

# N-Heterocyclic Carbene Catalyzed Nucleophilic Acylation of Trifluoromethyl Ketimines

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**Abstract:** An efficient N-heterocyclic carbene (NHC)-catalyzed nucleophilic acylation of trifluoromethyl ketimines has been developed. The combination of *N*-aryl trifluoromethyl ketimines with various furan-2-carbaldehydes leads chemoselectively to the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketones in moderate to very good yields (32–87%) providing ready access to this pharmaceutically important class of compounds.

**Key words:** organocatalysis, N-heterocyclic carbenes, aldehyde/ketimine cross-coupling,  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketones, umpolung

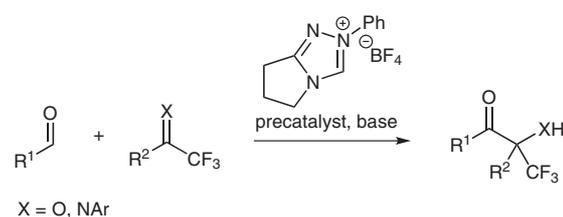
The catalytic nucleophilic addition of an acyl-anion equivalent to carbonyl compounds and Michael acceptors, known as benzoin and Stetter reactions, respectively, belong to the most prominent and powerful synthetic tools in carbene organocatalysis.<sup>1</sup> Their broad synthetic applicability has its origins in the early days of organic chemistry<sup>2</sup> and have evolved from there to become highly established transformations in organic synthesis with a great number of both inter- and intramolecular as well as enantioselective versions.<sup>3</sup>

However, the use of imines as electrophilic partners in carbene-catalyzed acyl anion additions have been studied much less, in spite of the pharmacologically importance of the resulting  $\alpha$ -amino-ketones.<sup>4</sup> Since, generally, two electrophiles (aldehyde and imine) are exposed to the carbene catalyst during the reaction course, the electronic nature of the imine component needs to be balanced carefully between: (i) being reactive enough to compete with the aldehyde in the reaction with the Breslow intermediate and (ii) being too reactive, leading ultimately to stable and unreactive catalyst–imine adducts.<sup>5</sup> Nevertheless, a few research groups were able to fulfill this challenging task by employing iminium salts formed in situ,<sup>6</sup> arylsulfonylamides as acylimine precursors<sup>7</sup> and *N*-phosphinoylimines<sup>5b</sup> in combination with acylsilanes in carbene-catalyzed acyl anion additions. Recently You et al. reported a thiazolium-derived NHC-catalyzed cross-coupling of aldehydes with *N*-aryl imines under thermodynamic control.<sup>8</sup>

Besides these excellent contributions there is, to the best of our knowledge, no literature precedence for reports on

the use of ketimines, particularly trifluoromethyl ketimines, as electrophilic components in carbene-catalyzed nucleophilic acylations.

In a recent communication we have reported on a crossed direct intermolecular benzoin-type reaction by employing aromatic and heteroaromatic aldehydes and aromatic trifluoromethyl ketones (X = O; Scheme 1).<sup>9</sup>



**Scheme 1** Crossed direct intermolecular benzoin-type reactions

Previous mechanistic observations revealed fast and reversible formation of the homo-benzoin product prior to the actual transformation,<sup>8,10</sup> and the good results we obtained for the generation of the  $\alpha$ -hydroxy- $\alpha$ -trifluoromethyl ketones inspired us to broaden the substrate scope of this crossed direct intermolecular benzoin-type reaction by using trifluoromethyl ketimines as electrophiles (X = NAr). We started our investigations by screening different aromatic and heteroaromatic aldehydes **1** and trifluoromethyl ketimine **2** in the presence of 10 mol% triazolium salt **4** and 20 mol% base in THF (Scheme 2, Table 1). Unfortunately, the reactivity of the benzaldehyde turned out to be insufficient for this transformation since even after a prolonged reaction time, only trace amounts of the product **3** could be observed (entry 3). However, by using the more reactive heteroaromatic furfural, the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketone **3** was formed with a promising preliminary yield of 45% (entry 4). By changing the employed base from DBU to Cs<sub>2</sub>CO<sub>3</sub>, the initial result could be enhanced to 87% yield (entry 5). Subsequently, other heteroaromatic aldehydes such as thiophen-2- and indol-2-carbaldehyde were tested; however, they showed no activity in this transformation (entries 6 and 7).

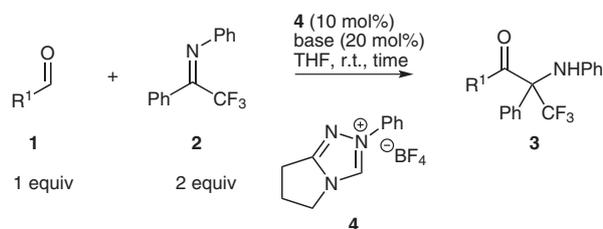
Under the best conditions (10 mol% triazolium salt **4** and 20 mol% Cs<sub>2</sub>CO<sub>3</sub> in THF), other *N*-aryl trifluoromethylated ketimines **6** and furan-carbaldehyde derivatives **5** were then tested (Scheme 3, Table 2).

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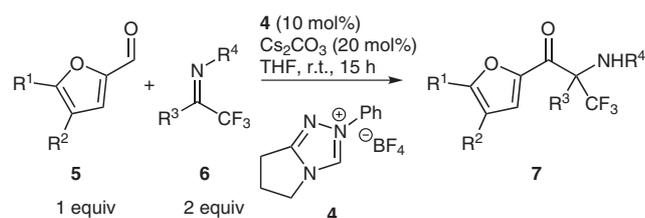


**Scheme 2** NHC-catalyzed aldehyde/trifluoromethyl ketimine cross-couplings

**Table 1** Substrate Screening for the Direct Intermolecular Benzoin-Type Reaction of Aldehydes with Trifluoromethyl Ketimines

Entry	R <sup>1</sup>	Base	Time (h)	Yield (%) <sup>a</sup>
1	Ph	DBU	15	0
2	Ph	Cs <sub>2</sub> CO <sub>3</sub>	15	0
3	Ph	DBU	3d	trace
4	2-furanyl	DBU	15	45
5	2-furanyl	Cs <sub>2</sub> CO <sub>3</sub>	15	87
6	2-thiophenyl	Cs <sub>2</sub> CO <sub>3</sub>	15	0
7	2-indolyl	Cs <sub>2</sub> CO <sub>3</sub>	15	0

<sup>a</sup> Yield of the isolated pure product.



**Scheme 3** Direct intermolecular benzoin-type reaction of furan-2-carbaldehydes with trifluoromethyl ketimines

**Table 2** Substrate Scope of the NHC-Catalyzed Aldehyde/Trifluoromethyl Ketimines Cross Coupling

7	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Yield (%) <sup>a</sup>
a	H	H	Ph	Ph	87
b	H	H	Ph	4-MeOC <sub>6</sub> H <sub>4</sub>	66
c	H	H	4-ClC <sub>6</sub> H <sub>4</sub>	Ph	69
d	H	H	4-BrC <sub>6</sub> H <sub>4</sub>	4-MeOC <sub>6</sub> H <sub>4</sub>	55
e	Me	H	Ph	Ph	32
f	Me	Me	Ph	Ph	59
g	4-ClC <sub>6</sub> H <sub>4</sub>	H	Ph	Ph	72
h			Ph	Ph	52

<sup>a</sup> Yield of the isolated pure product.

Eight different  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketones **7a–h** could be isolated in moderate to very good yields (32–87%; Table 2). Besides furfural, the best results concerning the furancarbaldehyde component in combination with trifluoromethyl ketimine **2** were obtained with 5-(4-chlorophenyl)furan-2-carbaldehyde (**7g**; 71% yield) followed by 4,5-dimethylfuran-2-carbaldehyde (**7f**; 59% yield) and benzofuran-2-carbaldehyde (**7h**; 51% yield). It is worth noting that the use of 5-methylfuran-2-carbaldehyde in the reaction of trifluoromethyl ketimine **2**, resulted in remarkably low levels of product formation (32% yield) of the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketone **7e**. By changing the ketimine substituent R<sup>4</sup> from *N*-phenyl to the more electron-rich *N*-4-methoxyphenyl, a decrease in yield from 87% to 66% was observed in the formation of the cross-product **7b**. A similar decrease in yield was also found when R<sup>3</sup> was modified to the slightly more electron-poor *para*-chlorophenyl group (**7c**; 69% yield). When both R<sup>3</sup> and R<sup>4</sup> groups were changed to *para*-chlorophenyl and *para*-methoxyphenyl groups, the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketone **7d** could be obtained in 55% yield. Noteworthy is the fact that the excess ketimine component **6** employed could be easily regained for further use during the separation of the reaction mixture by column chromatography.

In summary, we have developed the first NHC-catalyzed nucleophilic acylation of ketimines. The cross-couplings of *N*-aryl trifluoromethyl ketimines with furancarbaldehydes chemoselectively afforded the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketones in moderate to very good yields (32–87%). The product  $\alpha$ -amino ketones bearing a quaternary stereocenter and a trifluoromethyl group are useful synthetic building blocks and valuable pharmaceutical intermediates, which can be readily accessed via this novel protocol.

All reactions were performed in oven-dried glassware under a slight positive pressure of argon. All solvents were dried by conventional methods. Toluene and THF were freshly distilled from Na/Pb alloy under argon. The furanyl-2-carbaldehydes and other starting materials and reagents were purchased from commercial suppliers and used without further purification. The *N*-aryl trifluoromethyl ketimines **6a**, **6b** and **6d** were prepared according to literature procedures.<sup>11</sup> Preparative column chromatography: Merck silica gel 60, particle size 0.040–0.064 mm (230–240 mesh, flash). Analytical TLC: silica gel 60, F254 plates from Merck, Darmstadt. IR spectra were taken on a Perkin–Elmer FT-IR 1760 spectrophotometer. <sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F NMR spectra were recorded on Varian Gemini 300, Mercury 300 or Inova 400 spectrometers and all measurements were performed with TMS as internal standard. High resolution mass spectra were acquired on a Finnigan MAT 95 spectrometer. Microanalyses were obtained with a Vario EL element analyzer. Melting points were determined with a Tottoli melting point apparatus and are uncorrected.

***N*-[1-(4-Chlorophenyl)-2,2,2-trifluoroethylidene]aniline (6c)**  
1-(4-Chlorophenyl)-2,2,2-trifluoroethanone (1.25 g, 6.00 mmol) and triphenylphosphine-phenylimine (2.12 g, 6.00 mmol) were dissolved in toluene (25 mL) and refluxed at 120 °C for 24 h. Afterwards, the reaction mixture was treated repeatedly with *n*-pentane, whereupon triphenylphosphine oxide precipitated out of the solu-

tion. The precipitate was filtered off and the solvent was removed under reduced pressure. Purification via Kugelrohr distillation (bp 120 °C, 0.1 bar) afforded the pure ketimine **6c**.

Yield: 1.50 g (88%); yellow oil.

IR (film): 3441, 3066, 2918, 2850, 1941, 1906, 1789, 1715, 1660, 1593, 1540, 1489, 1450, 1400, 1384, 1330, 1266, 1232, 1198, 1135, 1094, 1018, 971, 903, 836, 776, 750, 693, 637, 578, 546, 495 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.04–7.19 (m, 6 H), 6.96 (t,  $J$  = 7.0 Hz, 1 H), 6.64 (d,  $J$  = 7.0 Hz, 2 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 155.5 [q,  $J$  = 34.1 Hz, C(N)CF<sub>3</sub>], 146.7, 136.6, 130.1, 128.9, 128.9, 128.2, 125.6, 120.3, 119.7 (q,  $J$  = 278.7 Hz, CF<sub>3</sub>).

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -69.93 (CF<sub>3</sub>).

MS (EI, 70 eV):  $m/z$  (%) = 283 (46) [M<sup>+</sup>], 262 (12), 216 (31), 215 (15), 214 (100), 139 (28), 118 (21), 77 (57), 51 (25).

Anal. Calcd for C<sub>14</sub>H<sub>9</sub>ClF<sub>3</sub>N: C, 59.28; H, 3.20; N, 4.94. Found: C, 59.07; H, 2.99; N, 5.28.

### Synthesis of the $\alpha$ -Amino- $\alpha$ -trifluoromethyl Ketones **7a–h**;

#### General Procedure

The aldehyde **5** (0.5 mmol, 1.0 equiv), trifluoromethyl ketimine **6** (1.0 mmol, 2.0 equiv), and the precatalyst **4** (14 mg, 0.05 mmol, 0.1 equiv) were dissolved in THF (1.5 mL), treated with Cs<sub>2</sub>CO<sub>3</sub> (33 mg, 0.10 mmol, 0.2 equiv) and stirred at r.t. for 15 h. Afterwards, the reaction mixture was directly purified by flash chromatography on silica gel (*n*-pentane–Et<sub>2</sub>O, 7:2) to afford the corresponding  $\alpha$ -amino- $\alpha$ -trifluoromethyl ketone **7**.

#### 3,3,3-Trifluoro-1-(furan-2-yl)-2-phenyl-2-(phenylamino)propan-1-one (**7a**)

Yield: 0.150 g (87%); colorless solid; mp 152 °C.

IR (film): 3432, 3127, 3061, 2927, 2738, 2927, 2320, 2110, 2029, 1989, 1744, 1666, 1601, 1555, 1500, 1455, 1434, 1390, 1312, 1265, 1236, 1199, 1165, 1086, 1023, 999, 956, 924, 880, 843, 817, 749, 691 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.44–7.46 (m, 2 H), 7.40–7.41 (m, 1 H), 7.30–7.34 (m, 3 H), 6.91 (t,  $J$  = 7.8 Hz, 2 H), 6.60 (t,  $J$  = 7.3 Hz, 1 H), 6.56 (d,  $J$  = 3.7 Hz, 1 H), 6.44 (d,  $J$  = 7.9 Hz, 2 H), 6.25–6.24 (m, 1 H), 5.78 (s, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 180.2, 149.4, 147.3, 143.1, 133.5, 129.0, 128.7, 128.6, 124.4 (q,  $J$  = 289.4 Hz, CF<sub>3</sub>), 123.0, 120.1, 116.8, 112.4, 111.6, 72.4 (q,  $J$  = 26.9 Hz, CCF<sub>3</sub>).

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -67.20 (CF<sub>3</sub>).

MS (EI, 70 eV):  $m/z$  (%) = 345 (3) [M<sup>+</sup>], 251 (14), 250 (100), 180 (29), 172 (16), 95 (34), 77 (50), 51 (16).

HRMS:  $m/z$  calcd for C<sub>19</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>2</sub>: 345.0977; found: 345.0973.

#### 3,3,3-Trifluoro-1-(furan-2-yl)-2-(4-methoxyphenylamino)-2-phenylpropan-1-one (**7b**)

Yield: 0.124 g (66%); yellow solid; mp 183 °C.

IR (film): 3415, 3157, 3124, 3065, 3009, 2964, 2913, 2841, 2321, 2160, 2067, 1989, 1955, 1744, 1659, 1587, 1556, 1513, 1453, 1386, 1330, 1294, 1251, 1150, 1081, 1037, 1011, 954, 926, 883, 819, 767, 701 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.40–7.42 (m, 3 H), 7.28–7.31 (m, 3 H), 6.54 (d,  $J$  = 4.1 Hz, 1 H), 6.49 (d,  $J$  = 8.9 Hz, 2 H), 6.41 (d,  $J$  = 8.9 Hz, 2 H), 6.24 (dd,  $J$  = 6.2, 1.7 Hz, 1 H), 5.45 (s, 1 H), 3.58 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 186.4, 153.8, 153.5, 147.5, 136.7, 133.8, 129.0, 128.8, 128.5, 124.3 (q,  $J$  = 289.3 Hz, CF<sub>3</sub>), 122.8, 119.5, 114.0, 112.3, 73.1 (q,  $J$  = 31.0 Hz, CCF<sub>3</sub>), 55.44.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -67.22 (CF<sub>3</sub>).

MS (EI, 70 eV):  $m/z$  (%) = 375 (15) [M<sup>+</sup>], 281 (17), 280 (100), 210 (20), 202 (13), 95 (22).

Anal. Calcd for C<sub>20</sub>H<sub>16</sub>F<sub>3</sub>NO<sub>2</sub>: C, 64.00; H, 4.30; N, 3.73. Found: C, 64.20; H, 4.32; N, 3.83.

#### 2-(4-Chlorophenyl)-3,3,3-trifluoro-1-(furan-2-yl)-2-(phenylamino)propan-1-one (**7c**)

Yield: 0.141 g (69%); colorless solid; mp 182 °C.

IR (film): 3430, 3126, 3057, 2925, 2845, 2543, 2323, 2172, 2105, 2020, 1907, 1834, 1798, 1735, 1665, 1603, 1556, 1499, 1456, 1436, 1409, 1390, 1316, 1266, 1237, 1200, 1165, 1098, 1021, 956, 921, 877, 830, 806, 764, 736, 689, 666 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.39–7.42 (m, 3 H), 7.29 (d,  $J$  = 8.9 Hz, 2 H), 6.91–6.95 (m, 2 H), 6.71 (d,  $J$  = 3.7 Hz, 1 H), 6.64 (t,  $J$  = 7.3 Hz, 1 H), 6.42 (d,  $J$  = 7.9 Hz, 2 H), 6.30 (dd,  $J$  = 3.7, 1.7 Hz, 1 H), 5.75 (s, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 179.6, 149.3, 147.8, 147.8, 135.2, 132.1, 129.9, 129.7, 129.2, 124.2 (q,  $J$  = 289.3 Hz, CF<sub>3</sub>), 123.2, 119.6, 116.9, 112.5, 72.1 (q,  $J$  = 27.4 Hz, CCF<sub>3</sub>).

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -67.28 (CF<sub>3</sub>).

MS (EI, 70 eV):  $m/z$  (%) = 379 (3) [M<sup>+</sup>], 286 (20), 285 (12), 284 (58), 216 (12), 214 (38), 172 (18), 95 (63), 77 (100), 51 (35).

Anal. Calcd for C<sub>19</sub>H<sub>13</sub>ClF<sub>3</sub>NO<sub>2</sub>: C, 60.09; H, 3.45; N, 3.69. Found: C, 59.99; H, 3.40; N, 3.69.

#### 2-(4-Bromophenyl)-3,3,3-trifluoro-1-(furan-2-yl)-2-(4-methoxyphenylamino)propan-1-one (**7d**)

Yield: 0.125 g (55%); yellow solid; mp 117 °C.

IR (film): 3401, 3143, 3126, 3066, 3033, 3001, 2957, 2930, 2899, 2833, 2324, 2161, 2082, 2011, 1989, 1969, 1859, 1782, 1736, 1666, 1590, 1555, 1513, 1491, 1455, 1406, 1389, 1315, 1289, 1254, 1231, 1201, 1164, 1118, 1104, 1083, 1026, 1012, 954, 923, 883, 821, 805, 768, 730, 710, 688, 667 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.47–7.50 (m, 3 H), 7.36 (d,  $J$  = 8.3 Hz, 2 H), 6.76 (d,  $J$  = 3.6 Hz, 1 H), 6.58 (d,  $J$  = 8.9 Hz, 2 H), 6.47 (d,  $J$  = 8.9 Hz, 2 H), 6.37 (dd,  $J$  = 3.7, 1.6 Hz, 1 H), 5.47 (s, 1 H), 3.66 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 180.1, 153.8, 149.4, 149.4, 144.2, 135.7, 132.0, 130.2, 128.4, 124.1 (q,  $J$  = 289.21 Hz, CF<sub>3</sub>), 123.0, 119.8, 114.1, 112.5, 72.9 (q,  $J$  = 26.53 Hz, CCF<sub>3</sub>), 55.4.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -67.32 (CF<sub>3</sub>).

MS (EI, 70 eV):  $m/z$  (%) = 453 (5) [M<sup>+</sup>], 360 (60), 358 (69), 290 (11), 288 (13), 202 (13), 135 (26), 123 (13), 12 (26), 108 (20), 107 (32), 95 (100), 92 (24), 77 (35), 64 (11).

Anal. Calcd for C<sub>20</sub>H<sub>15</sub>BrF<sub>3</sub>NO<sub>2</sub>: C, 52.88; H, 3.33; N, 3.08. Found: C, 52.99; H, 3.04; N, 3.07.

#### 3,3,3-Trifluoro-1-(5-methylfuran-2-yl)-2-phenyl-2-(phenylamino)propan-1-one (**7e**)

Yield: 0.058 g (32%); colorless solid; mp 151 °C.

IR (film): 3645, 3433, 3122, 3062, 2923, 2858, 2197, 2162, 2114, 1987, 1658, 1600, 1498, 1434, 1366, 1306, 1263, 1234, 1199, 1166, 1087, 1026, 993, 970, 938, 913, 878, 844, 816, 797, 751, 692, 654 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.43–7.45 (m, 2 H), 7.28–7.31 (m, 3 H), 6.87–6.91 (m, 2 H), 6.60 (t,  $J$  = 7.3 Hz, 1 H), 6.41–6.43 (m, 3 H), 5.87–5.89 (m, 2 H), 2.43 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 179.1, 159.5, 148.2, 143.2, 134.0, 129.0, 128.9, 128.5, 127.4 (q,  $J$  = 289.7 Hz, CF<sub>3</sub>), 125.9, 125.3, 119.0, 116.8, 109.6, 72.4 (q,  $J$  = 27.8 Hz, CCF<sub>3</sub>), 14.1.

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta = -67.04$  ( $\text{CF}_3$ ).

MS (EI, 70 eV):  $m/z$  (%) = 359 (10) [ $\text{M}^+$ ], 251 (15), 250.1 (100), 180 (17), 109 (10), 77 (12).

Anal. Calcd for  $\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_2$ : C, 66.85; H, 4.49; N, 3.90. Found: C, 66.88; H, 4.54; N, 3.95.

**1-(4,5-Dimethylfuran-2-yl)-3,3,3-trifluoro-2-phenyl-2-(phenyl-amino)propan-1-one (7f)**

Yield: 0.110 g (59%); yellow solid; mp 180 °C.

IR (film): 3647, 3418, 3122, 3021, 2924, 2857, 2322, 2120, 1991, 1944, 1743, 1651, 1602, 1501, 1437, 1370, 1311, 1287, 1262, 1234, 1147, 1076, 1035, 987, 949, 877, 832, 741, 693  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.42\text{--}7.44$  (m, 2 H), 7.27–7.31 (m, 3 H), 6.87–6.91 (m, 2 H), 6.59 (t,  $J = 7.3$  Hz, 1 H), 6.42 (d,  $J = 8.1$  Hz, 2 H), 6.30 (s, 1 H), 5.91 (s, 1 H), 2.11 (s, 3 H), 1.72 (s, 3 H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 178.8, 155.9, 146.8, 143.3, 134.0, 128.8, 128.8, 128.5, 128.5, 127.0, 124.5$  (q,  $J = 289.5$  Hz,  $\text{CF}_3$ ), 118.9, 118.3, 116.8, 72.0 (q,  $J = 30.3$  Hz,  $\text{CCF}_3$ ), 12.1, 9.6.

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta = -67.01$  ( $\text{CF}_3$ ).

MS (EI, 70 eV):  $m/z$  (%) = 374 (19), 373 (60) [ $\text{M}^+$ ], 251 (67), 250 (100), 180 (45), 172 (29), 123 (46), 77 (47).

Anal. Calcd for  $\text{C}_{21}\text{H}_{18}\text{F}_3\text{NO}_2$ : C, 67.55; H, 4.86; N, 3.75. Found: C, 67.25; H, 4.78; N, 3.76.

**1-[5-(4-Chlorophenyl)furan-2-yl]-3,3,3-trifluoro-2-phenyl-2-(phenylamino)propan-1-one (7g)**

Yield: 0.164 g (72%); yellow solid; mp 119 °C.

IR (film): 3636, 3371, 3059, 2958, 2920, 2852, 2541, 2342, 2118, 1906, 1712, 1666, 1602, 1560, 1503, 1468, 1435, 1414, 1362, 1312, 1267, 1213, 1170, 1122, 1095, 1029, 945, 924, 883, 820, 800, 751, 709, 670, 645, 597, 531, 503, 463  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.49$  (d,  $J = 7.8$  Hz, 2 H), 7.43 (d,  $J = 8.7$  Hz, 2 H), 7.28–7.35 (m, 5 H), 6.88–6.92 (m, 2 H), 6.81 (d,  $J = 3.8$  Hz, 1 H), 6.60 (t,  $J = 6.0$  Hz, 1 H), 6.49 (d,  $J = 3.8$  Hz, 1 H), 6.44 (d,  $J = 7.9$  Hz, 2 H), 5.87 (s, 1 H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 179.4, 157.6, 148.7, 143.1, 135.6, 133.7, 129.1, 129.0, 129.0, 128.4, 128.4, 127.1, 126.4, 125.2, 124.5$  (q,  $J = 287.1$  Hz,  $\text{CF}_3$ ), 119.2, 116.9, 108.0, 72.4 (q,  $J = 27.2$  Hz,  $\text{CCF}_3$ ).

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta = -67.09$  ( $\text{CF}_3$ ).

MS (EI, 70 eV):  $m/z$  (%) = 455 (34) [ $\text{M}^+$ ], 251 (47), 250.2 (100), 205 (12), 180 (31), 172 (22), 149 (19), 77 (32).

HRMS:  $m/z$  calcd for  $\text{C}_{25}\text{H}_{17}\text{ClF}_3\text{NO}_2$ : 455.0899; found: 455.0895.

**1-(Benzofuran-2-yl)-3,3,3-trifluoro-2-phenyl-2-(phenyl-amino)propan-1-one (7h)**

Yield: 0.103 g (52%); yellow solid; mp 196 °C.

IR (film): 3645, 3431, 3144, 3060, 2924, 2855, 2324, 2173, 2107, 1976, 1950, 1913, 1817, 1665, 1604, 1544, 1524, 1501, 1476, 1436, 1348, 1314, 1286, 1260, 1232, 1165, 1111, 1081, 1060, 1035, 1001, 954, 937, 913, 889, 873, 845, 742, 689  $\text{cm}^{-1}$ .

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.49\text{--}7.53$  (m, 2 H), 7.40 (d,  $J = 8.0$  Hz, 1 H), 7.30–7.36 (m, 5 H), 7.08–7.14 (m, 1 H), 6.88–6.92 (m, 3 H), 6.59 (t,  $J = 7.3$  Hz, 1 H), 6.49 (d,  $J = 8.0$  Hz, 2 H), 5.75 (s, 1 H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 182.6, 155.3, 149.2, 143.1, 133.4, 129.4, 129.2, 128.7, 126.5, 125.8, 124.4$  (q,  $J = 289.6$  Hz,  $\text{CF}_3$ ),

124.0, 123.7, 120.7, 119.6, 112.3, 111.1, 105.6, 72.6 (q,  $J = 27.2$  Hz,  $\text{CCF}_3$ ).

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta = -67.12$  ( $\text{CF}_3$ ).

MS (EI, 70 eV):  $m/z$  (%) = 395 (27) [ $\text{M}^+$ ], 251 (42), 250.2 (100), 180 (33), 172 (22), 145 (22), 89 (12), 77 (35).

Anal. Calcd for  $\text{C}_{23}\text{H}_{16}\text{F}_3\text{NO}_2$ : C, 69.87; H, 4.08; N, 3.54. Found: C, 70.30; H, 4.16; N, 3.35.

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