SUPPORTING INFORMATION

Synthesis of Stable Seleno[3,4-*b*]quinoxaline Derivatives

Emad Aqad, M. V. Lakshmikantham, Michael P. Cava*

Department of Chemistry, University of Alabama, Tuscaloosa,

Box 870336, Alabama 35487-0336.

Email Address mcava@bama.ua.edu

Experimental Section

Bis(cyanomethyl) selenide (5): Chloroacetonitrile (3.82 g, 3.22 mL, 50.59 mmol) was added at room temperature during 30 min. to a colorless solution of sodium selenide prepared from selenium (2 g, 25.33 mmol) and sodium borohydride (2 g, 52.90 mmol) in 40 mL of water under nitrogen atmosphere. The mixture was stirred for additional 1h. The aqueous solution was exteracted with CH_2Cl_2 (2x25 mL) and the combined organic layer was dried over sodium sulfate. Evaporation of the solvent and recrystallization from methanol gave 3.17 g (79%) of the selenide as colorless crystals: mp 42^0C. ^{1}H NMR ($CDCl_3$) δ = 3.52 (s, 4H). ^{13}C NMR ($CDCl_3$) δ = 17.15, 114.9. MS m/e (relative intensity): 160 M, (100), 133 (40), 80 (80). Anal. Calcd. for $C_4H_4N_2Se$: C, 30.21; H, 2.53; N, 17.61. Found: 30.32; H, 2.55; N, 17.68.

2,5-Dicyano-3,4-dihydroxyselenophene (7): To a stirred solution of sodium ethoxide, prepared from Na (0.90 g) and absolute ethanol (60 ml), under nitrogen atmosphere was added simultaneously diethyl oxalate (2.75 g, 2.57 mL, 18.87 mmol) and bis(cyanomethyl) selenide (3.00 g, 18.87 mmol) during 1 hour. The mixture was stirred for additional 15 hour at room temperature. The resulting precipitate of the disodium salt of 2,5-dicyano-3,4-

dihydroxyselenophene was filtered off and washed with ether. The salt was highly hygroscopic and was added immediately to aqueous solution of 35% sulfuric acid (15 mL) at 0^0C. The resulting precipitate of the product was filtered, washed with cold water and dried. Recrystallization from acetonitrile gave **7,** 1.58 g (39% based on the selenide **5**), as pale yellow microcrystals: mp 196-197^0C (dec.). ^{1}H NMR (DMSO-d_6) δ = 5.01 (s, 2OH). ^{13}C NMR (DMSO-d_6) δ = 87.23, 114.37, 154.95. MS m/e (relative intensity): 214 (M, 100), 195 (63), 187 (56). Anal. Calcd. for $C_6H_2N_2O_2Se$: C, 33.82; H, 0.95; N, 13.15. Found: C, 33.98, H, 1.01, N, 13.21.

1,3-Dicyano-4,9-dihydroseleno[3,4-*b*]quinoxaline (8): 2,5-Dicyano-3,4-dihydroxyselenophene (**7**) (0.50 g, 2.35 mmol) and *o*-phenylenediamine were suspended in AcOH (10 mL) and refluxed for 30 min. The reaction mixture was cooled to room temperature. The precipitate was collected and washed with cold ethanol. After drying (air), pure product (0.54, 80%) was obtained. An analytical sample was prepared by recrystallization from AcOH: mp > 300 ^{0}C. ^{1}H NMR (DMSO-d_6) δ = 6.65 (dd, *J* = 6.3, 2.5 Hz , 2H), 6.72 (dd, *J* = 6.3, 2.5 Hz), 9.99 (s, 2H). ^{13}C NMR (DMSO-d_6) δ = 113.92, 115.05, 122.32, 125.0,128.09, 142.96. MS m/e (relative intensity): 286 (M, 23), 285 (M-H, 15), 283 (M – 2H, 74), 279 (13), 160 (14). 158 (100). Anal. Calcd. for $C_{12}H_6N_4Se$: C, 50.54; H, 2.12; N, 19.65. Found: C, 50.48; H, 2.09; N, 19.73.

1,3-Dicyanoseleno[3,4-*b*]quinoxaline (4): Iodobenzene diacetate (0.22 g, 0.70 mmol) was added to a stirred solution of 1,3-dicyano-4,9-dihydroseleno[3,4-b]quinoxaline (**8**) (0.2 0 g. 0.70 mmol) in dichloromethane (25 mL). The mixture was stirred for 3h. The volume was reduced to about 5 ml and passed through short column (SiO_2/CH_2Cl_2). The orange fraction was collected and evaporated to give orange-red crystals (0.12 g, 60%): mp > 300^0C. ^{1}H NMR (DMSO-d_6) δ = 7.85 (dd, *J* = 7.2, 3.1 Hz, 2H), 8.08 (dd, *J* = 7.1, 3.1 Hz). ^{13}C NMR (DMSO-d_6) δ = 117.8, 124.6, 132.8, 136.7, 144.6, 145.6. MS m/e (relative intensity): 284 (M, 100), 267 (54), 268 (74), 160 (64), 156 (51). Anal. Calcd. for $C_{12}H_4N_4Se$: C, 50.90; H, 1.42; N, 19.79. Found: C, 50.80; H, 1.38; N, 19.83.

Dihydroseleno[3,4-*b*]quinoxaline (10): To a colorless solution of sodium selenide prepared from selenium (0.50 g, 6.33 mmol) and sodium borohydride (0.5 g, 12.26 mmol) in 20 ml water at room temperature, was added dropwise, a solution of 2,3-bis(bromomethyl)-quinoxaline[1] (2.0 g, 6.33 mmol) in THF (80 mL). The reaction mixture was stirred for 5h. The mixture was poured into water (100 mL). Extraction with methylene chloride (3x30 mL) and subsequent recrystallization of the residue from ethanol gave **10** (0.81 g, 55%) as colorless microcrystals: mp 148-149 ^{0}C. ^{1}H NMR ($CDCl_3$) δ = 4.37 (s, 2H) 7.36 (dd, *J* = 8.1 Hz , 2H), 8.02 (dd, *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$) δ = 26.0, 128.9, 130.0, 140.2, 156.7. MS m/e (relative intensity): .236 (M, 100), 234 (55), 233 (59), 155 (34), 154 (35), 141 (21). Anal. Calcd. for: $C_{10}H_8N_2Se$ C, 51.08; H, 3.43; N, 11.91. Found: C, 51.14; H, 3.49; N, 11.97

1,3-Diethoxycarbonylseleno[3,4-*b*]quinoxaline (11): To a stirred solution of dihydroseleno[3,4-b]quinoxaline (**10**) (0.50 g, 2.12 mmol) in dry THF (25 mL) under N_2 was added iodobenzene diacetete (0.69 g, 2.14 mmol) at 0^{0}C. The mixture was stirred at the same temperature for 2h. It was then cooled to -78 ^{0}C followed by addition of 1.70 mL of 2.5M BuLi in hexane. The reaction mixture was maintained at the same temperature for another 30 min and ethyl chloroformate (0.0.46 g, 4.4 mmol) was added and the mixture was stirred overnight at room temperature. The reaction mixture was poured over crushed ice. The crude product was extracted into CH_2Cl_2 (3x15 mL). The organic phase was dried and concentrated. The oily residue was subject to column chromatography (SiO_2), using hexane:methylene chloride 1:1. Evaporation of the eluant and recrystallization of the residue from ethanol gave **10** as yellow microcrystals. Yield: 0.22 g (28% based on **10**): mp 135-136 ^{0}C. ^{1}H NMR ($CDCl_3$) δ: 8.02 (dd, *J* = 7.1 3.1 Hz, 2H), 7.30 (dd, *J* = 7.1 3.1 Hz, 2H), 4.45 (q, *J* = 7.2 Hz, 4H), 1.34 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 166.8, 151.1, 138.0, 127.1, 123.15, 61.7, 14.61. MS m/e (relative intensity): 378 (M, 100), 333 (38), 288 (46), 260 (70). 218 (37). Anal. Calcd. for $C_{16}H_{14}N_2O_4Se$: C, 50.94; H, 3.74; N, 7.43. Found: C, 50.88; H, 3.67; N, 7.39.

---

[1] Pohmer, J.; Lakshmikantham M. V.; Cava, M. P. *J. Org. Chem.* **1995**, 60. 8283.

1,3-Diformyl-4,9-dihydroseleno[3,4-*b*]quinoxaline (12): Vilsmeier reagent was prepared from 0.25 mL of DMF and 0.30 ml of $POCl_3$ in dry CH_2Cl_2 (20 mL) was added to solution of dihydroseleno[3,4-b]quinoxaline (**10**) (0.25g, 1.06 mmol). The mixture was stirred at room temperature for 5h and was poured into $NaHCO_3$ solution. The sticky precipitate was extracted into CH_2Cl_2 (2x20 mL). The residue from the extract was chromatographed on silica-gel (eluent CH_2Cl_2) to give diformyl derivative **12** (0.13g, 46%). mp > 300^0C. ^{1}H NMR (DMSO-d_6) δ: 6.45 (dd, *J* = 6.8, 3.1 Hz), 6.78 (dd, *J* = 6.8, 3.1), 9.41 (s, 2H). ^{13}C NMR ($CDCl_3$) δ: 113.1, 114.0, 122.5, 128.6, 139.9, 140.8, 182.4MS m/e (relative intensity): 292 (M, 100), 217 (38), 243 (42). Anal. Calcd. for $C_{12}H_8N_2O_2Se$: C, 49.50; H, 2.77; N, 9.62. Found: C, 49.55; H, 2.69; N, 9.57.

1,3-Diformylseleno[3,4-*b*]quinoxaline (13): Iodobenzene diacetate (0.22 g, 0.68 mmol) was added to a stirred solution of 1,3-diformyl-4,9-dihydroseleno[3,4-b]quinoxaline (**12**) (0.20 g. 0.68 mmol) in dichloromethane (10 mL). The mixture was stirred for 3h. The volume was reduced to about 5 mL and passed through short column (SiO_2/CH_2Cl_2). The orange fraction was collected and evaporated to give orange-red crystals (0.11 g, 56%): mp > 300^0C. ^{1}H NMR (DMSO-d_6) δ: 7.86 (dd, *J* = 7.56, 3.2 Hz), 8.25 (dd, *J* = 7.6, 3.2). ^{13}C NMR (DMSO-d_6) δ: 129.9, 132.7, 137.0, 1146.0, 146.3, 184.5MS m/e (relative intensity): 290 (M, 100), 262 (33), 186 (42), 207 (36), 191 (28), 136 (39). Anal. Calcd. for $C_{12}H_6N_2O_2Se$: C, 49.85; H, 2.09; N, 9.69. Found: C, 49.76; H, 2.03; N, 9.64.

1,3-Bis(2-thienylmethylene)-1,3-dihydrothieno[3,4-*b*]quinoxaline (14): dihydroseleno[3,4-b]quinoxaline (**10**) (0.50 g, 2.12 mmol), 2-thiophenecarboxaldehyde (0.47 g, 4.25 mmol), and potassium *tert*-butoxide (0.52 g, 4.64 mmol) were added to dry diethyl ether and stirred overnight. The solution was neutralized byaddition of 10% HCl solution. The solvent was evaporated, and the residue was purified by column chromatography (SiO_2, CH_2Cl_2:hexane 4:1), followed by recrystallization (toluene), to give dark red crystals (0.64g, 71%): mp > 300^0C. ^{1}H NMR ($CDCl_3$) δ: 7.21 (dd. *J* = 4.9, 3.9 Hz, 2H), 7.46 (d, *J* = 3.6 Hz, 2H), 7.55 (d, *J* = 5.0 Hz, 2H), 7.74 (dd, *J* = 6.6, 3.2 Hz, 2H), 8.1 (dd, *J* = 6.5, 3.3, 2H), 8.7 (s, 2H). ^{13}C NMR (DMSO-d_6) δ: 120.5, 127.6, 128.2, 128.4, 129.4, 130.1, 130.3, 141.2, 142.1, 152.0. MS m/e (relative intensity): 424 (M, 100), 423 (89), 422 (55), 343 (19), 211 (10), 108 (11). Anal.

Calcd. For $C_{20}H_{12}N_2S_2Se$: C, 56.73; H, 2.86; N, 6.62; S, 15.15. Found: C, 56.78; H, 2.86; N, 6.62; S, 14.96.