A Simple and Efficient Method for the Preparation of 1-Benzyloxy-5-hydroxynaphthalene

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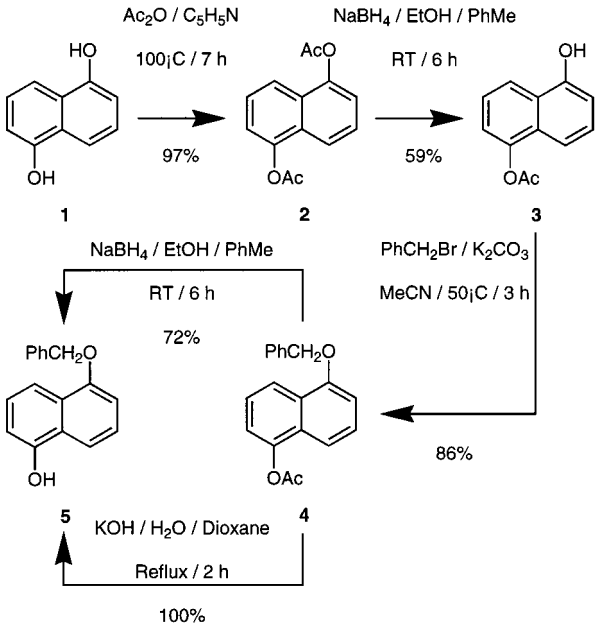
Abstract: 1,5-Dihydroxynaphthalene is a versatile π-electron rich aromatic ring system which has been employed widely for the construction of mechanically-interlocked molecular compounds and supramolecular complexes. A much-needed procedure for its transformation into 1-benzyloxy-5-hydroxynaphthalene has been developed. It involves *(i)* bisacetylation of 1,5-dihydroxynaphthalene, *(ii)* reductive removal of one of the two acetyl groups, *(iii)* benzylation, and *(iv)* cleavage of the remaining acetyl group.

Key words: 1,5-dihydroxynaphthalene, protection, deprotection

Recently, a number of template-directed synthetic procedures affording 1,5-dioxynaphthalene-containing catenanes,[1] double helices,[2] molecular knots,[3] pseudorotaxanes,[4] rotaxanes,[5] and self-complexing macrocycles[6] have been developed. These procedures all involve the syntheses of appropriate 1,5-dioxynaphthalene-based polyethers which are employed subsequently as templates for the construction of molecular assemblies or supramolecular arrays. Often, the syntheses of these templates require the monoprotection of 1,5-dihydroxynaphthalene. The method of choice[3,4a,7] for the monoprotection has been the direct monoalkylation of 1,5-dihydroxynaphthalene with $PhCH_2Br$ in the presence of K_2CO_3. However, this procedure is not easy to reproduce[7] or to carry out on a reasonable scale[7] and, as a result, alternative and low yielding routes, avoiding the monoprotection of 1,5-dihydroxynaphthalene, have been devised and used[3,7] for large scale syntheses of templates. Here, we report a simple and efficient four-step procedure (Scheme) for the synthesis of 1-benzyloxy-5-hydroxynaphthalene.

Acetylation of **1** with Ac_2O in C_5H_5N was carried out[8] using a modification of a literature procedure.[9] The resulting diacetate **2** can be isolated[8] in large quantities (*ca.* 30 g) and in very high yield (97%). The reductive removal of one of the two acetyl groups was achieved[10] by treating **2** with $NaBH_4$ in a mixture of EtOH and PhMe (1:3) to afford[11] the monoacetate **3** in good yield (59%). The free hydroxyl group of **3** was alkylated with $PhCH_2Br$ in the presence of K_2CO_3 in MeCN to afford[12] **4** in a yield of 86%. The remaining acetyl group of **4** can then be removed, either by reduction, or by hydrolysis. Treating **4** with $NaBH_4$ in a mixture of EtOH and PhMe (1:3) gave[13] 1-benzyloxy-5-hydroxynaphthalene (**5**) in a 72% yield.



Scheme

Similarly, reaction of **4** with KOH in a mixture of H_2O and dioxane (2:3) afforded[14] the benzyl ether **5** in a quantitative yield. In both instances, the benzyl group 'survived' the reaction conditions required for the deprotection.

1-Benzyloxy-5-hydroxynaphthalene can be now prepared in an overall yield of 49% starting from the commercially available 1,5-dihydroxynaphthalene. Thus, this procedure offers the possibility of preparing rapidly and efficiently large quantities of such an indispensable intermediate for the construction of 1,5-dihydroxynaphthalene-based polyethers, both acyclic and cyclic.

References and Notes

(1) For recent examples of catenanes based on macrocyclic components containing 1,5-dioxynaphthalene ring systems, see: a) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Angew. Chem. Int. Ed.*, **1998**, *37*, 333; b) Ashton, P. R.; Boyd, S. E.; Menzer, S.; Pasini, D.; Raymo, F. M.; Spencer N.; Stoddart, J. F.; White, A. J. P.; Williams,

D. J.; Wyatt, P. G. *Chem. Eur. J.*, **1998**, *4*, 299; c) Ballardini, R.; Balzani, V., Gandolfi, M. T.; Gillard R. E.; Stoddart, J. F.; Tabellini, E. *Chem. Eur. J.*, **1998**, *4*, 449; d) Amabilino, D. B.; Ashton, P. R.; Stoddart, J. F. White, A. J. P.; Williams, D. J. *Chem. Eur. J.*, **1998**, *4*, 460; e) Ashton, P. R.; Balzani, V.; Credi, A.; Kocian, O.; Pasini, D.; Prodi, L.; Spencer, N.; Stoddart, J. F., Tolley, M. S.; Venturi, M. *Chem. Eur. J.*, **1998**, *4*, 590; f) D. B. Amabilino, P. R. Ashton, S. E. Boyd, J. Y. Lee, S. Menzer, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc.*, **1998**, *120*, 4295; g) Menzer, S; White, A. J. P.; Williams, D. J.; Belohradsky, M.; Hamers, C.; Raymo, F. M.; Shipway, A. N.; Stoddart, J. F. *Macromolecules*, **1998**, *31*, 295; g) Try, A. C.; Harding, M. M.; Hamilton, D. G.; Sanders, J. K. M. *Chem. Commun.*, **1998**, 723; h) Hamilton, D. G.; Feeder, N.; Prodi, L.; Teat, S. J.; Clegg, W.; Sanders, J. K. M. *J. Am. Chem. Soc.*, **1998**, *120*, 1096; i) Hamilton, D. G.; Sanders, J. K. M. *Chem. Commun.*, **1998**, 1749.

(2) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *Makromol. Chem., Macromol. Symp.*, **1992,** *54/55*, 441.

(3) Ashton, P. R.; Matthews, O. A.; Menzer, S.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Liebigs Ann./Recueil*, **1997**, 2485.

(4) For some examples of pseudorotaxanes based on components containing 1,5-dioxynaphthalene ring systems, see: a) Ashton, P. R.; Chrystal, E. J. T.; Mathias, J. P.; Parry, K. P.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Tetrahedron Lett.*, **1987**, *28*, 6367; b) Ballardini, R.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; Venturi, M.; Philp, D.; Ricketts, H. G.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.*, **1993**, *32*, 1301; c) Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Langford, S. J.; Menzer, S.; Prodi, L.; Stoddart, J. F.; Venturi, M.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.*, **1996**, *35*, 978; d) Asakawa, M.; Dehaen, W.; L'abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Org. Chem.*, **1996**, *61*, 9591; e) Asakawa, M.; Ashton, P. R.; Boyd, S. E.; Brown, C. L.; Gillard, R. E.; Kocian, O.; Raymo, F. M.; Stoddart, J. F.; Tolley, M. S.; White, A. J. P.; Williams, D. J. *J. Org. Chem.*, **1997**, *62*, 26; f) Ashton, P. R.; Balzani, V.; Kocian, O.; Prodi, L.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.*, **1998**, In press; g) Balzani, V.; Credi, A.; Langford, S. J.; Montalti, M.; Raymo, F. M.; Stoddart, J. F. *New J. Chem.*, **1998**, In press.

(5) a) Ashton, P. R.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S. *Synlett*, **1994**, 789; b) Ashton, P. R.; Huff, J.; Menzer, S.; Parsons, I. W.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.*, **1996**, *2*, 31; c) Amabilino, D. B.; Ashton, P. R.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.*, **1995**, 747; d) Asakawa, M.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Belohradsky, M.; Gandolfi, M. T.; Kocian, O.; Prodi, L.; Raymo, F. M.; Stoddart, J. F.; Venturi, M. *J. Am. Chem. Soc.*, **1997**, 119, 302; e) Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Eur. J. Org. Chem.*, **1998**, In press; f) Ashton, P. R.; Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Eur. J. Org. Chem.*, **1998**, Submitted.

(6) a) Ashton, P. R.; Ballardini, R.; Balzani, V.; Boyd, S. E.; Credi, A.; Gandolfi, M. T.; Gómez-Lopéz, M.; Iqbal, S.; Philp, D.; Preece, J. A.; Prodi, L.; Ricketts, H. G.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.*, **1997**, *3*, 152; b) Wolf, R.; Asakawa, M.; Ashton, P. R.; Gómez-López, M.; Hamers, C.; Menzer, S.; Parsons, I. W.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Williams, D. J. *Angew. Chem. Int. Ed.*, **1998**, *37*, 975.

(7) Hamilton, D. G.; Davies, J. E.; Prodi, L.; Sanders, J. K. M. *Chem. Eur. J.*, **1998**, *4*, 608.

(8) A solution of **1** (20 g) in Ac_2O (100 mL) and C_5H_5N (110 mL) was heated for 7 h at 100°C under an atmosphere of N_2. After cooling down to room temperature, the remaining Ac_2O was destroyed by adding carefully H_2O. The resulting mixture was poured into H_2O (1 L) and stirred for 20 min. The precipitate was filtered off, washed with H_2O, air dried, and passed through a plug of SiO_2 using CH_2Cl_2/Me_2CO (99:1) as eluant to afford **2** (29.5 g, 97%) as a yellow solid. M.p. = 158–159°C. EIMS: *m/z* (%) = 244 (53) $[M]^+$, 202 (100), 160 (49), 131 (10). ^{1}H–NMR ($CDCl_3$): δ = 2.47 (6H, s), 7.30 (2H, dd, *J* = 7 and 1 Hz), 7.51 (2H, dd, *J* = 8 and 7 Hz), 7.79 (2H, dd, *J* = 8 and 1 Hz). ^{13}C–NMR ($CDCl_3$): δ = 21.0, 118.8, 119.3, 126.0, 128.1, 129.0, 146.7, 169.3. Anal. calcd for $C_{14}H_{12}O_4$: C = 68.85, H = 4.95; found: C = 68.67, H = 5.10.

(9) Jung, M. E.; Hagenah, J. A. *J. Org. Chem.*, **1987**, *52*, 1889.

(10) For a discussion on the mechanism of the reduction of acetyl groups with $NaBH_4$, see: Piancatelli, G.; Corsano, S. *Gazz. Chim. Ital.*, **1971**, *101*, 204.

(11) A mixture of **2** (5.0 g), $NaBH_4$ (0.38 g), EtOH (25 mL), and PhMe (75 mL) was stirred for 6 h at room temperature under an atmosphere of N_2. The solution was diluted with Et_2O (200 mL) and washed with H_2O (2 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexane/ CH_2Cl_2/Me_2CO 15:4:1) to yield **3** (2.46 g, 59%) as a white solid. M. p. = 145–147.5°C. EIMS: *m/z* (%) = 202 (75) $[M]^+$, 160 (100), 131 (60), 103 (11). ^{1}H–NMR ($CDCl_3$): δ = 2.47 (3H, s), 5.53 (1H, s), 6.74 (1H, dd, *J* = 8 and 1 Hz), 7.24–7.31 (2H, m), 7.39–7.46 (2H, m), 8.04 (1H, dd, *J* = 9 and 1 Hz). ^{13}C–NMR ($CDCl_3$): δ = 21.0, 109.2, 113.6, 118.7, 120.0, 124.6, 125.8, 126.6, 128.0, 146.4, 151.6, 169.9. Anal. calcd for $C_{12}H_{10}O_3$: C = 71.28, H = 4.98; found: C = 71.30, H = 5.04.

(12) A degassed solution of **3** (1.0 g) in MeCN (20 mL) was added slowly to a degassed suspension of $PhCH_2Br$ (1.0 g), K_2CO_3 (0.8 g), and 18-crown-6 (*ca.* 50 mg) in MeCN (20 mL) mantained at 50°C under an atmosphere of N_2. The mixture was heated for a further 3 h at 50°C and, after cooling down to room temperature, was concentrated under reduced pressure. The residue was partitioned between H_2O and Et_2O (containing a small amount of Me_2CO). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to afford **4** (1.3 g, 86%), after washing with hexane, as a white solid. M.p. = 131–132°C. EIMS: *m/z* (%) = 292 (38) $[M]^+$, 250 (32), 159 (9), 131 (5), 91 (100). ^{1}H–NMR ($CDCl_3$): δ = 2.46 (3H, s), 5.26 (2H, s), 6.92 (1H, d, *J* = 7 Hz), 7.27 (1H, dd, *J* = 8 and 1 Hz), 7.36–7.54 (8H, m), 8.26 (1H, dd, *J* = 9 and 1 Hz). ^{13}C–NMR ($CDCl_3$): δ = 21.0, 70.2, 105.8, 113.6, 118.8, 120.4, 124.7, 126.6, 127.1, 127.4, 127.9, 128.0, 128.6, 136.8, 146.4, 154.6, 169.5. Anal. calcd for $C_{19}H_{16}O_3$: C = 78.06, H = 5.52; found: C = 78.06, H = 5.50.

(13) A mixture of **4** (4.53 g), $NaBH_4$ (0.68 g), EtOH (25 mL), and PhMe (75 mL) was stirred for 6 h at room temperature under an atmosphere of N_2. The solution was diluted with Et_2O (200 mL) and washed with H_2O (2 × 200 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, *(i)* CH_2Cl_2, *(ii)* Me_2CO] to yield **5** (2.79 g, 72%) as a white solid. M. p. = 135.5°C. EIMS: *m/z* (%) = 250 (57) $[M]^+$, 159 (18), 131 (24), 103 (11), 91 (100). ^{1}H–NMR ($CDCl_3$): δ = 5.21 (1H, s), 5.26 (2H, s), 6.86 (1H, dd, *J* = 8 and 1 Hz), 6.93 (1H, d, *J* = 8 Hz), 7.29–7.45 (5H, m), 7.53–7.55 (2H, m), 7.78 (1H, d, *J* = 8 Hz), 7.96 (1H, dd, *J* = 9 and 1 Hz). ^{13}C–NMR ($CDCl_3$): δ = 70.1, 105.9, 109.5, 113.9, 115.0, 125.2, 125.2, 125.4, 127.1, 127.3, 127.9, 128.6, 137.1, 151.1, 154.4. Anal. calcd for $C_{17}H_{14}O_2$: C = 81.58, H = 5.64; found: C = 81.40, H = 5.82.

(14) A solution of KOH (2.00 g) in H_2O (50 mL) was added to a degassed solution of **4** (1.95 g) in dioxane (50 mL) and the mixture was heated for 2 h under reflux and an atmosphere of N_2. After cooling down to room temperature, the solution was diluted with H_2O (300 mL) and extracted with CH_2Cl_2 (2 × 300 mL). The combined organic phases were dried ($MgSO_4$) and the solvent was removed under reduced pressure to afford **5** (1.67 g, 100%) as a white solid.