First Synthesis of β -Keto Sulfoxides by a Palladium-Catalyzed Carbonylative Suzuki Reaction

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Supporting Information

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General methods. Proton magnetic resonance and carbon magnetic resonance were recorded at 300 MHz and 75 Hz respectively with a Bruker AC-300. Chemical shifts are reported in δ ppm relative to the CHCl_3 peak at 7.20 ppm (^1H) or 77.0 ppm (^{13}C). High Resolution Mass Spectra were determined on a Fisons VG Autospec instrument. All melting points are uncorrected and were recorded on a Cambridge Instruments apparatus. Reactions were monitored by analytical thin layer chromatography using commercial aluminium sheets pre-coated (0.2mm layer thickness) with silica gel 60 F₂₅₄ (E.Merck). Product purification by flash chromatography was performed using E. Merck Silica Gel (230-400 mesh).

Preparation of starting materials.

Synthesis of bromomethyl phenyl sulfoxide 1.¹ To a solution of methyl phenyl sulfoxide (10 mmol) and anhydrous pyridine (22 mmol) in dry acetonitrile (40 mL) cooled at -40°C under an argon atmosphere was added dropwise a solution of bromine (20 mmol) in dry acetonitrile (20 mL) at -20°C. The mixture was stirred first at -40°C for 1h and then overnight at room temperature. The solvent was evacuated in vacuum and the residue was redissolved in dichloromethane. The organic layer was washed with Na₂S₂O₃ (0.02N, 30 mL), dried over anhydrous Na₂SO₄ and concentrated to dryness. The crude material was purified by flash column chromatography (hexane:ethyl acetate 5:1) to yield sulfoxide **1** (80%). ¹H-NMR (300 MHz, CDCl₃): δ 4.26-4.36 (AB, J= 12.3 Hz, 2H) 7.69-7.47 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃): δ 49.5 (t), 125.5 (d), 129.7 (d), 132.5 (d), 141.9 (s); HRMS (E.I.) m/z (M⁺) calcd. for C₇H₇BrOS 217.9401, obsd 217.9363.

Palladium catalyzed three component Suzuki-Miyaura reaction with bromomethyl phenyl sulfoxide. General Procedure.

A mixture of α-bromo sulfoxide **1** (0.4 mmol), boronic acid **2** (0.8 mmol) CsF (1.6 mmol) and Pd(PPh₃)₄ (0.04 mmol) was added to a flask fitted with a reflux condenser and a septum inlet. The flask was fluxed with carbon monoxide and then charged with THF (6 mL). The mixture was stirred at 60°C under an atmospheric pressure of carbon monoxide. After the appropriate time, the mixture was cooled at room temperature, quenched with water (10 mL) and extracted with diethyl ether (2 x 15mL) and with dichloromethane (3 x 15 mL). The combined organic extracts were dried with Na₂SO₄ and evaporated under reduced pressure.

¹ Cinquini, M.; Colonna, S. *J.Chem. Soc. Perkin I* **1972**, 1883.

1-phenyl-2-(phenylsulfinyl)ethanone **3a**.²

Yield: 80%; m.p.: 68-72 °C; ¹H-NMR δ 4.29 (d, J= 14.1 Hz, 1H), 4.45 (d, J= 14.1 Hz, 1H), 7.41-7.88 (m, 10H); ¹³C-NMR δ 66.0 (t), 124.2 (d), 128.7 (d+d), 129.3 (d), 131.5 (d), 134.1 (d), 135.9 (s), 143.2 (s), 191.3 (s); HRMS (E.I.) m/z (M⁺) calcd. for C₁₄H₁₂O₂S 244.0558, obsd. 244.0569.

1-(4-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3b**.³

Yield: 95%; m.p.: 89-91°C; ¹H-NMR δ 3.78 (s, 3H), 4.16 (d, J= 14 Hz, 1H), 4.44 (d, J= 14 Hz, 1H), 6.83 (d, J= 9 Hz, 1H), 7.30-7.40 (m, 3H), 7.50-7.60 (m, 2H), 7.80 (d, J=9Hz, 1H); ¹³C-NMR δ 55.5 (q), 65.8 (t), 113.9 (d), 124.1(d), 129.1 (s), 129.2 (d), 131.2 (d), 131.4 (d), 143.3 (s), 164.0(s), 190.4(s); HRMS (E.I.) m/z (M⁺) calcd. for C₁₅H₁₄O₃S 274.0663, obsd.274.0644.

1-(3-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3c**.⁴

Yield: 88%; m.p.: 67-70 °C; ¹H-NMR δ 3.83 (s, 3H), 4.27 (d, J= 15 Hz, 1H), 4.55 (d, J= 14.2 Hz, 1H), 7.05-7.39 (m, 4H), 7.40-7.50(m, 3H), 7.60-7.70 (m, 2H); ¹³C-NMR δ 55.5 (q), 66.2 (t), 112.5 (d), 120.9 (d), 121.6 (d), 124.3 (d), 129.3 (d), 129.8 (d), 131.6 (d), 137.3 (s), 143.3 (s), 160.1 (s), 191.1 (s); HRMS (E.I.) m/z (M⁺) calcd. for C₁₅H₁₄O₃S 274.0663, obsd. 274.0669.

² Batigalia, F.; Zaldini-Hernandes, M.; Ferreira, A. G.; Malvestiti, Ivani; C. *Tetrahedron* **2001**, 57, 9669.

³ Olivato, P. R.; Guerrero, S. A.; Zukerman-Schpector, J. *Acta Cryst. Sect. B* **2000**, B56(1), 112

⁴ Satoh, T.; Fujii, T.; Yamakawa, K *Bull. Chem. Soc Jpn* **1990**, 63, 1266.

1-(2-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3d**.

Yield: 85%; m.p.: 80-83 °C; $^1\text{H-NMR}$ δ 3.90 (s, 3H), 4.44 (d, J = 14.7 Hz, 1H), 4.75 (d, J = 14.7 Hz, 1H), 6.90-7.05 (m, 2H), 7.47-7.54 (m, 4H), 7.68-7.74 (m, 3H); $^{13}\text{C-NMR}$ δ 55.6 (q), 71.2 (t), 111.6 (d), 121.0 (d), 124.6 (d), 126.0 (s), 129.1 (d), 131.0 (d), 131.2 (d), 135.2 (d), 144.0 (s), 159.1 (s), 192.0 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{15}\text{H}_{14}\text{O}_3\text{S}$ 274.0663, obsd. 274.0667.

1-(2-methylphenyl)-2-(phenylsulfinyl)ethanone **3e**.

Yield: 88%; oil; $^1\text{H-NMR}$ δ 2.47 (s, 3H), 4.27 (d, J = 14.5 Hz, 1H), 4.56 (d, J = 14.5 Hz, 1H), 7.23-7.28 (m, 2H), 7.41 (t, J = 7.8 Hz, 1H), 7.50-7.52 (m, 3H), 7.64 (d, J = 7.8 Hz, 1H), 7.69-7.72 (m, 2H); $^{13}\text{C-NMR}$ δ 21.5 (q), 68.2 (t), 124.2 (d), 125.8 (d), 129.3 (d), 129.9 (d), 131.5 (d), 132.2 (d), 132.6 (d), 135.5 (s), 139.7 (s), 143.2 (s), 193.9 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{15}\text{H}_{14}\text{O}_2\text{S}$ 258.0715, obsd. 258.0719.

1-(4-bromophenyl)-2-(phenylsulfinyl)ethanone **3f**.⁵

Yield: 54%; m.p.: 90-94°C; $^1\text{H-NMR}$ δ 4.26 (d, J = 14.1 Hz, 1H), 4.50 (d, J = 15 Hz, 1H), 7.50-7.75 (m, 9H); $^{13}\text{C-NMR}$ δ 65.6 (t), 124.2 (d), 129.4 (d), 129.7 (d), 130.3 (d), 131.7 (d), 132.1 (s), 134.8 (s), 142.9 (s), 190.4 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{14}\text{H}_{11}\text{BrO}_2\text{S}$ 321.9663, obsd. 321.9655

⁵ Issa, Y. M.; Etaiw, S. H.; El Ansary, A. L. *Indian J. Chem., Sect. A*: **1979**, 18A, 480.

1-(2-bromophenyl)-2-(phenylsulfinyl)ethanone **3g**.

Yield: 45%; oil; $^1\text{H-NMR}$ δ 4.40 (d, J = 14.4 Hz, 1H), 4.57 (d, J = 14.4 Hz, 1H), 7.31-7.71 (m, 9H); $^{13}\text{C-NMR}$ δ 68.6 (t), 119.4 (s), 124.3 (d), 127.7 (d), 129.4 (d), 130.0 (d), 131.6 (d), 132.8 (d), 133.7 (d), 139.5 (s), 143.0 (s), 194.31 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{14}\text{H}_{11}\text{BrO}_2\text{S}$ 321.9663, obsd. 321.9657.

2-(phenylsulfinyl)-1-(4-(trifluoromethyl)phenyl)ethanone **3h**.

Yield: 77%; m.p.: 128-131°C; $^1\text{H-NMR}$ δ 4.33 (d, J = 13.9 Hz, 1H), 4.52 (d, J = 13.9 Hz, 1H), 7.43-7.44 (m, 3H), 7.59-7.61 (m, 2H), 7.65 (d, J = 8.1 Hz, 1H); 7.93 (d, J = 8.1 Hz, 1H); $^{13}\text{C-NMR}$ δ 65.6 (t), 123.3 (q, J = 271.8 Hz), 124.1 (d), 125.8 (d), 129.2 (d), 129.4 (d), 131.8 (d), 135.2 (q, J = 32.9 Hz), 138.7 (s), 142.8 (s), 190.6 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{15}\text{H}_{11}\text{O}_2\text{F}_3\text{S}$ 312.0431, obsd. 312.0434.

2-(phenylsulfinyl)-1-(2-(trifluoromethyl)phenyl)ethanone **3i**.

Yield: 33%; m.p.: 70-74 °C; $^1\text{H-NMR}$ δ , 4.19 (d, J = 14.7 Hz, 1H), 4.41 (d, J = 14.7 Hz, 1H), 7.52-7.73 (m, 9H); $^{13}\text{C-NMR}$ δ 69.2 (t), 123.3 (q, J = 272 Hz), 124.2 (d), 125.1 (d), 127.8 (d), 129.5 (d), 131.1 (d), 131.7 (d), 132.1 (d), 138.1 (s), 142.9 (s), 194.6 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{15}\text{H}_{11}\text{O}_2\text{F}_3\text{S}$ 312.04318, obsd. 312.0437.

1-(3-nitrophenyl)-2-(phenylsulfinyl)ethanone **3k**.

Yield: 55%; m.p.: 118-120°C; $^1\text{H-NMR}$ δ 4.38 (d, J = 13.8 Hz, 1H), 4.50 (d, J = 13.8 Hz, 1H), 7.49-7.51 (m, 3H), 7.64-7.69 (m, 3H), 8.23 (d, J =7.8 Hz, 1H) 8.41 (dd, J = 7.8 and 1.2 Hz, 1H), 8.63(d, J =1.2 Hz,1H), $^{13}\text{C-NMR}$ δ 65.0 (t), 123.6 (d), 124.0 (d), 128.1 (d), 129.5(d), 130.1 (d), 131.8 (d), 134.3 (d), 137.4 (s), 142.4 (s), 148.3 (s), 189.4 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{14}\text{H}_{11}\text{NO}_4\text{S}$ 289.0408, obsd. 289.0410.

2-(phenylsulfinyl)-1-(3-thienyl)ethanone **3l**.

Yield: 99%; m.p.: 90-94°C; $^1\text{H-NMR}$ δ 4.10 (d, J = 13.5 Hz, 1H), 4.34 (d, J = 13.5 Hz, 1H), 7.23 (dd, J =5.1 and 2.8 Hz, 1H), 7.40-7.44 (m, 4H), 7.58-7.61 (m, 2H), 8.00 (dd, 2.8 and 0.9 Hz, 1H); $^{13}\text{C-NMR}$ δ 66.8 (t), 124.1 (d), 126.8 (d), 126.9 (d), 129.3 (d), 131.5 (d), 134.8(d), 141.5 (s), 143.0 (s), 184.9 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_2\text{S}_2$ 250.0122, obsd. 250.0110.

2-(phenylsulfinyl)-1-(2-thienyl)ethanone **3m**.⁶

Yield: 72%; oil; $^1\text{H-NMR}$ δ 4.18 (d, J = 13.3 Hz, 1H), 4.43 (d, J = 13.3 Hz, 1H), 7.11 (dd J = 4.7 and 4 Hz, 1H), 7.48-7.51 (3H), 7.67-7.71 (m, 4H); $^{13}\text{C-NMR}$ δ , 66.3 (t), 124.2 (d), 128.5 (d), 129.3 (d), 131.7 (d), 134.4 (d), 135.9 (d), 143.0 (s), 143.6 (s), 183.3 (s); HRMS (E.I.) m/z (M^+) calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_2\text{S}_2$ 250.0122, obsd.250.0110.

⁶ Kunick, C.; Messinger, P. *Chem. Ber.* **1986**, 119, 1429.

(4-bromobenzyl)phenyl sulfoxide **4f**⁷

Yield: 9%; m.p.: 155-159 °C ¹H-NMR (CDCl₃): δ 3.92-4.02 (AB, 2H, J= 12.7 Hz), 6.82 (d, J= 8.4 Hz, 2H), 7.35-7.47 (m, 7H); ¹³C-NMR (CDCl₃): δ 62.4 (t), 122.6 (s), 124.3 (d), 127.9 (s), 129.0 (d), 131.3 (d), 131.5 (d), 131.9 (d), 142.3 (s); HRMS: calcd for C₁₃H₁₁BrOS 293.9714 found 293.9714.

(4-trifluoromethylbenzyl)phenyl sulfoxide **4h**⁸

Yield: 23%; m.p.: 141 °C (subl.); ¹H-NMR (CDCl₃): δ 3.99-4.13 (AB, 2H, J= 12.7 Hz), 7.08 (d, J= 8.1 Hz, 2H), 7.35-7.51 (m, 7H); ¹³C-NMR (CDCl₃): δ 62.5 (t), 123.9 (q, J= 272.1), 124.2 (d), 125.2 (q, J= 3.7 Hz), 129.0 (d), 130.5 (q, J= 26.7), 130.6 (d), 131.4 (d), 133.0 (d), 142.2 (s); HRMS: calcd for C₁₄H₁₁F₃OS 284.0483 found 284.0479.

⁷ Rodríguez, N.; Cuenca, A.; Ramírez de Arellano, C.; Medio-Simón, M.; Peine, D.; Asensio, G. *J. Org. Chem.* **2004**, 69, 8070.

⁸ Kersten, M.; Wenschuh, E. *Phosphorus, Sulfur and Silicon and the Related Elements* **1993**, 80(1-4), 81.

Bromomethyl phenyl sulfoxide **1**

1-phenyl-2-(phenylsulfinyl)ethanone **3a**.

1-(4-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3b**.

1-(3-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3c**

1-(2-methoxyphenyl)-2-(phenylsulfinyl)ethanone **3d**.

1-(2-methylphenyl)-2-(phenylsulfinyl)ethanone **3e**.

1-(4-bromophenyl)-2-(phenylsulfinyl)ethanone **3f**.

1-(2-bromophenyl)-2-(phenylsulfinyl)ethanone **3g**.

2-(phenylsulfinyl)-1-(4-(trifluoromethyl)phenyl)ethanone **3h**

2-(phenylsulfinyl)-1-(2-(trifluoromethyl)phenyl)ethanone **3i**

1-(3-nitrophenyl)-2-(phenylsulfinyl)ethanone **3k**

2-(phenylsulfinyl)-1-(3-thienyl)ethanone **3l**.

2-(phenylsulfinyl)-1-(2-thienyl)ethanone **3m**.

(4-bromobenzyl)phenyl sulfoxide **4f**

(4-trifluoromethylbenzyl)phenyl sulfoxide **4h**