Supporting information

A Detailed Study of the Intramolecular Hydroamination of
N-(ortho-alkynyl)aryl-N'-Substituted Trifluoroacetamidines and
Bromodifluoroacetamidines

Jiangtao Zhu,a Haibo Xie,a Zixian Chen,a Shan Li,a Yongming Wu a,*

a Key laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of
Sciences, 345 Lingling Road, Shanghai 200032, China
Fax: (+86) 21-64166128. E-mail: ymwu@mail.sioc.ac.cn

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General:

Melting points were measured on a Melt-Temp apparatus and uncorrected. 1H NMR spectra were recorded in CDCl3 on a Bruker AM-300 spectrometer (300 MHz) with TMS as internal standard. 13C NMR spectra were taken on a Bruker AM-400 (100 MHz) spectrometer. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Elemental analysis was performed by the Analytical Laboratory of Shanghai Institute of Organic Chemistry. Mass spectra were recorded by EI methods. HRMS (EI) was measured on Waters Micromass GCT Premier mass spectrometer. Solvents and reagents were purchased from commercial sources and used as received. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure and petroleum ether/ethyl acetate combination was used as the eluent.
1. Synthesis of \( \text{2} \) from the corresponding acetimidoyl chloride and amine.

\[
\begin{array}{c}
\text{R}_1^1
\end{array} + \begin{array}{c}
\text{R}_2^2 \text{NH}_2 \\
\text{Et}_3\text{N}
\end{array}
\rightarrow
\begin{array}{c}
\text{N} \\
\text{RF}
\end{array}
\begin{array}{c}
\text{R}_1^1 \\
\text{NHR}_2^2
\end{array}
\text{DMF, 80}^\circ\text{C}
\]

A 50 mL flask was charged fluorinated acetimidoyl chloride \( \text{1} \) (6 mmol), the corresponding amine (7.2 mmol), triethylamine (727 mg, 7.2 mmol), DMF (20 mL). The resulting mixture was stirred at 80 °C for 2 h. Water (10 mL) was added to the mixture, which was then extracted with ethyl acetate (20 mL × 3). The combined organic layers were washed by saturated salt water, dried over MgSO\(_4\) and concentrated in vacuo, giving a residue which was subjected to silica gel chromatography to furnish the pure product \( \text{2} \).

\( \text{N-Benzyl-2,2,2-trifluoro-N'}-(2-\text{phenylethynyl})\text{-phenyl})\text{acetimidamide (2a)} \)

\[
\begin{array}{c}
\text{F}_3\text{C}
\end{array}
\begin{array}{c}
\text{N} \\
\text{NHBn}
\end{array}
\]

\(^1\text{H NMR (300 MHz, CDCl}_3\): } \delta \text{ 7.81 – 6.61 (m, 14H), 5.26 (brs, 1H), 4.47 (brs, 2H); MS (EI): m/z (\%): 278 (20.83) [M\(^+\)], 91 (100.00); Anal. Calcd. for C\(_{22}\)H\(_{17}\)F\(_3\)N\(_2\): C, 73.01; H, 4.53; N,7.40; Found: C,72.94; H, 4.65; N, 7.25; IR (film): v 3426, 3063, 3030, 1680, 1530, 1493, 1206, 1148, 754 cm\(^{-1}\).}

\( \text{2,2,2-trifluoro-N'}-(2-\text{phenylethynyl})\text{-phenyl})\text{acetimidamide (2b)} \)

\[
\begin{array}{c}
\text{F}_3\text{C}
\end{array}
\begin{array}{c}
\text{N} \\
\text{NH}_2
\end{array}
\]

\(^1\text{H NMR (300 MHz, CDCl}_3\): } \delta \text{ 7.67 – 7.23 (m, 7H), 7.11 (t, } J = \text{ 7.6 Hz, 1H), 6.96 (d, } J = \text{ 7.9 Hz, 1H), 4.92 (brs, 2H); MS (EI): m/z (\%): 288 (61.40) [M\(^+\)], 193 (100.00); HRMS (EI) Calcd. for C\(_{16}\)H\(_{17}\)F\(_2\)N\(_2\): 288.0874, Found: 288.0880; IR (film): v 3464, 3388, 3323, 3160, 1681, 1593, 1493,}
N-Cyclohexyl-2,2,2-trifluoro-N′-(2-(phenylethynyl)phenyl)acetimidamide (2d)

\[ \text{F}_3\text{C} \quad \text{NH} \quad \text{Ph} \]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.82 – 6.34 (m, 9H), 4.88 (brs, 1H), 3.67 (brs, 1H), 2.31 – 1.80 (s, 2H), 1.80 – 0.93 (m, 8H); MS (EI): m/z (%): 370 (49.84) [M$^+$], 288 (100.00); HRMS (EI) Calcd. for C$_{22}$H$_{21}$F$_3$N$_2$: 370.1657, Found: 370.1658; IR (film): $\nu$ 3285, 2922, 2851, 1655, 1544, 1187, 1151, 752 cm$^{-1}$.

2,2,2-Trifluoro-N-(4-methoxyphenyl)-N′-(2-(phenylethynyl)phenyl)acetimidamide (2e)

\[ \text{F}_3\text{C} \quad \text{NH} \quad \text{Ph} \]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.85 – 6.10 (m, 14H), 3.73 (s, 3H); MS (EI): m/z (%): 394 (8.08) [M$^+$], 204 (100.00); Anal. Calcd. for C$_{23}$H$_{17}$F$_3$N$_2$O: C, 70.04; H, 4.34; N, 7.10; Found: C, 70.21; H, 4.32; N, 7.06; IR (film): $\nu$ 3383, 3057, 2851, 1668, 1510, 1243, 1147, 1033, 754 cm$^{-1}$.

2,2,2-Trifluoro-N-(4-nitrophenyl)-N′-(2-(phenylethynyl)phenyl)acetimidamide (2g)

\[ \text{F}_3\text{C} \quad \text{NH} \quad \text{Ph} \]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.54 – 6.61 (m, 14H); MS (EI): m/z (%): 409 (100.00) [M$^+$]; Anal. Calcd. for C$_{22}$H$_{14}$F$_3$N$_3$O: C, 64.55; H, 3.45; N, 10.26; Found: C, 64.73; H, 3.54; N, 10.23; IR (film): $\nu$ 3377, 1682, 1580, 1541, 1508, 1337, 1163, 1128, 754 cm$^{-1}$.
N-benzyl-N’-(2-((4-chlorophenyl)ethynyl)phenyl)-2,2,2-trifluoroacetimidamide (2h)

\[\text{N-benzyl-N’-(2-((4-chlorophenyl)ethynyl)phenyl)-2,2,2-trifluoroacetimidamide (2h)}\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.68 – 6.62 (m, 13H), 5.29 (brs, 1H), 4.46 (brs, 2H); MS (EI): m/z (%): 412 (15.32) [M$^+$], 91 (100.00); HRMS (EI) Calcd. for C$_{23}$H$_{16}$ClF$_3$N$_2$: 412.0954; Found: 421.0955; IR (film): ν 3426, 3057, 3030, 1678, 1530, 1493, 1207, 1147, 828, 751 cm$^{-1}$.

N-Benzyl-2,2,2-trifluoro-N’-(2-(p-tolylethynyl)phenyl)acetimidamide (2i)

\[\text{N-Benzyl-2,2,2-trifluoro-N’-(2-(p-tolylethynyl)phenyl)acetimidamide (2i)}\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.59 – 6.71 (m, 13H), 5.25 (brs, 1H), 4.43 (brs, 2H), 2.36 (s, 3H); MS (EI): m/z (%): 392 (2.52) [M$^+$], 204 (100.00); Anal. Calcd. for C$_{24}$H$_{19}$F$_3$N$_2$: C, 73.46; H, 4.88; N, 7.14; Found: C, 73.53; H, 4.89; N, 7.07; IR (film): ν 3426, 3068, 3035, 2927, 1681, 1526, 1510, 1207, 1147, 816, 750 cm$^{-1}$.

N-Benzyl-2-bromo-2-difluoro-N’-(2-(phenylethynyl)phenyl)acetimidamide (2j)

\[\text{N-Benzyl-2-bromo-2-difluoro-N’-(2-(phenylethynyl)phenyl)acetimidamide (2j)}\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.60 – 6.87 (m, 14H), 5.22 (brs, 1H), 4.39 (brs, 2H); MS (EI): m/z (%): 438 (6.97) [M$^+$], 91 (100.00); Anal. Calcd. for C$_{23}$H$_{17}$BrF$_2$N$_2$: C, 62.88; H, 3.90; N, 6.38; Found: C, 63.08; H, 3.92; N, 6.34; IR (film): ν 3426, 3063, 3052, 1673, 1520, 1493, 1110, 919, 857, 754 cm$^{-1}$.

2-Bromo-N-butyl-2,2-difluoro-N’-(2-(phenylethynyl)phenyl)acetimidamide (2k)
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.50 – 6.87 (m, 9H), 4.93 (brs, 1H), 3.14 (brs, 2H), 1.49 (brs, 2H), 1.29 – 1.24 (m, 2H), 0.82(t, $J$ = 6.9 Hz, 3H); MS (EI): m/z (%): 404 (4.22) [M$^+$], 187 (100.00); HRMS (EI) Calcd. for C$_{20}$H$_{19}$BrF$_2$N$_2$: 404.0700, Found: 404.0702; IR (film): $\nu$ 3421, 3057, 2959, 2932, 2862, 1673, 1523, 1493, 1174, 1112, 911, 755 cm$^{-1}$.

2-Bromo-$N$-cyclohexyl-2,2-difluoro-$N'$-(2-(phenylethynyl)phenyl)acetimidamide (2l)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.50 – 6.87 (m, 9H), 4.83 (brs, 1H), 3.46 (brs, 1H), 1.99 (brs, 2H), 1.64 – 1.10 (m, 8H); MS (EI): m/z (%): 430 (31.10) [M$^+$], 98 (100.00); Anal. Calcd. for C$_{22}$H$_{21}$BrF$_2$N$_2$: C, 61.26; H, 4.91; N, 6.49; Found: C, 61.40; H, 4.95; N, 6.45; IR (film): $\nu$ 3415, 3046, 2931, 2854, 1668, 1515, 1493, 1472, 1170, 1110, 896, 754 cm$^{-1}$.

$N$-Allyl-2-bromo-2,2-difluoro-$N'$-(2-(phenylethynyl)phenyl)acetimidamide (2m)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.78 – 6.63 (m, 9H), 5.84 (brs, 1H), 5.40 – 4.75 (m, 3H), 3.83 (brs, 2H); MS (EI): m/z (%): 388 (43.08) [M$^+$], 254 (100.00); HRMS (EI) Calcd. for C$_{19}$H$_{13}$BrF$_2$N$_2$: 388.0387, Found: 388.0393; IR (film): $\nu$ 3421, 3057, 3019, 1673, 1518, 1493, 1473, 1174, 1112, 924, 755 cm$^{-1}$.

2-Bromo-2,2-difluoro-$N$-(4-methoxyphenyl)-$N'$-(2-(phenylethynyl)phenyl)acetimidamide (2n)
$^{1}$H NMR (300 MHz, CDCl$_3$): $\delta$ 9.14 – 6.28 (m, 14H), 4.00 (s, 3H); MS (EI): m/z (%): 454 (26.09) [M$^+$], 375 (100.00); Anal. Calcd. for C$_{23}$H$_{17}$BrF$_2$N$_2$O: C, 60.67; H, 3.76; N, 6.15; Found: C, 60.96; H, 3.93; N, 6.10; IR (film): v 3388, 3063, 2829, 1673, 1582, 1510, 1442, 1240, 1146, 754 cm$^{-1}$.

$N$-Benzyl-2-bromo-2,2-difluoro-$N'$-(2-(hex-1-yn-1-yl)phenyl)acetimidamide (2o)

$^{1}$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.51 – 6.55 (m, 9H), 5.06 (brs, 1H), 4.23 (brs, 2H), 2.51 – 2.01 (m, 2H), 1.71 – 1.10 (m, 4H), 0.84 (t, $J$ = 5.7 Hz, 3H); MS (EI): m/z (%): 418 (3.57) [M$^+$], 91 (100.00); HRMS (EI) Calcd. for C$_{21}$H$_{21}$BrF$_2$N$_2$: 418.0856, Found: 418.0858; IR (film): v 3421, 3068, 3053, 2954, 2932, 2873, 1674, 1520, 1477, 1171, 1116, 917, 749 cm$^{-1}$.

2-Bromo-2,2-difluoro-$N'$-(2-(hex-1-yn-1-yl)phenyl)-$N$-(4-methoxyphenyl)acetimidamide (2p)

$^{1}$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.64 – 5.87 (m, 9H), 3.73 (s, 3H), 2.68 – 2.21 (m, 2H), 1.81 – 1.37 (m, 4H), 1.11 – 0.68 (m, 3H); MS (EI): m/z (%): 434 (17.06) [M$^+$], 355 (100.00); Anal. Calcd. for C$_{21}$H$_{21}$BrF$_2$N$_2$O: C, 57.94; H, 4.86; N, 6.44; Found: C, 58.09; H, 4.95; N, 6.39; IR (film): v 3383, 2954, 2927, 1668, 1504, 1240, 1147, 1085 cm$^{-1}$.

$N$-Benzyl-2-bromo-2,2-difluoro-$N'$-(2-((4-methoxyphenyl)ethynyl)phenyl)acetimidamide (2q)
1H NMR (300 MHz, CDCl₃): δ 7.63 – 6.60 (m, 13H), 5.20 (brs, 1H), 4.39 (brs, 2H), 3.83 (s, 3H);
MS (EI): m/z (%): 468 (10.48) [M⁺], 91 (100.00); Anal. Calcd. for C₂₄H₁₉BrF₂N₂O: C, 61.42; H, 4.08; N, 5.97; Found: C, 61.69; H, 4.14; N, 5.94; IR (film): ν 3431, 3068, 3035, 2927, 2829, 1673, 1605, 1510, 1474, 1248, 1173, 1108, cm⁻¹.

2-Bromo-N-butyl-N'-(2-ethynylphenyl)-2,2-difluoroacetimidamide (2s)

1H NMR (300 MHz, CDCl₃): δ 7.44 – 6.84 (m, 4H), 4.93 (brs, 1H), 3.18 (s, 1H), 3.15 – 3.12 (m, 2H), 1.60 – 0.80 (m, 7H); MS (EI): m/z (%): 328 (30.58) [M⁺], 116 (100.00); HRMS (EI) Calcd. for C₁₄H₁₅BrF₂N₂: 328.0387; Found: 328.0381; IR (film): ν 3426, 3298, 3063, 3019, 2103, 1673, 1591, 1521, 1475, 1170, 1114, 917, 849, 750 cm⁻¹.

N-Benzyl-2-bromo-N'-(2-ethynylphenyl)-2,2-difluoroacetimidamide (2r)

1H NMR (300 MHz, CDCl₃): δ 7.44 – 6.84 (m, 9H), 5.24 (brs, 1H), 4.37 (brs, 2H), 3.19 (s, 1H); MS (EI): m/z (%): 362 (0.96) [M⁺], 91 (100.00); HRMS (EI) Calcd. for C₁₇H₁₃BrF₂N₂: 362.0230; Found: 362.0228; IR (film): ν 3426, 3298, 3063, 3019, 2103, 1673, 1591, 1521, 1475, 1170, 1114, 917, 849, 750 cm⁻¹.

2-Bromo-N-cyclohexyl-N'-(2-ethynylphenyl)-2,2-difluoroacetimidamide (2t)
\[ \text{BrF}_2\text{C}\equiv\text{NH} \]

\[ \text{BrF}_2\text{C}=\text{N} \equiv \text{H} \]

\[ \text{N} \equiv \text{Allyl-2-bromo-N'}-(2-ethynylphenyl)-2,2\text{-difluoroacetimidamide (2u)} \]

\[ \text{BrF}_2\text{C}\equiv\text{NH} \]

\[ \text{BrF}_2\text{C}=\text{N} \equiv \text{H} \]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.44 – 6.84 (m, 4H), 4.80 (brs, 1H), 3.17 (s, 1H), 2.01-1.13 (m, 11H); MS (EI): m/z (%): 354 (4.50) [M$^+$], 55 (100.00); HRMS (EI) Calcd. for C$_{16}$H$_7$BrF$_2$N$_2$: 345.0543; Found: 345.0541; IR (film): v 3415, 3310, 2932, 2855, 2018, 1670, 1592, 1518, 1474, 1171, 1113, 896 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.44 – 6.80 (m, 4H), 5.85 (brs, 1H), 5.21 – 5.14 (m, 3H), 3.82 (brs, 2H), 3.19 (s, 1H); MS (EI): m/z (%): 312 (36.27) [M$^+$], 115 (100.00); HRMS (EI) Calcd. for C$_{13}$H$_{11}$BrF$_2$N$_2$: 312.0074; Found: 312.0076; IR (film): v 3428, 3301, 2911, 2097, 1676, 1522, 1475, 1174, 924 cm$^{-1}$.
3a
$3b$

![Chemical structure of compound 3b](image)

$3c$

![Chemical structure of compound 3c](image)
3e
3h
3i

3i
3j

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$3m$
3t
6d
Figure 1. X-Ray Crystal Structure of 3j
Figure 2. X-Ray Crystal Structure of 4j'

Figure 3. X-Ray Crystal Structure of 4e