

Dendro-shaped blocks with arylsulfanyl fragments based on *p*-toluic acid

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Experimental

Melting points of compounds **3**, **4d-f** were determined on a Boetius Kofler's hot stage. Melting points of compounds **1**, **4a-c** were determined on a Mettler Toledo FP 900 Thermosystem instrument. The IR spectra are recorded on a Vector 22 instrument in KBr. Molecular masses and elemental composition were determined by mass spectrometry on a Thermo Electron Corporation DFS device (nominal ionization energy 70 eV). For chromatographic mass spectrometry (GC-MS), an HP 5890 chromatograph with a mass-selective detector HP 5971 was used. The energy of ionizing electrons is 70 eV. The separation of the substances was carried out with a HP-5 column of 30 m × 0.25 mm × 0.25 μm, carrier gas - helium, flow rate 1 ml min⁻¹. The thermostate temperature was 50-280 °C, the temperature of the ion source was 173 °C. NMR spectra were measured with Bruker AV-400 (¹H, 400 MHz), DRX-500 (¹H, 500 MHz, ¹³C, 125 MHz), Bruker AV-300 (¹³C, 75 MHz, ¹⁹F, 282 MHz) spectrometers in CDCl₃ and DMSO-d₆, the signals of deuterated solvents were used as references.

The course of the reactions and the purity of the products were carried out by GC-MS data and ¹H NMR spectroscopy.

3,5-Bis(chloromethyl)-4-methylbenzoic acid 1.

Method A. Sulfuric acid (93%, 4.0 ml) was added dropwise to a mixture of *p*-toluic acid (1.20 g, 8.8 mmol) and bis(chloromethyl) ether (2.8 ml, 32.6 mmol) with stirring and cooling in an ice bath, maintaining the temperature in the range of 12-15 °C. The mixture was stirred at this temperature for more 4 hours (until a homogeneous mass was formed), then it was brought to room temperature and kept for 24 hours. The mixture was poured into ice water, the precipitate was filtered off, washed with water to pH 7, and dried in air at 60 °C until constant weight. Yield of the material thus obtained: 1.62 g. The product was analyzed by GC-MS and ¹H NMR spectroscopy (solution in DMSO-d₆).

Method B. *p*-Toluic acid (5.0 g, 36.8 mmol) and bis(chloromethyl) ether (12 ml, 0.14 mol) were mixed. Then, 100% H₂SO₄ (15 ml) was added dropwise with stirring and cooling in an ice bath maintaining the temperature in the range of 12-15 °C. The mixture was stirred at this temperature until a homogeneous solution was formed (~4 h), then it was brought to room temperature and kept for 24 h. The mixture was poured into ice water, the precipitate formed was filtered off, washed with water to pH 5-6 and dried in air at 105-115 °C to constant weight. Yield of the material thus obtained: 7.43 g. The product was analyzed by ¹H NMR spectroscopy (solution in DMSO-d₆).

Method C. Similarly, from *p*-toluic acid (10.2 g, 75 mmol), bis(chloromethyl) ether (25 ml, 0.29 mol) and 100% H₂SO₄ (30 ml) at 30 °C, followed by keeping for 2 days and after the similar workup, product (16.37 g) was obtained with m.p. 170 - 175 °C. The yield of crude acid **1** was 94%. The crude acid **1** (2.42 g) was treated with stirring 3 times with water (100 ml) until a neutral pH aqueous extraction was reached, then it was filtered and dried at 105-115 °C. After vacuum (0.05-0.07 Torr) sublimation at 145 to 160 °C, purified acid **1** (2.14 g, 82%) was obtained, m.p. 200 - 202 °C.

Method D. Oleum (30%, 5.5 ml) was added dropwise to a mixture of *p*-toluic acid (1.88 g, 13.8 mmol) and bis(chloromethyl) ether (4.5 ml, 52.4 mmol) with stirring and cooling in an ice bath, maintaining the temperature in the range 12-15 °C. The mixture was stirred at this temperature for more 4 h, then the temperature was brought to ~20°C, and the mixture was kept for 24 hours. The mixture was poured into ice water, the precipitate formed was filtered off, washed with water to pH = 7 and dried in air at 60 °C until constant weight. The resulting substance (3.05 g), according to was a mixture of acid **1** and its chloromethyl ester **3** in a 3:1 ratio (¹H NMR, DMSO-d₆). The mixture was separated by recrystallization from hexane. The precipitate was filtered off yielding 2.00 g (62%) of pure 3,5-bis(chloromethyl)-4-methylbenzoic acid **1**. The second product, chloromethyl 3,5-bis(chloromethyl)-4-methylbenzoate **3** (0.77 g, 20%) was

isolated from the filtrate after evaporation and chromatography on silica gel (eluent: hexane – benzene, 1:1).

3,5-Bis(chloromethyl)-4-methylbenzoic acid 1. The yield is 82%. M.p. 200-202.5 °C (C₆H₆) (lit. m.p. 192-193 °C, M. M. Dashevskii et.al, *J. Appl. Chem. USSR*, 1972, **45**, 1087). IR spectrum, ν , cm⁻¹: 2982, 2711, 2617, 1684, 1610, 1427, 1315, 1267, 1241, 925, 746, 674, 604, 571. ¹H NMR (400 MHz, CDCl₃), δ : 2.54 (s, 3H, CH₃), 4.66 (s, 4H, CH₂), 8.05 (s, 2H, H^{2,6}), 8.07 (br. s, 1H, COOH). ¹³C NMR (100 MHz, DMSO-d₆) δ : 14.5, 44.8, 128.8, 131.5, 137.4, 142.4, 166.8. MS (EI), m/z : 232.0050 [M]⁺. (Calc. for: C₁₀H₁₀Cl₂O₂, m/z : 232.0052).

Chloromethyl 3,5-bis(chloromethyl)-4-methylbenzoate 3. The yield is 20%. M.p. 104-106 °C (hexane). IR spectrum, ν , cm⁻¹: 3066, 3050, 2987, 2926, 2854, 1736, 1608, 1437, 1340, 1309, 1263, 1221, 1182, 1149, 1103, 1018, 773, 742, 729, 709, 663, 598. ¹H NMR (400 MHz, CDCl₃) δ : 2.53 (s, 3H, CH₃), 4.65 (s, 4H, CH₂), 5.94 (s, 2H, OCH₂), 8.01 (s, 2H, H^{2,6}). MS (EI), m/z : 279.9820 [M]⁺. (Calc. for: C₁₁H₁₁Cl₃O₂, m/z : 279.9819).

Hydrolysis of ester 3. Ester **3** (0.28 g, 1 mmol) and 93% H₂SO₄ (8 ml) were mixed with cooling, and the suspension was stirred at 12-15 °C for 4 h, then brought to room temperature and stirring continued for the more two days. Then ice was added, the precipitate was filtered off, washed with water to pH ~7, and dried in air at 60 °C until constant weight. The yield of acid **1** was 0.20 g (87%).

3,5-Bis(4-tert-butylphenylsulfanylmethyl)-4-methylbenzoic acid 4b. Yield is 94% (*procedure A*), 95% (*procedure C*). M.p. 222 °C (decomp.) (C₆H₆). IR spectrum, ν , cm⁻¹: 3420, 3076, 2964, 2931, 2904, 2868, 2704, 2596, 2536, 1682, 1605, 1487, 1419, 1304, 1244, 1119, 1014, 946, 827, 758, 555. ¹H NMR (400 MHz, DMSO-d₆) δ : 1.21 (s, 18H, C(CH₃)₃), 2.25 (s, 3H, CH₃), 4.24 (s, 4H, SCH₂), 7.25 (d, 4H, H^{3',5'}, J (H^{2'}-H^{3'}) 8 Hz), 7.32 (d, 4H, H^{2',6'}, J (H^{2'}-H^{3'}) 8 Hz), 7.61 (s, 2H, H^{2,6}). ЯМР ¹³C (75 MHz, DMSO-d₆+CDCl₃) δ , 15.0, 35.0, 31.3, 37.3, 126.1, 130.0, 130.1, 130.3, 132.6, 136.3, 140.6, 149.5, 167.6. MS (EI), m/z : 492.2148 [M]⁺. (Calc. for: C₃₀H₃₆O₂S₂, m/z : 492.2151). Found (%): C, 72.97; H, 7.30; S, 12.98. Calc. for C₃₀H₃₆O₂S₂ (%): C, 73.14; H, 7.31; S, 13.01.

3,5-Bis(4-chlorophenylsulfanylmethyl)-4-methylbenzoic acid 4c. Yield is 80 % (*procedure B*), 84% (*procedure C*). M.p. 200-201.5°C (C₆H₆). IR spectrum, ν , cm⁻¹: 3435, 3076, 2926, 2854, 2598, 2536, 1687, 1608, 1574, 1475, 1421, 1389, 1306, 1248, 1172, 1093, 1010, 820, 810, 756 486. ¹H NMR (400 MHz, DMSO-d₆) δ : 2.42 (s, 3H, CH₃), 4.32 (s, 4H, SCH₂), 7.36 (s, 8H, H^{2',3',5',6'}), 7.70 (s, 2H, H^{2,6}). ЯМР ¹³C (75 MHz, ДМСО-d₆) δ , 14.9, 36.0, 128.2, 129.2, 130.3, 131.3, 131.4, 135.1, 136.4, 141.6, 166.9. MS (EI), m/z : 448.0111. [M]⁺. (Calc. for:

$C_{22}H_{18}Cl_2O_2S_2$, m/z : 448.0120.). Found (%): C, 58.72; H, 4.03; Cl 16.05; S, 13.78. Calc. for $C_{22}H_{18}Cl_2O_2S_2$ (%): C, 58.80; H, 4.01; Cl 15.81; S, 14.25.

4-Methyl-3,5-bis(pentafluorophenylsulfanylmethyl)benzoic acid 4d. Yield is 89% (*procedure C*). M.p. 193-194 °C. IR spectrum, ν , cm^{-1} : 3440, 3008, 2923, 2707, 2601, 2539, 1695, 1637, 1608, 1513, 1484, 1419, 1305, 1249, 1092, 979, 862, 760, 748, 580. 1H NMR (500 MHz, DMSO- d_6) δ : 2.44 (s, 3H, CH_3), 4.18 (s, 4H, CH_2), 7.26 (s, 2 H_{ar}). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 14.6, 37.1, 107.7 [td, 2J (CF) 21 Hz, 3J (CF) 3 Hz], 127.5, 130.2, 135.9, 137.2 [dt, CF, 1J (CF) 248 Hz, 2J (CF) 15 Hz], 141.2 [dm, CF, 1J (CF) 254 Hz], 141.3, 147.6 [dd, CF, 1J (CF) 244 Hz, 2J (CF) 6 Hz], 166.7. ^{19}F NMR (282 MHz, DMSO- d_6), δ : 0.6 [m, $2F^{3',5'}$], 9.8 [t, $F^{4'}$, J ($F^{4'}-F^{3'},F^{5'}$) 22 Hz] 30.3 m [$2F^{2',6'}$]. MS (EI), m/z : 559.9953 [M] $^+$. (Calc. for: $C_{22}H_{10}F_{10}O_2S_2$, m/z : 559.9957). Found (%): C, 47.25; H, 1.78; F 34.03; S, 11.33. Calc. for $C_{22}H_{10}F_{10}O_2S_2$ (%): C, 47.15; H, 1.80; F 33.90; S, 11.44.

4-Methyl-3,5-bis{[2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl]sulfanylmethyl}-benzoic acid 4e. Yield 90% (*procedure C*). M.p. 205-206 °C. IR spectrum, ν , cm^{-1} : 3432, 2926, 2854, 2712, 2604, 2546, 1701, 1643, 1610, 1477, 1423, 1330, 1254, 1190, 1151, 978, 829, 758, 748, 715, 584. 1H NMR (500 MHz, DMSO- d_6) δ 2.56 (s, 3H, CH_3), 4.41 (s, 4H, CH_2), 7.42 (s, 2 H_{ar}). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 14.7, 36.7, 108.0 [qt, 2J (CF) 34 Hz, 3J (CF) 13 Hz], 119.2 [t, 2J (CF) 21 Hz], 120.7 [q, CF_3 , 1J (CF) 274 Hz], 127.9, 130.3, 135.6, 143.4 [dd, CF, 1J (CF) 259 Hz, 2J (CF) 17 Hz], 147.1 [dd, CF, 1J (CF) 246 Hz, 2J (CF) 13 Hz], 166.5. ^{19}F NMR (282 MHz, DMSO- d_6), δ : 20.7 [m, $2F^{3',5'}$], 31.5 [m, $2F^{2',6'}$], 106.8 [t, (CF_3), J ($F^{CF_3}-F^{3'},F^{5'}$) 21 Hz]. MS (EI), m/z : 659.9885 [M] $^+$. (Calc. for: $C_{24}H_{10}F_{14}O_2S_2$, m/z : 659.9893). Found (%): C, 43.46; H, 1.54; F, 39.99; S, 9.66. Calc. for $C_{24}H_{10}F_{14}O_2S_2$ (%): C, 43.65; H, 1.53; F, 40.27; S, 9.71.

3,5-Bis(4-chloro-2,3,5,6-tetrafluorophenylsulfanylmethyl)-4-methylbenzoic acid 4f. Yield 84% (*procedure C*). M.p. 242-244 °C. IR spectrum, ν , cm^{-1} : 3425, 2983, 2968, 2712, 2604, 2544, 1695, 1623, 1610, 1475, 1450, 1425, 1319, 1308, 1256, 1198, 1143, 960, 823, 758, 615, 581, 451. 1H NMR (500 MHz, DMSO- d_6) δ 2.46 (s, 3H, CH_3), 4.23 (s, 4H, CH_2), 7.27 (s, 2 H_{ar}). ^{13}C NMR (125 MHz, DMSO- d_6), δ , 14.7, 37.0, 111.9 [t, 2J (CF) 21 Hz,], 112.2 [t, 2J (CF) 19 Hz], 127.6, 130.2, 135.9, 141.4, 143.6 [dd, CF, 1J (CF) 250 Hz, 2J (CF) 17 Hz], 147.4 [dd, CF, 1J (CF) 248 Hz, 2J (CF) 11 Hz], 168.6. ^{19}F NMR (282 MHz, DMSO- d_6), δ 21.1 [m, $2F^{3',5'}$], 30.1 [m, $2F^{2',6'}$]. MS (EI), m/z : 591.9362 [M] $^+$. (Calc. for: $C_{22}H_{10}Cl_2F_8O_2S_2$, m/z : 591.9366). Found (%): C, 43.86; H, 1.71; Cl, 11.74; F, 25.69; S, 10.50. Calc. for $C_{22}H_{10}Cl_2F_8O_2S_2$ (%): C, 44.53; H, 1.70; Cl, 11.95; F, 25.62; S, 10.81.