

(Z)-3-*p*-Tolylsulfinylacrylonitriles as Chiral Dipolarophiles: Reactions with Diazoalkanes.

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Supporting Information

Experimental Section

General Methods. All reactions were performed in flame-dried glassware equipped with rubber septa under positive pressure of argon. Flash chromatography was carried out with silica gel 60 (230-400 mesh ASTM), and silica gel F254 plates were used for preparative TLC. NMR spectra were determined in CDCl₃ solutions at 200 (or 300) and 50.3 (or 75) MHz for ¹H and ¹³C-NMR, respectively.

Compounds **1a-d** were synthesized and purified according to procedure described in ref 1. In order to verify the optical purity of **1a** to be used as the substrate in further reactions, it is necessary to check it by NMR using Yb(hfc)₃ as the LSR (substrate-LSR molar ratio 1:0.3).

1,3-Dipolar Cycloadditions. General Procedure. To a solution of (Z)-3-*p*-tolylsulfinylacrylonitrile (**1**) (1 mmol) in anhydrous Et₂O (substrates **1a-c**) or MeOH (substrate **1d**) (2 mL), cooled at the indicated temperature (see Table 1), was added a 0.95M solution of diazoalkane in Et₂O (10 equiv). The resulting mixture was stirred under the conditions shown in Table 1 and evaporated. The residue was purified as indicated in each case.

(3S,4S)-3-*n*-Butyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (4b**):** It was obtained by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-*n*-butyl-3-(*p*-tolylsulfinyl)propenenitrile (**1b**) with diazomethane as a white solid. It was crystallized from hexane: mp 97-98 °C; [α]_D²⁰ = +40.6° (c 1,

CHCl₃); ¹H-NMR δ 7.56 and 7.38 (AA'BB'system, 4H), 5.28 (dd, 1H, *J* = 4.9 and 19.2), 4.89 (dd, 1H, *J* = 8.7 and 19.2), 2.88 (dd, 1H, *J* = 4.9 and 8.7), 2.44 (s, 3H), 1.90 (m, 2H), 1.65 (m, 2H), 1.35 (m, 2H), 0.89 (t, 3H, *J* = 7.0) ; ¹³C-NMR δ 143.0, 138.5, 130.4 (2C), 124.3 (2C), 114.4, 89.0, 75.5, 62.5, 37.5, 26.4, 22.2, 21.4, 13.6; IR (CH₂Cl₂) 2959, 2930, 2870, 2242, 1493, 1466, 1380, 1085, 1044 cm⁻¹; MS (FAB) 290 (100) [*M*⁺+1], 262 (20), 150 (7), 140 (88), 125 (8), 92 (13); HRMS (FAB) C₁₅H₂₀N₃OS requires 290.132709. Found 290.133495. Anal. Calcd for C₁₅H₁₉N₃OS: C, 62.28; H, 6.57; N, 14.53; S, 11.07. Found: C, 62.08; H, 6.51; N, 14.35; S, 11.42.

(3*S*,4*S*)-3-*tert*-Butyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (4c): It was obtained by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-*t*-butyl-3-(*p*-tolylsulfinyl)propenenitrile (**1c**) with diazomethane as a white solid. It was crystallized from hexane: mp 80-82 °C; [*α*]_D²⁰ = +26.9° (c 1, CHCl₃); ¹H-NMR δ 7.51 and 7.36 (AA'BB'system, 4H), 5.35 (dd, 1H, *J* = 4.8 and 19.9), 4.50 (dd, 1H, *J* = 9.1 and 19.9), 2.91 (dd, 1H, *J* = 4.8 and 9.1), 2.42 (s, 3H), 1.10 (s, 9H); ¹³C-NMR δ 142.5, 138.0, 130.2 (2C), 123.6 (2C), 114.1, 97.9, 75.0, 58.7, 39.4, 24.8 (3C), 21.1; IR (CH₂Cl₂) 2972, 2239, 1492, 1472, 1086, 1051cm⁻¹; MS (FAB) 290 (100) [*M*⁺+1], 262 (15), 246 (6), 167 (4), 150 (7), 140 (33), 125 (6), 108 (5), 91 (11), 77 (7); HRMS (FAB) C₁₅H₂₀N₃OS requires 290.132709. Found 290.132235. Anal. Calcd for C₁₅H₁₉N₃OS: C, 62.28; H, 6.57; N, 14.53; S, 11.07. Found: C, 61.91; H, 6.72; N, 13.88; S, 11.32.

(3*S*,4*S*)-3-Benzyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (4d): It was obtained by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-benzyl-3-(*p*-tolylsulfinyl)propenenitrile (**1d**) with diazomethane as a yellow solid. It was crystallized from hexane: mp 91-92 °C; [*α*]_D²⁰ = +77.1° (c 1, CHCl₃); ¹H-NMR δ 7.35 (m, 7H), 7.08 (m, 2H), 5.19 (dd, 1H, *J* = 5.1 and 19.4), 4.24 (dd, 1H, *J* = 8.6 and 19.4), 3.38 and 3.17 (AB system, 2H, *J* = 14.1), 2.94 (dd, 1H, *J* = 5.1 and 8.6), 2.42 (s, 3H); ¹³C-NMR δ 142.7, 138.2, 131.5, 130.4 (2C), 130.2 (2C), 129.0 (2C), 128.4, 124.0 (2C), 114.7, 89.4, 75.4, 60.8, 42.6, 21.4; IR (CH₂Cl₂) 3033, 2972, 2925, 2360, 1494, 1085, 1048 cm⁻¹; MS (FAB) 324 (100) [*M*⁺+1], 296 (26), 279 (5), 247 (6), 231 (12), 184 (11), 155 (11), 140 (63), 123 (24), 91 (85); HRMS (FAB) C₁₈H₁₈N₃OS requires 324.117059. Found 324.117787. Anal. Calcd for C₁₈H₁₇N₃OS: C, 66.87; H, 5.26; N, 13.00; S, 9.91. Found: C, 66.44; H, 5.42; N, 12.56; S, 10.12.

(3S,4S,5S)-3-*n*-Butyl-5-methyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (5b):

It was obtained by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-*n*-butyl-3-(*p*-tolylsulfinyl)propenenitrile (**1b**) with diazoethane as a white solid. It was crystallized from hexane: mp 101-102 °C; $[\alpha]_D^{20} = -201.3^\circ$ (c 1, CHCl₃); ¹H-NMR δ 7.63 and 7.39 (AA'BB' system, 4H), 5.28 (q, 1H, *J* = 7.0), 2.45 (s, 3H), 2.40 (d, *J* = 7.0), 1.75 (m, 2H), 1.60 (m, 2H), 1.40 (d, 3H, *J* = 7.0), 1.28 (m, 2H), 0.85 (t, 3H, *J* = 7.0); ¹³C-NMR δ 143.1, 138.8, 130.4 (2C), 124.6 (2C), 114.1, 89.2, 86.4, 69.3, 38.5, 26.4, 22.1, 21.4, 19.3, 13.6; IR (KBr) 3036, 3020, 2973, 2247, 1492, 1468, 1082, 1039 cm⁻¹; MS (FAB) 304 (62) [M⁺+1], 276 (11), 248 (100), 164 (9), 140 (33), 123 (25), 109 (15), 91 (11); HRMS (FAB) C₁₆H₂₂N₃OS requires 304.148359. Found 304.148030. Anal. Calcd for C₁₆H₂₁N₃OS: C, 63.34; H, 6.98; N, 13.85; S, 10.57. Found: C, 63.28; H, 6.66; N, 13.95; S, 11.04.

(3S,4S,5S)-3-*tert*-Butyl-5-methyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile

(5c): It was obtained by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-*t*-butyl-3-(*p*-tolylsulfinyl)propenenitrile (**1c**) with diazoethane as a white solid. It was crystallized from hexane: mp 99-100 °C; $[\alpha]_D^{20} = -106.3^\circ$ (c 1, CHCl₃); ¹H-NMR δ 7.52 and 7.39 (AA'BB' system, 4H), 5.35 (q, 1H, *J* = 7.3), 2.45 (s, 3H), 2.42 (d, 1H, *J* = 7.3), 1.15 (s, 9H), 1.10 (d, 3H, *J* = 7.3); ¹³C-NMR δ 142.7, 138.4, 130.4 (2C), 123.8 (2C), 113.9, 98.7, 83.4, 65.9, 38.6, 25.5 (3C), 21.4, 18.2; IR (KBr) 2985, 2971, 2240, 1492, 1469, 1089, 1061 cm⁻¹; MS (FAB) 304 (100) [M⁺+1], 276 (11), 248 (7), 164 (5), 139 (14), 123 (14), 109 (5), 91 (4); HRMS (FAB) C₁₆H₂₂N₃OS requires 304.148359. Found 304.148748.

(3S,4S,5S)-3-Benzyl-5-methyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (5d):

It was obtained as a syrup by 1,3-dipolar cycloaddition reaction of (*R,Z*)-2-benzyl-3-(*p*-tolylsulfinyl)propenenitrile (**1d**) with diazoethane: $[\alpha]_D^{20} = -55.6^\circ$ (c 1, CHCl₃); ¹H-NMR δ 7.35 and 7.39 (AA'BB' system, 4H), 7.28 (m, 4H), 6.94 (m, 1H), 5.22 (q, 1H, *J* = 7.3), 3.47 and 2.98 (AB system, 2H, *J* = 14.2), 2.46 (d, 1H, *J* = 7.1), 2.45 (s, 3H), 0.88 (d, 3H, *J* = 7.3); ¹³C-NMR δ 142.8, 138.1, 131.5, 130.5 (2C), 130.3 (2C), 128.8 (2C), 128.3, 124.2 (2C), 114.2, 89.3, 86.4, 66.4, 43.1, 21.3, 18.0; IR (CH₂Cl₂) 3062, 3033, 2981, 2935, 2240, 1494, 1454, 1086, 1046 cm⁻¹.

(3S,4S)-3-*n*-Butyl-4-[(*R*)-*p*-tolylsulfinyl]-2,3,4,5-tetrahydro-3*H*-pirazole-3-carbonitrile (6b):

1 mmol of (3S,4S)-3-*n*-butyl-4-[(*R*)-*p*-tolylsulfinyl]-4,5-dihydro-3*H*-pirazole-3-carbonitrile (**4b**) was solved

in 2 mL of THF-H₂O (9:1) and treated with an excess of Al(Hg). The mixture was stirred at rt for 20 min and then filtered and the solid salts washed with THF. The filtrate was dried (MgSO₄) and concentrated to afford a white solid in 92% yield. It was crystallized from AcOEt-hexane: mp 116-117 °C; $[\alpha]_D^{20} = +31.8^\circ$ (c 1, CHCl₃); ¹H- δ 7.55 and 7.36 (AA'BB' system, 4H), 3.82 (bs, 1H), 3.78 (m, 1H), 3.05 (m, 2H), 2.43 (s, 3H) 1.72-1.18 (m, 6H), 0.91 (7, 3H, *J* = 6.9); ¹³C-NMR δ 142.1, 138.5, 130.1 (2C), 124.0 (2C), 118.6, 73.5, 67.1, 47.5, 37.1, 27.2, 22.1, 21.5, 21.2, 13.5. Anal. Calcd for C₁₅H₂₁N₃OS: C, 61.83; H, 7.26; N, 14.42; S, 11.00. Found: C, 61.61; H, 6.81; N, 14.41; S, 11.49.