Copper-Catalyzed Decarboxylation of α,β-Unsaturated Carboxylic Acids with N-Fluorobenzenesulfonimide: Synthesis of Enamines

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A R T I C L E     I N F O

A B S T R A C T

A highly efficient and easy protocol Copper-catalyzed decarboxylative amination of α,β-unsaturated carboxylic acids with N-Fluorobenzenesulfonimide as a nitrogen source and an oxidant has been developed. The present protocol, which includes C-N bond formation in one step through addition, oxidation, and decarboxylation processes, leads to the desired enamine products. Thus the results of the experiments have shown that this study is the novel example of copper-catalyzed decarboxylative atom transfer radical of α,β-unsaturated carboxylic acids. In addition, a wide range of enamines with different substitution patterns was prepared and different groups such as chloro, bromo, fluoro, methyl, and methoxy were employed to give products in moderate to excellent yield. The mechanistic investigations revealed that the catalytic cycle was initiated by the oxidation of Cu (I) with NFSI to provide the nitrogen-centered radical species. Finally, all the products were characterized by 1H NMR, 13C NMR, and HRMS spectra.

G R A P H I C A L   A B S T R A C T
Introduction

The enamine motif represents an increasingly valuable functional group found in many pharmaceutical agents, and bioactive molecules [1-3]. Enamides also constitute an important class of synthetic intermediates [4,5]. Because of their high reactivity, they form an important group functional for the preparation of heterocyclic compounds [6]. Most enamine synthesis involves the direct condensation of ketone with a secondary amine in the presence of a base [7]. The first general synthesis for the preparation of enamine was proposed by Mannich and Davidsen in 1936 [8]. According to this method, an aldehyde and a secondary amine react, in the presence of potassium carbonate. This procedure is rarely used in the context of total synthesis or complex molecules. Along the same lines, Wittig and Meyer reported a modification to the Mannich-Davidsen method for the preparation of enamines of single chain aldehydes using ether as the solvent and a single amine equivalent, but this method involves again the distillation of the products [9]. In 1952 Heyl and Herr reported the synthesis of ketone enamines by azeotropic reflux in the benzene, toluene, or xylene of the carbonyl compound in the presence of an excess of the secondary amine [10]. This study has been extended to several ketones by the Stork group [11,12]. Nowadays this method remains the most used for the formation of cyclic ketone enamines. A new enamine synthesis was published in 1967 by White and Weingarten [13]. In this case study, TiCl₄ serves as both a catalyst and a dehydrator. This method made possible the formation of enamines of acyclic ketones (i.e. methyl ketones), and hindered ketones [14]. Imines resulting from the condensation of primary amines with carbonyl compounds can be converted into enamines.

Scheme 1. Decarboxylative C-N bond Formation

This procedure applies more particularly in the case of the enamines of methyl ketones which, other than in a basic medium, usually give secondary products of aldol condensation [15]. By the same principle, an imine can also be acylated in the presence of a base and the resulting enamide can be reduced to obtain the desired enamine [16]. This acylation method was found to be much less attractive because of the reductions which are difficult to control. The preparation of enamines remains a challenge in organic synthesis. Recently, a very large regioselective amination: synthesis of enamines had been developed [17]. So, in 2015 Zhao proposed the organoselenium catalysis enables an efficient route to enamines in excellent regio- and stereoselectivity, but that reaction was limited by the presence of a base [18]. To overcome this limitation, Jia and Jiao disclosed in 2010, a Cu-catalyzed oxidative amidation of propiolic acids via decarboxylation under air (Scheme 1a), but the propiolic acid derivatives inhibit the formation of diynes by forming by-products during this transformation [19]. We find that it is clear that organic chemists should focus their attention on the discovery of new methods for the synthesis of enamines. The literature informs us that the preparation of enamines starting from radical decarboxylation, in the presence of a nitrogen source, has not been explored. The decarboxylation reaction is one of the major applications for the formation of the
carbon-nitrogen bond (C-N) and the synthesis of enamines [20-21]. To build molecules containing a C-N bond via radical decarboxylation followed by amination, we herein reported a copper-catalyzed decarboxylative amination of α, β-unsaturated carboxylic acid derivatives in the presence of N-fluorobenzenesulfonimide as the source of nitrogen and a powerful oxidant to form enamines with an improved pharmacological profile (Scheme 1b).

**Experimental**

**Materials and methods**

**Chemicals and Materials.**

All materials were purchased and used as received. The melting points of the products formed were obtained using an electronic device called the Beijing XT4A micro melting point. Reagents (derived from α, β-unsaturated carboxylic acid 1, and NFSI) were purchased from qualified suppliers. The proton NMR spectrum was obtained at room temperature on a scale of 600 MHz, 500 MHz, and 400 MHz. 13C NMR was obtained at room temperature on a scale of 125 MHz, 150 MHz. The chemical shift (δ) is reported in parts per million (ppm) relative to standard TMS (0 ppm for 1H) and CDCl3 (77.0 ppm for 13C). Mass was determined using Bruck microtof. The coupling constant (J) was expressed in Hz. The signals were described according to the following rules: s = singuar, d = doublet, t = triplet, q = quadruplet, m = multiplet. All reactions were monitored by thin layer chromatography (TLC) using the 0.2 mm silica gel plates. The products were separated by column chromatography using silica gel as the stationary phase.

**Operating protocol for the synthesis of product 2.**

Cinnamic acid 1a (29.6 mg, 0.2 mmol), NFSI (126 mg, 0.4 mmol) and Cu (OTf)2 (7.7 mg, 0.02 mmol) were placed in a Schlenk-tube containing a magnetic stirrer under nitrogen atmosphere. 1,2-dichloroethene (2 mL) was added as a solvent. This mixture was stirred for 24 hours at a temperature of 70 ºC and gradually monitored by thin layer chromatography (TLC). The result of the mixture was extracted with dichloromethane (3 × 10 mL). Then, the organic phase was dried with anhydrous Na2SO4. After evaporation of the solvent, the residue was purified by column chromatography using silica gel as the solid phase and petroleum ether/ethyl acetate (25: 1, v: v) as the eluent to produce the enamine 2a (70.15 mg; 88%) as a white solid.

**Results and Discussion**

We started our investigation by reacting cinnamic acid 1a (0.25 mmol) with N-Fluorobenzenesulfonimide or NFSI (2.0 equiv) in 2 mL of DCE as solvent at a temperature of 70 ºC for 24 h (Table 1). When the reaction was carried out in the absence of copper as the catalyzing agent, no product was found (Table 1, entry 1). However, when the reaction was studied in the presence of Cu(OAc)2 (10 mol %) as the catalyst, 2 mL of DCE at 70 ºC (Table 1, entry 2), the corresponding product (E) -N-(phenylsulfonyl)-N-styrylbenzenesulfonamide 2a was isolated in a yield of 17%. Different solvents such as DMF, PhCN, CH3OH, and toluene were examined (Table 1, entries 3 to 6). Only a trace of the desired product was observed. Using Cu(OTf)2 as a catalyst in DCM at 70 ºC (Table 1, entry 7), enamine 2a was obtained with a yield of 40%. When we replaced DCE instead of DCM under the same conditions as above, product 2a was obtained at 71% (Table 1, entry 10). A variety of additives such as TFA and acetic acid were also used but the yield of product 2a was not above 71% (Table 2, entries 12-14). To our surprise, when the reaction was carried out in the presence of 10% Phen = 1,10-phenanthroline while keeping the conditions of (Table 1, entry 10), enamide 2a was obtained with a yield of 84% (Table 1, entry 15). Different kinds of copper were tested in this study (CuCl, CuBr, Cul, and CuCl2), but none of them were effective for this reaction (Table 1, entry 16-19).

To explore the application of this protocol, different substrates were examined (Table 2).
The reaction between cinnamic acid 1a with N-Fluorobenzenesulfonimide (NFSI) allowed compound 2a to be synthesized with a yield of 84%. Several functional groups such as fluoro, bromo, chloro, and methoxy in para, ortho, and meta position of the benzenic nucleus were accepted during this reaction, enamide 2 was synthesized with a satisfactory yield (Table 2): 2b (80%), 2c (77%), 2d (79%), 2e (57%), and 2g (74%). The electron-donating groups in the ortho, para, and meta position, such as methyl, tert-butyl or t-Bu, dimethyl were tolerant during this transformation, the products were obtained with a yield of 2h (59%), 2i (57%), 2j (51%), 2k (47%) and 2l (38%). But electron-withdrawing groups such as CF3 and NO2 did not affect the course of this reaction. After 36 hours of reaction, only the traces of 2m and 2n were observed.

Scheme 2. The reaction of cinnamic acid 1a (0.25 mmol) with N-Fluorobenzenesulfonimide

Table 1. Optimization of Reaction Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Solvent</th>
<th>Additive (equiv)</th>
<th>T (ºC)</th>
<th>Yield (%)b</th>
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<td>-</td>
<td>DCE</td>
<td>-</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Cu(OAc)2</td>
<td>DCE</td>
<td>-</td>
<td>70</td>
<td>17</td>
</tr>
<tr>
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<td>Cu(OAc)2</td>
<td>DMF</td>
<td>-</td>
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<td>trace</td>
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<tr>
<td>4</td>
<td>Cu(OAc)2</td>
<td>PhCN</td>
<td>-</td>
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</tr>
<tr>
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<td>Cu(OAc)2</td>
<td>CH3OH</td>
<td>-</td>
<td>70</td>
<td>trace</td>
</tr>
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<td>CH3CN</td>
<td>-</td>
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<tr>
<td>9</td>
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<td>-</td>
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<td>-</td>
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<td>DCE</td>
<td>TFA (2.0)</td>
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<tr>
<td>19d</td>
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<td>DCE</td>
<td>-</td>
<td>70</td>
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aReaction conditions: 1a (0.2 mmol), NFSI (2.0 equiv), Cat (10 mol%), additives (x equiv), and solvent (2 mL) under N2 atmosphere at 70 ºC for 24 h. bYield of the isolated product. cThe reaction was performed in the presence of 10% of Phen = 1,10-phenanthroline. dZn(OTf)2 (10 mol%), TFA = trifluoroacetic acid, DMF = dimethylformamide, DCM = dichloromethane, DCE = 1,2-dichloroethene. Ac = Acetic acid.
Scheme 3. The reaction of α, β-unsaturated carboxylic acid derivatives (1) in the presence of N-fluorobenzenesulfonimide

Table 2: Decarboxylation of α, β-unsaturated carboxylic acid derivatives (1) in the presence of N-fluorobenzenesulfonimide under the action of copper as a catalyst.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates 1</th>
<th>Products 2</th>
<th>Entry</th>
<th>Substrates 1</th>
<th>Products 2</th>
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<td>1a</td>
<td>10</td>
<td>COOH</td>
<td>1j</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2a, 84%, 24 h</td>
<td></td>
<td></td>
<td>2j, 51%, 24 h</td>
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<tr>
<td>2</td>
<td>Br</td>
<td>1b</td>
<td>11</td>
<td></td>
<td>1k</td>
</tr>
<tr>
<td></td>
<td>COOH</td>
<td>2b, 88%, 24 h</td>
<td></td>
<td></td>
<td>2k, 47%, 24 h</td>
</tr>
<tr>
<td>3</td>
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<td>1c</td>
<td>12</td>
<td></td>
<td>1l</td>
</tr>
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<td>COOH</td>
<td>2c, 77%, 24 h</td>
<td></td>
<td></td>
<td>2l, 38%, 36 h</td>
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<tr>
<td>4</td>
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<td>1d</td>
<td>13</td>
<td></td>
<td>1m</td>
</tr>
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<td>COOH</td>
<td>2d, 78%, 24 h</td>
<td></td>
<td></td>
<td>2m, trace, 36 h</td>
</tr>
<tr>
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<td>Br</td>
<td>1e</td>
<td>14</td>
<td></td>
<td>1n</td>
</tr>
<tr>
<td></td>
<td>COOH</td>
<td>2e, 57%, 24 h</td>
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<td>2n, trace, 36 h</td>
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<tr>
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<td>1f</td>
<td>15</td>
<td></td>
<td>2o</td>
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<tr>
<td></td>
<td>COOH</td>
<td>2f, 80%, 24 h</td>
<td></td>
<td></td>
<td>2o, 8%, 36 h</td>
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<tr>
<td>7</td>
<td></td>
<td>1g</td>
<td></td>
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<tr>
<td></td>
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<tr>
<td>8</td>
<td></td>
<td>1h</td>
<td></td>
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<tr>
<td></td>
<td>COOH</td>
<td>2h, 99%, 24 h</td>
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Analysis of $^{13}$C NMR and $^1$H NMR spectrum

*(E)-N-(phenylsulfonyl)-N-styrylbenzenesulfonamide (2a)*

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (70.15 mg, 88%); Tf: 170 – 173 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.53 (d, $J$ = 14.0 Hz, 1H, =CH-N), 6.70 (d, $J$ = 14.0 Hz, 1H, Ar-CH=), 7.35 (m, 5H, Ar-H), 7.57 (t, $J$ = 7.6 Hz, 4H, S-Ar-H in 3 and 5 position), 7.70 (t, $J$ = 7.2 Hz, 2H, S-Ar-H in 4 position), 8.00 (d, $J$ = 7.2 Hz, 4H, S-Ar-H in 2 and 6 position). $^{13}$C NMR (125 MHz; CDCl$_3$): $\delta$ = 119.3, 127.2, 128.1, 128.7, 129.0, 129.3, 133.6, 133.9, 139.0, 139.4. HRMS (ESI-TOF) calculated for C$_{20}$H$_{17}$NNaO$_4$S$_2$, [M+Na]+ 422.0497 found 422.0512.

*(E)-N-(4-fluorostyryl)-N-(phenylsulfanyl)benzenesulfonamide (2b)*

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (73.36 mg, 88%); Tf: 154 – 157 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.45 (d, $J$ = 13.6 Hz, 1H, =CH-N), 6.65 (d, $J$ = 13.2 Hz, 1H, Ar-CH=), 7.05 (t, $J$ = 8.4 Hz, 2H, Ar-H in 2 and 6 position), 7.35 (m, 2H, Ar-H in 3 and 5 position), 7.55 – 7.57 (t, $J$ = 8.0 Hz, 4H, S-Ar-H in 3 and 5 position), 7.69 (t, $J$ = 7.2 Hz, 2H, S-Ar-H in 4 position), 8.00 (d, $J$ = 7.2 Hz, 4H, S-Ar-H in 2 and 6 position). $^{13}$C NMR (125 MHz; CDCl$_3$): $\delta$ = 119.3, 127.2, 128.2, 128.8, 129.1, 129.3, 133.7, 133.9, 139.1, 139.4. HRMS (ESI-TOF) calculated for C$_{20}$H$_{16}$FNNaO$_4$S$_2$, [M+H]+ 440.0402 found 440.0513.

*(E)-N-(4-bromostyryl)-N-(phenylsulfanyl)benzenesulfonamide (2c)*

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (73.75 mg, 77%); Tf: 152 – 154 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.53 (d, $J$ = 13.6 Hz, 1H, =CH-N), 6.64 (d, $J$ = 14.0 Hz, 1H, Ar-CH=), 7.22 (d, $J$ = 8.4 Hz, 2H, Ar-H in 2 and 6 position), 7.48 (d, $J$ = 8.4 Hz, 2H, Ar-H in 3 and 5 position), 7.57 (t, $J$ = 8.0 Hz, 4H, S-Ar-H in 3 and 5 position), 7.70 – 7.67 (m, 2H, S-Ar-H in 4 position), 8.00 (d, $J$ = 0.8 Hz, 4H, S-Ar-H in 2 and 6 position). $^{13}$C NMR (125 MHz; CDCl$_3$): $\delta$ = 119.3, 127.2, 128.1, 128.7, 129.0, 129.3, 133.6, 133.9, 139.0, 139.4. HRMS (ESI-TOF) calculated for C$_{20}$H$_{17}$BrNNaO$_4$S$_2$, [M+Na]+ 477.9777; found 477.9790.

*(E)-N-(4-chlorostyryl)-N-(phenylsulfanyl)benzenesulfonamide (2d)*

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (74.30 mg, 79%); Tf: 153 – 154 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.51 (d, $J$ = 14.0 Hz, 1H, =CH-N), 6.66 (d, $J$ = 13.0 Hz, 1H, Ar-CH=), 7.32 (m, 4H, Ar-H), 7.57 – 7.58 (t, $J$ = 7.6 Hz, 4H, S-Ar-H in 3 and 5 position), 7.69 (t, $J$ = 7.6 Hz, 2H, S-Ar-H in 4 position), 7.99 (d, $J$ = 7.6 Hz, 4H, S-Ar-H in 2 and 6 position). $^{13}$C NMR (125 MHz; CDCl$_3$): $\delta$ = 119.9, 128.1, 128.3, 129.0, 129.1, 132.1, 134.0, 137.4, 139.3. HRMS (ESI-TOF) calculated for C$_{20}$H$_{16}$ClNNaO$_4$S$_2$, [M+Na]+ 456.0107 found 456.0304.

*(E)-N-(3-bromostyryl)-N-(phenylsulfanyl)benzenesulfonamide (2e)*

Reaction conditions: 1 (0.2 mmol), NFSI (0.4 mmol), Cu(OTf)$_2$ (10 mol%) in DCE (2 mL) under N$_2$ atmosphere. Isolated yield.
Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (54.31 mg, 57%); Tf: 149 – 151 °C; 1H NMR (400 MHz, CDCl3): δ = 6.56 (d, J = 13.6 Hz, 1H, =CH-N), 6.65 (d, J = 14.0 Hz, 1H, Ar-CH=), 7.23 (d, J = 8.0 Hz, 1H, Ar-H in 4 position). 7.28 (m, 1H, Ar-H in 2 position), 7.46 (d, J = 7.6 Hz, 1H, Ar-H in 6 position), 7.51 (m, 1H, Ar-H in 5 position), 7.58 (t, J = 7.6 Hz, 4H, S-Ar-H in 3 and 5 position), 7.70 (t, J = 7.2 Hz, 2H, S-Ar-H in 4 position), 7.99 (d, J = 8.4 Hz, 4H, S-Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 120.8, 122.9, 125.8, 128.1, 129.1, 129.8, 130.3, 132.1, 134.1, 135.8, 136.8, 139.3. HRMS (ESI-TOF) calculated for C20H16BrNNaO4S2, [M+Na]+ 499.9596 found 499.9888.

(E)-N-(4-methylstyryl)-N-(phenylsulfonyl)benzenesulfonamide (2f)

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid blanc (72 mg, 80%); Tf: 132 – 134°C; 1H NMR (400 MHz, CDCl3): δ = 2.36 (s, 3H, CH3), 6.46 (d, J = 13.6 Hz, 1H, =CH-N), 6.64 (d, J = 14.0 Hz, 1H, Ar-CH=), 7.15 (d, J = 8.0 Hz, 2H, Ar-H in 2 and 6 position), 7.26 (d, J = 1.2 Hz, 2H, Ar-H in 3 and 5 position), 7.56 (t, J = 8.0 Hz, 4H, S-Ar-H in 3 and 5 position), 7.68 (t, J = 4.4 Hz, 2H, S-Ar-H in 4 position), 7.99 (d, J = 8.0 Hz, 4H, Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 21.3, 118.3, 127.1, 128.1, 129.0, 129.4, 130.8, 133.9, 139.3, 139.5, 139.6. HRMS (ESI-TOF) calculated for C21H19NNaO4S2, [M+Na]+ 436.0653 found 436.0702.

(E)-N-(4-(tert-butyl)styryl)-N-(phenylsulfonyl)benzenesulfonamide (2h)

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (53.70 mg; 59%); Tf: 135 – 138 °C; 1H NMR (400 MHz, CDCl3): δ = 1.32 (s, 9H, C(CH3)3), 6.49 (d, J = 14.0 Hz, 1H, =CH-N), 6.66 (d, J = 13.2 Hz, 1H, Ar-CH=), 7.31 (d, J = 8.4 Hz, 2H, Ar-H in 2 and 6 position), 7.38 (d, J = 8.4 Hz, 2H, Ar-H in 3 and 5 position), 7.57 (t, J = 8.0 Hz, 4H, S-Ar-H in 3 and 5 position), 7.66 (t, J = 6.4 Hz, 2H, S-Ar-H in 4 position), 7.98 (d, J = 7.6 Hz, 4H, S-Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 31.1, 34.7, 118.5, 125.7, 127.0, 128.1, 129.0, 130.9, 133.9, 139.1, 139.5, 152.8. HRMS (ESI-TOF) calculated for C24H26NO4S2, [M+H]+ 456.1298 found 456.1289.

(E)-N-(4-methylstyryl)-N-(phenylsulfonyl)benzenesulfonamide (2i)

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (42.22 mg; 57%); Tf: 130 – 133 °C; 1H NMR (400 MHz, CDCl3): δ = 2.35 (s, 3H, CH3), 6.37 (d, J = 13.2 Hz, 1H, =CH-N), 6.60 (d, J = 13.2 Hz, 1H, Ar-CH=), 6.87 (d, J = 8.4 Hz, 2H, Ar-H in 2 and 6 position), 7.3 (d, J = 8.0 Hz, 2H, S-Ar-H in 3 and 5 position), 7.57 (t, J = 7.6 Hz, 2H, S-Ar-H in 3 and 5 position), 8.00 (d, J = 7.6 Hz, 4H, S-Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 21.3, 34.7, 119.1, 124.4, 127.8, 127.9, 128.1, 128.6, 129.0, 133.6, 133.9, 135.9, 138.4, 139.2. HRMS (ESI-TOF) calculated for C21H19NNaO4S2, [M+Na]+ 436.0653 found 436.0623.

(E)-N-(2-methylstyryl)-N-(phenylsulfonyl)benzenesulfonamide (2j)

Purified by column chromatography (eluent: petroleum ether / EtOAc = 25: 1); white solid (63.39 mg; 74%); Tf: 130 – 131 °C; 1H NMR (400 MHz, CDCl3): δ = 3.82 (s, 3H, CH3-O), 6.37 (d, J = 13.2 Hz, 1H, 1H, =CH-N), 6.60 (d, J = 13.2 Hz, 1H, Ar-CH=), 6.87 (d, J = 8.4 Hz, 2H, Ar-H in 2 and 6 position), 7.3 (d, J = 8.8 Hz, 2H, Ar-H in 3 and 5 position), 7.56 (t, J = 8.4 Hz, 4H, S-Ar-H in 3 and 5 position), 7.67 (t, J = 7.2 Hz, 2H, S-Ar-H in 4 position), 8.00 (d, J = 7.6 Hz, 4H, S-Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 55.3, 114.1, 117.0, 126.2, 128.1, 128.7, 129.0, 133.9, 139.2, 139.5, 160.5. HRMS (ESI-TOF) calculated for C21H19NNaO4S2, [M+Na]+ 456.0653 found 456.0701.

(E)-N-(4-tert-butylstyril)-N-(phenylsulfonyl)benzenesulfonamide (2h)
Purified by column chromatography (eluent: petroleum ether / EtOAc = 25:1); white solid (42.12 mg; 51%); Tf: 130 – 133 °C; 1H NMR (400 MHz, CDCl3): δ = 2.23 (s, 3H, CH3-Ar), 6.37 (d, J = 13.2 Hz, 1H, Ar-H), 6.89 (d, J = 13.2 Hz, 1H, Ar-H), 7.19 (m, 2H, Ar-H in 5 position), 7.24 (m, 1H, Ar-H), 7.39 (d, J = 7.2 Hz, 1H, Ar-H), 7.58 (t, J = 7.2 Hz, 4H, S-Ar-H in 3 and 5 position), 7.68 (t, J = 7.2 Hz, 2H, S-Ar-H in 4 position), 8.01 (d, J = 7.6 Hz, 4H, S-Ar-H in 2 and 6 position). 13C NMR (125 MHz; CDCl3): δ = 19.6, 120.2, 126.2, 126.3, 128.1, 129.1, 129.2, 130.4, 132.8, 133.9, 136.6, 137.9, 139.5. HRMS (ESI-TOF) calculated for C21H20NO4S2, [M+H]+ 414.0833 found 414.0828.

(E)-N-(2,4-dimethylstyril)-N-(phenylsulfonyl)benzenesulfonamide (2k)
Purified by column chromatography (eluent: petroleum ether / EtOAc = 25:1); white solid (40.13 mg, 47%); Tf: 151 – 154 °C; 1H NMR (400 MHz, CDCl3): δ = 6.65 (d, J = 13.5 Hz, 1H, =CH-N), 6.85 (d, J = 13.5 Hz, 1H, Ar-CH=N), 7.49 – 7.51 (m, 2H, Ar-H), 7.55-7.59 (m, 4H, Ar-H), 7.69 (t, J = 7.5 Hz, 2H, S-Ar-H), 7.75 (s, 1H, S-Ar-H), 7.82 (d, J = 5.5 Hz, 3H, S-Ar-H), 8.02 (d, J = 7 Hz, 4H, S-Ar-H). 13C NMR (125 MHz; CDCl3): δ = 119.5, 123.2, 126.7, 126.8, 127.7, 128.2, 128.5, 129.1, 131.11, 133.2, 133.6, 134.0, 139.1, 139.5. HRMS (ESI-TOF) calculated for C24H19NNaO4S2, [M+Na]+ 472.0653 found 472.0701.

(E)-N-(2-(naphthalen-2-yl)vinyl)-N-(phenylsulfonyl)benzenesulfonamide (2l)
Purified by column chromatography (eluent: petroleum ether / EtOAc = 25:1); white solid (34.12mg, 38%); Tf: 127 – 128°C; 1H NMR (500 MHz, CDCl3): δ = 6.65 (d, J = 13.5 Hz, 1H, =CH-N), 6.85 (d, J = 13.5 Hz, 1H, Ar-CH=N), 7.49 – 7.51 (m, 2H, Ar-H), 7.55-7.59 (m, 4H, Ar-H), 7.69 (t, J = 7.5 Hz, 2H, S-Ar-H), 7.75 (s, 1H, S-Ar-H), 7.82 (d, J = 5.5 Hz, 3H, S-Ar-H), 8.02 (d, J = 7 Hz, 4H, S-Ar-H). HRMS (ESI-TOF) calculated for C24H19NNaO4S2, [M+Na]+ 472.0653 found 472.0701.

Figure 1. 1H NMR and 13C NMR spectrum of compound 2a Control Experiments for this reaction
When the reaction was studied under the action of oxygen O2 replacing nitrogen, product 2a was observed, but with a low yield of 17% (Scheme 4). In addition, we observed 11% of product 2a when the reaction was tested in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (Scheme 5), which assumes that a radical mechanism has been operated [22].

**Proposed mechanism**

To our knowledge, the detailed mechanism for this reaction is not yet well elucidated, but based on the results of the experimental control, we propose a cyclic mechanism involving the species Cu(I), Cu(II), and Cu(III) (Scheme 6). The initial step is the formation of the active intermediate Cu(I), which is formed via the reduction of the Cu(II) [23-30] species. Oxidation of the Cu(I) species by the NFSI produces the species Cu (III) A [31] which stabilizes into a radical, species Cu (II) B [32-36]. The addition reaction between species B and α, β-unsaturated carboxylic acid 1 leads to species C Cu(II) and the radical intermediate D. Species C and D react to give complex E which in turn undergoes decarboxylation to form the final product 2 and regenerate the catalyst Cu(I).
In conclusion, we have described a novel decarboxylation reaction leading to enamines between α, β-unsaturated carboxylic acid derivatives and N-fluorobenzenesulfonimide (NFSI) as a nitrogen source and also an oxidant in the presence of copper as a catalyst. This method offers an alternative way to realize a C-N bond and get access to β-Amino Styrenes 2. Besides this remarkable synthetic versatility, this protocol features many other advantages such as using simple substrates, atom-economical reactions, as well as high product yields. The highest yield in this series is that leading to product 2b (88%). Mechanistic investigations revealed that the catalytic cycle via nitrogen-centered radical has been appropriately discussed as well and application of this protocol to modify biologically active compounds is still ongoing in our laboratory.

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