Harnessing photo-excited anions in BHAS reactions

and

mechanistic insights into borrowing hydrogen catalysis

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A thesis submitted for the partial fulfillment of the degree of Doctor of Philosophy



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Dedicated to my beloved family

Declaration

I do hereby declare that the work presented in this thesis titled "Harnessing photoexcited anions in BHAS reactions and mechanistic insights into borrowing hydrogen catalysis" has been carried out by me under the supervision of Dr. Debashis Adhikari in the Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, India.

This work has not been submitted in part or full for a degree, diploma, or fellowship to any other university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly with due acknowledgements of collaborative work and discussions. This thesis is a bonafide record of original work done by me, and all sources listed within have been detailed in the bibliography.

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In my capacity as the supervisor of the candidate's thesis work, I certify that the above statements by the candidate are true to the best of my knowledge.

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Synopsis

Chapter 1: Introduction to C-C cross-coupling reactions via base promoted homolytic aromatic substitution (BHAS).

The synthesis of biaryls bears great importance in organic chemistry, as the unit is seen in a large number of core structural motifs that are found in molecules having tremendous medicinal, agrochemical, and pharmaceutical importance. Henceforth, there is a strong interest in furnishing C-C bonds in biaryls by easily accessible routes. Thus, direct C-H arylation of arenes has gained tremendous attention as it can bypass double preactivation for both participating substrates. In the domain of single electron transfer catalysis, simple organic additives in conjunction with KO^tBu are very effective for facile electron transfer. SET from potential electron donor species generates an aryl radical from Ar-X substrate with the liberation of leaving group (X). The aryl radical then attacks a coupling partner benzene ring to form a cyclohexadienyl radical. Cyclohexadienyl radical can be further deprotonated in the presence of a base, and the radical anion will be sufficiently reducing to promote SET to another substrate. In this way, the catalytic cycle becomes sustainable. There are several literature reports with tailor-made, well-designed electron donor species being super electron donors. Also there are several methods involving electrochemical reduction, photoexcitation.



Figure 1. General catalytic cycle for BHAS reaction.

In our work, We have been able to endow transition-metal-free BHAS (Basepromoted homolytic aromatic substitution) protocol that involves commercially available, inexpensive organic molecules to conduct C–C cross-coupling reactions at room temperature under visible light irradiation via a radical pathway. Profound understanding of the initiation pathway reveals multiple initiator species to be responsible for aryl radical generation via single electron transfer. This protocol has been explored successfully in carrying out coupling reactions with various arene partners.

Chapter 2: Aromatization as the driving force for single electron transfer towards C–C cross-coupling reactions.



Figure 2. Increasing reactivity of different phenazine cores based on aromaticity gain.

Aromaticity is a dictating force for a plethora of reactions, and a molecule may elicit a specific pattern of reactivity, if it is propelled by a thermodynamic driving force to gain aromaticity. We wondered whether a small organic molecule can facilitate SET to break an aryldiazonium bond, where the aromatic gain of the said initiator molecule will shepherd the process. Herein we present a small molecule, dihydrophenazine (DPh), that has a clear driving force to gain aromaticity upon undergoing 2e–/2H+ redox processes. The deprotonated form of dihydrophenazine (DPh) is a potent initiator under photochemical conditions that can efficiently generate aryl radicals *via* SET. Using this methodology, a series of arenes and heteroarenes have

been cross-coupled with aryl radicals at room temperature. Photochemical activation of DPh anions and the subsequent electron transfer to substrate aryldiazonium salts have been proved by Stern–Volmer analysis. Detailed mechanistic studies including interception of important reaction intermediates prove the aromaticity-driven SET as the key step to generate aryl radicals towards radical-promoted cross-coupling reactions.

Chapter 3: Deciphering the single electron transfer ability of fluorene under photoredox conditions.



Figure 3. Initiation network involving multiple key species for electron transfer.

In this chapter, we report fluorene as a radical initiator in its deprotonated form, to promote SET under photochemical conditions, leading to C–C cross-coupling reactions. A thorough mechanistic trial including the Stern–Volmer experiment substantiates the photoinduced electron transfer. Multiple key species en route to electron transfer have been isolated or separately synthesized to emphasize the radical

amplifying effect of fluorene by offering an initiation network, rather than a unique single initiation pathway. The radical initiator is further different from the bulk of previous work as hydrocarbons have not been examined to enable electron transfer at their deprotonated state. The efficiency of SET is demonstrated by a plethora of C–C cross-coupling reactions spanning benzene, pyrrole and thiophene as arene substrates.

Chapter 4: Single electron transfer catalysis by diphenylthiourea under visible light photoredox conditions.



Figure 4. Single electron transfer from deprotonated diphenyl thiourea.

We report diphenylthiourea (DPTU) as a potent photocatalyst at its deprotonated stage that can promote reductive bond cleavage chemistry on aryl bromide substrates. An easy deprotonation of the DPTU molecule by a strong base KOtBu and subsequent photoexcitation makes it a fairly strong reductant that promotes SET. The excited-state potential for the deprotonated thiourea was calculated to be $Eox^* = -2.54$ V vs SCE that shows promise for reductive cleavage of strong aryl bromide bonds. Leveraging on the reductive capacity of DPTU anion, an aryl radical was generated under blue light excitation and such aryl radical was exploited in isoindolinone, oxindole formation and C-C cross-coupling reactions. Encouragingly, the deprotonated form of DPTU was crystallized in the presence of a crown ether and catalysis was conducted with the isolable crystalline material to substantiate the role of putative anionic species in photocatalysis. The fate of DPTU after electron transfer was also traced to conclude that multiple species in the reaction solution helped to build a sufficient aryl radical concentration.



Chapter 5: Ligand-redox mediated radical hydrogenation relevant to borrowing hydrogen catalysis.

Figure 5. Ligand radical mediated radical hydrogenation mechanism.

Borrowing hydrogen (BH) or hydrogen autotransfer is a multistep catalytic method for the construction of C–C bonds, which consists of consecutive dehydrogenation of alcohol and hydrogenation of in situ generated unsaturated compounds. In our previous works, we have developed a Ni-based catalyst supported by redox active azo-phenolate ligand, which can handle these consecutive (de)hydrogenation steps efficiently. The first dehydrogenation step has been well investigated and indicated a ligand radical promoted hydrogen atom abstraction to be instrumental. This study prompted us to investigate the hydrogenation of the *in situ* generated imine or olefinic bond. There is a growing body of literature in olefinic hydrogenation promoted by metal hydride of Earth-abundant metals, where radical mechanism is followed. In the present report, we thoroughly study the mechanistic details of a nickel catalysed α alkylation of ketones with secondary alcohols. In this mechanistic picture, we showcase the olefinic hydrogenation of an enone to happen, completely bypassing the involvement of a metal hydride. This pathway is also radical promoted, where a single electron reduction of the substrate olefin and a subsequent hydrogen atom transfer step are most critical. A series of control reactions, detection of critical reaction intermediates, and radical probe experiments provide compelling proofs for such radical-promoted olefinic hydrogenation. The experimental clues, further aided by DFT calculations altogether suggest the precise one-electron chemistry where the involvement of metal-hydride is not required. Notably, the redox non-innocence of the azophenolate backbone, as well as imposed noninnocence of the substrate olefin, when bound to the catalyst molecule makes such mechanism feasible.

Chapter 6: DFT-guided mechanistic insights into chemo-divergence: a mixed explicit-implicit solvent description to dictate the chemoselectivity.



Figure 6. Role of protic solvent to dictate the chemoselectivity in nitrile reduction towards amine formation.

Nitrile reduction has been a well-known method to produce amine building blocks. Controlling the selectivity of such reduction processes toward various amines is still a challenging task. Recently, we reported the chemoselective synthesis of primary and secondary amines by a manganese catalyst via nitrile hydrogenation, employing ammonia-borane as the hydrogen source. During the optimization of the reaction, we observed a significant dependence of product selectivity on the reaction medium. Specifically, in hexane, primary amine is obtained, while in isopropanol a secondary amine is generated. In the present report, we showcase a mixed explicit-implicit solvation by a protic solvent and try to evaluate the key factors that regulate the observed product selectivity. We have also investigated the origin of solvent dependent chemoselectivity in nitrile hydrogenation via borrowing hydrogen method.

The explicit solvent effect involving polar protic isopropanol favors imine metathesis by proton hopping through stepwise addition and elimination steps to produce secondary amine as the final product. The aprotic solvent *n*-hexane is incapable of such proton migration and inhibits the solvent-assisted imine metathesis to give only primary amines as the final product. This DFT study provides a recipe for the choice of solvents that can dictate chemoselectivity in product formation.

Contents

Declaration	iv
Acknowledgments	vi
Aim of the thesis	viii
Table of Contents	X
Abbreviations	xiv
Chapter 1. Introduction to BHAS reactions	1
1.1. Significance of bi-aryl scaffolds	2
1.2. Synthetic protocols for biaryls : a step towards transition metal-free protocols over metal catalysis	2
1.3. Development of BHAS as transition-metal free approach	4
1.4. Different mode of aryl radical generation: XAT pathways for radical coupling	13
1.5. General trend of reduction potential of commonly used aryl radical precursors	15
1.6. Summarized overview of the sequential development of BHAS methodology	15
1.7. References	16
Chapter 2. Aromatization as the driving force for single electron transfer towards C–C cross-coupling reactions	19
2.1. Introduction	20
2.2. Results and discussion	21
2.3. Conclusions	29
2.4. Experimental section	29

2.5. References	44
Chapter 3. Deciphering the single electron transfer ability of fluorene under photoredox conditions	47
3.1. Introduction	48
3.2. Results and discussion	49
3.3. Conclusions	57
3.4. Experimental section	58
3.5. References	75
Chapter 4. Single electron transfer catalysis by diphenylthiourea under visible light photoredox conditions	77
4.1. Introduction	78
4.2. Results and discussion	79
4.3. Conclusions	86
4.4. Experimental section	86
4.5. References	97
Chapter 5. Ligand-redox mediated radical hydrogenation relevant to borrowing hydrogen catalysis	99
5.1. Introduction	100
5.2. Results and discussion	102
5.3. Conclusions	111
5.4. Experimental section	111
5.5. References	122
Chapter 6. DFT-guided mechanistic insights into chemo-divergence: a	126

mixed explicit-implicit solvent description to dictate the chemoselectivity	
6.1. Introduction	127
6.2. Computational details	128
6.3. Results and discussion	129
6.4. Conclusions	136
6.5. Co-ordinates for optimized geometries	137
6.6. References	154

Abbreviations

А	Ampere
a, b, c	Lattice parameters (X-ray)
atm	Atmospheric (unit of pressure)
a.u	Arbitrary units
aq.	Aqueous
BHAS	Base promoted homolytic aromatic substitution
^t Bu	Tert-butyl
°C	Degree celsius (0 °C= 273.15 k)
calcd	Calculated
CCDC	Cambridge crystallographic data centre
d	Doublet
d dd	Doublet Doublet of doublet
d dd DFT	Doublet Doublet of doublet Density functional theory
d dd DFT DMF	Doublet Doublet of doublet Density functional theory Dimethylformamide
d dd DFT DMF DMSO	Doublet Doublet of doublet Density functional theory Dimethylformamide Dimethylsulfoxide
d dd DFT DMF DMSO EL	Doublet Doublet of doublet Density functional theory Dimethylformamide Dimethylsulfoxide Electroluminescence
d dd DFT DMF DMSO EL equiv	Doublet Doublet of doublet Density functional theory Dimethylformamide Dimethylsulfoxide Electroluminescence Equivalent
d dd DFT DMF DMSO EL equiv	Doublet Doublet of doublet Density functional theory Dimethylformamide Dimethylsulfoxide Electroluminescence Equivalent Hour/s
d dd DFT DMF DMSO EL equiv h HOMO	Doublet Doublet of doublet Density functional theory Dimethylformamide Dimethylsulfoxide Electroluminescence Equivalent Hour/s Highest ocupied molecular orbital

Hz	Hertz
IC	Internal conversion
IL	Interligand transition
ISC	Intersystem crossing
J	coupling constant
K	Kelvin
LUMO	Lowest unoccupied molecular orbital
m	Multiplet (NMR)
mg	milli gram(s)
min	minute(s)
mL	milliliter(s)
mmol	milli mole(s)
MS	Mass spectrometry
m/z	Mass-to-charge ratio
NMR	Nuclear magnetic resonance
OLED	Organic light-emitting diodes
PC	Photocatalyst
ppm	parts per million
RT	Room temperature
s	singlet
t	triplet
THF	Tetrahydrofuran

TMS	Tetramethylsilane
TLC	Thin layer chromatography
UV-VIS	Ultraviolet-visible spectroscopy
Å	Ångström (1 Å = $10-10$ m)
α, β, γ	interaxial angles (X-ray)
λ	wavelength
λ_{ex}	wavelength of the excitation wavelength
λ_{max}	wavelength of the emission maximum
μ(Μ-Κα)	absorption co-efficient of the radiation source M (X-ray)

Publication details

- Bains, A. K.; <u>Kundu, A.</u>; Yadav, S.; Adhikari, D. * Borrowing Hydrogen-Mediated N-Alkylation Reactions by a Well-Defined Homogeneous Nickel Catalyst. ACS Catal. 2019, 9, 9051.
- Jana, A.; Das, K.; <u>Kundu, A.</u>; Thorve, P. R.; Adhikari, D. *; Maji, B. * A Phosphine-Free Manganese Catalyst Enables Stereoselective Synthesis of (1 + n)-Membered Cycloalkanes from Methyl Ketones and 1, n-Diols. *ACS Catal.* 2020, *10*, 2615.
- Bains, A. K.; Dey, D.; Yadav, S.; <u>Kundu, A.</u>; Adhikari. D. *; Nickel Catalysed Construction of Benzazoles via Hydrogen Atom Transfer Reactions. *Catal. Sci. Technol.* 2020, 10, 6495.
- Sarkar, K.; Das, K.; <u>Kundu, A.</u>; Adhikari, D.*; Maji, B.*; Phosphine-Free Manganese Catalyst Enables Selective Transfer Hydrogenation of Nitriles to Primary and Secondary Amines Using Ammonia–Borane. *ACS Catal.*, 2021, *11*, 2786.
- Kundu, A.[#]; Dey, D.[#]; Pal, S.; Adhikari, D.*; Pyrazole-Mediated C-H Functionalization of Arene and Heteroarenes for Aryl-(Hetero)aryl Cross-Coupling Reactions. *J. Org. Chem.* 2021, *86*, 15665.
- Bains, A. K.; <u>Kundu, A.</u>; Maiti, D.*; Adhikari, D.*; Ligand-redox Assisted Nickel Catalysis Toward Stereoselective Synthesis of (n+1)-membered Cycloalkanes from 1,n-diols with Methyl Ketones. *Chem. Sci.*, **2021**, *12*, 14217.
- Dey, D.[#]; <u>Kundu, A.[#]</u>; Roy, M.; Pal, S.; Adhikari. D.*; Aromatization as the driving force for single Electron Transfer Towards C-C Cross Coupling Reactions. *Catal. Sci. Technol.* 2022, *12*, 1934.
- Singh, V.; <u>Kundu, A.</u>; Singh, K.; and Adhikari, D.*; Redox-noninnocence of Formazanate Ligand Applied to catalytic formation of α-ketoamides. *Chem Commun.* 2022, 58, 6630.
- Bains, A.; Biswas, A.; <u>Kundu, A.</u>; Adhikari, D.*; Nickel-catalysis Enabling αalkylation of Ketones by Secondary Alcohols. *Adv. Synth. & Catal.*, 2022, 364, 2815.
- Dey, D.[#]; <u>Kundu, A.[#];</u> Mandal, B.; Roy, M.; Adhikari, D.*; Deciphering Single Electron Transfer Ability of Fluorene Under Photoredox Conditions. *Catal. Sci. Technol.* 2022, *12*, 7322.

- Singh, K.; <u>Kundu. A.;</u> Adhikari, D.*; Ligand-Based Redox: Catalytic Applications and Mechanistic Aspects. ACS Catal. 2022, 12, 13075.
- Singh, R.[#]; Bains, A[#]; <u>Kundu, A.[#]</u>; Jain, H. ; Yadav, S.; Dey, D.; Adhikari. D.* Mechanistic Elucidation of an Alcohol Oxidation Reaction Promoted by Nickel Azophenolate Complex. *Organometallics*, **2023**, *42*, 1759.
- Baguli, S.; <u>Kundu, A.</u>; Nath. S.; Adhikari. D.*; Mukherjee. D.*; A Donor– Acceptor Cyclopropane by Intramolecular C(sp3)–H Activation at a Cyclic(alkyl)(amino)carbene Center and Its Fascinating Ring-Opening Chemistry. *Org. Lett.*, **2023**, *25*, 3141.
- Mandal, C.; <u>Kundu, A.</u>; Das. S.; Adhikari. D.*; Mukherjee. D.*; A 2-Anilidomethylpyridine Ligand Framework Showcasing Hydride Storage and Transfer Abilities in Its Aluminum Chemistry. *Chem. Eur. J.*, **2023**, *29*, e2023011.
- Bains, A.; <u>Kundu, A.</u>; Adhikari, D.*; Mechanistic Elucidation of a Radical-Promoted Hydrogenation Relevant to Borrowing Hydrogen Catalysis. *ChemCatChem.*, 2023, 15, e202300586.
- Dey, D.[#]; <u>Kundu, A.[#]</u>; Roy, M.; Singh, V.; Maji, S.; Adhikari, D.*; Single Electron Transfer Catalysis by Diphenylthiourea Under Visible Light Photoredox Conditions. *Org. Chem. Front.*, **2023**, *10*, 5248-5253.
- Halder, S.[#]; Mandal, S.[#]; <u>Kundu, A.</u>; Mandal, B.; Adhikari, D.*; Super-Reducing Behavior of Benzo[*b*]phenothiazine Anion under Visible-light Photoredox Condition. *J. Am. Chem. Soc.*, **2023**, *145*, 22403.
- Kundu, A.; Mandal, B.; Maji, B.; Adhikari, D.*; DFT-Guided Mechanistic Insights into Chemo-divergence: a Mixed Explicit-Implicit Solvent Description to Dictate the Chemoselectivity. J. Phys. Chem. A, 2023, 127, 10068.
- Das, K. [#]; <u>Kundu, A.</u>[#]; Sarkar, K.; Adhikari, D.*; Maji, B.*; Catalytic Acceptorless Dehydrogenative Borylation of Styrenes Enabled by a Molecularly Defined Manganese Complex. *Chem. Sci.*, **2024**, *15*, 1098.
- 20. Bansal, S.[#]; Biswas, A.[#]; <u>Kundu, A.</u>[#]; Adhikari, M.; Singh, S.*; Adhikari, D.*; Ambiphilic Alcohol Dehydrogenation by BICAAC Mimicking Metal-Ligand Cooperativity. *ACS Catal.*, **2024**, *14*, 8087.
- Singh, V.; <u>Kundu, A.</u>; Hazari, A. S.; Weisser, K.; Adhikari, D.*; Exclusively Ligand Redox-Promoted C-H Tertiary Alkylation of Heteroarenes. *ACS Catal*, 2024, <u>Just accepted.</u>

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Chapter 1

Introduction to BHAS reactions

1.1. Significance of bi-aryl scaffolds

Bi-aryl scaffolds are one of the most fascinating cores in the organic chemistry domain.¹⁻² Such frameworks are made up of aromatic rings that have properties different from each other which includes them to the list of quite important building blocks for the formation of complex molecules. These complex molecules serve as integral structural components in bio-active compounds³ (Figure 1.1 as demonstrative examples), polymers⁴, liquid crystals⁵, organic optoelectronics⁶, agrochemicals⁷ etc. The structural diversity as well as tuneable electronic properties assures to regulate how it interacts, how well it works, how selective it is, and how effective it is. As science advances, it is probable that bi-aryl-containing compounds will continue to play a vital role in further development in abovementioned areas. Therefore there is significant urge for the development of new improved cross-coupling methods to synthesize bi-aryls.



Figure 1.1. Examples of bio-active molecules with bi-aryl cores.

1.2. Synthetic protocols for biaryls: a step towards transition metal-free protocols over metal catalysis.

From classical methods involving metal-driven cross-coupled reactions to cutting-edge techniques that make use of transition metal complexes, bi-aryl synthesis is already in advanced mode in terms of synthetic strategies.⁸⁻⁹ Getting familiar with

A. Traditional transition-metal catalysed cross-coupling reactions



B. Transition-metal catalysed decarboxylative couplings



C. Transition-metal catalysed direct arylation



Figure 1.2. Synthetic routes towards bi-aryl scaffolds.

these synthetic strategies not only enables us to get target molecules,. Despite of the numerous applications of metal catalysts towards cross-coupling reactions, there are several disadvantages of these processes. Heavy transition metals (e.g. palladium, platinum etc.) are costly, toxic and harmful to the environment. There are strict guidelines regarding the limit of trace metal impurity in various products imposed by the regulatory agencies. For this quality control, the removal of trace metal impurity has become a great challenge in terms of cost-efficiency, detection, complex sampling and sample preparation protocols. To tackle these issues and considering the importance of bi-aryl cores in medicinal and pharmaceutical industries, there is a severe urge for new synthetic protocols relying on transition metal-free conditions. This has led to the evolution of a new pathway of transition metal-free cross

coupling reactions, which is facilitated by the utilization of base-mediated homolytic aromatic substitution (BHAS) method.



Figure 1.3. Advantages of transition metal-free catalysis.

1.3. Development of BHAS as transition-metal free approach



Figure 1.4. Proposed chain propagation pathway using alkylmercury halides as precursors.

Understanding the chemical reactivity is one of the most active research area in organic chemistry. In this direction C-H functionalization covers a broad research area. Electrophilic aromatic substitution reactions are most common approach for aromatic C-H functionalization. In this context of aromatic substitution reactions, though homolytic alkylation can be used to introduce alkyl radicals onto certain substrates, yet this is not a viable method for most of the aromatic substrates for C-H functionalization because of very

low yields. However, many exceptions are there, where protonated hetero-aromatic compounds were alkylated efficiently with alkyl radicals, as investigated by Minisci. With base like DABCO, oxidative substitution reactions between unsaturated hydrocarbon and alkylmercury halide-generated alkyl radicals, (Figure 1.4), were also reported.¹⁰⁻¹³

1.3.1. Neutral and anionic organic super electron donors in BHAS.

Transition-metal centered radical mediated cyclization of epoxy olefin has been reported earlier.¹⁴ Following that thread, Murphy and co-workers developed a metal-free protocol for such type of reaction using organic electron-rich tetrathiafulvalene (TTF) as an organic electron donor.¹⁵



Figure 1.5. Proposed chain propagation pathway using alkyl halides as precursors.

To generate aryl radicals, aryl diazonium salts are already well known precursors.¹⁶ However, given the instability of these salts and their costs, other aryl radical precursors such as aryl halides were much sought after. The advantages associated with aryl chlorides are their ready availability, cheaper cost, safer handling.



Figure 1.6. Proposed chain propagation pathway using alky halides as precursors.







Figure 1.7. Multiple redox states several organic electron donors.



Figure 1.8. Multiple redox states several organic electron donors.
In 2014, Doni and Murphy summarised several neutral organic super electron donors and their rodox-reactivity towards challenging transformations.¹⁷ They showed examples of organic molecules with multiple redox states. For TTF, the potential for first oxidation is +0.34 V and the corresponding second oxidation occurs at +0.81 V *vs.* SCE in MeCN.¹⁸



Figure 1.9. Multiple redox states several organic electron donors.

Murphy group also reported several diketopiperazine molecules as electron donor initiators in BHAS mediated metal-free cross-coupling reactions.¹⁹



Figure 1.10. Catalytic use of organic SED.

In 2019 Murphy group developed a very interesting methodology where organic super electron donors can work in catalytic manner. They reported a benzimidazolium based system where the active electron donor species was regenerated with NaBH₄.²⁰

Kwong group reported 2-pyridyl carbinol as additive for single electron transfer initiated cross-coupling process.²¹ Later in 2017, Murphy group provided deep mechanistic insight into the initiation step and concluded that double deprotonation generates the potent electron donor species.²²



Figure 1.11. a) C-C cross coupling reaction using 2-pyridyl carbinol as additive . b) active electron donor species generated in situ from 2-pyridyl carbinol.

In 2015, Himmel group performed detailed analysis of the key parameters which are accountable for the electron donor strength. In that work, gas-phase ionization energy and the experimentally-derived redox potential in solution were correlated for further prediction of molecules with high reducing power.²³ These results also pinpoints the cruciality of molecular volume in regulating the reduction potential in solution. Later they reported the synthesis of the molecule where two redox-active guanidine moieties were attached through a bridge.²⁴ Hansmann group also developed several carbene based organic redox-active systems.²⁵

The detailed initiation mechanism for simple super electron donors (SED) are always a debated area, since the exact nature of the SED in solution requires significant structural/spectroscopic/kinetic probation. In 2016, Jiao revisited the initiation mechanism of the radical chain reactions. For their purpose, they took the combination of N,N'-dimethylethylenediamine (DMEDA) and t-BuOK as model reaction, which is one of the most efficient and representative reaction system for these radical reactions. A combined approach of kinetic studies, deuterium labelling experiments and DFT-calculations revealed a network of electron transfer steps instead of a single radical initiation pathway. A structurally simple diamine actually plays dual role of "radical regulator" and "radical amplifier" for the initiation process.²⁶ Towards this line, later they also reported very unusual reactivity of N-methyl aniline as strong electron donor towards aryl bromide bond activation.²⁷ They hypothesized that electron-rich heteroarenes will be more effective, but the results were not that inspiring. Even putting an extra aromatic ring to stabilise the N-centered radical also did

not show the expected performance. Next, they hypothesised that ring-strain might be a driving factor to enhance the reactivity and started screening various cyclic aromatic amines. Among them, indoline showed the highest efficiency as promoter under 80 °C, where gain of aromaticity upon consecutive deprotonation and electron transfer are the key towards their superb reactivity.²⁸



Figure 1.12. a) Unexpected reactivity using N-methyl anines as additive. b) Aromaticity gain as a driving force while indoline has been used as promoter.

In 2017, Jiao group reported pyridine catalysed borylation of aryl halides, where they developed a selective cross-coupling protocol for aryl radical and a pyridine stabilised boryl radical.²⁹ Later in 2018, they disclosed the initiation mechanism by detailed analysis involving isolation and thorough characterisation of the active species. In that work, they showed special type of boryl–pyridine based organic super electron donor species were the potent electron donors for the electron transfer process.³⁰



Figure 1.13. Diboron based organic super electron donors.

In 2019 König group reported visible light absorbing 9-anthrolate anions enabling aryl chloride bond activation via single electron transfer.³¹



Figure 1.14. visible light absorbing 9-anthrolate anion precursors.

Very recently, Melchiorre group reported a readily available indole thiolate organocatalyst anion as organic super electron donor species which enables challenging aryl chloride bond activation and birch reduction (figure 1.15).³²



Figure 1.15. indole thiolate organocatalyst anion as organic super electron donor.

Rui Shang and co-workers reported *o*-phosphinodiarylamide, *o*-phosphinolphenolate, *o*-phosphinothiophenolate anions as reductive photocatalysts in dehalogenative and deaminative radical cross-coupling reactions. These photocatalysts are also well-performing towards activation of trifluoromethyl groups for defluoroalkylation with alkenes, aryl chlorides.³³⁻³⁵



Figure 1.16. *o*-phosphinodiarylamide, *o*-phosphinolphenolate, *o*-phosphinothiophenolate anions used as reductive photocatalysts.

Mandal group has demonstrated different redox states of different phenalenyl (PLY) and utilised that in several bond activation methods. They started investigating the redox non-innocence of the PLY backbone supported by redox-silent metal ions and used ligand backbone for redox reservoir.³⁶⁻³⁷ Later they utilised the ligand directly into bond activation catalysis.³⁸⁻³⁹ Cationic form of PLY also has been used to show the Lewis acidity and redox dual reactivity.⁴⁰ They showed switching between mono and doubly reduced PLY and enabled challenging aryl chloride bond activation without any external stimuli.⁴¹ Later with the similar concept they have performed Heck-coupling⁴² and C-N cross-coupling reactions⁴³ smoothly.



Figure1.17. Different redox states of phenalenyl (PLY) based hydrocarbon.

Recently from our own group, we showed different type of imido anions enabling activation of strong aryl chloride bonds. A NNN trianionic pincer has been introduced as strong photoreductant.⁴⁴ Then a phenothiazine based imido anion, which is anti-aromatic in nature in its ground state also proved to be highly reducing at its excited state.⁴⁵Along the similar goal,

Bezdek group developed phospineoxide based robust organic redox systems which can perform two electron cycling.⁴⁶

1.3.2. Electron primed photo-redox and conPET catalysis.

In 2014, Köenig group introduced the concept conPET to be used in bond activation via electron transfer catalysis.⁴⁷ Later Bernhard Dick group showed Rhodamine 6G to adopt ConPET pathway in presence of isopropyl amine.⁴⁸



Figure 1.18. Schematic diagram for ConPET catalysis.

Wickens group established the concept of electron-primed photoredox catalysis that enables aryl chloride bond activation for radical coupling. Utilising this strategy, they surpassed the energetic limitation of light by priming the photocatalyst with electron via electrochemical reduction before the excitation.⁴⁹

Scott group isolated and characterised some of those radical anions generated after one electron reduction which led them to study the specific reactivity of those anions towards catalytic reactions.⁵⁰ This also provides experimental insights on the mechanism of high-profile conPET reactions.



Confirmed ArCl reduction under photoirradiation

Figure 1.19. Isolated and characterised radical anions (DIPP = 2,6-diisopropylphenyl).

1.4. Different mode of aryl radical generation: XAT pathways for radical coupling.



Figure 1.20. Photocatalytic reaction of aryl halides with tin(II) acetate to generate arylstannane(IV) reagents and its proposed mechanistic pathway.

Dilman group developed an easy-to-handle, cheap, atom-efficient methodology for the synthesis of monoorganotin(IV) derivatives from aryl halide precursors.⁵¹ This procedure involves a XAT step for aryl radical generation. These organo-tin derivatives can be used directly for Liebeskind–Srogl cross-coupling reaction without isolation or purification of the organo-tin derivative.

1.5. General trend of reduction potential of commonly used aryl radical precursors



Figure 1.21. Reduction potential window for the popular substrates of cross-coupling reactions.

When a relatively strong bond is targeted for cleavage via SET, a prior knowledge of the reduction potential of the targeted bonds are essential. Figure 1.21 tabulates the popular substrates used in cross-coupling reactions in the order of corresponding reduction potentials. Since aryl-diazonium tetrafluoroborates have reduction potentials close to zero with respect to SHE, these bonds can be activated very easily via single electron transfer. In comparison, aryl halides are challenging to cleave and their reduction potentials follow the trend -Cl <-Br <-I, that means the aryl iodides are in general easy to cleave among a variety of halides.

1.6. Summarised overview of the sequential development of BHAS methodology



Figure 1.22. Progress chart of BHAS methodology in chronological term.

1.7. References

1. Medici, F.; Resta, S.; Puglisi, A.; Rossi, S.; Raimondi, L.; Benaglia, M. Electrochemical Organic Synthesis of Electron-Rich Biaryl Scaffolds: An Update. *Molecules* **2021**, *26*, 6968.

2. Di Maso, M. J.; Grove, C. I.; Shaw, J. T. Chapter 10 - Studies in the Synthesis of Biaryl Natural Products: The 6,6'-Binaphthopyranones. In *Strategies and Tactics in Organic Synthesis*, Harmata, M., Ed. Academic Press: 2014; Vol. 10, pp 225-248.

3. Baudoin, O.; Guéritte, F. Natural Bridged Biaryls with Axial Chirality and Antimitotic Properties. In *Studies in Natural Products Chemistry*, Atta ur, R., Ed. Elsevier: 2003; Vol. 29, pp 355-417.

4. Iseki, T.; Mabesoone, M. F. J.; Koenis, M. A. J.; Lamers, B. A. G.; Weyandt, E.; de Windt, L. N. J.; Buma, W. J.; Palmans, A. R. A.; Meijer, E. W. Temperature-dependent modulation by biaryl-based monomers of the chain length and morphology of biphenyl-based supramolecular polymers. *Chem. Sci.* **2021**, *12*, 13001-13012.

5. Solladie, G.; Gottarelli, G. Liquid crystals and chirality : application to the determination of absolute configurations and to the conformational analysis of biaryls. *Tetrahedron* **1987**, *43*, 1425-1437.

6. Tominaga, M.; Nishino, K.; Morisaki, Y.; Chujo, Y., Synthesis, characterization, and optoelectronic study of three biaryl-fused closo-o-carboranes and their nido-[C2B9]– species. *J. Organomet. Chem.* **2015**, *798*, 165-170.

7. Chen, T.; Xiong, H.; Yang, J.-F.; Zhu, X.-L.; Qu, R.-Y.; Yang, G.-F. Diaryl Ether: A Privileged Scaffold for Drug and Agrochemical Discovery. *J. Agric. Food Chem.* **2020**, *68*, 9839-9877.

 Yuan, S.; Chang, J.; Yu, B. Construction of Biologically Important Biaryl Scaffolds through Direct C–H Bond Activation: Advances and Prospects. *Top Curr Chem* 2020, *378*, 23.

9. Ashenhurst, J. A. Intermolecular oxidative cross-coupling of arenes. *Chem Soc Rev* 2010, *39*, 540-548.

10. Russell, G. A.; Kim, B. H.; Kulkarni, S. V. Electron transfer processes. 48. Freeradical alkylations of enones involving proton transfers. *J. Org. Chem.* **1989**, *54*, 3768-3770.

11. Russell, G. A.; Chen, P.; Yao, C. F.; Kim, B. H. tert-Butylation of .alpha.,.beta.-Unsaturated Nitriles by tert-Butylmercury Halides in the Presence of Iodide Ion. *J. Am. Chem. Soc.* **1995**, *117*, 5967-5972.

12. Russell, G. A.; Kulkarni, S. V.; Khanna, R. K. Electron transfer process. 49. Radical and ionic reactions of (benzoylmethyl)mercurials. *The Journal of Organic Chemistry* **1990**, *55*, 1080-1086.

13. Russell, G. A.; Chen, P.; Kim, B. H.; Rajaratnam, R. Homolytic Base-Promoted Aromatic Alkylations by Alkylmercury Halides 1. *J. Am. Chem. Soc.* **1997**, *119*, 8795-8801.

14. Nugent, W. A.; RajanBabu, T. V. Transition-metal-centered radicals in organic synthesis. Titanium(III)-induced cyclization of epoxy olefins. *J. Am. Chem. Soc.* **1988**, *110*, 8561-8562.

15. Lampard, C.; Murphy, J. A.; Lewis, N. Tetrathiafulvalene as a catalyst for radical– polar crossover reactions. *J. Chem. Soc., Chem. Commun.* **1993**, 295-297.

16. Galli, C. Radical reactions of arenediazonium ions: An easy entry into the chemistry of the aryl radical. *Chem. Rev.* **1988**, *88*, 765-792.

17. Doni, E.; Murphy, J. A. Evolution of neutral organic super-electron-donors and their applications. *ChemComm* **2014**, *50*, 6073-6087.

18. Murphy, J. A. Discovery and Development of Organic Super-Electron-Donors. J. Org. Chem. 2014, 79, 3731-3746.

19. Cumine, F.; Zhou, S.; Tuttle, T.; Murphy, J. A. A study of diketopiperazines as electron-donor initiators in transition metal-free haloarene–arene coupling. *Org. Biomol. Chem.* **2017**, *15*, 3324-3336.

20. Rohrbach, S.; Shah, R. S.; Tuttle, T.; Murphy, J. A. Neutral Organic Super Electron Donors Made Catalytic. *Angew. Chem. Int. Ed.* **2019**, *58*, 11454-11458.

21. Wu, Y.; Choy, P. Y.; Kwong, F. Y. Direct intermolecular C–H arylation of unactivated arenes with aryl bromides catalysed by 2-pyridyl carbinol. *Org. Biomol. Chem.* **2014**, *12*, 6820-6823.

22. Barham, J. P.; Coulthard, G.; Kane, R. G.; Delgado, N.; John, M. P.; Murphy, J. A. Double Deprotonation of Pyridinols Generates Potent Organic Electron-Donor Initiators for Haloarene–Arene Coupling. *Angew. Chem. Int. Ed.* **2016**, *55*, 4492-4496.

23. Eberle, B.; Hübner, O.; Ziesak, A.; Kaifer, E.; Himmel, H.-J. What Makes a Strong Organic Electron Donor (or Acceptor)? *Chem. Eur. J.* **2015**, *21*, 8578-8590.

24. Wild, U.; Hübner, O.; Enders, M.; Kaifer, E.; Himmel, H.-J. Connecting Organic Redox-Active Building Blocks through Mild Noncatalytic C–H Activation. *Eur. J. Org. Chem.* **2022**, 2022, e202200349.

25. Antoni, P. W.; Golz, C.; Hansmann, M. M. Organic Four-Electron Redox Systems Based on Bipyridine and Phenanthroline Carbene Architectures. *Angew. Chem. Int. Ed.* **2022**, *61*, e202203064.

26. Zhang, L.; Yang, H.; Jiao, L. Revisiting the Radical Initiation Mechanism of the Diamine-Promoted Transition-Metal-Free Cross-Coupling Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 7151-7160.

27. Yang, H.; Zhang, L.; Jiao, L. N-Methylanilines as Simple and Efficient Promoters for Radical-Type Cross-Coupling Reactions of Aryl Iodides. *Chem. Eur. J.* **2017**, *23*, 65-69.

28. Yang, H.; Chu, D.-Z.; Jiao, L. Aromatization modulates the activity of small organic molecules as promoters for carbon–halogen bond activation. *Chem. Sci.* **2018**, *9*, 1534-1539.

29. Zhang, L.; Jiao, L. Pyridine-Catalyzed Radical Borylation of Aryl Halides. J. Am. Chem. Soc. 2017, 139, 607-610.

30. Zhang, L.; Jiao, L., Super electron donors derived from diboron. *Chem. Sci.* **2018**, *9*, 2711-2722.

31. Schmalzbauer, M.; Ghosh, I.; König, B. Utilising excited state organic anions for photoredox catalysis: activation of (hetero)aryl chlorides by visible light-absorbing 9-anthrolate anions. *Farad. Disc.* **2019**, *215*, 364-378.

32. Wu, S.; Schiel, F.; Melchiorre, P. A General Light-Driven Organocatalytic Platform for the Activation of Inert Substrates. *Angew. Chem. Int. Ed.* **2023**, *62*, e202306364.

33. Shen, N.; Liu, C.; Zhang, X.; Shang, R., o-Phosphinodiarylamides as Reductive Photocatalysts for Dehalogenative and Deaminative Cross-Couplings. *ACS Catal.* **2023**, *13*, 11753-11761.

34. Shen, N.; Li, R.; Liu, C.; Shen, X.; Guan, W.; Shang, R. Photocatalytic Cross-Couplings of Aryl Halides Enabled by o-Phosphinophenolate and o-Phosphinothiophenolate. *ACS Catal.* **2022**, *12*, 2788-2795.

35. Liu, C.; Shen, N.; Shang, R. Photocatalytic defluoroalkylation and hydrodefluorination of trifluoromethyls using o-phosphinophenolate. *Nat. Commun.* **2022**, *13*, 354.

36. Chakraborty, S.; Ahmed, J.; Shaw, B. K.; Jose, A.; Mandal, S. K. An Iron-Based Long-Lived Catalyst for Direct C–H Arylation of Arenes and Heteroarenes. *Chem. Eur. J.* **2018**, *24*, 17651-17655.

37. Sen, T. K.; Mukherjee, A.; Modak, A.; Ghorai, P. K.; Kratzert, D.; Granitzka, M.; Stalke, D.; Mandal, S. K. Phenalenyl-Based Molecules: Tuning the Lowest Unoccupied Molecular Orbital to Design a Catalyst. *Chem. Eur. J.* **2012**, *18*, 54-58.

38. Ahmed, J.; P, S.; Vijaykumar, G.; Jose, A.; Raj, M.; Mandal, S. K. A new face of phenalenyl-based radicals in the transition metal-free C–H arylation of heteroarenes at room temperature: trapping the radical initiator via C–C σ -bond formation. *Chem. Sci.* **2017**, *8*, 7798-7806.

39. Singh, B.; Ahmed, J.; Biswas, A.; Paira, R.; Mandal, S. K. Reduced Phenalenyl in Catalytic Dehalogenative Deuteration and Hydrodehalogenation of Aryl Halides. *J. Org. Chem.* **2021**, *86*, 7242-7255.

40. Ahmed, J.; Chakraborty, S.; Jose, A.; P, S.; Mandal, S. K. Integrating Organic Lewis Acid and Redox Catalysis: The Phenalenyl Cation in Dual Role. *J. Am. Chem. Soc.* **2018**, *140*, 8330-8339.

41. Ahmed, J.; Datta, P.; Das, A.; Jomy, S.; Mandal, S. K., Switching between mono and doubly reduced odd alternant hydrocarbon: designing a redox catalyst. *Chem. Sci.* **2021**, *12*, 3039-3049.

42. Banik, A.; Mandal, S. K. Tuning Redox States of Phenalenyl-Based Molecules by Consecutive Reduction toward Transition Metal-Free Heck-Type C–C Cross-Coupling. *ACS Catal.* **2022**, *12*, 5000-5012.

43. Sil, S.; Santha Bhaskaran, A.; Chakraborty, S.; Singh, B.; Kuniyil, R.; Mandal, S. K. Reduced-Phenalenyl-Based Molecule as a Super Electron Donor for Radical-Mediated C–N Coupling Catalysis at Room Temperature. *J. Am. Chem. Soc.* **2022**, *144*, 22611-22621.

44. Singh, V.; Singh, R.; Hazari, A. S.; Adhikari, D. Unexplored Facet of Pincer Ligands: Super-Reductant Behavior Applied to Transition-Metal-Free Catalysis. *JACS Au* **2023**, *3*, 1213-1220.

45. Halder, S.; Mandal, S.; Kundu, A.; Mandal, B.; Adhikari, D. Super-Reducing Behavior of Benzo[b]phenothiazine Anion Under Visible-Light Photoredox Condition. *J. Am. Chem. Soc.* **2023**. *41*, 22403–22412.

46. Käch, D.; Gasser, A. C.; Wettstein, L.; Schweinzer, C.; Bezdek, M. J. Phosphine Oxide-Functionalized Terthiophene Redox Systems. *Angew. Chem. Int. Ed.* **2023**, *62*, e202304600.

47. Ghosh, I.; Ghosh, T.; Bardagi, J. I.; König, B. Reduction of aryl halides by consecutive visible light-induced electron transfer processes. *Science* **2014**, *346*, 725-728.

48. Brandl, F.; Bergwinkl, S.; Allacher, C.; Dick, B. Consecutive Photoinduced Electron Transfer (conPET): The Mechanism of the Photocatalyst Rhodamine 6G. *Chem. Eur. J.* **2020**, *26*, 7946-7954.

49. Cowper, N. G. W.; Chernowsky, C. P.; Williams, O. P.; Wickens, Z. K. Potent Reductants via Electron-Primed Photoredox Catalysis: Unlocking Aryl Chlorides for Radical Coupling. *J. Am. Chem. Soc.* **2020**, *142*, 2093-2099.

50. Horsewill, S. J.; Hierlmeier, G.; Farasat, Z.; Barham, J. P.; Scott, D. J. Shining Fresh Light on Complex Photoredox Mechanisms through Isolation of Intermediate Radical Anions. *ACS Catal.* **2023**, *13*, 9392-9403.

51. Zemtsov, A. A.; Supranovich, V. I.; Levin, V. V.; Dilman, A. D. Photocatalytic Reaction of Aryl Halides with Tin(II) Acetate to Generate Arylstannane(IV) Reagents. *ACS Catal.* **2023**, 12766-12773.

Chapter 2

Aromatization as the driving force for single electron transfer towards C–C cross-coupling reactions

For the purpose of this thesis, the work of chapter 2 is adapted with permission from (Dey. D. [#]; Kundu. A. [#]; Roy. M.; Pal. S.; Adhikari. D.*, *Catal. Sci. Technol.* **2022**, *12*, 1934. Title: Aromatization as the driving force for single electron transfer towards C–C cross-coupling reactions.)

2.1. Introduction

Synthesis of biaryl motifs under transition-metal-free conditions has garnered tremendous research focus recently, primarily owing to the lower expense and environmental benignity associated with the approach.^{1, 2} In this regard, direct C–H functionalization of an arene or heteroarene ring is very much desirable, so that the process can be step-economic by easily obviating a bond prefunctionalization step.^{3, 4} For such C–H functionalization reactions, one of the elegant methods is to promote the reaction by a radical, where such radical steers a substitution reaction on an arene or heteroarene to fabricate a biaryl product, often referred to as base-promoted homolytic aromatic substitution (BHAS).⁵⁻⁷ The generation of such a radical in the reaction medium is often triggered by a single electron transfer (SET) event. Multiple small molecules, either in their neutral or monoanionic form have been observed to be sufficiently reducing in character so that they promote SET and break a C–X bond (X = halide, diazonium, iodonium etc.).⁸⁻¹⁴ Intuitively, different molecules have varying reducing ability en route to aryl radical generation, which is dictated by the electronic nature of the reducing species.





Aromaticity is a dictating force for a plethora of reactions, and a molecule may elicit a specific pattern of reactivity, if it is propelled by a thermodynamic drive to gaining aromaticity. We wondered, whether a small organic molecule can facilitate SET event to break an aryl diazonium bond, where aromatic gain of the said initiator molecule will shepherd the process. Herein we present a small molecule dihydrophenazine (DPh), that has a clear driving force to gain aromaticity upon undergoing $2e^{-}/2H^{+}$ redox processes. Phenazine has been deployed earlier as a reusable oxidant leaving the end product of this process as dihvdrophenazine.¹⁵ Such a reduced product can be further oxidized easily to phenazine in aerobic milieu. Our recent work on alcohol oxidation by an azo promoted redox also leaves a hydrazo end product which can be easily oxidized under aerobic atmosphere.¹⁶⁻²⁰ The conceptual resemblance between these two molecules inspired us to choose DPh, so that an electron transfer can be leveraged en route to its 2e- oxidation to phenazine (Scheme 1). Notably, phenazine derivatives have been exploited in the photochemical redox processes in last few years.²¹ Miyake and co-workers have shown that the diaryl dihydrophenazine can be an efficient photoreductant to generate an alkyl radical from alkylbromide, which leads to atom transfer radical polymerization (ATRP) reaction.^{22, 23} Furthermore, radical cations of diaryl dihydrophenazine has been generated by an external oxidant NOPF₆, and the role of oxidized form was studied towards ATRP reactions under photoexcitation.²⁴ However, photoredox chemistry of dihydrophenazine in its anionic form has not been explored earlier. In this report, we disclose how a deprotonated form of DPh, can initiate electron transfer under photochemical condition, and how the engendered radical can facilitate cross-coupling reactions via C-H functionalization.

2.2. Results and discussion

The search for new reductants and associated processes that result in clean carbon-carbon bond formation by free radical reactions largely originates from difficulties associated with inorganic SET reductants. Tin-hydride donors, previously used are very toxic and their replacement with an innocuous organic electron donor is highly desirable. ²⁵

Towards this end, electron donating reagents based on organic molecules have shown great promise as reducing agents. Organic species can act as electron donors and lead to spontaneous reaction with a substrate that has ample oxidizing power, or they can be induced to donate electron under electrochemical or photochemical conditions.^{26, 27} Some previous reports including our recent work showcased the potential of aromatic heterocycles in their deprotonated form.²⁸ We reasoned that the deprotonated form of 9,10-dihydrophenazine (L1, Scheme 1) may be suitable for promoting electron transfer to a substrate molecule.²⁸ The

deprotonation of **L1** is fully feasible under this basic condition as the measured pKa is 5.5 in DMSO medium. We further anticipated that **L1** can be converted to its fully aromatic form, phenazine upon undergoing $2e^{-}/2H^{+}$ process, so that there could be a thermodynamic drive behind such electron transfer processes.

We started testing this hypothesis using L1 in the C–H arylation reaction of arene and heteroarenes with aryldiazonium as the coupling partner. When the arylation of 4-chloro phenyl diazonium tetrafluoroborate was attempted in the presence of 5 mol% L1 and 1.2 equiv of base in DMSO, 4-chloro biphenyl (2m) was

 Table 2.1. Optimisation Table

	_		2m		
entry	L	KO ^t Bu (equiv)	Solvent	time (h)	yield (%)
	(mol %)				
1	-	1.2	DMSO	10	12
2	5	1.2	DMSO	10	55
3	10	1.2	DMSO	10	80
4	15	1.2	DMSO	10	82
5	10	-	DMSO	10	trace
6	10	0.2	DMSO	10	40
7	10	1.2	MeCN	10	53
8^{a}	10	1.2	DMSO	10	14
9	10	1.2	DMSO	6	62
10	10	1.2	DMSO	16	82

 $F_{4}BN_{2} \longrightarrow CI + \bigcup \xrightarrow{L1, KO'Bu} CI \longrightarrow 2m$

Reaction conditions: ^a reaction was conducted in dark.

isolated in 55% yield under visible light irradiation conditions at room temperature (Table1, entry 2). Gratifyingly, increasing the amount of initiator molecule to 10 mol% increased the yield of the product to 80% (Table1, entry 3). The presence of base is also crucial as the lack of it does not give any product (Table 1, entry 5 and 6). DMSO as a solvent is important for the reactions, as switching to acetonitrile keeping other conditions identical affected the

reaction, by lowering the product yield to 53% (Table 1, entry 7). To investigate the effect of light on this reaction, the reaction was further performed under completely dark conditions, affording a 14% yield of the product (Table 1, entry 8), which indicates that the reaction is light-driven. Similarly, in absence of the initiator molecule, only 12% of **2m** was isolated. The optimized conditions for the reaction revealed the reaction time to be 10 h, while reduction of time to 6 h diminished the yield of **2m** to 62% (Table 1, entry 9). Providing extra reaction time for 16 h did not improve the product yield (Table 1, entry 10), henceforth all further reactions were conducted for only 10 h. Minimal yield under only base promoted condition (Table 1, entry 1) is fully consistent with Murphy's observation, where relatively higher loading of KO^tBu gives some background reaction.²⁹ Among light sources, a white LED lamp worked best. We note on passing, that the reaction also affords comparable yield of products when the reaction vessel is exposed to diffused light in a typical laboratory set up. After screening various combinations it was established the routed in highest yield.



Reaction conditions: L1 (10 mol%), aryldiazonium salt (0.5 mmol), KO^tBu (0.6 mmol), benzene (10 mmol), DMSO (2 mL), visible light, 10h.

After extensive optimization of the reaction conditions, we explored the substrate scope over a variety of aryl diazonium salts along with benzene as the arene coupling partner. The aryl diazonium salts were chosen as the aryl partner, as N_2 is released as a by-product from the reaction, making the reduction easier.^{30, 31} As disclosed earlier, the chloro substituted

diazonium salt gave 80% yield within 10 h. 4-tolyl, and 2-tolyl diazonium salts were affording the respective biphenyls **2b**, and **2d** in 72-82% yields. Similarly, *m*-xylyl diazonium salt reacted with benzene to furnish biphenyl product **2c** in 74% yield. Electron donating -OMe group present in *o*-, *m*- *p*- positions of the phenyl group were well tolerated under the reaction conditions affording the respective biphenyl products **2f**-**2h** in 69-75% yields. Analogously, electron withdrawing groups like, $-CF_3$, $-NO_2$, -CN in the aryl diazonium salts were also tolerated well under the reaction conditions and the respective biphenyls (**2h**-**2j**) formed smoothly in 62-74% yields. For simple phenyl diazonium salt, the yield of the biphenyl **2m** was 75%. Interestingly, other halogen substituted phenyl diazonium salts were also competent substrate molecules to efficiently couple benzene offering the biphenyls **2k**-**2l**, **2n**-**2r** in good to very good yields.





Reaction conditions: L1 (10 mol%), aryldiazonium salt (0.5 mmol), KO^tBu (0.6 mmol), mesitylene (10 mmol), DMSO (2 mL), visible light irradiation for 10h.

After that, we utilized the optimized conditions for the C–H arylation of a substituted arene such as mesitylene. In that case, a variety of aryl diazonium salts afforded moderate to good yields (58-67%) of biphenyl products (**3a-3f**). Importantly, electron donating methyl, methoxy or electron withdrawing -CF₃, -CN substituents were all tolerant to the reaction conditions and furnished the respective biphenyl products smoothly.

Next, we investigated the applicability of the reaction protocol towards different heterocycles as a coupling partner for this cross-coupling reaction. At first, we applied the arylation protocol for C-2 functionalization of thiophene with different diazonium salts as coupling partner, affording 60-69 % yields of the corresponding biphenyl products (**4a-4d**; **4e-4i**). The regioselective arylation at the C-2 position is dictated

by the large HOMO coefficient at this specific carbon that steers the attack of an aryl radical.³² Good yields were obtained for the products where aryldiazonium salts contained both electron donating or withdrawing groups. Likewise, another heterocycle furan underwent the cross-coupling transformations and gave products **5a**-**5i** in moderate to good yields. The yields of the activated and un-activated aryl coupling partners are similar.





Reaction conditions: L1 (10 mol%), aryldiazonium salt (0.5 mmol), KO^tBu (0.6 mmol), furan/thiophene (10 mmol), DMSO (2 mL), visible light, 10h.

Finally, benzofuran was successfully arylated under the same conditions affording 2arylbenzofuran in modest yields (**6a-6d**). The product yields are also similar both for activated and unactivated aryldiazonium salts. However, the reaction protocol failed to arylate pyridine and pyrazine type of electron deficient heteroarenes. The span of multiple aryldiazonium salts as well as different arene substrates support the generality of the process under very mild reaction conditions.

We finally inquired whether other aryl radical source such as aryl halide is amenable to this reaction condition. To examine this, we tested 4-iodo anisole as the substrate to couple with benzene. Interestingly, the initiator is capable of cleaving such iodo substrate so that the final product **2a** can be realized in 75% isolated yield. Furthermore, the same reaction with 4-bromo anisole under otherwise identical reaction conditions afforded 49% of the biaryl product.



Table 2.5. Substrate scope of benzofuran with aryldiazonium salts.

Reaction conditions: L1 (10 mol%), aryldiazonium salt (0.5 mmol), KO^tBu (0.6 mmol), benzofuran (5mmol), DMSO (2 mL), visible light, 10h.

Upon successfully exploring the substrate scope, we were very interested to understand the mechanism of the arylation reaction. The transition metal-free cross-coupling reactions are often considered to follow a radical chain mechanism, where chain propagation is accepted as a part of BHAS reaction. In comparison, the radical initiation step varies among catalysts and hence deserves special attention. Elucidating the mechanism is also important for knowing the molecular basis of such initiation step and to spearhead the design of other potent initiator molecules in cross-coupling reactions. At the outset, to eliminate the presence of trace element in the reaction mixture, that might be catalyzing the reaction, we conducted an ICP-MS analysis on the batch of KO^tBu used. Pleasingly, no trace metal was detected in KO^tBu, confirming the reaction to be transition metal-free in nature. To further establish that single electron transfer happens from the initiator, engendering a radical species, we performed a control reaction in presence of 1 equiv of TEMPO. In corroboration with our hypothesis, no biphenyl product was isolated under this condition. Additionally, use of TEMPO helped us isolating the aryl radical (*p*-chloro phenyl) intermediate in its intercepted form by this radical quencher. The arrested radical was further authenticated by high-resolution mass spectrometry to give a peak at 268.1453 amu.³³

We have previously disclosed that the reaction is light-promoted. Having these evidences in hand, we predict that the monodeprotonated form of **L1**, is sufficiently reducing at its excited state to promote single electron transfer (SET) to aryldiazonium salts to generate an aryl radical. The light-mediated nature of the reaction strongly suggests that such SET might not be feasible at the ground state. Indeed, a control reaction of isolated **L1**^{\cdot} mixed with aryldiazonium salt under dark condition did not forge any biaryl product. This is intuitive that upon light absorption, the excited state of **L1**^{\cdot} becomes more reducing in nature so that

electron transfer to break an aryldiazonium bond is facilitated. To unambiguously establish that electron transfer occurs from the excited **L1**⁻, a fluorescence quenching of the molecule was conducted. Notably, the rich photophysical properties of phenazine derivatives likely originate from π -conjugation to the pyrazine core, and that has been exploited earlier as fluorescent tracers or dyes for medicinal and electronic applications. ^{34, 35}

To our gratification, a sequential quenching of fluorescence intensity was clearly visible with the increasing aryl diazonium salt concentration, proving an oxidative quenching to operate. Multiple examples of photocatalysed SET events have been reported to generate an aryl radical from aryldiazonium salts, but traditional Ru, Ir-based photocatalysts were deployed in those cases. Indeed, breaking

Fig. 2.1. a) Stern-Volmer quenching plot for L1⁻ treated with 4-chlorobenzenediazonium tetrafluoroborate, b) Yield comparison among various initiators and NICS Calculation



the aryldiazonium salt by a Ru photocatalyst started in 1980 by Deronzier.^{36, 37} Since then, many other works involved

photocatalytic generation of aryl radical from these salts employing these expensive photocatalysts.³⁸⁻⁴⁰ Sanford have also used Ru catalyst under photochemical conditions to generate an aryl radical, along the Pd-catalyzed directed C–H bond activation reactions.⁴¹ It is interesting to note that deprotonated from of the dihydrophenazine is sufficiently reducing at its excited state so that it can replace expensive traditional photocatalysts. Meanwhile, the UV-vis spectrum of the L1⁻ affirms the feasibility of its photoexcitation. While light green colored L1 absorbs at 355 nm, its deprotonation immediately makes the absorption broad band to shift to 550 nm. Such a red-shift as a result of deprotonation clearly suggests that the deprotonated form of the initiator can be photoexcited by visible light. Furthermore, the

appearance of dark violet color of the mixture upon deprotonation of **L1** is also consistent with its broad absorption starting at 460 nm.

It is logical that the SET from L1⁻ generates an aryl radical from aryl diazonium salt with the liberation of N₂. The aryl radical then attacks a benzene ring to form a cyclohexadienyl radical. Cyclohexadienyl radical can be further deprotonated in presence of KO^tBu, and the radical anion will be sufficiently reducing to promote SET to the substrate aryl diazonium salts (Scheme 2). In this way, the catalytic cycle can be sustainable, and the role of L1 is proved to be an initiator. Importantly, a second electron transfer must happen from the initiator, since the molecule can be deprotonated further, and upon photoexcitation this radical anion will likely be more reducing to facilitate SET. This step is very much necessary for L1 to gain aromaticity at the end of the electron transfer processes. To validate this hypothesis and to trace the fate of the initiator molecule, we scrutinized the reaction mixture at the end of a standard reaction and isolated the fully aromatized phenazine product (L1a). This confirms that L1 undergoes a complete $2e^{7}/2H^{+}$ redox process during promoting the radical-based coupling, en route to gaining aromaticity. To substantiate our assertion further, we chose two other heterocyclic backbones, which are similar to L1 but with different extent of gain in aromaticity. In this regard, we examined 1,2,3,4-tetrahydrohydroquinoxaline (L2) and tetrahydropyrazine (L3) as two initiator molecules for the cross-coupling reactions under identical photoexcited conditions. Indeed, these initiator molecules afforded 38% and 28% of the biaryl product **2m** respectively. It is intuitive that gain in aromaticity in the final product of the initiator will facilitate the rate of electron transfer. To get a quantitative idea, we resorted on quantifying the aromaticity in these three rings utilizing a popular aromaticity index. Along this direction, nucleus-independent chemical shift, $NICS_{zz}(1)$ has been used profusely⁴² where a ghost atom bq is kept at 1 Å above the plane of the aromatic ring.^{43, 44} Such a calculation at B3LYP/6-31G* level of theory^{45, 46} quantified the value for aza skeleton of the phenazine to be -12.75. Conversely, the NICS values in quinoxaline (L2a) and pyrazine (L3a) ring are -10.32 and -10.23 respectively. These metrices, although describe the local aromaticity in the chosen ring, rightly reflects the difference in aromaticity gain in L1 compared to its close congeners. From these evidences, we conclude that for the deprotonated heterocycles, gain in aromaticity could be the driving force for SET, which essentially enables them as initiator. Jiao has recently established a system where gain of aromaticity has been pointed as the driving force for electron transfer from indoline,⁴⁷ finally converting the promoter to indole. As delineated through the mechanistic cycle (Scheme 2), at least two phenazine-based species are responsible to participate in SET. There is a clear precedent of multiple species being engaged in such SET processes, where the initiator molecule traverses through different intermediate forms that are capable of reducing a substrate molecule. Sometimes, tiny concentration of radical species builds up in the presence of KO^tBu, while their concentration is not sufficient to propagate a radical chain. The role of our initiator is to proliferate the cycle by two consecutive electron transfer processes, so that it can behave as a powerful radical amplifier. This nicely aligns with Jiao's observation where a deprotonated diamine backbone involved in multiple electron transfer enhancing the concentration of radical initiator in the reaction mixture. ⁴⁸

Scheme 2.2. Proposed catalytic cycle.



2.3. Conclusions

In Summary, we showed a DPh molecule is capable of promoting SET under photochemical conditions, at its deprotonated form to break a bond in aryldiazonium salts and generate an aryl radical. Such an aryl radical has been utilized to build a synthetic protocol for C–C cross-coupling chemistry including a large array of arene and heteroarenes. The governing principle behind such electron transfer is the aromaticity gain which thermodynamically drives such electron transfer. We hope, this work will help designing further initiator molecules that can steer radical-promoted C–H functionalization reactions.

2.4. Experimental section

2.4.1. General Considerations:

All starting compounds employed in this study were procured from commercial suppliers and were used without further purification. All chemicals were purchased from Sigma Aldrich, Avra, TCI, Alfa Aeaser, GLR innovations. Glasswares were dried overnight at 160 °C. Benzene was dried by heating over sodium with benzophenone as indicator. Solvents such as ether, acetone were used as received from the commercial suppliers. For thin layer chromatography (TLC), silica-coated aluminium foils with fluorescent indicator 254 nm (from Merck) were used. Column chromatography was performed using SD Fine silica gel 60-120 mesh using a gradient of ethyl acetate and hexane as mobile phase. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. ¹H NMR and ¹³C NMR spectra were recorded on a 400 MHz Bruker Biospin Advance III FT-NMR spectrometer. Fluorescence quenching experiments were carried out in a Cary Eclipse Fluorescence Spectrofluorometer. UV-Vis was recorded using Varian Cary 60 (Agilent technologies) spectrophotometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: s=singlet, d=doublet, t=triplet, q=quartet and m=multiplet. Chemical shifts (δ) are quoted to the nearest 0.01 ppm relative to tetramethylsilane (δ 0.00 ppm) in CDCl₃(δ 7.26 ppm) or (CD₃)₂SO (δ 2.50 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm) or $(CD_3)_2SO$ (δ 39.5 ppm).

2.4.2. General Procedure for synthesis of Aryl diazonium tetrafluoroborate.

Substituted diazonium salts were prepared following the reported literature. Substituted aniline (10 mmol) was dissolved in 5 mL distilled water at room temperature. Then 5 mL of 46% hydrofluoroboric acid was added to the mixture at 0-5 °C. Sodium nitrite (0.7 g) was dissolved in 2 mL of water and cooled down to 0-5 °C separately. Now this cooled sodium nitrite solution was added dropwise over the course of 10 minutes to the main reaction mixture and the resulting mixture was stirred for 30 min, maintaining the temperature at 0-5 °C. After that the precipitate was collected by filtration and the residue was washed with ice-cooled distilled water. The precipitate was dissolved in minimum amount of acetone and then diethyl ether was added. The crystals of the respective diazonium salts were collected from the solution, washed with diethyl ether and dried under vacuum.

2.4.3. Reaction procedure for C-H arylation of benzene and mesitylene.

In a Schlenk flask aryldiazonium salt (0.5 mmol), KO^tBu (0.6 mmol) and the initiator molecule (L1) (10 mol%) were dried for 30 mins in a Schlenk line. After that DMSO (1 mL) and arene (10 mmol) was added to the reaction mixture under argon atmosphere. The reaction

mixture was stirred under visible light irradiation for 10 h in an argon atmosphere at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Purification by column chromatography with EtOAc/hexane afforded the corresponding product. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

2.4.4. Reaction procedure for C-H arylation of thiophene and furan.

In a Schlenk flask aryl diazonium salt (0.5 mmol), KO^tBu (0.6 mmol) and the additive ligand (L1) (10 mol%) were dried for 30 mins in a Schlenk line. After that DMSO (1 mL) and heteroarene (10 mmol) was added to the reaction mixture under argon atmosphere. The reaction mixture was stirred under visible light irradiation for 10 h in an argon atmosphere at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Purification by column chromatography with EtOAc/hexane afforded the corresponding product. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

2.4.5. Reaction procedure for C-H arylation of benzofuran.

In a Schlenk flask aryl diazonium salt (0.5 mmol), KO^tBu (0.6 mmol) and the additive ligand (**L1**) (10 mol%) were dried for 30 mins in a well-equipped Schlenk line. After that DMSO (1 mL) and benzofuran (5 mmol) was added to the reaction mixture under argon atmosphere. The reaction mixture was stirred under visible light irradiation for 10 h in an argon atmosphere at room temperature. After the completion of the reaction, dichloro methane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Purification by column chromatography with EtOAc/hexane afforded the corresponding product. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

2.4.6. Radical quenching experiment:

In a schlenk flask aryl diazonium salt (0.5 mmol), KO^tBu (0.6 mmol) and additive (10 mol%) were dried for 30 mins in a well-equipped schlenk line. After that DMSO (1mL) and benzene (10 mmol) were added to the reaction mixture and different amount of TEMPO was added in the reaction mixture at argon atmosphere. The reaction mixture was stirred under visible light irradiation for 10 h under an argon atmosphere at room temperature.

S.No	TEMPO equivalence	Yield (%)
1.	0.6 equiv	15
2.	1 equiv	trace

Table 2.6.: Yield of the product with different loading of TEMPO:

2.4.7. Trapping the intermediate:

In a schlenk flask aryl diazonium salt (0.5 mmol), KO^tBu (0.6 mmol) and additive (10 mol%) were dried for 30 mins in a well-equipped schlenk line. After that DMSO (1 mL) was added dropwise to the reaction mixture and TEMPO (0.6 mmol) was added in the reaction mixture under argon atmosphere. The reaction mixture was stirred for 10 h under visible light irradiation at room temperature. The desired intermediate was characterised by ESI-MS. (M+H⁺ = 268.1453).



2.4.8. ICP-MS Analysis of KO^tBu:

This analysis was conducted on Agilent's 7700X instrument, following a method AOAC 999.10. The contents of transition metal elements (Cu, Pd, Ni, Co and Fe) were found to be less than detection limit (0.1 ppm).

Entry	Parameter	Results			
		Result-1	Result-2		
1.	Copper	BDL (MDL: 0.1 mg/kg)	BDL (MDL: 0.1 mg/kg)		
2.	Palladium	BDL (MDL: 0.1 mg/kg)	BDL (MDL: 0.1 mg/kg)		
3.	Iron	2.26 mg/kg	2.26 mg/kg		
4.	Nickel	BDL (MDL: 0.1 mg/kg)	BDL (MDL: 0.1 mg/kg)		
5.	Cobalt	BDL (MDL: 0.1 mg/kg)	BDL (MDL: 0.1 mg/kg)		

Table 2.7.: ICP-MS analysis on the contents (in ppm) of transition metals in KO^tBu

BDL: Below Detection Limit, MDL: Method Detection Limit





Figure 2.2. UV-visible spectra of L1 (blue) and L1+ KO^tBu (red) mixture in DMSO.

2.4.10. Fluorescence quenching experiment and Stern-Volmer plot:

Fluorescence quenching experiments were performed using a PerkinElmer LS 55 Fluorescence Spectrometer. In each experiment, measurement was carried out mixing 10^{-6} M solution of L1 and KO^tBu in DMSO with appropriate amount of quencher in quartz cuvette. The sample solutions were previously degassed with argon. The solution was irradiated at 470 nm, and the emission intensity was overserved at 579 nm. Plots were derived according to the Stern-Volmer equation and K_{sv} was calculated. Stern-Volmer equation is the following

$$\mathbf{I}_0 / \mathbf{I} = 1 + K_{sv}[\mathbf{Q}]$$

Where I_0 is the fluorescence intensity without the quencher, I is the intensity with the quencher, [Q] is the concentration of added quencher and *Ksv* is the Stern-Volmer quenching constant.



Figure 2.3. Emission spectra of L1 and KO^tBu mixture in DMSO with different amount of 4chlorobenzene diazonium tetrafluoroborate.

2.4.11. Analytical data:

4-chlorophenylbenzene (2a) :



¹H NMR (400 MHz, CDCl₃) δ 7.55 (m, 4H), 7.42 (m, 5H).¹³C NMR (100 MHz, CDCl₃) δ 140.1, 139.8, 133.5, 129.0, 129.0, 128.5, 127.7, 127.1.

4-methylphenylbenzene (2b):



¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.8 Hz, 2H), 7.63 (d, J = 7.8 Hz, 2H), 7.55 (t, J = 7.7 Hz, 2H), 7.48 – 7.42 (m, 1H), 7.38 (d, J = 7.8 Hz, 2H), 2.52 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 141.3, 138.4, 137.3, 137.1, 131.3, 129.6, 128.8, 127.1, 127.1, 21.2.

3,5-dimethylphenylbenzene (2c):



¹H NMR (400 MHz, CDCl₃) δ 7.68 (t, *J* = 5.6 Hz, 2H), 7.51 (q, *J* = 5.9 Hz, 2H), 7.46 – 7.38 (m, 1H), 7.32 (d, *J* = 6.4 Hz, 2H), 7.10 (s, 1H), 2.49 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 141.6, 141.4, 138.4, 129.0, 128.8, 127.3, 127.2, 125.2, 21.5.

2-methylphenylbenzene (2d):



¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.44 (m, 2H), 7.39 (m, 3H), 7.33 – 7.28 (m, 4H), 2.33 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.1, 135.5, 130.4, 129.9, 129.3, 128.2, 127.4, 126.9, 125.9, 76.8, 20.6.

4-methoxyphenylbenzene (2e):



¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 8.8 Hz, 4H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.35 – 7.28 (m, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 140.9, 133.9, 128.8, 128.2, 126.8, 126.7, 114.3, 55.4.

3-methoxyphenylbenzene (2f):



¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, J = 7.2, 1.3 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.37 (td, J = 7.5, 7.1, 3.7 Hz, 2H), 7.21 (dt, J = 7.7, 1.3 Hz, 1H), 7.18 – 7.13 (m, 1H), 6.92 (ddd, J = 8.2, 2.6, 1.0 Hz, 1H), 3.88 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 160.0, 142.9, 141.2, 129.9, 128.9, 127.6, 127.3, 119.8, 113.0, 112.8, 55.4.

2-methoxyphenylbenzene (2g):



¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, J = 8.4 Hz, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.39 (t, J = 7.1 Hz, 3H), 7.10 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 8.7 Hz, 1H), 3.86 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 156.5, 138.6, 131.0, 130.8, 129.7, 128.7, 128.1, 127.0, 120.9, 111.3, 55.6.

4-trifluoromethylphenylbenzene (2h):



¹H NMR (400 MHz, CDCl₃) δ 7.70 (s, 4H), 7.61 (d, J = 7.1 Hz, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.42 (t, J = 7.8 Hz, 1H).¹³C NMR (100 MHz, CDCl₃) δ 144.9, 139.9, 129.1, 128.3, 127.6, 127.4, 125.8 (q, J = 3.7 Hz), 123.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.4.

2,4-dinitrophenylbenzene (2i):



¹H NMR (400 MHz, CDCl₃) δ 8.71 (d, J = 2.3 Hz, 1H), 8.47 (dd, J = 8.6, 2.3 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 6.7 Hz, 3H), 7.37 – 7.32 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 149.2, 147.0, 142.4, 135.3, 133.4, 129.7, 129.2, 127.8, 126.6, 119.8.

4-cyanophenylbenzene (2j):



¹H NMR (400 MHz, CDCl₃) δ 7.71 (q, *J* = 8.0 Hz, 4H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 145.8, 139.3, 132.7, 129.2, 128.8, 127.9, 127.4, 119.1, 111.0.

4-bromophenylbenzene (2k):



¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.53 (m, 4H), 7.45 (td, *J* = 8.6, 2.2 Hz, 4H), 7.40 – 7.35 (m, 1H).¹³C NMR (100 MHz, CDCl₃) δ 140.3, 140.1, 132.0, 129.0, 128.9, 127.8, 127.1, 121.7.

4-bromophenylbenzene (2l):



¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 7.3 Hz, 1H), 7.50 – 7.43 (m, 5H), 7.39 (d, J = 6.8 Hz, 2H), 7.27 – 7.22 (m, 1H).¹³C NMR (100 MHz, CDCl₃) δ 142.6, 141.2, 133.2, 131.4, 129.5, 128.8, 128.1, 127.7, 127.5, 122.7.

Biphenyl (2m):



¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.62 (d, 2H, J = 8 Hz), 7.46 (t, 4H, J = 8Hz), 7.37 (t, 1H, J = 8 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 128.9, 127.4, 127.3.

3-chlorophenylbenzene (2n):



¹H NMR (400 MHz, CDCl₃) δ 7.65 – 7.56 (m, 3H), 7.48 (t, J = 7.5 Hz, 3H), 7.43 – 7.33 (m,

3H). ¹³C NMR (100 MHz, CDCl₃) δ 143.2, 139.9, 134.8, 130.1, 129.0, 128.0, 127.4, 127.4, 127.2, 125.4.

2-chlorophenylbenzene (2o):



¹H NMR (400 MHz, CDCl₃) δ 7.59 – 7.49 (m, 5H), 7.49 – 7.31 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 140.6, 139.5, 132.6, 131.5, 130.0, 129.6, 128.6, 128.2, 127.7, 126.9.

3,5-dichloro-1,1'-biphenyl (2p):



¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.52 (m, 2H), 7.49 – 7.39 (m, 5H), 7.35 (t, J = 1.9 Hz, 1H).¹³C NMR (100 MHz, CDCl₃) δ 144.3, 138.6, 135.4, 129.1, 128.6, 127.2, 127.16, 125.7.

4-fluorophenylbenzene (2q):



¹H NMR (400 MHz, CDCl₃) δ 7.56 (dt, *J* = 9.2, 2.6 Hz, 4H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.15 (t, *J* = 8.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 162.6 (d, *J* = 247.4 Hz), 140.37, 137.4 (d, *J* = 3 Hz), 129.0, 128.8 (d, *J* = 8 Hz), 127.4, 127.2, 115.7 (d, *J* = 21.2 Hz).

2-fluorophenylbenzene (2r):



¹H NMR (400 MHz, CDCl₃) δ 7.52 (dt, J = 8.2, 1.5 Hz, 2H), 7.41 (m, 3H), 7.36 – 7.31 (m, 1H), 7.31 – 7.24 (m, 1H), 7.17 (td, J = 7.5, 1.3 Hz, 1H), 7.12 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 159.9 (d, J = 248.3 Hz), 136.0, 130.9 (d, J = 5 Hz), 129.3, 129.2 (d, J = 3 Hz), 129.1 (d, J = 8.1 Hz), 128.6, 127.8, 124.4 (d, J = 5 Hz), 116.2 (d, J = 23.2 Hz).

2-Phenylmesitylene (3a):



¹H NMR (400 MHz, CDCl₃) δ 7.49 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 6.8 Hz, 2H), 7.03 (s, 2H), 2.42 (s, 3H), 2.09 (s, 6H).¹³C NMR (100 MHz, CDCl₃) δ 141.2, 139.2, 136.7, 136.1, 129.4, 128.5, 128.2, 126.6, 21.2, 20.9.

1-Methyl-4-mesitylbenzene (3b):



¹H NMR (400 MHz, CDCl₃) δ 7.22 (d, J = 7.6 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 6.94 (s, 2H), 2.40 (s, 3H), 2.33 (s, 3H), 2.01 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 139.1, 138.1, 136.6, 136.3, 136.1, 129.3, 129.2, 128.1, 21.4, 21.2, 20.9.

1-Methoxy-4-mesitylbenzene (3c):



¹H NMR (400 MHz, CDCl₃) δ 7.08 – 7.03 (m, 2H), 6.99 – 6.92 (m, 4H), 3.86 (s, 3H), 2.33 (s, 3H), 2.01 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 138.8, 136.6, 133.4, 130.4, 128.2, 113.9, 55.3, 21.2, 20.9.

1-Trifluoromethyl-4-mesitylbenzene (3d):



¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 6.99 (s, 2H), 2.37 (s, 3H), 2.02 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 145.2, 137.8, 137.4, 135.8, 129.9, 129.2, 128.9, 128.4, 125.5 (q, J = 3.7 Hz), 21.2, 20.8.

1-Cyano-4-mesitylbenzene (3e):



¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 6.98 (s, 2H), 2.36 (s, 3H), 1.99 (s, 6H).¹³C NMR (100 MHz, CDCl₃) δ 146.5, 137.7, 137.2, 135.4, 132.4, 130.4, 128.4, 110.7, 21.2, 20.7.

1-Chloro-4-mesitylbenzene (3f):



¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.98 (s, 2H), 2.37 (s, 3H), 2.04 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 139.6, 137.9, 137.0, 136.0, 132.6, 130.9, 128.77, 128.3, 21.2, 20.8.

2-(phenyl) thiophene (4a):



¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 2H), 7.35 – 7.25 (m, 3H), 7.09 (q, *J* = 3.1, 1.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 144.6, 134.5, 129.0, 128.1, 127.6, 126.1, 124.9, 123.2.

2-(4-methylphenyl) thiophene (4b):



¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.28 (dd, *J* = 11.1, 4.2 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 4.4 Hz, 1H), 2.39 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 144.7, 137.5, 131.8, 129.7, 128.1, 126.0, 124.4, 122.7, 21.3.

2-(4-ethylphenyl) thiophene (4c):



¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, J = 7.9 Hz, 2H), 7.29 (dt, J = 18.2, 6.4 Hz, 4H), 7.11 (d, J = 4.2 Hz, 1H), 2.71 (d, J = 7.8 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 143.8, 132.0, 128.5, 128.4, 128.0, 126.5, 126.1, 124.4, 122.7, 28.7, 15.7.

2-(4-methoxyphenyl) thiophene (4d):



¹H NMR (400 MHz, CDCl₃) δ 7.58 – 7.54 (m, 2H), 7.25 – 7.20 (m, 2H), 7.07 (dd, J = 5.1, 3.6 Hz, 1H), 6.96 – 6.90 (m, 2H), 3.84 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 159.3, 144.4, 128.0, 127.4, 127.3, 124.0, 122.2, 114.4, 55.5.

2-(4-trifluoromethylphenyl) thiophene (4e):


¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.40 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.37 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.12 (dd, *J* = 5.1, 3.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 128.5, 126.7, 126.4, 126.0 (q, *J* = 3.7 Hz), 124.6.

2-(4-cyanophenyl) thiophene (4f):



¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.63 (m, 4H), 7.43 – 7.38 (m, 2H), 7.13 (dd, J = 5.1, 3.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 142.2, 138.7, 128.7, 127.2, 126.2, 125.2, 119.0, 110.6, 77.5, 76.8.

2-(4-bromophenyl) thiophene (4g):



¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.46 (m, 4H), 7.30 (dd, J = 4.5, 1.6 Hz, 2H), 7.09 (d, J = 4.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 132.1, 128.4, 127.6, 125.4, 123.6, 121.4.

2-(4-chlorophenyl)thiophene (4h):



¹H NMR (400 MHz, CDCl₃) δ 7.60 – 7.54 (m, 2H), 7.41 – 7.36 (m, 2H), 7.35 – 7.31 (m, 2H), 7.12 (dd, J = 5.1, 3.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.1, 133.2, 132.9, 129.0, 128.2, 127.6, 127.1, 125.2, 123.5.

2-(3-chlorophenyl)thiophene (4i):



¹H NMR (400 MHz, CDCl₃) δ 7.55 (s, 1H), 7.42 (d, J = 7.5 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.23 – 7.15 (m, 2H), 7.05 – 7.01 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 142.8, 136.2, 134.9, 128.2, 127.5, 126.0, 125.7, 124.2, 124.0.

2-phenyl furan (5a):



¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 8.6 Hz, 2H), 7.53 (s, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.32 (t, J = 6.9 Hz, 1H), 6.72 (d, J = 3.4 Hz, 1H), 6.53 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 154.1, 142.1, 131.0, 128.8, 127.4, 123.9, 111.7, 105.1.

2-(4-methylphenyl) furan (5b):



¹H NMR (400 MHz, CDCl₃) δ 7.57 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 1.8 Hz, 1H), 7.19 (d, J = 7.9 Hz, 2H), 6.59 (d, J = 3.3 Hz, 1H), 6.46 (m, 1H), 2.36 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 154.3, 141.8, 137.3, 129.5, 128.4, 123.9, 111.7, 104.3, 21.4.

2-(4-ethylphenyl) thiophene (5c):



¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.58 (m, 2H), 7.45 (d, J = 1.0 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 6.60 (d, J = 4.2 Hz, 1H), 6.46 (m, 1H), 2.67 (m, 2H), 1.26 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 154.3, 143.7, 141.8, 128.6, 128.3, 124.0, 111.7, 104.4, 28.8, 15.7.

2-(4-methoxyphenyl) furan (5d):



¹H NMR (400 MHz, CDCl₃) δ 7.66 – 7.62 (m, 2H), 7.46 (dd, J = 1.8, 0.8 Hz, 1H), 6.95 (d, J = 8.9 Hz, 2H), 6.54 (dd, J = 3.3, 0.8 Hz, 1H), 6.47 (dd, J = 3.3, 1.8 Hz, 1H), 3.84 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 154.1, 141.5, 125.3, 124.1, 114.2, 111.6, 103.5, 55.4.

2-(4-trifluoromethylphenyl) furan (5e):

F₃C

¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 1.8 Hz, 1H), 6.77 (d, J = 3.4 Hz, 1H), 6.52 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 152.6, 143.2, 134.1, 129.2, 128.9, 125.8(q, J = 3.7 Hz), 125.7, 123.9, 112.1, 107.1.

2-(4-cyanophenyl) furan (5f):



¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 7.54 (s, 1H), 6.81 (d, J = 3.5 Hz, 1H), 6.53 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 152.1, 143.8, 134.8, 132.7, 124.1, 112.4, 110.4, 108.3.

2-(4-bromophenyl) furan (5g):



¹H NMR (400 MHz, CDCl₃) δ 7.54 (m, 4H), 7.50 (d, J = 1.8 Hz, 1H), 6.66 (m, 1H), 6.50 (dd, J = 3.4, 1.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 152.9, 142.4, 131.8, 129.8, 125.3, 121.1,

111.9, 105.6.

2-(4-chlorophenyl) furan (5h):



¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.58 (m, 2H), 7.47 (s, 1H), 7.37 – 7.33 (m, 2H), 6.64 (t, J = 2.5 Hz, 1H), 6.48 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 153.0, 142.4, 133.1, 129.5, 129.0, 125.1, 111.9, 105.6.

2-phenyl benzofuran (6a):



¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 7.1 Hz, 2H), 7.60 (d, *J* = 6.8 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.34 (m, 1H), 7.30 (td, *J* = 8.1, 7.6, 1.5 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.04 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 156.3, 154.9, 138.7, 129.6, 129.5, 127.9, 125.0, 124.1, 123.0, 120.9, 111.2, 100.7, 21.6.

2-(4-methylphenyl)benzofuran (6b):



¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 8.2 Hz, 2H), 7.60 – 7.56 (m, 1H), 7.53 (d, J = 8.7 Hz, 1H), 7.31 – 7.21 (m, 4H), 6.98 (s, 1H), 2.41 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 156.3, 154.9, 138.7, 129.6, 129.5, 127.9, 125.0, 124.1, 123.0, 120.9, 111.2, 100.7, 21.6.

2-(4-methoxyphenyl)benzofuran (6c):



¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.77 (m, 2H), 7.58 – 7.54 (m, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.28 – 7.20 (m, 2H), 7.02 – 6.96 (m, 2H), 6.90 (s, 1H), 3.87 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 160.1, 156.2, 154.8, 129.6, 126.6, 123.9, 123.5, 123.0, 120.7, 114.4, 111.1, 99.8, 55.5.

2-(4-trifluoromethylphenyl)benzofuran (6d):



¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 6.5 Hz, 1H), 7.55 (d, J = 9.0 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.29 – 7.24 (m, 1H), 7.14 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 155.2, 154.3, 133.8, 130.1, 129.0, 125.9 (q, J = 3.7 Hz), 125.2, 125.1, 123.4, 121.4, 111.5, 103.4.

2.5. References

1. Corbet, J.-P.; Mignani, G., Selected Patented Cross-Coupling Reaction Technologies. *Chem. Rev.* **2006**, *106*, 2651-2710.

2. Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M., Aryl–Aryl Bond Formation One Century after the Discovery of the Ullmann Reaction. *Chem. Rev.* **2002**, *102*, 1359-1470.

3. McGlacken, G. P.; Bateman, L. M., Recent advances in aryl–aryl bond formation by direct arylation. *Chem. Soc. Rev.* **2009**, *38*, 2447-2464.

4. Wencel-Delord, J.; Glorius, F., C–H bond activation enables the rapid construction and late-stage diversification of functional molecules. *Nat. Chem.* **2013**, *5*, 369-375.

5. Stephenson, C. R. J.; Studer, A.; Curran, D. P., The renaissance of organic radical chemistry – deja vu all over again. *Beilstein J. Org. Chem.* **2013**, *9*, 2778-2780.

6. Studer, A.; Curran, D. P., Organocatalysis and C□H Activation Meet Radical- and Electron-Transfer Reactions. *Angew. Chem. Int. Ed.* **2011**, *50*, 5018-5022.

7. Bolton, R.; Williams, G. H., Homolytic arylation of aromatic and polyfluoroaromatic compounds. *Chem. Soc. Rev.* **1986**, *15*, 261-289.

8. Murphy, J. A., Discovery and Development of Organic Super-Electron-Donors. J. Org. Chem. 2014, 79, 3731-3746.

9. Yang, H.; Zhang, L.; Jiao, L., N-Methylanilines as Simple and Efficient Promoters for Radical-Type Cross-Coupling Reactions of Aryl Iodides. *Chem. Eur. J.* **2017**, *23*, 65-69.

 Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F.
 Y.; Lei, A., Organocatalysis in Cross-Coupling: DMEDA-Catalyzed Direct C–H Arylation of Unactivated Benzene. *J. Am. Chem. Soc.* 2010, *132*, 16737-16740.

Zhou, S.; Doni, E.; Anderson, G. M.; Kane, R. G.; MacDougall, S. W.; Ironmonger,
 V. M.; Tuttle, T.; Murphy, J. A., Identifying the Roles of Amino Acids, Alcohols and 1,2-

Diamines as Mediators in Coupling of Haloarenes to Arenes. J. Am. Chem. Soc. 2014, 136, 17818-17826.

 Dewanji, A.; Murarka, S.; Curran, D. P.; Studer, A., Phenyl Hydrazine as Initiator for Direct Arene C–H Arylation via Base Promoted Homolytic Aromatic Substitution. *Org. Lett.* 2013, *15*, 6102-6105.

13. Ahmed, J.; Chakraborty, S.; Jose, A.; P, S.; Mandal, S. K., Integrating Organic Lewis Acid and Redox Catalysis: The Phenalenyl Cation in Dual Role. *J. Am. Chem. Soc.* **2018**, *140*, 8330-8339.

Chandrashekar, H. B.; Maji, A.; Halder, G.; Banerjee, S.; Bhattacharyya, S.; Maiti,
D., Photocatalyzed borylation using water-soluble quantum dots. *Chem. Commun.* 2019, 55, 6201-6204.

15. Chun, S.; Chung, Y. K., Transition-Metal-Free Poly(thiazolium) Iodide/1,8-Diazabicyclo[5.4.0]undec-7-ene/Phenazine-Catalyzed Esterification of Aldehydes with Alcohols. *Org. Lett.* **2017**, *19*, 3787-3790.

16. Bains, A. K.; Kundu, A.; Yadav, S.; Adhikari, D., Borrowing Hydrogen-Mediated N-Alkylation Reactions by a Well-Defined Homogeneous Nickel Catalyst. *ACS Catal.* **2019**, *9*, 9051-9059.

17. Bains, A. K.; Kundu, A.; Maiti, D.; Adhikari, D., Ligand-redox assisted nickel catalysis toward stereoselective synthesis of (n+1)-membered cycloalkanes from 1,n-diols with methyl ketones. *Chem. Sci.* **2021**, *12*, 14217-14223.

Bains, A. K.; Biswas, A.; Adhikari, D., Nickel-catalysed chemoselective C-3 alkylation of indoles with alcohols through a borrowing hydrogen method. *Chem. Commun.* 2020, *56*, 15442-15445.

19. Bains, A. K.; Dey, D.; Yadav, S.; Kundu, A.; Adhikari, D., Nickel catalysed construction of benzazoles via hydrogen atom transfer reactions. *Catal. Sci. Technol.* **2020**, *10*, 6495-6500.

20. Bains, A. K.; Adhikari, D., Mechanistic insight into the azo radical-promoted dehydrogenation of heteroarene towards N-heterocycles. *Catal. Sci. Technol.* **2020**, *10*, 6309-6318.

21. Pearson, R. M.; Lim, C.-H.; McCarthy, B. G.; Musgrave, C. B.; Miyake, G. M., Organocatalyzed Atom Transfer Radical Polymerization Using N-Aryl Phenoxazines as Photoredox Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 11399-11407.

22. Lim, C.-H.; Ryan, M. D.; McCarthy, B. G.; Theriot, J. C.; Sartor, S. M.; Damrauer, N. H.; Musgrave, C. B.; Miyake, G. M., Intramolecular Charge Transfer and Ion Pairing in N,N-

Diaryl Dihydrophenazine Photoredox Catalysts for Efficient Organocatalyzed Atom Transfer Radical Polymerization. *J. Am. Chem. Soc.* **2017**, *139*, 348-355.

23. Theriot, J. C.; Lim, C.-H.; Yang, H.; Ryan, M. D.; Musgrave, C. B.; Miyake, G. M., Organocatalyzed atom transfer radical polymerization driven by visible light. *Science* **2016**, *352*, 1082-1086.

24. Corbin, D. A.; McCarthy, B. G.; van de Lindt, Z.; Miyake, G. M., Radical Cations of Phenoxazine and Dihydrophenazine Photoredox Catalysts and Their Role as Deactivators in Organocatalyzed Atom Transfer Radical Polymerization. *Macromolecules* **2021**, *54*, 4726-4738.

25. Crespi, S.; Fagnoni, M., Generation of Alkyl Radicals: From the Tyranny of Tin to the Photon Democracy. *Chem. Rev.* **2020**, *120*, 9790-9833.

26. Sun, C.-L.; Gu, Y.-F.; Huang, W.-P.; Shi, Z.-J., Neocuproine–KOtBu promoted intramolecular cross coupling to approach fused rings. *Chem. Commun.* **2011**, *47*, 9813-9815.

27. Zhao, H.; Shen, J.; Guo, J.; Ye, R.; Zeng, H., A macrocyclic aromatic pyridone pentamer as a highly efficient organocatalyst for the direct arylations of unactivated arenes. *Chem. Commun.* **2013**, *49*, 2323-2325.

Kundu, A.; Dey, D.; Pal, S.; Adhikari, D., Pyrazole-Mediated C–H Functionalization of Arene and Heteroarenes for Aryl–(Hetero)aryl Cross-Coupling Reactions. *J. Org. Chem.* 2021, 86, 15665-15673.

29. Zhou, S.; Anderson, G. M.; Mondal, B.; Doni, E.; Ironmonger, V.; Kranz, M.; Tuttle, T.; Murphy, J. A., Organic super-electron-donors: initiators in transition metal-free haloarene–arene coupling. *Chem. Sci.* **2014**, *5*, 476-482.

30. Babu, S. S.; Muthuraja, P.; Yadav, P.; Gopinath, P., Aryldiazonium Salts in Photoredox Catalysis – Recent Trends. *Adv. Synth. Catal.* **2021**, *363*, 1782-1809.

31. Liu, J.; Jiang, J.; Zheng, L.; Liu, Z.-Q., Recent Advances in the Synthesis of Nitrogen Heterocycles Using Arenediazonium Salts as Nitrogen Sources. *Adv. Synth. Catal.* **2020**, *362*, 4876-4895.

32. Caramella, P.; Cellerino, G.; Corsico Coda, A.; Gamba-Invernizzi, A.; Gruenanger, P.; Houk, K. N.; Marinone Albini, F., Selectivity in cycloadditions. 5. Cycloadditions of nitrile oxides to furan. Competing mechanisms and regiochemistry. *J. Org. Chem.* **1976**, *41*, 3349-3356.

33. Mondal, A.; Sharma, R.; Pal, D.; Srimani, D., Manganese catalyzed switchable C-alkylation/alkenylation of fluorenes and indene with alcohols. *Chem. Commun.* **2021**, *57*, 10363-10366.

34. Wang, P.; Xie, Z.; Tong, S.; Wong, O.; Lee, C.-S.; Wong, N.; Hung, L.; Lee, S., A Novel Neutral Red Derivative for Applications in High-Performance Red-Emitting Electroluminescent Devices. *Chem. Mater.* **2003**, *15*, 1913-1917.

35. Lindner, B. D.; Paulus, F.; Appleton, A. L.; Schaffroth, M.; Engelhart, J. U.; Schelkle, K. M.; Tverskoy, O.; Rominger, F.; Hamburger, M.; Bunz, U. H. F., Electron-transporting phenazinothiadiazoles with engineered microstructure. *J. Mater. Chem. C* **2014**, *2*, 9609-9612.

36. Cano-Yelo, H.; Deronzier, A., Photocatalysis of the Pschorr reaction by tris-(2,2'-bipyridyl)ruthenium(II) in the phenanthrene series. *J. Chem. Soc.*, *Perkin Trans.* **1984**, 1093-1098.

37. Cano-Yelo, H.; Deronzier, A., Photo-oxidation of tris(2,2'-bipyridine)ruthenium(II) by para-substituted benzene diazonium salts in acetonitrile. Two-compartment photoelectrochemical cell applications. *J. Chem. Soc., Faraday Trans. 1* **1984,** *80*, 3011-3019.

38. Hari, D. P.; Schroll, P.; König, B., Metal-Free, Visible-Light-Mediated Direct C–H Arylation of Heteroarenes with Aryl Diazonium Salts. *J. Am. Chem. Soc.* **2012**, *134*, 2958-2961.

39. Gomes, F.; Narbonne, V.; Blanchard, F.; Maestri, G.; Malacria, M., Formal base-free homolytic aromatic substitutions via photoredox catalysis. *Org. Chem. Front.* **2015**, *2*, 464-469.

40. Gauchot, V.; Sutherland, D. R.; Lee, A. L., Dual gold and photoredox catalysed C–H activation of arenes for aryl–aryl cross couplings. *Chem. Sci.* **2017**, *8*, 2885-2889.

41. Kalyani, D.; McMurtrey, K. B.; Neufeldt, S. R.; Sanford, M. S., Room-Temperature C–H Arylation: Merger of Pd-Catalyzed C–H Functionalization and Visible-Light Photocatalysis. *J. Am. Chem. Soc.* **2011**, *133*, 18566-18569.

42. Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R., Nucleus-Independent Chemical Shifts (NICS) as an Aromaticity Criterion. *Chem. Rev.* **2005**, *105*, 3842-3888.

43. Schleyer, P. v. R.; Manoharan, M.; Wang, Z.-X.; Kiran, B.; Jiao, H.; Puchta, R.; van Eikema Hommes, N. J. R., Dissected Nucleus-Independent Chemical Shift Analysis of π -Aromaticity and Antiaromaticity. *Org. Lett.* **2001**, *3*, 2465-2468.

44. Schleyer, P. v. R.; Jiao, H.; Hommes, N. J. R. v. E.; Malkin, V. G.; Malkina, O. L., An Evaluation of the Aromaticity of Inorganic Rings: Refined Evidence from Magnetic Properties. *J. Am. Chem. Soc.* **1997**, *119*, 12669-12670.

45. Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993**, *98*, 5648-5652.

46. Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **1988**, *37*, 785-789.

47. Yang, H.; Chu, D.-Z.; Jiao, L., Aromatization modulates the activity of small organic molecules as promoters for carbon–halogen bond activation. *Chem. Sci.* **2018**, *9*, 1534-1539.

48. Zhang, L.; Yang, H.; Jiao, L., Revisiting the Radical Initiation Mechanism of the Diamine-Promoted Transition-Metal-Free Cross-Coupling Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 7151-7160.

Chapter 3

Deciphering the single electron transfer ability of fluorene under photoredox conditions

For the purpose of this thesis, the work of chapter 3 is adapted with permission from (Dey. D. [#]; Kundu. A. [#]; Mandal. B.; Roy. M.; Adhikari. D.*, Catal. Sci. Technol. **2022**, *12*, 7322. Title: Deciphering the single electron transfer ability of fluorene under photoredox condition.)

3.1. Introduction

Single electron transfer (SET)-based C–X bond cleavage to generate a carbon-based radical has lately emerged as an important tool to facilitate cross-coupling chemistry without involving transition metal catalysts.¹⁻³ In radical-mediated cross-coupling reactions, usually there exist a chain propagation step, where one of the pertinent intermediates is capable of transferring electron to a substrate molecule.⁴ This process often converts the role of the starting molecule to just an initiator, which usually builds sufficient concentration of a radical intermediate to push the reaction in the forward direction. The chain propagation part of the catalytic cycle is well-understood, while the initiation step challenges chemists profusely.⁵ The diversity, and in cases, the simplicity of initiator molecules warrants detailed study to sketch the underlying principles behind their success. Previous attempts by Murphy, Jiao have delineated the mechanistic picture for this step and provided crucial information regarding the nature of the active initiator and its fate.⁵⁻⁹ Inarguably, a thorough understanding regarding radical initiation process is pivotal to delineating the design principles for new promoter molecules.





Prior reports in radical-promoted cross-coupling chemistry demonstrated small organic molecules which in combination with a base, converts these into an efficient electron initiator.¹⁰⁻¹⁴ Several carbanion and amides have also shown their utility in such SET-mediated cross-coupling reactions.¹⁵⁻¹⁹ However, pure hydrocarbons have not been exploited earlier as a reductant to promote SET-mediated cross-coupling reactions. To this end, we discovered that a simple organic molecule such as deprotonated fluorene is a potent initiator that can reductively cleave a C–I bond under photochemical conditions. Intriguingly, upon electron transfer the fluorene anion generates a radical and its dimeric form is also capable of

performing electron transfer further.

3.2. Results and discussions

3.2.1. Optimisation of reaction conditions

 Table 3.1. Optimisation table.

	-	Fluorene base Benzene, 24 h visible light	-		
Entry	Additive (mol%)	Base (equiv.)	Solvent	Yield ^a (%)	
1	5	KO ^t Bu (1)	Benzene	40	
2	10	$KO^{t}Bu(1)$	Benzene	44	
3	15	$\mathrm{KO}^{\mathrm{t}}\mathrm{Bu}\left(1\right)$	Benzene	43	
4	5	KO ^t Bu (2)	Benzene	46	
5	10	KO ^t Bu (2)	Benzene	50	
6	15	KO ^t Bu (2)	Benzene	49	
7	5	KO ^t Bu (3)	Benzene	60	
8	10	KO ^t Bu (3)	Benzene	73	
9	-	KO ^t Bu (3)	Benzene	7	
10	15	KO ^t Bu (3)	Benzene	72	
11 ^b	10	KO ^t Bu (3)	Benzene	5	
12	20	NaO ^t Bu (3)	Benzene	10	
13	20	NaOH (3)	Benzene	trace	
14	20	KOH (3)	Benzene	trace	
15	20	TEA (3)	Benzene	-	
16	20	NaOMe (3)	Benzene	trace	
17	20	$Na_2CO_3(3)$	Benzene	trace	
18	20	K ₃ PO ₄ (3)	Benzene	-	
19	20	$Cs_2CO_3(3)$	Benzene	trace	

^a NMR yields, ^b reaction is performed under dark conditions.

The fate of the initiator is fully traced so that electronic nature and the electron initiation

aptitude of these multiple species can be fully understood. Fluorene (**1**) and its derivatives have rich photophysical properties that have been exploited in photoelectric materials, semiconductor devices as well as solar cells.²⁰⁻²¹ We surmised that the methylene group at the 9-position of fluorene is sufficiently acidic so that deprotonation is feasible and the resulting anion will be sufficiently reducing to break an Ar–I bond. Having this hypothesis in mind, we set a cross-coupling protocol with fluorene as an initiator in benzene, *p*-iodo anisole as a substrate and KO^tBu as the base to generate anisole radical. The reaction was successful only under visible light irradiation, where the desired biphenyl product was isolated in 73% yield at room temperature. A thorough optimization study revealed that 10 mol% loading of fluorene, in the presence of 3 equiv. of base afforded maximum product yield (Table 1, entry 8). As a base, KO^tBu is effective while NaO^tBu results only 10% of the cross-coupled product (Table 1, entry 12).

3.2.2. Mechanistic investigations to disclose the initiation path

The successful cross-coupling between an arene and aryl iodide prompted us to investigate the details of the mechanism. Since, aryl iodide is a good source of aryl radical upon SET $(E^{o}_{red} = -1.59 \text{ to } -2.24 \text{ V vs SCE})^{22}$, this is intuitive that the reaction is radical-mediated. To prove this conjecture, we performed the reaction in the presence of a radical inhibitor TEMPO and observed no product formation when the inhibitor was mixed in 1 equivalent. The Pk_a of the methylenic protons (22 in DMSO)²³ supports that deprotonation is completely feasible in the presence of a strong base such as KO^tBu. Hence, the deprotonated form of fluorene 1a, under photochemical condition becomes sufficiently reducing so that it can initiate SET to cleave an Ar-I bond.²⁴ To prove the importance of carbanion generation, we wanted to perform a control reaction with isolated 1a. Along this direction, we deprotonated 1 separately and prepared 1a by encapsulating the potassium cation with 18-crown-6. The need for photoexcitation is clearly established by dissolving 1a in benzene upon shinning visible light for a successful cross-coupling reaction, while the dark reaction under otherwise identical conditions did not afford any biaryl product. While examining the absorption property of 1 under visible light, we found no absorption in this region of electromagnetic spectrum. Interestingly, the deprotonation leads to a red shift and **1a** exhibits an absorption maximum at 552 nm. In striking contrast, treatment of 1 with NaO^tBu did not lead to any absorption in the visible region akin to deprotonation-driven absorption in the visible region and also corroborated well with the incompetent nature of the base for this cross-coupling reaction. Similar discrepancy between the usage of KO^tBu vs NaO^tBu was also documented

by Murphy²⁵⁻²⁶ and alluded to the difference in deprotonating ability in conjunction with the stabilization of the carbanion by the respective alkali metal cations.



Fig. 3.1. a) Proposed chain initiation process featuring **1a**. **b)** Emission spectra of **1a** in MeCN with different amounts of 4-iodo anisole addition. **c)** Stern-Volmer quenching for **1a**.

To ascertain the photoinduced electron transfer from 1a, we performed a Stern-Volmer quenching experiment, with the sequential addition of substrate aryl iodide. A clear fluorescence quenching of 1a was observed bearing a linear correlation with increasing concentration of the quencher substrate, proving the photoinduced electron transfer. Upon SET to ArI, the initiator 1a converts it to a fluorenyl radical, 1b. Such radicals 1b may dimerize to form the bifluorene 1c. Importantly, 1c possesses acidic hydrogens which can be further deprotonated, thus facilitating subsequent electron transfer. To probe the role of dimer 1c in electron transfer initiation. Gratifyingly, the reaction afforded 61% yield of the desired biaryl product at room temperature under only photochemical conditions. A carbanion 1d that will be generated from 1c via deprotonation, will further generate a radical species 1e after electron transfer under visible light irradiation.²⁷ The deprotonation of the methylenic hydrogen in 1e will result in a radical anion species 1f, which ideally is a more potent reductant than 1d. Likely, the photoexcited form 1f* conducts SET to generate an aryl radical and converts itself in the olefinic-dimer molecule, bifluoronylidene 1g.²⁸



Fig. 3.2. Proposed radical-chain initiation process featuring 1d.

To prove the intermediacy of the dimer **1g** in the catalytic cycle, we synthesized the molecule separately and examined its ability to promote C-C cross-coupling reaction. The visible lightpromoted reaction starting with 1g forged the biaryl product in 65% yield. We further discovered that the double bond in 1g can be reduced by KO^tBu upon photochemical conditions so that it can regenerate radical anion **1f**. A ground state reduction of **1g** by KO^tBu was not feasible, since the analogous dark reaction failed to generate any desired product. This is likely anticipated, as an electron rich olefin can only be reduced at a fairly negative potential, -1.61 V (vs Fc⁺/Fc) (see ESI for the voltammogram) and a mild reductant like KO^tBu ($E_{ox}^{o} = 0.1$ V) is incompetent in reducing it at its ground-state.²⁶ Once 1f is regenerated by this additional route, the radical initiation step continues in the presence of sustained promoters. To collect compelling evidence for the photoreduction of 1g, we mixed 1g with KO^tBu and exposed it to visible light for 5 minutes. The resulting solution changed its color from yellow to dark brown immediately, indicating a delocalized radical anion might have formed in the reaction mixture. When such brown-colored solution was interrogated via X-band EPR spectroscopy, a clear signal emerged at g = 2.004 proving the generation of an organic radical (Figure 3.3c). The signal is broad and that might be attributed to the extended spin delocalization of the radical. As revealed through DFT computation, the reduced species housed the spin density majorly on the olefinic part of the molecule with some delocalization on the adjacent aromatic rings (Figure 3.3d).



Fig. 3.3. (a) Proposed chain initiation process featuring **1g**. (b) Reaction of Fluorene with I_2 in presence of KO^tBu. (c) X-band (9.32 GHz) EPR signal of **1f** obtained from **1g** and KO^tBu mixture after shining visible light at rt. (d) Computed excess positive spin density in **1f** at isosurface 0.005 (e bohr⁻³)^{1/2}.

It is clear from the discussion that multiple species formed from 1 can perform SET and all contribute during the radical initiation step. To scrutinize the fate of 1 during this radical initiation step, we performed a reaction of fluorene with KO^tBu under visible light, but

instead of the substrate molecule, iodine was used as an electron acceptor. It has been shown earlier that iodine can be a terminal oxidant so that the species generated from **1** en route to multiple SET steps can be interrogated. Running the reaction for 24 h at room temperature resulted in a large amount of **1g** with a tiny amount of unknown product. Upon column chromatographic separation and crystallization, the identity of the product was authenticated as the fluorene trimer, **1h** (Figure 3.3b). The isolated **1h** was further characterized by ¹H and ¹³C NMR spectroscopies along with high-resolution mass spectrometric data. The formation of **1h** can only be explained by the attack of **1b** to **1g** followed by a hydrogen atom abstraction. The isolation of **1h** from the mixture of **1**, KO^tBu and iodine establishes unequivocally that **1g** is a bona fide intermediate during the SET processes.



Fig. 3.4. General cycle for BHAS mediated C-C cross-coupling reaction.

Among a large array of molecules that have proved to be efficient initiators, radical initiation step is not often thoroughly interrogated. It has been often conceived that once a tiny amount of aryl radical is generated which is responsible for initiating the reaction, usual product formation is managed by the chain propagation step. However, Jiao has argued that a tiny concentration of an aryl radical might not be adequate to conduct a cross-coupling reaction at an appreciable rate. Building up of radical concentration can amplify the reaction rate.⁷ In our case, we have found at least three different intermediates enabling SET processes, including starting initiator **1**. The present example clearly showcases a radical initiation mechanistic network rather than a single and unique initiation pathway that is responsible for this radical-

promoted cross-coupling reaction. The rest part of the reaction is via chain propagation, which is well-known for BHAS reactions (Fig. 3.4). The engendered aryl radical through initiation step, attacks benzene to form phenylcyclohexadienyl radical, which is further deprotonated by KO^tBu to give aryl radical anion. This highly reducing aryl radical anion transfers one electron to another aryl halide bond to complete the chain process.

3.2.3. Substrate Scope

 Table 3.2. Substrate scope for C-C cross-coupling reaction



Reaction conditions: **1** (10 mol%), aryl halide (0.5 mmol), KO^tBu (1.5 mmol), benzene (2 mL), visible light, 24 h. ^{*}isolated yields.

Finally, to prove that the iodoarene does not generate benzyne and such an intermediate is not responsible for the successful cross-coupling chemistry, a 2,6-dimethyl phenyliodide was chosen.^{26, 29} At the end of the reaction employing standard conditions, expected 2,6-dimethyl-1,1'-biphenyl (8%) and **3a** (22%) was isolated in total 30% yield. The primary reason for the low yield from the reaction is the loss of xylene as a volatile by-product, whose formation can be explained via the hydrogen atom abstraction by a xylyl radical. The formation of xylene and the biphenyl unambiguously dismisses the contribution of benzyne mechanism towards the biphenyl formation, since the formation of benzyne is not possible for the chosen

substrate. To examine the generality of this fluorene-promoted electron transfer protocol, we studied the scope of multiple aryliodide substrates. A series of aryliodide was used as the source of the aryl radical and was successfully coupled to unactivated benzene. Pleasingly, all substrate molecules were converted to a respective biaryl in high yields. As showcased in the table 1, phenyl, p-^tBu iodobenzene (**2a-2b**) were all converted to the respective biphenyls (**3a-3b**) in 60-79% yields.

Similarly, 2-methyl iodobenzene or 3,5-dimethyl phenyl iodide reacted under the photocatalytic protocol efficiently to give the biphenyl products **3c-3d** in 70-71% yields. Both electron donating and withdrawing groups were well tolerated to furnish respective biphenyl products (**3e-3i**) in 58-81% yields. Furthermore, naphthyliodide was a potential substrate to furnish the 1-phenyl naphthalene in moderate 50% yield. Some of the heterocycles such as 2-methoxy pyridyl and thiophene reacted with benzene smoothly under this reaction protocol to afford the biaryl products **3k-3l** in 56-59% yields. The method was further effective in scaling-up the reaction, as the synthesis of **3e** afforded 56% isolated yield in a gram-scale reaction (See ESI, section 6).





Reaction conditions: **1** (10 mol%), aryl halide (0.5 mmol), KO^tBu (1.5 mmol), thiophene (1.5 mL), visible light, 24 h, isolated yields.

To prove further the generality of the protocol, we examined thiophene as the arene partner for the cross-coupling reaction. Using thiophene as a coupling partner, tolyl and xylyl iodides afforded the respective hetero-biaryl products (**4a-4b**) in 59-61% yields (Table 3).

Gratifyingly, highly electron withdrawing -CN, electron donating -OMe, and mildly donating -F groups in the aryl iodide component were all tolerant to the reaction conditions to furnish **4c-4e** in 56-68% yields. Additionally, the scope of the reaction was further extended to N-methylpyrrole as the arene coupling partner (Table 4). When the latter arene was used, several aryl iodides afforded the desired products (**5a-5c**) in 50-54% yields.

Notably, the reducing power of the fluorene anion is not limited to breaking only aryl iodide bonds. We investigated the same reaction switching to aryl bromides as halide substrate and found encouraging result. When 4-bromo anisole was examined as a model bromo substrate, the desired biaryl product was isolated in 55 % yield (See ESI, section 8). Arguably, the room temperature reaction is an improvement over multiple radical-mediated thermal reactions starting with aryliodide substrates that often needed a reaction temperature of 80-120 °C.^{15, 30-33} Achieving the reducing excited state of a carbanion promotes Ar–I bond cleavage in a much easier manner compared to the electron transfer from the ground state of an additive-KO^tBu blend under thermal conditions.





Reaction conditions: **1** (10 mol%), aryl halide (0.5 mmol), KO^tBu (1.5 mmol), *N*-methylpyrrole (1.5 mL), visible light, 24 h, isolated yields.

3.3. Conclusions

In conclusion, this report describes how a carbanion of an organic hydrocarbon molecule fluorene can behave as an efficient initiator during radical-promoted cross-coupling reactions under visible light initiation condition. Along the reductive cleavage of aryliodide, the parent initiator generates multiple intermediates which also enables SET, thus overall having an amplifying effect on the reaction efficiency. We believe such knowledge will be helpful in designing other radical initiators to steer cross-coupling reactions under very mild conditions.

3.4. Experimental Section

3.4.1. General procedure for the synthesis of C–C cross-coupling reaction of aryl halides with benzene.



In a pressure tube, aryl iodide (0.5 mmol), KO^tBu (1.5 mmol) and fluorene (10 mol%) were taken in a glove box. After that dry benzene (2 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Subsequent purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.2. Synthetic procedure of 9H,9'H-9,9'-bifluorene (1c).



1c was synthesized following literature procedure.¹ A 100 mL oven-dried Schlenk flask was charged with 1.0 g (4.5 mmol) of fluorene under nitrogen flow. The solid was then dissolved in 40 mL of diethyl ether and cooled to -78 °C. A syringe was used to add 4 mL (5 mmol) of 1.6 M n-butyllithium in hexanes to the cooled solution, then allowed to stir at ambient temperature for 2.5 h upon which the solution turned red. The red solution was again cooled to -78 °C before the addition of 0.6 g (4.5 mmol) of cobalt(II) chloride. After 1 h of stirring at ambient temperature, saturated solutions of NaCl (10 mL) and NH₄Cl (10 mL) were added. The aqueous layer was extracted with 3×15 mL portions of dichloromethane, and

magnesium sulfate was added to the organic phase. After filtration, solvent was removed under vacuum and the resulting solid was washed with pentane and ether to give 482 mg (65% yield) of 9H,9'H-9,9'-bifluorene (**1c**). The authenticity of the product was confirmed by ¹H and ¹³C NMR spectroscopies. ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 7.6 Hz, 4H), 7.29 (d, *J* = 8.7 Hz, 4H), 7.09 (t, *J* = 7.0 Hz, 4H), 6.96 (d, *J* = 7.8 Hz, 4H), 4.85 (s, 2H).¹³C NMR (100 MHz, CDCl₃) δ 144.8, 141.6, 127.4, 126.8, 124.2, 119.8, 49.9.

3.4.3. Synthetic procedure of 9,9'-bifluorenylidene(1g).



1g was synthesized following literature procedure.³ In an oven-dry 250 mL round bottom flask, zinc dust (74 mmol) and TiCl₄ (37.5 mmol) were added in 40 mL dry THF solvent under N₂ atmosphere at 0 °C. Then, the mixture was transferred to the 20 mL THF solutions of fluorenone (10 mmol) via cannula. After that the reaction mixture was refluxed for 24 h, then the reaction mixture was cooled and quenched with a saturated aqueous solution of NH₄Cl. The organic products were extracted in ethyl acetate. The organic layer was dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. The crude product was purified by column chromatography to give the desired product **1g** in 983 mg (60% yield) as a red solid. The authenticity of the product was confirmed by ¹H NMR and ¹³C NMR spectroscopies. ¹H NMR (400 MHz, CDCl₃) δ 8.39 (d, *J* = 7.8 Hz, 4H), 7.71 (d, *J* = 7.5 Hz, 4H), 7.36 – 7.31 (m, 4H), 7.24 – 7.18 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 138.4, 129.3, 127.0, 126.9, 120.0

3.4.4. Synthesis of 9,9'-bifluorenylidenyl radical anion.



In a glove box, 9,9'-bifluorenylidene (2 mmol) was dissolved in THF (3 mL) giving an intense yellow color. Then potassium (2.1 mmol) and 18-crown-6 (2.1 mmol) were added to the solution. The reaction mixture was stirred at room temperature for 5 minutes during which a dark brown colored solution ensued. The reaction mixture was dried further to isolate **1f**.

3.4.5. Gram-scale synthesis of 3g



In a sealed tube, 4-iodoanisole (4.3 mmol, 1 g), KO^tBu (12.9 mmol, 1.4 g) and fluorene (10 mol%) were taken in a glove box. After that dry benzene (16 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Subsequent purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product in 56 % isolated yield. The biaryl product was fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.6. C-C cross coupling reaction of 4-iodo anisole with thiophene as a coupling partner



In a sealed tube, aryl iodide (0.5 mmol), KO^tBu (1.5 mmol) and fluorene (10 mol%) were taken in a glove box. After that dry thiophene (1.5 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Subsequent purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product. The hetero-biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.7. C-C cross coupling reaction of 4-iodo anisole with N-methyl pyrrole as a coupling partner



In a sealed tube, aryl iodide (0.5 mmol), KO¹Bu (1.5 mmol) and fluorene (10 mol%) were taken in a glove box. After that dry N-methyl pyrrole (1.5 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Subsequent purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product. The hetero-biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.8. C-C cross coupling reaction of 4-bromo anisole with benzene as a coupling partner



In a sealed tube, 4-bromoanisole (0.5 mmol), KO^tBu (1.5 mmol) and fluorene (10 mol%) were taken in a glove box. After that dry benzene (2 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Subsequent purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product in 55 % isolated yield. The biaryl product was fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.8. Reaction of fluorene with I₂ in the presence of KO^tBu



In an oven-dried Schlenk flask, **1** (1 mmol), KO^tBu (1.5 mmol) and I₂ (2 mmol) were mixed under inert atmosphere. After that dry benzene (2 mL) was added to the reaction mixture. The reaction mixture was stirred under visible light irradiation for 24 h under inert atmosphere at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Purification by column chromatography with EtOAc/hexane afforded **1g** (40%) and **1h** (14%).

9H,9''H-9,9':9',9''-terfluorene (1h):



1h was fully characterized by ¹H and ¹³C NMR spectroscopies. ¹H NMR (400 MHz, CDCl₃) δ 8.52 (d, *J* = 7.5 Hz, 2H), 7.87 – 7.79 (m, 2H), 7.62 – 7.52 (m, 4H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 7.0 Hz, 2H), 6.88 – 6.80 (m, 2H), 6.51 (t, *J* = 8.2 Hz, 2H), 6.30 (d, *J* = 7.7 Hz, 2H), 5.41 (s, 2H), 5.35 (d, *J* = 7.8 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 146.3,144.3, 143.9, 143.7, 141.7, 141.0, 136.2, 128.1, 127.6, 127.4, 126.9, 126.8, 126.0, 124.6, 123.6, 120.4, 119.3, 118.8.

3.4.9. C-C cross-coupling reaction taking 9H,9'H-9,9'-bifluorene(1c) as initiator



In a pressure tube 4-iodoanisole (0.5 mmol), KO^tBu (1.5 mmol) and **1c** (10 mol%) were charged in a glove box. After that dry benzene (2 mL) was added to the reaction mixture and the tube was securely closed. The reaction mixture was stirred under visible light irradiation for 24 h in N₂ atmosphere at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Further purification by column chromatography with EtOAc/hexane combination as the eluent afforded the corresponding product in 61% yield. The biaryl product (**3g**) was fully characterized by ¹H and ¹³C NMR spectroscopies.

When the same reaction was repeated under dark condition, no product was isolated.





Inside the glove box, a pressure tube was charged with 4-iodoanisole (0.5 mmol), KO^tBu (1.5 mmol) and **1g** (10 mol%). After that dry benzene (2 mL) was added to the reaction mixture and the tube was closed properly. The reaction mixture was stirred under visible light irradiation for 24 h under N₂ atmosphere at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under the reduced pressure. Further purification by column chromatography with hexane afforded the corresponding product in 64% yield. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies. When the same reaction was repeated under dark condition, no product was isolated.





Inside a glove box, a pressure tube was charged with 2,6-dimethyl iodobenzene (0.5 mmol), KO^tBu (1.5 mmol) and fluorene (10 mol%). After that dry benzene (2 mL) was added to the reaction mixture and the tube was tightly closed. The reaction mixture was stirred under visible light irradiation for 24 h at room temperature. After the completion of the reaction, dichloromethane was added to the mixture and extracted. Then the resulting solution was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Purification of the crude mixture by column chromatography with hexane afforded 2,6-dimethyl-1,1'-biphenyl (8%) and **3a** (22%) in overall 30% yield. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

3.4.12. Electron paramagnetic resonance spectroscopy

In a solution of **1g** (0.05 mmol, 17 mg) in toluene, KO^tBu (0.07 mmol, 8 mg) was added. The reaction mixture was irradiated with visible light. The light exposure was continued for 5 minutes during which the yellow color of the solution was changed to dark brown. The X-band EPR measurement of this solution was carried out at room temperature. A sharp signal at g = 2.004 was observed, which indicated the formation of an organic radical anion.

3.4.13. Radical quenching experiment:

To a solution of fluorene (0.1 mmol), KO^tBu (1.5 mmol), 4-iodoanisole (0.5 mmol) in benzene (2 mL), TEMPO (1 equiv, 0.5 mmol) were added. The reaction mixture was stirred for 24 h under visible light irradiation. The reaction was quenched fully and no desired biaryl product was obtained. The TEMPO-adduct was detected by mass spectrometry (M+H = 264.1927).

3.4.14. Cyclic voltammetry:

To prepare **1a**, 3.5 mg of fluorene and 3 mg of KH (30 % w/w in mineral oil) were taken in 1 mL of dry THF and strirred for 10 min. Then the solution was filtered through PTFE filter. Then 19 mL THF of 0.1 M (nBu_4N)PF₆ solution was added to the filtrate as the supporting electrolyte. A three-electrode set-up was used to determine the reduction potential where glassy carbon was the working electrode, a Pt wire as the counter and Ag/AgCl containing 1M KCl solution as the reference electrode, respectively. The shown voltammogram was collected with a scan rate of 100 mV sec⁻¹. The peak positions for the anodic and cathodic waves were internally referenced with respect to ferrocene/ferrocinium couple.

The CV data was collected by dissolving **1g** (4 mg) in 15 mL THF with a 0.1 M (nBu_4N)PF₆ solution as the supporting electrolyte. A three-electrode set-up was used to determining the reduction potential where glassy carbon was the working electrode, a Pt wire as the counter and Ag/AgCl containing 1M KCl solution as the reference electrode, respectively. The shown voltammogram was collected with a scan rate of 100 mV sec⁻¹. The peak positions for the anodic and cathodic waves were internally referenced with respect to ferrocene/ferrocinium couple.



Figure 3.5. (a) Cyclic voltammogram of 1a. (b) Cyclic voltammogram of 1g.

3.4.15. The UV-Visible absorption experiments:



Figure 3.6. UV-visible spectra of 1a in MeCN.



Figure 3.7. UV-visible spectra of 1d in THF.



Figure 3.8. UV-visible spectra of 1g in THF.

3.4.15. Fluorescence quenching experiment and Stern-Volmer plot:

In this experiment, measurements were carried out on a 10^{-6} M solution of **1a** in MeCN with appropriate amount of quencher in quartz cuvette. The sample solutions were previously degassed with argon. The solution was irradiated at 515 nm, and the emission intensity was examined at 571 nm. Plots were derived according to the Stern-Volmer equation and K_{SV} was calculated. Stern-Volmer equation is the following

 $I_0/I = 1 + K_{SV}[Q]$

Where I_0 is the fluorescence intensity without the quencher, I is the intensity in the presence of the quencher, [Q] is the concentration of added quencher and K_{SV} is the Stern-Volmer quenching constant.

3.4.16. Computational data:

All calculations were carried out using Density Functional Theory as implemented in the Gaussian09⁶ quantum chemistry programs. The geometries of stationary points were optimized with the B3LYP density functional theory. We used 6-31G(d) basis set for elements H, C. Harmonic force constants were computed at the optimized geometries to characterize the stationary points as minima. Spin density of the radical was visualized through Gaussview.

Coordinates:

1f

02

C -4.00267700 2.46740500 -1.28110300 C -2.73257900 2.94453000 -1.65401700 C -1.58946600 2.18672100 -1.43922100 C -1.70672600 0.92846300 -0.82186700 C -2.99838500 0.43715800 -0.48069000 C -4.13991800 1.20886800 -0.70465300 H -4.88162600 3.07815400 -1.46514900 H -2.64785300 3.91711300 -2.13104800 H -0.61659700 2.55042600 -1.76056800 H -5.12558900 0.82719800 -0.44790900 C -1.43703000 -1.22669000 -0.01008300 C -0.99627300 -2.43931900 0.56401600 C -1.92442200 -3.30616500 1.13629000 C -3.29313800 -2.99302100 1.16308900 C -3.74390700 -1.78702400 0.62935400 C -2.82953900 -0.90282800 0.05861600 H 0.05408100 -2.72136000 0.53315600 H -1.58274900 -4.24908400 1.55527100 H -3.99856800 -3.69007300 1.60523900 H -4.80024500 -1.53081600 0.67198800 C -0.70679900 -0.08128600 -0.52946300

```
C 0.70645200 0.08162300 -0.52965300
C 1.70632400 -0.92810800 -0.82229100
C 1.43676300 1.22693300 -0.01019100
C 1.58899900 -2.18628400 -1.43982600
C 2.99803600 -0.43688600 -0.48114500
C 0.99604600 2.43940400 0.56427200
C 2.82927100 0.90303100 0.05834400
C 2.73207300 -2.94409200 -1.65480100
H 0.61610300 -2.54991200 -1.76117600
C 4.13953400 -1.20860800 -0.70529600
C 1.92425000 3.30612800 1.13662600
H -0.05433700 2.72135400 0.53370500
C 3.74370600 1.78712100 0.62917100
C 4.00221700 -2.46705700 -1.28190200
H 2.64728800 - 3.91660100 - 2.13197200
H 5.12523500 -0.82699200 -0.44858400
C 3.29298600 2.99300300 1.16318900
H 1.58261000 4.24892900 1.55589800
H 4.80004600 1.53089800 0.67165900
H 4.88113500 - 3.07780500 - 1.46610300
H 3.99845500 3.68997100 1.60540800
K 0.00146400 -0.00102800 2.28103100
```

3.4.17. Analytical data:

Biphenyl (3a) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 61 mg, 79%). ¹H NMR (400 MHz, CDCl₃) δ 7.64 (dd, J = 8.3, 1.3 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.43 – 7.35 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 128.9, 127.4, 127.3.

4-(tert-butyl)-1,1'-biphenyl (3b) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 63 mg, 60%). ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 7.3 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 1.49 (s, 9H).¹³C NMR (100 MHz, CDCl₃) δ 150.3, 141.2, 138.5, 128.8, 127.2, 127.1, 126.9, 125.8, 34.6, 31.5.

3,5-dimethyl-1,1'-biphenyl (3c) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a yellow oil (yield: 65 mg, 71%). ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.5 Hz, 7H), 7.58 – 7.52 (m, 9H), 7.49 – 7.43 (m, 4H), 7.36 (s, 8H), 7.13 (s, 3H), 2.52 (s, 30H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 141.4, 141.2, 138.2, 128.9, 128.6, 127.2, 127.1, 125.1, 21.4.

2-methyl-1,1'-biphenyl (3d) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 59 mg, 70%). ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.49 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 3H), 7.41 – 7.33 (m, 4H), 2.40 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.1, 135.4, 130.4, 129.9, 129.3, 128.2, 127.4, 126.9, 125.9, 20.6.

4-methoxy-1,1'-biphenyl (3e) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 75 mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.47 (m, 4H), 7.39 (t, *J* = 7.1 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 140.9, 133.9, 128.8, 128.3, 126.8, 126.8, 114.3, 55.4.

3-methoxy-1,1'-biphenyl (3f) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 66 mg, 72%). ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 7.6 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.16 (s, 1H), 6.92 (dd, *J* = 8.2, 2.7 Hz, 1H), 3.89 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 160.1, 142.9, 141.2, 129.9, 128.9, 127.6, 127.3, 119.8, 113.0, 112.8, 55.4.

2-fluoro-1,1'-biphenyl (3g) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 71 mg, 82%). ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.42 – 7.30 (m, 2H), 7.25 – 7.14 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 161.1, 158.7, 136.0, 130.9, 130.9, 129.3, 129.2, 129.2, 129.1, 129.1, 128.6, 127.8, 124.5, 124.5, 116.3, 116.1.

4-(trifluoromethyl)-1,1'-biphenyl (3h) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 80 mg, 72%). ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 4H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 144.9, 139.9, 129.1, 128.3, 127.6, 127.4, 125.9, 125.9, 125.8, 125.8, 123.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.33.

[1,1'-biphenyl]-4-carbonitrile (3i) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 78 mg, 87%). ¹H NMR (400 MHz, CDCl₃) δ 7.75 – 7.66 (m, 4H), 7.59 (dd, J = 6.9, 1.6 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.46 – 7.40 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 145.8, 139.3, 132.7, 129.2, 128.8, 127.9, 127.4, 119.1, 111.0.

1-phenylnaphthalene (3j) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 51 mg, 50%). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.92 (m, 2H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.50 (m, 6H), 7.47 (dd, *J* = 5.4, 1.6 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 140.8, 140.3, 133.9, 131.7, 130.1, 128.3, 127.7, 127.3, 127.0, 126.1, 125.8, 125.4.

2-methoxy-3-phenylpyridine (3k) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless oil (yield: 55 mg, 59%). ¹H NMR (400 MHz, CDCl₃) δ 8.21 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.62 (dd, *J* = 14.6, 7.1 Hz, 3H), 7.46 (t, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 6.99 (dd, *J* = 7.3, 5.0 Hz, 1H), 4.02 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 160.9, 145.8, 138.6, 136.8, 129.2, 128.3, 127.6, 124.7, 117.2.

3-phenylthiophene (3l) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 45 mg, 56%). ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, *J* = 7.3 Hz, 2H), 7.53 – 7.41 (m, 5H), 7.37 (t, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 142.4, 135.9, 128.9, 127.2, 126.6, 126.4, 126.3, 120.4

4-methyl-1,1'-biphenyl (3m) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a yellow oil (yield: 53 mg, 63%). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.9 Hz, 2H), 7.50 (d, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 141.3, 138.5, 137.2, 129.6, 128.8, 127.1, 127.1, 21.2.

4-fluoro-1,1'-biphenyl (3n) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 71 mg, 82%). ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.42 – 7.30 (m, 2H), 7.25 – 7.14 (m, 2H). ¹³C

NMR (100 MHz, CDCl₃) δ 161.1, 158.7, 136.0, 130.9, 130.9, 129.3, 129.2, 129.2, 129.1, 129.1, 128.6, 127.8, 124.5, 124.5, 116.3, 116.1.

2-methoxy-6-phenylnaphthalene (30) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 53 mg, 45%). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 1.8 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.75 – 7.69 (m, 3H), 7.52 – 7.46 (m, 2H), 7.41 – 7.35 (m, 1H), 7.23 – 7.16 (m, 2H), 3.95 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 157.9, 141.3, 136.5, 133.9, 129.8, 129.3, 128.9, 127.4, 127.3, 127.2, 126.2, 125.7, 119.3, 105.6.

3-(trifluoromethyl)-1,1'-biphenyl (3p) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a white solid (yield: 82 mg, 74%). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 2.0 Hz, 1H), 7.78 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.44 – 7.39 (m, 1H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 142.1, 139.9, 130.6, 129.4, 129.1, 128.2, 127.3, 124.1, 124.0.

methyl [1,1'-biphenyl]-4-carboxylate (3q) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 59 mg, 70%). Spectroscopic data matched with the literature.^{24 1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.0 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 3.94 (s, 3H).¹³C NMR (100 MHz, Chloroform-*d*) δ 167.2, 145.8, 140.1, 130.2, 129.1, 129.0, 128.3, 127.4, 127.2, 52.3.

2-(3-methylphenyl)thiophene (4a) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 53 mg, 61%). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 7.3 Hz, 2H), 7.35 – 7.26 (m, 3H), 7.15 – 7.07 (m, 2H), 2.41 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 144.7, 138.6, 134.4, 128.9, 128.4, 128.1, 126.8, 124.8, 123.2, 123.1, 21.6.

2-(3,5-dimethylphenyl)thiophene (4b) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 56 mg, 59%).¹H NMR (400 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 4.7 Hz, 1H), 7.27 (d, *J* = 5.1 Hz, 3H), 7.08 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.95 (s, 1H), 2.37 (s, 6H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 144.8, 138.5, 134.3, 129.3, 127.9, 124.6, 123.9, 122.9, 21.4.

2-(4-cyanophenyl)thiophene (4c) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 63 mg, 68%).¹H NMR (400 MHz, Chloroform-*d*) δ 7.67 (q, *J* = 8.7 Hz, 4H), 7.43 – 7.37 (m, 2H), 7.13 (dd, *J* = 5.1, 3.7 Hz, 1H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 142.1, 138.7, 128.6, 127.2, 126.2, 125.2, 118.9, 110.6. **2-(4-methoyphenyl)thiophene (4d) :**



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 53 mg, 56%).¹H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.53 (m, 2H), 7.25 – 7.20 (m, 2H), 7.07 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.95 – 6.91 (m, 2H), 3.84 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 159.3, 144.4, 128.0, 127.4, 127.3, 123.9, 122.2, 114.4.

2-(4-fluorophenyl)thiophene (4e) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 60 mg, 67%). ¹H NMR (400 MHz,
Chloroform-*d*) δ 7.61 – 7.55 (m, 2H), 7.28 (d, *J* = 5.1 Hz, 1H), 7.26 (d, *J* = 3.6 Hz, 1H), 7.13 – 7.06 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 163.6, 161.2, 143.4, 130.8, 128.2, 127.8, 127.7, 124.9, 123.2, 116.0, 115.8.

2-(4-methoxyphenyl)-1-methyl-1H-pyrrole (5a):

The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 51 mg, 54%). Spectroscopic data matched with the literature.¹⁸ ¹H NMR (400 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.74- 6.69 (m, 1H), 6.21 (t, *J* = 3.1 Hz, 1H), 6.18 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.86 (s, 3H), 3.65 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 158.7, 134.5, 130.1, 126.0, 123.1, 113.9, 108.1, 107.7, 55.4, 35.0.

1-methyl-2-(m-tolyl)-1H-pyrrole (5b) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 45 mg, 52%). Spectroscopic data matched with the literature.^{19 1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.18 (m, 2H), 7.13 (d, *J* = 7.3 Hz, 1H), 6.71 (s, 1H), 6.21 (d, *J* = 2.9 Hz, 2H), 3.67 (s, 3H), 2.40 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 138.1, 134.9, 133.4, 129.6, 128.3, 127.7, 125.9, 123.6, 108.6, 107.8.

1-methyl-2-(naphthalen-1-yl)-1H-pyrrole (5c) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 52 mg, 50%). Spectroscopic data matched with the literature.^{20 1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (t, *J* = 7.6 Hz, 2H), 7.73 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.49 (dq, *J* = 15.9, 7.8 Hz, 4H), 6.83 (s, 1H), 6.32 (t, *J* = 3.0 Hz, 1H), 6.28 (s, 1H), 3.40 (s, 3H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 133.8, 133.4, 132.3, 131.4, 128.9, 128.3, 128.3, 126.4, 126.4, 126.0, 125.3, 122.6, 110.1, 107.7, 34.6.

3.5. References

1. McGlacken, G. P.; Bateman, L. M., Recent advances in aryl–aryl bond formation by direct arylation. *Chem. Soc. Rev.* **2009**, *38*, 2447-2464.

2. Murphy, J. A., Discovery and Development of Organic Super-Electron-Donors. J. Org. Chem. 2014, 79, 3731-3746.

3. Sun, C.-L.; Shi, Z.-J., Transition-Metal-Free Coupling Reactions. *Chem. Rev.* 2014, *114*, 9219-9280.

4. Studer, A.; Curran, D. P., Organocatalysis and C-H Activation Meet Radical- and Electron-Transfer Reactions. *Angew, Chem., Int. Ed.* **2011**, *50*, 5018-5022.

5. Zhang, L.; Yang, H.; Jiao, L., Revisiting the Radical Initiation Mechanism of the Diamine-Promoted Transition-Metal-Free Cross-Coupling Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 7151-7160.

6. Barham, J. P.; Coulthard, G.; Kane, R. G.; Delgado, N.; John, M. P.; Murphy, J. A., Double Deprotonation of Pyridinols Generates Potent Organic Electron-Donor Initiators for Haloarene–Arene Coupling. *Angew, Chem., Int. Ed.* **2016**, *55*, 4492-4496.

7. Patil, M., Mechanistic Insights into the Initiation Step of the Base Promoted Direct C– H Arylation of Benzene in the Presence of Additive. *J. Org. Chem.* **2016**, *81*, 632-639.

8. Zhou, S.; Doni, E.; Anderson, G. M.; Kane, R. G.; MacDougall, S. W.; Ironmonger, V. M.; Tuttle, T.; Murphy, J. A., Identifying the Roles of Amino Acids, Alcohols and 1,2-Diamines as Mediators in Coupling of Haloarenes to Arenes. *J. Am. Chem. Soc.* **2014**, *136*, 17818-17826.

9. Zhou, S.; Anderson, G. M.; Mondal, B.; Doni, E.; Ironmonger, V.; Kranz, M.; Tuttle, T.; Murphy, J. A., Organic super-electron-donors: initiators in transition metal-free haloarene–arene coupling. *Chem. Sci.* **2014**, *5*, 476-482.

 Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F.
 Y.; Lei, A., Organocatalysis in Cross-Coupling: DMEDA-Catalyzed Direct C–H Arylation of Unactivated Benzene. *J. Am. Chem. Soc.* 2010, *132*, 16737-16740.

11. Sun, C.-L.; Gu, Y.-F.; Huang, W.-P.; Shi, Z.-J., Neocuproine–KOtBu promoted intramolecular cross coupling to approach fused rings. *Chem. Commun.* **2011**, *47*, 9813-9815.

12. Budén, M. E.; Guastavino, J. F.; Rossi, R. A., Room-Temperature Photoinduced Direct C–H-Arylation via Base-Promoted Homolytic Aromatic Substitution. *Org. Lett.* **2013**, *15*, 1174-1177.

13. Wu, Y.; Wong, S. M.; Mao, F.; Chan, T. L.; Kwong, F. Y., Intramolecular Direct C–H Bond Arylation from Aryl Chlorides: A Transition-Metal-Free Approach for Facile Access of Phenanthridines. *Org. Lett.* **2012**, *14*, 5306-5309.

Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S., KO^tBu Mediated Synthesis of Phenanthridinones and Dibenzoazepinones. *Org. Lett.* 2012, *14*, 2838-2841.

15. Qiu, Y.; Liu, Y.; Yang, K.; Hong, W.; Li, Z.; Wang, Z.; Yao, Z.; Jiang, S., New Ligands That Promote Cross-Coupling Reactions between Aryl Halides and Unactivated Arenes. *Org. Lett.* **2011**, *13*, 3556-3559.

16. Schmalzbauer, M.; Ghosh, I.; König, B., Utilising excited state organic anions for photoredox catalysis: activation of (hetero)aryl chlorides by visible light-absorbing 9-anthrolate anions. *Faraday Discuss.* **2019**, *215*, 364-378.

 Kundu, A.; Dey, D.; Pal, S.; Adhikari, D., Pyrazole-Mediated C–H Functionalization of Arene and Heteroarenes for Aryl–(Hetero)aryl Cross-Coupling Reactions. *J. Org. Chem.* 2021, *86*, 15665-15673.

18. Dey, D.; Kundu, A.; Roy, M.; Pal, S.; Adhikari, D., Aromatization as the driving force for single electron transfer towards C–C cross-coupling reactions. *Catal. Sci. Technol.* **2022**, *12*, 1934-1940.

19. Yang, H.; Zhang, L.; Jiao, L., N-Methylanilines as Simple and Efficient Promoters for Radical-Type Cross-Coupling Reactions of Aryl Iodides. *Chem.*– *Eur. J.* **2017**, *23*, 65-69.

20. Thomas, S. W.; Joly, G. D.; Swager, T. M., Chemical Sensors Based on Amplifying Fluorescent Conjugated Polymers. *Chem. Rev.* **2007**, *107*, 1339-1386.

21. Grimsdale, A. C.; Leok Chan, K.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B., Synthesis of Light-Emitting Conjugated Polymers for Applications in Electroluminescent Devices. *Chem. Rev.* **2009**, *109*, 897-1091.

22. Pause, L.; Robert, M.; Savéant, J.-M., Can Single-Electron Transfer Break an Aromatic Carbon–Heteroatom Bond in One Step? A Novel Example of Transition between Stepwise and Concerted Mechanisms in the Reduction of Aromatic Iodides. *J. Am. Chem. Soc.* **1999**, *121*, 7158-7159.

23. Bordwell, F. G.; Drucker, G. E.; McCollum, G. J., Stabilization of carbanions by polarization of alkyl groups on nonadjacent atoms. *J. Org. Chem.* **1982**, *47*, 2504-2510.

24. Schmalzbauer, M.; Marcon, M.; König, B., Excited State Anions in Organic Transformations. *Angew, Chem., Int. Ed.* **2021**, *60*, 6270-6292.

Barham, J. P.; Coulthard, G.; Emery, K. J.; Doni, E.; Cumine, F.; Nocera, G.; John, M.
P.; Berlouis, L. E. A.; McGuire, T.; Tuttle, T.; Murphy, J. A., KO^tBu: A Privileged Reagent for Electron Transfer Reactions? *J. Am. Chem. Soc.* 2016, *138*, 7402-7410.

Nocera, G.; Young, A.; Palumbo, F.; Emery, K. J.; Coulthard, G.; McGuire, T.; Tuttle, T.; Murphy, J. A., Electron Transfer Reactions: KO^tBu (but not NaO^tBu) Photoreduces Benzophenone under Activation by Visible Light. *J. Am. Chem. Soc.* 2018, *140*, 9751-9757.

27. La Porte, N. T.; Martinez, J. F.; Hedström, S.; Rudshteyn, B.; Phelan, B. T.; Mauck, C. M.; Young, R. M.; Batista, V. S.; Wasielewski, M. R., Photoinduced electron transfer from rylenediimide radical anions and dianions to Re(bpy)(CO)₃ using red and near-infrared light. *Chem. Sci.* 2017, *8*, 3821-3831.

28. Pogodin, S.; Agranat, I., Theoretical Notions of Aromaticity and Antiaromaticity: Phenalenyl Ions versus Fluorenyl Ions. *J. Org. Chem.* **2007**, *72*, 10096-10107.

29. Cumine, F.; Zhou, S.; Tuttle, T.; Murphy, J. A., A study of diketopiperazines as electron-donor initiators in transition metal-free haloarene–arene coupling. *Org. Biomol. Chem.* **2017**, *15*, 3324-3336.

30. Yong, G.-P.; She, W.-L.; Zhang, Y.-M.; Li, Y.-Z., Direct arylation of unactivated aromatic C–H bonds catalyzed by a stable organic radical. *Chem. Commun.* **2011**, *47*, 11766-11768.

31. Zhao, H.; Shen, J.; Guo, J.; Ye, R.; Zeng, H., A macrocyclic aromatic pyridone pentamer as a highly efficient organocatalyst for the direct arylations of unactivated arenes. *Chem. Commun.* **2013**, *49*, 2323-2325.

32. Song, Q.; Zhang, D.; Zhu, Q.; Xu, Y., p-Toluenesulfonohydrazide as Highly Efficient Initiator for Direct C–H Arylation of Unactivated Arenes. *Org. Lett.* **2014**, *16*, 5272-5274.

33. Chen, W.-C.; Hsu, Y.-C.; Shih, W.-C.; Lee, C.-Y.; Chuang, W.-H.; Tsai, Y.-F.; Chen, P. P.-Y.; Ong, T.-G., Metal-free arylation of benzene and pyridine promoted by amino-linked nitrogen heterocyclic carbenes. *Chem. Commun.* **2012**, *48*, 6702-6704.

Chapter 4

Single electron transfer catalysis by diphenylthiourea under visible light photoredox conditions

For the purpose of this thesis, the work of chapter 4 is adapted with permission from (Dey. D.#; Kundu. A.#; Roy. M.; Singh. V.; Maji. S.; Adhikari. D.*,Org. Chem. Front., 2023, 10, 5248. Title: Single electron transfer catalysis by diphenylthiourea under visible light photoredox conditions.)

4.1. Introduction

Photochemical pathways to reductively cleave a bond, lately became immensely popular, as the source of energy is quite abundant and cheap.¹⁻² There is a constant search for molecules that can undergo a chemical transformation and in turn becomes converted to a highly reducing species upon photoexcitation. König has shown that many molecules are extremely good photoreductant when the light absorbing species becomes an anion.³⁻⁴ Often, such anions at its excited state directly cleaves a C-X bond in a reductive fashion.⁵ This is in opposed to the popular photocatalyst $Ru(bpy)_3^{2+}$ where a sacrificial reductant such as tertiary amine is required to reduce the photocatalyst. In SET-based reductive cleavage, it is frequently conceived that once an aryl radical is generated, a chain propagation step can pursue to successfully make the process catalytic. However, focused study to delineating the initiation pathway that builds up a sufficient concentration of the radical process is scarce. To fill this void, we choose a small molecule diphenylthiourea (DPTU), that in its deprotonated form becomes a potent reductant upon photoexcitation (Scheme 4.1).



Scheme 4.1. C-C cross coupling reaction via photoinduced electron transfer from deprotonated diphenyl thiourea.

Previously, thiourea has been utilized in photocatalytic reactions showcasing its activity in guanylation reaction.⁶ Furthermore, thiols has been shown to promote thiol-ene reaction under visible light initiation, where R-SH photoreduced either 9-mesityl-10-methyl acridinium tetrafluoroborate or a ruthenium photocatalyst generating a thiyl radial .⁷⁻⁹ In the cross-coupling reaction of thiols with aryl and heteroaryl halides under photochemical conditions, often thiol species reduced the excited state of the Ir-photocatalyst.¹⁰ Beyond the role of a photoreductant, sulfur anions have also been utilized in the formation of various

electron donor-acceptor complexes and hydrogen atom transfer catalysis.¹¹⁻¹² Along this line, sulfur anions have directly generated a thiyl radical to promote C-S cross-coupling reaction in the absence of a separate photocatalyst.¹³⁻¹⁴ Our keen interest in anionic photochemistry involving amido anions¹⁵⁻¹⁶, carbanions^{19,17} as potent SET catalyst made us to posit that anion of DPTU at its photoexcited state might be sufficiently reducing to cleave aryl halide bonds. In the present work we showcase that deprotonated DPTU can easily cleave aryl bromide bonds to generate aryl radicals that has been utilized for a host of useful chemical transformations. Furthermore, a thorough mechanistic study sheds light on how multiple intermediate species from DPTU helps to build the adequate concentration of aryl radicals so that the follow up reaction can proceed at a reasonable rate.

4.2. Results and Discussions

4.2.1. Optimisation of reaction conditions

Our initial foray in SET-promoted cross-coupling reactions started with the screening of a set of urea and thiourea molecules. We surmised the presence of deprotonable hydrogens in these array of chosen molecules will generate a stable anion in situ and upon photoexcitation they will be potent reductants. Having this idea in mind, we chose the cross-coupling of *p*-bromo anisole and benzene as the model reaction and screened the possible urea-based photocatalysts (L1-L4). As evident through the optimization reactions, simple urea (L1) failed to afford any cross-coupled product (Table 4.1, entry 1). Similarly, when diphenylurea (L2) and thiourea (L3) were examined to catalyze the reaction, formation of tiny amount of product was observed (entry 2 & 3). In the contrary, DPTU (L4) upon 10 mol% loading gave the desired biphenyl 2a in 29% yield (entry 4). Encouragingly, increasing the catalyst loading to 20 mol% improved the product yield to moderate 55% within 12 h (entry 5). Extending the reaction time to 24 h significantly increased the product yield to 93% (entry 6). The base KO^tBu is required in 3 equivalents, while decrease of its loading affect the yield of cross-coupled product in a detrimental manner (entries 7-8). Optimization of the condition revealed that blue LED lamp is most suitable for the reaction. Separate control reaction in presence of thiourea L4, base, light proves all these components to be indispensable and the reaction fails in the absence of any one (entry 9-11). Extensive screening of base disclosed that KO^tBu is the most efficient one, while other bases such as NaO^tBu, Et₃N, KOH, NaOH, K_2CO_3 were proved to exhibit very poor conversion. Notably, the failure of L2 despite having a very similar architecture to L4 hints to sulfur's speacial role in electron transfer

catalysis. We hypothesize that amide anion form L2 is less stable, as the sulfur has been replaced by oxygen, that makes a significant difference in the anionic stability and that in turn affects its catalytic activity.

MeOBr 1a	+ 💭 📙	and (x mol%) O ^t Bu (y eq.) Blue LED	MeO-	2a
H_2N NH_2 O L1		H ₂ N NH ₂ S L3	H L4	

 Table 4.1. Optimisation table.

Entry	L (mol %)	Base (equiv)	Time (h)	Yield ^b (%)
1	L1 (20)	KO ^t Bu (3 eq.)	24	-
2	L2 (20)	KO ^t Bu (3 eq.)	24	9
3	L3 (20)	KO ^t Bu (3 eq.)	24	17
4	L4 (10)	KO ^t Bu (3 eq.)	12	29
5	L4 (20)	KO ^t Bu (3 eq.)	12	55
6	L4 (20)	KO ^t Bu (3 eq.)	24	93
7	L4 (20)	KO ^t Bu (1 eq.)	12	15
8	L4 (20)	KO ^t Bu (2 eq.)	12	34
9	-	KO ^t Bu (3 eq.)	24	-
10	L4 (20)	-	24	-
11 ^a	L4 (20)	KO ^t Bu (3 eq.)	24	-
12	L4 (5)	KO ^t Bu (3 eq.)	12	22
13	L4 (10)	KO ^t Bu (3 eq.)	12	29
14	L4 (15)	KO ^t Bu (3 eq.)	12	37

Reaction conditions: Aryl bromide (0.5 mmol), ligand (x mol%), base (y equiv.), benzene (2 mL), blue LED, room temperature. ^areaction was conducted in dark. ^bNMR yield.

4.2.2. Mechanistic Probation

Evaluating the details of the radical initiation step is critical to design other small molecule photocatalysts. This makes us intrigued regarding the reaction mechanism for the photocatalytic process. The molecule **L4** does not absorb within visible range and appears colorless. However, when deprotonated in situ, the color of the solution changes to greenish yellow and generates the deprotonated DPTU (7) (Scheme 2). Upon photoexcitation, 7

performs SET to the aryl bromide to generate the aryl radical while itself becomes converted to a thiyl radical. This SET from the deprotonated thiol reminisces the thiyl radical (8) generation from the excited state of deprotonated 2-mercaptobenzoxazole, which reduces the dye Rose Bengal along the preparation of aminobenzoxazoles.¹⁸



Scheme 4.2. Aryl radical initiation pathway by deprotonated L4.



Scheme 4.3. (a) Radical trapping experiment with TEMPO. (b) C-C cross-coupling reaction with isolated deprotonated form (7a) of L4. (c) C-C cross-coupling reaction with 2-anilinobenzothiazole (11).

To prove the process proceeds through the intermediacy of a radical, we performed a control reaction in the presence of radical quencher TEMPO. Upon addition of one equivalent of

TEMPO the reaction ceases entirely. As a strong evidence to this SET and aryl radical generation, we were able to intercept the putative aryl radical as its TEMPO adduct and



Figure 4.1. ORTEP of **7a** drawn with 50% probability ellipsoids. hydrogen atoms except the important one is omitted for clarity.

collected a high-resolution mass spectrometric signature for the same (Scheme 3a). Intuitively, such radical 8 can drive a SOMO-philic attack to the adjacent phenyl ring, so that a five-membered ring 9 containing sulfur and nitrogen can form. The deprotonable cyclohexenyl hydrogen in 9 can be abstracted by the strong base KO^tBu. The resulting radical anion 10 is a strongly reducing species and can promote SET further to cleave another aryl bromide bond. At the end of this electron transfer, a 2-anilinobenzothiazole 11 forms. As a compelling proof for this sequence of electron transfer, **11** was isolated from a stoichiometric reaction and was characterized by NMR spectroscopy (Section 4.3, ESI). To prove the conjecture further that, the reaction starts upon deprotonation of L4 and the anion is responsible for photoexcited electron transfer, we attempted to isolate the key species. Accordingly, we deprotonated L4 with KO^tBu and tried to isolate the deprotonated product in the presence of 18-crown-6 (7a). Gratifyingly, keeping the THF solution for 4 days at room temperature grew diffractable-quality crystals. Upon solid-state X-ray diffraction of 7a, the structure of the deprotonated DPTU was fully analyzed. As evident form the crystal structure (Figure 4.1) the DPTU anion is interacting with countercation potassium through the sulfur end. However, the primarily ionic interaction is reflected in relatively large distance between sulfur and potassium (3.23 Å). To prove that, only upon the excitation of visible light, such an anion promotes SET, a reaction was started with 7a. Gratifyingly, a cross-coupling reaction with 4-methoxy bromobenzene afforded 91% yield of the product 3a (Scheme 3b).

However, the deprotonated anion is not capable of promoting the reductive cleavage a Ar-Br bond in its ground state. This is evidenced through a drak reaction, where no product formation was observed in strong agreement with the optimization table. The **7a** contains a 18-C-6 macrocycle, that physically separates the crown-encapsulated potassium from the delocalized sulfur anion. It is intuitive that less stabilization of the DPTU anion might be making it a slightly better reductant compared to the potassium-stabilized version of the latter, where potassium can come closer to the anion. To verify this possibility, two parallel reactions were run; one in the presence of 18-C-6, and another in its absence keeping all other reduction conditions identical. Interestingly, the reaction with crown ether-encapsulated potassium resulted in 6% higher yield than that of the other one.

The photophysical property of the anion is in good agreement with its reducing behavior. While the parent L4 shows maximum absorbance at 305 nm, the band displays a significant red shift upon deprotonation. The maximum absorption of the anion is at 355 nm, with a tail portion extended to 400 nm. The ground state oxidation potential of the thiolate anion was found to be +0.15 V vs SCE as measured by cyclic voltammetry. The value is much favorable to tolyl thiol in acetonitrile that occurs at a potential of +0.83 V vs SCE.¹⁹ The E_{0.0} energy was estimated from the average of excitation energy and emission energy maxima. The excited state potential calculated from ground state oxidation potential corrected by E_{0,0} was found to be -2.54 V vs SCE. This potential window matches with expected redox potential range for aryl bromide bonds. To gather a concrete proof for the excited-state electron transfer, we attempted to study the fluorescence quenching of 7 by sequential addition of aryl bromide. However, the experiment did not provide definitive clue due to the overlapping emission of **11** anion with that of **7**. It can be further noted that there is a N-H present in 2anilinobenzothiazole, which can be easily deprotonated under the basic condition of the reaction. It is logical to enquire, whether deprotonated 2-anilinobenzothiazole is also capable of performing SET upon photoexcitation. To address this conjecture, we set a cross-coupling reaction starting with 2-anilinobenzothiazole as the photocatalyst. However, only 11% crosscoupled product was isolated from the reaction (Scheme 3c), proving 2-anilinobenzothiazole as not an efficient SET agent. This result is perhaps intuitive, as the anion of 11 is too stabilized by the phenyl ring to abate its reducing ability considerably. Apparently, the 7 and 10 both efficiently conduct the reductive cleavage of aryl bromide. This reinforces the fact that some of the reaction intermediates along with the starting photocatalyst build up sizeable concentration of the aryl radical which is required for the somophilic attack to another substrate molecule. By this way the effect of radical is amplified and it offers a network of initiation pathways in contrary to the unique species capable of promoting reductive cleavage.

4.2.3. Substrate Scope

Table 4.3. Scope of biaryls



Having the optimized condition in hand, we extended the scope of this corss-coupling reaction. A large variety of potential. Consistent with this thought, the fluoro substituent was fully retained and the product **2f** was isolated in 75% yield. Importantly, two heterocyclic bromides, namely 2-methoxy-3-pyridyl bromide and thiophene bromide were proved to be effective cross-coupling partners under this photochemical reaction to afford the products **2g**-**2h** in 71-72% yields.

Table 4.4. Scope of intramolecular cyclization of o-bromo-N,N-dialkylarylamides



After that, we switched our attention to apply this photochemical methodology to fabricate isoindolinone rings from 2-bromo-N,N-dialkylbenzamide substrates. As can be anticipated, the reaction would start by the reductive cleavage of the C-Br bond of **3a**, to engender an aryl radical which will in turn conduct a 1,5-HAT process.¹⁵ Following this reductive cleavage of C-Br bond by DPTU, an isoindolinone 4a was obtained in 65% yield (Table 3). A quick optimization study revealed that tetrahydrofuran is an appropriate solvent for the reaction and the best yield of product is obtained upon 20% loading of L4. When 2-bromo-N-isopropyl-Nmethylbenzamide was chosen as the substrate, the resulting aryl radical was selectively generating the isopropyl radical upon 1,5-HAT. The respective isoindolinone 4b was formed in 63% yield. In these set of reactions, the tertiary radical stability dictates the regioselective hydrogen atom abstraction. Interestingly, a competition between benzyl and isopropyl groups as the hydrogen atom donor showed the formation of tertiary radical generation. Thus, 2bromo-N-isopropyl-N-benzylbenzamide under the photochemical condition led to the formation of isoindolinone 4c in 55% yield. Furthermore, a fluoride substituent in the bromobenzamide retained the fluoride and furnished the product 4d in 72% yield. Notably, a prior methodology accomplished the similar photochemical transformation to isoindolinone formation utilizing *fac*-Ir(ppy)₃ as the photocatalyst.²⁰ It is very encouraging to note that the anion generated from DPTU is a potent reductive photocatalyst that can accomplish the same job.

Upon successfully achieving the isoindolinone formation from bromo-substituted benzamides, we attempted to cleave aryl bromide bonds of *o*-bromo-anilides towards the formation of oxindoline rings. These set of products are

Table 4.5. Scope of intramolecular cyclization of N-(o-bromoaryl)-N-methylalkylamide



considered as privileged motifs since a tetra-substituted carbon centers at the 3-position are frequently found in pharmaceutically important molecules or bioactive natural products.²¹⁻²² When *o*-anilide aryl bromide, **5a** was examined under the DPTU photocatalytic conditions, the product **6a**, 3,3-dimethyl oxindole was isolated in 73% yield (Table 4). Similarly, -OMe substituted *o*-bromo-anilide, **5b** smoothly converted to the desired product **6b** in 70% yield. Analogously, the -Me substituted variant afforded **6c** in 68% yield. Finally, when the starting anilide substrate contained both chloro and bromo groups, aryl bromide bond was cleaved retaining the C-Cl bond so that the product **6d** can be isolated in 72% yield.

4.3. Conclusions

In conclusion, we present diphenylthiourea to be an efficient photocatalyst at its deprotonated form that leads to a plethora of reaction spanning from C-C cross-coupling reaction to isoindolinone formation. This example also is a nice contribution to the pool of anion photochemitsry that often makes the species significantly reducing in nature. The stability of the thiyl radical upon SET is a good driving force, and the fate of the photocatalyst molecule was thoroughly traced to disclose an initiation network in opposed to one unique electron transfer pathway. This knowledge is important to develop sulfur-based photocatalysts and other small organic molecules that will be capable of presenting reductive bond cleavage protocols.

4.4. Experimental Section

4.4.1. General procedure for Synthesis of biaryls taking aryl halide as substrates.

In an oven dried pressure tube aryl bromide (0.5 mmol), KO^tBu (1.5 mmol) and diphenylthiourea, L4 (20 mol%) were added inside a glove box. After that dry benzene (2 mL) was added to the reaction mixture. The reaction mixture was stirred for 24 h under visible light irradiation in an inert atmosphere at room temperature. The reaction flask was placed 7-8 cm away from the LED source. Purification by column chromatography with EtOAc/hexane afforded the corresponding product. The biaryl products were fully characterized by ¹H and ¹³C NMR spectroscopies.

4.4.2. Synthesis of cyclic amide taking amido-halides as substrates

An oven-dried Schlenk flask with a magnetic stirring bar was charged with 2-Bromo-N,Ndialkylbenzamide (0.5 mmol), catalyst L4 (20 mol%) and KO^tBu (1.5 mmol) under N_2 atmosphere. 1 mL of dry and degassed THF was added to above reaction mixture. The reaction mixture was stirred under blue light at room temperature for 24 hours. Solvent was removed under rotary evaporator. The desired product was isolated by column chromatography using hexane/ethyl acetate mixture. The pure product was analyzed by NMR spectroscopy.

4.4.3. Radical quenching experiment

In an oven-dried pressure tube 4-bromoanisole (1 mmol), KO^tBu (3 mmol), L4 (20 mol%), and TEMPO (2 mmol) were added inside a glove box. After that dry benzene (2 mL) was added to the reaction mixture under an argon atmosphere. The reaction mixture was stirred for 24 h under visible light irradiation in an argon atmosphere at room temperature. The reaction was fully quenched and no desired product was isolated from the reaction mixture.

Entry	TEMPO (equiv)	Yield (%)
1.	0.5	5%
2.	2.0	-

4.4.4. Trapping the radical intermediate:

In an oven-dried pressure tube 4-bromoanisole (1 mmol), KO^tBu (3 mmol), L4 (20 mol%) and TEMPO (0.6 mmol) were added inside a glove box. After that dry benzene (2 mL) was added to the reaction mixture under an inert atmosphere. The reaction mixture was stirred for 24 h under visible light irradiation in an inert atmosphere at room temperature. Then the crude reaction mixture was subjected to HRMS. The desired intermediate was characterised by high-resolution ESI-MS. (M+H⁺ = 264.1938).



4.4.5. Reaction of diphenylthiourea with I₂ in the presence of KO^tBu.



In an oven-dried Schlenk flask, L4 (1 mmol), KO^tBu (2.2 mmol), and I₂ (2 mmol) were mixed under an inert atmosphere. After that dry benzene (2 mL) was added to the reaction mixture. The reaction mixture was stirred under visible light irradiation for 24 h under an inert atmosphere at room temperature. After the completion of the reaction, excess I₂ was quenched with saturated sodium thiosulfate solution and the mixture was extracted with EtOAc. Then the resulting solution was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography with EtOAc/hexane afforded **11** (58%). ¹H NMR (400 MHz, CDCl₃) δ 9.34 (s, 1H), 7.63 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.53 – 7.49 (m, 2H), 7.42 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.35 – 7.30 (m, 1H), 7.21 – 7.13 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 165.4, 151.4, 140.1, 129.7, 126.3, 124.6, 122.4, 121.0, 120.7, 119.3. Spectroscopic data matched with the literature.¹²

4.4.6. Catalysis with isolated 11.



To confirm that **11** is an intermediate species in this electron transfer catalysis, 4bromoanisole (0.5 mmol), KO^tBu (1.5 mmol), and **11** (20 mol%) were added to an ovendried pressure tube along with 2 mL of dry benzene. The reaction mixture was stirred at room temperature for 24 h under visible light irradiation. Column chromatographic purification by EtOAc/hexane mixture afforded the corresponding product in 11% yield.

4.4.7. Detection of the potential single electron donor species.



In a 10 mL reaction vial **L4** (1 mmol), KO^tBu (1.1 mmol), and 18-crown-6 (1.1 mmol) were charged under the inert atmosphere of a glove box. 5 mL THF was added to the mixture and stirred for 20 mins. The stir bar was removed and the solution was kept at room temperature. After four days the solution afforded pale yellowish needle-shaped crystals.

4.4.8. Spectroscopic experiments:



Figure 4.2. UV-visible spectra of L4 (10^{-4} M) in MeCN.



Figure 4.3. UV-visible spectra of deprotonated DPTU, $7 (10^{-4} \text{ M})$ in MeCN.



Figure 4.4. Emission spectra of deprotonated DPTU, **7** (10^{-4} M) in MeCN (excitation wavelength = 380 nm).

4.4.9. Cyclic voltammetry experiment for deprotonated DPTU, 7

We attempted to determine the oxidation potential of deprotonated DPTU (7) by cyclic voltammetry. To prepare deprotonated L4, 2.28 mg of N,N'-Diphenylthiourea and 3 mg of KH (30 % w/w in mineral oil) were taken in 1 mL of dry MeCN and stirred for 10 min. Then the solution was filtered through PTFE filter. Then 19 mL MeCN solution of 0.1 M (nBu₄N)PF₆ was added to the filtrate as the supporting electrolyte. To evaluate the ground-state oxidation, a three-electrode set-up was used where glassy carbon was the working electrode, a Pt wire as the counter and Ag/AgCl containing 2 M KCl solution as the reference electrode, respectively. The shown voltammogram (Figure 4.5) was collected with a scan rate of 100 mV sec-1. The peak positions for the anodic and cathodic waves were internally referenced with respect to Fc^+/Fc couple.



Figure 4.5. CV of 1 mM of **7** dissolved in acetonitrile along with 0.1 M solution of tetrabutylammonium hexafluorophosphate salt as an electrolyte.

4.4.10. $E_{0,0}$ calculation for 7.

Excitation wavelength = 380 nm Emission max = 428 nm Average wavelength = 404 nm $E_{0,0} = 1240/404 \text{ eV} = 3.07 \text{ eV}$ $E_{\text{ox}}^* = E_{\text{ox}} - E_{\text{o,o}}$ $E_{\text{ox}}^* = 0.53 - 3.07 = -2.54 \text{ V vs SCE}$

4.4.11. Analytical data

4-methoxy-1,1'-biphenyl (2a):



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 82 mg, 89%).¹H NMR (400 MHz, CDCl₃) δ 7.55 (t, *J* = 8.2 Hz, 4H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 159.2, 141.0, 133.9, 128.9, 128.3, 126.9, 126.8, 114.3, 55.5.

4-methyl-1,1'-biphenyl (2b):



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 71 mg, 85%).¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 2.40 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 141.3, 138.5, 137.2, 129.6, 128.8, 127.1, 127.1, 21.2.

biphenyl (2c):



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 66 mg, 86 %).¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.63 (m, 2H), 7.51 (q, *J* = 7.6 Hz, 2H), 7.42 (d, *J* = 5.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 128.9, 128.9, 127.4, 127.3, 127.3.

[1,1'-biphenyl]-4-carbonitrile (2d) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield:79 mg, 88%).¹H NMR (400 MHz, CDCl₃) δ 7.75 – 7.67 (m, 4H), 7.61 – 7.57 (m, 2H), 7.51 – 7.46 (m, 2H), 7.46 – 7.41 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 145.8, 139.3, 132.7, 128.8, 127.8, 127.3, 119.1, 111.0.

4-(trifluoromethyl)-1,1'-biphenyl (2e) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 87 mg, 78 %).¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 4H), 7.64 – 7.59 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H).¹³C NMR (100 MHz, CDCl₃) δ 144.9, 139.9, 129.1, 128.3, 127.6, 127.4, 125.9, 125.9, 125.8, 125.8.¹⁹F NMR (376 MHz, CDCl₃): δ -62.33.

2-fluoroy-1,1'-biphenyl (2f):



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 65 mg, 75%).¹H NMR (400 MHz, CDCl₃) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 3H), 7.36 (dt, *J* = 24.6, 6.4 Hz, 2H), 7.25 – 7.12 (m, 2H).¹³C NMR (100 MHz, CDCl₃) δ 158.7, 136.0, 130.9, 130.9, 129.3, 129.2, 129.2, 129.1, 129.0, 128.6, 127.8, 124.5, 124.5, 116.3, 116.1.¹⁹F NMR (376 MHz, CDCl₃): δ -115.86.

2-methoxy-3-phenylpyridine (2g):



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 66 mg, 71%).¹H NMR (400 MHz, CDCl₃) δ 8.21 (dd, *J* = 5.0, 2.0 Hz, 1H), 7.65 – 7.58 (m, 3H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 6.99 (dd, *J* = 7.3, 5.0 Hz, 1H), 4.02 (s, 3H).¹³C NMR (100 MHz, CDCl₃) δ 160.9, 145.8, 138.6, 136.8, 129.2, 128.3, 127.6, 124.7, 117.1, 53.6, 53.5.

3-phenylthiophene (2h) :



The compound was purified by column chromatography (silica gel 60–120 mesh) with hexane to give the product as a colourless solid (yield: 58 mg, 72%).¹H NMR (400 MHz, CDCl₃) δ 7.72 – 7.63 (m, 2H), 7.52 – 7.50 (m, 1H), 7.49 – 7.41 (m, 4H), 7.40 – 7.33 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 142.4, 135.9, 128.9, 127.2, 126.6, 126.4, 126.3, 120.4.

2-isopropyl-3,3-dimethylisoindolin-1-one (4a)



The compound was purified by column chromatography (silica gel) with 10 % mixture of ethyl acetate in hexane to give the product as a white solid (68 mg, 65%).¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 3.62 (hept, *J* = 6.8 Hz, 1H), 1.53 (d, *J* = 6.9 Hz, 6H), 1.44 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 151.3, 132.0, 131.3, 127.9, 123.2, 120.7, 63.3, 44.6, 25.5, 20.5.

2,3,3-trimethylisoindolin-1-one (4b)



The compound was purified by column chromatography (silica gel) with 10 % mixture of ethyl acetate in hexane to give the product as a white solid (55 mg, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 6.8 Hz, 1H), 7.39 (t, J = 7.3 Hz, 2H), 3.00 (s, 3H), 1.42 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 151.6, 131.5, 130.9, 128.0, 123.6, 120.7, 62.1, 25.0, 23.9.

2-benzyl-3,3-dimethylisoindolin-1-one (4c)



The compound was purified by column chromatography (silica gel) with 10 % mixture of ethyl acetate in hexane to give the product as a white solid (67 mg, 55%). ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.44 (t, *J* = 6.9 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 3H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.22 (d, *J* = 7.2 Hz, 1H), 4.75 (s, 2H), 1.35 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 167.9, 152.0, 138.7, 131.8, 130.4, 128.5, 128.0, 127.8, 127.2, 123.8, 120.7, 63.2, 42.6, 26.3.

5-fluoro-2-isopropyl-3,3-dimethylisoindolin-1-one (4d)



The compound was purified by column chromatography (silica gel) with 10 % mixture of ethyl acetate in hexane to give the product as a white solid (79 mg, 72%). ¹H NMR (400 MHz, CDCl₃) δ 7.74 (dd, *J* = 8.3, 5.1 Hz, 1H), 7.12 – 7.06 (m, 1H), 7.01 (dd, *J* = 8.2, 2.2 Hz, 1H), 3.62 (hept, *J* = 6.8 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 6H), 1.47 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 163.8 (¹J_{C-F}= 251 Hz), 153.7 (³J_{C-F}= 9 Hz), 128.1 (⁴J_{C-F}= 2 Hz), 125.4 (³J_{C-F}= 9 Hz), 115.5 (²J_{C-F}= 24 Hz), 108.3 (²J_{C-F}= 23 Hz), 63.1, 44.8, 25.5, 20.6. ¹⁹F NMR (376 MHz, CDCl₃): δ -108.0

1,3,3-trimethylindolin-2-one (6a)



The compound was purified by column chromatography (silica gel) with 5 % mixture of ethyl acetate in hexane to give the product as a colorless oil (63 mg, 73%).¹H NMR (400 MHz, CDCl₃) δ 7.29 – 7.23 (m, 1H), 7.20 (d, *J* = 6.1 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 3.22 (s, 3H), 1.37 (s, 6H).¹³C NMR (101 MHz, CDCl₃) δ 181.5, 142.8, 136.0, 127.8, 122.6, 122.4, 108.1, 44.3, 26.3, 24.5.

5-methoxy-1,3,3-trimethylindolin-2-one (6b)



The compound was purified by column chromatography (silica gel) with 10 % mixture of ethyl acetate in hexane to give the product as a colorless oil (72 mg, 70%).¹H NMR (400 MHz, CDCl₃) δ 6.81 (d, *J* = 2.3 Hz, 1H), 6.77 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 3.79 (s, 3H), 3.17 (s, 3H), 1.34 (s, 6H).¹³C NMR (101 MHz, CDCl₃) δ 181.1, 156.1, 137.3, 136.2, 111.6, 110.1, 108.3, 55.9, 44.7, 26.4, 24.5.

1,3,3,5-tetramethylindolin-2-one (6c)



The compound was purified by column chromatography (silica gel) with 5 % mixture of ethyl acetate in hexane to give the product as a yellow oil (63 mg, 68%).¹H NMR (400 MHz, CDCl₃) δ 7.06 (d, *J* = 7.8 Hz, 1H), 7.03 (s, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 3.19 (s, 3H), 2.35 (s, 3H), 1.36 (s, 6H).¹³C NMR (101 MHz, CDCl₃) δ 181.5, 140.4, 136.0, 132.1, 128.0, 123.3, 107.8, 44.3, 26.4, 24.5.

5-chloro-1,3,3-trimethylindolin-2-one (6d)



The compound was purified by column chromatography (silica gel) with 5 % mixture of ethyl acetate in hexane to give the product as a yellow solid (75 mg, 72%).¹H NMR (400 MHz, CDCl₃) δ 7.22 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 3.19 (s, 3H), 1.35 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 180.9, 141.3, 137.6, 128.0, 127.7, 123.0, 109.0, 44.6, 26.4, 24.4.

4.5. References

1. Melchiorre, P., Introduction: Photochemical Catalytic Processes. Chem. Rev. 2022, 122, 1483-1484.

2. Romero, N. A.; Nicewicz, D. A., Organic Photoredox Catalysis. *Chem. Rev.* 2016, *116*, 10075-10166.

3. Schmalzbauer, M.; Marcon, M.; König, B., Excited State Anions in Organic Transformations. *Angew. Chem. Int. Ed.* **2021**, *60*, 6270-6292.

4. Fox, M. A., The photoexcited states of organic anions. *Chem. Rev.* **1979**, *79*, 253-273.

5. Wang, S.; Wang, H.; König, B., Light-Induced Single-Electron Transfer Processes involving Sulfur Anions as Catalysts. *J. Am. Chem. Soc.* **2021**, *143*, 15530-15537.

6. Saetan, T.; Sukwattanasinitt, M.; Wacharasindhu, S., A Mild Photocatalytic Synthesis of Guanidine from Thiourea under Visible Light. *Org. Lett.* **2020**, *22*, 7864-7869.

7. Tyson, E. L.; Niemeyer, Z. L.; Yoon, T. P., Redox Mediators in Visible Light Photocatalysis: Photocatalytic Radical Thiol–Ene Additions. *J. Org. Chem.* **2014**, *79*, 1427-1436.

8. Zhao, G.; Kaur, S.; Wang, T., Visible-Light-Mediated Thiol–Ene Reactions through Organic Photoredox Catalysis. *Org. Lett.* **2017**, *19*, 3291-3294.

9. Santandrea, J.; Kairouz, V.; Collins, S. K., Continuous Flow Science in an Undergraduate Teaching Laboratory: Photocatalytic Thiol–Ene Reaction Using Visible Light. *J. Chem. Edu.* **2018**, *95*, 1073-1077.

10. Oderinde, M. S.; Frenette, M.; Robbins, D. W.; Aquila, B.; Johannes, J. W., Photoredox Mediated Nickel Catalyzed Cross-Coupling of Thiols With Aryl and Heteroaryl Iodides via Thiyl Radicals. *J. Am. Chem. Soc.* **2016**, *138*, 1760-1763.

11. Li, H.; Liu, Y.; Chiba, S., Leveraging of Sulfur Anions in Photoinduced Molecular Transformations. *JACS Au* **2021**, *1*, 2121-2129.

12. Li, H.; Chiba, S., Synthesis of α -tertiary amines by polysulfide anions photocatalysis via single-electron transfer and hydrogen atom transfer in relays. *Chem Catal.* **2022**, *2*, 1128-1142.

13. de Pedro Beato, E.; Spinnato, D.; Zhou, W.; Melchiorre, P., A General Organocatalytic System for Electron Donor–Acceptor Complex Photoactivation and Its Use in Radical Processes. *J. Am. Chem. Soc.* **2021**, *143*, 12304-12314.

14. Cuadros, S.; Horwitz, M. A.; Schweitzer-Chaput, B.; Melchiorre, P., A visible-light mediated three-component radical process using dithiocarbamate anion catalysis. *Chem. Sci.* **2019**, *10*, 5484-5488.

15. Singh, V.; Singh, R.; Hazari, A. S.; Adhikari, D., Unexplored Facet of Pincer Ligands: Super-Reductant Behavior Applied to Transition-Metal-Free Catalysis. *JACS Au* **2023**, *3*, 1213-1220.

 Kundu, A.; Dey, D.; Pal, S.; Adhikari, D., Pyrazole-Mediated C–H Functionalization of Arene and Heteroarenes for Aryl–(Hetero)aryl Cross-Coupling Reactions. *J. Org. Chem.* 2021, *86*, 15665-15673.

17. Dey, D.; Kundu, A.; Mandal, B.; Roy, M.; Adhikari, D., Deciphering the single electron transfer ability of fluorene under photoredox conditions. *Catal. Sci. Technol.* **2022**, *12*, 7322-7327.

18. Rattanangkool, E.; Sukwattanasinitt, M.; Wacharasindhu, S., Organocatalytic Visible Light Enabled SNAr of Heterocyclic Thiols: A Metal-Free Approach to 2-Aminobenzoxazoles and 4-Aminoquinazolines. *J. Org. Chem.* **2017**, *82*, 13256-13262.

19. Bordwell, F. G.; Zhang, X.-M.; Satish, A. V.; Cheng, J. P., Assessment of the Importance of Changes in Ground-State Energies on the Bond Dissociation Enthalpies of the O-H Bonds in Phenols and the S-H Bonds in Thiophenols. *J. Am. Chem. Soc.* **1994**, *116*, 6605-6610.

20. Dai, P.; Ma, J.; Huang, W.; Chen, W.; Wu, N.; Wu, S.; Li, Y.; Cheng, X.; Tan, R., Photoredox C–F Quaternary Annulation Catalyzed by a Strongly Reducing Iridium Species. *ACS Catal.* **2018**, *8*, 802-806.

21. Zhou, F.; Liu, Y.-L.; Zhou, J., Catalytic Asymmetric Synthesis of Oxindoles Bearing a Tetrasubstituted Stereocenter at the C-3 Position. *Adv. Synth. Catal.* **2010**, *352*, 1381-1407.

22. Marti, C.; Carreira, Erick M., Construction of Spiro[pyrrolidine-3,3'-oxindoles] – Recent Applications to the Synthesis of Oxindole Alkaloids. *Eur. J. Org. Chem.* **2003**, *2003*, 2209-2219.

Chapter 5

Mechanistic elucidation of a radical-promoted hydrogenation relevant to borrowing hydrogen catalysis

For the purpose of this thesis, the work of chapter 5 is adapted with permission from (Bains. A.; Kundu, A.; Adhikari. D.*, *ChemCatChem.*, **2023**, *15*, e202300586. Title: Mechanistic elucidation of a radical-promoted hydrogenation relevant to borrowing hydrogen catalysis.)

5.1. Introduction

The hydrogenation of a double bond, either polar carbonyl or imine, or relatively nonpolar olefin by homogeneous catalysis is a very important reaction in organic synthesis.^[1] Multiple hydrogenation methodologies have been developed over the course of last few decades, among which hydrogen-transfer reactions have attracted tremendous focus.^[2] These methods became more popular owing to their simplicity, and favorable properties of the reductant alcohols replacing the high pressure of hydrogen gas required for this purpose. The hydrogen transfer by most of the transition metal catalysts follows a hydridic route, by the intermediacy of metal-hydride. In the recent developments of olefin hydrogenation, several Earth-abundant metal catalysts are becoming prominent that follow radical mechanism, primarily by the homolytic cleavage of the M-H bond. This is in strong contrast to polar carbonyl hydrogenation via Noyori mechanism which relied on non-radical, metal-ligand (M-L) bifunctional operation.^[3] Both thermal and photochemical activation of the metal-hydride bond to promote its homolytic cleavage has been established recently. Chirik^[4], Schneider^[5], and Peters^[6] group have showcased cobalt catalysts that hydrogenate an olefin via hydrogen atom transfer (HAT) or proton-coupled electron transfer (PCET). Chirik has recently shown that a relatively weak cobalt hydride bond in a trigonal bipyramidal environment, can hydrogenate styrene under thermal conditions, while the activity is significantly enhanced under blue light activation.^[4] Peters group demonstrated that under electrocatalytic reduction condition, an olefin can be reduced following concerted proton-electron transfer, where a cobaltocenium redox mediator transferred the H-atom equivalent.^[6] Schneider has also shown that a light-activated, in situ-generated, three-coordinate Co(I) center binds H₂ to give a dihydrogen complex, that enables stepwise hydrogenation of a variety of olefins following HAT.^[5]

Along metal-hydride based hydrogenation, homolytic cleavage of the former to generate a hydrogen atom and olefination by the H-atom is known as MHAT mechanism.^[7] In this direction, Poli and Holland showed that an iron hydride can steer alkene cross-coupling reactions where an extremely weak M–H bond causes the alkene to undergo irreversible HAT.^[8]



Figure 5.1. Metal hydride (via MHAT) and CPET promoted hydrogenation of an olefin.

There is a burgeoning interest in developing base-metal catalysts instead of much toxic, less abundant, and more expensive precious metals for important chemical transformations.^[9] Such Earth-abundant metals are also playing a crucial role in borrowing hydrogen (BH) catalysis^[10] employing alcohols as an inexpensive and benign source of alkyl building blocks.^[11] The crucial hydrogenation step required in a BH reaction, either by precious metals or Earth-abundant metals invokes the intermediacy of a metal hydride. In stark contrast, a hydrogenation via radical pathway, adopting one-electron HAT without the involvement of metal hydride is very much rare in BH catalysis.^[12] Our current interest is focused to base metal-catalysis where ligand-based redox plays a preeminent role^[13] Along the mechanistic probation of an α -alkylation reaction,^[14] we present in this report a complementary radical mechanism of hydrogenation to an olefinic bond, which completely bypasses the traditional metal-hydride pathway (Figure 5.1). Interestingly, such radical-based hydrogenation is chemoselective and reduces only the double bond of an enone substrate sparing the carbonyl functionality.



Nickel-catalysed α -alkylation of ketones by secondary alcohols

● Ligand-redox assisted hydrogenation ● Radical-driven discrete 1e⁻ chemistry

Figure 5.2. Ligand-dominated hydrogenation of olefin in an enone, en route to β , β '-disubstituted ketone formation.

5.2. Results and Discussion

To endeavor C-alkylation of a ketone by utilizing secondary alcohol as the source of alkyl group, we recently forged β , β -disubstituted ketone products utilizing nickel catalyst **1**. ^[14] The starting ketone in this reaction is *ortho*-di- substituted phenyl acetophenone, and the steric protection of the aryl ketone is very much required to stop detrimental condensation and Cannizaro-type reactions. ^[15]

The major design principle behind our catalyst **1** is the redox-responsive azo arm in the azophenolate ligand, which is easy to reduce given its low-lying π^* orbital.^[16] Indeed, sequential 2e⁻/2H⁺ reduction of the azo leads to the hydrazo form of the catalyst (1^{H,H}) and such conversion facilitates easy dehydrogenation of an alcohol.^[17] We anticipate at this point that the monoreduced azo, and its capability to store hydrogen may provide an entry point to radical-promoted olefinic hydrogenation reactions. Notably, some other base metal catalysts comprising of cobalt^[18], manganese^[19] and iron^[20] are also known for such C-alkylation with secondary alcohol, which drive the hydrogenation component of the reaction by the respective metal hydrides, following conventional M-L cooperativity or redox-neutral pathway.

In the present work we unravel the mechanism of the C-alkylation reaction, specifically focusing on the olefin hydrogenation step. At the beginning of the reaction, a secondary alcohol is dehydrogenated by **1** (Figure 5.2), whose mechanism is close to the radical-promoted dehydrogenation delineated previously.^[21]

At the end of such dehydrogenation reaction the catalyst remains in the form of $\mathbf{1}^{\mathbf{H},\mathbf{H}}$ that will be used to hydrogenate an *in situ*-generated enone. We previously disclosed that both 1phenyl ethanol and cyclohexanol were appropriate secondary alcohol substrates that afforded β , β -dialkylated products in 69% and 82% yields.^[14] To mechanistically interrogate the hydrogenation of enone further, we chose cyclohexanol as the model substrate. Sometimes cyclohexanol can be dehydrogenated in the presence of a simple base if there is a hydrogen acceptor present, so that an Meerwein–Ponndorf–Verley (MPV) pathway^[22] may follow to give the desired product. To examine whether MPV mechanism may afford the product in the present case, we performed a control reaction in the presence of hydrogen acceptor benzophenone. No dehydrogenation or the subsequent α -alkylation took place in the absence of catalyst **1**. Further control reaction proves that reaction does not proceed in the presence of only base in absence of a catalyst (Figure 5.3a).

To prove that the reaction utilizes hydrogen stripped from the secondary alcohol, we chose deuterium substituted 1-phenyl ethanol. The reaction under identical reaction conditions disclosed altogether 87% *d*-incorporation at α - and β -position of the carbonyl group in the product (Figure 5.3b). Notably, in the β , β -dialkylated product, *d*-incorporation at the β -position of the enone (80%) is lot higher than the α -position (7%). Such a predominant *d*-incorporation at the β -position indicates a stable radical generation at the benzylic position that facilitated further HAT. This in turn strongly supports the mode of olefin reduction that is facilitated by



Figure 5.3. a) Catalyst-free control reaction in the presence of a sacrificial source of hydride,b) Deuterium labelling experiment.

monoreduced azo group (vide infra). To authenticate that hydrogen from the alcohol is stored in the hydrazo-form of the catalyst, we performed the reaction under inert condition, and isolated $\mathbf{1}^{\mathbf{H},\mathbf{H}}$ in 65% yield (Figure 5.4a). The molecule $\mathbf{1}^{\mathbf{H},\mathbf{H}}$ is a critical intermediate en route to the olefinic hydrogenation and this intermediate has been well characterized by NMR, IR spectroscopies as well as high-resolution ESI-mass spectrometry.^[13b]



Figure 5.4. a) Hydrogenation of azo to the hydrazo form $(1^{H,H})$, b) Hydrogenation of the intermediate enone.

We shall show in the following discussion that this intermediate stage is the entry point for olefin hydrogenation of an enone, and that is completely driven by a radical mechanism. Meanwhile, the resulting ketone from the secondary alcohol dehydrogenation undergoes an aldol condensation reaction with substrate *ortho*-di-substituted phenyl acetophenone to form an enone in the presence of a strong base such as KO^tBu. Logically, a selective hydrogenation of the olefinic part in an enone is required to result the final α -alkylated product of the ketone.

This raises an important question; how this stored hydrogen in the ligand motif is delivered back to the in situ-generated enone. In stark difference to all postulated mechanisms relying on metal-ligand cooperativity,^[3c, 23] we propose that our catalyst system hydrogenates the enone via radical pathway. To substantiate this claim, we studied the hydrogenation of the enone separately, where intermediate $1^{H,H}$ in the presence of KO^tBu was used as the source of hydrogen. The role of KO^tBu in this reaction is dual in nature; beyond being a good base, it also behaves as a mild reductant to reduce the intact azo motif in 1^{H,H}.^[21] This olefin hydrogenation on a pre-synthesized chalcone happens smoothly (Figure 5.4b) to result the final alkylated product in 58% yield. As alluded, the same reaction is completely arrested when 1 equiv of TEMPO was added to the reaction mixture. Dissecting the α -alkylation reaction in two major parts; alcohol dehydrogenation and olefinic hydrogenation of the enone and explicitly arresting the second part by a radical quencher strongly indicates that the hydrogenation of the olefin is also promoted by radical reaction. In the nickel catalyst, the enone binds through the olefin end, while the detachment of one of the phenolate arm creates the required unsaturation in the pseudo square-planar geometry of nickel. Notably, a proton from the hydrazo motif can scramble with phenolate arm that remains as a detached phenol arm. Upon binding to nickel, the bound olefin is reduced by the mono-reduced azo, while the resulting carbon-centric radical is stabilized by nickel coordination. Indeed, a good covalency developed between nickel and the enone can have the radical in a delocalized form, where the nickel is partially reduced. Computationally, we observed a significant amount of nickel-based spin in the intermediate where enone remains in the bound form to the catalyst molecule (Figure 5.5a). This is akin to many organic radicals that are well stabilized when coordinated to a redox-responsive metal center.^[24] The enone binding is also reminiscent of substratedriven redox activity that steers catalysis.^[24] In the present case the enone substrate is not redox active until it binds to the nickel center (Figure 5.5b). Since the binding is followed by electron transfer from mono-reduced azo functionality, the bound enone elicits its redox activity and governs the one-electron mediated subsequent steps.


Figure 5.5. (a) Computationally-derived spin density picture of intermediate II (iso surface = 0.004), where (*E*)-1,3-diphenylbut-2-en-1-one has been used as the model enone substrate. (b) Schematic for synergistic redox activity at the ligand and substrate bound to the metal. 'S' designates the substrate.

To substantiate our claim for the intermediacy of the radical in this process, we chose a radical-clock substrate and conducted the hydrogenation with our catalyst. Accordingly, when radical-clock substrate 3 (Figure 5.6a, iii) undergoes hydrogenation with $1^{H,H}$, the reduction leads to an olefinic radical, 4a (stabilized by the nickel center in actual catalytic cycle). Having a cyclopropyl ring connected to the radical, ring opening would follow, leaving the signature of radical generated. Furthermore, in the presence of a radical inhibitor TEMPO, this radical can be arrested in the form of an adduct, affording 4b. Encouragingly, scrutiny of the reaction mixture by high-resolution ESI mass spectrometry disclosed a M+H peak at 372.2892 amu that proves the intermediacy of 4a in the reaction (Figure 5.6a). Quite expectedly, when the reaction was performed on the radical-probe substrate 3 in presence of catalyst 1 and a hydrogen donor substrate 1-phenyl ethanol, under identical reaction conditions, cyclopropyl ring-opened products (Figure 5.6b) were isolated in major amount (80%). In contrary, the ring was retained in only 10% of the α -alkylated product (Figure 5.7). In the product distribution, predominant formation of ring-opened product indicates the hydrogen atom transfer step is slower than the cyclopropyl ring rearrangement. The cyclopropyl ring-opening from the radical-clock substrate, and the interception of the putative radical intermediate provide compelling evidence for the intermediacy of the radical during the hydrogenation.



Figure 5.6. a) Interception of radical intermediates, b) Ring opening of radical-probe substrate.

As we will discuss below, this carbon-based radical undergoes a HAT step from the hydrazo arm of the catalyst to form a C–H bond in the intermediate structure (Figure 5.7). In the catalytic cycle, this carbon-centric radical intermediate is **II** (Figure 5.8). To shed further light on the electronic structures of the important intermediates as well as to better understand the HAT step, we resorted on a high-level DFT computational study. We have been able to optimize the geometry of intermediate **II** (M06-2X functional^[26]), and found that this intermediate only costs 3.2 kcal mol⁻¹ with respect to the reference state comprising of all components of reaction infinitely apart. In this intermediate, nickel has an active role to stabilize the extra electron that is donated from the reduced azo backbone. In this intermediate structure nickel also changes it geometry to a distorted tetrahedral one (Figure 5.7). A significant precedence for metal stabilization to the organic radical is found in natural enzymes, conferring stability to otherwise high-energy intermediates.^[25] In the



Figure 5.7. Potential energy surface for olefin hydrogenation path with computationally optimized geometries of **II** (the olefin-bound intermediate to nickel), optimized TS_{II-III} for HAT (upon which a C–H bond is formed from N–H), **III** (Ni-alkyl intermediate after hydrogenation of the olefinic bond via HAT)

present case, enone is bound to the nickel center in an η^1 fashion (Ni...C_a = 2.90 Å, while Ni...C_{β} = 3.53 Å), where significant π -backdonation likely stabilizes the intermediate. Additionally, as a conclusive proof for such a radical's involvement in the reaction, TEMPOadduct of the putative carbon-based radical (cyclohexanol as the substrate) was analyzed by ESI-mass spectrometry and a signature peak was found at 400.3205 amu (M+H) (Figure 5.6a). Additionally, when 1-phenyl ethanol was used as the secondary alcohol substrate, the corresponding enone-reduced radical was arrested via its TEMPO-adduct, detected at 450.3361 amu. In this adduct, the source of proton could be a substrate alcohol, or even the in situ-generated water from the condensation step. A clear HAT happens in the intermediate II where a hydrogen atom migrates from the N-H bond to the carbon-centric radical, that forms by electron reorganization. The radical generation at the benzylic position is much preferable over its generation at the α -position to the carbonyl center. This is strongly supported by the dlabelling experiment performed earlier (vide supra). Computationally, the respective transition state (TS) for HAT was optimized which exhibited the salient C...H and N...H distances to be 1.32 and 1.37 Å, respectively (Figure 5.7). Apparently, this is a symmetric TS where hydrogen atom has been migrated half-way from the locus nitrogen atom to the terminus carbon atom.

The migration of the hydrogen atom is also very clear from the vibrational analysis, depicting the movement at an imaginary frequency of 1301 cm⁻¹. An alternative view of looking at the step as a proton transfer followed by electron transfer was considered. However, the driving force for proton transfer from the N-H is not clear, and this electronic rearrangement to generate a carbon-centric radical makes the HAT more feasible over proton transfer. Notably, our reduction reaction fails for unactivated olefin such as styrene. That also indicates the proposed reduction of the olefin is probable when such substrate possesses a low-lying π^* orbital. This reduction is also important to facilitate the subsequent HAT step. The calculated barrier (ΔG_{sol}^{\dagger}) for the TS computed at 6-311G*/M06-2X) level^[26] is 23.1 kcal mol⁻¹ from the reference state. Upon HAT, the intermediate III forms which is also a stable intermediate in the potential energy surface. The Ni...C_{α} bond length in the optimized structure of **III** is found to be 2.22 Å, and much akin to **II**, the azo radical is stabilized *via* nickel coordination (Figure 5.7c). We note that both in intermediate II and TS_{II-III} one of the phenol rings enjoys π - π stacking interaction with a phenyl ring of the chosen enone substrate. In the computationally optimized intermediate II, the distance between the centroids of the putative rings is only 3.4 Å. Such a noncovalent interaction contributes some stability to the intermediate and the respective TS, and supports this mode of olefin binding to nickel. The α -alkylated product liberation step requires a protonation of the nickel-bound alkyl end. This protonation is facile by phenol arm which shuttles the proton from the hydrazo group. As a viable alternative, the nickel-alkyl bond homolysis may also happen and the resulting alkyl radical may abstract Hatom from the phenol. Given the data in hand, we prefer the protonation pathway since solvent assisted proton shuttling is very common. Upon protonation, the α -alkylation product is ejected out, while the phenolate arm of the ligand is restored which re-coordinates the nickel center. As an alternative, the incoming substrate alcohol or even ^tBuOH may protonate the nickel-bound alkyl group to release product and the generated alkoxide may coordinate the metal center. As a completely different choice to the radical mechanism, we considered the intermediacy of nickel-hydride that would promote two-electron mechanism. The formation of nickel hydride intermediate supposedly from β -hydride elimination from the intermediate $\mathbf{1}^{H,H}$ was interrogated computationally. This probation led to a very high-energy, three-coordinate nickel hydride along with the detachment of the azo-phenolate arm. Such a high energy intermediate and unusual geometry dismisses the intermediacy of nickel hydride in the present system.



Figure 5.8. Plausible mechanistic cycle for radical-promoted olefin hydrogenation.

This radical promoted hydrogenation is reminiscent of a recent imine hydrogenation by a polarity-matched HAT.^[27] As proposed in that report, the imine is reduced under photoinitiated condition, whether $Ru(bpy)_3^{2+}$ reduces the imine by single electron transfer and the alkyl radical abstracts a hydrogen atom from thiol. It is also noteworthy that the observed chemoselectivity associated with the process reduces the olefin keeping the carbonyl intact. Usually, given a polar carbonyl and non-polar olefin present together, hydride-based mechanism reduces both functionalities.^[28] It is interesting that switch to ligand-assisted base metal catalyst^[29] not only changes the mechanistic paradigm, but also offers the complementary chemoselectivity that is different from canonical hydrogenations. We attribute this chemoselectivity to the preferential binding of olefin onto nickel over carbonyl binding and the subsequent reduction of the bound functionality. Logically, a ketone binding to nickel and its one-electron reduction to ketyl radical is a high energy process that deters the carbonyl reduction. During the hydrogenation of enone, the chemoselective reduction to the olefinic motif sparing the carbonyl is very consistent with our α -alkylation reaction by primary alcohol, where the final product is always a ketone.^[30] Recently, a rich chemistry has spawned from transition metal hydrides, where the hydrides are behaving as a hydrogen atom donor toward hydrogenation of alkenes.^[31] Indeed, back in 1977 Halpern performed seminal chemically induced dynamic nuclear polarization (CIDNP) experiments to claim that atom subsequent manganese hydride followed hydrogen transfer to promote hydrogenation.^[12] Notably, elegant studies of other metal hydride mediated HAT, popularly

known as MHAT have indicated concerted proton electron transfer (CPET)^[32] from M–H intermediates to a C–C π -bond of olefin. Encouragingly, such processes can also be rendered catalytic in the presence of stoichiometric silane that helps in the regeneration of the active catalyst.^[7a] As a demonstration to the applicability of such reduction, Vanderwal has showed a highly efficient HAT-initiated polyene cyclization for the stereo-controlled construction of terpenoid scaffolds.^[33] Our mechanistic profile contrasts all these features, by completely avoiding the metal hydride, where both the proton and electron equivalent remain stored in the azo-ligand backbone. A successful C-alkylation reaction with a broad substrate scope further promises that the radical-promoted pathway can be complementary and equally effective as compared to metal-ligand cooperativity-driven hydrogenation reactions.

5.3. Conclusions

Through a detailed mechanistic interrogation, we show a hydrogenation protocol of enone that relies on a radical-promoted pathway, assisted by ligand-redox. The observed method is significantly different from recent radical-based hydrogenation reactions invoking a metal hydride, both under thermal or photochemical means. While majority of the polar bond hydrogenations adopt Noyori-type classical hydride-based pathways, this radical-promoted reaction likely offers an orthogonal avenue. This study demonstrates that a complete switching in the mechanistic paradigm may offer heavily ligand-assisted base metal catalysis as a complementary approach to their precious metal analogues.

5.4. Experimental section

5.4.1. General Considerations

All the starting compounds employed in this study were procured from commercial suppliers and were used without further purification. Potassium tert-butoxide, potassium hydroxide, and o-phenylene diamine were purchased from Sigma Aldrich. Glassware was dried overnight at 160 °C. Solvents such as methanol, ethanol, and toluene were used as received from the suppliers. For thin-layer chromatography (TLC), 60 F254 precoated silica gel (Merck) was used. Column chromatography was performed using SD Fine silica gel 60–120 mesh using a gradient of ethyl acetate and hexane as the mobile phase. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. IR spectra were recorded on a PerkinElmer FT IR spectrometer as KBr pellets, as indicated, with v_{max} in inverse cm. 1 H NMR and 13C NMR spectra were recorded on a 400 MHz Bruker Biospin Advance III FT- NMR spectrometer. NMR shifts were reported as delta (δ) units in parts per million (ppm) and coupling constants (J) in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Chemical shifts (δ) are quoted to the nearest 0.01 ppm relative to CDCl₃ (δ 7.26 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in CDCl₃ (δ 77.1 ppm).

5.4.2. Synthesis of 1

The azo-phenolate ligand (L) was synthesized following our reported procedure.^[21] A dark brown-colored crystalline solid in 79% yield. The desired product was fully characterized by ¹H and ¹³C NMR spectroscopy. ¹H NMR (400 MHz, CDCl₃): δ 8.45–8.44 (m, 2H), 7.35–7.25 (m, 5H), 1.29 (s, 9H), 1.01 (s, 9H). ¹³C{H} NMR (100 MHz, CDCl₃): δ 148.8, 144.3, 139.5, 130.8, 128.6, 125.7, 124.8, 124.8, 122.4, 122.1, 35.7, 34.3, 31.6, 29.5 ppm.

5.4.3. Preparation of Ni(H₂L)L, 1^{H,H}

In a 25 mL Schlenk flask, 1 mmol **1** was suspended in THF solution of 1 mmol benzyl alcohol and 1 mmol KO^tBu and connected to a condenser under nitrogen flow. The solution was heated to reflux for 4 h. The color of the solution became maroon quickly. After that the reaction was exposed to air and the mixture was dried in vacuo. The obtained crude reaction mixture was washed with dry hexane (5 mL × 3 times). The crystalline red color precipitate was dried, and collected in 461 mg amount, 68% yield. The desired product was fully characterized by ¹H and ¹³C{¹H} NMR spectroscopy.^[21] ¹H NMR (400 MHz, C₆D₆): δ 8.33–8.31 (d, *J* = 8.0 Hz, 2H), 7.75–7.66 (m, 3H), 7.10–7.08 (d, *J* = 8.0 Hz, 3H), 6.91–6.83 (m, 6H), 4.14 (s, br, 2H), 1.29 (s, 18H), 1.02 (s, 18H). ¹³C{H} NMR (100 MHz, C₆D₆): δ 155.1 (Ar), 151.1(Ar), 150.9(Ar), 148.0(Ar), 143.9(Ar), 141.7(Ar), 139.6(Ar), 138.3(Ar), 137.7(Ar), 130.7(Ar), 130.6(Ar), 129.4(Ar), 128.5(Ar), 127.8(Ar), 125.9(Ar), 124.8(Ar), 122.3(Ar), 35.7(CMe₃), 35.6(CMe₃), 34.4(CMe₃), 34.0(CMe₃), 31.5(*Me*), 31.3(*Me*), 29.8(*Me*), 29.6(*Me*) ppm. HRMS (ESI) m/z: [M + H]⁺ Calcd for C₄₀H₅₂N₄NiO₂, 679.3522; found 679.3467

5.4.5. Synthesis of 1-Mesitylethan-1-one (2a) and, 1-(2,3,4,5,6-Pentamethylphenyl) ethan-1-one (2b)

Aryl ketone were prepared according to the following literature.^[19] To a solution of mesitylene (600.9 mg, 5 mmol) or pentamethylbenzene (741.2 mg, 5 mmol) in DCM (100 mL), acetyl chloride (0.475 mL, 6 mmol) was added and cooled to 0 °C. Later, AlCl₃ (723.8 mg, 5.42 mmol) was added portion wise over the course of 10 minutes. The resulting mixture

was then warmed up to room temperature. The mixture was stirred for 4 h. After completion of the reaction (checked via TLC), crushed ice was added into the reaction mixture. The final crude product was extracted with dichloromethane (50 mL \times 3 times) and dried over sodium sulphate. The pure products **2a**, **2b** were obtained through flash column chromatographic (hexane/ethyl acetate, 10:0.5) separation. Yield of the products; **2a** (867 mg, 85%), **2b** (855 mg, 90%).

5.4.6. Synthesis of radical-probe substrate (3-Cyclopropyl-1-mesitylprop-2-en-1-one, 3)

To a solution of NaOH (1 mmol) in H₂O (3 mL), ethanolic solution of 1-mesitylethan-1-one (**2a**) was added at 0 °C. To it, cyclopropane carboxaldehyde (1 mmol) was introduced dropwise. The mixture was then allowed to warm to room temperature and stirred for 2 h. The reaction mixture concentrated *in vacuo*. The residue was purified by column chromatography using hexane/ethyl acetate (100:1) as an eluent to afford pure product. The desired product 3cyclopropyl-1-mesitylprop-2-en-1-one (**3**) is fully characterized by ¹H, ¹³C NMR spectroscopies. Yellow oil (166 mg, 78%); Eluent combination: hexane/diethyl ether (100:1). ¹H NMR (400 MHz, CDCl₃) δ 6.81 (d, *J* = 0.5 Hz, 2H), 6.38 (d, *J* = 15.6 Hz, 1H), 5.98 – 5.92 (m, 1H), 2.27 (s, 3H), 2.13 (s, 6H), 1.66 – 1.56 (m, 1H), 1.01 – 0.94 (m, 2H), 0.60 – 0.55 (m, 2H); ¹³C{H} NMR (101 MHz, CDCl₃) δ 200.7, 157.6, 138.0, 137.3, 133.9, 129.6, 128.2, 21.1, 19.3, 15.1, 9.4 ppm; IR (KBr pellet): 2900, 2871, 1710, 1563, 1345, 1230, 1096, 1023, 814, 704 cm⁻¹; HRMS (ESI) m/z: [M + H]⁺ Calcd for: C₁₅H₁₈O 215.1435; Found 215.1428

Cyclopentyl(mesityl)methanone (5): Yellow oil (85 mg, 80%), eluent combination: hexane/diethyl ether (100:1). ¹H NMR (400 MHz, CDCl₃) δ 6.83 (s, 2H), 3.27 – 3.19 (m, 1H), 2.27 (s, 3H), 2.21 (s, 6H), 1.91 – 1.84 (m, 4H), 1.78 – 1.74 (m, 2H), 1.63 – 1.58 (m, 2H); ¹³C{H} NMR (101 MHz, CDCl₃) δ 214.2, 140.2, 138.3, 133.0, 128.7, 53.4, 29.9, 26.1, 21.1, 19.7 ppm. The NMR spectroscopic data agrees with the literature report.^[34]

3-Cyclopropyl-1-mesitylpropan-1-one (6): Yellow oil (10 mg, 10%), eluent combination: hexane/ethyl acetate (100:5). ¹H NMR (400 MHz, CDCl₃) δ 6.84 (s, 2H), 2.83 – 2.79 (m, 2H), 2.28 (s, 3H), 2.20 (s, 6H), 1.64 – 1.59 (m, 2H), 1.41 – 1.32 (m, 1H), 0.83 – 0.73 (m, 1H), 0.48 – 0.41 (m, 2H), 0.09 (m, 2H); ¹³C{H} NMR (101 MHz, CDCl₃) δ 213.8, 139.3, 138.3, 133.4, 128.6, 52.4, 28.3, 26.0, 21.1, 19.7 ppm; IR (KBr pellet): 3101, 2767, 2192, 1710,

1503, 1302, 1198, 1121, cm⁻¹; HRMS (ESI) m/z: $[M + H]^+$ Calcd for C₁₅H₂₀O 217.1592; Found 217.1584.

5.4.7. Control experiments

A) Radical quenching experiments



A 15 mL pressure tube was charged with 5 mol% of **1**, 0.5 mmol of 1-mesitylethan-1-one (**2a**), KO^tBu (0.5 mmol) in 5 mL toluene. To this mixture 1 mmol of 1-(4-methylphenyl) ethanol and x equiv of TEMPO was charged. The reaction flask was purged with an inert gas for few minutes before closing the flask tightly. The reaction mixture was stirred at 130 $^{\circ}$ C for 24 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The nmr yield of the reaction decreased drastically with the addition of TEMPO, and complete quenching of reaction was observed when it was administered in 1 equivalent.

Table S1: Product yield upon varying equivalence of radical quencher

entry	TEMPO equivalence	yield (%)
1.	0.5 equiv	12 %
2.	1 equiv	n.r.



A 15 mL pressure tube was charged with 0.5 mmol of $1^{H,H}$, 0.5 mmol of 1,3-diphenylbut-2en-1-one,¹ KO^tBu (0.5 mmol) in 5 mL toluene. To the reaction mixture, 1 equiv of TEMPO was charged. The reaction flask was purged with an inert gas for few minutes before closing the flask tightly. This reaction mixture was refluxed at 130 °C for 12 h. The formation of the

desired product 1,3-diphenylbutan-1-one was not observed.

B) Hydrogenation of intermediate chalcone



A 15 mL pressure tube was charged with 0.5 mmol of $1^{H,H}$, 0.25 mmol of 1,3-diphenylbut-2en-1-one¹, KO^tBu (0.25 mmol) in 5 mL toluene. The reaction flask was purged with an inert gas for few minutes before closing the flask tightly. This reaction mixture was refluxed at 130 °C for 12 h. 1,3-Diphenylbutan-1-one² was observed as a desired product in 58% isolated yield.





C) Experiment with a radical-probe substrate



A 15 mL pressure tube was charged with 5 mol% of **1**, 0.5 mmol of 3-cyclopropyl-1mesitylprop-2-en-1-one (**3**), 0.6 mmol of 1-phenyl ethanol, KO^tBu (0.5 mmol) in 5 mL toluene. The reaction flask was purged with an inert gas for few minutes before closing the flask tightly. This reaction mixture was refluxed at 130 °C for 12 h. The reaction mixture was cooled to room temperature upon completion and concentrated *in vacuo*. The residue was purified by column chromatography using hexane/ethyl acetate (100:1) as an eluent to afford pure products. The desired products are characterized by ¹H, ¹³C NMR spectroscopies.

D) Detection of radical intermediate arrested by TEMPO



A 15 mL pressure tube was charged with 5 mol% of **1**, 0.5 mmol of 3-cyclopropyl-1mesitylprop-2-en-1-one (**3**), KO^tBu (0.5 mmol) in 5 mL toluene. To it, 0.5 equiv TEMPO was added. The reaction flask was purged with an inert gas for few minutes before closing the flask tightly. This reaction mixture was refluxed at 130 °C for 5 h. The crude was subjected to HRMS (ESI) for characterization. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{37}NO_2$ 372.2903; Found 372.2892

E) Deuterium incorporation studies

	α-position, 2H	β-position, 1H
Signal δ	3.52	2.99
Integral value	1.86	0.2
Calculated percentage	${(2.00-1.86)/2.00}*100 = 7\%$	${(1.00-0.20)/1.00}*100 = 80\%$

D-labelled Alcohol conversion, monitored by ¹H NMR for scheme 1:

Scheme 1:



5.4.7. Computational Details

All calculations were carried out using Density Functional Theory as implemented in the Gaussian09^[38] quantum chemistry programs. The geometries of stationary points and transition states (TS) were optimized with M06-2X functional. We used double- ζ basis set with the relativistic effective core potential of Hay and Wadt (LANL2DZ)^[39.40] for the nickel atom and 6-31G* basis set for other elements (H, C, O, and N). The geometries were optimized without any symmetry constraints. Harmonic force constants were computed at the optimized geometries to characterize the stationary points as minima or saddle points. The zero-point vibrational corrections were determined from the harmonic vibrational frequencies to convert the total energies E^e to E⁰. The rigid-rotor harmonic-oscillator approximation was applied for evaluating the thermal and entropic contribution that were necessary to obtain the enthalpies, H₂₉₈ and Gibbs free energies, G₂₉₈ at 298 K. To get accurate energies of the optimized geometry using 6-311G* triple- ζ basis set^[41] for light atoms (H, C, N, O). Implicit solvent effects of toluene were considered and solvent correction was done using the polarized continuum model.^[42]

To decrease the computational cost, (i) tert-butyl groups in the ligand were replaced by methyl and (ii) the methyl groups in the phenyl substituent of pentamethyl acetophenone were replaced with hydrogens and all the calculations were carried out with this truncated framework.

Optimized structure of some intermediates



Figure 5.9. (a) Representation of pi-pi stacking phenomenon in intermediate II and TS_{II-III} (b) optimised structure of hypothetical tricoordinate Ni^(I)hydride species. During the optimization of this intermediate one of the azophenolate ligand departs.

Coordinates of optimized geometries of intermediates and transition states

1				0	1.63357900	-0.27942200	-0.82896100
$\Delta G(sol) =$	-1620.25 Hartre	e		Н	0.06722700	-4.25134100	-1.20292300
. ,				Н	1.69574200	-1.54728700	1.69282100
0.1				Н	3.76064500	-5.21098900	0.79239900
C	0.77803000	-2.82150800	0.22593200	Н	-3.76027000	5.21144000	-0.79326300
Ċ	1.77076900	-2.48289800	1.14508700	Н	-0.06722500	4.25150700	1.20260000
С	2.83600900	-3.35000500	1.35736600	Н	-1.69549200	1.54760800	-1.69343800
Н	3.60404400	-3.08991400	2.07845100	Н	-6.06286700	-0.17744900	0.58666200
С	2.92255400	-4.53968500	0.63579100	Н	-3.65869100	-3.44477400	-0.80195000
С	1.93313500	-4.86315200	-0.29132400	Н	6.06275800	0.17706100	-0.58578000
Н	2.00160500	-5.78537200	-0.85942400	Н	3.65857000	3.44410700	0.80347400
С	0.85234800	-4.01143000	-0.49478000	С	4.05393900	-1.41899700	-1.50442700
С	-2.59674200	-1.73825900	-0.05205400	Н	3.46422200	-2.18989800	-1.00089200
С	-2.67031700	-0.42643200	0.50752200	Н	3.64429400	-1.32206300	-2.51601500
С	-3.97011600	0.10424300	0.78152500	Н	5.09122400	-1.75506200	-1.58094400
С	-5.08121200	-0.60946200	0.39493100	С	6.28545800	2.59866200	0.61627900
С	-5.01833300	-1.88745400	-0.21982900	Н	6.82354800	2.04971300	1.39699500
С	-3.77791100	-2.44325400	-0.39793300	Н	6.96579200	2.70211400	-0.23576100
Ν	-0.32147200	-1.91881700	0.07615300	Н	6.07059300	3.59963200	0.99902800
Ν	-1.43829100	-2.47578800	-0.09101900	С	-6.28562600	-2.59960800	-0.61426900
0	-1.63367200	0.27967000	0.82832900	Н	-6.96570200	-2.70275100	0.23801500
Ni	-0.00006400	0.00006600	-0.00031300	Н	-6.82401100	-2.05109400	-1.39508800
С	-0.77790100	2.82173800	-0.22639200	Н	-6.07074300	-3.60072800	-0.99661500
С	-1.77052800	2.48321800	-1.14570500	С	-4.05397500	1.41930200	1.50392600
С	-2.83568300	3.35039500	-1.35812400	Н	-3.64378200	1.32298100	2.51534800
Н	-3.60362900	3.09035900	-2.07932300	Н	-3.46470300	2.19011000	0.99971700
С	-2.92225300	4.54007100	-0.63654400	Н	-5.09130100	1.75515800	1.58078000
С	-1.93294300	4.86345300	0.29072000				
Н	-2.00143200	5.78566500	0.85883000	^t BuO ⁻			
С	-0.85224100	4.01166100	0.49431800	$\Delta G(sol)$	= -232.833 Hartre	e	
С	2.59662800	1.73804100	0.05254500				
С	2.67020200	0.42643500	-0.50755200	-11			
С	3.97003400	-0.10426300	-0.78143500	С	0.12550300	0.13337900	-0.00003700
С	5.08109800	0.60912000	-0.39418400	С	0.72012000	0.85893400	1.25664100
С	5.01819000	1.88685600	0.22113000	Н	0.34122300	1.88895600	1.27061900
С	3.77779400	2.44274300	0.39906600	Н	0.34093100	0.35638500	2.15572000
Ν	0.32145000	1.91892600	-0.07641900	Н	1.82164600	0.88671400	1.30518300
Ν	1.43826800	2.47571400	0.09137400	С	0.71983700	-1.31783500	0.00008800

Н	0.34065500	-1.84492200	0.88500700	С
Н	0.34078700	-1.84502000	-0.88482800	Н
Н	1.82135800	-1.37392000	0.00017300	C
C	0.72030900	0.85879500	-1.25670500	C
н ч	0.34125500	0.33014800	-2.155/8/00	C
H	1.82184300	0.88656900	-1.30508400	C
0	-1.19688200	0.13359300	-0.00013700	Č
				С
1-phenyl e	thanol			Ν
$\Delta G(sol) =$	-385.71 Hartree			N
<u>.</u>				O NE
01	1 10002000	2 (7805500	0 12248400	INI C
0 C	1.18983900	-3.6/895500	0.13348400	C
н	1 97052600	-2.93982900	-0.52882400	Ċ
C	2.05597800	-3.31114300	-2.11064000	Н
С	2.39230800	-2.37067500	-3.08478800	С
С	1.68146100	-4.59621300	-2.50650800	C
С	2.36060000	-2.70755400	-4.43489200	H
H	2.67792800	-1.36541200	-2.78162000	C
С	1.64425500	-4.93404200	-3.85662100	C
п С	1.41722800	-3.99129200	-1.74431700	Č
H	2.62195200	-1.96627600	-5.18406900	С
Н	1.34911500	-5.93568600	-4.15478000	С
Н	1.95406800	-4.25444100	-5.87661500	С
С	3.50369300	-3.30592800	-0.06082600	N
Н	3.53495900	-3.05404800	1.00242900	N
H	3.68546000	-4.37859200	-0.17485900	Н
н Н	4.29153200	-2./3804400	-0.38309300	Н
11	0.51507000	-5.51727100	-0.23124000	Н
				Н
Acetopher	none			Н
01				Н
$\Delta G(sol) =$	-384.57 Hartree			С
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0 C	1.94496600	-3.85//1300	0.1/903400	Ċ
C	2.20033100	-3.00415900	-0.04441800	С
C	2.40192300	-2.35615300	-3.09198300	С
C	1.73554100	-4.59909100	-2.49366200	H
С	2.30843000	-2.68951600	-4.44035100	С
Н	2.69866900	-1.35041900	-2.81003300	H
C	1.64220700	-4.93157000	-3.83854900	Н
H	1.51847800	-5.32219500	-1.71420700	Н
н	2 53175600	-3.9/009300	-4.81338000	Н
H	1.34639400	-5.93424900	-4.13090100	Н
Н	1.85610000	-4.23544100	-5.86544900	С
С	2.61078700	-1.60925400	-0.21864800	Н
Н	1.91125000	-0.86352200	-0.60983900	C
Н	2.61932000	-1.56671600	0.87014900	0 C
Н	3.60583000	-1.36388900	-0.60358000	C
				С
				С
II				Н
-12				С
$\Delta G(sol) =$	-2314.261929 H	Iartree		H
С	-0.96638800	2.44401400	-1.86800600	С ц
C	0.40257400	2.82417300	-1.84030300	Н
C	0.78956300	4.12700300	-2.10691400	Н
H	1.84975800	4.3/413/00	-2.0/531600	C
C	-0.14200200	J.11/1/400	-2. 4 2013000	

1.849758004.37413700-2.07531600-0.145863005.11717400-2.42813600

-1.48588500	4.74603800	-2.50084000
-2.23581900	5.48645500	-2.77448000
-1.90063800	3.44421000	-2.23402700
-3.05848300	-0.42069000	-1.55159900
-2.36969600	-1.32683200	-2.38606000
-2.71557400	-2.68197400	-2.38606000
-3.77839100	-3.12229300	-1.59663300
-4.50424100	-2.23777600	-0.79813600
-4.12078300	-0.89844800	-0.77548500
-1 29147300	1 16334300	-1 51216000
-2 70740500	0.93359400	-1 52975400
-1 37803200	-0.923/8000	-3 21957500
-0.08197800	-0.18720400	-0.55279800
0.24700300	2 15602000	1 64016100
-0.24700500	2.13726600	1 33312100
-1.00771500	2.13720000	2 25020200
-2.54004800	-2.39911200	1.00652000
-3.39312900	-2.38310000	1.99032900
-2.11/13100	-3.06244600	2 20045000
-0./3411/00	-3.09/13200	3.80043900
-0.41945000	-3.43/30/00	4./091/300
0.18189600	-2.03222300	2.88430700
2.826/6300	-1./4128300	-0.08936000
2./549/400	-0./5945100	-1.14543400
3.9/9/1100	-0.51909400	-1.88534900
5.12844100	-1.19428000	-1.57484200
5.20361700	-2.153/3400	-0.52555100
4.05851000	-2.40131300	0.18189900
0.64867600	-1.649/9300	0.65510600
1.82033900	-2.1247/400	0.75729000
1.72104000	-0.09915100	-1.46541300
-2.94865100	3.1/822500	-2.308/4/00
1.14241500	2.05493400	-1.62986000
0.16516500	6.13/00300	-2.63136500
-2.64154200	-3.44244300	4.22109000
1.2396/300	-2.00345700	5.11442900
-1.93331300	1 25340600	2 53810400
-0.98230700	1.23349000	2.33810400
-2 22724700	1.39403800	1 95635100
-2.22724700	2 98076500	1.16589400
-3 46419100	1 21881600	2 22673000
-3 307/3100	3 53123200	0.68621200
-1 26972200	3.46244600	0.03021200
-4 64839000	1 76591400	1 74145800
-3 49330500	0.30055200	2 80631100
-4 62137000	2 93082800	0.97722100
-3 35129700	4 42125400	0.06743000
-5.59392400	1.27477700	1.95498200
-5.54471000	3.36073100	0.60109900
-1.06152000	-0.04904000	-2.87586600
0.18324100	1.38321100	1.86829400
0.16353600	1.87611100	0.89932800
1.49319700	0.85300900	2.31623200
1.61129300	0.07449600	3.25367700
2.72092900	1.28386600	1.56654200
2.73777400	2.35336300	0.66775500
3.89995900	0.56663600	1.80086800
3.91561400	2.68797600	0.00376000
1.84273100	2.93346900	0.46999600
5.07188300	0.89726800	1.13549500
3.86213500	-0.26691900	2.49417300
5.07840200	1.95652300	0.22832600
3.91716700	3.51581200	-0.69946200
5.97085800	0.31029000	1.29769600
5.98766100	2.20310200	-0.31297100
-1.13814300	0.56187300	3.86655200
-1.46696100	-0.47370900	3.71257900

C H

и	0 10604400	0 51722800	4 40758200	п	0 77451800	2 77621100	0 211/2500
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тс				ч	1 18832800	2 42077000	0.45171600
				11	1.18832800	-2.42977000	-0.451/1000
$\Delta G(sol) = -2$	2314.22 Hartre	e		С	3.82796600	-0.92797600	-2.85030700
Imaginary fi	requency $= -13$	00.67 cm^{-1}		Н	2.22319700	0.35150800	-3.54036100
-12	1 5			С	4.18399100	-1.94434900	-1.96553900
-1 <u>2</u>	1 20200500	2 10250000	1 5(122400	11	2 40274600	2 26050200	0.40949200
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П С	1 12022700	4.07052(00	1.75402(00	11	2 16027100	1 40026000	1 96002100
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C	-2.8/098500	3.800/3/00	1.93723300		2.15400000	1 70500500	2.72001000
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IN .	-2.4//90900	-0.23841100	1.210/2800		7.54824200	0.11015000	0.00703000
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C	3.14144400	-0.22322900	1.22192800	t	_		
С	4.17388700	-1.07983500	1.76263900	'Bu	1O ⁻		
С	5.47926900	-0.94921700	1.36252700	٨G	i(sol) = -232.725 Hartre	e	
Ĉ	5 90212500	0.02/30300	0.42125800	0.2		-	
C	5.90212500	0.02430300	0.42123800	02		o 1 - 6 6 0 10 0	
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Ν	2.79004400	1.69911500	-0.37363200	н	0 34254200	1.89233400	1.29283200
0	1 0/07/200	0.38572000	1 62206400	11	0.2//20000	0 3/101200	2 15457000
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H_2O			
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01			
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C	0.10257500	-2.70737500	-1.20+03+00
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H H H H C H C O C C C C C H C H C H H H C H

H H

H H H

H C H

H H H H H H H H H H H H H H H

H H

5.5. References

(a) Pher G. Andersson, I. J. M., *Modern Reduction Methods*. Wiley-VCH Verlag Gmbh & Co., Weinheim, 2008; (b) Wang, Y.; Huang, Z.; Leng, X.; Zhu, H.; Liu, G.; Huang, Z., Transfer Hydrogenation of Alkenes Using Ethanol Catalyzed by a NCP Pincer Iridium Complex: Scope and Mechanism. *J. Am. Chem. Soc.* 2018, *140*, 4417-4429; (c) Parker, P. D.; Hou, X.; Dong, V. M., Reducing Challenges in Organic Synthesis with Stereoselective Hydrogenation and Tandem Catalysis. *J. Am. Chem. Soc.* 2021, *143*, 6724-6745; (d) Etayo, P.; Vidal-Ferran, A., Rhodium-catalysed asymmetric hydrogenation as a valuable synthetic tool for the preparation of chiral drugs. *Chem. Soc. Rev.* 2013, *42*, 728-754.

2. (a) Mikhailine, A. A.; Maishan, M. I.; Lough, A. J.; Morris, R. H., The Mechanism of Efficient Asymmetric Transfer Hydrogenation of Acetophenone Using an Iron(II) Complex Containing an (S,S)-Ph2PCH2CH=NCHPhCHPhN=CHCH2PPh2 Ligand: Partial Ligand Reduction Is the Key. *J. Am. Chem. Soc.* **2012**, *134*, 12266-12280; (b) Huang, Z.; Wang, Y.; Leng, X.; Huang, Z., An Amine-Assisted Ionic Monohydride Mechanism Enables Selective Alkyne cis-Semihydrogenation with Ethanol: From Elementary Steps to Catalysis. *J. Am. Chem. Soc.* **2021**, *143*, 4824-4836; (c) Broggi, J.; Jurčík, V.; Songis, O.; Poater, A.; Cavallo, L.; Slawin, A. M. Z.; Cazin, C. S. J., The Isolation of [Pd{OC(O)H}(H)(NHC)(PR3)] (NHC = N-Heterocyclic Carbene) and Its Role in Alkene and Alkyne Reductions Using Formic Acid. *J. Am. Chem. Soc.* **2013**, *135*, 4588-4591.

3. (a) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R., The Catalyst Precursor, Catalyst, and Intermediate in the RuII-Promoted Asymmetric Hydrogen Transfer between Alcohols and Ketones. *Angew. Chem., Int. Ed.* **1997**, *36*, 285-288; (b) Yamakawa, M.; Ito, H.; Noyori, R., The Metal–Ligand Bifunctional Catalysis: A Theoretical Study on the Ruthenium(II)-Catalyzed Hydrogen Transfer between Alcohols and Carbonyl Compounds. *J. Am. Chem. Soc.* **2000**, *122*, 1466-1478; (c) Noyori, R.; Yamakawa, M.; Hashiguchi, S., Metal–Ligand Bifunctional Catalysis: A Nonclassical Mechanism for Asymmetric Hydrogen Transfer between Alcohols and Carbonyl Compounds. *J. Org. Chem.* **2001**, *66*, 7931-7944.

4. Mendelsohn, L. N.; MacNeil, C. S.; Tian, L.; Park, Y.; Scholes, G. D.; Chirik, P. J., Visible-Light-Enhanced Cobalt-Catalyzed Hydrogenation: Switchable Catalysis Enabled by Divergence between Thermal and Photochemical Pathways. *ACS Catal.* **2021**, *11*, 1351-1360. Sang, S.; Unruh, T.; Demeshko, S.; Domenianni, L. I.; van Leest, N. P.; Marquetand, P.;
 Schneck, F.; Würtele, C.; de Zwart, F. J.; de Bruin, B.; González, L.; Vöhringer, P.; Schneider,
 S., Photo-Initiated Cobalt-Catalyzed Radical Olefin Hydrogenation. *Chem. Eur. J.* 2021, 27, 16978-16989.

6. Derosa, J.; Garrido-Barros, P.; Peters, J. C., Electrocatalytic Reduction of C–C π -Bonds via a Cobaltocene-Derived Concerted Proton–Electron Transfer Mediator: Fumarate Hydrogenation as a Model Study. *J. Am. Chem. Soc.* **2021**, *143*, 9303-9307.

7. (a) Green, S. A.; Crossley, S. W. M.; Matos, J. L. M.; Vásquez-Céspedes, S.; Shevick, S. L.; Shenvi, R. A., The High Chemofidelity of Metal-Catalyzed Hydrogen Atom Transfer. *Acc. Chem. Res.* 2018, *51*, 2628-2640; (b) Crossley, S. W. M.; Obradors, C.; Martinez, R. M.; Shenvi, R. A., Mn-, Fe-, and Co-Catalyzed Radical Hydrofunctionalizations of Olefins. *Chem. Rev.* 2016, *116*, 8912-9000.

8. Kim, D.; Rahaman, S. M. W.; Mercado, B. Q.; Poli, R.; Holland, P. L., Roles of Iron Complexes in Catalytic Radical Alkene Cross-Coupling: A Computational and Mechanistic Study. *J. Am. Chem. Soc.* **2019**, *141*, 7473-7485.

9. (a) Bullock, R. M., Reaction: Earth-Abundant Metal Catalysts for Energy Conversions. *Chem* **2017**, *2*, 444-446; (b) Chirik, P. J.; Wieghardt, K., Radical Ligands Confer Nobility on Base-Metal Catalysts. *Science* **2010**, *327*, 794-795.

10. (a) Mondal, A.; Sharma, R.; Pal, D.; Srimani, D., Recent Progress in the Synthesis of Heterocycles through Base Metal-Catalyzed Acceptorless Dehydrogenative and Borrowing Hydrogen Approach. *Eur. J. Org. Chem.* 2021, 2021, 3690-3720; (b) Das, K.; Waiba, S.; Jana, A.; Maji, B., Manganese-catalyzed hydrogenation, dehydrogenation, and hydroelementation reactions. *Chem. Soc. Rev.* 2022, *51*, 4386-4464; (c) Subaramanian, M.; Sivakumar, G.; Balaraman, E., Recent advances in nickel-catalyzed C–C and C–N bond formation via HA and ADC reactions. *Org. Biomol. Chem.* 2021, *19*, 4213-4227; (d) Freitag, F.; Irrgang, T.; Kempe, R., Cobalt-Catalyzed Alkylation of Secondary Alcohols with Primary Alcohols via Borrowing Hydrogen/Hydrogen Autotransfer. *Chem. Eur. J.* 2017, *23*, 12110-12113; (e) Elangovan, S.; Neumann, J.; Sortais, J.-B.; Junge, K.; Darcel, C.; Beller, M., Efficient and selective N-alkylation of amines with alcohols catalysed by manganese pincer complexes. *Nat. Commun.* 2016, *7*, 12641; (f) Zell, T.; Milstein, D., Hydrogenation and Dehydrogenation Iron Pincer Catalysts Capable of Metal-Ligand Cooperation by

Aromatization/Dearomatization. *Acc. Chem. Res.* **2015**, *48*, 1979-1994; (g) Gunanathan, C.; Milstein, D., Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science* **2013**, *341*, 1229712.

11. (a) K. Bains, A.; Ankit, Y.; Adhikari, D., Bioinspired Radical-Mediated Transition-Metal-Free Synthesis of N-Heterocycles under Visible Light. *ChemSusChem* 2021, *14*, 324-329; (b)
Bains, A. K.; Ankit, Y.; Adhikari, D., Pyrenedione-Catalyzed α-Olefination of Nitriles under Visible-Light Photoredox Conditions. *Org. Lett.* 2021, *23*, 2019-2023.

 Sweany, R. L.; Halpern, J., Hydrogenation of .alpha.-methylstyrene by hydridopentacarbonylmanganese (I). Evidence for a free-radical mechanism. *J. Am. Chem. Soc.* 1977, *99*, 8335-8337.

13. (a) Singh, K.; Kundu, A.; Adhikari, D., Ligand-Based Redox: Catalytic Applications and Mechanistic Aspects. *ACS Catal.* 2022, *12*, 13075-13107; (b) Bains, A. K.; Singh, V.;
Adhikari, D., Homogeneous Nickel-Catalyzed Sustainable Synthesis of Quinoline and Quinoxaline under Aerobic Conditions. *J. Org. Chem.* 2020, *85*, 14971-14979; (c) Biswas,
A.; Bains, A. K.; Adhikari, D., Ligand-assisted nickel catalysis enabling sp3 C–H alkylation of 9H-fluorene with alcohols. *Catal. Sci. Technol.* 2022, *12*, 4211-4216; (d) Bains, A. K.;
Kundu, A.; Maiti, D.; Adhikari, D., Ligand-redox assisted nickel catalysis toward stereoselective synthesis of (n+1)-membered cycloalkanes from 1,n-diols with methyl ketones. *Chem. Sci.* 2021, *12*, 14217-14223; (e) Bains, A. K.; Adhikari, D., Mechanistic insight into the azo radical-promoted dehydrogenation of heteroarene towards N-heterocycles. *Catal. Sci. Technol.* 2020, *10*, 6309-6318.

14. Bains, A. K.; Biswas, A.; Kundu, A.; Adhikari, D., Nickel-Catalysis Enabling α-Alkylation of Ketones by Secondary Alcohols. *Adv. Synth. Catal.* **2022**, *364*, 2815-2821.

15. Akhtar, W. M.; Armstrong, R. J.; Frost, J. R.; Stevenson, N. G.; Donohoe, T. J., Stereoselective Synthesis of Cyclohexanes via an Iridium Catalyzed (5 + 1) Annulation Strategy. *J. Am. Chem. Soc.* **2018**, *140*, 11916-11920.

16. McLoughlin, E. A.; Waldie, K. M.; Ramakrishnan, S.; Waymouth, R. M., Protonation of a Cobalt Phenylazopyridine Complex at the Ligand Yields a Proton, Hydride, and Hydrogen Atom Transfer Reagent. *J. Am. Chem. Soc.* **2018**, *140*, 13233-13241.

17. Sengupta, D.; Bhattacharjee, R.; Pramanick, R.; Rath, S. P.; Saha Chowdhury, N.; Datta, A.; Goswami, S., Exclusively Ligand-Mediated Catalytic Dehydrogenation of Alcohols. *Inorg. Chem.* 2016, *55*, 9602-9610.

 Chakraborty, P.; Gangwar, M. K.; Emayavaramban, B.; Manoury, E.; Poli, R.;
 Sundararaju, B., α-Alkylation of Ketones with Secondary Alcohols Catalyzed by Well-Defined Cp*CoIII-Complexes. *ChemSusChem* **2019**, *12*, 3463-3467.

19. Waiba, S.; Jana, S. K.; Jati, A.; Jana, A.; Maji, B., Manganese complex-catalysed α -alkylation of ketones with secondary alcohols enables the synthesis of β -branched carbonyl compounds. *Chem. Commun.* **2020**, *56*, 8376-8379.

20. Bettoni, L.; Gaillard, S.; Renaud, J.-L., Iron-Catalyzed α -Alkylation of Ketones with Secondary Alcohols: Access to β -Disubstituted Carbonyl Compounds. *Org. Lett.* **2020**, *22*, 2064-2069.

21. Bains, A. K.; Kundu, A.; Yadav, S.; Adhikari, D., Borrowing Hydrogen-Mediated N-Alkylation Reactions by a Well-Defined Homogeneous Nickel Catalyst. *ACS Catal.* **2019**, *9*, 9051-9059.

22. Klomp, D.; Hanefeld, U.; Peters, J. A., Transfer Hydrogenation Including the Meerwein-Ponndorf-Verley Reduction. In *The Handbook of Homogeneous Hydrogenation*, 2006; pp 585-630.

23. (a) Ikariya, T.; Blacker, A. J., Asymmetric Transfer Hydrogenation of Ketones with
Bifunctional Transition Metal-Based Molecular Catalysts. *Acc. Chem. Res.* 2007, *40*, 1300-1308; (b) Xu, R.; Chakraborty, S.; Bellows, S. M.; Yuan, H.; Cundari, T. R.; Jones, W. D.,
Iron-Catalyzed Homogeneous Hydrogenation of Alkenes under Mild Conditions by a
Stepwise, Bifunctional Mechanism. *ACS Catal.* 2016, *6*, 2127-2135; (c) Coufourier, S.;
Gaignard Gaillard, Q.; Lohier, J.-F.; Poater, A.; Gaillard, S.; Renaud, J.-L., Hydrogenation of
CO2, Hydrogenocarbonate, and Carbonate to Formate in Water using Phosphine Free
Bifunctional Iron Complexes. *ACS Catal.* 2020, *10*, 2108-2116; (d) Seck, C.; Mbaye, M. D.;

Coufourier, S.; Lator, A.; Lohier, J.-F.; Poater, A.; Ward, T. R.; Gaillard, S.; Renaud, J.-L., Alkylation of Ketones Catalyzed by Bifunctional Iron Complexes: From Mechanistic Understanding to Application. *ChemCatChem* **2017**, *9*, 4410-4416; (e) Chakraborty, S.; Lagaditis, P. O.; Förster, M.; Bielinski, E. A.; Hazari, N.; Holthausen, M. C.; Jones, W. D.; Schneider, S., Well-Defined Iron Catalysts for the Acceptorless Reversible Dehydrogenation-Hydrogenation of Alcohols and Ketones. *ACS Catal.* **2014**, *4*, 3994-4003.

24. (a) Lyaskovskyy, V.; de Bruin, B., Redox Non-Innocent Ligands: Versatile New Tools to Control Catalytic Reactions. *ACS Catal.* **2012**, *2*, 270-279; (b) Broere, D. L. J.; van Leest, N. P.; de Bruin, B.; Siegler, M. A.; van der Vlugt, J. I., Reversible Redox Chemistry and Catalytic C(sp3)–H Amination Reactivity of a Paramagnetic Pd Complex Bearing a Redox-Active o-Aminophenol-Derived NNO Pincer Ligand. *Inorg. Chem.* **2016**, *55*, 8603-8611.

25. Ulas, G.; Lemmin, T.; Wu, Y.; Gassner, G. T.; DeGrado, W. F., Designed metalloprotein stabilizes a semiquinone radical. *Nat. Chem.* **2016**, *8*, 354-359.

26. Zhao, Y.; Truhlar, D. G., The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **2008**, *120*, 215-241.

27. (a) P. Roberts, B., Polarity-reversal catalysis of hydrogen-atom abstraction reactions:
concepts and applications in organic chemistry. *Chem. Soc. Rev.* 1999, 28, 25-35; (b) Guo, X.;
Wenger, O. S., Reductive Amination by Photoredox Catalysis and Polarity-Matched
Hydrogen Atom Transfer. *Angew. Chem., Int. Ed.* 2018, *57*, 2469-2473.

28. (a) Babu, R.; Subaramanian, M.; Midya, S. P.; Balaraman, E., Nickel-Catalyzed Guerbet
Type Reaction: C-Alkylation of Secondary Alcohols via Double (de)Hydrogenation. *Org. Lett.* 2021, 23, 3320-3325; (b) El-Sepelgy, O.; Matador, E.; Brzozowska, A.; Rueping, M., CAlkylation of Secondary Alcohols by Primary Alcohols through Manganese-Catalyzed
Double Hydrogen Autotransfer. *ChemSusChem* 2019, *12*, 3099-3102.

29. van der Meer, M.; Rechkemmer, Y.; Peremykin, I.; Hohloch, S.; van Slageren, J.; Sarkar,
B., (Electro)catalytic C–C bond formation reaction with a redox-active cobalt complex. *Chem. Commun.* 2014, *50*, 11104-11106.

30. Bains, A. K.; Biswas, A.; Adhikari, D., Nickel-Catalyzed Selective Synthesis of α-Alkylated Ketones via Dehydrogenative Cross-Coupling of Primary and Secondary Alcohols. *Adv. Synth. Catal.* **2022**, *364*, 47-52.

31. (a) Shevick, S. L.; Wilson, C. V.; Kotesova, S.; Kim, D.; Holland, P. L.; Shenvi, R. A., Catalytic hydrogen atom transfer to alkenes: a roadmap for metal hydrides and radicals. *Chem. Sci.* 2020, *11*, 12401-12422; (b) Ma, X.; Herzon, S. B., Non-classical selectivities in the reduction of alkenes by cobalt-mediated hydrogen atom transfer. *Chem. Sci.* 2015, *6*, 6250-6255; (c) Iwasaki, K.; Wan, K. K.; Oppedisano, A.; Crossley, S. W. M.; Shenvi, R. A., Simple, Chemoselective Hydrogenation with Thermodynamic Stereocontrol. *J. Am. Chem. Soc.* 2014, *136*, 1300-1303.

Weinberg, D. R.; Gagliardi, C. J.; Hull, J. F.; Murphy, C. F.; Kent, C. A.; Westlake, B. C.;
 Paul, A.; Ess, D. H.; McCafferty, D. G.; Meyer, T. J., Proton-Coupled Electron Transfer.
 Chem. Rev. 2012, *112*, 4016-4093.

33. Vrubliauskas, D.; Vanderwal, C. D., Cobalt-Catalyzed Hydrogen-Atom Transfer Induces Bicyclizations that Tolerate Electron-Rich and Electron-Deficient Intermediate Alkenes. *Angew. Chem., Int. Ed.* **2020,** *59*, 6115-6121.

34. Jana, A.; Das, K.; Kundu, A.; Thorve, P. R.; Adhikari, D.; Maji, B., A Phosphine-Free Manganese Catalyst Enables Stereoselective Synthesis of (1 + n)-Membered Cycloalkanes from Methyl Ketones and 1,n-Diols. *ACS Catal.* **2020**, *10*, 2615-2626.

35. Deng, K.; Huai, Q-Y.; Shen, Z-L.; Li, H-J.; Liu, C.; Y-C.; Wu, Y-C., Rearrangement of Dypnones to 1,3,5-Triarylbenzenes. *Org. Lett.* **2015**, *17*, 1473-1476.

36. Chakraborty, P.; Gangwar, M. K.; Emayavaramban, B.; Manoury, E.; Poli, R.; Sundararaju, B., α-Alkylation of Ketones with Secondary Alcohols Catalyzed by Well-Defined Cp*Co^{III}-Complexes. *ChemSusChem.* **2019**, *12*, 3463-3467.

37. Wübbolt, S.; Cheong, C. B.; Frost, J. R.; Christensen, K. E.; Donohoe, T. J., A Vinyl Cyclopropane Ring Expansion and Iridium-Catalyzed Hydrogen Borrowing Cascade. *Angew. Chem. Int. Ed.* **2020**, *59*, 11339–11344.

38. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16 Rev. C.01*, Wallingford, CT, 2016.

39. Hay, P. J.; Wadt, W. R., Ab initio effective core potentials for molecular calculations.Potentials for K to Au including the outermost core orbitals. *J. Chem. Phys.* 1985, 82, 299-310.

40. Wadt, W. R.; Hay, P. J., Ab initio effective core potentials for molecular calculations. Potentials for main group elements Na to Bi. *J. Chem. Phys.* **1985**, *82*, 284-298.

41. Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J.A., Self-consistent molecular orbital methods. XX. A basis set for correlated wave functions. *J. Chem. Phys.* **1980**, *72*, 650–654.

42. (a) Tomasi, J.; Mennucci, B.; Cammi, R., Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105*, 2999-3094. (b) Cossi, M.; Barone, V.; Cammi, R.; Tomasi, J., Ab initio study of solvated molecules: a new implementation of the polarizable continuum model. *Chem. Phys. Lett.* **1996**, *255*, 327-335. (c) Cancès, E.; Mennucci, B.; Tomasi, J., A new integral equation formalism for the polarizable continuum model: Theoretical background and applications to isotropic and anisotropic dielectrics. *J. Chem. Phys.* **1997**, *107*, 3032-3041. (d) Barone, V.; Cossi, M., Quantum Calculation of Molecular Energies and Energy Gradients in Solution by a Conductor Solvent Model. *J. Phys. Chem. A* **1998**, *102*, 1995-2001.

Chapter 6

DFT-Guided Mechanistic Insights into Chemodivergence: a Mixed Explicit-Implicit Solvent Description to Dictate the Chemoselectivity

For the purpose of this thesis, the work of chapter 6 is adapted with permission from (Kundu. A.; Mandal. B.; Maji. B.; Adhikari. D.*, *J. Phys. Chem. A* **2023**. *127*, 10068-10074. Title: DFT-Guided Mechanistic Insights into Chemo-divergence: a Mixed Explicit-Implicit Solvent Description to Dictate the Chemoselectivity.)

6.1. -Introduction

In homogeneous catalysis, solvent has a strong influence in dictating the catalytic outcome. Sometimes this effect is so prominent that different solvent systems lead to the formation of different products displaying high selectivity. Often such selectivity switch is an intriguing question and computational modeling can be an effective tool to offer detailed insight into the governing factors.¹⁻⁴ Detailed evaluation of the reaction path describing a critical role of the reaction medium on it generates a macroscopic-level view that also tells us about the varying solubility of multiple intermediates along the reaction pathway. Such a molecular level depiction also demonstrates the direct interaction of solvent molecule with substrates, intermediates and transition states. There are several prior reports, where solvent's crucial participation has been elucidated by extensive DFT calculations.⁵⁻⁶ Several reports from Schoenebeck group showed effect of solvent to show reverse regioselectivity for Pd-catalysed cross-coupling reactions.⁷⁻⁸ On a similar note, Bai and Lan groups reported distinctly different catalytic reactions performed by a Rh-catalyst in different



Scheme 6.1. (a) Previous work, (b) Basic overview of iso-propanol assistance in the additionelimination path to dictate the reaction outcome.

solvent medium. Furthermore, Pidko group showed how explicit solvent modeling helped to understand the mechanism of solvent-assisted Meerwin-Pondrof-Verley (MPV) pathway in a

Mn(I)-catalyzed transfer hydrogenation reaction.⁹ In a similar note, role of protic solvent in base-promoted enolization has also been investigated.¹⁰

Nitrile reduction has been a popular method to produce amine building blocks.¹¹⁻¹⁴ Controlling the selectivity of such reduction processes towards various amines is still a challenging task. Recently, we reported the chemoselective synthesis of primary and secondary amines by a manganese catalyst via nitrile hydrogenation, employing ammoniaborane as the hydrogen source.¹⁵ During optimizing the reaction, we observed a significant dependence of product selectivity on the reaction medium. Specifically, in hexane primary amine is obtained, whilst in isopropanol a secondary amine is generated. In this present report we endeavor a mixed explicit-implicit solvation by a protic solvent and try to evaluate the key factors to regulate the observed product selectivity.



Scheme 6.2. (a) Model catalysts chosen towards studying solvent-dependent chemoselectivity. (b) Sequential steps for the formation of Mn-bound imine upon hydride insertion.

6.2. Computational details:

All calculations were carried out using Density Functional Theory as implemented in the Gaussian16¹⁶ quantum chemistry programs. The geometries of stationary points and transition states (TS) were optimized in gas phase with B3LYP-D3BJ functional.¹⁷⁻²¹ We used double- ζ basis set with the relativistic effective core potential of Hay and Wadt (LANL2DZ)^{22,23} for the manganese atom and 6-31G* basis set for other elements (H, C, O, N, S). The geometries were optimized without any symmetry constraints. Harmonic force constants were computed at the optimized geometries to characterize the stationary points as

minima or saddle points. The zero-point vibrational corrections were determined from the harmonic vibrational frequencies to convert the total energies E^e to E^0 . The rigid-rotor harmonic oscillator approximation was applied for evaluating the thermal and entropic contribution that were necessary to obtain the enthalpies, H₂₉₈ and Gibbs free energies, G₂₉₈ at 298 K. To get accurate energies, optimized structures were re-evaluated by additional single point energy calculations using 6-311G* triple- ζ basis set for light atoms (H, C, O, N, S). The solvent correction was done using the polarized continuum model.²⁴⁻²⁷



6.3. Results and discussions:

Figure 6.1. Pictorial representation of two different faces of the catalyst at its resting state (a) I and (b) I' to be available as reaction site.

Two manganese catalysts are selected for the study: their ligand backbones differ by a thiomethoxy and a thiophene side arm (Scheme 2a). These two catalysts, which we describe as Mn1 and Mn2 have been reported to enable nitrile hydrogenation in our previous report that demonstrates different product selectivity in different solvents (n-hexane and isopropanol).¹⁵ We plan to use both manganese catalysts so that we validate the generality of our findings regarding the solvent's role, irrespective of some modification in the ligand motif. The solvent's role in directly dictating the product outcome has been highlighted in literature earlier. ²⁸⁻²⁹ Sunoj group recently reviewed the role of protic solvents in several organic transformations.³⁰ Solvent's particular role in modulating secondary sphere via non-covalent interactions has also been documented.³¹ Furthermore, Chandra and co-workers disclosed that active participation of water molecule in lowering down the energy barrier for

a path that consists of proton transfer combined with nucleophilic attack via proton hopping.^{32,33}.



Scheme 6.3. Mechanistic sketch for the solvent assisted vs. non-assisted pathway.

6.3.1. Potential energy surface considering face F1 as the reactive site for Mn1 catalyst:

As detailed in our previous report, the precatalyst in presence of a base quickly becomes converted to a Mn-imido species (intermediate I) as the catalytically active species. This manganese species is responsible to exhibit metal-ligand cooperativity and to drive the alcohol bond activation as a starting point of hydrogen borrowing reactions.^{15, 34} We began our mechanistic analysis with this intermediate I, that represents a Y-shaped TBP geometry under the geometric influence of pincer ligand, and possesses singlet spin ground state. A close examination of the geometrically optimized intermediate I reveals two different faces (namely faces F1 & F2) to be available as reaction sites (as shown in Figure 6.1a). In our study we will consider approach of the substrate molecules from two different faces and the energetics will be compared in two different solvents, specifically nonpolar aprotic hexane and polar protic isopropanol. With these chosen combinations, four alternative pathways towards imine metathesis require comparison to detect the most favorable one. Path A will be operational via F1-face, and the protic solvent iso-propanol will assist the process, The same

sequence of events when happens from the F1-face, without the assistance of a solvent, we designate that as path C. Similarly, Path B describes the imine metathesis through F2-face, with the participation from solvent iso-propanol. Pathway D remains same to pathway B on other aspects except the solvent is hexane, that does not provide any help in imine metathesis step. The intermediate I dehydrogenates ammonia-borane in a metal-ligand bifunctional manner and stores those hydrogen equivalents in intermediate IIA, generating a manganese hydride while following path A. This is followed by nitrile insertion into the Mn-hydride resulting a Mn-bound imine intermediate IIIA via path A. The analogous intermediate via path B is IIIB. Notably, the imine metathesis from the intermediate IIIA is the origin of chemodivergence demonstrated through the reaction. In dictating the chemodivergent nature of the reaction, protic solvent has a preponderant role. There are multiple reports in support of such solvent-assisted pathway where the solvent proton assists the pathway heavily. Such proton hopping phenomenon is well-established for polar protic solvents and has been described as Grotthuss mechanism.³⁵ In close relevance to our work, there are studies where proton or hydrogen bond assisted imine metathesis catalysis has been examined.36,37 The nucleophilic amine attack to the imine-form is much facilitated when the imine is metalbound, rather than when it is free. This amine can either be the final product of double hydrogenation of substrate nitrile or an externally added amine. The attack indicates the higher electrophilicity of the imine carbon at its metal-bound state. This hypothesis correlates well with the experimental observation where unsymmetrical amine forms exclusively from a starting nitrile and an externally added amine.¹⁵ This imine metathesis process consists of two distinct steps such as addition followed by elimination, in a stepwise manner. Initially, the amine attacks the carbon center of Mn-bound imine in intermediate IIIA and transfers a proton to the imine nitrogen in a concerted manner, resulting a Mn-bound hemiaminal



Figure 6.2. Potential energy surface diagram comparing the solvent assisted vs. non-assisted pathway for the Mn1 catalyst.

intermediate IVA. This specific step is assisted by iso-propanol and passes through TS-IA posing a transition barrier of 29.4 kcal/mol from intermediate IIIA. We note that when proton transfer is involved, quantum mechanical tunneling may contribute to keep the barrier moderate, however it is not going to impact the solvent-dependent chemoselectivity which is the focus of the current study. While the same step is computed in n-hexane, the nonavailability of the solvent proton makes the corresponding **TS-IC** very high in energy, showcasing a barrier of 55.5 kcal/mol. The unfavorable character of this path directly relates to the lack of solvent participation (via proton hopping) in this case. To complete the imine metathesis process, an elimination step from intermediate IVA is required, which results in intermediate VA upon releasing the resulting imine. The free imine will be subsequently reduced to afford the final product, a secondary amine (via intermediates VI-VIII). This step possesses a transition state barrier of 18.8 kcal/mol (TS-IIA) from the lowest energy intermediate. Corroborating with the previous solvent-assisted pathway, such low barrier originates from the assistance of iso-propanol via proton-hopping. As can be anticipated, the solvent non-assisted elimination pathway is unfavorable, posing a high energy barrier of 35.5 kcal/mol (TS-IIC) in n-hexane.

6.3.2. Potential energy surface considering face F2 as reactive site for Mn1 catalyst:

In this section we will consider the same set of phenomena that will be operated from face **F2**. Considering face **F2** of **Mn1** as reactive site, intermediate **IIB** can be the starting point where the reducing equivalent hydrogen is stored in the form of manganese hydride and an N-H (Figure 6.2). The amine attack coupled with a proton transfer event on the Mn(I)-bound imine, passes through **TS-ID** posing an energy barrier of 57.3 kcal/mol in hexane. Such solvent non-assisted step leads to the formation of intermediate **IVB**. But in iso-propanol, the transition state (**TS-IB**) barrier significantly reduces to 32.4 kcal/mol where solvent assists via proton hopping. In comparison to the favorable pathway from face **F1**, the transition state **TS-1B** is ~3 kcal/mol higher than the corresponding TS, **TS-IA**. This energy difference between two TSs might be attributed to the steric factor posed by methyl group, which makes face **F2** less accessible reaction site. Then the elimination of the secondary imine crosses an energy barrier of 37.5 kcal/mol in n-hexane via **TS-IID** (non-assisted pathway), while isopropanol-assisted path proceeds along **TS-IIB** (solvent-assisted pathway) comprising a barrier of 20.8 kcal/mol.



Figure 6.3. Potential energy surface diagram comparing the solvent-assisted vs. non-assisted pathway for the Mn2 catalyst.

	Γ	VIn1	Mn2			
Solvent	TS	Barrier (kcal/mol)	TS	Barrier (kcal/mol)		
	Fa	ce F1	F	Face F1'		
Iso-propanol	TS-IA	29.4	TS-IA'	25.0		
	TS-IIA	18.8	TS-IIA'	20.6		
n-hexane	TS-IC	55.5	TS-IC'	46.0		
	TS-IIC	35.5	TS-IIC'	39.5		
	Face F2		F	'ace F2'		
Iso-propanol	TS-IB	32.4	TS-IB'	31.2		
	TS-IIB	20.8	TS-IIB'	18.2		
n-hexane	TS-ID	57.3	TS-ID'	44.7		
	TS-IID	37.5	TS-IID'	35.7		

 Table 6.1.
 Tabulated transition barriers from the lowest energy intermediates of the corresponding catalytic cycles for the corresponding transition states.

6.3.3. Potential energy surface considering face F1' as reactive site for Mn2 catalyst:

We have shown in the above two sections that solvent-assistance provide low-energy pathways, by specifically affording stabilizing interaction in the transition states. To examine, whether this set of observation ingeneral, we applied the same on a different manganese catalyst **Mn2** (Figure 6.3) having slightly different ligand backbone. In our prior experimental work the same catalyst was used offering similar efficiency to **Mn1**. For **Mn2**, we again considered two reactive faces (**F1**' & **F2**' in Figure 6.1b). Upon treatment with ammonia-borane, **Mn2** leads to the catalytic resting state **I**' displaying a Y-shaped TBP geometry. It also remains as singlet in its ground state.^{15, 34} **I**' dehydrogenates ammonia-borane and stores the hydrogen equivalents through face **F1**' to engender intermediate **IIA**' which will further hydrogenate the nitrile substrate to give intermediate **IIIA**'. Likewise the earlier pathways, an imine metathesis happens via sequential addition and elimination steps.

The isopropanol-assisted path for amine addition to the Mn-bound imine overcomes a transition barrier of 25.0 kcal/mol via **TS-IA**' to engender intermediate **IVA**'. Then intermediate **IVA**' undergoes an elimination step to complete the imine metathesis process. On the other hand, without any solvent assistance in n-hexane, the amine addition traverses through a transition barrier of 46.0 kcal/mol via **TS-IC**'. The isopropanol-assisted elimination path costs an energy barrier of 20.6 kcal/mol, while the energy barrier for the non-assisted path in n-hexane, is 39.5 kcal/mol.

6.3.4. Potential energy surface considering face F2' as the reactive site for Mn2 catalyst:

In this section, we will look at the same set of phenomena discussed earlier for **Mn2**, but they will operate from the side of face **F2'**. Following the similar path described earlier in the previous section, intermediate **IIB'** will be generated, storing the hydrogen equivalents in **F2'** face (Figure 6.3). Then hydride insertion into nitrile will give the Mn-bound imine intermediate **IIIB'**. Amine addition will be facilitated with the assistance of isopropanol having an energy barrier of 31.2 kcal/mol (**TS-IB'**), while in n-hexane the barrier for **TS-ID'** is quite high, 44.7 kcal/mol. Amine addition leads to the formation of intermediate **IVB'**, which is prepared to undergo elimination as a final step of imine metathesis process. In n-hexane the transition barrier for this elimination step is calculated to be 35.7 kcal/mol (**TS-IID'**). On the other hand, isopropanol assisted elimination traverses through a barrier of 18.2 kcal/mol (**TS-IIB'**) and such a low barrier befits the proton-assisted pathway.

Taking all the above discussions into account, we can clearly infer that both catalytic manganese systems follow the general trend and the transition barriers for imine metathesis step are significantly reduced by the help of protic solvent. This favors the formation of an imine. That is further hydrogenated at a later phase to give the observed secondary amine.¹⁵

6.4. Conclusions

In this report, we have investigated the underpinnings of the chemo-divergent feature observed in a Mn(I)-catalyzed hydrogenation of nitrile reaction. We have shown polar protic solvent iso-propanol helps the imine metathesis step to be operative predominantly before the hydrogenation step to selectively result secondary amines. Proton hopping phenomenon plays a significant role towards this transformation. While n-hexane is unable to provide such assistance towards the imine metathesis step, and likely leads to primary amine as the final product. We believe that such detailed understanding regarding active solvent participation in
dictating chemoselectivity will help in further reaction design where a specific product is desirable, suppressing the formation of another.

01

6.5. **Co-ordinates for optimized geometries**



I			
01			
Mn	1.13801000	1.41043400	1.18275300
0	-1.45990700	2.78585600	1.27335200
0	1.52350900	1.73975700	-1.72092300
Ν	2.13750000	3.10397800	1.59842200
С	2.99149400	3.01761100	2.63737500
С	2.01252200	4.28530700	0.95720800
Н	1.31319700	4.29893200	0.12975800
С	3.61362100	5.32864200	2.40389600
Н	4.18966300	6.19349000	2.71859200
С	2.72768500	5.41396800	1.32602200
Н	2.59164000	6.33989800	0.77774700
С	3.05513400	1.66499100	3.27385600
Н	4.10840800	1.32643500	3.28799100
Н	2.76579000	1.76283000	4.33840800
С	2.28112500	-0.58197200	3.18235300
Н	3.20670600	-0.66268200	3.77092400
Н	1.46516600	-0.71323000	3.91547100
С	-0.43647600	2.23198100	1.18549500
С	1.32311700	1.60897100	-0.58135000
С	3.74378800	4.11289200	3.06479500
Н	4.42020000	4.00001300	3.90653500
Ν	2.20063300	0.73747500	2.56286300
С	2.27252200	-1.75813700	2.22927300
С	3.23502100	-2.76349700	2.37237900
С	1.31351900	-1.91196300	1.21564000
С	3.25618800	-3.87983000	1.53546300
Н	3.98632200	-2.66264600	3.15171300
С	1.33273600	-3.02317600	0.36783900
С	2.30325900	-4.01192900	0.52679900
Н	4.02183100	-4.63895100	1.66772000
Н	0.58494900	-3.10425400	-0.41506500
Н	2.31467200	-4.87351700	-0.13412700
S	0.08156300	-0.65168500	0.89552300
С	-1.04110800	-0.87492300	2.32670100
Н	-1.87023800	-0.18098400	2.17189400
Н	-1.41227800	-1.90193500	2.34623400
Н	-0.53764900	-0.62748600	3.26220900



IIA/IIC

Mn	0.93968700	1.51092300	1.37665200
0	-0.92106800	2.03628900	3.62578100
0	-0.74393600	2.76679100	-0.67912200
Ν	2.08875000	3.15116500	1.64359600
С	3.00899700	3.06497700	2.63286100
С	2.06143300	4.27874200	0.90683900
Н	1.31943200	4.30983400	0.11923200
С	3.87937300	5.24980300	2.14041100
Н	4.57508300	6.06061500	2.33230400
С	2.92802000	5.34370600	1.12582600
Н	2.85490900	6.22706200	0.50026100
С	2.94966400	1.78734300	3.42202800
Н	3.91102400	1.57802200	3.91496200
Н	2.18139600	1.87144000	4.20175900
С	2.28719400	-0.56569300	3.23401400
Н	3.06541900	-0.73703900	3.99232500
Н	1.33345400	-0.45661100	3.76130600
С	-0.14855100	1.83750900	2.77035600
С	-0.11458800	2.25472500	0.15814800
С	3.91927000	4.08198300	2.90070200
Н	4.64523600	3.95513300	3.69794900
Ν	2.52989900	0.70346800	2.52134100
С	2.28031500	-1.73466300	2.27965700
С	3.23652800	-2.74425600	2.43531500
С	1.36550800	-1.83570500	1.21515600
С	3.29306100	-3.83248100	1.56435700
Н	3.94882900	-2.67231300	3.25368300
С	1.43023900	-2.91985700	0.33586900
С	2.38799100	-3.91955700	0.50839100
Н	4.04524500	-4.60245500	1.70831100
Н	0.72431100	-2.97007300	-0.48721500
Н	2.42664800	-4.75743200	-0.18147800
S	0.09847400	-0.59522700	0.90417900
С	-1.14135600	-1.16684500	2.13428800
Н	-1.98778800	-0.48100100	2.05555600
Н	-1.46110900	-2.18410000	1.89599700
Н	-0.74371100	-1.12181800	3.15039200
Н	3.25101200	0.55327100	1.81740700
Н	1.85866400	1.16768900	0.07430900



IIIA/IIIC

01			
Mn	1.12091700	1.37576300	1.42576700
0	-0.40388700	2.92071000	-0.55150200
0	3.17312100	0.48701000	-0.52845300
Ν	2.32050400	2.89963300	2.01560600
С	3.31232300	2.56844100	2.87340400

С	2.17348900	4.19160100	1.67221100	Ν	2.26180400	2.91667600	1.53465400
Н	1.35547700	4.41110100	0.99762100	С	3.41749700	2.58236500	2.15313500
С	4.04114700	4.85493400	3.02237500	С	2.04578300	4.21225800	1.23996300
Н	4.71158400	5.61305400	3.41511400	Н	1.11351400	4.43456800	0.73633100
С	3.01162600	5.19441900	2.14625200	С	4.13338300	4.87893800	2.21115200
Н	2.84927500	6.22044300	1.83399800	Н	4.85833700	5.63955000	2.48375600
С	3.39322200	1.10578500	3.22750500	С	2.95095500	5.21892800	1.55635500
Н	4.01962800	0.57192000	2.50091200	Н	2.72057000	6.24692600	1.29856400
Н	3.85372300	0.97861000	4.21948600	С	3.61055700	1.11127600	2.41651000
С	1.92845700	-0.86680400	3.55004000	Н	4.09326600	0.63772000	1.55022600
Н	2.66625100	-1.10869500	4.32797400	Н	4.27212600	0.96448600	3.28431900
Н	0.94287900	-0.98260500	4.00821000	С	2.29174700	-0.91425300	2.95745900
С	0.21890000	2.28277800	0.19819700	Н	3.18567100	-1.16835600	3.54421200
С	2.36720800	0.80441600	0.24950200	Н	1.43597000	-1.06903100	3.62125300
С	4.18408100	3.52013400	3.39565100	С	-0.23464700	2.33310900	0.31218500
Н	4.95969000	3.21209200	4.08974800	С	1.87714300	0.93052300	-0.26942200
N	2.03968900	0.55011000	3.16123100	С	4.36473700	3.53847600	2.51209000
С	2.07415200	-1.84356500	2.40856100	Н	5.26926500	3.22756000	3.02494500
С	3.10627400	-2.78390900	2.42725500	Ν	2.29304200	0.51280600	2.61158400
С	1.16778600	-1.86467000	1.33023800	С	2.19596400	-1.85305100	1.77649800
С	3.25874700	-3.71869000	1.40089500	С	3.22092200	-2.77225500	1.54076200
Н	3.80500300	-2.77891700	3.26051200	С	1.08012900	-1.86379100	0.91558200
С	1.31893400	-2.79848200	0.30320400	С	3.16106300	-3.67562600	0.47752800
С	2.36258800	-3.72579000	0.33558700	Н	4.08306900	-2.77638000	2.20340000
Н	4.07637500	-4.43258300	1.43568600	С	1.01851500	-2.76598800	-0.14840300
Н	0.61875100	-2.78853800	-0.52599700	С	2.05600300	-3.67395800	-0.36932600
Н	2.47101500	-4.44526500	-0.47047400	Н	3.97747300	-4.37268500	0.31319000
S	-0.10222600	-0.60975900	1.09241300	Н	0.15753300	-2.74450900	-0.80894300
С	-1.27268400	-0.89794800	2.47774600	Н	1.99863400	-4.36854200	-1.20197100
Н	-2.23933600	-0.52003100	2.13775200	S	-0.23241100	-0.63273300	1.00768000
Н	-1.34674900	-1.96944700	2.67465900	С	-1.17512300	-1.15663500	2.49038700
Н	-0.97469400	-0.33047800	3.35937500	Н	-2.02252600	-0.47117000	2.56762000
N	-0.12171400	1.94807200	2.88822300	Н	-1.53782800	-2.17538200	2.34005700
С	-1.93406300	3.04448000	4.09631100	Н	-0.58601900	-1.09794500	3.40715000
С	-3.05555600	3.87601900	3.98099500	Ν	0.15203600	1.83867600	3.05898400
С	-1.60108500	2.53482700	5.36027000	С	-0.43168400	3.11542000	3.39598000
С	-3.82931900	4.19289900	5.09802300	Н	0.10997100	3.89224000	2.82798400
Н	-3.31843000	4.27366900	3.00261700	С	-0.21695200	3.42918400	4.87445200
С	-2.36957800	2.84842800	6.47651200	С	1.00444800	3.97626700	5.28553100
Н	-0.72763900	1.89373300	5.43572700	С	-1.17923800	3.12448100	5.84165500
С	-3.48864900	3.67958400	6.35026100	С	1.26522800	4.20740900	6.63490000
H	-4.69699500	4.83888600	4.99178500	Н	1.75524500	4.21570700	4.53461500
H	-2.10033600	2.44773900	7.45084100	С	-0.92120900	3.35283800	7.19528900
H	-4.08868800	3.92400100	7.22271600	Н	-2.12945300	2.71503200	5.51250000
H	1.38300900	1.10049600	3.73668900	С	0.30084100	3.89395400	7.59738800
C	-1.13024200	2.71422800	2.88676600	Н	2.21694500	4.63697100	6.93858300
H	-1.51887700	3.20561200	1.97091400	H	-1.67870100	3.11274600	7.93756200
				H	0.49969900	4.07610200	8.65021700
				Н	-0.50200600	1.13825800	3.41125800



IVA/IVC			
01			
Mn	0.96128000	1.38550500	1.21198100
0	-1.01891600	3.00236400	-0.23640000
0	2.48344400	0.67782600	-1.23029700

1.87714300	0.93052300	-0.26942200
4.36473700	3.53847600	2.51209000
5.26926500	3.22756000	3.02494500
2.29304200	0.51280600	2.61158400
2.19596400	-1.85305100	1.77649800
3.22092200	-2.77225500	1.54076200
1.08012900	-1.86379100	0.91558200
3.16106300	-3.67562600	0.47752800
4.08306900	-2.77638000	2.20340000
1.01851500	-2.76598800	-0.14840300
2.05600300	-3.67395800	-0.36932600
3.97747300	-4.37268500	0.31319000
0.15753300	-2.74450900	-0.80894300
1.99863400	-4.36854200	-1.20197100
-0.23241100	-0.63273300	1.00768000
-1.17512300	-1.15663500	2.49038700
-2.02252600	-0.47117000	2.56762000
-1.53782800	-2.17538200	2.34005700
-0.58601900	-1.09794500	3.40715000
0.15203600	1.83867600	3.05898400
-0.43168400	3.11542000	3.39598000
0 10997100	3 89224000	2 82798400
-0.21695200	3 42918400	4 87445200
1 00444800	3 97626700	5 28553100
-1 17923800	3 12448100	5 84165500
1 26522800	4 20740900	6 63490000
1.20522000	4 21570700	4 53461500
-0.92120900	3 35283800	7 19528900
-2 12945300	2 71503200	5 51250000
0 3008/100	3 89395400	7 59738800
2 21694500	4 63697100	6 93858300
-1 67870100	3 11274600	7 93756200
0.49969900	4 07610200	8 65021700
-0.50200600	1 13825800	3 41125800
1 73487800	1.05727700	3 31393100
-1 86390400	3 14346600	3.06375600
-1.06/05800	2 68066200	2 16352200
2 /1016700	2.00000200	2.10332200
-2.41710700	4.495753000	2.93278100
1 80010200	5 1353/300	2,28603300
-1.80910200	1 43825100	2.28003300
-3.83029400	4.43823100	2.43800900
-4.92208800	4.40743800	1.06212400
-4.07994800	4.55529000	1.00212400
-0.22/02000	4.30309300	4 38046100
-4./3901000	4.4042/100	4.36900100
-3.38334600	4.24483300	0.3/033400
-3.23998400	4.3024/400	0.5/185800
-0.40131000	4.222/8900	1.40339/00
-1.00233800	4.20009000	0.40452700
-3.33/40000	4.10105/00	-0.49452/00
-/.4//30000	4.14551700	1.08029900

Н Ν Н

С

Η

H C C C C H C H C H

С Н Н



V	A/	V	C
0	1		

Mn	0.99570500	1.32920300	1.07753300
0	-0.64896200	2.59975300	-0.99899200
0	3.15864200	0.44184100	-0.74466600
Ν	2.08290900	2.97780100	1.53831500
С	3.03968200	2.80866000	2.47997500
С	1.90938700	4.20747200	1.01724500
Н	1.13071400	4.29666700	0.26975300
С	3.66240300	5.13001300	2.36875900
Н	4.27676400	5.96383200	2.69411900
С	2.67604000	5.30249700	1.39875300
Н	2.49417600	6.26921900	0.94142800
С	3.18972900	1.40482900	3.00464600
Н	3.91143800	0.85457900	2.38494100
Н	3.58618300	1.42388900	4.03231300
С	1.89244900	-0.65000700	3.42313700
Н	2.61625600	-0.75795100	4.24336500
Н	0.90412000	-0.81589900	3.85958700
С	0.02421600	2.07010600	-0.20796100
С	2.29968300	0.75924500	-0.02366400
С	3.83792900	3.86234500	2.91885300
Н	4.58577200	3.68255800	3.68484200
Ν	1.89848900	0.72880600	2.91044800
С	2.16908100	-1.70297700	2.37727900
С	3.27517700	-2.54488300	2.50779400
С	1.31533200	-1.88578000	1.27233900
С	3.55068800	-3.53657700	1.56358000
Н	3.93479600	-2.41510800	3.36263000
С	1.58863900	-2.87586400	0.32685100
С	2.70572400	-3.70176600	0.46952600
Н	4.42386600	-4.17112300	1.68366100
Н	0.92622000	-2.98983100	-0.52530400
Н	2.91038400	-4.46652700	-0.27374900
S	-0.05007400	-0.77152700	0.90012000
С	-1.22408800	-1.06108000	2.28525800
Н	-2.22458600	-0.88001600	1.88476000
Н	-1.15206500	-2.09983300	2.61373600
Н	-1.03305400	-0.36232400	3.10119200
Ν	-0.33563800	1.98533200	2.50728400
Н	-0.33836200	3.00861100	2.51441700
Н	-1.30903500	1.74895300	2.30556600
Н	1.12640400	1.26795900	3.35798700



IIB/IID 0 1

01			
Mn	0.93968700	1.51092300	1.37665200
0	-0.92106800	2.03628900	3.62578100

0	-0.74393600	2.76679100	-0.67912200
Ν	2.08875000	3.15116500	1.64359600
С	3.00899700	3.06497700	2.63286100
С	2.06143300	4.27874200	0.90683900
Н	1.31943200	4.30983400	0.11923200
С	3.87937300	5.24980300	2.14041100
Н	4.57508300	6.06061500	2.33230400
С	2.92802000	5.34370600	1.12582600
Η	2.85490900	6.22706200	0.50026100
С	2.94966400	1.78734300	3.42202800
Η	3.91102400	1.57802200	3.91496200
Η	2.18139600	1.87144000	4.20175900
С	2.28719400	-0.56569300	3.23401400
Η	3.06541900	-0.73703900	3.99232500
Н	1.33345400	-0.45661100	3.76130600
С	-0.14855100	1.83750900	2.77035600
С	-0.11458800	2.25472500	0.15814800
С	3.91927000	4.08198300	2.90070200
Η	4.64523600	3.95513300	3.69794900
Ν	2.52989900	0.70346800	2.52134100
С	2.28031500	-1.73466300	2.27965700
С	3.23652800	-2.74425600	2.43531500
С	1.36550800	-1.83570500	1.21515600
С	3.29306100	-3.83248100	1.56435700
Η	3.94882900	-2.67231300	3.25368300
С	1.43023900	-2.91985700	0.33586900
С	2.38799100	-3.91955700	0.50839100
Η	4.04524500	-4.60245500	1.70831100
Η	0.72431100	-2.97007300	-0.48721500
Η	2.42664800	-4.75743200	-0.18147800
S	0.09847400	-0.59522700	0.90417900
С	-1.14135600	-1.16684500	2.13428800
Η	-1.98778800	-0.48100100	2.05555600
Н	-1.46110900	-2.18410000	1.89599700
Н	-0.74371100	-1.12181800	3.15039200
Н	3.25101200	0.55327100	1.81740700
Н	1.85866400	1.16768900	0.07430900



IIIB/IIID 0 1

Mn	1.32441800	1.58186100	1.46566800
0	-0.05234400	3.11244500	-0.63360300
0	3.21319100	0.22459200	-0.37131500
N	2.60052000	3.07216600	1.97150000
С	3.53544700	2.75633600	2.89599900
С	2.53226900	4.34539400	1.54249800
Н	1.75920300	4.55919700	0.81536900
С	4.35910200	5.01420900	2.94567700
Н	5.04192800	5.76703800	3.32708600
С	3.39148300	5.33954600	1.99674000
Н	3.29123700	6.34942400	1.61369700
С	3.54551900	1.31288100	3.32407800
Н	4.17819800	0.72816400	2.64257800
Н	3.96621000	1.21007700	4.33596300
С	2.04819800	-0.63534500	3.54171100

Н	2.70840200	-0.90956000	4.37744300
С	0.50540800	2.47763900	0.16748800
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С	4.42276400	3.70042500	3.40511200
Н	5.14892300	3.40305100	4.15513600
Ν	2.17937000	0.79694700	3.22743800
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С	-1.97122900	2.96384000	3.97644900
С	-3.16276700	3.68938100	3.85156600
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Н	-3.40453800	4.14667100	2.89403900
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Н	-0.75845900	1.78191600	5.28366600
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Н	-4.95029900	4.39856700	4.82441700
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С	-1.07207100	2.78906000	2.80248500
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С	-2.01710400	-1.37264300	4.82401100
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Н	1.19153200	-1.52577700	5.92269500
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Н	-0.39287300	-2.45871400	0.64193100
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С	2.17096700	4.32557100	1.35102800
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Н	4.91434900	5.72029400	2.77524000
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Н	2.84399000	6.35706000	1.49010500
С	3.67393900	1.19810800	2.51578900
Н	4.16780800	0.75925300	1.63748900
Н	4.32065000	1.01091000	3.38623400

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-0.21970100	3.64444900	4.88567500
0.98527500	4.22152800	5.30497800
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-0.35036100	1.28536700	3.56417200
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-1.81291100	3.22610500	3.05227100
-1.88848000	2.67014900	2.20371900
-2.39112400	4.54848800	2.80470400
-2.38377200	5.10326300	3.75022100
-1.78719500	5.13408600	2.08504100
-3.80158000	4.41460500	2.28695700
-4.88673400	4.34748600	3.16804200
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-6.18426200	4.17220300	2.68773600
-4.70648400	4.43257200	4.23685600
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-7 01822100	4 12823100	3 38340900
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1 13045100	-1 41652400	3 42095600
-1 28572500	-1 69830300	3 53780400
1 23033600	-2 11536200	4 62875600
-1 16322500	-2.11330200	4 74040000
-2 26433900	-1.51262200	3 1066/000
0 10130100	-2 60548100	5 28517200
2 21381700	-2.00346100	5.065/3300
_2.21301700	-2.20070100	5.00343300
-2.03085700	-2.73919300	5.24/99000
0.2121/200	-3.13934200	0.22413100
-0.00114900	-1.37010100	0.12024900
	-1.13277300	-0.83993400
1.04142/00	-1.90013/00	0.2229/000
-0.00001300	-2.45561000	0.25220800
2.54936200	-1.299/3/00	1.78024400





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0	3.45671100	0.44130900	-0.74386200
Ν	2.08954500	2.95501200	1.57805500
С	2.96530800	2.82962700	2.60077500
С	1.81841500	4.19203900	1.12055300
Н	1.10981200	4.24889500	0.30357600
С	3.30067100	5.20894400	2.70830900
Н	3.76932500	6.08202300	3.15178400
С	2.40225700	5.33724600	1.65030500
Н	2.14660300	6.30782000	1.23870200
С	3.25656800	1.41610300	3.02594800
Н	4.08809500	1.02593700	2.42146500
Н	3.57627600	1.38572400	4.07919000
С	2.32836200	-0.84456400	3.01061100
Н	2.97679300	-0.98164700	3.88866600
С	0.22851900	1.98476700	-0.31272300
С	2.56202400	0.76248900	-0.06436400
С	3.57923800	3.93194300	3.19004200
Н	4.26556000	3.78231300	4.01762400
Ν	2.08405200	0.58314700	2.76953100
S	0.05359600	-0.79806500	0.74000000
Ν	-0.22202300	1.70541600	2.40654400
Н	-0.41520200	2.70933800	2.37477600
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Н	1.23670200	0.93567900	3.26987500
С	1.03432400	-2.01703600	-0.21350500
Н	0.50774900	-2.97365500	-0.23764000
Н	1.12779700	-1.61553500	-1.22490500
Н	2.03177200	-2.14028200	0.21227500
С	-0.01010400	-1.64669300	2.32477200
С	-1.18643800	-2.34057400	2.62171200
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С	-1.32720100	-3.01552500	3.83424700
Н	-1.99169000	-2.34449000	1.89367400
С	0.88204700	-2.28349700	4.46700900
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Н	-2.24535400	-3.55265300	4.05289100
Н	1.68737000	-2.25339200	5.19654800
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01			
Mn	0.91445200	1.36471300	1.38571000
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Ν	2.06356600	2.98476900	1.63078700
С	2.93378500	2.92138100	2.66237000
С	2.02217300	4.10901200	0.88524600
Н	1.30777000	4.10531600	0.07071200
С	3.73278100	5.14432600	2.20635300
Н	4.38321400	5.98371700	2.43231600
С	2.83510100	5.20351600	1.13729200
Н	2.76285300	6.08324300	0.50701500
С	2.91362000	1.62535900	3.41935200
Н	3.93181100	1.19066400	3.41471900

Н	2.68445100	1.82949800	4.48312500
С	1.92175100	-0.57886800	3.40967900
Н	2.93761400	-0.99626800	3.51284700
Н	1.48703400	-0.55851900	4.42621000
С	-0.58060700	2.32297900	1.19149700
С	1.15210800	1.23625400	-0.37568800
С	3.77808900	3.98682200	2.97531500
Н	4.46098400	3.89627700	3.81446300
Ν	1.95061900	0.74674200	2.80987300
С	1.13496900	-1.46091400	2.49144500
С	1.41345800	-2.65033500	1.89579900
S	-0.26323300	-0.69958300	1.74685500
С	0.50950900	-2.97049700	0.81898600
Н	2.26371700	-3.26696400	2.16716000
С	-0.40781400	-1.99628000	0.57639900
Н	0.56524900	-3.89071600	0.24724800
Н	-1.21082900	-1.98659900	-0.14735800

Mn

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IIA'/IIC'			
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	0.17600200	1.30314400	1 22260500
0	-0.1/099200	2.408/8300	-1.52509500
U N	2.22827200	0.57727100	-0.71303200
N C	2.22827200	3.05278300	1.52044700
C	3.11119800	2.95800200	2.54051000
C	1.95983300	4.27633500	1.0258/000
Н	1.24261800	4.306/0900	0.21508200
C	3.45523500	5.33890800	2.57418400
Н	3.93048800	6.22378800	2.98566900
C	2.55241200	5.43450100	1.5168/800
Н	2.29802800	6.39231700	1.07557700
C	3.38170300	1.55612100	3.03718300
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С	2.23063600	-0.67353300	3.20700000
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С	0.47335400	1.93915300	-0.47729400
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Н	4.41804900	3.95084300	3.92768500
Ν	2.14218000	0.78034600	2.90587400
Н	-0.01594300	1.68707100	1.70246800
Н	1.41141000	1.20769100	3.46706700
С	2.00056100	-1.46874600	1.95897100
С	2.80157900	-2.36735500	1.32489700
S	0.59800400	-1.05540900	0.97061600
С	2.30816000	-2.74983000	0.02868600
Н	3.74034500	-2.72063800	1.73888500
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IIIA'/IIIC' 0 1

Mn	1.45324200	1.35770600	1.38254500
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Ν	2.51626000	2.97399700	2.00587300
С	3.36318900	2.76843300	3.04304400
С	2.32636200	4.23431500	1.57393600
Н	1.63110300	4.35087900	0.75206600
С	3.83413400	5.12274700	3.21187900
Н	4.34342900	5.95555800	3.68664000
С	2.96648500	5.32983700	2.14142900
Н	2.77420300	6.32355100	1.75149600
С	3.57156900	1.33138600	3.46253200
Н	4.36644700	0.89281200	2.84432000
Н	3.90530800	1.28880700	4.50997300
С	2.43315900	-0.89838100	3.37441600
Н	3.48259400	-1.20196600	3.44482600
Н	1.94632200	-1.19601700	4.31197800
С	0.53186300	2.13607300	0.07991600
С	2.75738700	0.74514300	0.28463000
С	4.02684200	3.82068600	3.66827400
Н	4.68432700	3.61343700	4.50668800
Ν	2.34667300	0.57146200	3.21390500
Ν	0.11047300	1.84494100	2.78402900
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Н	-3.14317800	4.09151500	2.76701200
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S	0.27862300	-1.02910100	1.55325800
С	1.56314500	-2.82439200	0.21834700
Н	3.34050500	-2.98201100	1.55295900
С	0.42795000	-2.07485300	0.16379100
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Ő	2 40786200	0 59828600	-1 32507200
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C	2 84567200	2 20242600	1.20437100
C	2.84307300	3.30343000	0.85007700
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C II	2.02030400	5.70057500	1.90237900
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C	1.46496300	5.53677700	1.1536/900
Н	0.85820400	6.38000600	0.84534000
С	3.59250800	2.04073600	2.33642900
Н	4.26289900	1.77881900	1.50612700
Н	4.22223000	2.21968000	3.22075900
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Ν	2.65053100	0.93829500	2.51275700
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C	2.41216700	-1.38619600	1.80891200
Č	2.81461200	-2.29044900	0.87406600
S	0.65445700	-1 24519900	1 82022000
C C	1 72595500	-2.88729600	0.14920700
н	3 85885500	-2 49828400	0.66591800
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н	1 86032900	-3 63009300	-0 62912600
н	-0.46878300	-2 67208800	0.14853500
C	-1 45055200	4 78204100	2 73469800
Č	_2 00017800	5 20060/00	1 584/1800
Č	-0.87553700	5 69588500	3 64001700
~	0.01000000	2.02200200	2.0-001/00

1.51660100	1.16744600	0.81896200
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01			
Mn	1.43831500	1.21959800	0.91813800
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0	3.85368500	0.33660600	-0.56378000
Ν	2.26289800	2.98993700	1.49822600
С	2.97097300	2.97674300	2.65379100
С	2.05563800	4.17432500	0.88992200
Н	1.48263500	4.13598000	-0.02834600
С	3.25246400	5.36803000	2.58915500
Н	3.63331800	6.28925200	3.01905300
С	2.53450100	5.37742800	1.39442700
Н	2.33662000	6.29962600	0.85863700
С	3.24317600	1.62136900	3.26594500
Н	4.17805800	1.23075800	2.83951400
Н	3.39730600	1.72570500	4.35109900
С	2.39142600	-0.72682900	3.23843500
Н	3.45053400	-0.90002800	3.45607300
Н	1.82700200	-1.00132200	4.13975100
С	0.55562300	1.79629800	-0.51010700
С	2.90605800	0.68303200	0.01762400
С	3.46606900	4.14735700	3.22450800
Н	4.01400200	4.09235600	4.15996700
Ν	2.17094300	0.69739500	2.91683100
Ν	-0.12866300	1.68492700	2.17975000
Н	-0.30775700	2.69201300	2.16577100
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С	2.01026200	-1.58426000	2.06441800
С	2.73074200	-2.54319200	1.41947000
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Н	3.69793100	-2.88880600	1.76896000
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С	-2.12747600	6.65912800	1.33926500
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Н	-0.40980200	5.33006000	4.54815000
С	-1.53252700	7.56203300	2.22777800
Η	-2.62126100	7.02383100	0.44191600
Η	-0.46309300	7.74993600	4.08942700
Η	-1.56399300	8.63001700	2.03412000

0	-0.03900200	2.22280700	-1.44176900
0	4.00212900	0.61712000	-0.71369500
Ν	2.23243700	2.95329200	1.50850400
С	3.03772500	2.90407500	2.59795000
С	1.91816500	4.16321000	1.00776700
Н	1.26599200	4.15810300	0.14341300
С	3.20398300	5.30196300	2.68385700
Н	3.57876700	6.21098000	3.14373100
С	2.38400700	5.35200100	1.55824400
Н	2.09667500	6.29673900	1.10916400
С	3.38419600	1.51730200	3.08520000
Н	4.23584400	1.13294100	2.50829700
Н	3.67665100	1.53805100	4.14537500
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Н	2.65200200	-1.09379600	4.03630000
С	0.60294000	1.77883400	-0.57655400
С	3.03896900	0.80327700	-0.08141100
С	3.52776200	4.05276100	3.21107300
Н	4.15778000	3.96189200	4.09052700
Ν	2.24888100	0.63124600	2.81453000
Н	0.06862100	1.53227900	1.59000200
Н	1.43788000	0.90634400	3.36518200
С	1.28146700	-1.51833800	2.44538700
С	0.24533800	-2.11318900	3.10067800
S	0.87970400	-1.23273100	0.75855900
С	-0.89447500	-2.35001100	2.25685300
Н	0.26880900	-2.34827700	4.16000600
С	-0.72274100	-1.88354600	0.98884400
Н	-1.80028300	-2.84008700	2.59632000
Н	-1.40372100	-1.94302300	0.15100300
Η	3.39284200	-1.06313400	2.41969500

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IIIB'/IIID'		
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Mn	1.55526800	1.52471600
0	0.10374700	2.95755200
0	3.54980100	0.26217200
Ν	2.82190900	3.01615500
С	3.70977200	2.72354300
С	2.77734300	4.27701200

2.04391600 4.46653100

4.52439300 4.98742200

5.18519800 5.75152700

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3.52897400 6.28406600

3.72034200 1.28780600

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4.08788000 1.22744700

2.16942800 -0.68841200

2.77921100 0.75492200

4.56582000 3.68624700

5.25317200 3.41157200

2.37220200 0.75063500

0.24380700 2.14449200

 $2.35001600 \quad -0.96548200 \quad 4.54746300$

0.69843900 2.36705600 0.12389500

-1.93419500 2.38437900 3.86812400

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-0.68276400

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0.35045700

3.48345400

4.27740800

3.26269700

2.80490200

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С	-3.31873000	2.41793800	3.66100800
С	-1.44804100	2.41569800	5.18324900
С	-4.20211500	2.47881500	4.73958900
Н	-3.69968000	2.39065900	2.64187000
С	-2.32486300	2.47916700	6.26130000
Н	-0.37189300	2.38679600	5.32570000
С	-3.70754400	2.50898200	6.04440600
Н	-5.27439300	2.50305900	4.56283800
Н	-1.93612200	2.50550300	7.27652400
Н	-4.39193300	2.55648600	6.88722900
Н	1.67542500	1.29210100	3.80153800
С	-1.01302300	2.26338300	2.70498900
Н	-1.55216200	2.23957400	1.73490000
С	0.74724100	-0.99079500	3.13177700
С	-0.34712700	-1.06939700	3.94157100
S	0.26382400	-0.86534500	1.44465400
С	-1.58915600	-1.04403200	3.22516000
Н	-0.28013500	-1.09311600	5.02393100
С	-1.42274500	-0.91366000	1.87911700
Н	-2.55951200	-1.09464700	3.70503300
Н	-2.17903500	-0.88109900	1.10726900
Н	2.88146600	-1.24126300	2.87547400



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0	2.70458500	0.60541600	-1.23096400
Ν	2.47691700	3.00453900	1.53312200
С	3.60828200	2.72724700	2.22585900
С	2.19774300	4.29139900	1.25237000
Н	1.28643900	4.46660800	0.69462800
С	4.16639700	5.06418500	2.37985400
Н	4.81975400	5.86174100	2.71937100
С	3.01233800	5.34504600	1.65153800
Н	2.73252500	6.36249500	1.40116600
С	3.89592000	1.26384200	2.46956300
Н	4.43858100	0.85166000	1.60715500
Н	4.53925100	1.14419900	3.35390900
С	2.65118100	-0.90131000	2.67505300
Н	3.20245200	-1.28715100	1.80901200
Н	3.15777300	-1.25647100	3.58415200
С	-0.02386700	2.31677700	0.29252400
С	2.11988700	0.93035500	-0.27798200
С	4.46265200	3.73353000	2.66857300
Н	5.34745900	3.46835400	3.23830100
Ν	2.62161000	0.56526200	2.58954400
Ν	0.39379900	1.80716200	3.03478000
С	-0.30043600	3.02426500	3.37971700
Н	0.18078200	3.84869500	2.82144400
С	-0.11720500	3.33973500	4.86242200
С	1.06748800	3.95365200	5.28665500
С	-1.06780300	2.97406800	5.81945100

С	1.30337100	4.19239600	6.63908500
Н	1.80919600	4.23914000	4.54298900
С	-0.83429800	3.20936000	7.17658500
Н	-1.98856000	2.51049800	5.47900300
С	0.35072900	3.81830700	7.59186000
Н	2.22615000	4.67454700	6.95319000
Н	-1.58238700	2.92117000	7.91130700
Н	0.52999800	4.00608700	8.64725600
Н	-0.19080800	1.03381500	3.36490000
Н	2.03267300	0.98539200	3.34240800
Ν	-1.72784100	2.94300200	3.03989700
Н	-1.79533800	2.43576900	2.16091100
С	-2.37284600	4.24805400	2.88088100
Н	-2.37680200	4.74584500	3.85745700
Н	-1.80914800	4.90432500	2.18977500
С	-3.78314600	4.07518100	2.37423100
С	-4.85468200	3.93325600	3.26284900
С	-4.03024400	3.98931500	0.99879200
С	-6.14933800	3.72119600	2.78922100
Н	-4.66660400	3.98913800	4.33223400
С	-5.32357800	3.77305100	0.52071200
Н	-3.20009100	4.08429200	0.30323600
С	-6.38719200	3.64130800	1.41521100
Н	-6.97298400	3.61917500	3.49100000
Н	-5.50079900	3.71116400	-0.54976200
Н	-7.39561200	3.47823300	1.04456000
С	1.22416800	-1.36259900	2.68341600
С	0.45234800	-1.73833000	3.74323300
S	0.22542000	-1.04802600	1.26903000
С	-0.95032100	-1.78612600	3.43871500
Н	0.86065900	-1.93182800	4.72949300
С	-1.22889700	-1.41295500	2.15763800
Н	-1.71119300	-2.07768500	4.15385400
Н	-2.18860000	-1.37165500	1.66118900

H₂N H N CO CO

VB'/VD'

01			
Mn	1.42080300	1.14442300	1.01483500
0	-0.19375600	2.06985900	-1.26456700
0	3.84691200	0.41294500	-0.53160700
Ν	2.21918800	2.94276100	1.53924400
С	3.01258000	2.95069700	2.63799600
С	1.93901500	4.11794400	0.94440200
Н	1.29956400	4.06222100	0.07196100
С	3.23980300	5.34567400	2.53996900
Н	3.63473700	6.27694400	2.93401200
С	2.42890800	5.33387500	1.40649400
Н	2.16953700	6.24900600	0.88506100
С	3.33441400	1.60153300	3.23882800
Н	4.23796200	1.20202400	2.75606300
Н	3.55595700	1.70738400	4.31200100
С	2.43761500	-0.72444300	3.29761000
Н	3.34673900	-1.07070900	2.79025100
Н	2.57336800	-0.88600300	4.37750100
С	0.46942800	1.67900800	-0.39013500
С	2.88904800	0.68405500	0.07464900
С	3.52829400	4.13339700	3.16225000

Н	4.14884800	4.09510600	4.05204100
Ν	2.23197000	0.68986000	2.96495700
Ν	-0.11906600	1.57555000	2.29939300
Н	-0.50410100	2.50855400	2.13730800
H	-0.91262900	0.94810700	2.14481600
H	1.314/1400	1.04329000	3.32818600
C	1.22126000	-1.46//5000	2.83269500
C	0.18351400	-1.96//1300	3.56086800
S	0.82063200	-1.43013/00	1.12101400
U U	-0.95170000	-2.33027800	2.75929000
н С	0.20276700	-2.03/91900	4.04327800
С ц	-0.77399300	-2.00419900	1.45452000
н	-1.44806100	-2.70483100	0.61146900
	1.11000100	2.23017700	0.01140900
TS-IA			
01			
Mn	0.93687400	0.96243700	1.17230200
0	-0.61372000	1.54205500	-1.28485100
0	3.03891100	-0.20226500	-0.52899900
Ν	1.97439500	2.71779400	1.13424400
С	3.03919900	2.77621600	1.96654200
С	1.70129600	3.78492900	0.35989600
Н	0.82914400	3.70921800	-0.27646100
С	3.56772600	5.00506500	1.23892600
Н	4.18524600	5.89650300	1.28924400
С	2.47159500	4.94188000	0.38112000
Н	2.18715100	5.77512600	-0.25136700
C	3.28380900	1.53449100	2.78677200
H	3.95012100	0.84909000	2.24829500
H C	3.76543400	1./9446200	3.74075000
U U	2.07638700	-0.39631700	3.77164900
н u	2.816/2400	-0.28998000	4.57676000
п	0.06126700	-0.30934800	4.24037700
C	2 19854000	0.23274400	0.14922700
C	3 84868400	3 90489600	2 04711800
н	4 68039500	3 91874300	2 74397800
N	1.99814600	0.85285300	2.98497300
C	2.39917900	-1.61743600	2.94973400
Č	3.59441000	-2.30694600	3.16375100
С	1.50746600	-2.10219200	1.97255600
С	3.91922600	-3.44410900	2.42097200
Н	4.28272700	-1.94251800	3.92275000
С	1.83158100	-3.23812800	1.22874700
С	3.03570200	-3.90981200	1.45076300
Н	4.85882400	-3.95812500	2.60022700
Н	1.13822000	-3.58805600	0.47076800
Н	3.27731000	-4.79166800	0.86509400
S	0.01483500	-1.21592400	1.49351100
C	-1.03702600	-1.31431500	3.00072300
H	-2.05303500	-1.52028700	2.66095100
H	-0.68697800	-2.133/3200	3.03103500
н u	-1.01446200	-0.34/40000	3.30/11000
п N	1.3/030400	1.4//28000	2.49/01400 2.56008800
C	-0.04003800	3 03/53300	2.50090000
н	-0.5415870200	3 61348800	1 64872100
C	0.21632500	3 73585500	3 62585400
Č	0 72403000	5 02246400	3 40248500
Č	0 46374700	3 11071600	4 85798800
Č	1.50328200	5.65201100	4.37139400
й	0.51198000	5.51758300	2.46089000
C	1.24305900	3.73967800	5.82759100
Н	0.01664800	2.13705400	5.03786200
С	1.77335900	5.00972600	5.58241500
Н	1.90314700	6.64444000	4.18165900

н	1.42743900	3.24803300	6,77920400
н	2 38113400	5 50140000	6 3 3 7 0 0 7 0 0
N	-2 55951400	3 74783700	2 86014400
ц	2.01020600	2 00000000	2.00014400
Г	-2.91029000	2.99009900	2.19479700
C II	-2.80415400	5.10980700	2.414/0300
Н	-3.95095600	5.24//6000	2.28004600
Н	-2.55199900	5.81636700	3.19349400
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Н	-1.42052600	1.49227900	1.88605500
С	-2.15760800	5.46939700	1.11629000
С	-1.48768000	6.69287900	1.00295600
С	-2.15066800	4.58512100	0.02431000
Č	-0.81584900	7.03833000	-0.17313900
н	-1 48255300	7 38001200	1 84662900
C	1 47170000	4 02020000	1.04002000
с u	2 60820100	4.52525000	0.12252100
п	-2.00829100	5.59558500	0.12232100
C	-0.80520400	6.15428300	-1.25316800
Н	-0.30359500	7.99477000	-0.24212900
Н	-1.45675400	4.22404900	-1.97243600
Н	-0.28504400	6.41756200	-2.17085400
Н	-2.89616600	3.57192600	3.80416900
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Н	-4.76383300	1.48421200	0.28201400
		1110121200	0.20201.00
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M	0.007722000	0.72619000	1 02 42 (700
MII	0.98773200	0.75018900	1.02420700
0	-0.35191100	0.89906900	-1.61185600
0	3.11538000	-0.85103000	-0.23778800
N	1.91068700	2.53743200	0.79021900
C	2.95439300	2.76258500	1.61821800
С	1.49492600	3.53858400	-0.00814500
Н	0.63069600	3.33256700	-0.62702700
С	3.19935900	5.01164600	0.81286100
Н	3.69800700	5.97587800	0.82869300
С	2.10745700	4.78686200	-0.02356800
н	1 70464200	5 56461600	-0 66084000
C	3 31265800	1 60351300	2 50925800
с u	3.00165000	0.02006400	1.08362700
11	2.92159700	1.05271500	2 41946200
H	3.82158700	1.95271500	3.41840300
C	2.33298300	-0.400/9500	3.5532/100
Н	3.12815100	-0.25612800	4.29785200
С	0.11235900	0.81497900	-0.55513700
С	2.27615400	-0.20292800	0.25166400
С	3.62293500	3.98233400	1.65140700
Н	4.44641700	4.12382100	2.34377500
Ν	2.08011900	0.85894600	2.82091000
С	1.07698000	-0.84013800	4,26568000
Č	1.06209300	-0.85713500	5 66450500
C	0.11316200	1 1/185000	3 57002500
C	-0.11310200	1 15208600	6 27502800
C U	-0.1012/000	-1.13508000	0.57505800
H	1.97554100	-0.61624200	6.20230200
C	-1.28304300	-1.42515300	4.28996800
С	-1.28039200	-1.43073100	5.68514000
Н	-0.08675300	-1.15528400	7.46093300
Н	-2.19726300	-1.62168100	3.73984500
Н	-2.19669300	-1.64705600	6.22608300
S	-0.24206400	-1.11612100	1.78822600
C	0.56277600	-2.71314700	1.39116500
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н	1 60525000	_2 73712500	1 71//1200
н	0.00/20000	_3 53012000	1 85210400
11	1 400 49 200	-3.33012000	2 41921100
H	1.49948600	1.449/1600	3.41821100
IN C	-0.69/93400	1.09518400	2.01549400
C	-0.56930100	2.96407200	2.33824700
Н	-0.65076400	3.75610700	1.59709600
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С	0.83095600	4.58121500	3.63260800	С	4.76429500	-1.73212700	2.33304200
С	0.11160200	2,53299900	4,70503500	С	2.40182300	-2.09640700	2.62404700
Ĉ	1 5/1588800	4 92775500	1 7790/900	Č	4 91698600	-3.02772100	1 83503000
	0.92090200	4.72710500	4.77904900	C	<i>4.)</i> 10/0000	-5.02772100	2 41 45 (700
п	0.82080500	3.23/10300	2.70081000	П	3.03144800	-1.08132400	2.41450700
C	0.82355700	2.88185600	5.85140600	C	2.55279200	-3.3929/400	2.12665600
Н	-0.46493200	1.61488500	4.65440700	С	3.80715100	-3.86143900	1.73216200
С	1.54980200	4.07683800	5.88789500	Н	5.89795200	-3.37756000	1.52862500
Н	2.10106400	5.86147000	4.80929800	Н	1.67804500	-4.02958800	2.04078600
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н	2 10475700	4 35005800	6 78121100	S	0 70530600	-1 56589800	2 92397500
N	2.10473700	2 62082200	2 60680400	C C	0.76550000	1.26282600	4 72026000
IN IV	-2.02331200	3.02083300	2.09089400	C	0.00740300	-1.20383000	4.75020900
Н	-2.94517700	3.003/9100	1.88304900	Н	-0.38921000	-1.18929300	5.00013100
С	-2.89183400	5.04451500	2.49792600	Н	1.11099700	-2.11634300	5.24896600
Н	-3.97286400	5.23819900	2.38256900	Н	1.17134100	-0.33758000	5.00522600
Н	-2.56802000	5.59855200	3.38810500	Н	2.17833100	1.75090900	3.17145700
0	-2.94888400	2.07028200	0.55954500	Ν	-0.27963400	1.62813300	3.21805800
о U	1 43227500	1 66545800	1 25015000	C	0.15380000	3 37201700	3 86034700
	-1.43227300	5 (0292000	1.23913900	C	0.13389900	2 72804(00	2 97070400
C	-2.16/23/00	5.60282000	1.28240200	Н	0.46138500	3.73804600	2.87970400
C	-1.43/71200	6.79228700	1.38984800	С	1.36394400	3.10993500	4.72071800
С	-2.21997100	4.94446400	0.04131300	С	2.56234800	3.76460700	4.39570100
С	-0.77863600	7.33424800	0.28307200	С	1.36540700	2.24295600	5.82487100
Н	-1.38362200	7.30057600	2.35028800	С	3.73106700	3.54289900	5.12656100
C	-1 55322900	5 48470000	-1 05948400	Ĥ	2 57167100	4 44526600	3 54768100
с u	2 72620400	2 07845100	0.04206200	II C	2.57107100	2 02200500	6 56267200
п	-2.72039400	5.97845100	-0.04296200	C	2.52939400	2.02500500	0.30207300
C	-0.83891600	6.68225500	-0.94916600	Н	0.45121300	1./2906100	6.10082100
Н	-0.22307700	8.26308100	0.38546800	С	3.71955800	2.66632100	6.21298500
Н	-1.59809000	4.96435500	-2.01312000	Н	4.64755600	4.05808800	4.85118700
Н	-0.33680400	7.10399900	-1.81675800	Н	2.50744900	1.34683400	7.41324900
н	-3.01082900	3,27645200	3,57325900	Н	4.62546600	2,49034700	6.78582300
C	-3 90000900	1 06841800	0 51895700	н	-0 57204300	1 10211500	4 04333500
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S-IB'			
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1	0 60404000	0 46402700	1 (5070500
In	0.60494000	0.46403/00	1.659/9500
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, [-1 11414600	2.47945100	0.09388300
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,	-0.02048000	4.31773400	-0.17789500
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ч	-4.93798700	2 96389300	7.56895300	ч	2 87374700	-0.33286700	5.065555400
C II	-4 58316600	6 02105400	7.30893300 5.48476900	II C	0.21563300	-0.33280700	4 63605600
н	-2 76937800	5 69418500	4 34669900	н	0.66739600	-1 56957200	6 72172600
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C	3.30395300	0.00/38000	3.09967800	C	2.41130400	2.98281100	1.80657100
н u	5./1020100 4.12654700	-0.33493300	2.2550/500	U	1.12492200	3./313/800	0.03294000
П	4.13054/00	0.36221800	5.72156200	H	0.3/20/300	5.48812000	-0./0592500
C	-0.99823000	0.1/303900	1.01554500	U U	2.01208000	5.2/414/00 6.26518600	1.10410500
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C C	0.33367800	1.05605200	0.54651000	C II	2 73751000	1 75505400	2 88603800
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Ċ	1 57591500	-2 07862900	1 92564200	Ċ	3 04708800	4 21948000	2 34612600
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н	4.11918200	-1.51045500	4.09895800	N	1.58012500	0.86964700	2.80000300
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C C	1 1 1 0 7 2 4 0 0	1 60280600	2 70452200	C C	2 04817500	2 17526600	156412200
C II	-1.110/2400	-1.00289000	2.70435500	C	-2.04817300	-2.1/350000	4.30412200
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ч	-2 1/531800	2,55016400	0.75459800	н	1.77619500	-2 51891300	1 30068600
II C	1 22001400	2.55010400	0.75457800	11	0.21115600	2 40042000	0.05201500
C	-1.55001400	4.07084300	2.00870500	п	0.51113600	-5.49042900	0.95201500
C	-1.83/06400	5.07088300	1.1/1/0100	Н	0.69492700	1.35386600	3.08008300
С	-0.49406900	4.43638800	3.06867700	N	-0.74068700	1.57812800	1.97277100
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Н	-2.47496200	4.78786000	0.33617600	Н	-2.22355900	2.41921800	0.64126200
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C	-0 67464500	6 76620200	2 44289900	Ċ	-0.61806100	4 46410000	2 86259700
с u	1 00051400	7 17726200	0.71670500	C C	1 48058500	6 30/77300	0.05457500
11	-1.00001400	(04252000	4 11122200		-1.48058500	4 (0494100	0.04021500
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Ν	-2.86733400	2.17780500	2.74730200	Н	-0.24966100	3.71854200	3.56292600
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н	-2 12022700	1 27936600	2 83568400	н	-0 49145900	7 79220300	2 16316300
C C	-1 19389000	0.92207200	1 30252800	N	-2 787/3300	2 11234600	2.68768100
C	-4.4 <i>)</i> 58 <i>)</i> 000	0.72207200	0.05475600	IN C	-2.78745500	2.11234000	2.00700100
C	-5.81584900	0.61434900	0.954/5600	C	-4.21819500	2.02020000	2.32200800
C	-3.452/6600	0.1/232800	0.74532200	Н	-4.8128/500	2.03119200	3.24239200
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Н	-2.42116300	0.38745800	1.01030700	С	-5.91243500	0.43404400	1.38882600
С	-5.05090300	-1.16977000	-0.48615600	С	-3.59564900	0.04081500	0.84201200
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и П	2 00068500	1 42852000	0.57660000	с u	-0.20000000	1 01727000	1 00177100
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Н	-2.82014800	2.76243800	3.58442400	Н	-2.54373900	0.28946400	0.93352900
				С	-5.31267100	-1.43366300	-0.02370100
TS-IIC				Н	-7.33484400	-0.94747200	0.55477200
				Н	-3.19762700	-1.65273300	-0.40935900
01				Н	-5.60144600	-2.29950800	-0.61301900
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0	_0.71821/00	1 56/62200	-1 57562200	и П	2.05755400	-1 05037100	2 86/08000
0	2 21205500	0.01026500	-1.57502500	п	2.37505000	-1.0373/100	2.00490000
U N	5.21205500	-0.21050500	-0.49030300	mc.	ID		
IN	1.66/91600	2.79572400	0.989/5100	TS-	ID		
C	2.47625800	2.98291400	2.05648800	01			
С	1.41982000	3.84768800	0.18846600	Mn	0.71797800	0.89109600	0.59570800
Н	0.75500200	3.66124400	-0.64454900	0	-1.12186000	0.67623000	-1.69489900
С	2.79062500	5.30294600	1.50977600	0	2.83772000	-0.63287200	-0.80218800

N	1 71602700	2 64600200	0.05122600	TS IID			
N C	2.86220700	2.04009200	0.03123000	13-11D			
C	2.86230700	2.90498100	0.72226300	0.1			
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Н	0.37068700	3.28526600	-1.38491600	Mn	0.60323500	0.87455600	0.60419900
С	3.22802300	4.90834800	-0.55666100	0	-1.15153000	0.66186100	-1.75584700
Н	3.81882500	5.78920200	-0.78889200	0	2.66650100	-0.91013900	-0.52809200
С	2.03612800	4.64983700	-1.22952200	Ν	1.63957100	2.58305400	0.01252900
Н	1.64766600	5.31606200	-1.99006800	С	2.74839000	2.88248600	0.72610600
С	3.22197000	1.92989800	1.82025800	С	1.26596400	3.41550600	-0.97677800
Н	3.80255700	1.09040700	1.41988200	Н	0.35368800	3.16412800	-1.50107000
Н	3.83338100	2,43383300	2.58330300	С	3.13781800	4.86092700	-0.58312200
C	2 12992000	0 45849600	3 50105200	н	3 72114900	5 74838300	-0.80886500
н	2.91286000	0.80927100	4 18833700	C	1 98756600	4 55822700	-1 30713700
и и	1 10137200	0.00527100	4.05003600	с u	1.62350200	5 10566000	2 10308400
C	0.29290900	0.49009100	4.03773000		2.00421500	1 02402400	1 82804000
C	-0.38289800	0.73080800	-0.80202000	C	2 70020200	1.92402400	1.44415400
C	2.00174400	-0.04966500	-0.23980900	H	3.70020300	1.098/9400	1.44415400
C	3.6401/200	4.02420800	0.43968000	H	3.68342200	2.4349/100	2.61380900
Н	4.5460/100	4.2039/500	1.00982800	C	2.08487500	0.26/17/00	3.35339000
Ν	1.97153200	1.40116000	2.38176800	Н	2.87496100	0.54546000	4.06561500
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С	3.66164500	-1.52132400	3.46897700	С	1.85297500	-0.19462800	-0.09383100
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С	1.89387600	-3.06855000	1.99713500	С	0.82156900	-0.02751200	4.12811900
Ĉ	3.11991400	-3.60751100	2,39019600	Ċ	0.78561500	0.28489700	5,48978800
н	4 96674900	-3 23434200	3 43786800	Č	-0 34777300	-0 54294200	3 53257800
н	1 10808000	-3 66003300	1 41081000	C C	-0.36810200	0.10012400	6 25211800
и П	3 37570800	4 62607200	2 11/70000	с ц	1 67351000	0.70486600	5.05371400
п с	0.00092000	-4.02007200	2.114/0900	П	1.07331000	0.70480000	1 2021 (000
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C	-1.0/4/8400	-0.95450700	3.09307900	C	-1.52118400	-0.39/58/00	5.65207500
H	-2.02672700	-0.57461500	2.71497000	H	-0.36572900	0.360/8300	7.30610600
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Ĉ	0 22769100	3 68539100	5 49332200	C	-0 85343400	3 53675100	1 80492100
н	-1 47389200	2 90896800	4 40010700	н	-0 27463500	4 00683700	0.99715000
C	1 85320100	4 88210800	4 16748100	II C	-0.18012500	3 86203500	3 126/3000
U U	1.05520100	4.07728600	2.05040200	C C	0.70172200	3.60203500	4 22085 500
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C II	1.42586500	4.40/13000	5.40697300	C	1.05228100	4.50890900	5.18404500
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H	2.76638700	5.46/69900	4.09281100	H	-1.//9/1900	3.013/2000	4.28111300
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C	-1.04490900	3 82721200	-2 50729700		_2 163/2000	1 07002200	-0 /8730200
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Η	-2.00467100	2.28862400	1.39553600	Н	-2.84030500	2.97880500	-0.92159000
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Н	2.44223300	-0.60362500	2.79484500	TS-IIC'			
TS-IC'				0 1			
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C	3.99485100	3.16518200	0.34955800	H	2.84205600	4.43272000	0.69309600
н	5.50/50200	3.03013300	-0.40064800	U U	4.38080300	4.24445500	3.71009400
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н	5 79609400	4 14026100	-0 27486100	II C	2 42319000	0.98642900	3 51535900
C	3 36440400	0.72020700	2 99585600	н	3 02020300	0.24430800	2 96685600
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C	-1.02000400	4.30381100	2.04011800	C C	-0.93999200	5 44212800	2 02200000
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C	-3 12401700	6 44200600	2,97966500	Н	-1 69249700	6 18699200	0.30174100
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Ν	-2.17537000	2.22826200	1.98125900	С	-3.63962500	3.06835600	2.39476000
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Н	-1.60117100	1.23248300	0.26256300	H	-3.35331300	2.27874600	1.69241300
H	-3.044/2800	0.5/31/600	1.048/0600	H	-1.5440/600	2.85225100	3.14/75900
н С	-1.18158/00	1.80693400	2.55552400	C C	-4.39822300	2.49084500	3.30323100
C	-3.42000000	2.32914000	0.12500700	C C	-3.86066000	1 / 1002900	<i>1</i> 26680400
C	-2 88190500	3 02832200	-1 24150900	C	-6 30568300	2 49622600	5.06264900
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Н	-5.67265200	4.64608000	-2.33252200	Н	-2.50640100	4.46251400	3.47612300
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C	0.75477600	-0.92896200	3.35794900	C	-1.70789700	-1.44853700	3.53587000
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C	1.43584000	2.92771400	-0.3258/800	C
C U	-0.77305500	2.70652200	-1.01018300	H
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C	-0.69345900	3 85043100	-1 79823500	н
н	-1 57282200	4 19377900	-2 32981600	C II
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C	2.84474600	1.09821500	2.69855600	Н
Н	3.87749400	1.13421900	2.33622200	Н
Н	2.81162700	1.62270300	3.66056300	С
С	-1.34415100	-0.04832700	0.48349800	С
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Н	2.53781000	4.60570400	-1.08360600	Ν
Ν	1.93460800	1.81028900	1.75973400	Н
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Ν	-0.98334600	1.95344000	2.23845300	C
С	-0.70850100	3.39565100	2.57499500	Н
Н	0.12852700	3.77388200	1.94613500	C
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H C	-2.28528300	3.1/641400	4.74129600	C II
U U	1.30183000	4.03012200	3.73842000	H C
п С	0.41727300	4.13027000	5.01897500 6.73598400	Ч
н	-1 64462500	3 31357600	7 1 5232200	н
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С	2.28893500	-2.65871700	2.65438600	Н
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Н	-2.17054700	6.04342300	2.04779700	C
C	-2.85171900	5.20694900	0.20548600	C
C C	-3.12988300	4.101/3300	-0.093/4900	C
C	-2.70320700	0.29422000	1.26401900	U TT
с н	-4.47403700	4.10340400	-1.20401800	п
C	-3.79020200	6 32200200	-1 84575300	с u
н	-2 10987300	7 11770000	-0.45111200	C II
Ċ	-4.39789700	5.25707500	-2.15075500	н
Ĥ	-5.16669000	3.35763800	-1.48242200	Н
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ГS-IID'

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)	-2.50851200	0.29198700	-0.46965500
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	2.33297400	0.58378000	2.93243800
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N	-1.14043600	2.00663300	2.31557500
-	-1.16818900	3.50254200	2.50919100
1	-0.94896000	3.98027300	1.54218900
	-0.13521200	3.95552700	3.52043300
	-0.29632100	3.62102700	4.8/441300
-	1.01910300	4.65072800	3.13/15500
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1	-1.226/0200	3.14267900	5.16643300
	2.01444500	4.96240200	4.07065500
1 7	1.13013200	4.94/13800	2.09/50800
J	1.80130000	4.58810100	5.40518900
1 T	0.55450800	5.05802900	0.84991400
1	2.90101000	3.30040200	5.75522000
1	2.03034300	4.62924600	2 22022200
n N	-0.93937800	3 50556000	2 02115700
л Т	-2.33819700	2 29311800	2.92115700
ן. ר	1 20426600	2.29311800	2.43930000
7	0.71841200	0 22128400	4 91109700
S	0.04570700	-1 01802400	2 74615100
, ,	-0 58800100	-0 32937300	5 14918800
ł	1.24123900	0.85866900	5.61525600
7	-1.09104500	-0.99256400	4.07037600
Ŧ	-1.12597300	-0.21701300	6.08361500
Ŧ	-2.03683100	-1.50818900	3.97740900
7	-3.30570900	4.67143700	2.30951900
ł	-2.92195400	5.66769900	2.60135700
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2	-3.38308600	4.63356800	0.78069200
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2	-3.83858300	3.38841800	-1.26306800
H	-3.96035300	2.56536600	0.72258500
2	-3.16985300	5.70301000	-1.39837900
ł	-2.78677800	6.67684000	0.48786600
2	-3.54790600	4.51966800	-2.03471500
ł	-4.12622900	2.45748900	-1.74418800
H	-2.94084000	6.58896100	-1.98667100
ł	-3.61910400	4.47688800	-3.11853600

6.6. References

1. Harvey, J. N.; Himo, F.; Maseras, F.; Perrin, L., Scope and Challenge of Computational Methods for Studying Mechanism and Reactivity in Homogeneous Catalysis. *ACS Catal.* **2019**, *9*, 6803-6813.

2. Poree, C.; Schoenebeck, F., A Holy Grail in Chemistry: Computational Catalyst Design: Feasible or Fiction? *Acc. Chem. Res.* **2017**, *50*, 605-608.

 Sperger, T.; Sanhueza, I. A.; Schoenebeck, F., Computation and Experiment: A Powerful Combination to Understand and Predict Reactivities. *Acc. Chem. Res.* 2016, 49, 1311-1319.

4. Vogiatzis, K. D.; Polynski, M. V.; Kirkland, J. K.; Townsend, J.; Hashemi, A.; Liu, C.; Pidko, E. A., Computational Approach to Molecular Catalysis by 3d Transition Metals: Challenges and Opportunities. *Chem. Rev.* **2019**, *119*, 2453-2523.

5. Norjmaa, G.; Ujaque, G.; Lledós, A., Beyond Continuum Solvent Models in Computational Homogeneous Catalysis. *Top. Catal* **2022**, *65*, 118-140.

 Sunoj, R. B.; Anand, M., Microsolvated transition state models for improved insight into chemical properties and reaction mechanisms. *Phys. Chem. Chem. Phys.* 2012, *14*, 12715-12736.

7. Proutiere, F.; Schoenebeck, F., Solvent Effect on Palladium-Catalyzed Cross-Coupling Reactions and Implications on the Active Catalytic Species. *Angew. Chem. Int. Ed.* **2011**, *50*, 8192-8195.

8. Proutiere, F.; Schoenebeck, F., Orthogonal Selectivities under Pd(0) Catalysis with Solvent Polarity: An Interplay of Computational and Experimental Studies. *Synlett* **2012**, *23*, 645-648.

9. Krieger, A. M.; Sinha, V.; Li, G.; Pidko, E. A., Solvent-Assisted Ketone Reduction by a Homogeneous Mn Catalyst. *Organometallics* **2022**, *41*, 1829-1835.

10. Wachter, N. M.; Rani, N.; Zolfaghari, A.; Tarbox, H.; Mazumder, S., DFT investigations of the unusual reactivity of 2-pyridinecarboxaldehyde in base-catalyzed aldol reactions with acetophenone. *J. Phys. Org. Chem.* **2020**, *33*, e4048.

11. Garduño, J. A.; García, J. J., Toward Amines, Imines, and Imidazoles: A Viewpoint on the 3d Transition-Metal-Catalyzed Homogeneous Hydrogenation of Nitriles. *ACS Catal.* **2020**, *10*, 8012-8022.

12. Sharma, D. M.; Punji, B., 3 d Transition Metal-Catalyzed Hydrogenation of Nitriles and Alkynes. *Chem. Asian J.* **2020**, *15*, 690-708.

13. Lévay, K.; Hegedűs, L., Recent Achievements in the Hydrogenation of Nitriles Catalyzed by Transitional Metals. *Curr. Org. Chem.* **2019**, *23*, 1881-1900.

14. Bagal, D. B.; Bhanage, B. M., Recent Advances in Transition Metal-Catalyzed Hydrogenation of Nitriles. *Adv. Synth. Catal.* **2015**, *357*, 883-900.

15. Sarkar, K.; Das, K.; Kundu, A.; Adhikari, D.; Maji, B., Phosphine-Free Manganese Catalyst Enables Selective Transfer Hydrogenation of Nitriles to Primary and Secondary Amines Using Ammonia–Borane. *ACS Catal.* **2021**, *11*, 2786-2794.

 Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16 Rev. C.01*, Wallingford, CT, 2016.

17. Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlationenergy formula into a functional of the electron density. *Phys. Rev. B* **1988**, *37*, 785-789.

18. Vosko, S. H.; Wilk, L.; Nusair, M., Accurate spin-dependent electron liquid correlation energies for local spin density calculations: a critical analysis. *Can. J. Phys.* **1980**, *58*, 1200-1211.

19. Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. J. Chem. Phys. 1993, 98, 5648-5652.

20. Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J., Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994**, *98*, 11623-11627.

21. Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H., A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.* **2010**, *132*.

22. Hay, P. J.; Wadt, W. R., Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals. *J. Chem. Phys.* **1985**, *82*, 299-310.

23. Wadt, W. R.; Hay, P. J., Ab initio effective core potentials for molecular calculations. Potentials for main group elements Na to Bi. *J. Chem. Phys.* **1985**, *82*, 284-298.

24. Tomasi, J.; Mennucci, B.; Cammi, R., Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105*, 2999-3094.

25. Cossi, M.; Barone, V.; Cammi, R.; Tomasi, J., Ab initio study of solvated molecules: a new implementation of the polarizable continuum model. *Chem. Phys. Lett.* **1996**, *255*, 327-335.

26. Cancès, E.; Mennucci, B.; Tomasi, J., A new integral equation formalism for the polarizable continuum model: Theoretical background and applications to isotropic and anisotropic dielectrics. *J. Chem. Phys.* **1997**, *107*, 3032-3041.

27. Barone, V.; Cossi, M., Quantum Calculation of Molecular Energies and Energy Gradients in Solution by a Conductor Solvent Model. *J. Phys. Chem. A* **1998**, *102*, 1995-2001.

28. Wang, B.; Cao, Z., Hydration of Carbonyl Groups: The Labile H_3O^+ Ion as an Intermediate Modulated by the Surrounding Water Molecules. *Angew. Chem. Int. Ed.* **2011**, *50*, 3266-3270.

29. Zahn, D., Theoretical Study of the Mechanisms of Acid-Catalyzed Amide Hydrolysis in Aqueous Solution. *J. Phys. Chem. B* **2003**, *107*, 12303-12306.

30. Das, M.; Gogoi, A. R.; Sunoj, R. B., Molecular Insights on Solvent Effects in Organic Reactions as Obtained through Computational Chemistry Tools. *J. Org. Chem.* **2022**, *87*, 1630-1640.

31. Alassad, Z.; Nandi, A.; Kozuch, S.; Milo, A., Reactivity and Enantioselectivity in NHC Organocatalysis Provide Evidence for the Complex Role of Modifications at the Secondary Sphere. *J. Am. Chem. Soc.* **2023**, *145*, 89-98.

32. Dutta, S.; Chandra, A., A Multiple Proton Transfer Mechanism for the Charging Step of the Aminoacylation Reaction at the Active Site of Aspartyl tRNA Synthetase. *J. Chem. Inf. Model.* **2023**, *63*, 1819-1832.

33. Dutta, S.; Chandra, A., Free Energy Landscape of the Adenylation Reaction of the Aminoacylation Process at the Active Site of Aspartyl tRNA Synthetase. *J. Phys. Chem. B* **2022**, *126*, 5821-5831.

34. Jana, A.; Das, K.; Kundu, A.; Thorve, P. R.; Adhikari, D.; Maji, B., A Phosphine-Free Manganese Catalyst Enables Stereoselective Synthesis of (1 + n)-Membered Cycloalkanes from Methyl Ketones and 1,n-Diols. *ACS Catal.* **2020**, *10*, 2615-2626.

35. Agmon, N., The Grotthuss mechanism. Chem. Phys. Lett. 1995, 244, 456-462.

36. Burland, M. C.; Meyer, T. Y.; Baik, M.-H., Proton as the Simplest of All Catalysts for [2 + 2] Cycloadditions: DFT Study of Acid-Catalyzed Imine Metathesis. *J. Org. Chem.* **2004**, *69*, 6173-6184.

37. Schaufelberger, F.; Seigel, K.; Ramström, O., Hydrogen-Bond Catalysis of Imine Exchange in Dynamic Covalent Systems. *Chem. Eur. J.* **2020**, *26*, 15581-15588.