An Improved Synthesis of 4-Hydroxy-2,4,6-cycloheptatrien-1-one (4-Hydroxytropone)

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Synopsis. 4-Hydroxytropone was prepared in an overall yield of 61% from 5-hydroxytropolone via tosylation, $LiAlH_4$-reduction, acetolysis with acetic trifluoroacetic anhydride in situ, and hydrolysis.

4-Hydroxytropone (**1**) is a fundamental isomer of tropolone, but its syntheses are far from being practical; the photocycloadditions of 3-acetoxy-2-cyclopenten-1-one with 1,2-dichloroethene[1] or 3-methoxy-2-cyclopenten-1-one with acetylene[2] are impractical since an excess of the starting enone is required or the yields are not so high. Also, acid substitution of 4-bromotropone[3] or ring-enlargement of *p*-dimethoxybenzene[4] are not adequate for preparative operations since the yields are poor.

We describe here an improved synthesis of **1** from 5-hydroxytropolone (**2**), which is obtained from the photooxidation of tropone and the subsequent NEt_3-treatment of the resultant 4,7-epidioxy-2,5-cycloheptadien-1-one.[5] The tosylation of **2** gave 2,5-bis(*p*-tolylsulfonyloxy)tropone (**3**) in 93% yield. Treatment of **3** with $LiAlH_4$ in dry tetrahydrofuran led to 4-(*p*-tolylsulfonyloxy)tropone (**4**) in 87% yield via a selective 1,8-reduction (Chart 1).

When **4** was heated at 80 °C in acetic trifluoroacetic anhydride prepared in situ from acetic anhydride, trifluoroacetic anhydride, and acetic acid,[6] 4-acetoxytropone (**5**) was obtained in 84% yield. Hydrolysis of **5** with aqueous acetic acid afforded the desired **1** in 90% yield, the overall yield of **1** from **2** being 61%.

Experimental

2,5-Bis(*p*-tolylsulfonyloxy)tropone (3): Et_3N (8 cm^3) was added to a THF solution (70 cm^3) of 5-hydroxytropolone (**2**, 2.0 g, 14.5 mmol) and TsCl (7.0 g, 36.7 mmol) at 0 °C and the mixture was stirred overnight at room temperature. The precipitates were filtered off and the filtrate was condensed under reduced pressure. The residue was chromatographed on a silica-gel column (hexane : EtOAc=3 : 1—1 : 1) to give the product, which was washed with hexane to give **3**, yield: 6.01 g (93%), colorless crystals, mp 129—129.5 °C (hexane–EtOAc); ^1H NMR ($CDCl_3$) δ=2.45 (3H, s), 2.48 (3H, s), 6.61 (1H, dm, J=10.3 Hz), 6.94 (1H, dd, J=13.2, 2.6 Hz), 7.05 (1H, dd, J=13.2, 0.7 Hz), 7.26 (1H, d, J=10.3 Hz), 7.35 (2H, dm, J=8.4 Hz), 7.39 (2H, dm, J=8.4 Hz), 7.77 (2H, dm, J=8.4 Hz), and 7.88 (2H, dm, J=8.4 Hz); ^{13}C NMR ($CDCl_3$) δ=22.1, 22.2, 123.0, 128.0, 128.9 (4C), 130.1 (2C), 130.7 (2C), 131.9, 133.5, 134.3, 141.2, 146.2, 147.0, 153.1, 154.5, and 178.5; UV (MeOH) 227.7 (ε 39500), 263.2 (sh, 4200), 275.4 (3800), and 318.6 nm (8700); IR (KBr) 1601, 1374, 1352, 1190, 1178, 1046, 831, and 678 cm^{-1}; MS m/z 446 (M^+, 1), 382 (92.2), 227 (27.5), 155 (100), and 91 (11.1). Found: C, 56.49; H, 4.17%. Calcd for $C_{21}H_{18}O_7S_2$: C, 56.48; H, 4.07%.

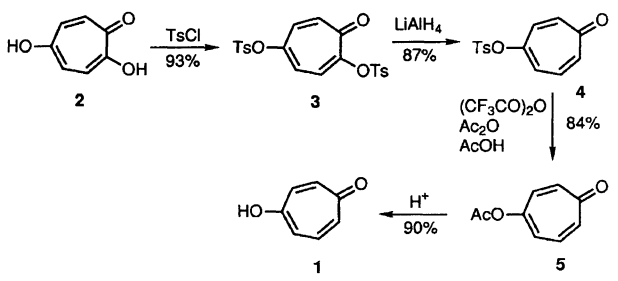

Chart 1.

4-(*p*-Tolylsulfonyloxy)tropone (4): A THF solution (70 cm^3) of 2,5-bis(*p*-tolylsulfonyloxy)tropone (**3**, 2.0 g, 4.48 mmol) and $LiAlH_4$ (138.2 mg, 3.64 mmol) was stirred at 0 °C for 30 min. The mixture was quenched by the sequential addition of water and 2 M HCl (M=mol dm^{-3}). The resulting suspension was extracted with ether. The organic layer was washed with sat. NaCl solution, dried over Na_2SO_4, and evaporated. The residue was chromatographed on a silica-gel column (hexane : EtOAc=3 : 1—2 : 1) to give **4**, yield: 1.07 g (87%), colorless crystals, mp 84—85 °C (ether); ^1H NMR ($CDCl_3$) δ=2.48 (3H, s), 6.65—6.7 (1H, m), 6.84 (1H, dd, J=12.8, 2.6 Hz), 6.89—7.04 (3H, m), 7.39 (2H, dm, J=8.4 Hz), and 7.77 (2H, dm, J=8.4 Hz); ^{13}C NMR ($CDCl_3$) δ=21.8, 126.6, 128.5 (2C), 130.2 (2C), 131.8, 133.7, 133.8, 141.2, 141.6, 146.4, 153.0, and 186.4; UV (MeOH) 227.4 (ε 30400), 277.0 (sh, 3700), 304.5 (8200), and 311.5 nm (sh, 8000); IR (KBr) 1587, 1375, 1195, 1179, 1084, and 794 cm^{-1}; MS m/z 276 (M^+, 25.9), 155 (67.6), and 91 (100). Found: C, 60.64; H, 4.33%. Calcd for $C_{14}H_{12}O_4S$: C, 60.85; H, 4.39%.

4-Acetoxytropone (5): A mixture of 4-(*p*-tolylsulfonyloxy)tropone (**4**, 478.2 mg, 1.73 mmol), acetic anhydride (8.5 cm^3), acetic acid (0.9 cm^3), and trifluoroacetic anhydride (0.6 cm^3) was heated overnight in a sealed tube at 80 °C. The solvents were then removed in vacuo and the residue was chromatographed on silica gel (hexane : EtOAc=3 : 1—2 : 1) to give **5**, yield: 238.8 mg (84%), a brown oil; ^1H NMR ($CDCl_3$) δ=2.30 (3H, s), 6.71—6.76 (1H, m), and 6.89—7.13 (4H, m); ^{13}C NMR ($CDCl_3$) δ=21.0, 124.9, 134.3, 134.5, 140.7, 141.1, 154.6, 168.9, and 186.9; UV (MeOH) 227.0 (ε 18900), 306.7 (7500), and 312.5 nm (7500); IR (oil) 1764, 1643, 1581, 1529, 1370, 1195, and 1141 cm^{-1}; MS m/z 165 (M^++1, 22.4), 122 (19.1), 94 (100), and 43 (57.5). Found: m/z 164.0470 (M^+). Calcd for $C_9H_8O_3$: M, 164.0473.

4-Hydroxytropone (1): A solution of 4-acetoxytropone (**5**, 642.2 mg, 3.91 mmol) in aqueous 50% acetic acid (20 cm^3) was heated at 90 °C for 10 h. The volatile material

was then removed in vacuo to give **1**, yield: 429.5 mg (90%), pale yellow crystals, mp 205.5—207 °C (decomp) (lit,[3] mp 212 °C (decomp)); ^{1}H NMR ($CDCl_3$) δ=6.76 (2H, dm, J=11.0 Hz), 7.17—7.19 (2H, m), and 7.28 (1H, t, J=11.0 Hz); ^{13}C NMR ($CDCl_3$) δ=124.5 (2C), 139.6 (2C), 141.2, and 177.7 (2C).

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