Synthesis of Conjugated Dienes via Palladium-Catalysed Aerobic Dehydrogenation of Unsaturated Acids and Amides

Meledath Sudhakaran Keerthana and Masilamani Jeganmohan*

Department of Chemistry, Indian Institute of Technology, Madras-600036, India

E-Mail: mjeganmohan@iitm.ac.in

Electronic Supporting Information (ESI)

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Experimental Section

General information: All reactions were carried out under the air atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with nitrogen prior to use (three times). Dry solvents were used for the reaction. Column chromatographical purifications were performed using SiO₂ (120-200 mesh ASTM) from Avra Pvt. Ltd., India. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Commercially available metal salts and acids were purchased from Sigma-Aldrich and Spectrochem. Pvt. Ltd., India and used without further purification. Starting Materials: Starting materials 1a-1p, 3a-3f, 5a-5e and 7a-7f were prepared by known literature procedures.¹-⁶


Pd(OAc)₂ (5.0 mol %), L₅ (5 mol %), Cu(OAc)₂·H₂O (20 mol %), and Amide 1 (50.0 mg, 1 equiv.) were taken in a 15 mL Schlenk tube. Acetonitrile (1.0 mL) was added to the reaction mixture via syringe. Then, pivalic acid (50 mol %) was added to the solution, followed by the addition of Acetonitrile (2.0 mL). The tube was sealed using screw cap under air and the reaction mixture was allowed to stir at 100 °C for 24 h in an oil bath. After cooling to the ambient temperature, the reaction mixture was diluted with CH₂Cl₂, filtered through Celite, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure product 2.

Optimization Studies:

The reaction was initially studied using various ligands and most of them inhibited the reaction (Scheme 1). However, N-Ac-glycine L₁ gave the desired dehydrogenated product 2a in 32% yield. When the ligand was switched from L₁ to N-Ac-alanine L₂ the reaction yield was reduced to 21%. Further, the reaction was probed using various phosphorous, sulphur and nitrogen-based ligands. When 1,10-phenanthroline L₃ was used, the dehydrogenated product 2a was produced with a yield of 16%. A trace amount of product was observed when pyridin-2-ol L₄ was used. 1,2-bis(diphenylphosphaneyl)ethane L₆ and 1,3-bis(diphenylphosphaneyl)propane L₇ generated the product 2a with a yield of 48 and 27% respectively. However, the best results were observed when 1,2-bis(phenylsulfinyl)ethane L₅ was used. In this case, the yield of the product 2a was improved to 89%.
The reaction was next screened with various additives such as AcOH, pivalic acid 1-adamantane carboxylic acid, mesitylenic acid, and benzoic acid (entries 1-5). AcOH gave the desired product 2a in 58% yield (entry 1). In the case of pivalic acid, the expected product 2a was isolated in 89% yield (entry 2). Other additives were found to be ineffective for the reaction. The reaction was further examined using various oxidants (20 mol %) such as Ag$_2$CO$_3$, AgOAc, Ag$_2$O, benzoquinone, PhI(OAc)$_2$, K$_2$S$_2$O$_8$, (NH$_4$)$_2$S$_2$O$_8$, Cu(OAc)$_2$ and Cu(OAc)$_2$·H$_2$O (entry 6-13). Among them, Cu(OAc)$_2$·H$_2$O was very effective, giving the dehydrogenated product 2a in 89% yield (entry 2). AgOAc and PhI(OAc)$_2$ gave the desired product in 20 and 35% respectively (entry 7 and 10). Cu(OAc)$_2$ was partially effective, providing the desired product 2a in 58% yield (entry 13). Other oxidants were found to be ineffective. The reaction was further examined with various solvents such as 1,2-dichloroethane, 1,2-dichlorobenzene, N,N-dimethylformamide (DMF), toluene, 1,2-dimethoxyethane (DME), methanol, CF$_3$CH$_2$OH, 1,4-dioxane, DMSO, CH$_3$CN and THF (entry 13-22). Among them, CH$_3$CN was very effective, giving the expected product 2a in 89% yield (entry 2). DMF provided trace amount of product (entry 15). CF$_3$CH$_2$OH gave the product 2a in 24% yield (entry 20). 1,4-Dioxane and DMSO and were partially effective, yielding the dehydrogenated product 2a in 58% and 43% yields, respectively (entry 21-22). Optimal yield of 89% for product 2a was obtained when the reaction was carried out under air in the presence of 20 mol % of Cu(OAc)$_2$·H$_2$O along with 50 mol % of pivalic acid in acetonitrile solvent. Control experiment revealed that the reaction does not proceed in absence of ligand and pivalic
acid (entry 23-24). The yield of product 2a was reduced to 20% in absence of Cu(OAc)$_2$·H$_2$O (entry 26). Trace amount of product was formed when O$_2$ was used as the sole oxidant (entry 27).

Scheme S2. α β-Dehydrogenation of β-Substituted Amide 1a

Table 1. Optimization Table

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>L (mol %)</th>
<th>Additive</th>
<th>Oxidant</th>
<th>Solvent</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>AcOH</td>
<td>Cu(OAc)$_2$·H$_2$O</td>
<td>CH$_3$CN</td>
<td>58%</td>
</tr>
<tr>
<td>2</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>Cu(OAc)$_2$·H$_2$O</td>
<td>CH$_3$CN</td>
<td>89%</td>
</tr>
<tr>
<td>3</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>Adm-1-COOH</td>
<td>Cu(OAc)$_2$·H$_2$O</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>Mesitylene carboxylic acid</td>
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<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>Benzoic acid</td>
<td>Cu(OAc)$_2$·H$_2$O</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>Ag$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
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<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>AgOAc</td>
<td>CH$_3$CN</td>
<td>20%</td>
</tr>
<tr>
<td>8</td>
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<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>Ag$_3$O</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
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<td>L5 (5 mol %)</td>
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<td>Benzoquinone</td>
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<td>NR</td>
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<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>Phl(OAc)$_2$</td>
<td>CH$_3$CN</td>
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<tr>
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<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>K$_2$S$_2$O$_8$</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
<td>12</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>(NH$_4$)$_2$S$_2$O$_8$</td>
<td>CH$_3$CN</td>
<td>NR</td>
</tr>
<tr>
<td>13</td>
<td>Pd(OAc)$_2$</td>
<td>L5 (5 mol %)</td>
<td>PivOH</td>
<td>Cu(OAc)$_2$</td>
<td>CH$_3$CN</td>
<td>58%</td>
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<tr>
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<td>L5 (5 mol %)</td>
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<td>1,2-dichloroethane</td>
<td>NR</td>
</tr>
<tr>
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<td>L5 (5 mol %)</td>
<td>PivOH</td>
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<td>1,2-dichlorobenzene</td>
<td>NR</td>
</tr>
<tr>
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<td>PivOH</td>
<td>Cu(OAc)$_2$·H$_2$O</td>
<td>DMF</td>
<td>trace</td>
</tr>
</tbody>
</table>
2. General Procedure for α β-Dehydrogenation of β-Substituted Acid 7.

Pd(OAc)$_2$ (10.0 mol %), L5 (10 mol %), Cu(OAc)$_2$H$_2$O (20 mol %), and Acid 7 (50.0 mg, 1 equiv.) were taken in a 15 mL Schlenk tube. Acetonitrile (1.0 mL) was added to the reaction mixture via syringe. Then, pivalic acid (50 mol %) was added to the solution, followed by the addition of Acetonitrile (2.0 mL). The tube was sealed using screw cap under air and the reaction mixture was allowed to stir at 100 °C for 24 h in oil bath. After cooling to the ambient temperature, the reaction mixture was diluted with CH$_2$Cl$_2$, filtered through Celite, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure product 8.

**Mechanistic Investigation**

Pd(OAc)$_2$ (5.0 mol %), Cu(OAc)$_2$H$_2$O (20 mol %), and Amide 1a (50.0 mg, 1 equiv.) were taken in a 15 mL Schlenk tube. Acetonitrile (1.0 mL) was added to the reaction mixture via syringe. Further, pivalic acid (50 mol %) was added to the solution. Then, D$_2$O (2 equiv.) was added followed by addition of acetonitrile (1 mL). The tube was sealed using screw cap under air and the reaction mixture was allowed to stir at 100 °C for 24 h in oil bath. After cooling to the ambient temperature, the reaction mixture was diluted with CH$_2$Cl$_2$, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column.
using hexane and ethyl acetate as eluent to give pure product D-2a in 56% yield. No deuterium incorporation was observed in the product. However, unreacted starting material D-1a was recovered in 38% yield with 45% deuterium incorporation at the α-carbon atom.

\[
\text{\textbf{\textit{1}}}H \text{ and } \text{\textit{13}}C \text{ NMR spectra of compound D-1a in CDCl}_3 \text{ at 400MHz:}
\]

**COSY Spectra of D-1a:** From COSY NMR, it can be observed that proton $H_a$ at ($\delta = 2.33$ ppm) is strongly correlated with alkene proton $H_b$ at ($\delta = 5.4$ ppm). Similarly, the alkene proton $H_b$ at ($\delta = 5.4$ ppm) shows a correlation with methyl proton at ($\delta = 1.6$ ppm).
$^1$HNMR spectra of compound D-2a in CDCl$_3$ at 400 MHz:

Reference:

Spectral Data of All Compounds:

**(2E,4E)-N-Benzylhexa-2,4-dienamide (2a):**

![Structure (2a)](image)

Prepared according to General Procedure 1; white solid; eluent (20% ethyl acetate : hexane); yield is 89%. $^1$H NMR (400 MHz, CDCl₃): δ 7.35 – 7.23 (m, 5H), 6.45 – 5.96 (m, 3H), 5.78 (d, $J = 15.0$ Hz, 1H), 4.47 (d, $J = 5.8$ Hz, 2H), 1.82 (d, $J = 6.1$ Hz, 3H). $^{13}$C$^1$H NMR (101 MHz, CDCl₃): δ 166.4, 141.6, 137.9, 129.7, 128.7, 127.8, 127.4, 121.3, 43.6, 18.6. HRMS (ESI/Q-TOF): [M + Na]$^+$ Calcd for C₁₃H₁₃NONa 224.1051; Found 224.1059.

**(2E,4E)-N-(3,4-Dimethoxybenzyl)hexa-2,4-dienamide (2b):**

![Structure (2b)](image)

Prepared according to General Procedure 1; half-white solid; eluent (25% ethyl acetate: hexane); yield is 85%. $^1$H NMR (400 MHz, CDCl₃): δ 7.14 (d, $J = 12.5$ Hz, 5H), 6.37 – 5.87 (m, 2H), 5.75 (d, $J = 15.0$ Hz, 1H), 4.43 (d, $J = 5.7$ Hz, 2H), 2.32 (s, 3H), 1.82 (d, $J = 6.1$ Hz, 3H). $^{13}$C$^1$H NMR (101 MHz, CDCl₃): δ 166.28, 141.46, 137.83, 137.14, 135.36, 129.71, 129.34, 129.25, 128.69, 127.88, 121.40, 43.43, 21.09, 18.57. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd for C₁₄H₁₅NONa 238.1208; Found 238.1219.

**/(2E,4E)-N-(4-Methoxybenzyl)hexa-2,4-dienamide (2c):**

![Structure (2c)](image)

Prepared according to General Procedure 1; white solid; eluent (20% ethyl acetate: hexane); yield is 88%. $^1$H NMR (400 MHz, CDCl₃): δ 7.17 (d, $J = 8.2$ Hz, 3H), 6.82 (d, $J = 8.2$ Hz, 2H), 6.07 (m, $J = 15.1$, 8.8 Hz, 2H), 5.78 (d, $J = 15.0$ Hz, 1H), 4.37 (d, $J = 5.7$ Hz, 2H), 3.76 (s, 3H), 1.81 (d, $J = 6.3$ Hz, 3H). $^{13}$C$^1$H NMR (101 MHz, CDCl₃): δ 166.4, 158.9, 141.3,
137.8, 130.5, 129.7, 129.1, 121.5, 114.0, 114.0, 55.2, 43.1, 18.5. HRMS (ESI/Q-TOF) m/z: [M + Na]^+ Calcd for C_{14}H_{17}NO_{2}Na 254.1157; Found 254.1142.

(2E,4E)-N-(4-Fluorobenzyl)hexa-2,4-dienamide (2d):

![Chemical Structure](image)

Prepared according to General Procedure 1; yellow-white solid; eluent (20% ethyl acetate:hexane); yield is 78%. 1H NMR (400 MHz, CDCl_3): δ 7.38 – 7.10 (m, 3H), 6.97 (t, J = 8.6 Hz, 2H), 6.23 – 5.97 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 4.42 (d, J = 5.9 Hz, 2H), 1.82 (d, J = 6.0 Hz, 3H). 13C{1H} NMR (101 MHz, CDCl_3): δ 166.4, 159.0, 141.3, 137.8, 130.5, 129.7, 129.1, 121.5, 114.0, 114.0, 55.2, 43.1, 18.5. HRMS (ESI/Q-TOF) m/z: [M + Na]^+ Calcd for C_{13}H_{16}FNONa 242.0957; Found 242.0968.

(2E,4E)-N-Butylhexa-2,4-dienamide (2e):

![Chemical Structure](image)

Prepared according to General Procedure 1; yellow-white solid; eluent (25% ethyl acetate:hexane); yield is 75%. 1H NMR (400 MHz, CDCl_3): δ 7.16 (dd, J = 15.1, 10.7 Hz, 1H), 6.30 – 5.77 (m, 3H), 3.31 (m, J = 7.2, 5.7 Hz, 2H), 1.81 (dd, J = 6.8, 1.4 Hz, 3H), 1.52 (m, J = 6.9, 6.0, 1.6 Hz, 2H), 1.46 – 1.26 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H). 13C{1H} NMR (101 MHz, CDCl_3): δ 166.8, 140.5, 137.0, 129.8, 122.2, 39.3, 31.7, 20.1, 18.4, 13.7. HRMS (ESI/Q-TOF) m/z: [M + Na]^+ Calcd for C_{13}H_{16}FNONa 190.1208; Found 190.1211

(2E,4E)-N-(Tert-butyl)hexa-2,4-dienamide (2f):

![Chemical Structure](image)

Prepared according to General Procedure 1; white solid; eluent (25% ethyl acetate in hexane); yield is 73%. 1H NMR (400 MHz, CDCl_3): δ 7.35 – 6.84 (m, 1H), 6.56 – 5.96 (m, 3H), 5.82 (d, J = 15.0 Hz, 1H), 1.80 (d, J = 6.4 Hz, 3H), 1.38 (d, J = 1.9 Hz, 9H). 13C{1H} NMR (101
1H NMR (400 MHz, CDCl₃): δ 7.37 – 6.66 (m, 2H), 6.30 – 5.60 (m, 3H), 3.12 (m, J = 5.7, 5.0 Hz, 3H), 1.81 (d, J = 6.7 Hz, 2H), 0.85 (m, 6H).

13C{¹H} NMR (101 MHz, CDCl₃): δ 166.9, 140.5, 137.0, 129.8, 122.2, 47.0, 28.5, 20.2, 20.1, 18.4. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₀H₁₈NO 168.1388; Found 168.1396.

Prepared according to General Procedure 1; white solid; eluent (25% ethyl acetate:hexane); yield is 80%.

(2E,4E)-N-Isobutylhexa-2,4-dienamide (2g):

1H NMR (400 MHz, CDCl₃): δ 8.39 – 7.46 (m, 3H), 7.30 (m, J = 10.9, 10.4, 4.7 Hz, 2H), 7.09 (t, J = 7.3 Hz, 1H), 6.26 – 5.64 (m, 3H), 1.96 – 1.53 (d, 3H).

13C{¹H} NMR (101 MHz, CDCl₃): δ 165.5, 140.7, 137.2, 129.8, 122.2, 48.2, 33.2, 25.5, 24.9, 18.5. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₂H₁₉NO NaN 216.1358; Found 216.1358.

(2E,4E)-N-Cyclohexylhexa-2,4-dienamide (2h):

1H NMR (400 MHz, CDCl₃): δ 7.16 (dd, J = 15.0, 10.4 Hz, 1H), 6.34 – 5.47 (m, 3H), 3.84 (dt, J = 7.4, 3.5 Hz, 1H), 1.94 (dd, J = 12.8, 3.9 Hz, 2H), 1.82 (d, J = 6.4 Hz, 3H), 1.77 – 1.65 (m, 2H), 1.62 (m, J = 12.9, 3.8 Hz, 1H), 1.48 – 1.28 (m, 2H), 1.17 (m, J = 11.9, 3.7 Hz, 3H). 13C{¹H} NMR (101 MHz, CDCl₃): δ 165.5, 140.7, 137.2, 129.8, 122.2, 48.2, 33.2, 25.5, 24.9, 18.5. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₂H₁₉NO Na 216.1364; Found 216.1358.

(2E,4E)-N-Phenylhexa-2,4-dienamide (2i):

1H NMR (400 MHz, CDCl₃): δ 8.39 – 7.46 (m, 3H), 7.30 (m, J = 10.9, 10.4, 4.7 Hz, 2H), 7.09 (t, J = 7.3 Hz, 1H), 6.26 – 5.64 (m, 3H), 1.96 – 1.53 (d, 3H).

13C{¹H} NMR (101 MHz, CDCl₃): δ 165.5, 140.7, 137.2, 129.8, 122.2, 48.2, 33.2, 25.5, 24.9, 18.5. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₂H₁₉NO NaN 216.1358; Found 216.1358.
MHz, CDCl₃): 166.5, 163.3, 141.7, 138.1, 134.3, 129.6, 129.4, 121.2, 115.5, 115.3, 42.9, 18.6.

HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₂H₁₃NO₂ Na 210.0895; Found 210.0898.

(2E,4E)-N-(p-Tolyl)hexa-2,4-dienamide (2j):

![Structure of (2E,4E)-N-(p-Tolyl)hexa-2,4-dienamide (2j)]

Prepared according to General Procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 84%. ¹H NMR (400 MHz, CDCl₃): δ 7.81 – 7.03 (m, 3H), 6.68 – 6.03 (m, 1H), 6.16 (m, 2H), 6.52 – 5.72 (m, 2H), 5.39 – 4.81 (m, 1H), 3.19 (d, J = 7.4 Hz, 3H), 1.86 (d, J = 5.1 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 164.9, 142.6, 138.7, 137.0, 135.3, 129.7, 129.0, 127.3, 124.2, 121.8, 120.0, 18.6, 14.0. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₃H₁₅NO₂ Na 224.1051; Found 224.1062.

(2E,4E)-N-(4-Chlorophenyl)hexa-2,4-dienamide (2k):

![Structure of (2E,4E)-N-(4-Chlorophenyl)hexa-2,4-dienamide (2k)]

Prepared according to General Procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 74%. ¹H NMR (400 MHz, CDCl₃): δ 7.97 – 7.52 (m, 3H), 7.30 – 7.09 (dd, J = 9.1, 5.6 Hz, 2H), 6.48 – 5.78 (m, 1H), 6.31 – 5.72 (m, 2H), 2.12 – 1.54 (m, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃): 166.5, 141.7, 138.1, 134.3, 134.2, 129.6, 129.4, 121.2, 115.5, 115.3, 42.8, 18.6.

(2E,4E)-N-(4-Bromophenyl)hexa-2,4-dienamide (2l):

![Structure of (2E,4E)-N-(4-Bromophenyl)hexa-2,4-dienamide (2l)]

Prepared according to General Procedure 1; white solid; eluent (20% ethyl acetate : hexane); yield is 79%. ¹H NMR (400 MHz, CDCl₃): δ 9.79 (s, 1H), 8.80 (d, J = 1.5 Hz, 1H), 8.74 (dd, J = 4.2, 1.7 Hz, 1H), 8.10 (dd, J = 8.2, 1.7 Hz, 1H), 7.62 – 7.37 (m, 4H), 6.24 – 5.94 (m, 2H), 1.82 (d, J = 6.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 166.1, 148.1, 142.4, 138.7,
136.4, 131.3, 129.8, 127.5, 122.4, 121.8, 121.5, 116.8, 112.0. **HRMS (ESI/Q-TOF) m/z:** [M + H]⁺ Calcd for C₁₂H₁₃BrNO 266.0181; Found 266.0188.

**(2E,4E)-N-(3,4-Dimethylphenyl)hexa-2,4-dienamide (2m):**

![Image](attachment:image.png)

Prepared according to General Procedure 1; white solid; eluent (25% ethyl acetate:hexane); yield is 70%. **¹H NMR (400 MHz, CDCl₃):** δ 7.51 (d, J = 45.1 Hz, 1H), 7.35 – 7.15 (m, 1H), 6.94 (d, J = 7.3 Hz, 2H), 6.25 – 5.79 (m, 3H), 2.27 (s, 3H), 2.17 (s, 3H), 1.82 (d, J = 6.4 Hz, 3H). **¹³C{¹H} NMR (101 MHz, CDCl₃):** δ 164.9, 142.1, 138.2, 133.2, 131.1, 129.8, 127.1, 123.9, 121.9, 20.9, 18.6, 17.8. **HRMS (ESI/Q-TOF) m/z:** [M + Na]⁺ Calcd for C₁₄H₁₇NONa 238.1208; Found 238.1211.

**(2E,4E)-N-Methoxy-N-methylhexa-2,4-dienamide (2n):**

![Image](attachment:image.png)

Prepared according to General Procedure 1; white solid; eluent (4% ethyl acetate in hexane); yield is 89%. **¹H NMR (400 MHz, CDCl₃):** δ 7.44 – 7.09 (m, 1H), 6.82 (d, J = 8.2 Hz, 1H), 6.08 (m, 1H), 5.78 (m, J = 15.0 Hz, 1H), 4.37 (s, J = 5.8 Hz, 3H), 3.76 (s, 3H), 1.81 (d, J = 6.3 Hz, 3H). **¹³C{¹H} NMR (101 MHz, CDCl₃):** δ 166.4, 141.3, 121.5, 114.0, 55.2, 43.1, 18.5. **HRMS (ESI/Q-TOF) m/z:** [M + Na]⁺ Calcd for C₈H₁₅NO₂Na 178.0844; Found 178.0835.

**(2E,4E)-N-(Thiophen-2-ylmethyl)hexa-2,4-dienamide (2o):**

![Image](attachment:image.png)

Prepared according to General Procedure 1; white solid; eluent (18% ethyl acetate:hexane); yield is 68%. **¹H NMR (400 MHz, CDCl₃):** δ 7.41 – 7.13 (m, 2H), 6.97 (t, J = 8.6 Hz, 2H), 6.23 – 6.01 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 4.42 (d, J = 5.9 Hz, 2H), 1.82 (d, J = 6.0 Hz, 6.0 Hz,
$^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 166.5, 141.7, 138.1, 134.2, 129.6, 129.4, 121.2, 115.5, 115.3, 42.8, 18.6.

($2E,4E$)-N-(Naphthalen-2-yl)hexa-2,4-dienamide (2p):

Prepared according to general procedure 2; white solid; eluent (20% ethyl acetate:hexane); yield is 66%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.79 (s, 1H), 8.77 – 8.10 (d, $J$ = 8.2 Hz, 2H), 7.74 – 7.11 (m, 1H), 7.38 (d, $J$ = 4.2 Hz, 6H), 6.38 – 5.77 (m, 2H), 1.82 (d, $J$ = 6.5 Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 166.1, 148.1, 142.4, 138.7, 136.4, 129.8, 127.5, 123.1, 122.4, 121.8, 121.5, 116.7, 112.5, 111.99, 27.0. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{16}$NO 238.1232; Found 238.1241.

($2E,4E$)-N,5-Diphenylpenta-2,4-dienamide (4a):

Prepared according to general procedure 1; white solid; eluent (18% ethyl acetate:hexane); yield is 80%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.85 (s, 1H), 8.08 (dd, $J$ = 42.3, 5.8 Hz, 2H), 7.9 (dd, $J$ = 15.7, 11.4 Hz, 1H), 7.88 (d, $J$ = 8.2 Hz, 1H), 7.62 – 7.31 (m, 5H), 7.31 – 7.00 (m, 2H), 6.94 – 6.51 (m, 2H), 5.96 (d, $J$ = 11.1 Hz, 1H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 164.8, 148.1, 142.8, 140.7, 138.5, 136.6, 136.4, 134.7, 128.8, 128.0, 127.6, 127.5, 125.2, 121.6, 121.6, 120.8, 116.5. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd for C$_{17}$H$_{15}$NONa 272.1051; Found 272.1056.

($2E,4E$)-5-(4-Methoxyphenyl)-N-phenylpenta-2,4-dienamide (4b):

Prepared according to General Procedure 1; white solid; eluent (18% ethyl acetate:hexane); yield is 84%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.84 (s, 1H), 8.79 (dd, $J$ = 26.7, 5.8 Hz, 2H), 7.90 (d, $J$ = 8.2 Hz, 1H), 7.59 – 7.33 (m, 5H), 6.96 – 6.74 (m, 4H), 6.27 (d, $J$ = 14.8 Hz, 1H), 3.77 (s, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 165.4, 147.4, 144.0, 143.9, 141.3, 138.4, 136.0,
133.4, 130.9, 128.9, 127.9, 127.4, 121.3, 116.0, 110.1, 52.3. HRMS (ESI/Q-TOF) m/z: [M + H]⁺ Calcd for C₁₈H₁₈NO₂ 280.1338; Found 280.1332.

(2E,4E)-N-Phenyl-5-(p-tolyl)penta-2,4-dienamide (4c):

Prepared according to general procedure 1; yellow solid; eluent (18% ethyl acetate:hexane); yield is 79%. ¹H NMR (400 MHz, CDCl₃): δ 9.85 (s, 1H), 8.01 (dd, J = 39.9, 5.7 Hz, 2H), 7.95 (dd, J = 15.6, 11.4 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.54 – 7.33 (m, 4H), 7.08 (d, J = 7.8 Hz, 2H), 6.80 – 6.64 (m, 2H), 5.94 (d, J = 11.1 Hz, 1H), 2.28 (s, 3H).¹³C{¹H} NMR (101 MHz, CDCl₃): δ 164.9, 148.1, 143.1, 140.8, 139.0, 138.9, 136.4, 133.9, 129.4, 128.6, 128.0, 127.5, 124.3, 121.6, 121.5, 120.2, 116.5, 21.4. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd for C₁₈H₁₇NONa 286.1208; Found 286.1213.

(2E,4E)-5-(4-Bromophenyl)-N-phenylpenta-2,4-dienamide (4d):

Prepared according to general procedure 1; white solid; eluent (22% ethyl acetate:hexane); yield is 73%. ¹H NMR (400 MHz, CDCl₃): 10.64 (s, 1H), 8.2 (m, 3H), 8.0 (dd, J = 8.3, 1.4 Hz, 1H), 7.88 (d, J = 8.5 Hz, 3H), 7.62 (d, J = 8.4 Hz, 2H), 7.52 (dt, J = 15.3, 7.5 Hz, 3H), 7.43 – 7.38 (m, 1H).¹³C{¹H} NMR (101 MHz, CDCl₃): δ 164.8, 152.1, 148.1, 142.8, 140.7, 138.5, 136.6, 136.4, 134.7, 128.7, 128.0, 127.6, 127.5, 125.2, 121.6, 120.8, 116.5.

(2E,4E)-5-(4-Fluorophenyl)-N-phenylpenta-2,4-dienamide (4e):

Prepared according to general procedure 1; white solid; eluent (18% ethyl acetate:hexane); yield is 68%. ¹H NMR (400 MHz, CDCl₃): δ 9.93 (s, 1H), 8.90 – 8.74 (m, 2H), 7.9 (d, J = 8.2 Hz, 1H), 7.75 (d, J = 15.5 Hz, 1H), 7.63 – 7.22 (m, 9H), 6.73 (d, J = 15.5 Hz, 1H).¹³C{¹H} NMR (101 MHz, CDCl₃): δ 164.2, 148.2, 142.1, 138.5, 137.3, 136.5, 134.8, 134.6, 130.9, 128.9, 128.7, 128.1, 127.5, 126.8, 126.5, 121.6, 116.9. HRMS (ESI/Q-TOF) m/z: [M + Na]⁺ Calcd C₁₇H₁₄FNONa 290.0957; Found 290.0964.
(2E,4E)-5-(3,4-Dimethylphenyl)-N-phenylpenta-2,4-dienamide (4f):

\[
\text{Me} \quad \text{Me} \quad \text{O} \quad \text{N} \quad \text{H}
\]

Prepared according to general procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 75%. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 9.97 (s, 1H), 8.79 - 8.18 (m, 2H), 8.16 (d, J = 8.1 Hz, 1H), 7.53 – 7.15 (m, 8H), 6.29 (d, \(J = 5.4\) Hz, 1H), 2.32 (s, 3H), 2.10 (s, 3H).\(^{13}\)C\{\(^1\)H\} NMR (101 MHz, CDCl\(_3\)): \(\delta 167.8, 148.1, 139.8, 138.5, 138.1, 136.4, 134.7, 134.1, 131.8, 129.4, 128.4, 127.9, 127.4, 126.4, 121.6, 121.2, 116.8, 45.1, 21.2. HRMS (ESI/Q-TOF) \(m/z\): \([\text{M} + \text{Na}]^+\) Calcd C\(_{19}\)H\(_{19}\)NONa 300.1364; Found 300.1364.

\(\text{(E)}\)-N-Benzylpenta-2,4-dienamide (6a):

\[
\text{CH}_3\quad \text{CH}_3\quad \text{O} \quad \text{N} \quad \text{H}
\]

Prepared according to general procedure 1; white solid; eluent (25% ethyl acetate:hexane); yield is 75%. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.16 (dd, J = 15.0, 10.4 \text{ Hz}, 1H), 6.28 – 5.64 (m, 4H), 3.85 (m, \(J = 7.4, 3.3 \text{ Hz}, 1H), 1.99 – 1.86 (m, 2H), 1.71 (dt, J = 13.3, 3.9 \text{ Hz}, 2H), 1.62 (dt, \(J = 12.9, 3.8 \text{ Hz}, 1H), 1.46 – 1.27 (m, 2H), 1.17 (m, \(J = 11.8, 6.1 \text{ Hz}, 3H).\(^{13}\)C\{\(^1\)H\} NMR (101 MHz, CDCl\(_3\)): \(\delta 165.5, 140.7, 137.2, 129.8, 122.2, 48.2, 33.2, 25.5, 24.9, 18.5. \)HRMS (ESI/Q-TOF) \(m/z\): \([\text{M} + \text{H}]^+\) Calcd for C\(_{11}\)H\(_{18}\)NO 180.1388; Found 180.1395.

\(\text{(E)}\)-N-Isobutylpenta-2,4-dienamide (6b):

\[
\text{Me} \quad \text{OH}
\]

Prepared according to general procedure 1; white solid; eluent (18% ethyl acetate:hexane); yield is 80%. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.17 (d, J = 8.2 \text{ Hz}, 3H), 6.82 (d, \(J = 8.2 \text{ Hz}, 3H), 6.07 (m, \(J = 15.1, 8.8 \text{ Hz}, 2H), 5.78 (d, \(J = 15.0 \text{ Hz}, 1H), 4.37 (d, \(J = 5.7 \text{ Hz}, 2H), 3.76 \text{ s, 3H).} \(^{13}\)C\{\(^1\)H\} NMR (101 MHz, CDCl\(_3\)): \(\delta 166.4, 158.9, 141.3, 137.8, 130.5, 129.7, 129.1, 121.5, 114.0, 114.0, 55.2, 43.1. \)
(E)-N-(4-Bromophenyl)penta-2,4-dienamide (6c):

![Chemical structure](image)

Prepared according to general procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 72%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65 – 7.47 (m, 3H), 7.38 (d, $J = 8.9$ Hz, 3H), 7.28 (m, 3H), 6.96 (s, 2H), 6.03 (d, $J = 14.6$ Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$): $\delta$ 171.5, 146.9, 142.4, 136.2, 129.2, 128.8, 127.7, 126.9, 124.9, 116.7. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ Calcd for C$_{11}$H$_{12}$NO 174.0919; Found 174.0928.

(E)-N-(p-Tolyl)penta-2,4-dienamide (6d):

![Chemical structure](image)

Prepared according to general procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 73%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.84 (s, 1H), 8.79 (dd, $J = 26.7, 5.8$ Hz, 2H), 8.10 (d, $J = 8.2$ Hz, 1H), 7.49 – 7.36 (m, 3H), 6.82 (d, $J = 15.8, 8.2$ Hz, 1H), 6.27 (d, $J = 14.8$ Hz, 1H), 3.77 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$): $\delta$ 170.6, 159.5, 143.0, 134.0, 130.4, 128.6, 127.7, 126.3, 125.0, 122.6, 120.9, 37.8.

(E)-N-(4-Chlorophenyl)penta-2,4-dienamide (6e):

![Chemical structure](image)

Prepared according to general procedure 1; white solid; eluent (24% ethyl acetate:hexane); yield is 68%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76 – 7.68 (m, 1H), 7.46 (d, $J = 8.3$ Hz, 2H), 7.13 (d, $J = 8.3$ Hz, 2H), 6.72 (d, $J = 11.3$ Hz, 1H), 6.35 (t, $J = 11.6$ Hz, 1H), 5.98 (d, $J = 15.2$ Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$): $\delta$ 171.8, 142.1, 137.6, 134.9, 131.8, 130.8, 127.7, 123.6, 123.1, 122.6, 122.0. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd C$_{11}$H$_{10}$ClINa 230.0349; Found 230.0354.

(2E,4E)-5-Phenylpenta-2,4-dienoic acid (8a):

![Chemical structure](image)
Prepared according to General Procedure 2; half white solid; eluent (28% ethyl acetate:hexane); yield is 86%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.54 (dd, $J = 25.8$, 10.0 Hz, 3H), 7.38 (d, $J = 8.9$ Hz, 3H), 6.97 (t, $J = 14.8$ Hz, 2H), 6.03 (d, $J = 14.6$ Hz, 1H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): δ 171.5, 146.9, 142.9, 142.3, 141.7, 136.2, 136.0, 128.8, 127.7, 124.9, 116.7. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd for C$_{11}$H$_{10}$O$_2$Na 197.0578; Found 197.0576.

$^{(2E,4E)}$-5-(p-Tolyl)penta-2,4-dienoic acid (8b):

Prepared according to General Procedure 2; half white solid; eluent (30% ethyl acetate:hexane); yield is 84%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.45 (dd, $J = 15.1$, 10.3 Hz, 1H), 7.31 (d, $J = 7.7$ Hz, 2H), 7.11 (d, $J = 7.8$ Hz, 2H), 6.83 (dd, $J = 20.7$, 12.9 Hz, 2H), 5.90 (d, $J = 15.4$ Hz, 1H), 2.30 (s, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): δ 170.6, 159.5, 143.0, 133.9, 132.1, 130.9, 128.6, 127.4, 127.1, 126.3, 120.9, 37.9. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd for C$_{12}$H$_{12}$O$_2$Na 211.0735; Found 211.0744.

$^{(2E,4E)}$-5-(4-Chlorophenyl)penta-2,4-dienoic acid (8c):

Prepared according to general procedure 2; Half white solid; eluent (28% ethyl acetate:hexane); yield is 77%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.82 – 7.51 (m, 1H), 7.46 (d, $J = 8.1$ Hz, 2H), 7.30 – 7.01 (m, 3H), 6.72 (d, $J = 11.3$ Hz, 1H), 6.35 (t, $J = 11.6$ Hz, 1H), 5.98 (d, $J = 15.2$ Hz, 1H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): δ 171.5, 148.6, 146.9, 142.4, 136.2, 129.2, 128.8, 127.7, 126.9, 124.9, 116.7.

$^{(2E,4E)}$-5-(4-Bromophenyl)penta-2,4-dienoic acid (8d):
Prepared according to general procedure 2; Half white solid; eluent (25% ethyl acetate:hexane); yield is 79%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76 – 7.68 (m, 1H), 7.46 (d, $J = 8.3$ Hz, 2H), 7.13 (d, $J = 8.3$ Hz, 2H), 6.72 (d, $J = 11.3$ Hz, 1H), 6.35 (t, $J = 11.6$ Hz, 1H), 5.98 (d, $J = 15.2$ Hz, 1H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 171.8, 142.1, 137.6, 134.9, 131.8, 130.8, 127.7, 123.6, 123.1, 122.6, 122.0. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd for C$_{11}$H$_9$BrO$_2$Na 274.9684; Found 274.9690.

Methyl (2$E$,4$E$)-hexa-2,4-dienoate (8e):

Prepared according to general procedure 2; Yellow solid; eluent (15% ethyl acetate:hexane); yield is 38%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.51 – 7.03 (m, 1H), 6.44 – 6.04 (m, 2H), 5.78 (d, $J = 15.4$ Hz, 1H), 3.73 (d, $J = 1.4$ Hz, 3H), 1.85 (d, $J = 5.7$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 167.7, 145.2, 139.4, 129.7, 118.5, 51.4, 18.6, 18.6.

(2$E$,4$E$)-5-(Benzo[d][1,3]dioxol-5-yl)-1-(piperidin-1-yl)penta-2,4-dien-1-one (10)

Prepared according to general procedure 1; white solid; eluent (20% ethyl acetate:hexane); yield is 69%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.16 (dd, $J = 15.1$, 10.7 Hz, 2H), 6.30 – 5.81 (m, 4H), 3.31 (m, $J = 7.2$, 5.7 Hz, 3H), 1.81 (dd, $J = 6.8$, 1.4 Hz, 3H), 1.62 – 1.43 (m, 2H), 1.46 – 1.28 (m, 2H), 0.91 (t, $J = 7.4$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 166.8, 140.5, 137.0, 129.8, 122.2, 39.3, 31.7, 20.1, 18.4, 13.7. HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ Calcd C$_{17}$H$_{19}$NO$_3$Na 308.1263; Found 308.1269.

(2$E$,4$E$)-hexa-2,4-dienoic acid (12)

Prepared according to general procedure 2; Half white solid; eluent (25% ethyl acetate:hexane); yield is 82%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.43 – 7.26 (m, 1H), 6.33 – 6.09 (m, 2H), 5.78 (d, $J = 15.4$ Hz, 1H), 1.88 (d, $J = 5.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 172.9,
147.4, 140.8, 129.7, 118.2, 18.7. **HRMS (ESI/Q-TOF) m/z:** [M + Na]$^+$ Calcd for C$_6$H$_8$O$_2$Na 135.0422; Found 135.0429.
Copies of NMR Spectra

$^1$H and $^{13}$C spectra of compound 2a:
$^1$H and $^{13}$C spectra of compound 2b:
$^1$H and $^{13}$C spectra of compound 2c:
$^1$H and $^{13}$C spectra of compound 2d:
$^1$H and $^{13}$C spectra of compound 2e:
$^1$H and $^{13}$C spectra of compound 2f:
$^1$H and $^{13}$C spectra of compound 2g:
$^1\text{H}$ and $^{13}\text{C}$ spectra of compound 2h:
$^1$H and $^{13}$C spectra of compound 2i:
$^1$H and $^{13}$C spectra of compound 2j:
$^1$H and $^{13}$C spectra of compound 2k:
$^1$H and $^{13}$C spectra of compound 2l:
$^1$H and $^{13}$C spectra of compound 2m:
$^1$H and $^{13}$C spectra of compound 2n:
$^1$H and $^{13}$C spectra of compound 2o:
$^1$H and $^{13}$C spectra of compound 2p:
$^1$H and $^{13}$C spectra of compound 4a:
$^1$H and $^{13}$C spectra of compound 4b:
$^1$H and $^{13}$C spectra of compound 4c:
$^1$H and $^{13}$C spectra of compound 4d:
$^1$H and $^{13}$C spectra of compound 4e:
$^1$H and $^{13}$C spectra of compound 4f:
$^1\text{H}$ and $^{13}\text{C}$ spectra of compound 6a:
$^1$H and $^{13}$C spectra of compound 6b:
$^1$H and $^{13}$C spectra of compound 6c:
$^1$H and $^{13}$C spectra of compound 6d:
$^1$H and $^{13}$C spectra of compound 6e:
$^{1}$H and $^{13}$C spectra of compound 8a:
$^1$H and $^{13}$C spectra of compound 8b:
$^1$H and $^{13}$C spectra of compound 8c:
$^1$H and $^{13}$C spectra of compound 8d:
$^1$H and $^{13}$C spectra of compound 8e:
$^1$H and $^{13}$C spectra of compound 10:
$^1$H and $^{13}$C spectra of compound 12: