SYNTHESIS OF FUNCTIONALIZED *N*-SULFONYLAMIDINES FROM *N*-SULFONYLKETENIMINES AND 2-AMINO BENZIMIDAZOLE

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GRAPHICAL ABSTRACT

Abstract *The synthesis of a novel class of *N*-(1*H*-benzo[*d*]imidazol-2-yl)-2-alkyl-*N'*-sulfonylamidines via a copper-catalyzed three-component coupling reaction of 1*H*-benzo[*d*]imidazol-2-amine, sulfonyl azides and terminal alkynes is described.*

Keywords Amidines; copper iodide; *N*-sulfonylketenimines; tosyl azide; terminal alkyne

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EXPERIMENTAL

All chemicals were obtained commercially and used without further purification. M.p.: *Electrothermal-9100* apparatus. IR Spectra: *Shimadzu-IR-460* spectrometer; bond positions in cm^{-1} . ^1H - and ^{13}C -NMR Spectra: *Bruker DRX-500 Avance* instrument at 400.1 and 100.6 MHz, resp.; δ in ppm, J in Hz. MS: *Finnigan-MAT-8430EI-MS* mass spectrometer; at 70 eV; in m/z (rel. %). Elemental analyses: *Vario EL III CHNOS* elemental analyzer.

General Procedure for the Preparation of Compounds 5

To a mixture of alkyne **1** (1 mmol), sulfonyl azide **2** (1.2 mmol), CuI (0.1 mmol), and Et_3N (1 mmol) in DMF (3 mL) was slowly added 2-amino-benzoimidazole (1.5 mmol). The mixture was stirred at room temperature. After completion of the reaction [about 8 h; TLC (AcOEt/hexane 1:3) monitoring], the mixture was diluted with CH_2Cl_2 (2 mL) and aqueous NH_4Cl solution (3 mL), stirred for 30 min, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 mL $\times$ 3) and the combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography [silica gel (230-400 mesh; Merck), AcOEt/hexane 1:3] to give product.

***N*-(1*H*-benzo[d]imidazol-2-yl)-2-phenyl-*N'*-tosylacetamidine 5.** Yield: 0.32 g (80%); cream powder; m.p. = 156-159 °C. IR (KBr): 3160 (NH), 3030 (NH), 1448 (C=N), 1375 (SO_2), 1178 cm^{-1} (SO_2). ^1H NMR (400 MHz, CDCl_3): δ_{H} = 2.48 (3H, s, Me), 4.25 (2H, s, CH_2), 7.29-7.35 (3H, m, Ph), 7.40 (2H, d, $^3J_{\text{HH}}$ = 7.9 Hz, Ar), 7.48 (2 H, d, $^3J_{\text{HH}}$ = 7.5 Hz, Ar), 7.57 (1 H, t, $^3J_{\text{HH}}$ = 7.4 Hz, Ar), 7.62 (1 H, t, $^3J_{\text{HH}}$ = 7.4 Hz, Ar), 7.91 (2 H, d, $^3J_{\text{HH}}$ = 7.9 Hz, Ar), 8.02 (1 H, d, $^3J_{\text{HH}}$ = 7.4 Hz, Ar), 8.26 (1 H, d, $^3J_{\text{HH}}$ = 7.4 Hz, Ar), 9.59 (1 H, s, NH), 10.48 (1 H, s, NH). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} = 30.8 (Me), 47.6 (CH_2), 123.3 (CH), 123.6 (CH), 127.2 (C), 127.9 (CH), 128.2 (2 CH), 128.6 (CH), 129.5 (2 CH), 130.2 (CH), 130.8 (C), 131.4 (2 CH), 133.8 (2 CH), 141.7

(C), 142.8 (C), 148.2 (C), 158.1 (C), 166.0 (C). MS (EI, 70 eV): m/z (%) = 404 (M^+ , 5), 328 (10), 313 (13), 287 (16), 249 (32), 155 (100), 91 (70), 77 (54). Anal. calcd. for $C_{22}H_{20}N_4O_2S$ (404.13): C, 65.33; H, 4.98; N, 13.85%. Found: C, 65.69; H, 5.02; N, 13.94%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-2-phenyl-*N'*-(phenylsulfonyl)acetimidamide 5b.**

Yield: 0.32 g (82%); cream powder; m.p. = 132-134 °C. IR (KBr): 3137 (NH), 3003 (NH), 1448 (C=N), 1376 (SO₂), 1181 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 4.28 (2H, s, CH₂), 7.30-7.37 (3H, m, Ph), 7.49 (2H, d, ³ J_{HH} = 7.8 Hz, Ar), 7.59 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 7.66-7.74 (3H, m, Ph), 7.77 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 8.00-8.06 (3H, m, Ph), 8.29 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 9.72 (1H, s, NH), 10.88 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 46.9 (CH₂), 122.9 (CH), 123.7 (CH), 127.3 (CH), 128.0 (2 CH), 128.2 (CH), 128.7 (CH), 129.2 (2 CH), 130.3 (CH), 130.7 (2 CH), 133.6 (2 CH), 134.5 (C), 136.4 (C), 145.6 (C), 148.7 (C), 158.7 (C), 167.1 (C). MS (EI, 70 eV): m/z (%) = 390 (M^+ , 1), 313 (6), 299 (10), 273 (18), 249 (16), 141 (100), 132 (21), 91 (38), 77 (50), 78 (31). Anal. calcd. for $C_{21}H_{18}N_4O_2S$ (390.12): C, 64.60; H, 4.65; N, 14.35%. Found: C, 64.93; H, 4.69; N, 14.42%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(methylsulfonyl)-2-phenylacetimidamide 5c.**

Yield 0.24 g (74%); cream powder, m.p. = 122-124 °C. IR (KBr): 3324 (NH), 3010 (NH), 1448 (C=N), 1369 (SO₂), 1176 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 3.68 (3H, s, Me), 4.35 (2H, s, CH₂), 7.31-7.35 (3H, m, Ph), 7.50 (2H, d, ³ J_{HH} = 7.8 Hz, Ar), 7.60 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 7.66 (1H, t, ³ J_{HH} = 7.7 Hz, Ar), 8.05 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 8.32 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 9.77 (1H, s, NH), 10.89 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 30.8 (Me), 46.0 (CH₂), 122.6 (CH), 123.2 (C), 123.9 (CH), 128.4 (CH), 129.2 (CH), 129.4 (2 CH), 130.0 (CH), 133.2 (2 CH), 133.4 (C), 147.9 (C), 159.2 (C), 165.0 (C). MS (EI, 70 eV): m/z (%) = 328 (M^+ , 5),

252 (6), 273 (10), 211 (18), 196 (16), 91 (23), 78 (100), 77 (50). Anal. calcd. for C₁₆H₁₆N₄O₂S (328.10): C, 58.52; H, 4.91; N, 17.06%. Found: C, 58.21; H, 4.95; N, 17.17%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-tosylhexanamidine 5d.** Yield 0.24 g, (62%); cream powder, mp: 111-113 °C, IR (KBr): 3224 (NH), 3039 (NH), 1490 (C=N), 1368 (SO₂), 1179 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 0.92 (3H, t, ³J_{HH} = 6.9 Hz, Me), 1.39-1.45 (2H, m, CH₂), 1.48-1.54 (2H, m, CH₂), 2.17-2.21 (2H, m, CH₂), 2.49 (3H, s, Me), 3.24 (2H, t, ³J_{HH} = 6.9 Hz, CH₂), 7.41 (2H, d, ³J_{HH} = 7.9 Hz, Ar), 7.64 (1H, t, ³J_{HH} = 7.5 Hz, Ar), 7.72 (1H, t, ³J_{HH} = 7.5 Hz, Ar), 7.91 (2H, d, ³J_{HH} = 7.9 Hz, Ar), 8.08 (1H, d, ³J_{HH} = 7.5 Hz, Ar), 8.37 (1H, d, ³J_{HH} = 7.5 Hz, Ar), 9.39 (1H, s, NH), 10.98 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 14.7 (Me), 19.2 (CH₂), 22.5 (CH₂), 22.9 (CH₂), 30.8 (Me), 31.6 (CH₂), 127.2 (CH), 128.1 (2 CH), 128.8 (CH), 129.7 (CH), 130.9 (CH), 131.4 (2 CH), 141.8 (C), 142.7 (C), 145.8 (C), 148.0 (C), 160.7 (C), 164.9 (C). MS (EI, 70 eV): *m/z* (%) = 384 (M⁺, 5), 313 (7), 293 (20), 229 (16), 155 (100), 91 (74), 77 (30), 76 (32), 71 (54). Anal. calcd. for C₂₀H₂₄N₄O₂S (384.16): C, 62.48; H, 6.29; N, 14.57%. Found: C, 62.69; H, 6.33; N, 14.66%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(phenylsulfonyl)hexanimidamide 5e.** Yield 0.21 g (57%); cream powder, m.p. = 119-122 °C. IR (KBr): 3348 (NH), 3066 (NH), 1451 (C=N), 1377 (SO₂), 1180 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 0.89 (3H, t, ³J_{HH} = 6.9 Hz, Me), 1.37-1.44 (2H, m, CH₂), 1.46-1.54 (2H, m, CH₂), 2.17-2.21 (2H, m, CH₂), 3.39 (2H, t, ³J_{HH} = 6.9 Hz, CH₂), 7.61 (2H, t, ³J_{HH} = 7.9 Hz, Ar), 7.70-7.78 (2H, m, Ph), 7.98 (1H, t, ³J_{HH} = 7.5 Hz, Ar), 8.06 (2H, d, ³J_{HH} = 7.9 Hz, Ar), 8.13 (1H, d, ³J_{HH} = 7.5 Hz, Ar), 8.40 (1H, d, ³J_{HH} = 7.5 Hz, Ar), 9.51 (1H, s, NH), 10.33 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 14.7 (Me), 19.3 (CH₂), 22.9 (CH₂), 30.8 (CH₂), 31.7 (CH₂), 127.2 (2 CH), 128.5 (2 CH), 129.3 (CH), 129.6 (CH), 130.4 (CH), 131.7 (CH), 136.5 (C), 139.4 (CH), 144.0 (C), 145.4 (C), 162.0 (C), 166.8

(C). MS (EI, 70 eV): m/z (%) = 370 (M^+ , 7), 299 (17), 253 (20), 229 (34), 141 (100), 125 (23), 77 (41), 76 (33). Anal. calcd. for $C_{19}H_{22}N_4O_2S$ (370.15): C, 61.60; H, 5.99; N, 15.12%. Found: C, 61.21; H, 6.04; N, 15.21%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(methylsulfonyl)hexanimidamide 5f.** Yield 0.16 g (53%); cream powder, m.p. = 100-103 °C. IR (KBr): 3387 (NH), 3043 (NH), 1449 (C=N), 1376 (SO₂), 1181 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 0.90 (3H, t, ³ J_{HH} = 6.9 Hz, Me), 1.35-1.42 (2H, m, CH₂), 1.44-1.50 (2H, m, CH₂), 2.11-2.18 (2H, m, CH₂), 3.10 (3H, s, Me), 3.37 (2H, t, ³ J_{HH} = 6.9 Hz, CH₂), 7.71 (1H, t, ³ J_{HH} = 7.9 Hz, Ar), 7.78 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 8.10 (1H, d, ³ J_{HH} = 7.9 Hz, Ar), 8.40 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 9.21 (1H, s, NH), 10.10 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 14.6 (Me), 19.2 (CH₂), 23.0 (CH₂), 30.7 (CH₂), 31.6 (CH₂), 33.0 (Me), 121.3 (CH), 124.4 (CH), 129.4 (CH), 130.4 (CH), 132.5 (C), 144.1 (C), 162.1 (C), 165.5 (C). MS (EI, 70 eV): m/z (%) = 308 (M^+ , 7), 237 (7), 229 (20), 191 (23), 176 (20), 78 (100), 77 (26). Anal. calcd. for $C_{14}H_{20}N_4O_2S$ (308.13): C, 54.52; H, 6.54; N, 18.17%. Found: C, 54.27; H, 6.50; N, 18.26%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-tosylpentanimidamide 5g.** Yield 0.24 g (65%); cream powder, m.p. = 102-105 °C. IR (KBr): 3354 (NH), 3044 (NH), 1444 (C=N), 1306 (SO₂), 1180 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 1.02 (3H, t, ³ J_{HH} = 6.9 Hz, Me), 1.49-1.63 (2H, m, CH₂), 1.78-1.92 (2H, m, CH₂), 2.50 (3H, s, Me), 3.05 (2H, t, ³ J_{HH} = 6.9 Hz, CH₂), 7.41 (2H, d, ³ J_{HH} = 7.9 Hz, Ar), 7.59 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 7.66 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 7.93 (2H, d, ³ J_{HH} = 7.9 Hz, Ar), 8.04 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 8.30 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 8.62 (1H, s, NH), 9.64 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 14.5 (Me), 21.5 (CH₂), 22.4 (CH₂), 23.0 (Me), 24.8 (CH₂), 123.8 (CH), 128.1 (2 CH), 128.4 (CH), 128.6 (CH), 128.7 (CH), 130.1 (2 CH), 141.8 (C), 142.9 (C), 144.7 (C), 147.8 (C), 148.0 (C), 159.1 (C). MS (EI, 70 eV):

m/z (%) = 370 (M^+ , 4), 253 (9), 229 (18), 155 (100), 91 (36), 77 (38), 57 (32). Anal. calcd. for $C_{19}H_{22}N_4O_2S$ (370.15): C, 61.60; H, 5.99; N, 15.12%. Found: C, 62.09; H, 6.04; N, 15.26%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(phenylsulfonyl)pentanimidamide 5h.** Yield 0.22 g, (62%); cream powder, m.p. = 98-100 °C. IR (KBr): 3333 (NH), 3098 (NH), 1404 (C=N), 1387 (SO₂), 1144 cm⁻¹ (SO₂). ¹H NMR (400 MHz, CDCl₃): δ_H = 0.98 (3H, t, ³ J_{HH} = 6.9 Hz, Me), 1.51-1.57 (2H, m, CH₂), 2.14-2.23 (2H, m, CH₂), 2.52 (2H, t, ³ J_{HH} = 6.9 Hz, CH₂), 7.64 (2H, t, ³ J_{HH} = 7.9 Hz, Ar), 7.70-7.75 (2H, m, Ph), 7.96 (1H, t, ³ J_{HH} = 7.5 Hz, Ar), 8.01 (2H, d, ³ J_{HH} = 7.9 Hz, Ar), 8.08 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 8.37 (1H, d, ³ J_{HH} = 7.5 Hz, Ar), 9.31 (1H, s, NH), 9.87 (1H, s, NH). ¹³C NMR (100.6 MHz, CDCl₃): δ_C = 14.5 (Me), 21.5 (CH₂), 23.0 (CH₂), 26.2 (CH₂), 121.7 (2 CH), 124.1 (2 CH), 127.1 (CH), 128.0 (CH), 130.4 (CH), 131.6 (CH), 138.7 (CH), 131.6 (C), 132.9 (C), 136.5 (C), 145.6 (C), 160.1 (C). MS (EI, 70 eV): m/z (%) = 356 (M^+ , 10), 299 (15), 224 (28), 132 (44), 141 (100), 125 (23), 77 (25), 76 (30). Anal. calcd. for $C_{18}H_{20}N_4O_2S$ (356.13): C, 60.65; H, 5.66; N, 15.72%. Found: C, 61.02; H, 5.70; N, 15.81%.

***N*-(1*H*-benzo[d]imidazol-2-yl)-2-phenyl-*N'*-tosylacetamidine (5a):**

***N*-(1*H*-benzo[d]imidazol-2-yl)-2-phenyl-*N'*-(phenylsulfonyl)acetimidamide (5b):**

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N*'-(methylsulfonyl)-2-phenylacetimidamide (5c):**

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-tosylhexanamide (5d):**

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(phenylsulfonyl)hexanimidamide (**5e**):**

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(methylsulfonyl)hexanimidamide (5f):**

N-(1*H*-benzo[d]imidazol-2-yl)-*N'*-tosylpentanimidamide (5g):

***N*-(1*H*-benzo[d]imidazol-2-yl)-*N'*-(phenylsulfonyl)pentanimidamide (5h):**

BRUKER

Current Data Parameters
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PROCNO 1

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BRUKER

Current Data Parameters
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d12 0.00002000 sec

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SFO1 100.6204965 MHz

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PL2 -4.00 dB
PL12 18.50 dB
PL13 18.50 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
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GB 0
PC 1.40