Electronic Supplementary Material (ESI) for Chemical Communications

Pd(II)-Catalyzed Decarboxylative Cross-Coupling of Oxamic Acids with Potassium Phenyltrifluoroborates under Mild Conditions

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Supporting information

Table of contents

I.General Information ·····S2

II.Experimental Section·····S3

III.References ·····S7

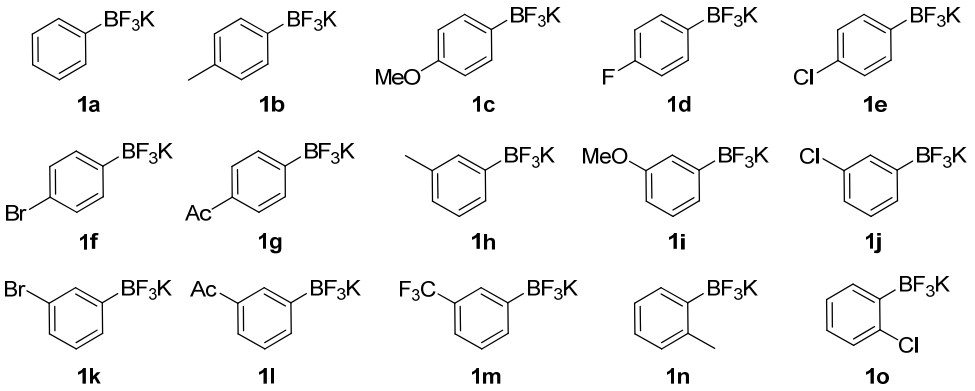
IV.Spectra·····S8

I. General Information

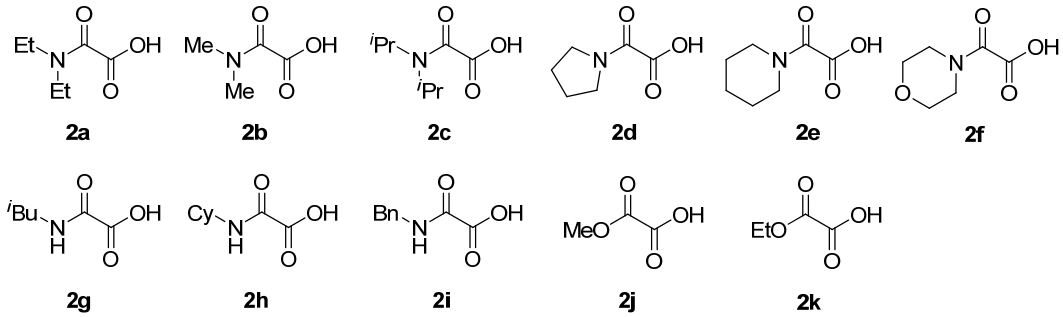
All reactions were carried out in oven-dried glassware. Pd (II) catalysts, Ag_2CO_3, $K_2S_2O_8$ and $(NH_4)_2S_2O_8$ were purchased from Acros or Sigma-Aldrich. Dimethyl sulfoxide (DMSO) were purchased from Sigma-Aldrich and used directly. All other solvents and commercially available reagents (Boronic acids, KHF_2, amines and oxalic acid derivativers) were purchased from Fisher, Sigma-Aldrich, Acros or TCI and used directly. For TLC analysis, precoated plates (w/h F254, Dynamic Adsorbents Inc, 0.25 mm thick) were used; for air-flashed column chromatography, Flash Silica Gel (Dynamic Adsorbents Inc, 32-63 μm) was used. The ^1H and ^{13}C NMR spectra were obtained on a Bruker 500 MHz NMR Fourier transform spectrometer. ^1H NMR data was reported as: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR data was reported in terms of chemical shift (δ ppm). The infrared spectra were obtained using a Thermo Nicolet IR 330 Spectrometer. High resolution mass (HRMS) analysis was obtained using a Thermo Electron Corporation MAT 95XP-Trap MS system with Electrospray Ionization (ESI).

II. Experimental Section

Preparation of starting materials:



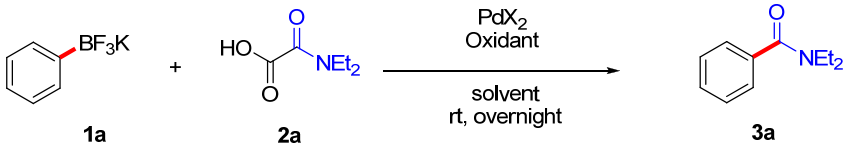
Potassium phenyltrifluoroborates (**1**)



Oxalic acid derivatives (**2**)

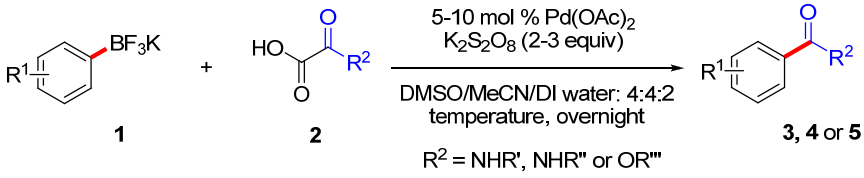
Potassium phenyltrifluoroborates (**1a**, **1b**, and **1c**), and oxamic acids (**2b**, **2j**, and **2k**) were purchased from Sigma-Aldrich, TCI or Acros. Other potassium aryltrifluoroborates were prepared from boronic acids with KHF_2 according to the reported procedure.[1] *N*,*N*-diethyloxamic acid (**2a**) and 2-oxo-2-(piperidin-1-yl)acetic acid (**2e**) were prepared from diethyl oxalate with the corresponding amines according to the reported procedure.[2,3] Other oxamic acids (**2c**, **2d**, **2f**, **2g**, **2h**, and **2i**) were prepared from the corresponding amines with methyl oxalyl chloride according to the reported protocol.[4]

General procedure of reaction conditions optimization (Table 1)



An 8 mL vial was charged with $PhBF_3K$ (**1a**, 0.3 mmol), *N*,*N*-diethyloxamic acid (**2a**, 0.6 mmol), oxidant, Pd source, followed by solvents (6 mL in total). After stirring at room temperature overnight, the reaction was quenched by the addition 3 mL of water. The resulting mixture was extracted with EtOAc (5 mL x 3) and the combined organic phases were dried over Na_2SO_4. After removal of the solvents, the crude ^1H NMR yields were measured with CH_2Br_2 as the internal standard. The isolated yield was obtained by flash chromatography column on silica gel (gradient eluent of EtOAc in Hexanes: 0 ~ 30%, v/v) (entry 4, Table 1).

General procedure of the optimal reaction conditions



General procedure of the optimal reaction conditions I (Entries **1**, **3**, and **5**, Table 2 and all entries in Table 3)

An 8 mL vial was charged with $ArBF_3K$ (**1**, 0.3 mmol), *N*,*N*-disubstituted oxamic acids (**2**, 0.6 mmol, 2 equiv), $K_2S_2O_8$ (2 or 3 equiv), followed by $Pd(OAc)_2$ (DMSO solution, 5 or 10 mol %), CH_3CN and DI water (DMSO: CH_3CN: DI water = 4/4/2, v/v/v, 6 ml in total). After stirring at room temperature overnight, the reaction was quenched by the addition of 3 mL of water. The resulting mixture was extracted with EtOAc (5 mL x 3). The combined organic phase was dried over Na_2SO_4, and then concentrated via vacuum. The desired product was obtained after purification by flash chromatography column on silica gel (gradient eluent of EtOAc in Hexanes: 0 ~ 30%, v/v).

General procedure of the optimal reaction conditions II (Entries 2 and 5 in Table 2)

An 8 mL vial was charged with $ArBF_3K$ (**1**, 0.3 mmol), oxamic acids (**2**, 0.6 mmol, 2 equiv), $K_2S_2O_8$ (3 equiv), Ag_2CO_3 (20 mol %), followed by $Pd(OAc)_2$ (DMSO solution, 10 mol %), CH_3CN and DI water (DMSO: CH_3CN: DI water = 4/4/2, v/v/v, 6 ml in total). After stirring at room temperature overnight, the reaction was quenched by the addition of 3 mL of water. The resulting mixture was extracted with EtOAc (5 mL x 3). The combined organic phase was dried over Na_2SO_4, and then concentrated via vacuum. The desired product was obtained after purification by flash chromatography column on silica gel (gradient eluent of EtOAc in Hexanes: 0 ~ 30%, v/v).

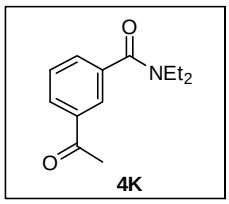
General procedure of the optimal reaction conditions III (Entries 9 and 10 in Table 2)

An 8 mL vial was charged with $ArBF_3K$ (**1**, 0.3 mmol), oxalic acid derivatives (**2**, 0.6 mmol, 2 equiv), $K_2S_2O_8$ (3 equiv), followed by $Pd(OAc)_2$ (DMSO solution, 10 mol %), CH_3CN and DI water (DMSO: CH_3CN: DI water = 4/4/2, v/v/v, 6 ml in total). After heating at 70 °C for 10 min, the mixture was cooled down to room temperature and stirred overnight. The reaction was quenched by the addition of 3 mL of water. The resulting mixture was extracted with EtOAc (5 mL x 3). The combined organic phase was dried over Na_2SO_4, and then concentrated via vacuum. The desired product was obtained after purification by flash chromatography column on silica gel (gradient eluent of EtOAc in Hexanes: 0 ~ 30%, v/v).

General procedure of the optimal reaction conditions IV (Entries 6, 7 and 8 in Table 2 and all entries in Table 4)

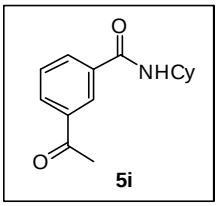
An 8 mL vial was charged with $ArBF_3K$ (**1**, 0.3 mmol), oxamic acid derivatives (**2**, 0.6 mmol, 2 equiv), $K_2S_2O_8$ (3 equiv), Ag_2CO_3 (20 mol %), followed by $Pd(OAc)_2$ (DMSO solution, 10 mol %), CH_3CN and DI water (DMSO: CH_3CN: DI water = 4/4/2, v/v/v, 6 ml in total). After heating at 70 °C for 10 min, the mixture was cooled down to room temperature and stirred overnight. The reaction was quenched by the addition of 3 mL of water. The resulting mixture was extracted with EtOAc (5 mL x 3). The combined organic phase was dried over Na_2SO_4, and then concentrated via vacuum. The desired product was obtained after purification by flash chromatography column on silica gel (gradient eluent of EtOAc in Hexanes: 0 ~ 30%, v/v).

NMR Data of New Products



3-Acetyl-*N*,*N*-diethylbenzamide (4k)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.97 (d, 1H, *J* = 8.0 Hz), 7.95 (s, 1H), 7.56 (d, 1H, *J* = 7.5 Hz), 7.49 (t, 1H, *J* = 7.5 Hz), 3.54 (br, 2H), 3.23 (br. 2H), 2.60 (s, 3H), 1.23 (br, 3H), 1.11 (br, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.4, 170.3, 137.8, 137.2, 130.8, 128.9, 128.8, 126.3, 43.4, 39.5, 26.7, 14.2, 12.9; HRMS (ESI) m/z calcd for $C_{13}H_{18}NO_2$ $[M+H]^+$ 220.1332, found 220.1336; IR (neat), ν: 2969, 2923, 2852, 1717,1685, 1631, 1534, 1321, 1253 cm^{-1}



3-Acetyl-*N*-cyclohexylbenzamide (5i)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.27 (s, 1H), 8.03 (d, 1H, *J* = 8.0 Hz), 7.99 (d, 1H, *J* = 8.0 Hz), 7.51 (t, 1H, *J* = 8.0 Hz), 6.20 (br, 1H), 4.05-3.90 (m, 1H), 2.62 (s, 3H), 2.15-1.95 (m, 2H), 1.80-1.70 (m, 2H), 1.68-1.60 (m, 1H), 1.45-1.35 (m, 2H), 1.30-1.15 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.5, 165.6, 137.1, 135.5, 131.6, 130.9, 128.9, 126.2, 49.0, 33.2, 26.7, 25.5, 24.9; HRMS (ESI) m/z calcd for $C_{15}H_{20}NO_2$ $[M+H]^+$ 246.1489, found 246.1492; IR (neat), ν: 3306, 2930, 2853, 1717,1684, 1634, 1534, 1251 cm^{-1}.

III. References:

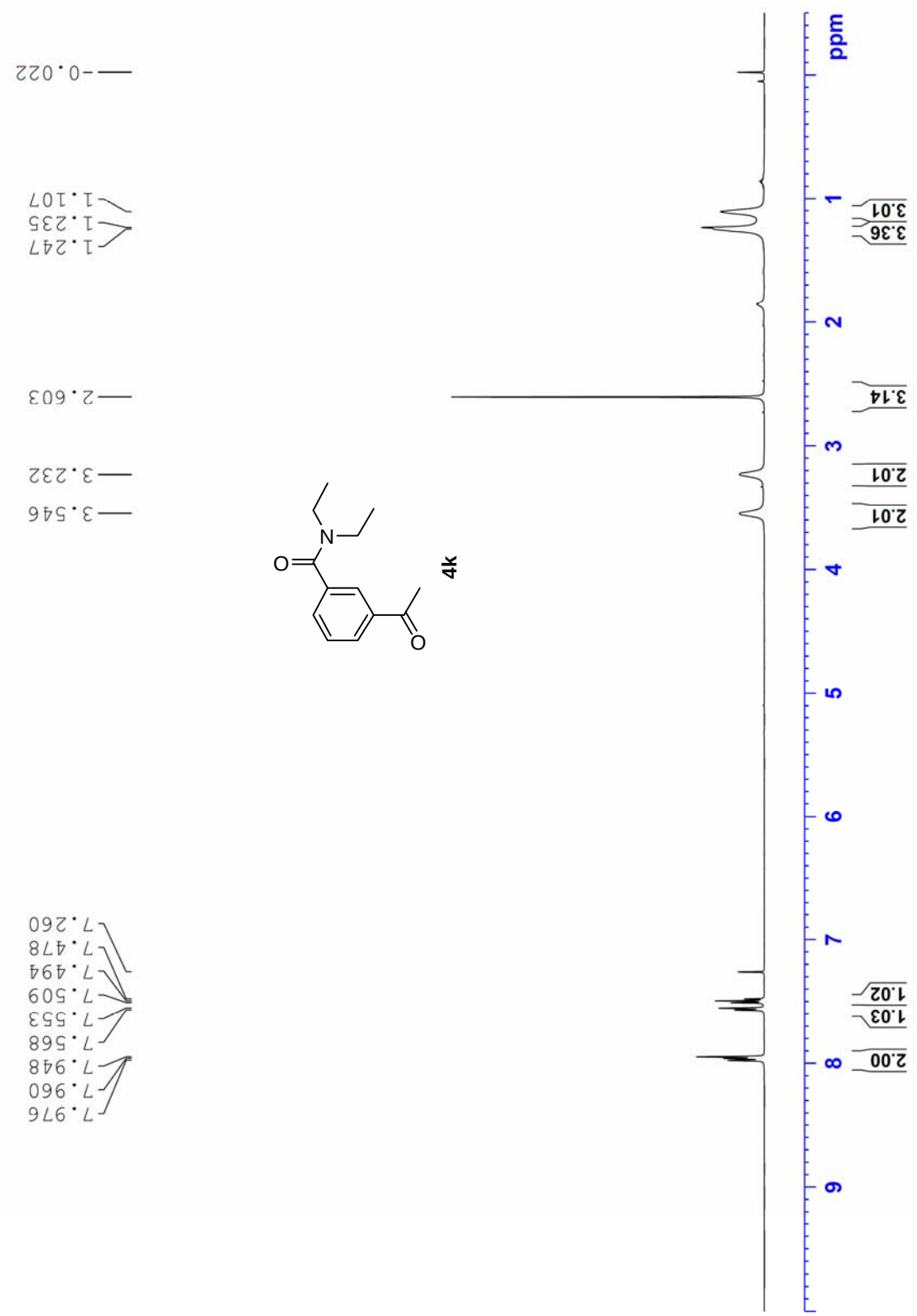
(1) G. A.Molander, W. Febo-Ayala, and L. Jean-Gerard, *Org. Lett.*, 2009, **11**, 3830.

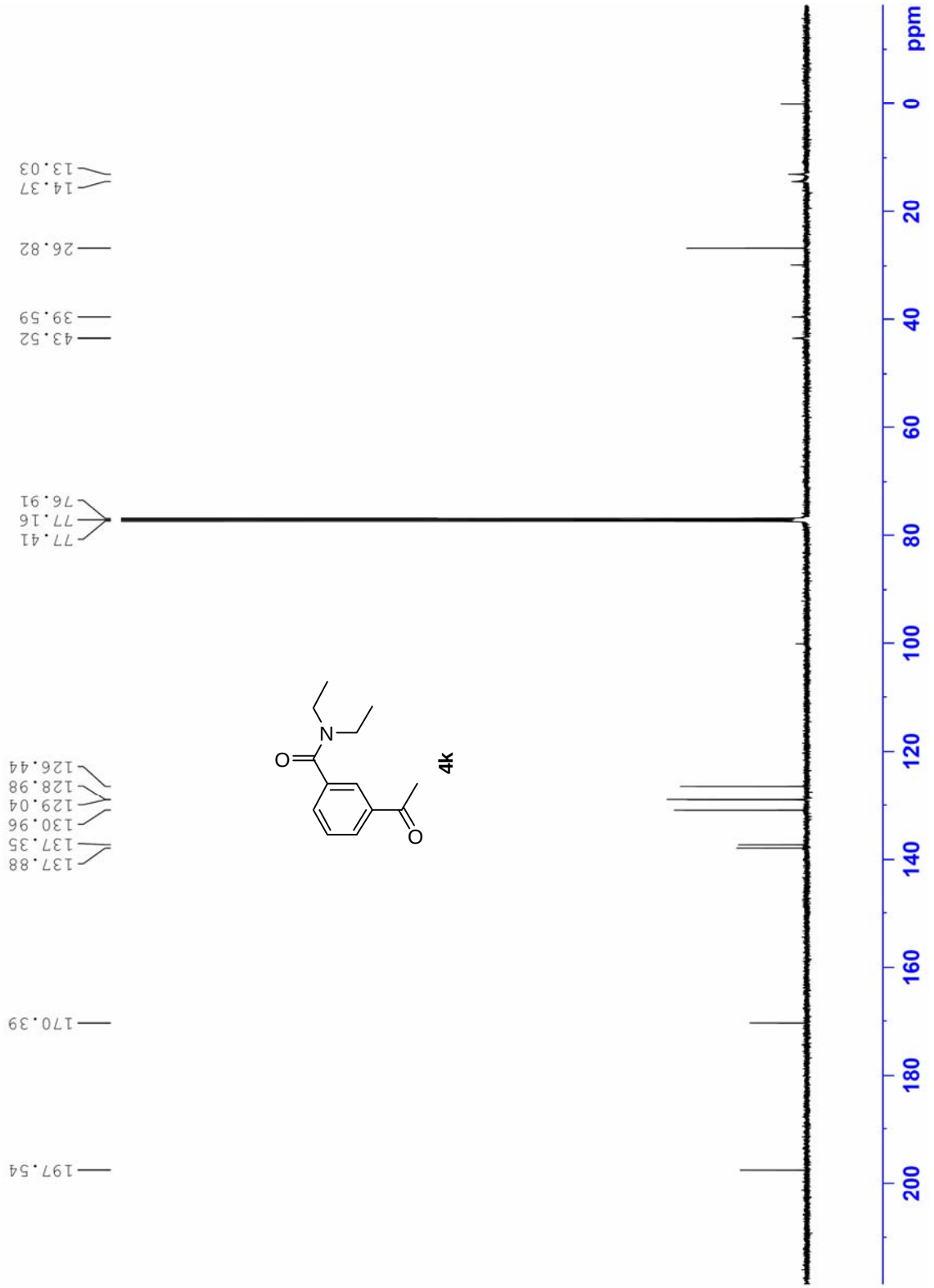
(2) R. Peters, M. Althaus, and A.-L. Nagy, *Org. Biomol. Chem.*, 2006, **4**, 498.

(3) F. Coppa, F. Fontana, E. Lazzarini, and F. Minisci, *Heterocycles*, 1993, **36**, 2687.

(4) I. M. Downie, M. J. Earle, H. Heaney, and K. F. Shuhaibar, *Tetrahedron*, 1993, **49**, 4015

IV. Spectra of New Products

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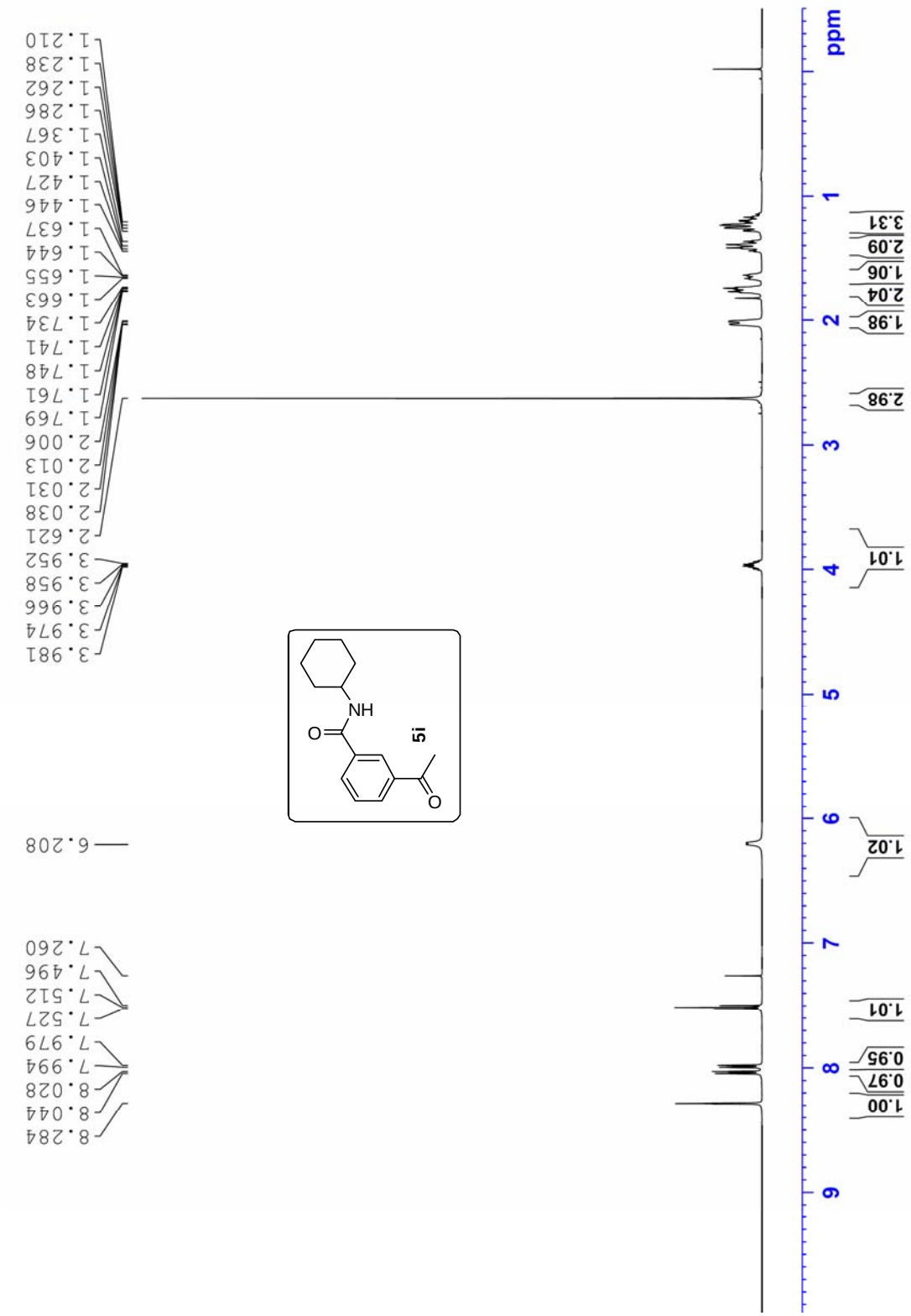
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