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The Development and Mechanistic Investigations of Various Catalytic Processes by Mesoporous Metal Oxides and Sulfides

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The Development and Mechanistic Investigations of Various Catalytic Processes by Mesoporous Metal Oxides and Sulfides

Biswanath Dutta, PhD

University of Connecticut, 2018

This thesis includes five chapters. The 1st Chapter provides a brief introduction of mesoporous materials and heterogeneous catalysis. Chapter 2 describes the coupling of anilines to azo dyes in the presence of mesoporous manganese oxide materials. In Chapter 3 an extension of the applicability of mesoporous manganese oxide catalysts to cross dehydrogenative coupling of N-Aryltetrahydroisoquinolines (sp³ C-H) with indoles (sp² C-H) was discussed. Moreover, in Chapter 4 the applicability of mesoporous cobalt sulfoselenide system was studied to producing hydrogen from water under electro-catalytic conditions. Finally, in Chapter 5, the future perspectives of the development of mesoporous materials has been discussed to extend their applicability to performing complicated chemical reactions.

Since past few decades, intense research is going on to develop the alternatives to fossil fuels and petroleum products. Also, to curb the menace of global warming, the development of green chemical pathways have been focused. These green chemical methodologies are intended to repel traditional pathways that often involve the use or production of toxic elements, environmentally unfriendly protocols, and non-reusable techniques. Therefore, to develop green chemical pathways for reactions, systems are designed using earth-abundant but non-toxic elements. Moreover, these reusable protocols are preferred to be operable under atmospheric conditions, and without any additives. These fundamentals of ‘green chemistry’, interested me in understand the surface chemistry and further the applications of mesoporous metal chalcogenides such as manganese oxides and cobalt sulfides.

In this thesis, the importance of different catalytic processes, their operational procedures, and fundamental details have been depicted. We have identified the active sites responsible for the excellent activity of all reported transformations. Detail investigation of the surface chemistry of
these heterogeneous catalytic processes is expected to facilitate the understanding and further the advancement of rather complicated procedures. Computational calculations were performed in all cases to support our experimental finding. These non-toxic, additive free catalytic protocols discussed here showed excellent reusability and environmentally benign waste (water) generation, which abides by the rules of Green Chemistry.
The Development and Mechanistic Investigations of Various Catalytic Processes by Mesoporous Metal Oxides and Sulfides

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Doctor of Philosophy Dissertation

The Development and Mechanistic Investigations of Various Catalytic Processes by Mesoporous Metal Oxides and Sulfides

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2018
To My Mom, Dad, and Elder Sister
Acknowledgments

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Reaction conditions: N-phenyltetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.) toluene (0.25 mL), 25 mg of catalyst (Meso MnOx-550), 100°C.

A$_{0}$: original concentration of substrate. A$_{t}$: concentration of substrate at time t. K: rate constant.

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Chapter 1: Introduction

1.1 Mesoporous Materials:

Mesoporous materials are types of porous materials which have a pore size between 2 to 50 nm as defined by IUPAC.\(^1\) In 1970, the first mesoporous materials were invented by Dr. Page,\(^2\) which, went unnoticed until Mobil Corporation Laboratories reproduced these in 1992.\(^3\) Since then, the field of mesoporous materials has expanded enormously, and thousands of research articles have been published relating to their formation and applications.\(^4\) Porous nanostructures of these materials are ideal for providing a high surface area scaffold to which active metals can be grafted. Resultantly, they have been recognized as popular heterogeneous catalytic systems.\(^5\) Moreover, their porous network is useful for shape-selective catalysis, adsorption, and optical properties compared to their nonporous counterparts.\(^6\)–\(^8\) Structural features such as pore size, pore volume, high surface area, nano-crystalline wall structure, tunable porous networks, unique morphologies (i.e., sphere, rods, cubes), and different meso-structures (i.e., 2D hexagonal, tetragonal, face-centered cubic) are controlled to modulate porous architectures and morphologies. Control over the morphology is required to modulate the adsorption of a material which is an integral part of the surface chemistry of heterogeneous systems.\(^9\)

Catalytic reactions on mesoporous support involve adsorption and diffusion of the reactants on solid surfaces, a reaction between the reactants on the active sites, and desorption of products besides the regeneration of the catalyst. Therefore, materials with a higher number of active sites which increases proportionally with the surface area, are the best candidates for heterogeneous catalysts. This leads to mesoporous-nanostructured materials as excellent catalytic systems. Interestingly, the intrinsic structural features of mesoporous-nanostructured materials have also been recognized to impact catalytic reactions.\(^9\),\(^10\) Therefore, mesoporous materials with high thermal, chemical and physical stability, non-toxicity, excellent reusability, and abundant resources have generated enormous interest for various industrial applications, in recent years.

1.2 Mesoporous Transition Metal Oxides

Various mesoporous materials, depending on different synthetic approaches, have been produced from elements throughout the periodic table. Among them, the development of mesoporous transition metal oxides (MTMO) have attracted much interest due to their applications
in heterogeneous catalysis.\textsuperscript{9,11–14} Despite many difficulties, numerous thermally stable MTMOs have been developed. Many of them, especially groups I-IV TMs such as Y, Ti, Hf, Zr, V, Nb, Ta, Cr, Mo, and W, can be synthesized in multiple ways.\textsuperscript{15–18} Some of the mesoporous groups I-IV TM oxides and their corresponding catalytic processes are summarized in Table 1.1. Multivalency, surface defects, and high surface area of these mesoporous transition metal oxide materials have been identified that lead to their excellent catalytic performance. While there are scopes of extending the catalytic applicability of known MTMOs, development of newer systems and investigation of their surface chemistry is extremely important.

**Table 1.1: Examples of some of the mesoporous transition metal oxide based catalysis.**

<table>
<thead>
<tr>
<th>Transition Metal oxides</th>
<th>Catalytic Applications</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium (Ti)</td>
<td>Photocatalysis- Dye degradation</td>
<td>19.</td>
</tr>
<tr>
<td>Manganese (Mn)</td>
<td>Thermal catalysis-volatile organic compounds, NOx, CO, and various organic moieties.</td>
<td>14.</td>
</tr>
<tr>
<td>Iron (Fe)</td>
<td>Thermal catalysis-Cyclohexane oxidation.</td>
<td>20.</td>
</tr>
<tr>
<td>Cobalt (Co)</td>
<td>Photochemical and photoelectrochemical – CO oxidation</td>
<td>21.</td>
</tr>
<tr>
<td>Nickel (Ni)</td>
<td>Electrocatalysis- Water oxidation</td>
<td>22.</td>
</tr>
<tr>
<td>Copper (Cu)</td>
<td>Thermal catalysis- Combustion catalyst</td>
<td>23.</td>
</tr>
<tr>
<td>Zirconium (Zr)</td>
<td>Thermal catalysis- Oxidative dehydrogenation butane</td>
<td>24.</td>
</tr>
<tr>
<td>Niobium (Nb)</td>
<td>Thermal catalysis- 5-Hydroxymethylfurfural Formation from Sugars</td>
<td>25.</td>
</tr>
<tr>
<td>Ruthenium (Ru)</td>
<td>Electro catalysis- Water oxidation</td>
<td>27.</td>
</tr>
<tr>
<td>Tantalum (Ta)</td>
<td>Photocatalysis- Water oxidation</td>
<td>28.</td>
</tr>
<tr>
<td>Tungsten (W)</td>
<td>Photocatalysis- Dye degradation</td>
<td>29.</td>
</tr>
</tbody>
</table>

**1.3 Catalytic Processes**

Catalysis has been defined as a process where the rate of a chemical reaction is altered due to the presence of a substance, termed as the catalysts, which do not cause any changes to themselves. This is due to the variation of the activation energy; the reaction rates are found to alter in the presence of a catalyst. The increment and decrement of energy barriers between reactants and
products are coined as negative and positive catalysis, respectively. Whereas, chemical processes that involve catalysts and reactants of the same phase and different phases are called homogeneous and heterogeneous catalysis, respectively.

Catalysis has widespread applications in chemical and pharmaceutical industries to produce various value-added products. For preparing various fine chemicals and drug molecules, numerous catalytic pathways have been explored to date. Among these oxidations and reductions of organic substrates such as alcohols, amines and hydrocarbons are of prime interest as they lead to the formation of various industrially important compounds. Conventional methods using peroxides (such as hydrogen peroxide), metal salts (such as potassium permanganate (KMnO₄), sodium dichromate (Na₂Cr₂O₇)), organo-catalysts, and ozone (O₃) are used for these oxidation reactions. Generation of a high amount of toxic wastes and complicated separation steps of these systems make them industrially and environmentally unfriendly. Therefore, the development of greener catalytic processes involving rationally designed catalysts is much needed. Catalytic systems developed using earth-abundant elements, aerobic atmosphere as the sole oxidant, and less harsh conditions are highly desirable. Though extensive research has been performed over the past decade to improve various catalytic processes, further improvement of most methods is required for commercializing them.

1.4 Heterogeneous Catalysis

Heterogeneous catalysis is a type of catalysis where the catalyst and the reactant remain in different physical states (solid, liquid or gas). This leads to an easier separation and recyclable method of the heterogeneous catalysts than corresponding homogeneous systems. However, due to the difference between the phases of reactants and catalysts, their reaction pathways usually vary from that of homogeneous systems. Therefore, to understand the surface chemistry of different heterogeneous systems, various surface properties are probed using different characterization techniques.

The primary objective of heterogeneous catalysis is to develop sustainable catalytic processes and promote green chemistry. Hence, natural abundance, non-toxicity, minimization of waste generation, and reusability are considered as the main features of an excellent heterogeneous catalyst. Moreover, excellent chemical and physical stability of heterogeneous catalysts make them useful for reactions involving harsh conditions.
1.5 References


(4) Kresge, C. T.; Leonowicz, M. E.; Roth, W. J.; Vartuli, J. C.; Beth, J. S.


(21) Gu, D.; Jia, C.-J.; Weidenthaler, C.; Bongard, H.-J.; Spliethoff, B.; Schmidt, W.; Schüth,


Chapter 2. Mesoporous Manganese Oxide Catalyzed Aerobic Oxidative Coupling of Anilines to Aromatic Azo Compounds

2.1 Abstract

Here we introduce an environmentally friendly approach of synthesizing symmetrical and asymmetrical aromatic azo compounds using air as the sole oxidant under mild reaction condition, in the presence of cost-effective and reusable mesoporous manganese oxide materials.

2.2 Background and Significance

Aromatic azo compounds are an important class of molecules used as dyes, food additives, pigments, indicators, therapeutic agents, and as precursors in the synthesis of natural products. Conventional methods of aromatic azo compound formation proceed via diazonium or nitrosobenzene intermediates (Scheme 1, Figure 2.1), using stoichiometric amounts of nitrite salts (NaNO₂) or other toxic oxidants. To make these conventional processes facile and more selective, catalytic pathways are followed. Up to now, a number of catalytic protocols have been developed towards the syntheses of azo derivatives by oxidation of aniline. However, the existing systems have several drawbacks, such as lower yields, undesirable over oxidation products, limited functional group compatibility, the assistance of additives, use of harsh reaction conditions (high pressure, high temperature) and poor reusability of the catalyst. In 2008, Corma and co-workers made a break-through, reporting a heterogeneous Au/TiO₂ mediated aromatic azo compound synthesis from corresponding aniline derivatives (Scheme 2, Figure 2.1).

In the following years, many crucial efforts were made to get moderate to good yields of azo derivatives such as a CuBr/pyridine/O₂ reaction system, a photo-catalytic pathway in the presence of Au/ZrO₂, and Pt or Pd nanowires in the presence of KOH. Recently, Corma’s group reported another way of preparing azo compounds from aromatic nitro compounds using Au/CeO₂ under high pressure of hydrogen. However, the use of precious metals (Au, Pt or Pd), high pressure, and assistance of bases make those processes industrially and environmentally unfriendly. Therefore, development of a cost-effective, efficient, heterogeneous catalysis for aromatic azo compound synthesis, which can be used under mild, atmospheric reaction conditions and with the absence of additives, is highly desirable.
In the past decade, the use of transition metal oxide based catalytic systems has drawn significant attention in the synthesis of small organic molecules. Recently, our group has introduced a new class of inverse micelle templated mesoporous manganese oxide materials [University of Connecticut (UCT) materials], which were found to be effective in different organic transformations such as the oxidation of alcohols, amines, and the oxidation/esterification of long chain alcohols and methylbenzoic acid production by oxidation of alkylbenzenes. These mesoporous manganese oxide (meso-MnOₓ) materials have versatile structural forms and high thermal stability which influence their catalytic activities. The redox cycle of manganese (Mn) along with its labile lattice oxygen molecules have been found to be the dominant factors in catalyzing different oxidation reactions. Herein, we demonstrate for the first time a facile, cost-effective approach for aerobic oxidative coupling of anilines, involving mesoporous manganese oxide (meso-MnOₓ) materials to synthesize diverse symmetric and asymmetric aromatic azo compounds. An absence of precious metal and additives, air as the sole oxidant, atmospheric conditions, and proper reusability make our catalytic protocol competitive with other existing systems.
2.3 Experimental Section

2.3.1 Synthesis

2.3.1.1 Preparation of meso-MnOx

The catalyst was synthesized following the procedure described in the literature. In a typical synthesis 5 g (0.02 mol) of manganese nitrate tetrahydrate (Mn(NO$_3$)$_2$·4H$_2$O) and 10 g (0.134 mol) of 1-butanol was added into a 120 mL beaker. To this solution 2 g (0.0034 mol) of poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) (Pluronic P123, PEO$_{20}$PPO$_{70}$PEO$_{20}$, molar mass 5750 g mol$^{-1}$) and 2 g (0.032 mol) of concentrated nitric acid (HNO$_3$) were added and stirred at room temperature until the solution became clear (light pink). The resulting clear solution was then kept in an oven at 120 °C for 3 h. The product was collected and washed with excess ethanol, centrifuged, and dried in a vacuum oven overnight. In the end, the dried black powders were subjected to a heating cycle. First, they were heated at 150 °C for 12 h and cooled down to room temperature under ambient conditions. The material was then subjected to a heating cycle. The material was then heated to 250 °C for 3 h, 350 °C for 2 h, 450 °C for 2 h, 550 °C for 1 h and 650 °C for 1 h, respectively.

2.3.1.2 Reaction procedure of aniline coupling

In a typical reaction, a mixture of aniline (1.0 mmol), meso Mn$_2$O$_3$ (50 mg) and toluene (0.5 mL) was added in a 25 mL round bottom flask equipped with a condenser. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After the reaction, the mixture was cooled, and the catalyst was removed by filtration. The product analysis was done using GC-MS (gas chromatography-mass spectrometry). The conversion was determined based on the concentration of aniline. Most reactions were repeated twice, and the average values were used. The products were isolated by silica gel column chromatography (n-hexane or a mixed solvent of n-hexane and dichloromethane was used as an eluent).

2.4 Characterization

2.4.1 Structural Characterization

2.4.1.1 X-ray Photoelectron spectroscopy (XPS):
2.4.1.2 Powder X-ray Diffraction (PXRD):

![Figure 2.2](image)

Figure 2.2. X-ray photoelectron spectra (XPS) of a) Mn 2p [of Meso-MnOx at different calcination temperatures, 150, 250, 350, 450, 550, 650 and AMO] and (b) O 1S [of Meso-MnOx at different calcination temperatures, 150, 250, 350, 450, 550, 650 and AMO] of meso MnOx.

![Figure 2.3](image)

Figure 2.3. Powder X-ray diffraction of meso MnOx at different calcination temperatures. The diffraction patterns at 450°C and 550°C calcinations can be indexed to Mn\(_2\)O\(_3\) phase, whereas calcination temperatures at 250°C and 350°C displayed an amorphous nature.
2.4.1.3 Scanning Electron Microscopic and high Resolution Transmission Electron Mictroscopic analysis (SEM and HR-TEM):

Figure 2.4 a) Scanning electron microscopy (SEM) showed the spherical morphology of the meso-MnOx-550. b) Transmission electron microscopy (TEM) displayed the lattice fringes of the meso-MnOx-550.

2.4.1.4 BET surface area and BJH pore size distribution:

Figure 2.5 a) Nitrogen adsorption isotherms of meso MnOx at different calcination temperatures. A type IV adsorption isotherm followed by a type I hysteresis loop were observed for all the materials, which confirmed the mesoporous structure. b) BJH pore size distribution of the same materials show a constant increase in pore diameter with increasing calcination temperatures.

2.5 Catalytic Reactions
2.5.1 Role of Manganese Oxides
2.5.2 Optimization of Reaction Conditions

According to the literature, metal oxide catalyzed oxidative coupling of aniline is initiated with the formation of radical intermediates, by transferring electrons from aniline to metal centers \[^{[8a]}\]. Then, the target molecule (azo benzene) is formed after successive exclusion of hydrogens and
electrons from the corresponding intermediates. Initially, we investigated the oxidative coupling of aniline as the model reaction for developing optimal reaction conditions. A comparative study was conducted to convert aniline 1a to trans-1,2-diphenyldiazone I aa using different phases of manganese oxide materials, synthesized by the UCT method (entry 1-9, Table 2.2). The Mn$^{3+}$ rich (as revealed from X-ray photoelectron spectra, Figure 2.2, Table 2.3) meso-MnOx material (meso MnOx-450), was found to be the best material in terms of conversion and selectivity (entry 3, Table 2.2). The meso MnOx-450 material had the crystalline Mn$_2$O$_3$ phase (Figure 2.3) with a mesoporous size distribution (Figure 2.5). The surface area was calculated to be 100 m$^2$g$^{-1}$, whereas the pore size was 5.3 nm (Table 2.3). Reaction with commercially available nonporous Mn$_2$O$_3$ produced only 3% of the target compound similar to catalyst-free conditions (entry 10-11, Table 2.2). This can be attributed to the presence of the mesoporous network of meso-Mn$_2$O$_3$, which not only provides a higher surface area (100 m$^2$g$^{-1}$) than commercial Mn$_2$O$_3$ (11 m$^2$g$^{-1}$) but also facilitates the adsorption and diffusion of aniline.

**Table 2.1 Optimization of oxidative coupling of aniline by meso-Mn$_2$O$_3$**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent Volume (mL)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>TON</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>10</td>
<td>24</td>
<td>71</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>2.</td>
<td>25</td>
<td>24</td>
<td>39</td>
<td>62</td>
<td>38</td>
</tr>
<tr>
<td>3.</td>
<td>5</td>
<td>24</td>
<td>75</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>4.</td>
<td>1</td>
<td>24</td>
<td>97</td>
<td>&gt;99</td>
<td>&lt;1</td>
</tr>
<tr>
<td>5.</td>
<td>0.5</td>
<td>8</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6.</td>
<td>no</td>
<td>36</td>
<td>58</td>
<td>21</td>
<td>79</td>
</tr>
<tr>
<td>7.</td>
<td>10</td>
<td>36</td>
<td>51</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

[a] Reaction condition: 1a (93 mg, 1.0 mmol), meso-Mn$_2$O$_3$ (50 mg, 0.32 mmol) toluene as solvent, 110°C, air balloon. [b] Determined by GC-MS. [c] TON = moles of aniline converted per mole of catalyst. [d] In presence of TBHP.

During the investigation of the effects of oxidants, a better conversion was observed for the reaction conducted under air or oxygen than nitrogen (entry 1-3, Table 2.5). This signifies the importance of aerial oxygen in the reaction. The effects of different solvents with variable polarities were also surveyed (entry 1-4, Table 2.6) and toluene emerged as the best solvent with...
97 % conversion. While optimizing the solvent amount, an optimal amount of 0.5 mL was found to be the best (> 99 % conversion, entry 5, Table 2.1). The formation of a trace amount of imines (benzylidene-phenyl-amine, I aa’) as the side product can be attributed to the condensation of benzaldehyde (from oxidation of toluene) with aniline. This undesirable benzaldehyde formation proportionally increased with the volume of toluene (entry 1-5, Table 2.1) reflecting higher selectivity towards undesirable imine I aa’ formation. Use of oxidative additives, such as TBHP (entry 6, Table 2.1) enhanced the benzaldehyde formation favoring an increase of imine selectivity to 79 %. Hence, after the extensive screening with all the parameters, 50 mg meso-MnO3, in 0.5 mL toluene at 110 °C under an air balloon were selected as the best-optimized reaction conditions (entry 5, Table 2.1) and pursued for the rest of this work.

Table 2.2 The catalytic results of aniline coupling reaction using different meso manganese oxide [a] (made by UCT method, numbers refer to maximum calcination temperature).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion [%][b]</th>
<th>Selectivity [%][b]</th>
<th>Yield [%][b]</th>
<th>TON [h⁻¹][c]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I aa</td>
<td>I aa’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Meso MnOx-250</td>
<td>17</td>
<td>41</td>
<td>59</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>Meso MnOx-350</td>
<td>55</td>
<td>86</td>
<td>14</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>Meso MnOx-450</td>
<td>71</td>
<td>70</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>Meso OMS-2-250</td>
<td>39</td>
<td>80</td>
<td>20</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>Meso OMS-2-350</td>
<td>34</td>
<td>77</td>
<td>23</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>Meso OMS-2-450</td>
<td>45</td>
<td>82</td>
<td>18</td>
<td>37</td>
</tr>
<tr>
<td>7</td>
<td>Meso MnOx-ε-250</td>
<td>49</td>
<td>74</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td>8</td>
<td>Meso MnOx-ε-350</td>
<td>59</td>
<td>81</td>
<td>19</td>
<td>48</td>
</tr>
<tr>
<td>9</td>
<td>Meso MnOx-ε-450</td>
<td>58</td>
<td>78</td>
<td>22</td>
<td>45</td>
</tr>
<tr>
<td>10</td>
<td>C-Mn2O3</td>
<td>3</td>
<td>100</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>No</td>
<td>3</td>
<td>100</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>12[d]</td>
<td>Mn(OAc)₃.2H₂O</td>
<td>29</td>
<td>100</td>
<td>0</td>
<td>29</td>
</tr>
</tbody>
</table>

[a] Reaction procedure: aniline 1 a (1 mmol) and catalyst (50 mg) were successively placed and mixed with toluene (10 mL) and refluxed at 110°C under air balloon for 24 hours. [b] Conversion, selectivity and yield were determined by GC-MS based on the concentration of anilines. [c] TOF = TON.h⁻¹, TON = no of amines converted per mole of catalyst. [d] Mn(OAc)₃.2H₂O (85 mg, 0.32 mmol).
Table 2.3 Summarization of XPS data of meso MnOx at different calcination temperature.

<table>
<thead>
<tr>
<th>Calcination temp. (°C)</th>
<th>Mn3+ (641.8 eV)</th>
<th>Mn4+ (643.9 eV)</th>
<th>O\textsubscript{lattice}</th>
<th>O\textsubscript{adsorbed}</th>
<th>O\textsubscript{adsorbed water}</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>73.5</td>
<td>26.5</td>
<td>47.5</td>
<td>40.5</td>
<td>12.0</td>
</tr>
<tr>
<td>350</td>
<td>79.3</td>
<td>20.7</td>
<td>65.8</td>
<td>26.2</td>
<td>8.0</td>
</tr>
<tr>
<td>450</td>
<td>81.2</td>
<td>18.8</td>
<td>71.5</td>
<td>22.7</td>
<td>5.8</td>
</tr>
</tbody>
</table>

Table 2.4 Structural characterizations of meso MnOx at different calcination temperatures.

<table>
<thead>
<tr>
<th>Calcination temp. (°C)</th>
<th>Surface area\textsuperscript{[a]} (m\textsuperscript{2}g\textsuperscript{-1})</th>
<th>Pore diameter\textsuperscript{[b]} (nm)</th>
<th>Crystal Str. \textsuperscript{[c]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>200</td>
<td>2.8</td>
<td>Amorphous</td>
</tr>
<tr>
<td>350</td>
<td>191</td>
<td>3.7</td>
<td>Amorphous</td>
</tr>
<tr>
<td>450</td>
<td>100</td>
<td>5.3</td>
<td>Mn\textsubscript{2}O\textsubscript{3}</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]} Calculated by BET method. \textsuperscript{[b]} Calculated by BJH method from the desorption branch of the isotherm. \textsuperscript{[c]} From powder XRD.

Table 2.5 The catalytic results using different oxidants.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Oxidant</th>
<th>Conversion [%]\textsuperscript{[b]}</th>
<th>Selectivity [%]\textsuperscript{[b]}</th>
<th>Yield [%]\textsuperscript{[b]}</th>
<th>TOF [\textsuperscript{h}\textsuperscript{-1}]\textsuperscript{[c]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meso MnOx-450</td>
<td>Air</td>
<td>25</td>
<td>&gt;98</td>
<td>25</td>
<td>0.197</td>
</tr>
<tr>
<td>2</td>
<td>Meso MnOx-450</td>
<td>N\textsubscript{2}</td>
<td>8</td>
<td>&gt;98</td>
<td>8</td>
<td>0.063</td>
</tr>
<tr>
<td>3</td>
<td>Meso MnOx-450</td>
<td>O\textsubscript{2}</td>
<td>28</td>
<td>&gt;96</td>
<td>27</td>
<td>0.229</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction condition: aniline 1 a (1 mmol), meso-MnO\textsubscript{3} (50 mg, 0.32 mmol), toluene (10 mL), 110 °C, air balloon, 4 h. \textsuperscript{[b]} Conversion, selectivity and yield were determined by GC-MS \textsuperscript{c} TOF = TON.\textsuperscript{h}\textsuperscript{-1}, TON = no of amines converted per mole of catalyst.

Table 2.6 The catalytic results using different solvents.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conversion [%]\textsuperscript{[b]}</th>
<th>Selectivity [%]\textsuperscript{[b]}</th>
<th>Yield [%]\textsuperscript{[b]}</th>
<th>TOF [\textsuperscript{h}\textsuperscript{-1}]\textsuperscript{[c]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>97</td>
<td>&gt;99</td>
<td>96</td>
<td>0.131</td>
</tr>
<tr>
<td>2</td>
<td>Dichloromethane</td>
<td>28</td>
<td>53</td>
<td>15</td>
<td>0.037</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>28</td>
<td>&gt;99</td>
<td>28</td>
<td>0.037</td>
</tr>
<tr>
<td>4</td>
<td>cyclohexane</td>
<td>48</td>
<td>&gt;99</td>
<td>48</td>
<td>0.063</td>
</tr>
<tr>
<td>5</td>
<td>Chlorobenzene</td>
<td>25</td>
<td>&gt;99</td>
<td>25</td>
<td>0.033</td>
</tr>
<tr>
<td>6</td>
<td>Benzonitrile\textsuperscript{[d]}</td>
<td>0</td>
<td>n/d</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction condition: aniline 1 a (1 mmol), catalyst meso-MnO\textsubscript{3}-450 (50 mg, 0.32 mmol), toluene (10 mL), 110 °C, air balloon, 24 h. \textsuperscript{[b]} Conversion, selectivity, and yield were determined by GC-MS based on the concentration of anilines. \textsuperscript{c} TOF = TON.\textsuperscript{h}\textsuperscript{-1}, TON = no of amines converted per mole of catalyst. \textsuperscript{[d]} Benzamide formation was observed. n/d: not determined. n/a: not applicable.
2.5.3 Substrate Scope
2.5.3.1 Oxidative Homo-coupling

Using the operationally simple and optimized reaction conditions, various aromatic azo compounds were synthesized, from their corresponding aniline derivatives, in order to evaluate the substrate scope. Diverse aniline derivatives, having electron rich (entry 2-5, Table 2.7) and electron deficient groups (entry 6, Table 2.7), produced their corresponding aromatic azo compounds with excellent yield (as high as 98 %) and selectivity (> 99 %). The reaction with a heteroatom containing aniline derivative, 1 g gave comparatively lower conversion (45 %) (entry 7, Table 2.7), with higher amounts of catalyst. This may be due to the poisoning of the metal center of the catalyst by coordination with N-heteroatoms.\textsuperscript{20} Excellent yield (82 %) of the azo compound I hh (entry 8, Table 2.7) from bulky 1-Naphthylamine 1 h indicated that steric hindrance did not have a significant impact in this reaction protocol. Moreover, survival of halo-substituted compounds such as 4-chloroaniline 1f, leading to the corresponding azo compound 2 ff (84 %) (entry 6, Table 2.7) is noteworthy, as preventing dehalogenation is a challenge for catalytic reactions involving halogen derivatives.\textsuperscript{21} This N,N coupling is only possible when the -NH\textsubscript{2} group is attached to an aromatic ring, or else imine was formed from the self-coupling of benzylamine 1 j (entry 10, Table 2.7).

Table 2.7 Aerobic oxidation of anilines to aromatic azo compounds by meso-Mn\textsubscript{2}O\textsubscript{3}. \textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>(\text{R}^1)</th>
<th>Time (h)</th>
<th>Conversion [%]\textsuperscript{[c][d]}</th>
<th>Selectivity of I [%]\textsuperscript{[c][d]}</th>
<th>TON\textsuperscript{[e]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(\text{C}_6\text{H}_5) (1 a)</td>
<td>8</td>
<td>&gt; 99</td>
<td>&gt; 99 (I aa) (93)</td>
<td>3.13</td>
</tr>
<tr>
<td>2.</td>
<td>4-Me-(\text{C}_6\text{H}_4) (1 b)</td>
<td>7</td>
<td>&gt; 99</td>
<td>&gt; 99 (I bb) (95)</td>
<td>3.13</td>
</tr>
<tr>
<td>3.</td>
<td>4-OMe-(\text{C}_6\text{H}_4) (1 c)</td>
<td>4</td>
<td>&gt; 99</td>
<td>&gt; 99 (I cc) (89)</td>
<td>3.13</td>
</tr>
<tr>
<td>4.</td>
<td>3,5-Me\textsubscript{2}-(\text{C}_6\text{H}_3) (1 d)</td>
<td>4</td>
<td>88</td>
<td>&gt; 99 (I dd)</td>
<td>2.78</td>
</tr>
<tr>
<td>5.</td>
<td>4-N(Me)\textsubscript{2}-(\text{C}_6\text{H}_4) (1 e)</td>
<td>8</td>
<td>&gt; 99</td>
<td>&gt; 99 (I ee)</td>
<td>3.13</td>
</tr>
<tr>
<td>6.</td>
<td>4-Cl-(\text{C}_6\text{H}_4) (1 f)</td>
<td>6</td>
<td>84</td>
<td>&gt; 99 (I ff)</td>
<td>2.65</td>
</tr>
<tr>
<td>7.\textsuperscript{[b]}</td>
<td>2-NH\textsubscript{2}-(\text{C}_6\text{H}_5)N (1 g)</td>
<td>12</td>
<td>45</td>
<td>&gt; 99 (I gg)</td>
<td>0.71</td>
</tr>
<tr>
<td>8.</td>
<td>1-Naphthyl (1 h)</td>
<td>12</td>
<td>82</td>
<td>&gt; 99 (I hh)</td>
<td>2.59</td>
</tr>
<tr>
<td>9.</td>
<td>2-Cl-4-Me-(\text{C}_6\text{H}_3) (1 i)</td>
<td>16</td>
<td>97</td>
<td>&gt; 99 (I ii)</td>
<td>3.06</td>
</tr>
<tr>
<td>10.</td>
<td>(\text{C}_6\text{H}_5\text{CH}_2) (1 j)</td>
<td>9</td>
<td>&gt; 99</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
[a] Reaction procedure: $R^1$ (1.0 mmol) and meso-Mn$_2$O$_3$ (50 mg, 0.32 mmol) were successively placed and mixed with toluene (0.5 mL). [b] 100 mg, [c] Determined by GC-MS based on the concentration of anilines. Numbers in parenthesis refer to yields of isolated products, [e] TOF = TON.h$^{-1}$, TON = no of amines converted per mole of catalyst.

### 2.5.3.2 Oxidative Hetero-coupling

The excellent activities of the meso-Mn$_2$O$_3$ mediated homocoupling of anilines inspired us to study the feasibility of the protocol in the synthesis of asymmetric aromatic azo compounds. Asymmetric aromatic azo compounds are usually synthesized by reacting diazonium salts with electron-rich aromatic compounds.$^5$ $^6$ Initially, reactions between different molar ratios of $p$-anisidine 1c and aniline 1a (entry 1-3, Table 2.8) were executed. The reaction with a molar ratio 1:3 of $p$-anisidine: aniline was selected as the optimum ratio for obtaining the asymmetric aromatic azo compound II ca ((4-Methoxy-phenyl)-phenyl-diazene) with 35% selectivity (entry 2, Table 2.8). Using this optimized condition, various structurally different aromatic aniline derivatives such as p-toluidine, 3,5-dimethylaniline, $p$-$N,N'$-dimethylaniline, $p$-chloroaniline, and napthylamine were reacted with aniline. The asymmetric aromatic azo compound II ba was synthesized from p-toluidine 1b and aniline 1a with 56% selectivity (entry 4, Table 2.8). The homocoupling of anilines with electron donating groups reacts much faster (entry 2-5, Table 2.7) than those with electron withdrawing groups (entry 6, Table 2.7).

### Table 2.8 Aerobic oxidative cross-coupling of aniline with different aniline derivatives.$^[[a]$]  

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>4-OMe-C$_6$H$_4$ (1c)</td>
<td>1/2</td>
<td>&gt; 99</td>
<td>28 (II ca)</td>
<td>28</td>
</tr>
<tr>
<td>2.</td>
<td>(1c)</td>
<td>1/3</td>
<td>&gt; 99</td>
<td>35 (II ca)</td>
<td>35</td>
</tr>
<tr>
<td>3.</td>
<td>(1c)</td>
<td>1/4</td>
<td>&gt; 99</td>
<td>37 (II ca)</td>
<td>37</td>
</tr>
<tr>
<td>4.</td>
<td>4-Me-C$_6$H$_4$ (1b)</td>
<td>1/3</td>
<td>&gt; 99</td>
<td>56 (II ba)</td>
<td>55</td>
</tr>
<tr>
<td>5.</td>
<td>3,5-Me$_2$C$_6$H$_3$ (1d)</td>
<td>3/1</td>
<td>&gt; 99</td>
<td>92 (II da)</td>
<td>91</td>
</tr>
<tr>
<td>6.</td>
<td>4-N(Me)$_2$C$_6$H$_4$ (1e)</td>
<td>3/1</td>
<td>&gt; 99</td>
<td>43 (II ea)</td>
<td>43</td>
</tr>
<tr>
<td>7.</td>
<td>4-Cl-C$_6$H$_4$ (1f)</td>
<td>3/1</td>
<td>&gt; 99</td>
<td>88 (II fa)</td>
<td>87</td>
</tr>
<tr>
<td>8.</td>
<td>1-Naphthyl (1i)</td>
<td>3/1</td>
<td>80</td>
<td>72 (II ia)</td>
<td>58</td>
</tr>
</tbody>
</table>
Reaction procedure: Total 1mmol $R^1$-NH$_2$ and Ph-NH$_2$ (according to the molar ratio mentioned above), meso-Mn$_3$O$_3$ (50 mg, 0.32 mmol), toluene (0.5mL), 110°C, air balloon, 12 h. [b] Molar ratio of aniline derivatives and aniline. [c] Determined by GC-MS based on the concentration of anilines. [d] Calculated based on self-coupled (I) and cross-coupled (II) products of the limiting reagent.

Therefore, during cross-coupling, a larger excess of electron deficient anilines was used to enhance the yield of the cross-coupled product (entry 1-4, Table 2.8). The molar ratio was flipped to 3:1 (entry 5-8, Table 2.8) for the reactions between aniline to aniline derivatives 1 d, 1 e, 1 f and 1 i, which required equal or more time for homocoupling compared to aniline, in order to get cross-coupled products with moderate 43-58 % (entry 6, 8, Table 2.8) to high 87-91 % (entry 5, 7, Table 2.8) yields.

2.5.4 Kinetic Studies

To investigate the kinetic aspect of the reaction between aniline and meso-Mn$_3$O$_3$, a time-dependent study was conducted (Figure 2.6). Formation of a minute amount of imine was tracked during the reaction which was due to the coupling between aniline and aldehyde (formed by oxidation of toluene). Kinetic experiments depicted a first-order rate equation with respect to aniline 1 a (Figure 2.7) having a rate constant of 0.32 h$^{-1}$. The apparent activation energy (Ea), determined from the Arrhenius plot in the temperature range of 20–110 °C (Figure 2.8), was 29.8 kJ mol$^{-1}$.

![Figure 2.6 Time-dependent Study. Reaction procedures were the same as discussed in Table 2. Formation of a minute amount of imine (I aa') was observed due to oxidation of toluene.](image-url)
**Figure 2.7** Kinetic study of the oxidative coupling of aniline by meso-Mn$_2$O$_3$: The reaction exhibited a first-order rate dependence with respect to aniline having the rate constant of 0.32 min$^{-1}$. Reaction procedure was the same as discussed in Table 2. $A_0$: original concentration of substrate. $A_t$: concentration of substrate at time t. K: rate constant.

**Figure 2.8** Arrhenius plot for oxidative coupling of aniline by meso Mn$_2$O$_3$: The apparent activation energy was estimated as 29.8 KJ mol$^{-1}$. Reaction conditions: aniline (1 mmol), catalyst (50 mg), solvent (0.5 mL), air balloon, 2 h. K: rate constant.
2.5.5 Reusability and Heterogeneity

To verify if the observed catalysis is the result of solid meso-MnO$_x$ or leached active metal species, the oxidative coupling of aniline was carried out and the catalyst was separated from the system after 3 hours of reaction (at about 64 % conversion of aniline). The filtrate was then kept under the same reaction conditions for the next 7 hours. Successive aliquots were taken out after each hour and analyzed by GC-MS, but no further production of azobenzene was observed (Figure 2.9). Moreover, inductively coupled plasma (ICP) analysis revealed a very low amount (79.6 ppb) of Mn in the filtrate. To check the reusability, the meso-Mn$_2$O$_3$ catalyst was retrieved by a simple filtration method from the reaction mixture with > 90 % recovery. The reused catalyst was washed with excess toluene and acetonitrile respectively, and finally reactivated at 250 °C (to remove the adsorbed species from the catalyst surface) for 50 minutes prior to reuse. The retrieved catalyst could be used for at least 5 times, though a slight gradual decrease of performance was observed. (Figure 2.10). All of these results verified that our catalytic system is truly heterogeneous, which is not only active but also has sustainability.

![Figure 2.9](image-url)

**Figure 2.9** Effect of removal of catalyst on the oxidative coupling of aniline: Reaction conditions were the same as discussed in Table 2. After 3 h, meso-Mn$_2$O$_3$ was removed by hot filtration (at about 64 % conversion).
Figure 2.10 Kinetic profiles of reusable experiments. Reaction conditions: aniline 1 a (1 mmol), meso-Mn$_2$O$_3$ (30 mg, 0.192 mmol), toluene (1 mL), 80 °C, air balloon. After each cycle, catalysts were washed with toluene and acetonitrile and reactivated at 250 °C for 50 minutes prior to reuse.

2.6 Discussions

In order to understand the mechanistic details of the catalytic process, several experiments were conducted. The presence of 2,6-Di-tert-butyl-4-methylphenol (a radical inhibitor) did not produce any trace of aromatic azobenzene. Rather, the reaction produced a coupled product 3 a-X (Figure 2.11) which validates the formation of intermediate 3 a (Figure 2.12). This isolation of the intermediate (by GC-MS) suggests that our mechanism is similar to that proposed by Corma and coworkers. They assumed the radical species (3) formed from aniline (1 a) was coupling with another molecule of aniline 1 a to form 4 (a compound with a 3 e- sigma bond) which after successive loss of a proton and an electron formed intermediate 6. Intermediate 6 goes through all the afore-mentioned steps once again to get to the final product 1 aa.

The generation of the radial intermediate 3 a caused the reduction of surface active Mn$^{3+}$ to Mn$^{2+}$, which leads to the facile release of labile lattice oxygen (Figure 2.12, Cycle 2). That lattice oxygen combines with the protons (4 H$^+$) and electrons (2 e$^-$) released in Cycle 1 to form water. The supply of oxygen from the air was crucial for this catalytic activity, as the loss of lattice oxygens should be replenished by oxygen from the air. This was consistent with our observation of diminished reaction rate when the reaction was performed under nitrogen only, instead of under air (entry 1-2, Table 2.3).
We performed a reaction with 1,2 diphenyl hydrazine 6 in the presence of meso-Mn$_2$O$_3$ under the optimized condition, producing azobenzene I aa in just 20 minutes. The same reaction did not occur in the absence of the catalyst. This suggests that the very fast reaction rate could be the reason for not trapping intermediate 7.

![N2H4](image)

**Figure 2.11** Intermediate Trapping: Reaction procedure: aniline 1 a (1 mmol), radical inhibitor (1.2 mmol), and meso-Mn$_2$O$_3$ (50 mg, 0.32 mmol) were successively placed and mixed with toluene (1 mL) and refluxed at 110°C under air balloon. The reaction mixture was analyzed by GC-MS after cooling to room temperature.

![Mechanism](image)

**Figure 2.12** The proposed mechanism of the reaction.

**Table 2.9** Aerobic oxidative cross-coupling of 1,2 diphenylhydrazine with different aniline derivatives,[a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion [%][b]</th>
<th>Selectivity of Iaa [%][b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>meso-Mn$_2$O$_3$</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2.</td>
<td>no</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

[a] Reaction procedure: 1,2 diphenylhydrazine 6 (1 mmol) and meso-Mn$_2$O$_3$ (50 mg, 0.32 mmol) were successively placed and mixed with toluene (0.5 mL) and refluxed at 110°C under air balloon for 20 minutes. [b] Determined by GC-MS based on the concentration of anilines.
2.7 Computational Calculations

To further validate the reaction mechanism, we also performed quantum mechanical computations, on the system in the gas phase, using density functional theory (DFT) as implemented in the Vienna ab initio package. In addition, to estimate the Mn oxidation states, DFT calculations were carried out on mesoporous manganese oxide (meso-MnOx). A DFT reaction energy profile in the gas phase is shown in Figure 2.13. The relative energies [Kcal mol$^{-1}$] are based on the summations of the total representative energies $E_{tot}$ of all species. Our DFT computation based Bader charge analysis provides support that in step 1, the active Mn$^{3+}$ species was reduced to Mn$^{2+}$ with the calculated charge on Mn found to be 2.18 e$^-$. In step 2 the generated radical is further stabilized by coupling with another molecule of aniline which readily loses a proton and an electron in steps 3 and 4 to give the more stable intermediate 1,2 diphenylhydrazine 6 (Table 2.9). In the subsequent steps, while transforming 6 to I aa, DFT computations had further supported that the suggested mechanism follows a similar pathway as from 1 a to 4 to obtain the end product.

![Figure 2.13 DFT of reaction energy profile in the gas phase.](image)

2.8 Conclusions

In conclusion, we have developed for the first time a facile, cost-effective, and mild reaction procedure for synthesizing diverse symmetric and asymmetric aromatic azo compounds using inexpensive meso-MnOx materials. A variety of aniline derivatives can undergo oxidative homocoupling and cross-coupling with moderate to excellent yields (35 - > 99 %). Air as the
terminal oxidant, absence of precious metals and additives, atmospheric conditions with proper reusability, makes our catalytic protocol superior to other reported systems. Through the mechanistic investigation, we were able to reveal the involvement of surface active Mn$^{3+}$ species, labile lattice oxygen, and radical intermediates towards the catalytic activity. A manganese mediated electron transfer mechanism from aniline was proposed, which was complemented by DFT calculations. Studies to understand and modify the reaction mechanism are underway to make the reaction more facile.

2.9 Analysis of Reaction Products

Characterization of typical products

2.9.1 Azobenzene (I aa): Yellow powder.

\[ \text{H NMR (400 MHz, CDCl}_3, \text{TMS): } \delta 7.96-7.94 (d, J = Hz, 4H), 7.57-7.48 (m, J = 36, 6H) \]
$^{13}$C NMR (101 MHz, CDCl$_3$, TMS): $\delta$ 152.71, 131.02, 129.12, 122.89
2.9.2 4,4'-Dimethylazobenzene (I bb): Yellow powder.

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{b} & \quad \text{c} & \quad \text{a} & \quad \text{d} & \quad \text{e} \\
\end{align*}
\]

\[^1H\text{ NMR (400 MHz, CDCl}_3, \text{TMS): } \delta 7.81 (d, J = 8 \text{ Hz}, 4\text{H}), 7.33 (d, J = 8 \text{ Hz}, 4\text{H}), 2.46 (6\text{H}), \]

\[\text{CHCl}_3, \text{H}_2\text{O}\]
$^{13}$C NMR (101 MHz, CDCl$_3$, TMS): $\delta$ 150.83, 141.19, 129.69, 122.71, 21.48.
2.9.3 4,4'-Dimethoxyazobenzene (I cc): Yellow powder.

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{, TMS): } & \delta 7.90 (d, J = 8 \text{ Hz}, 4\text{H}), 7.03 (d, J = 8 \text{ Hz}, 4\text{H}), 3.91 (6\text{H}), \\
\end{align*}
\]
$^{13}$C NMR (101 MHz, CDCl$_3$, TMS): δ 161.56, 147.10, 124.33, 114.16, 55.56.
2.10 References


Chapter 3. Cross Dehydrogenative Coupling of N-Aryltetrahydroisoquinolines (sp³ C-H) with Indoles (sp² C-H) Using Heterogeneous Mesoporous Manganese Oxide Catalyst

3.1 Abstract

We disclose a novel, heterogeneous catalytic approach for selective coupling of C1 of N-aryltetrahydroisoquinolines with C3 of indoles in the presence of mesoporous manganese oxides. Our work involves a detailed mechanistic investigation of the reaction on the catalyst surface, backed by the DFT computational studies, to understand the superior catalytic activity of manganese oxides.

3.2 Background and Significance

C-H bond activation reactions are currently under focus due to their applications for the formation of C-C bonds in the synthesis of complex natural products and pharmaceuticals. Con conventionally, C-C bond formation required functional group handles. In recent years, interest has grown in oxidative cross-coupling reactions, also known as cross-dehydrogenative coupling (CDC). The properties which make the cross-dehydrogenative coupling (CDC) reactions popular are their i) ‘atom economy’ ii) prior activation or leaving group free chemistry, and iii) cost-effective procedures. Moreover, many CDCs have only water as the by-product. Direct CDC of sp²-sp³ is recently gaining interest due to their prevalence in natural products.

Figure 3.1 Catalytic routes for oxidative dehydrogenative coupling of indoles with tetrahydroisoquinoline.

Among numerous substrates that can be exploited for C-C (sp²-sp³) coupling reactions using CDC, amines are most popular. Amines, in particular N-aryltetrahydroisoquinolines and indoles, have been used the most by different research groups due to their abundance and their prevalence in natural products. Pioneering studies by Murahashi and Li led to the development of
interesting procedures which include the discovery of different catalysts, oxidants, and nucleophiles. In multiple studies, toxic Cu or Fe salts were used as catalysts and TBHP or DTBP as oxidants. Studies have been reported to use different catalytic systems, such as PtCl₂/molecular sieves, NaAuCl₄/TBHP, Ru porphyrin/TBHP, V₂O₅/O₂, SBA-15 supported Fe(terpy)/TBHP, and phosphoric acid on dearomatic arylation of isoquinoline. Some metal free CDCs have also been reported using bases (KOtBu), Grignard reagents, and hypervalent iodines. Despite being interesting, these procedures lack operational simplicity and environmental friendliness. Moreover, none of the procedures claimed to be completely heterogeneous except the system using Fe(terpy)/TBHP, which however is industrially infeasible due to the aggregation of active sites. These existing systems mostly suffer from the a) use of toxic catalysts or oxidants, b) poor selectivity due to formation of by-products, c) use of bases or air sensitive Grignard reagents, d) operational complexity, and e) poor reusability of the catalysts. Therefore, the development of an i) efficient, ii) base / additive free, iii) non-toxic, iv) reusable and v) cost-effective catalytic system is required to meet the measures of green chemistry. No catalyst having all these properties together has been reported to date.

In recent years, transition metal-based catalytic processes have gained significant attention for the synthesis of small organic molecules. We have previously reported highly efficient methods to synthesize amines and azo compounds using mesoporous manganese oxides, synthesized by an inverse micelle assembled soft templated method. Versatile structural forms with high thermal stability and redox cycling of manganese (Mn) have been found to influence the catalytic and oxidizing properties of these materials, respectively. Intrigued by these findings, we explored their scope in CDC of N-aryltetrahydroisoquinolines with indoles.

Herein, we demonstrate a facile, additive, and toxic catalyst free, highly selective CDC between the C1 of N-aryltetrahydroisoquinolines and C3 of indoles using reusable meso-MnOx as catalyst. This is the first catalytic process to satisfy all measures of green chemistry and can compete with the selectivity, efficiency, and cost of existing systems.

Most procedures reported to date used i) oxidizing agents, such as TBHP, DTBP, and ii) toxic Cu(II)-Cu(I) chemistry, to form an intermediate (iminium ion) which couples with indoles. Therefore, the use of manganese oxide (MnOx), known for oxidative dehydrogenative catalysis, could be a better option to replace existing environmentally hazardous protocols. A comparative study of different phases of manganese oxide (Table 3.1), performed on a model
reaction between \( N \)-phenyltetrahydroisoquinoline (1a) (\( N \)-Ph-THIQ) and indole, revealed meso-MnO\( \text{X} \)-550 as the best catalyst with 42\% conversion (Table 3.1, entry 7). Thus, subsequent studies were continued with meso-MnO\( \text{X} \)-550 which has a spherical morphology, and crystalline Mn\(_2\)O\(_3\) phase (as revealed by the XRD, SEM and HR-TEM data, Figure 3.3 and 3.4) with BET surface area of 71 m\(^2\)/g (Figure 3.5, a) and mesoporous size distribution (pore diameter 6.6 nm) (Figure 3.5, b).

3.3 Material Synthesis

3.3.1 Preparation of meso-MnO\( \text{X} \)

The catalyst was synthesized following the procedure described in the literature.\(^{[1]}\) In a typical synthesis 5 g (0.02 mol) of manganese nitrate tetrahydrate (Mn (NO\(_3\))\(_2\)-4H\(_2\)O) and 10 g (0.134 mol) of 1-butanol were added into a 120 mL beaker. To this solution 2 g (0.0034 mol) of poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) (Pluronic P123, PEO\(_{20}\)PPO\(_{70}\)PEO\(_{20}\), molar mass 5750 g mol\(^{-1}\)) and 2 g (0.032 mol) of concentrated nitric acid (HNO\(_3\)) were added and stirred at room temperature until the solution became clear (light pink). The resulting clear solution was then kept in an oven at 120\(^\circ\)C for 3 h. The product was collected and washed with excess ethanol, centrifuged, and dried in a vacuum oven overnight. At the end, the dried black powders were subjected to a heating cycle. First, they were heated at 150\(^\circ\)C for 12 h and cooled down to room temperature under ambient conditions. The material was then subjected to a heating cycle. The material was then heated to 250\(^\circ\)C for 3 h, 350\(^\circ\)C for 2 h, 450\(^\circ\)C for 2 h, 550\(^\circ\)C for 1 h and 650\(^\circ\)C for 1 h, respectively.

3.3.2 Preparation of AMO (Amorphous Manganese Oxide)

The catalyst was synthesized following the procedure described in the literature.\(^{[2]}\) by the reduction of KMnO\(_4\) with oxalic acid at room temperature. Potassium permanganate solution (1.58 g, 0.01 mol of KMnO\(_4\) dissolved in 60 mL of distilled deionized water (DDW)) was added dropwise to the oxalic acid solution (2.28 g, 0.025 mol of oxalic acid dissolved in 100 mL of DDW) and kept stirring for 2 h at room temperature. The brown slurry obtained from the reaction was filtered to get the product. This slurry was washed several times with deionized water and dried at 90 \(^\circ\)C overnight to obtain the amorphous manganese oxide.
3.3.3 Reaction procedure of 1,2,3,4-tetrahydroisoquiniline to indole coupling

In a typical reaction, N substituted 1,2,3,4-tetrahydroisoquinoline (THIQ) (0.133 g, 1.0 mmol), meso Mn₂O₃ (50 mg) and toluene (0.5 mL) were added successively in a 25 mL round bottom flask equipped with a condenser.

The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After reaction, the reaction mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC-MS (gas chromatography mass spectrometry). The conversion was determined based on the concentration of N substituted 1,2,3,4-tetrahydroisoquinoline. Most reactions were repeated twice and the average values were used. The products were isolated by silica gel column chromatography (5:95 Ethyl acetate/petroleum ether was used as an eluent).

3.4 Characterization
3.4.1 Structural Characterization
3.4.1.1 X-ray Photoelectron spectroscopy (XPS):

![Figure 3.2 X-ray photoelectron spectra (XPS) of a) Mn 2p of Meso-MnOx at different calcination temperatures, 150, 250, 350, 450, 550, 650 and AMO and (b) O 1S of Meso-MnOx at different calcination temperatures, 150, 250, 350, 450, 550, 650 and AMO of meso MnOx.](image-url)
3.4.1.2 Powder X-ray Diffraction (PXRD):

Figure 3.3 a) Powder X-ray diffraction of meso MnOx at different calcination temperatures. The diffraction patterns at 450°C and 550°C calcinations can be indexed to Mn₂O₃ phase, whereas calcination temperatures at 250°C and 350°C displayed an amorphous nature.

3.4.1.3 Scanning Electron Microscopic and High-Resolution Transmission Electron Microscopic analysis (SEM and HR-TEM):

Figure 3.4 a) Scanning electron microscopy (SEM) showed the spherical morphology of the meso-MnOx-550. b) Transmission electron microscopy (TEM) displayed the lattice fringes of the meso-MnOx-550.
3.4.1.4 BET surface area and BJH pore size distribution:

![Figure 3.5](image)

**Figure 3.5** a) Nitrogen adsorption isotherms of meso MnOx at different calcination temperatures. A type IV adsorption isotherm followed by a type I hysteresis loop were observed for all the materials, which confirmed the mesoporous structure. b) BJH pore size distribution of the same materials show a constant increase in pore diameter with increasing calcination temperatures.

### 3.5 Catalytic Reactions

#### 3.5.1 Optimization of Reaction Conditions

Commercially available Mn$_2$O$_3$ (c-Mn$_2$O$_3$) (surface area 11 m$^2$/g) (Table 3.1, entry 9) and amorphous manganese oxide (AMO) (Table 3.1, entry 10) yielded only 23 % and 32 %, respectively, probably due to the lack of lattice oxygen, required active sites, and high surface area. Mn$^{3+}$ rich Mn(III) acetate, which lacked only labile lattice oxygens and high surface area (Table 3.1, entry 11), produced only 13 % conversion, while no reaction occurred in the absence of catalyst (Table 3.1, entry 12). These results suggest a probable combination of properties—high surface area, lattice oxygen and active sites—required for the reaction.

While investigating the effect of oxidants, their impact on both conversion and selectivity was discovered. A sharp drop in conversion was noted as the reaction atmosphere was switched from air or O$_2$ to N$_2$ (Table 3.3, entry 1, 4, 5). This demonstrates the importance of oxygen for the reaction. The selectivity dropped from > 99 % to 76 % in the presence of peroxides (H$_2$O$_2$ and TBHP), probably due to the formation of amine-peroxide by-product (Table 3.3, entry 2, 3). A similar oxidation of amines was observed under a high pressure oxygen atmosphere, which severely impacted the selectivity of the coupling reaction (Table 3.3, entry 6, 7). Solvent selection (Table 3.4, entry 1-5) and concentration (Table 3.5, entry 1-6) were optimized, where 0.25 mL
of toluene (Table 3.5, entry 2) emerged as the best solvent system for the reaction. Finally, the optimized ratio (1 to 1.2 equivalent) of 1a and Indole (2a) (Table 3.6, entry 4) was assessed prior to conducting experiments with different catalyst loading. After screening the reaction parameters, the optimum conditions for CDC of 0.25 mmol of N-phenyltetrahydroisoquinoline were determined to be 25 mg of meso-MnOx-550 catalyst in 0.25 mL of toluene at 100 °C and an indole to N-phenyltetrahydroisoquinoline (1a) ratio of 1.2 equivalents with the reaction conducted under an air balloon. Further investigations were continued under the optimized reaction conditions.

Table 3.1 Aerobic oxidative cross-coupling of N-phenyltetrahydroisoquinoline with indole in presence of different catalysts. a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%) b</th>
<th>Selectivity (%) b</th>
<th>TOF c (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. d</td>
<td>MnOx-150</td>
<td>17</td>
<td>&gt; 99</td>
<td>0.09</td>
</tr>
<tr>
<td>2. d</td>
<td>MnOx-250</td>
<td>26</td>
<td>&gt; 99</td>
<td>0.14</td>
</tr>
<tr>
<td>3. d</td>
<td>MnOx-350</td>
<td>35</td>
<td>&gt; 99</td>
<td>0.18</td>
</tr>
<tr>
<td>4. d</td>
<td>MnOx-450</td>
<td>39</td>
<td>&gt; 99</td>
<td>0.20</td>
</tr>
<tr>
<td>5. d, e</td>
<td>MnOx-450</td>
<td>30</td>
<td>76</td>
<td>0.16</td>
</tr>
<tr>
<td>6. d, f</td>
<td>MnOx-450</td>
<td>37</td>
<td>&gt; 99</td>
<td>0.19</td>
</tr>
<tr>
<td>7. d</td>
<td>MnOx-550</td>
<td>42</td>
<td>&gt; 99</td>
<td>0.22</td>
</tr>
<tr>
<td>8. d</td>
<td>MnOx-650</td>
<td>42</td>
<td>&gt; 99</td>
<td>0.22</td>
</tr>
<tr>
<td>9.</td>
<td>C-Mn₃O₃</td>
<td>32</td>
<td>&gt; 99</td>
<td>0.17</td>
</tr>
<tr>
<td>10.</td>
<td>AMO</td>
<td>23</td>
<td>&gt; 99</td>
<td>0.12</td>
</tr>
<tr>
<td>11. g</td>
<td>Mn(III) acetate</td>
<td>13</td>
<td>&gt; 99</td>
<td>0.07</td>
</tr>
<tr>
<td>12.</td>
<td>no</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

a Reaction conditions: N-phenyltetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.) toluene (0.5 mL), 25 mg of catalyst, 100 °C, 3 h. b Conversions and selectivities were determined by GC-MS. c TOF= TON/ hours, TON = no of moles of limiting reagent converted to product per mole of catalyst. d Mesoporous catalyst, e TBHP (1.5 eqv.), f toluene (1 mL), g Mn(OAc)₃·2H₂O (85 mg, 0.16 mmol).
3.5.2 Role of Manganese Oxides

*Table 3.2* Summarization of XPS data of meso MnOx at different calcination temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Calcination temp. (°C)</th>
<th>Mn$^{3+}$ (641.8 eV)</th>
<th>Mn$^{4+}$ (643.9 eV)</th>
<th>O lattice</th>
<th>O adsorbed</th>
<th>O adsorbed water</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>250</td>
<td>68.25</td>
<td>31.75</td>
<td>55.91</td>
<td>29.09</td>
<td>15</td>
</tr>
<tr>
<td>2.</td>
<td>350</td>
<td>68.83</td>
<td>31.17</td>
<td>62.8</td>
<td>25.86</td>
<td>11.3</td>
</tr>
<tr>
<td>3.</td>
<td>450</td>
<td>69.63</td>
<td>30.37</td>
<td>65.38</td>
<td>23.22</td>
<td>11.4</td>
</tr>
<tr>
<td>4.</td>
<td>550</td>
<td>70.61</td>
<td>29.39</td>
<td>63.83</td>
<td>26.72</td>
<td>9.45</td>
</tr>
<tr>
<td>5.</td>
<td>650</td>
<td>73.84</td>
<td>26.16</td>
<td>77.84</td>
<td>22.16</td>
<td>0</td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td>23.82</td>
<td>43.14</td>
<td>06.62</td>
<td>65.13</td>
<td>28.25</td>
</tr>
</tbody>
</table>

*a* XPS was performed on the sample after separating and washing from a reaction.

3.5.3 Role of Lattice Oxygens

*Table 3.3* The catalytic results using different oxidants.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Selectivity (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>GC Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>TON&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Air</td>
<td>42</td>
<td>&gt; 99</td>
<td>42</td>
<td>0.6</td>
</tr>
<tr>
<td>2.</td>
<td>H$_2$O$_2$</td>
<td>20</td>
<td>76</td>
<td>15</td>
<td>0.24</td>
</tr>
<tr>
<td>3.</td>
<td>TBHP</td>
<td>30</td>
<td>76</td>
<td>23</td>
<td>0.36</td>
</tr>
<tr>
<td>4.</td>
<td>N$_2$</td>
<td>25</td>
<td>100</td>
<td>25</td>
<td>0.39</td>
</tr>
<tr>
<td>5.</td>
<td>O$_2$</td>
<td>41</td>
<td>&gt; 99</td>
<td>41</td>
<td>0.64</td>
</tr>
<tr>
<td>6.</td>
<td>O$_2$</td>
<td>63</td>
<td>n.d</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>7.</td>
<td>O$_2$</td>
<td>82</td>
<td>n.d</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.) toluene (0.5 mL), 25 mg of catalyst (Meso MnOx-550), 100°C, 3 hours. <sup>b</sup> Conversions and selectivities were determined by GC-MS. <sup>c</sup> TON = no of moles of limiting reagent converted to product per mole of catalyst. <sup>d</sup>1.5 bar, <sup>e</sup>20 bar.

*Table 3.4* The catalytic results using different solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Selectivity (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>TON&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Toluene</td>
<td>42</td>
<td>&gt;99</td>
<td>42</td>
<td>0.65</td>
</tr>
<tr>
<td>2.</td>
<td>1,4-dioxane</td>
<td>&lt;1</td>
<td>&gt;99</td>
<td>&lt;1</td>
<td>0.02</td>
</tr>
<tr>
<td>3.</td>
<td>Acetonitrile</td>
<td>4</td>
<td>&gt;99</td>
<td>4</td>
<td>0.06</td>
</tr>
<tr>
<td>Entry</td>
<td>Solvent</td>
<td>Concentration</td>
<td>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Selectivity (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>---------------</td>
<td>------------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>1.</td>
<td>neat</td>
<td>n/a</td>
<td>45</td>
<td>&gt; 99</td>
<td>45</td>
</tr>
<tr>
<td>2.</td>
<td>0.25</td>
<td>100</td>
<td>68</td>
<td>&gt; 99</td>
<td>68</td>
</tr>
<tr>
<td>3.</td>
<td>0.5</td>
<td>50</td>
<td>42</td>
<td>&gt; 99</td>
<td>42</td>
</tr>
<tr>
<td>4.</td>
<td>1</td>
<td>25</td>
<td>37</td>
<td>&gt; 99</td>
<td>37</td>
</tr>
<tr>
<td>5.</td>
<td>2</td>
<td>12.5</td>
<td>15</td>
<td>&gt; 99</td>
<td>15</td>
</tr>
<tr>
<td>6.</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>&gt; 99</td>
<td>7</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.), toluene, 25 mg of catalyst (Meso MnOx-550), 100°C, 3h. <sup>b</sup> Conversions and selectivities were determined by GC-MS. <sup>c</sup> TON = no of moles of limiting reagent converted to product per mole of catalyst.

Table 3.6 The catalytic results of different N-phenyl tetrahydroisoquinoline to Indole ratio.<sup>a</sup>

<table>
<thead>
<tr>
<th>Entry</th>
<th>N-phenyl tetrahydroisoquinoline to Indole ratio</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Selectivity (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>TON&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1:0.5</td>
<td>11</td>
<td>&gt; 99</td>
<td>11</td>
<td>0.17</td>
</tr>
<tr>
<td>2.</td>
<td>1:1</td>
<td>28</td>
<td>&gt; 99</td>
<td>28</td>
<td>0.44</td>
</tr>
<tr>
<td>3.</td>
<td>1:1.2</td>
<td>42</td>
<td>&gt; 99</td>
<td>42</td>
<td>0.65</td>
</tr>
<tr>
<td>4.</td>
<td>1:1.5</td>
<td>40</td>
<td>&gt; 99</td>
<td>40</td>
<td>0.62</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.), toluene (0.5 mL) 25 mg of catalyst (Meso MnOx-550), 100°C, 3h. <sup>b</sup> Conversions and selectivities were determined by GC-MS. <sup>c</sup> TON = no of moles of limiting reagent converted to product per mole of catalyst.

Table 3.7 The catalytic results using different catalyst support.<sup>a</sup>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst Support</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Selectivity (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>TON&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Meso-CeO₂</td>
<td>2</td>
<td>&gt; 99</td>
<td>2</td>
<td>0.17</td>
</tr>
</tbody>
</table>
2. Meso-TiO$_2$ < 1 > 99 < 1 0.16
3. Meso-Fe$_2$O$_3$ 9 > 99 9 0.21
4. Meso-Co$_3$O$_4$ 18 > 99 18 0.43
5. Meso-Mn$_2$O$_3$ 42 > 99 42 0.66

$^a$ Reaction conditions: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.), toluene (0.5 mL) 25 mg of catalyst, 100°C, 3h. $^b$ Conversions and selectivities were determined by GC-MS. $^c$ TON = no of moles of limiting reagent converted to product per mole of catalyst.

Table 3.8 Aerobic oxidative cross-coupling of N-Phenyltetrahydroisoquinoline with indole under different reaction conditions.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Oxidant</th>
<th>Conversion (%)$^b$</th>
<th>Selectivity (%)$^b$</th>
<th>GC Yield (%)</th>
<th>TON$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Meso-250-MnOx</td>
<td>Air</td>
<td>26</td>
<td>&gt; 99</td>
<td>26</td>
<td>0.40</td>
</tr>
<tr>
<td>2.</td>
<td>Meso-250-MnOx</td>
<td>N$_2$</td>
<td>17</td>
<td>&gt; 99</td>
<td>17</td>
<td>0.26</td>
</tr>
<tr>
<td>3.</td>
<td>Meso-250-MnOx</td>
<td>Air</td>
<td>15</td>
<td>&gt; 99</td>
<td>15</td>
<td>0.23</td>
</tr>
<tr>
<td>4.</td>
<td>Meso-350-MnOx</td>
<td>Air</td>
<td>35</td>
<td>&gt; 99</td>
<td>35</td>
<td>0.54</td>
</tr>
<tr>
<td>5.</td>
<td>Meso-350-MnOx</td>
<td>N$_2$</td>
<td>23</td>
<td>&gt; 99</td>
<td>23</td>
<td>0.36</td>
</tr>
<tr>
<td>6.</td>
<td>Meso-350-MnOx</td>
<td>Air</td>
<td>25</td>
<td>&gt; 99</td>
<td>25</td>
<td>0.39</td>
</tr>
<tr>
<td>7.</td>
<td>Meso-450-MnOx</td>
<td>Air</td>
<td>39</td>
<td>&gt; 99</td>
<td>39</td>
<td>0.61</td>
</tr>
<tr>
<td>8.</td>
<td>Meso-450-MnOx</td>
<td>N$_2$</td>
<td>26</td>
<td>&gt; 99</td>
<td>26</td>
<td>0.40</td>
</tr>
<tr>
<td>9.</td>
<td>Meso-450-MnOx</td>
<td>Air</td>
<td>33</td>
<td>&gt; 99</td>
<td>33</td>
<td>0.51</td>
</tr>
<tr>
<td>10.</td>
<td>Meso-550-MnOx</td>
<td>Air</td>
<td>42</td>
<td>&gt; 99</td>
<td>42</td>
<td>0.65</td>
</tr>
<tr>
<td>11.</td>
<td>Meso-550-MnOx</td>
<td>N$_2$</td>
<td>27</td>
<td>&gt; 99</td>
<td>25</td>
<td>0.42</td>
</tr>
<tr>
<td>12.</td>
<td>Meso-550-MnOx</td>
<td>Air</td>
<td>38</td>
<td>&gt; 99</td>
<td>38</td>
<td>0.59</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.), Toluene (0.5 mL), 25 mg of catalyst, 100°C, 3h. $^b$ Conversions and selectivities were determined by GC-MS. $^c$ TON = no of moles of limiting reagent converted to product per mole of catalyst. $^d$ 1st Reuse.
3.5.4 Substrate Scope

3.5.4.4 Oxidative Homo-Coupling

To explore the generalizability of our protocol, we evaluated its scope in the presence of different \(N\)-aryl tetrahydroisoquinolines and indoles. Under optimized reaction conditions, \(N\)-phenyl tetrahydroisoquinoline (1a) and indole derivatives with electron-rich (Table 3.9, entry 3-5, 7) and electron-deficient (Table 3.9, entry 2, 6, 8) groups responded well and produced corresponding C-C coupled products with moderate (53-71\%) to high (78-98\%) conversion and excellent selectivity (>99\%). The result with 6-chloroindole (2b) (Table 3.9, entry 2) is noteworthy. It is common for such systems to undergo dehalogenation in the presence of heterogeneous catalysts. In the case of an ester-substituted indole (5-COOMe-indole), a maximum of 35\% yield (Table 3.9, entry 7) was obtained, probably due to steric hindrance. \(N\)-Methylindole (2g) yielded only 53\%; again, it is likely that steric hindrance played a role.

### Table 3.9
Cross-coupling of \(N\)-Phenyl tetrahydroisoquinolines (1a) with differently substituted indole derivatives in presence of meso-MnOx catalyst.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Indole</th>
<th>Conversion (%)(^b)</th>
<th>Selectivity (%)(^b)</th>
<th>TOF(^c) (h(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. (^d)</td>
<td>indole (2a)</td>
<td>98</td>
<td>&gt;99 (3aa) (89) (^j)</td>
<td>0.30</td>
</tr>
<tr>
<td>2. (^e)</td>
<td>6-Cl (2b)</td>
<td>80</td>
<td>&gt;99 (3ab) (72) (^j)</td>
<td>0.07</td>
</tr>
<tr>
<td>3. (^f)</td>
<td>2-Me (2c)</td>
<td>71</td>
<td>&gt;99 (3ac)</td>
<td>0.09</td>
</tr>
<tr>
<td>4. (^f)</td>
<td>5-Me (2d)</td>
<td>78</td>
<td>&gt;99 (3ad) (72) (^j)</td>
<td>0.10</td>
</tr>
<tr>
<td>5. (^f, i)</td>
<td>5-OMe (2e)</td>
<td>89</td>
<td>&gt;99 (3ae)</td>
<td>0.06</td>
</tr>
<tr>
<td>6. (^g, i)</td>
<td>5-COOMe (2f)</td>
<td>35</td>
<td>&gt;99 (3af)</td>
<td>0.05</td>
</tr>
<tr>
<td>7. (^g, i)</td>
<td>N-Me (2g)</td>
<td>53</td>
<td>&gt;99 (3ag)</td>
<td>0.07</td>
</tr>
<tr>
<td>8. (^h)</td>
<td>7-NO(_2) (2h)</td>
<td>98</td>
<td>&gt;99 (3ah) (91) (^j)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: amine derivative (0.25 mmol), indole derivative (1.2 eqv.), 100 °C, 0.25 mL toluene, 25 mg catalyst. \(^b\) Conversions and selectivities were determined by GC-MS. \(^c\) TOF = TON/ hours, TON = no of moles of
amine derivative converted to the product per mole of catalyst.\textsuperscript{d} 5 h, \textsuperscript{e} 18 h, \textsuperscript{f} 24 h, \textsuperscript{h} 3 h, \textsuperscript{i} 50 mg catalyst. \textsuperscript{j} numbers in parenthesis represents the isolated yields the products.

### 3.5.4.5 Oxidative Hetero-coupling

**Table 3.10** Cross-coupling of differently substituted N-aryl tetrahydroisoquinolines with different in presence of meso-MnOx catalyst.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>R\textsuperscript{1}</th>
<th>R\textsuperscript{2}</th>
<th>Conversion (%)\textsuperscript{c}</th>
<th>Selectivity (%)\textsuperscript{c}</th>
<th>TOF\textsuperscript{c} (h\textsuperscript{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. \textsuperscript{e}</td>
<td>1b</td>
<td>indole (2a)</td>
<td>83</td>
<td>&gt;99 (3ba)</td>
<td>0.08</td>
</tr>
<tr>
<td>2. \textsuperscript{f}</td>
<td>6-Cl (2b)</td>
<td>87</td>
<td>&gt;99 (3bb)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>3. \textsuperscript{e}</td>
<td>2-Me (2c)</td>
<td>87</td>
<td>&gt;99 (3bc)</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>4. \textsuperscript{e}</td>
<td>5-Me (2d)</td>
<td>85</td>
<td>&gt;99 (3bd)</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>5. \textsuperscript{f}</td>
<td>5-OMe (2e)</td>
<td>75</td>
<td>&gt;99 (3be)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>6. \textsuperscript{f}</td>
<td>N-Me (2g)</td>
<td>77</td>
<td>&gt;99 (3bg)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>7. \textsuperscript{e}</td>
<td>7-NO\textsubscript{2} (2h)</td>
<td>96</td>
<td>&gt;99 (3bh) (88) m</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>8. \textsuperscript{h}</td>
<td>1c</td>
<td>indole (2a)</td>
<td>83</td>
<td>&gt;99 (3ca)</td>
<td>0.22</td>
</tr>
<tr>
<td>9. \textsuperscript{h}</td>
<td>2-Me (2c)</td>
<td>94</td>
<td>&gt;99 (3cc) (84) m</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>10. \textsuperscript{e}</td>
<td>5-Me (2d)</td>
<td>71</td>
<td>&gt;99 (3cd)</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>11. \textsuperscript{e}</td>
<td>5-OMe (2e)</td>
<td>88</td>
<td>&gt;99 (3ce)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>12. \textsuperscript{e}</td>
<td>N-Me (2g)</td>
<td>87</td>
<td>&gt;99 (3cg)</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>13. \textsuperscript{i}</td>
<td>7-NO\textsubscript{2} (2h)</td>
<td>72</td>
<td>&gt;99 (3ch)</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>14. \textsuperscript{j, k}</td>
<td>1d</td>
<td>indole (2a)</td>
<td>28</td>
<td>&gt;99 (3da)</td>
<td>0.01</td>
</tr>
<tr>
<td>15. \textsuperscript{j, k}</td>
<td>2-Me (2c)</td>
<td>78</td>
<td>&gt;99 (3dc)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>16. \textsuperscript{j, k}</td>
<td>5-Me (2d)</td>
<td>55</td>
<td>&gt;99 (3dd)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>17. \textsuperscript{f}</td>
<td>N-Me (2g)</td>
<td>86</td>
<td>&gt;99 (3dg)</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: amine derivative (0.25 mmol), indole derivative (1.2 eqv.), 100 °C, 0.25 mL toluene, 25 mg catalyst. \textsuperscript{b} 1b = 4-Me-Ph; 1c = 4-OMe-Ph; 1d = 4-NO\textsubscript{2}-Ph. c Conversions and selectivities were determined by GC-MS. d TOF = TON/ hours, TON = no of moles of amine derivative converted to product per mole of catalyst. e12 h. f 24 h, g 18 h, h 6 h, i 30 h, j 36 h, k 50 mg catalyst. m numbers in parenthesis represents the isolated yields the products.
The excellent activity of the catalyst for coupling 1a with differently substituted indoles spurred us to investigate the effect of different N-substituted tetrahydroisoquinolines with indole derivatives. Superb reactivity was seen for electron rich N-aryl groups (N-(4-Me-Ph)-tetrahydroisoquinoline (1b) (Table 3.10, entry 1-7) and N-(4-OMe-Ph)-tetrahydroisoquinoline (1c) (Table 3.10, entry 8-13)), while sluggish rates of reaction were observed with an electron withdrawing N-aryl group (N-(4-NO2-Ph)-tetrahydroisoquinoline (1d) (Table 3.10, entry 14-17)). Depending on the amine and indole precursors used, reaction conditions were modified in several instances to optimize conversion (70 % to as high as 98 %) and selectivity (> 99 %). Taken together, the results demonstrate the broad utility of our protocol.

3.5.5 Reusability and Heterogeneity

To determine if the observed catalysis was resulting from leached active sites, the solid catalyst was separated from the reaction mixture by filtration after 3 h (at about 42 % conversion). The filtrate was then stirred under the optimized reaction conditions for 5 more hours. Aliquots collected after each hour were analyzed by GC-MS to track the progress of the reaction. No further increase in GC-MS yield after the first 3 hours (Figure 3.6), indicated the absence of leached active species in the solvent. For a more convincing result, the filtrate was analyzed by inductively coupled plasma mass spectrometry (ICP-MS), where the manganese (Mn) was found in very low
amount (165 ppm). To evaluate the reusability of the catalyst, separated (>90 % by filtration) catalyst was washed with toluene and ethanol to remove adsorbed organic compounds prior to reactivating at 250 °C for 1 hour. A similar approach was followed to recycle the catalyst after every cycle. Retrieved catalysts were successfully reused for three more cycles with a drop of activity of only 14 % (Figure 3.7).

![Figure 3.7 a) Reusability test of the catalyst. Reaction condition: N-phenyl tetrahydroisoquinoline (0.25 mmol), indole (1.2 eqv.), 100 °C, 0.50 mL toluene, 25 mg catalyst. Air balloon, 3 h. Turnover number (TON) = [reacted mol N-phenyl tetrahydroisoquinoline]/[total mol catalyst]. b) PXRD of meso MnOx-550 before and after fourth reuse. No noticeable changes were observed in the diffraction patterns after fourth reuse.](image-url)
3.5.6 Kinetic Studies

Kinetic studies (Figure 3.8) revealed a first-order rate equation (Figure 3.10) with respect to the amine (1a), having a rate constant of 0.24 h⁻¹. Similar time-dependent studies were conducted at different temperatures (25 °C, 50 °C and 75 °C) to determine the apparent activation energy (E_a) as 21.12 KJ/mol, from an Arrhenius plot (Figure 3.12).

To explore in more depth the reaction kinetics, a time-dependent reaction was performed between N-phenyltetrahydroisoquinoline (1a) and indole (2a) (Figure 3.9). Interestingly, an intermediate with a mass one-unit lower than 1a was tracked in the kinetic profile along with the expected coupled product (3aa) and unreacted substrates. That intermediate disappeared by the end of the reaction (Figure 3.9). To determine the nature of the intermediate, another time-dependent study was executed in the presence of 1,2,3,4-tetrahydroisoquinoline and indole (2a) under similar reaction conditions. Formation of the corresponding C-C coupled product with a lower rate of reaction (Figure 3.9) is consistent with the presence of a charged intermediate (see Figure 3.13, D), which was further supported by the reaction kinetics of its neutral counterpart (Figure. 3.16). The charge on nitrogen can be stabilized by the N-substituted aryl ring (depending on the electronic nature of the aryl ring), which would enhance the coupling rate. A significant decrease of turnover frequency (TOF) upon changing electron rich (4-Me-Ph (1b) and 4-OMe-Ph (1c)) groups with an electron deficient 4-NO₂-Ph (1d) group suggested the presence of a positive charge on the intermediate. The electron-deficient aryl ring also lowered the rate of reaction significantly (Table 3.10, entry 16), while the electron-rich aryl rings accelerated the rate (Table 3.10, entry 1, 9).

![Figure 3.8](image-url) Time-dependent Study. Reaction procedures were the same as discussed in Table 3.2. Formation of minute amount of imine intermediate was observed.
Evidence of charge stability by the incorporation of aryl groups. Reaction conditions were same as in Table 3.2. Reaction kinetics for both N-substituted (with Phenyl) and unsubstituted 1,2,3,4-tetrahydroisoquinolines were compared. Faster reaction kinetics was observed in case of N-aryltetrahydroisoquinoline. This probably caused, due to the better stability of the charged intermediate B (Figure 3.13).

Kinetic study of the oxidative cross-coupling of N-phenyltetrahydroisoquinoline with indole by meso-Mn$_3$O$_4$: The reaction exhibited a first-order rate dependence with respect to N-phenyltetrahydroisoquinoline, having the rate constant of 0.235 h$^{-1}$.
Figure 3.11 Kinetic study of the oxidative cross-coupling of N-phenyltetrahydroisoquinoline with indole by meso-Mn$_2$O$_3$: The reaction exhibited a first-order rate dependence with respect to N-phenyltetrahydroisoquinoline, having the rate constant of 0.544 h$^{-1}$.

Reaction conditions: N-phenyltetrahydroisoquinoline (0.25 mmol), indole (1.2 equiv.) toluene (0.25 mL), 25 mg of catalyst (Meso MnOx-550), 100°C. 

$A_0$: original concentration of substrate. $A_t$: concentration of substrate at time t. $K$: rate constant.

$K_{dTHIQN-Ph} / K_{dTHIQN-Ph}$ for the deprotonation of d-THIQ-N-Ph (THIQ-N-Ph to d-THIQ-N-Ph) = 0.544 / 0.218 = 2.49.

Figure 3.12 Arrhenius plot for oxidative coupling of N-phenyltetrahydroisoquinoline by meso Mn$_2$O$_3$: The apparent activation energy was estimated as 21.12 KJ mol$^{-1}$. Reaction conditions: N-phenyltetrahydroisoquinoline (0.25 mmol), catalyst (25 mg), solvent (0.5 mL), air balloon. $K$: rate constant.
Although the experiments described above demonstrate the presence of an iminium ion intermediate, they do not rule out radical intermediates. More experiments were conducted to explore this possibility. A radical trap (2,6-di-tert-butyl-4-methylphenol) was used to potentially couple with radical species that might be present. A reaction containing 1,2,3,4-tetrahydroisoquinoline, indole and the radical trap yielded an adduct of the trap and the amine (based on the mass spectra, Figure 3.15, c) instead of a C-C coupled product (Figure 3.15, b). This is consistent with the presence of a radical intermediate B (Figure 3.13). However, N-phenyltetrahydroisoquinoline failed to form the coupled product with the trap, probably due to steric hindrance of bulky groups (Figure 3.15, a).

Combining the evidence, we propose a mechanism, shown in Figure 3.13, for this meso-MnOx CDC. We assume the formation of radical intermediate B is driven by the reduction potential of manganese and that the active species removes an electron from the lone pair on the nitrogen. Reduction of surface active manganese is known to simultaneously release labile lattice oxygen molecules due to structural changes. Based on prior studies we believe these lattice oxygens deprotonate B to form intermediate C. Loss of an electron transforms C to D which is a stable intermediate which was tracked in minute amounts by GC-MS analysis (Figure 3.8). This intermediate (D) was reacted with indole to form the intermediate F, which after the subsequent loss of a proton produced the expected product G. The released lattice oxygen combines with the protons and electrons over the course of the reaction to produce water as a by-product.

The increase in conversion (Table 3.1) with the increment of calcination temperature (from 250 to 650 °C) prompted us to investigate the chemistry behind the efficiency of manganese oxides during the reaction. Significantly, the amount of Mn$^{3+}$, as revealed by X-ray photoelectron spectroscopic (XPS) analysis, increased with calcination temperatures (Table 3.2). This led us to presume a correlation between the amount of Mn$^{3+}$ and conversion. The facile transformation of Mn$^{3+}$ to Mn$^{2+}$ probably drove the reaction forward with increasing efficiency.

3.6 Discussion

Interestingly, the two reduction peaks were observed to shift closer to each other with rising calcination temperatures and eventually merged at 650 °C. This indicates a high probability of an Mn$^{3+}$ to Mn$^{2+}$ transformation, which probably facilitated the first (Figure 3.13, A to B) and third C to D (Figure 3.13) steps of the reaction. As mentioned above, the lattice oxygens released during
the Mn$^{3+}$ to Mn$^{2+}$ transformation are believed to deprotonate the intermediates (B and F) and catalyze the reaction. Thus, increased transformation of Mn$^{3+}$ to Mn$^{2+}$ may enhance the release of lattice oxygens and, hence, the reaction rate, as deprotonations are considered to be more energy demanding than electron abstractions. The growth of the lattice oxygen content (Table 3.2) with increasing calcination temperatures led us to design a comparative study to probe the enhanced accessibility of the lattice oxygens.

![Figure 3.13 The proposed reaction mechanism.](image)

A set of experiments was performed under nitrogen and air for each material to identify the role of different available oxygens. The reactions performed under a nitrogen atmosphere (Table 3.8, entry 2, 5, 8, 11), showed a dramatic drop in product formation compared to a reaction run under aerobic conditions (Table 3.8, entry 1, 4, 7, 10). This indicated a role for aerobic oxygens in catalyzing these reactions. The lower conversions that were observed for reactions under nitrogen, were presumably due to existing lattice oxygens. The increased efficiency under aerobic conditions supports the theory of a collected contribution from aerobic and lattice oxygens. The increase of conversion under nitrogen with calcination temperatures was probably
due to the increasing accessibility of the labile lattice oxygens (Table 3.8, entry 2, 5, 8, 11). Experiments to compare the reusability of all materials (Table 3.8, entries 3 (vs 1), 6 (vs 4), 9 (vs 7), 12 (vs 10)) showed that reusability increased with calcination temperature. This comparison of results of each material under air and nitrogen and of the first reuse shows agreement with the feasibility of Mn$^{3+}$ to Mn$^{2+}$ transformation and the availability of lattice oxygens with increased calcination temperatures.

### 3.7 Computational Calculations

![Energy profile of the reaction in the gas phase, as determined by DFT calculations.](image)

**Figure 3.14** Energy profile of the reaction in the gas phase, as determined by DFT calculations.

Density functional theory calculations were performed with a frozen core projector augmented wave method as implemented in Vienna Ab-Initio Simulation Package (VASP) code, to further validate our proposed reaction mechanism. Exchange and correlation interactions were treated using a generalized gradient approximation with the Perdew-Burke-Ernzerhof (PBE) function. To expand the crystal wave functions, a plane wave basis cutoff of 400 eV was used. In addition, to estimate the Mn oxidation states, DFT calculations were carried out on mesoporous manganese oxides (meso-MnOx).

Energy profiles for the C-C coupling reaction are shown in **Figure 3.14**. The energy corresponding to A was the reference energy. Under optimized conditions, the scope of the coupling reaction for the most feasible mechanism was investigated. The relative energies (Kcal mol$^{-1}$) are based on the summations of the representative total energies ($E_{\text{total}}$) of all species.
The reaction energy profiles shown in Figure 3.14 suggest that the steps A to B and C to D, where Mn$^{3+}$ abstracts electrons to form Mn$^{2+}$, are energetically more favorable. The steps B to C and F to G, which involve proton abstraction by lattice oxygens, are energetically unfavorable. The possibility of intermediate C' could be neglected due to its higher relaxed energy (135.62 kcal/mol) than intermediate C (76.69 kcal/mol). As per our DFT calculations, step F to G is energetically more favorable, probably due to the energy of aromatization, than B to C. This makes B to C the rate-determining step, which was supported by a primary kinetic isotope effect ($K_{\text{H}}/K_{\text{D}} = 2.49$, Figure 3.11). DFT computation based Bader charge analysis supports that, for intermediate B, the active Mn$^{3+}$ species was reduced to Mn$^{2+}$ with a calculated charge of 2.12 e- on Mn.

3.8 Conclusions

In conclusion, a unique noble metal free, non-toxic, reusable, and cost-effective catalytic protocol has been developed to couple various N-aryltetrahydroisoquinolines (sp$^3$ C-H) and Indoles (sp$^2$ C-H) with moderate to excellent yields (35–99 %), using mesoporous manganese oxides. The use of air and manganese oxides as the oxidants make our protocol interesting and appealing as compared to other reported systems. The mechanistic investigation led by experimental evidence and DFT computations validated the proposed mechanism. Studies showed the efficiency of manganese oxides and their role in the mechanism. Research to apply our protocol to other types of C-C coupling reactions is underway.

3.9 Analysis of Reaction Products

The GC-MS analyses were performed by a 7820A GC system connected with a mass detector of 5975 series MSD from Agilent Technologies, and a nonpolar cross-linked methyl siloxane column with dimensions of 12 in × 0.200 mm × 0.33 μm was used. The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker AVANCE III- 400 MHz spectrometer. $^1$H NMR spectra were collected at 400 MHz with chemical shift referenced to the residual peak in CDCl$_3$ (δ: H 7.26 ppm). $^{13}$C NMR spectra were collected at 100 MHz and referenced to the residual peak in CDCl$_3$ (δ: C 77.0 ppm). Multiplicities are written as s (singlet), d (doublet), t (triplet), and m (multiplet).
3.9.1 GC-MS to detect reaction intermediates

\[
\text{M.W.} = 365 \text{ g/mol}
\]
**Figure 3.15** Intermediate Trapping: Reaction procedure: a) N-phenyltetrahydroisoquinoline 1a (0.25 mmol), indole (1.2 eqv.), radical inhibitor (1.2 eqv.), and meso-Mn$_2$O$_3$ (25 mg, 0.16 mmol) were successively placed and mixed with toluene (0.5 mL) and refluxed at 100°C under air balloon. The reaction mixture was analyzed by GC-MS after cooling to room temperature. b) Instead of using N-phenyltetrahydroisoquinoline, 1, 2, 3, 4-tetrahydroisoquinoline was used under previously mentioned reaction condition. c) Mass-spectra of the trapped intermediates.

**Figure 3.16** Intermediate as a substrate. Reaction procedure: 3,4-dihydroisoquinoline (0.25 mmol), indole (1.2 mmol) and meso-Mn$_2$O$_3$ (25 mg, 0.16 mmol) were successively placed and mixed with toluene (0.25 mL) and refluxed at 100°C under air balloon. The reaction mixture was analyzed by GC-MS after cooling to room temperature.
3.9.2 NMR to detect reaction products

1-(1H-Indol-3-yl)-2-phenyl-1,2,3,4-tetrahydro-isoquinoline

Pale yellow solid; Yield - 71%; $^1$H NMR (CDCl$_3$, 400 MHz, ppm) $\delta$ 7.92 (s, 1H), 7.55 (d, $J = 7.1$ Hz, 1H), 7.40 (m, 1H), 7.31 (m, 2H), 7.23 (m, 2H), 7.15 (m, 4H), 7.04 (m, 2H), 7.01 (m, 1H), 3.63 (dd, $J = 7.7$, 4.6 Hz, 2H), 3.07 (m, 1H), 2.81 (dd, $J = 16.2$, 4.4 Hz, 1H);
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ 149.8, 137.4, 136.6, 135.6, 129.2, 128.8, 128.0, 126.7, 126.5, 125.7, 124.1, 122.1, 120.1, 119.6, 119.3, 118.1, 115.8, 111.0, 56.6, 42.3, 29.7, 26.6;
1-[4-(2-Methyl-propenyl)-1H-pyrrol-3-yl]-2-phenyl-1,2,3,4-tetrahydro-isoquinoline

1H NMR (CDCl3, 400 MHz, ppm) δ 7.82 (s, 1H), 7.26 9m, 4H), 7.17 (m, 3H), 7.04 (d, J = 8.2 Hz, 2H), 6.69 (d, J = 8.2 Hz, 1H), 6.78 (t, J = 7.2 Hz, 1H), 6.57 (d, J = 2.2 Hz, 1H), 6.14 (s, 1H), 3.64 (m, 2H), 3.07 (m, 1H), 2.80 (m, 1H);
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$, 150.0, 137.5, 135.5, 134.9, 129.1, 128.8, 128.1, 126.7, 126.6, 125.6, 124.4, 123.8, 119.6, 118.9, 118.2, 116.1, 56.6, 42.3, 29.7, 26.5, 21.6;
1-(6-Chloro-1H-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydro-isoquinoline

$^1$H NMR (CDCl₃, 400 MHz, ppm) $\delta$ 7.90 (s, 1H), 7.40 (d, $J$ = 8.6 Hz, 1H), 7.30 (d, $J$ = 1.7 Hz, 1H), 7.21 (m, 4H), 7.01 (d, $J$ = 8.2 Hz, 2H), 6.98 (dd, $J$ = 8.6, 1.8 Hz, 1H), 6.80 (t, $J$ = 7.3 Hz, 1H), 6.62 (d, $J$ = 2.0 Hz, 1H), 3.59 (m, 2H), 3.07 (ddd, $J$ = 16.0, 9.4, 6.1 Hz, 1H), 2.79 (ddd, $J$ = 16.3, 4.4, 4.4 Hz, 1H),
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ 149.8, 137.1, 136.9, 135.5, 129.2, 128.9, 128.1, 127.9, 126.8, 125.7, 125.1, 124.7, 121.1, 120.4, 119.5, 118.5, 116.2, 110.9, 56.6, 42.4, 29.7, 26.6;
1-(7-Nitro-1H-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydro-isoquinoline.

\[
\begin{align*}
\text{NO}_2
\end{align*}
\]

\(^1\text{H} \text{NMR (CDCl}_3, 400 \text{ MHz, ppm)} \delta 9.71 (s, 1H), 8.11 (d, \text{ } J = 8.1 \text{ Hz, } 1H), 7.86 (d, \text{ } J = 7.8 \text{ Hz, } 1H), 7.24 (m, 6H), 7.09 (t, \text{ } J = 8.0 \text{ Hz, } 1H), 7.04 (d, \text{ } J = 8.2 \text{ Hz, } 2H), 6.85 (t, \text{ } J = 7.2 \text{ Hz, } 1H), 6.80 (d, \text{ } J = 1.4 \text{ Hz, } 1H), 6.17 (s, 1H), 3.64 (ddd, \text{ } J = 13.0, 9.8, 4.9 \text{ Hz, } 1H), 3.54 (ddd, \text{ } J = 14.4, 10.0, 4.6 \text{ Hz, } 1H), 3.10 (ddd, \text{ } J = 16.2, 9.9, 3.3 \text{ Hz, } 1H), 2.80 (ddd, \text{ } J = 16.4, 8.2, 4.1 \text{ Hz, } 1H),
\]
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$ 149.7, 136.4, 135.4, 132.8, 130.0, 129.3, 128.5, 127.9, 127.0, 126.5, 125.9, 120.8, 119.3, 119.1, 119.1, 116.7, 56.5, 42.5, 29.7, 26.5;
1-(7-Nitro-1H-indol-3-yl)-2-(4-methyl phenyl)-1,2,3,4-tetrahydro-isoquinoline.

\[
\begin{align*}
\text{NO}_2
\end{align*}
\]

\[\text{H NMR (CDCl}_3, 300 \text{ MHz, ppm)} \delta 9.70 (s, 1H), 8.15, (d, J = 8.07 \text{ Hz, 2H}), 7.85 (d, J = 7.8 \text{ Hz, 2H}), 7.21 (m, 4H), 7.11 (t, J = 8.01 \text{ Hz, 1H}), 7.06 (d, J = 7.23 \text{ Hz, 1H}), 6.95 (t, J = 8.19 \text{ Hz, 1H}), 6.79 (d, 1H), 6.10 (s, 1H), 3.57 (m, J = 13.2, 9.96, 5.43 \text{ Hz, 1H}), 3.10 (ddd, J = 16.2, 9.9, 3.3 \text{ Hz, 2H}), 2.79 (ddd, J = 16.4, 8.2, 4.1 \text{ Hz, 2H}), 2.25 (s, 3H). \]
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) $\delta$ 147.73, 136.46, 132.42, 129.79, 129.17, 128.91, 128.69, 127.99, 126.93, 126.52, 125.84, 120.92, 119.34, 119.04, 117.59, 109.98, 56.85, 43.13, 29.70, 26.49, 20.44;
1-(2-Methyl-1H-indol-3-yl)-2(4-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline.

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{H} & \quad \text{O} \\
\end{align*}
\]

\(^1\)H NMR (CDCl3, 400 MHz, ppm) \(\delta\) 7.67 (s, 1H), 7.2 (m, 1H), 7.1 (m, 1H), 7.04 (m, 7H), 6.90 (d, J = 12.4 Hz, 2H), 6.7 (d, J = 8.7 Hz, 2H), 5.64 (s, 1H), 3.59 (m, 1H), 3.45 (m, 1H), 3.21 (m, 1H), 3.34 (m, 1H), 2.00 (s, 3H).
$^{13}$C NMR (CDCl$_3$, 100 MHz, ppm) δ 154.96, 145.61, 138.57, 135.07, 135.03, 133.58, 128.55, 128.49, 128.13, 126.03, 125.95, 123.48, 120.65, 119.57, 119.29, 113.82, 113.34, 109.99, 109.92, 59.32, 55.41, 48.68, 29.74 29.22, 11.97;

3.10 References

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Chapter 4. Partial Surface Selenization of Cobalt Sulfide Microspheres for Enhancing the Hydrogen Evolution Reaction

4.1 Abstract

Electrocatalysis of water is a scalable and sustainable source of the production of hydrogen (H\textsubscript{2}), a future energy carrier. This drive for clean energy inspired us to develop an inexpensive, readily producible, highly active, and stable catalyst to replace current state of the art platinum catalysts. Building on the promising hydrogen evolution reaction (HER) activity of many pyrites, their structural tuning by different metals/non-metals has been found to be effective in several instances. We present here one such effort by partial surface selenization of mesoporous cobalt sulfide material which displayed an outstanding long-term operational stability (for at least 25 hours) besides attaining a current density of 100 mA cm\textsuperscript{-2} at an overpotential of 160 mV versus the reversible hydrogen electrode (RHE) (in acidic media). A remarkably low Tafel slope (of 52 mV dec\textsuperscript{-1}) and high exchange current density (\(j_0\)) (of 70 µA cm\textsuperscript{-2}) make our catalyst superior to most existing systems. More importantly, using a variety of analytical techniques, electrochemical measurements, and theoretical calculations, we have analyzed the morphology, and identified a new sulfur-selenide species to be the key to improving the intrinsic activity of the material (as compared to the meso-CoS\textsubscript{2}). This study is expected to explain similar systems and modify approaches to enhancing the electrochemical activity of metal chalcogenides.

4.2 Background and Significance

The electrochemical hydrogen evolution reaction (HER) from water is believed to be the cleanest and most sustainable approach for hydrogen (H\textsubscript{2}) production to meet future terawatt energy demands.\textsuperscript{1,2} To produce hydrogen in a facile way for industrial applications, a highly active and robust catalyst is required which minimizes the energy barrier, here represented by the overpotential (\(\eta\)) of this process.\textsuperscript{3} To date, platinum (Pt) and its alloys are considered to be the most active HER catalysts due to their high stability and lowest overpotential (~25-35 mV of overpotential to achieve a geometrical current density of 10 mA cm\textsuperscript{-2}).\textsuperscript{4} However, the scarcity and high cost of platinum (Pt) limit its widespread application.\textsuperscript{5,6} Hence, to replace platinum (Pt), the development of a highly active (close to Pt), sustainable, and cost-effective catalyst is in urgent need. Inspired by this rising demand, scientists across the world have started exploring possibilities
of developing a hydrogen economy. This has led to various binary (such as metal oxides, nitrides, sulfides, selenides, phosphides, carbides, and borides) and ternary transition metal compounds (such as MoPS, WPS, CoPS, WSSe, MoSSe-NiSe, and bimetallic alloys) as HER catalysts. Among them, pyrite-type transition metal dichalcogenides (MX₂, where M = Fe, Co, or Ni and X = O, S or Se) have gained significant attention due to their natural abundance, excellent stability (under both acidic and basic solutions), and outstanding HER performance, which makes them attractive for industrial applications.

Transition metal pyrites are also known for various energy-related applications due to their metallic and semiconducting properties. However, in HER the electron donating property of chalcogenides is suggested to be a primary requirement. This requires the tuning of the electronic feature of X₂⁻ dumbbells in metal pyrites by varying the atomic ratio of elements, which is considered to be highly crucial to enhancing the hydrogen adsorption process. A recent study on cobalt phosphosulfide (CoPS) has successfully showcased how the replacement of sulfur by phosphorus tune the electronic structure of the catalyst to aid the hydrogen evolution reaction. Followed by this, various selenium doped or alloyed ternary metal pyrites such as WS₂(1-x)Se₂x and MoS₂(1-x)Se₂x were prepared, which exhibited excellent enhancement of HER activity compared to WS₂ and MoS₂, respectively. In CoPS, phosphorous (P) doping converted S₂⁻ to (SP)³⁻ dumbbells. This was shown to increase the surface electron density of the material which caused better adsorption of thermoneutral hydrogens. However, this enhancement of the negative charge of the anionic site is not possible in the selenium doped system, as the electronic nature of sulfur and selenium are comparable. Therefore, in the rush of unraveling the source of enhanced activity of rarely studied selenium doped metal pyrites, we initiated investigations. Herein, we demonstrate the synthetic route of a unique surface selenized mesoporous cobalt sulfide electrocatalyst, its excellent HER activity, chemical stability, and the determination of its surface active sites. Formation of these active sites and their effects were evaluated by electrochemical impedance spectroscopy (EIS), X-ray photoelectron spectroscopic (XPS) techniques, and active site blocking experiments. Moreover, Density Functional Theory (DFT) computed calculations confirm the stability of the material and our experimental findings.
4.3 Experimental Section

4.3.1 Material Synthesis

All chemicals were purchased from Sigma-Aldrich unless otherwise specified. Mesoporous-Co$_3$O$_4$, synthesized by a soft template mediated solvent evaporation induced self-assembly method,$^{45}$ was sulfurized to produce mesoporous-CoS$_2$, which was selenized to produce the mesoporous-CoSSe material.

**4.3.1.1 Synthesis of meso-Co$_3$O$_4$**

In a typical synthesis 0.02 mol of cobalt nitrate hexahydrate (Co(NO$_3$)$_2$·6H$_2$O) and 0.134 mol of 1-butanol were added to a 120 mL beaker. To this solution 0.00034 mol of poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol)(Pluronic P123, PEO20PPO70PEO20, molar mass 5800 g mol$^{-1}$) and 0.032 mol of concentrated nitric acid (HNO$_3$) were added successively and stirred at room temperature until the solution became clear (purple). The resulting clear solution was then kept in an oven at 120°C for 4 hours to get a light pink dry powder. The product was collected and washed with excess ethanol, centrifuged, and dried in a vacuum oven overnight to get rid of excess surfactants and remaining organics. In the end, the dried pink powder was subjected to a heating cycle of 150°C for 12 h and then to 250°C for 4 hours. These steps are supposed to remove all surfactants and control the mesoporosity of the material.$^{45}$

Figure 4.1 Schematic representation of the catalyst synthesis.
4.3.1.2 Synthesis of meso-CoS₂

The black powder obtained from the previous step was then placed in the center of a standard 1.5-inch (diameter) quartz tube using a ceramic boat. Another ceramic boat containing sulfur was placed next to the first boat. The quartz tube was kept inside a tube-furnace and Helium (He) gas was used to purge the reactor for 30 minutes to remove air. Then 5 % H₂S was mixed online with 95 % of Helium (He) to pass through the tube furnace with a feeding speed of 50 s.c.c.m. for 12 hours with a ramp rate of 1 °C/min up to 250 °C. The system was brought to room temperature before taking the sample out for further use.

4.3.1.3 Synthesis of meso-CoSSe-nh

The meso-CoS₂ powder obtained from the step mentioned above was placed in the center of a standard 1.5-inch (diameter) quartz tube (different than the one used for sulfurization to avoid contamination) using a ceramic boat. Another ceramic boat containing selenium was placed next to the first boat. The quartz tube was then kept inside a tube-furnace and Helium (He) gas was purged through the system for 30 minutes to remove air at a feeding speed of 50 s.c.c.m. Then, the temperature of the furnace was set to increase up to 250 °C for nᵗʰ hours with a ramp rate of 1 °C/min. The furnace was allowed to cool down to room temperature to take the sample out for further use.

4.4 Characterization

4.4.1 Structural Characterization and Analysis of Reaction Products

Since electrochemical HER is a surface phenomenon, this reaction has been reported to be highly dependent on the surface area of a material which is a direct measure of the number of active sites. This makes materials with a higher number of active sites of great interest. An increase in the number of active sites is believed to contribute towards the higher catalytic efficiency of materials by raising their rate of charge transfer and product diffusion. This led us to develop mesoporous cobalt sulfide and sulfoselenide materials, as mesopores are known to increase the surface area of a material. Consequently, a simple three-step synthetic protocol was implemented. This involved the synthesis of mesoporous cobalt oxide (meso-Co₃O₄) material by a soft template mediated solvent evaporation induced self-assembly method, developed by our
group, followed by its sulfurization to produce meso-CoS$_2$. Finally, a controlled selenization of this meso-CoS$_2$ material (at 250 °C for 12 hours) yielded the partially surface selenized meso-CoSSe-12h catalyst. The schematic representation of the synthetic protocol of these catalysts is shown in Figure 4.1 and thoroughly described in the methods section.

To comprehend the stability of the enlarged lattice structure of meso-CoSSe-12h, we compared the total energies of both meso-CoS$_2$ and meso-CoSSe-12h. Hence, lattice structures of CoS$_2$ and CoSSe were modeled using DFT calculations, assuming ~25 % of surface selenium (Figure 4.2) (based on the SEM-EDX mapping, as mentioned later).

The surface morphology of resulting meso-CoSSe-12h catalyst was analyzed by multiple characterization techniques. The crystal structure of this materials was measured using PXRD and compared with meso-CoS$_2$ (Figure 4.3, a). The PXRD pattern of meso-CoSSe-12h was indexed as a sulfur-deficient pyrite (CoS$_2$) system, identical with that of meso-CoS$_2$ (space group $Pa$-3, $a = 5.5385$ Å, ICSD collection code #86351). Nevertheless, a minor increment (of 0.0108 Å) of lattice constant ($a = 5.5493$ Å) was observed for meso-CoSSe-12h as compared to the meso-CoS$_2$ (Figure 4.3, b), depicting a small expansion of the unit cell. This could be due to the larger ionic radii of selenium than sulfur. Interestingly, this 0.2 % lattice strain, accumulated during the 0.0108 Å elongation of lattice constant upon selenium (Se) doping, is shown by DFT calculations to be driven thermodynamically, as the 0.2 % strained CoSSe leads to the lowest energy of the structure (Figure 4.3, c).
4.5 Discussion

Scanning electron microscopy (SEM; Figure 4.3, e.) revealed the structural morphology of meso-CoSSe-12h which was similar to cabbage-like layered nanospheres of meso-CoS$_2$ (Figure 4.3, d). Transmission electron microscopy was used to capture further details of these materials which revealed the presence of mesopores in both CoS$_2$ and CoSSe-12h catalysts. Larger ionic
radii of selenium (Se) as compared to sulfur (S) probably expanded the unit cells in meso-CoSSe-12h, which decreased the surface area (Figure 4.4, a) and porosity (Figure 4.3, g, h, and i).

![Figure 4.4](image)

**Figure 4.4** a) BET surface area, and b) BJH pore size distribution of meso-CoSSe-12h catalyst.

![Figure 4.5](image)

**Figure 4.5** Characterization on the meso-CoSSe-12h. (a) Raman shift of meso-CoS2 and meso-CoSSe-12h. (b) XPS spectra of Co 2p of meso-CoS2 and meso-CoSSe-12h. (c) XPS spectra of Se 3d of meso-CoSSe-12h. (d) XPS spectra of S 2p in meso-CoSSe-12h showing the effect of Se on the surface of meso-CoS2. (e) Auger images showing the average depth of Se from the surface.

Barrett–Joyner–Halenda (BJH) pore size distribution methods, used to measure pore sizes, also detected this decrease of pore diameter upon selenization (Figure 4.4, b). To determine the
uniformity of selenium in meso-CoSSe, high-resolution transmission electron microscopy (HR-TEM) of meso-CoSSe-12h was analyzed. These experiments showed the presence of similar lattice fringes at different areas. The elemental uniformity of Co, S, and Se in the meso-CoSSe-12h surface was further confirmed by SEM-EDX analysis as depicted in Figure 4.3, f.

Confocal micro-Raman spectra (Figure 4.5, a) of meso-CoS$_2$ displayed all five Raman active modes $E_g$ ($\sim$295 cm$^{-1}$), $T_g$ (1) ($\sim$330 cm$^{-1}$), $A_g$ ($\sim$395 cm$^{-1}$), $T_g$ (2) ($\sim$420 cm$^{-1}$) and $T_g$ (3) ($\sim$490 cm$^{-1}$). Here, the $A_g$ and $T_g$ (2) modes correspond to the in-phase and out of phase stretching vibrations of sulfide ($S_2^{-2}$) dumbbells of the pyrite lattice. $E_g$ is the pure librational mode of the same, and $T_g$ (1), $T_g$ (3) modes are combinations of both stretching and librational vibrations. Interestingly, all these modes were observed to be redshifted for meso-CoSSe-12h as compared to meso-CoS$_2$ (Figure 4.5, a). This is attributed to a larger unit cell for meso-CoSSe-12h than meso-CoS$_2$, validating our earlier findings from X-ray diffraction studies. More importantly, the presence of one set of these ($A_g$, $E_g$, and $T_g$) peaks suggested that the surface of meso-CoSSe-12h has a single uniform phase rather than a binary mixture of two different solid phases.

To further understand the details of the surface properties of meso-CoSSe-12h, XPS was utilized. An increase in binding energy of Co 2p in meso-CoSSe-12h as compared to meso-CoS$_2$ (Figure 4.5, b), was observed which implies the oxidation of Co. A decrease in the percentage of metallic Co (Co$^{0}$) (XPS peak at 778 eV) (Figure 4.5, b) further supported this phenomenon. Unlike the oxidation of cobalt (Co), a comparison of the 2p region of sulfur (S) displayed reduction upon selenization of meso-CoS$_2$. The expansion of the 2p peak towards lower binding energy was assumed to happen due to the formation of a new species. To understand this, the 2p regions of both materials were deconvoluted (Figure 4.5, d) and compared. This analysis shows formation of a new terminal sulfur-selenium species (denoted as SSe$^{-2}$) in meso-CoSSe-12h, besides the two pre-existing bridged (S$^{-2}$ and S$_2^{-2}$) and one terminal sulfur species. In the meso-CoSSe-12h catalyst only one type of selenium species was found to form as revealed by the single peak at 54.8 eV (Figure 4.5, c). This supports the homogeneity of sulfur and selenium moieties on the catalyst surface. More importantly, the generation of this new sulfur species at lowest binding energy indicates the weakening of Co-S bonds and further supports the oxidation of Co (Figure 4.5, b). Moreover, to know the surface composition of the material, SEM-EDX mapping was used, which yielded an empirical formula of CoS$_{1.32}$Se$_{0.67}$ (Figure 4.3, e, and Table. 4.1). This further supports the presence of all three elements (Co, S, and Se) on the surface of the material. The afore-
The mentioned empirical formula was very close to that of the DFT computed model of meso-CoSSe (Figure 4.2, CoS$_{1.5}$Se$_{0.5}$).

To further support this finding, the overall percentage of each element was measured using X-ray fluorescence (XRF) spectrometry, where the catalyst was digested by a mixture of HNO$_3$, HCl, and HF (9: 3: 8). XRF was used to detected the atomic ratio of different elements, to be 27 % of Co, 54 % for S, and 18 % for Se with an error bar of 0.5 % (Table. 4.1). Consequently, this generated an empirical formula of CoS$_2$Se$_{0.67}$. The comparison between the empirical formulas generated by XPS and XRF validates the presence of a higher percentage of Se on the surface of meso-CoSSe. This supports our prior assumption of surface selenization.

Table 4.1 Elemental compositions of the samples with different Co/S/Se contents prepared by varying the reaction time of CoSSe preparation.

<table>
<thead>
<tr>
<th>Catalysts</th>
<th>Co</th>
<th>S</th>
<th>Se</th>
<th>S:Se</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surface (SEM-EDX)</td>
<td>Bulk (XRF)</td>
<td>Surface (SEM-EDX)</td>
<td>Bulk (XRF)</td>
</tr>
<tr>
<td>Meso-CoS$_2$</td>
<td>34.99</td>
<td>33.33</td>
<td>65.01</td>
<td>66.67</td>
</tr>
<tr>
<td>Meso-CoSSe-6h</td>
<td>33.54</td>
<td>28.70</td>
<td>53.69</td>
<td>54.90</td>
</tr>
<tr>
<td>Meso-CoSSe-12h</td>
<td>33.40</td>
<td>27.27</td>
<td>44.13</td>
<td>54.54</td>
</tr>
<tr>
<td>Meso-CoSSe-18h</td>
<td>34.31</td>
<td>29.10</td>
<td>40.40</td>
<td>45.60</td>
</tr>
<tr>
<td>Meso-CoSSe-24h</td>
<td>36.88</td>
<td>28.57</td>
<td>33.33</td>
<td>42.85</td>
</tr>
<tr>
<td>c-CoSe$_2$</td>
<td>24.48</td>
<td>69.49</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 4.6 a) LSV Polarization curves, and b) Tafel plots of CoS$_2$, CoSSe (6h), CoSSe (12h), CoSSe (18h), CoSSe (24h), and c-CoSe$_2$ in 0.5 M H$_2$SO$_4$ electrolyte at a scan rate of 5 mV s$^{-1}$. 

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The percentages of surface elements (Co, S, and Se) were controlled by varying the selenization time (summarized in Table 4.1). Thus, to investigate the effect of Se content on meso-CoS₂, meso-CoSSe catalysts with different amounts of Se were evaluated using their polarization (LSV) curves. A continuous increase of HER activity with increasing Se content was observed. However, instead of obtaining a continuous increment, the material with 12 hours of selenization was found to be most active (Figure 4.6). The Tafel slope of that material also showed correlation with the LSV curve (Figure 4.6). Longer selenization time not only increased the amount of Se but also separated the material into two separate phases CoS₂ and CoSe₂. The content of CoSe₂ also increased with time. But due to our inability to achieve pure phase CoSe₂, commercial CoSe₂ was used to compare the activity of other materials. However, the activity of this commercial material was found to be extremely poor which can be attributed to the lack of active sites due to its bulk particles and lack of porosity.⁴⁴

4.6 Electrochemical Measurements and Discussions

All electrochemical characteristics related to the HER of both meso-CoS₂ and meso-CoSSe-12h catalysts were measured using a three-electrode (rotating disc electrode, RDE) electrochemical cell having 0.5 M H₂SO₄ (aq.) solution (see methods section) as the electrolyte. A constant catalyst loading of 0.2 mg cm⁻² on the graphite electrode (having resistance below 10 ohms) was used to compare the activity of different catalysts. The overpotential (ƞ) required to achieve a geometric current density of −10 mA cm⁻² was selected as the target parameter for their comparison and was measured by linear sweep voltammetry at a scan rate of 5 mV s⁻¹. The meso-CoSSe-12h catalyst achieved that (−10 mA cm⁻²) current density at an overpotential (ƞ) of −110 mV (versus the reversible hydrogen electrode, RHE) which was significantly lower (−358 mV vs. RHE) than that of the meso-CoS₂ catalyst (Figure 4.7, a). This activity was further compared to the reference electrode (Pt/ C), which required only ~35 mV (vs. RHE) of overpotential to reach the −10 mA cm⁻² current density, under similar conditions. All data were iR corrected, and the ohmic losses of the system were always < 8 Ω. To know the kinetics of the process, Tafel slopes were calculated from the extrapolation of the linear region of overpotential versus log J plot, where a lower slope symbolizes faster kinetics. Consequently, the reaction kinetics of meso-CoSSe-12h (Tafel slope of 52 mV dec⁻¹) was found to be faster than the meso-CoS₂ (Tafel slope of 116 mV dec⁻¹) (Figure 4.7, b). The benchmark Pt/C displayed faster kinetics due to its lower Tafel
Figure 4.7 Determination of HER activity. (a) LSV of meso-CoS$_2$, meso-CoSSe-12h, and Pt/C in 0.5 M H$_2$SO$_4$ at scan rate of 5 mV s$^{-1}$. (b) Tafel plots of all polarization curves mentioned in a. (c) Plot of TOF per active site under dynamic potential for meso-CoS$_2$ and meso-CoSSe-12h. (d) Plot showing the extraction of the double-layer capacitance ($C_d$) for meso-CoS$_2$ and meso-CoSSe-12h electrodes. (e) Hydrogen amount from theoretical calculations (black square) and experimental tests (red sphere) vs. time for the meso-CoSSe-12h catalyst at -20 mA for 120 min. The straight line represents the theoretically calculated amounts of H$_2$ assuming 100% Faradaic efficiency, and the scattered dots represent the point where produced H$_2$ were measured by gas chromatography. The overlapping of experimental data with that of the theoretical data indicates that nearly all of the current was used for H$_2$ evolution.

Figure 4.8 HER stability tests. (a) accelerated stability measurements by recording the polarization curves for the meso-cosse-12h catalyst before and after 1,000 cyclic voltammograms at a scan rate of 50 mV s$^{-1}$ under acidic conditions. (b) The plot of $\eta$ vs. time for the meso-cosse-12h catalyst at a constant cathodic current density of 100 mA cm$^{-2}$ under acidic conditions.
slope value of 36 mV dec\(^{-1}\). These values of the Tafel slope suggested a possible Volmer-Heyrovsky pathway during the HER, where the electrochemical desorption of hydrogen (H) is the rate-determining step.\(^{17}\) The intrinsic activity of active sites of a material is measured from the geometrical exchange current density at zero overpotential \((J_{0,\text{geometrical}})\). This activity is calculated from the intercept (at zero overpotential) of the fitting curve of the Tafel slope. Activities were 8 \(\mu\)A cm\(^{-2}\), 70 \(\mu\)A cm\(^{-2}\), and 890 \(\mu\)A cm\(^{-2}\) for meso-CoS\(_2\), meso-CoSSe-12h, and Pt/C, respectively (Figure 4.7, c). A sharp \(~9\) fold increment of \(J_{0,\text{geometrical}}\) for meso-CoSSe-12h as compared to the meso-CoS\(_2\) revealed the enhancement of the intrinsic activity of meso-CoS\(_2\) upon selenization. To understand more about the origin of this activity difference, their relative electrochemical surface areas were measured by extracting the double-layer capacitance \((C_{dl})\) using cyclic voltammetry (Figure 4.7, d).\(^{15}\) This showed that the electrochemical surface area of meso-CoSSe-12h (38.25 cm\(^2\)) was \(~2\) times higher than that of meso-CoS\(_2\) (17.50 cm\(^2\)). Therefore we assume, due to this higher electrochemically active surface area (\(~2\) times) and geometrical exchange current densities (\(~9\) times), that meso-CoSSe-12h exhibits better HER activity than meso-CoS\(_2\). To determine the faradic efficiency of the meso-CoSSe-12h catalyst, hydrogen gas was produced and quantified at an interval of 20 minutes for 2 hours using a pre-determined calibration curve obtained from GC-TCD (Figure 4.7, e). The experimental plot obtained from this process displayed \(~99\%\) fit to the theoretical graph, confirming an accurate conversion of cathodic current to \(H_2\) production.

![Figure 4.9 LSV Polarization curves of meso-CoS2, meso-CoSSe-12h, and Pt/C in 1 M KOH electrolyte at a scan rate of 5 mV s\(^{-1}\).](image-url)
To estimate the impact of Se doping in improving the activity of meso-CoS$_2$ in alkaline media (1 M KOH), the cathodic polarization curves of meso-CoSSe-12h and meso-CoS$_2$ catalysts were measured using linear sweep voltammetry (Figure 4.9, a and Note S2). This study showed a similar trend as for acidic media, confirming the drastic improvement of activity of meso-CoS$_2$ upon selenium (Se) doping. Moreover, excellent activities of meso-CoSSe-12h in both acidic and alkaline electrolytes distinguish this system from most metal sulfide systems such as CoS$_2$, MoS$_2$, and some metal phosphides (for example, Ni$_2$P), as they fail to perform under alkaline conditions.$^{2,32}$

To evaluate the stability of the meso-CoSSe-12h catalyst, an accelerated degradation study was performed under 0.5 M H$_2$SO$_4$ (aq.) solution as shown in (Figure 4.8, a). The cathodic polarization curve obtained after 1,000 continuous cycles of voltammograms (scan rate: 50 mV s$^{-1}$) exhibited a negligible increase in $\eta$ required to reach the current density of 100 mA cm$^{-2}$ as compared to its 1$^{st}$ polarization curve. Moreover, the catalyst was capable of generating this current density for at least 25 hours (Figure 4.7, b). This indicates excellent stability of the meso-CoSSe-12h catalyst with acidic electrolyte. The unique design, the presence of earth-abundant elements (Co, S, and Se), excellent acid-base stability, and an outstanding HER performance of our pyrite-type material may have fundamental and applied importance; and is one of the best catalytic systems reported so far for HER.

![Figure 4.10 LSV Polarization curves of meso-CoSSe-12h, Au@ meso-CoSSe-12h, Hist@meso-CoSSe-12h, and Au&Hist@meso-CoSSe-12h in 0.5 M H$_2$SO$_4$ electrolyte at a scan rate of 5 mV s$^{-1}$.](image)
To investigate the importance and contribution of each element of the catalyst, a few control experiments were performed. Individual active sites were blocked using specific reagents to measure the activity of remaining elements. HER polarization curves of these blocked materials were used to qualitatively estimate the role of individual active sites. To perform these experiments, three different electrodes were prepared following methods mentioned in Note S8. The conjugate Histidine which is an amino acid was selected for its excellent complexation ability with both Co (II)\(^ {47,48} \) and Co (III).\(^ {49} \) These strong tetrahedral complexes are expected to inhibit the cobalt species from participating in the HER process, which may help quantify the combined catalytic activity of sulfur and selenium. Similarly to block sulfur, the electrode catalyst was incubated with HAuCl\(_4\).3H\(_2\)O, which is known to reduce the Au\(^{3+}\) species to Au clusters\(^ {50} \) over sulfur atoms.\(^ {51} \) This phenomenon is anticipated to measure the combined catalytic effect of cobalt and selenium. However, when both Histidine and HAuCl\(_4\).3H\(_2\)O were used to incubating the catalyst, only selenium is expected to show catalytic activity.

The polarization curves of these differently blocked catalysts were measured by linear sweep voltammetry (LSV) and compared with the previously acquired LSV of unblocked meso-CoSSe-12h catalyst Figure 4.10. Expectedly, the catalytic activity of all blocked electrodes was found to be lower than that of the unblocked one. Among these active site blocked electrodes, the cobalt-blocked electrode (Hist@meso-CoSSe-12h) exhibited the best activity, indicating a comparatively significant role of sulfur and selenium in the process. Followed by this, the sulfur blocked electrode (Au@meso-CoSSe-12h) yielded a comparatively poor HER activity, which further declined for the sulfur and cobalt blocked electrode (Au&Hist@meso-CoSSe-12h) (Figure 4.10). This signifies a comparatively higher contribution by the combined effect of Co-Se (Au@meso-CoSSe-12h) than the sole contribution of selenium of the system (Hist@meso-CoSSe-12h). This study identified S-Se to be most important, supporting our prior conclusion of newly developed super-active sulfur-selenium species (Figure 4.5. d), in the CoSSe catalytic system.

4.7 Computational Calculations

DFT predicted lattice structures (Figure 4.2) were used to identify the most stable planes where adsorption can occur. These data suggest that the 1S layer termination of the \{001\} surface is found to be the most stable (Figure 4.11). As mentioned before, the adsorption of hydrogen is the most probable rate-determining step of this HER process. The determination of the free energy
change of this step is very crucial. These free energies ($\Delta G_H$) were calculated for all comparable surface sites. A reduction of free energy values for adsorption of hydrogen on both Co and S was seen in meso-CoSSe as compared to meso-CoS$_2$. Interestingly, a significant reduction of free energy was observed for sulfur (from 0.94 eV to 0.44 eV), as compared to the reduction on cobalt (from 0.33 eV to 0.22 eV). The free energy associated with the adsorption on Se was found to be 0.67 eV. This signifies the importance of Se in meso-CoSSe and validates its superior electrocatalytic HER activity over meso-CoS$_2$ as obtained experimentally. According to this DFT calculation, oxidation of Co sites was found to minimize the activation barrier, indicating faster kinetics for proton adsorption.

These studies inspired us to conduct a circuit model fitting analysis for electrochemical impedance spectroscopy (EIS) of both meso-CoS$_2$ and meso-CoSSe-12h materials to learn about their rates of charge transfer and electrochemically active interfaces (Figure 4.12). This study revealed a decrease of ohmic resistance in meso-CoSSe-12h as compared to meso-CoS$_2$, enhancing the charge transfer by ~100 times (Figure 4.12). However, the hemisphere obtained for meso-CoSSe-12h was significantly distorted as compared to that of meso-CoS$_2$. Therefore, we conducted simulation studies to generate equivalent circuits of experimentally obtained EIS spectra of both materials using various impedance elements (Figure 4.12). This revealed the co-existence of

![HER free energy diagram for {001} surface of meso-CoS$_2$ and meso-CoSSe, with H adsorption at Co and S sites.](image-url)
charge transfer resistance ($R_{ct}$) and adsorption resistance ($R_{ad}$), for both cobalt and sulfur interfaces of meso-CoS$_2$, representing the manifestation of Volmer-Heyrovsky steps (Figure 4.12). Interestingly, selenization caused a sharp decrease of the resistivities of all pre-existing interfaces (cobalt and sulfur), besides the generation of another electrochemically active interface (Figure 4.12). The agreement of this equivalent circuit with XPS studies confirms the development of a new sulfur-selenide species in meso-CoS$_2$ upon selenization (Figure 4.5, d).

These newly generated active sites or interfaces increased the total turnover frequency (TOF) of the HER process due to the combined effect of its enhanced electrochemical surface area, exchange current density, and reaction kinetics (suggested by the lowering of Tafel slope). TOF indicates the number of gaseous hydrogen molecules generated at unit time (per second). Hence, TOF is considered to be the most critical characteristic of a catalyst which reveals its intrinsic

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**Figure 4.12** EIS Nyquist plots recorded for (a) meso-CoSSe-12h and (b) meso-CoS$_2$ catalyst with the potential set at −0.25 V vs. RHE.

**Table 4.2** Summary of the electrochemical properties of meso-CoS$_2$, meso-CoSSe-12h, and Pt/C electrodes.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$I_f$ (mV vs. RHE) for $-10$ mA cm$^{-2}$</th>
<th>Tafel Slope (mV dec$^{-1}$)</th>
<th>$J_0$, (µA cm$^{-2}$)</th>
<th>$C_{dl}$ (mF cm$^{-2}$)</th>
<th>Relative surface area</th>
<th>TOF ($s^{-1}$)</th>
<th>Active site density (atoms cm$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>meso-CoS$_2$</td>
<td>358</td>
<td>116</td>
<td>8</td>
<td>0.70</td>
<td>1</td>
<td>0.104 × $</td>
<td>j</td>
</tr>
<tr>
<td>meso-CoSSe</td>
<td>56</td>
<td>52</td>
<td>70</td>
<td>1.53</td>
<td>2.18</td>
<td>0.047 × $</td>
<td>j</td>
</tr>
<tr>
<td>Pt/C</td>
<td>36</td>
<td>36</td>
<td>890</td>
<td>-</td>
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</tr>
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</table>

82
catalytic efficiency. To quantify the TOF of these catalysts, the thermodynamic potential was calculated using the exchange current density (0 V vs. RHE). This yielded a TOF value of 3.34 H₂ s⁻¹ for meso-CoSSe-12h, which is approximately four times larger than the meso-CoS₂ (0.83 H₂ s⁻¹) (see detailed calculation in Note S6.). Before this, we also calculated the electrochemically active surface area (Note S5), and the active site density (sites per cm²) (Note S5) of both meso-CoS₂ and meso-CoSSe materials. Despite the reduction of active site density, the TOF of meso-CoSSe-12h increased as compared to meso-CoS₂ due to its higher (~9 times) intrinsic activity (Note S6) and electrochemically active surface area (ECSA).

**4.8 Conclusions**

In conclusion, we successfully designed a readily producible surface selenized mesoporous cobalt sulfide with excellent stability in acidic media. This drastically enhanced the HER activity of the meso-CoS₂ catalyst. We confirmed that the development of new terminal sulfur-selenium species, besides the oxidation of Co, was responsible for the enhanced HER activity of meso-CoSSe-12h. This resulted in a decrease of reaction overpotential (from 358 to 110 mV, vs. RHE); and an increase of the Tafel slope (from 116 to 52 mV dec⁻¹), intrinsic activity (geometrical exchange current density) (from 8 to 70 µA cm⁻²), and turn over frequency (TOF) (from 0.83 to 3.34 H₂ s⁻¹). These combined effects resulted in the enhanced HER activity. The reaction kinetics of these systems were also supported by DFT calculations. A similar trend of reactivity of this earth abundant transition metal dichalcogenide catalyst was shown in basic media. Besides its excellent catalytic performance, outstanding stability (for at least 25 hours) and reusability (up to at least 1000 cycles), this system is fundamentally important for water splitting applications.

**4.9 Notes:**

**Note S1: Activity comparisons to other reported HER electrocatalysts in acid**

The HER activity of meso-CoSSe-12h was determined with a three electrode system having 0.5 M H₂SO₄ as the electrolyte. Hg/HgCl₂ was selected as the reference, whereas Pt/C was the benchmark electrode. The activity of meso-CoSSe-12h was compared with that of meso-CoS₂, and commercial-CoSe₂. Moreover, the activity of most of the reported metal sulfides were compared with our results.
We ran the linear swept voltammetry for comparing the activities of different electrodes and selected the overpotential ($\eta$) required to achieve 10 mAcm$^{-2}$ to be the main parameter of comparison as most papers reported this value. Despite the onset potential of a catalyst being the best indicator of its intrinsic activity, it is difficult to use for comparison due to the ambiguity in determining its value. Hence, by comparing the overpotential ($\eta$) required to achieve 10 mAcm$^{-2}$ for meso-CoSSe with previously reported materials, the activity of meso-CoSSe was higher than most of the metal sulfides reported to date. Some reported catalysts such as MoS$_2$/N-RGO$^3$, MoS|P$_{10}$, HP-NiSe$_2$ foam$^{18}$, MoS$_{2(1-x)}$Se$_{2x}$/NiSe$_2$,$^{19}$ CoPS NPls/carbon paper$^{23}$, Co-doped FeS$_2$ nanosheets$^{24}$, and metallic FeNiS nanosheet$^{25}$ have shown better activity than meso-CoSSe. However, if the catalyst preparation is taken into consideration, the meso-CoSSe synthesis is much easier and generates a highly stable system (at least 25 hours in acidic conditions).

**Note S2: HER activity in alkaline electrolyte**

The HER activities of meso-CoS$_2$, meso-CoSSe-12h, and Pt/C catalysts were determined under a freshly prepared 1 M KOH electrolyte using Ag/AgCl as the reference and Pt as the counter electrode. Interestingly, a similar trend of results (via linear swept voltammetry, Supplementary Figure 4.9, a) as that under acidic conditions was obtained for meso-CoS$_2$, meso-CoSSe, and Pt/C electrodes. The meso-CoSSe catalyst showed much higher HER activity than the meso-CoS$_2$ with a more positive onset potential ($\eta$) and a larger current density which indicates that the enhancement of activity of meso-CoS$_2$ upon surface selenization is consistent despite changing the electrolyte conditions.

**Note S3: Faradaic efficiency measurements**

To measure the Faradaic efficiency of the meso-CoSSe-12h catalyst, gaseous H$_2$ was produced in a sealed Pyrex glass reactor at a constant cathodic current density of 20 mA cm$^{-2}$. Produced H$_2$ was measured using a gas chromatography (GC) with thermal conductivity detector (TCD) and quantified from the pre-determined calibration curve. The calibration curve was prepared using different concentrations of H$_2$ and Ar. Gas samples of a reaction were collected at a time interval of 20 minutes and analyzed to get a plot of H$_2$ produced against time. Such reaction kinetics were determined and plotted for meso-CoSSe-12h as shown in Figure 4.3, d where an excellent correlation between the calculated (theoretical) and measured (experimental) amounts of H$_2$ gas was observed. This indicates near 100% efficiency of the catalyst.
The production of gaseous H\textsubscript{2} was further confirmed by comparing GC signals of H\textsubscript{2} from the reaction and the commercial supply. (**Figure 4.13**).

**Figure 4.13** GC signal of H\textsubscript{2}, as obtained from meso-CoSSe-12h catalyst as the working and Pt as the reference electrode (after 5 minutes of reaction).

**Note S4: Estimation of the electrochemical double-layer capacitance (C\textsubscript{dl}).**

To calculate the electrochemical double-layer capacitance for meso-CoS\textsubscript{2} and meso-CoSSe-12h, the cyclic voltammetry methods were used with different scan rates ranging from 10 mV/s to 60 mV/s with a step of 10 mV/s. The potential is scanned from 0.1 to 0.2 V vs RHE where no faradic current was detected.

The center of this working potential (*i.e.*, 0.15 V) was selected to calculate $\Delta J_0$ (vs RHE). Hence, we plotted the differences in current densities ($\Delta J = J_a - J_c$) at 0.15 V (vs. RHE) against the scan rates fit to a linear regression; Hence forth, the electrochemical double-layer capacitance was calculated using the formula below,

$$C_{dl} = \text{Slope of the } \Delta J_0 \text{ (vs RHE) vs scan rates plot}$$

**a. For meso-CoS\textsubscript{2}**

$$C_{dl} = \frac{(0.050 - 0.015) \text{ mA cm}^{-2}}{(60 - 10) \text{ mV s}^{-1}} = 0.0007 \text{ F} = 0.7 \text{ mF}$$

**b. For meso-CoSSe-12h**

$$C_{dl} = \frac{(0.095 - 0.02) \text{ mA cm}^{-2}}{(60 - 10) \text{ mV s}^{-1}} = 0.0015 \text{ F} = 1.5 \text{ mF}$$
**Note S5: Electrochemically active surface area (ECSA) and active sites density measurements**

Meso-CoS$_2$ and meso-CoSSe-12h electrodes, each with 212 μg cm$^{-2}$ of catalyst loading were subjected to ESCA in order to measure their corresponding electrochemical double-layer capacitance ($C_{dl}$). The $C_{dl}$ was determined from the scan-rate dependence of cyclic voltammetry, in a potential range where no Faradic reaction occurs. The Cyclic Voltammetric results of both meso-CoS$_2$ and meso-CoSSe-12h electrodes are shown in Figure 4.14.

![Figure 4.14](image)

**Figure 4.14** Double-layer capacitance measurements for determining the electrochemical active surface area of catalysts with mass loading 0.2 g cm$^{-2}$. All CVs were replotted keeping their center at the origin (zero current density, 0.00 mA cm$^{-2}$). (a) CVs measured for meso-CoS$_2$ in a non-Faradaic region at scan rate of 5 mV s$^{-1}$, 10 mV s$^{-1}$, 15 mV s$^{-1}$, 20 mV s$^{-1}$, 25 mV s$^{-1}$, 30 mV s$^{-1}$, 35 mV s$^{-1}$, 40 mV s$^{-1}$, 45 mV s$^{-1}$, 50 mV s$^{-1}$, 55 mV s$^{-1}$, and 60 mV s$^{-1}$. (b) CVs measured for meso-CoSSe-12h in a non-Faradaic region at scan rate of 5 mV s$^{-1}$, 10 mV s$^{-1}$, 15 mV s$^{-1}$, 20 mV s$^{-1}$, 25 mV s$^{-1}$, 30 mV s$^{-1}$, 35 mV s$^{-1}$, 40 mV s$^{-1}$, 45 mV s$^{-1}$, 50 mV s$^{-1}$, 55 mV s$^{-1}$, and 60 mV s$^{-1}$.

- **The ECSA can be calculated from the $C_d$ according to:**

\[
A_{ECSA}^{catalyst} = \frac{C_{dl}}{C_s}
\]

Where, $C_s$ is the specific capacitance of a flat standard electrode with 1 cm$^2$ of real surface area, which is generally in the range of 20 to 60 μF cm$^{-2}$.$^{10}$ Thus, the averaged value of 40 μF cm$^{-2}$ for the flat electrode, has been used to obtain:

\[
A_{ECSA}^{CoS_2} = \frac{0.70 \text{ mFcm}^{-2}}{40 \text{ μFcm}^{-2} \text{ per cm}^2_{ECSA}} = 17.50 \text{ cm}^2_{ECSA}
\]

\[
A_{ECSA}^{CoSSe} = \frac{1.53 \text{ mFcm}^{-2}}{40 \text{ μFcm}^{-2} \text{ per cm}^2_{ECSA}} = 38.25 \text{ cm}^2_{ECSA}
\]
• **Active sites density (sites cm\(^{-2}\)) = number of active sites per real surface area,**

For this the lattice parameters (as obtained from PXRD) were used to calculate the unit lattice volume.

<table>
<thead>
<tr>
<th>Refinement</th>
<th>Cubic side length, Å</th>
<th>Cubic volume, Å(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meso-CoS(_2)</td>
<td>5.5217</td>
<td>168.3534</td>
</tr>
<tr>
<td>Meso-CoSSe-12h</td>
<td>5.535</td>
<td>169.5998</td>
</tr>
</tbody>
</table>

For meso-CoS\(_2\) = \(\left(\frac{12 \text{ atoms/unit cell}}{168.3534 \text{ Å}^3/\text{unit cell}}\right)^2 = 1.72 \times 10^{15} \text{ atoms cm}^{-2}_{\text{real}}\) \(\text{(4)}\)

For meso-CoSSe-12h = \(\left(\frac{12 \text{ atoms/unit cell}}{169.5998 \text{ Å}^3/\text{unit cell}}\right)^2 = 1.71 \times 10^{15} \text{ atoms cm}^{-2}_{\text{real}}\) \(\text{(5)}\)

**Note S6: Exchange current density and Turnover frequency (TOF) calculations**

• **Exchange current density \((j_0)\):**

The exchange current density is the current that is available at zero overpotential. This available current density, expressed as \(j_0\), is measured by fitting \(j\) - \(E\) data to the Tafel equation. This value is solely dependent on the material under consideration, is considered to be an inherent property of each material.\(^{26}\)

We calculated this for meso-CoS, meso-CoSSe, and Pt/C. Obtained values are mentioned below:

\[\text{meso-CoS} = 8 \text{ μA}\]

\[\text{meso-CoSSe} = 70 \text{ μA}\]

\[\text{Pt/C} = 892 \text{ μA}\]

• **The per-site TOF value was calculated according to the following equation:**

\[
\text{TOF} = \frac{\# \text{ total hydrogen turnovers/cm}^2 \text{ geometric area}}{\text{number of active sites/cm}^2 \text{ geometric area}} = \frac{\# \text{ total hydrogen turnovers/cm}^2 \text{ geometric area}}{\text{active sites density}}
\]

\(\text{(6)}\)

The number of total hydrogen turnovers was calculated from the current density extracted from the LSV polarization curve.
According to this, the number of total hydrogen turnovers would be

\[
= ( |j| \text{ mA. cm}^{-2} ) \left( \frac{1}{\text{1000 mA}} \right) \left( \frac{1 \text{ mol e}^{-}}{96453.3 \text{ C}} \right) \left( \frac{1 \text{ mol}}{2 \text{ e}^{-}} \right) \left( \frac{6.022 \times 10^{23} \text{ molecules of H}_2}{1 \text{ mol H}_2} \right)
\]

\[= 3.12 \times 10^{15} \text{ molecules of H}_2 \text{ s}^{-1} \text{ cm}^{-2} \] (7)

Using the number of total hydrogen turnovers, active site density, and electrochemically active surface area; we converted the current density from the LSV polarization curve into TOF, as:

\[
\text{TOF} = \frac{\# \text{ total hydrogen turnovers} \times \text{absolute value of current density}}{\# \text{ active sites} \times \text{electrochemical active surface area}} \] (8)

\[
\text{TOF}_{\text{CoS}_2} = \frac{\left( 3.12 \times 10^{15} \frac{\text{H}_2/\text{s}}{\text{cm}^2 \text{ per mA/cm}^2} \right) \times |j|}{\left( 1.72 \times 10^{15} \text{ atoms/cm}^2 \text{ real} \right) \times (17.50 \text{ cm}^2 \text{ ECSA})} = 0.10365 \times |j| \text{ s}^{-1} \] (9)

\[
\text{TOF}_{\text{CoSSe}} = \frac{\left( 3.12 \times 10^{15} \frac{\text{H}_2/\text{s}}{\text{cm}^2 \text{ per mA/cm}^2} \right) \times |j|}{\left( 1.71 \times 10^{15} \text{ atoms/cm}^2 \text{ real} \right) \times (38.25 \text{ cm}^2 \text{ ECSA})} = 0.04770 \times |j| \text{ s}^{-1} \] (10)

Therefore, the TOF at thermodynamic potential (0 V vs RHE), with the \( j_0 \), where \( j_0 \) is the exchange current, would be:

\[
\text{TOF}_{\text{CoS}_2} (0 \text{ V}) = 0.10365 \times 8 = 0.83 \text{ H}_2 \text{ s}^{-1}.
\]

\[
\text{TOF}_{\text{CoSSe}} (0 \text{ V}) = 0.0477 \times 70 = 3.34 \text{ H}_2 \text{ s}^{-1}.
\]

**Note S7: Calibration of reference electrodes Hg/HgCl\_2 and Ag/AgCl.**

To calibrate the Hg/HgCl\_2 or Ag/AgCl electrode for use as a reference in 0.5 M H\_2SO\_4 or 1 m KOH electrolyte, respectively, a three electrode system having Pt wires as cathode and anode was used. Both the Hg/HgCl\_2 and Ag/AgCl electrodes were prepared by filling with saturated KCl solution having sufficient KCl crystals prior to use. The calibration was conducted after the electrolyte was H\_2\_- saturated for at least 30 minutes. Cyclic voltammetry was conducted at a scan rate of 1 mV s\(^{-1}\) and the average value of the two potentials at which the anodic and cathodic scans crossed zero current was calculated to be the thermodynamic potential for the hydrogen electrode reaction. According to these results shown in Supplementary Figure 4.15, a and Figure 4.15, b, the potential (vs RHE) in acidic or basic condition can be calculated from the Equations below,
**Figure 4.15** Calibration of a) Hg/HgCl₂, KCl (sat) reference electrode in 0.5 M H₂SO₄, and b) Ag/AgCl, KCl (sat) reference electrode in 1 M KOH solution.

In 0.5 M H₂SO₄, \( E \) (RHE) = \( E (\text{Hg/HgCl}_2) + 0.271 \) V,

While, in 1 M KOH, \( E \) (RHE) = \( E \) (Ag/AgCl) + 0.968 V.

**Note S8: Preparation of electrodes for active site blocking experiments**

To perform the active site blocking experiments, the meso-CoS|Se-12h catalyst was suspended in a solution of water, ethanol and Nafion (500 μL, 500 μL, and 40 μL) by prolonged sonication (2h). Three electrodes were prepared by drop-casting a certain amount (10 μL, with the mass loading of 0.212 mg cm⁻²) of this solution on pyrolytic graphite electrodes where they were allowed to dry overnight. These electrodes were further incubated for 4 hours with either 10 μM aqueous solution of HAuCl₄·3H₂O or 10 μM aqueous solution of histidine amino acid, prior to washing with DI water and drying under vacuum.

**Note S9: Density functional theory calculations of Hydrogen Evolution Reaction (HER)**

First-principles density functional theory (DFT) calculations are carried out to evaluate the HER catalytic activity of CoS₂ and CoSSe. DFT calculations are performed using Vienna ab initio simulation package (VASP), with the projector augmented wave method for the electronic-ion interaction and a Perdew-Burke-Ernzerhof form generalized gradient approximation (GGA) for the exchange-correlation potential. A plane wave basis sets wave function is expanded with a cutoff energy of 400 eV. The Brillouin zone integration was performed using a Monkhorst-Pack scheme, with a 3x3x1 k-point mesh. The surface is modelled by a 1x1 supercell of CoS₂ (001) surface, with a lattice constant of 5.520 Å. A vacuum of 15 Å is applied to minimize the interaction
between the top and bottom surfaces. For geometry optimizations, the top six surface layer volumes are allowed to relax until all forces converge to within 0.03 eV/Å, and the other layers are fixed to simulate the bulk environment.

To evaluate the effects of Se substitution on HER catalytic activity of CoS₂, DFT calculations are carried out with the (001) surface model of pristine CoS₂ and CoSSe with H adsorption at Co and S site. The relaxed crystal structures of CoS₂ and CoSSe surface slabs with H are shown in Figure 1.

The H adsorption energy is calculated as:

$$\Delta E_H = E_{\text{Surface-H}} - E_{\text{Surface}} - \frac{E_{H_2}}{2}$$

Where, $E_{\text{Surface-H}}$, $E_{\text{Surface}}$, and $E_{H_2}$ are the energies of the H-adsorbed surface, clean surface, and H₂ molecule, respectively.

The Gibbs free energy change of the HER are calculated using the following equation:

$$\Delta G_H = \Delta E_H + \Delta E_{ZPE} - T \Delta S$$

Where, $\Delta E_{ZPE}$ is the zero point energy correction and $\Delta S$ is the entropy change associated with H adsorption. $\Delta E_{ZPE}$ is estimated from vibrational frequency calculation to be 0.094 eV, and $T \Delta S$ is estimated to be -0.204 eV at 1 kbar and 300K. Therefore, $\Delta G_H$ can be expressed as

$$\Delta G_H = \Delta E_H + 0.30 \, eV$$
4.10 References


(42) Zou, X.; Zhang, Y.; Chem. Soc. Rev. 2015, 44, 5148-5180


Chapter 5. Future Perspectives

Reported procedures were developed with the fundamental goal of modifying existing protocols following the rules of “green chemistry”. The invented mesoporous transition metal oxides and sulfides were able to produce fine chemicals and green fuel (hydrogen) from raw materials with excellent efficiency. These additive-free, reusable, and heterogeneously catalyzed protocols were found to generate non-toxic wastes (mostly water) using air as the sole oxidant. As a future perspective, these materials can be (1) utilized for complex catalytic oxidation and other heterogeneous reactions, and (2) further tuned and optimized to improve the physicochemical properties that are responsible for different catalytic processes.

For a long-term perspective, metals oxides and sulfides can be modified to converting solar energy into transportable chemical energy. They can also be used as battery materials for energy storage devices. The development of numerous catalytic methodologies is highly desirable which are required to meet the exponentially rising demand for energy and petrochemicals.

In summary, this work highlights the structure-activity relationship of various robust, inexpensive, and thermally stable heterogeneous catalysts for different catalytic processes. The versatile nature of these materials is expected to open up newer avenues of catalysis research to secure future energy demands and develop alternative protocols for synthesizing fine chemicals.
Appendix

List of publications, patents and presentations

❖ PUBLICATIONS


❖ (TO BE) SUBMITTED ARTICLES

   “Mesoporous Cobalt/Manganese Oxide: A Highly Selective Bifunctional Catalyst for Amine-Imine Transformations and Investigations of its Surface Chemistry.”

   “Partial surface selenization of mesoporous cobalt sulfide nanospheres for excellent hydrogen evolution reaction and determination of their active sites.”

   “Mesoporous Copper Sulfide Catalyzed Transformation of Amines to Imines under Visible Light.”

   “Lithium Promoted Mesoporous Manganese Oxide Catalyzed Oxidation of Allyl Ethers.”

❖ PATENTS


❖ TALKS

Mesoporous Manganese Oxide Catalyzed Aerobic Oxidative Coupling Of Anilines To Aromatic Azo Compounds. *(Awarded for an Outstanding Presentation)* 253rd ACS Meeting (04/2017)