1 H, H-6), 1.76 (q, 2 H, 2 H-4, J = 7.8 Hz).

OM–DM of 1: 3-*epi*-Isoeucommiol 5 and Bicyclo Derivative 7. To the yellow suspension obtained by adding THF (2.5 mL) to a stirred solution of mercuric acetate (0.5 g, 1.57 mmol) in water (10 mL) was added 1 (0.5 g, 1.45 mmol). After 20 min, to the colorless solution, cooled at 0 °C, was added 6 N NaOH (5 mL), and then, slowly and under stirring, 0.5 M $NaBH_4$ solution (15 mL) in 2 N NaOH was added. After 15 min the reaction mixture was worked up as before to give a mixture **2–5** (236 mg, 87%). Successive addition of 0.1 N HCl (3 mL) gave, after usual workup, a mixture of **7** and **4** (191 mg, yield$_{1\rightarrow 7+4}$ = 78%) in GC ratio 4:1. Chromatographic separation ("washed silica gel") with $CHCl_3$–MeOH, 9:1, afforded pure **4** (14 mg), a 1:1 mixture of **4** and **7** (42 mg), and finally pure **7** (120 mg). ^{1}H NMR (300 MHz, D_2O): δ 5.54 (br s, 1 H, H-8), 4.99 (d, 1 H, H-1, $J_{1,5}$ = 7.8 Hz), 4.06 (dd, 2 H, 2 H-7′, J_{AB} = 15.0 Hz), 3.71–3.52 (cm, 2 H, 2 H-3), 3.53 (o, 2 H, 2 H-6′), 2.69 (cm, 1 H, H-5), 2.60 (br s, 1 H, H-6), 2.04–1.92 and 1.65–1.56 (cm, 2 H, 2 H-4). ^{13}C NMR (D_2O): δ 150.19 (s, C-7), 126.30 (d, C-8), 88.16 (d, C-1), 66.87 (t, C-3), 63.91 (t, C-6′), 59.89 (t, C-7′), 55.03 (d, C-6), 45.17 (d, C-5), 34.13 (t, C-4).

The above procedure, leading to the selective preparation of bicyclo derivatives **4** and **7**, could be shortened by starting from the Hg° filtration. The filtered solution was directly acidified with HCl (initially 6 N and then 2 N) until pH 3–4 (Congo Red). After being stirred overnight, the aqueous solution was neutralized with $NaHCO_3$ and then extracted in a liquid-liquid extractor with EtOAc (2 × 250 mL, 12 h). The EtOAc solution, dried (Na_2SO_4) and evaporated in vacuo, afforded the desired bicyclo derivative, which was purified as described.

Registry No. 1, 479-98-1; 2, 64274-29-9; 3, 64274-28-8; 4, 94707-63-8; 5, 116050-15-8; 6, 116004-75-2; 7, 116050-16-9.

Direct Lithiation of Hydroxyaromatics

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Since the pioneering work of Gilman and Wittig almost 50 years ago,[1] aromatic lithiation[2] has evolved as a powerful method for the introduction of a wide variety of functional groups and alkyl side chains at positions not easily available by other means (i.e. electrophilic aromatic substitution).

Though the mechanistic pathway for the heteroatom-facilitated lithiation is poorly understood, it is generally believed that coordination of the incoming lithium base with the available coordinating groups takes place prior to the actual hydrogen–lithium exchange step.[3] Accordingly, phenoxides are generally considered very poor ortho directors in metalation reactions, although it has been recently demonstrated that the direct metalation of phenol itself (ortho to the OH group) can be worked out by using the appropriate selection of reagents (*t*-BuLi/THP).[4] Moreover, in our recent work toward the synthesis of

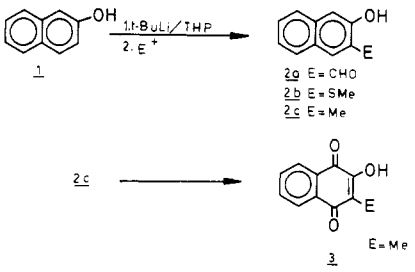


Figure 1.

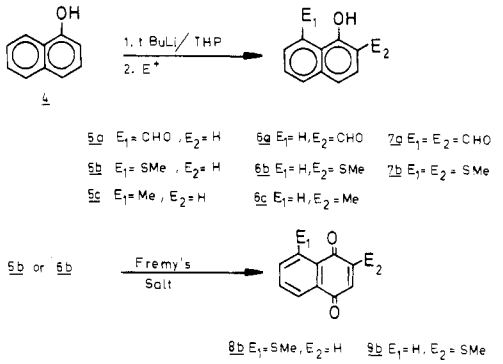


Figure 2.

quinones, we have been able to prove that substituted phenols can be metalated in a regioselective manner (ortho to other directors other than the OH group) by the action of *t*-BuLi/THP or, in appropriate cases, by *n*-BuLi/THF.[5]

Continuing with our efforts in the field, we now report our work on the direct lithiation of polycyclic aromatic systems containing an OLi group as the only directing group, namely, the lithium salts of naphthols, anthranols, and also some polyphenols. The major objective of our plan was to achieve the regioselective introduction of electrophiles onto mono and polyhydroxy benzenes, naphthalenes, and anthracenes. Obviously, if this goal were reached, a powerful methodology for the regioselective preparation of a variety of substituted polycyclic aromatics and many simple derivatives such as the corresponding quinones would be at hand.

In the event, direct lithiations were carried out under standard conditions, i.e. by operating with 25% M excess of *t*-BuLi, which was added in ca. 2 min to a concentrated solution (2 M) of the substrate in anhydrous tetrahydropyran,[6] at room temperature (see the Experimental Section). By so doing, a strongly exothermic reaction (to ca. 50 °C) takes place. It is worth noting in this context that running the reaction at lower temperature, decreasing the rate of addition of *t*-BuLi (15 min instead of 2 min), or working with more dilute solutions of either substrate (≤1 M) or lithium base (≤1.7 M) led to a significant decrease in yield of the final product and the subsequent recovery of unchanged starting material.

Treatment of 2-naphthol (1) under the above working conditions led to a viscous paste, which was then quenched with different electrophiles, namely DMF, $(MeS)_2$, MeI,

(1) (a) Gilman, H.; Bebb, R. L. *J. Am. Chem. Soc.* **1939**, *61*, 109. (b) Wittig, G.; Furhman, G. *Chem. Ber.* **1940**, *73*, 1197.

(2) Gilman, H.; Morton, J. W. *Org. React.* (*N.Y.*) **1954**, *8*, 258. Gschwend, H. W.; Rodriguez, H. *Org. React.* (*N.Y.*) **1979**, *26*, 1. Wakefield, B. J. *Organolithium* Compounds; Pergamon: New York, 1974. Narasimhan, N. S.; Mali, R. S. *Synthesis* **1983**, 957.

(3) Barnes, R. A.; Nehmsmann, L. J. *J. Org. Chem.* **1966**, *27*, 1939. See also ref 2.

(4) Posner, G. H.; Canella, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 2571.

(5) Saâ, J. M.; Morey, J.; Costa, A. *Tetrahedron Lett.* **1986**, *27*, 5125. Costa, A.; Saâ, J. M. *Tetrahedron Lett.* **1987**, *28*, 5551. Saâ, J. M.; Llobera, A.; Garcia-Raso, A.; Costa, A.; Deyâ, P. M. *J. Org. Chem.*, in press.

(6) THP is, at least partially, destroyed by the action of *t*-BuLi. It is premature to determine whether or not the resulting alkoxide plays a major role on the reaction mechanism by reacting with the organolithium derivatives present. See: Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9. Schlosser, M.; Strunck, S. *Tetrahedron Lett.* **1984**, *25*, 741 and references therein.

0022-3263/88/1953-5345$01.50/0

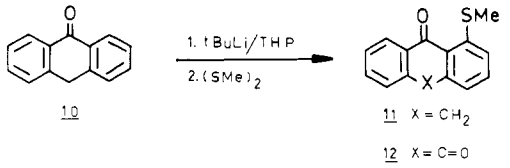


Figure 3.

thus furnishing the otherwise difficult-to-synthesize[7] 3-substituted 2-naphthols (**2**) (Figure 1). The corresponding 1-substituted or 1,3-disubstituted 2-naphthols (vide infra) were not detected in the above reaction mixtures, as indicated by ^{1}H NMR spectroscopy. The remarkable regioselectivity found parallels that observed by Gilman[8] who converted 2-naphthol into the corresponding 3-carboxylic acid derivative by stepwise treatment with *n*-BuLi/TMEDA and CO_2, though in very low isolated yield (7%).

The structures of compounds **2a** through **2c** were secured on the basis of their ^{1}H NMR spectra, which typically showed two appropriate singlets. Furthermore, slow oxidation of **2c** with Fremy's salt yielded the expected 1,2-naphthoquinone, which, on treatment[7a] with sodium dithionite followed by *t*-BuOK/O_2, provided naturally occurring phthiocol **3** whose physical and spectroscopic properties were found to be identical with those reported.[7a]

In striking contrast with the clean regioselectivity observed for the 2-naphthol case, treatment of 1-naphthol (**4**) with *t*-BuLi/THP under the above described conditions, followed by quenching with different electrophiles, furnished a separable mixture of compounds **5–7**, together with unreacted starting material **4** (Figure 2), in proportions which were dependent on the electrophile and also on the reaction conditions employed. Whereas the yield of **7a** could be easily improved by increasing the reaction time, that of **7b** could not be changed either by extending the reaction time or by adding excess of reagents. On the other hand, alkylation reactions provided a very complex mixture of mono-, di-, and polyalkylated products (treatment with MeI) or they did not occur at all (treatment with dimethylallyl bromide).

The structures of compounds **5** and **6** were established mainly on the basis of their ^{1}H NMR spectra (see the Experimental Section). As a further proof for these assignments, the isomeric naphthols **5b** and **6b** were converted (Fremy's salt)[9] into the corresponding 5-(methylthio)-1,4-naphthoquinone (**8b**) ("thiojuglone methyl ether") and its 2-methylthio analogue **9b**, respectively. The spectroscopic properties of the interesting[10,11] **8b** and **9b**

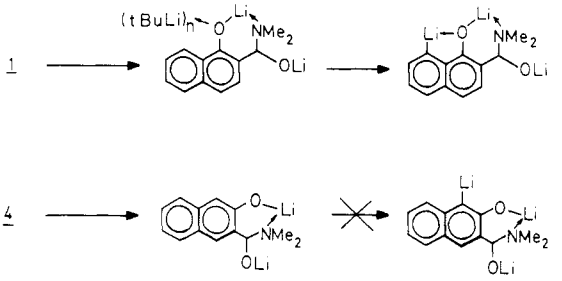


Figure 4.

were in full agreement with the proposed structures. That compound **7a** was the 2,8-diformyl-1-naphthol and not the 7,8- or 2,3-isomers, was unambiguously confirmed by means of its NOE difference spectrum, which showed the expected connectivity pattern.[12]

Similarly, the direct metalation of anthrone **10** (Figure 3), followed by treatment with dimethyl disulfide, furnished the easily oxidizable anthrone **11**, together with anthraquinone **12**.

Not totally unexpected, on the other hand, all attempts to achieve the direct metalation of 1,3-dihydroxybenzene[13] under the above set of standard conditions eventually provided (after quenching with D_2O, DMF, $(MeS)_2$) unchanged starting material in high yield. These results should not be taken, per se, as indicative of the inability of *t*-BuLi to deprotonate them, since, in all cases studied, the abundant precipitate formed did not dissolve on addition of either excess *t*-BuLi or anhydrous lithium chloride.

Our results confirm Posner's observations that an OLi group may act as an ortho-directing metalation group. However, no clear-cut explanation can be advanced to account for the observed regioselectivity of the direct metalation of naphthols. This is particularly so in the light of the report by Comins[14] regarding the metalation of α-amino alkoxides derived from naphthaldehydes on the one hand, and the metalation of (dimethylamino)-methylnaphthalenes[15a] and MOM-protected naphthols,[15b] on the other hand. Furthermore, the regioselective outcome of the lithiation of 1- and 2-alkoxy naphthalenes[15] has been shown to be highly dependent on the conditions

(7) (a) Lengthy synthesis of 3-substituted 2-naphthols have been recently published. See, for example: Ghera, E.; Ben-David, Y. *J. Org. Chem.* **1985**, *50*, 3355. Fields, D. L. *J. Org. Chem.* **1971**, *36*, 3002. Some direct synthesis based on the metalation of simple naphthalene derivatives failed. See: Watanabe, M.; Snieckus, V. *J. Am. Chem. Soc.* **1980**, *102*, 1457. Meyers, A. I.; Lutomski, K., unpublished results. (b) For the successful metalation of 1-substituted naphthalenes, see: Meyers, A.; Avila, W. B. *J. Org. Chem.* **1981**, *46*, 3881. Harvey, R. G.; Cortez, C.; Jacobs, S. A. *J. Org. Chem.* **1982**, *47*, 2120. Sibi, M. P.; Snieckus, V. *J. Org. Chem.* **1983**, *48*, 1935.

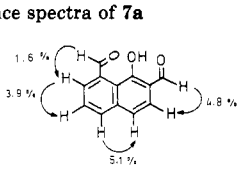
(8) Gilman, H.; Arntzen, C. E.; Webb, F. J. *J. Org. Chem.* **1945**, *10*, 374.

(9) Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.

(10) Juglones and derivatives are standard building blocks for the synthesis of anthracyclines. Presumably, by employing **8b** the 4-methylthio analogues of the clinical valuable anthracyclines could be obtained. See: *Tetrahedron* ("Symposia in Print", Guess Editor T. Ross Kelly) **1984**, *40*, 4537–4793. See also Krohn, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 790. Other interesting juglone analogues should be readily available from cheap 1-naphthol via lithiation.

(11) For a general overview of the synthetic approaches toward naphthoquinones, see: *Methoden Org. Chem. (Houben-Weyl)* **1983**, Band VII/3a Teil I. For more recent developments, see: Sibi, M. P.; Dankwardt, J. W.; Snieckus, V. *J. Org. Chem.* **1986**, *51*, 271. Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 1174. Liebeskind, L. S.; Iyer, S.; Jewell, C. F., Jr. *J. Org. Chem.* **1986**, *51*, 3065. Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3068. Moore, H. W.; Decker, O. H. W. *Chem. Rev.* **1986**, *86*, 821. Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iger, S.; Leeds, J. P. *Tetrahedron* **1985**, *41*, 5839. Wulff, W. D.; Tang, P.-C.; Chan, K.-S.; McCallum, J. S.; Yang, D. C.; Gilbertson, S. R. *Tetrahedron* **1985**, *41*, 5813. Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803.

(12) NOE diffference spectra of **7a**



(13) Gilman, H.; Willis, H. B.; Cook, T. H.; Webb, F. J.; Meals, R. N. *J. Am. Chem. Soc.* **1940**, *62*, 667.

(14) Comins, D. L.; Brown, J. D. *J. Org. Chem.* **1984**, *49*, 1078. Comins, D. L.; Brown, J. D.; Mantlo, N. B. *Tetrahedron Lett.* **1982**, *23*, 3979. Graybill, B. M.; Shirley, D. A. *J. Org. Chem.* **1966**, *31*, 1221.

(15) (a) Gay, R. L.; Hauser, C. R. *J. Am. Chem. Soc.* **1967**, *89*, 2297. (b) Kawikawa, T.; Kubo, I. *Synthesis* **1986**, 431.

(16) Narasimhan, N. S.; Mali, R. S. *Tetrahedron* **1975**, *31*, 1005. Shirley, D. A.; Cheng, C. F. *J. Organomet. Chem.* **1969**, *20*, 251.

of lithiation. To reconcile both our results and those already published we speculate that they reflect the different capacity of the lithium base (complexed with the appropriate heteroatom on the naphthalene derivative) to reach the different hydrogen atoms on the naphthalene nucleus (CIPE process).[17] In line with this interpretation, we feel that the unique behavior of the formylation reactions of metalated 1-naphthol is a consequence of stereoelectronics, i.e., the capacity of the intermediate α-aminoalkoxide in C-2 (or C-8) to internally chelate the adjacent lithium naphtholate at C-1 (see Figure 4), thus facilitating a subsequent metalation to take place at C-8 (or C-2) by coordinating with a second organolithium base. Alternatively, the α-aminoalkoxide at C-3 (derived from metalated 2-naphthol) can also chelate the lithium naphtholate at C-1, but the electron pairs on the ArOLi are not adequately disposed in space to allow (after coordination with a second lithium base) for an easy hydrogen–lithium exchange.

In summary the ortho functionalization of monohydroxy polycyclic aromatics via direct lithiation is an efficient methodology for the preparation of some simple though often difficult-to-synthesize derivatives.[7] The direct introduction of alkyl side chains on these systems is currently under investigation. The lithiation of the highly interesting polyhydroxy aromatics, which resisted metalation under our set of standard conditions, need to be pursued.

Experimental Section

General Methods. All melting points are uncorrected and were taken on a capillary melting point apparatus. The boiling points given refer to those observed during bulb-to-bulb distillations (Büchi GKR-50 apparatus). The starting materials were obtained from commercial suppliers and were used without purification. Anhydrous tetrahydropyran (THP) was obtained by distillation from sodium benzophenone ketyl immediately prior to use. Proton NMR spectra were obtained on a Varian FT-80A, Bruker WM-250, or Bruker WP-200SY spectrometers in $CDCl_3$ with Me_4Si as internal standard. Electron impact mass spectra were recorded on an Hewlett-Packard 5988A GC/MS operating at 70 eV ionizing energy. Infrared spectra were recorded on an Hitachi 260-10 infrared spectrophotometer. Elemental analyses were obtained at the Servei de Microanalisi del CSIC (Barcelona). Column chromatographies were performed on silica gel 60 (Macherey Nagel 70–230 mesh).

General Procedure for Lithiation of Hydroxy Aromatics. A flame-dried round-bottom flask, cooled under a stream of argon, was typically charged with 2 mmol of the hydroxy aromatic compound, dissolved in 1 mL (3 mL in the case of anthrone) of anhydrous THP. To the stirred solution, at room temperature (ca. 20–25 °C) was added dropwise 4.5 mmol of ca. 2 M *t*-BuLi in pentane via a syringe in approximately 2 min. Immediately a rapid evolution of heat and gases occurred, thus raising the temperature of the reaction mixture to ca. 50 °C. After the gas evolution subsided (15 min), the reaction mixture, which appeared as a highly viscous brownish material, was left to stir (with difficulty) for another 4 h.

A solution of the electrophile in THP was then added to the mixture at the appropriate temperature and, subsequently, left to stir for the adequate period of time. Standard workup involved careful addition of water and 1 M HCl until pH 5–6. The organic material was then extracted with ethyl acetate or ether. The extracts after being washed with brine and water were dried over anhydrous Na_2SO_4 and evaporated to dryness. The resulting residue (which contains some 6,6-dimethylheptan-1-ol) was chromatographed on silica gel and finally distilled or crystallized.

2-Hydroxy-3-naphthaldehyde (2a). A 0.29-g (2 mmol) sample of 2-naphthol was treated as indicated above with *t*-BuLi. To the resulting dark brown paste, at 0 °C was added dimethylformamide (1 mL) in THP (1 mL), and the mixture was left to stir for 24 h at room temperature. Extractive workup (ether) led to a crude material, which was chromatographed on silica gel (CH_2Cl_2), thus yielding 0.04 g of 1 and 0.21 g of **2a** (61% yield): mp 100–102 °C from CH_2Cl_2–hexane (lit.[16] mp 99–100 °C); IR (KBr) 3390, 3040, 2960, 1665, 1495, 1455, 1380, 1110, 880, 745 cm^{-1}; ^1H NMR δ 10.29 (s, 1 H, OH), 10.05 (s, 1 H), 8.10 (s, 1 H), 7.26 (s, 1 H), 7.90–7.20 (m, 4 H); EIMS, *m/e* (relative abundance) 172 (M^+, 100), 171 (64), 149 (58), 132 (8), 126 (15), 116 (13), 115 (63), 91 (30).

2-Hydroxy-3-(methylthio)naphthalene (2b). The dilithio derivative of 1 (2 mmol) generated as shown above was treated, at 0 °C, with dimethyl disulfide (1 mL) dissolved in THP (1 mL), and the mixture was stirred at room temperature for 2.5 h. Standard extractive workup (ethyl acetate) followed by chromatography (Cl_2CH_2) yielded **2b** (bp 110 °C/10^{-3} mmHg) as a yellow solid: mp 83–4 °C in 83% yield; IR (KBr) 3250, 1620, 1580, 1425, 1380, 1330, 1150, 1010, 950, 850 cm^{-1}; ^1H NMR δ 8.00 (s, 1 H), 7.31 (s, 1 H), 7.72–7.40 (m, 5 H), 2.42 (s, 3 H); EIMS, *m/e* (relative abundance) 190 (M^+, 100), 175 (20), 148 (11), 147 (67), 145 (11), 115 (22), 103 (10), 69 (12). Anal. Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.29; S, 16.85. Found: C, 69.49; H, 5.58; S, 16.65.

2-Hydroxy-3-methylnaphthalene (2c). The dilithio derivative of 1 (6 mmol) generated as illustrated in the general procedure was treated with methyl iodide (5 mL) in THP (6 mL) at −40 °C. Stirring was continued for an additional 4 h at −40 °C. Extractive workup (ether) followed by repeated chromatography (hexane–ether, 8:2) yielded **2c** (bp 120 °C/0.05 mmHg) in 46% yield: mp 155 °C from CH_2Cl_2–hexane (lit.[18] 156.5–157 °C); IR (KBr) 3540, 3050, 2940, 1620, 1602, 1515, 1395, 1345, 1245, 1195, 1155, 1095, 870 cm^{-1}; ^1H NMR δ 7.75–7.5 (m, 2 H), 7.57 (s, 1 H), 7.43–7.11 (m, 3 H), 7.05 (s, 1 H), 2.41 (s, 3 H); EIMS, *m/e* (relative abundance) 158 (M^+, 100), 157 (31), 140 (9), 139 (10), 129 (33), 128 (32), 127 (14), 115 (15).

Synthesis of Phthiocol 3. A methanolic solution (3 mL) of 0.2 g of **2c** was added all at once to 50 mL of a buffered solution (Na_2PO_4H, $NaPO_4H_2$, pH 6) of Fremy's salt (3 g). Stirring was continued for 30 min. Extractive workup (ethyl acetate) yielded an orange solid, which was then treated according to the procedure described by Ghera.[7a] Phthiocol was obtained as a crystalline solid, mp 173 °C (lit.[7a] mp 172–3 °C): IR (KBr) 3330, 1655, 1640, 1390, 1340, 1275, 1215, 1070, 940 cm^{-1}; ^1H NMR δ 8.21–7.90 (m, 2 H), 7.84–7.53 (m, 2 H), 2.10 (s, 2.10); EIMS, *m/e* (relative abundance) 188 (M^+, 100), 160 (21), 149 (11), 132 (31), 131 (46), 105 (24), 104 (16), 103 (12), 77 (27), 76 (20).

Preparation of 1-Hydroxynaphthalene-8-carboxaldehyde (5a) and 1-Hydroxynaphthalene-2,8-dicarboxaldehyde (7a). Method A. 1-Hydroxynaphthalene (2 mmol) (**4**) was lithiated as illustrated in the general procedure, and the resulting dark brown paste, at 0 °C, was treated with dimethylformamide (2 mmol) dissolved in THP (1 mL). The bath was removed, and stirring was continued for an additional 3 h. Workup as usual (ethyl acetate) followed by chromatography (Et_2O–CH_2Cl_2) provided **5a** in 40% yield and **7a** in 20% yield.

5a: mp 88–90 °C (pentane) (lit.[19] mp 92–6 °C); IR (CCl_4) 3060, 2940, 1665, 1590, 1450, 1265, 1250, 1215, 1195, 1000, 975 cm^{-1}; ^1H NMR δ 11.55 (s, 1 H), 9.83 (s, 1 H, disappears on addition of D_2O), 8.15–7.05 (m, 6 H); EIMS, *m/e* (relative abundance) 172 (M^+, 100), 171 (75), 155 (20), 144 (10), 126 (16), 116 (17), 115 (77), 105 (11), 89 (15), 77 (11).

7a: yellow needles; mp 146–8 °C (hexane–ethanol); IR (CCl_4) 3300, 3030, 2965, 2840, 1690, 1650, 1625, 1355, 1315, 1270 cm^{-1}; ^1H NMR (250 MHz) δ 11.17 (s, 1 H, C8–CHO), 10.07 (s, 1 H, C2–CHO), 8.05 (dd, 1 H, J = 7.2, 1.4 Hz, H7), 8.00 (dd, 1 H, J = 8.3, 1.4 Hz, H5), 7.72 (dd, 1 H, J = 8.3, 7.2 Hz, H6), 7.61 (d, 1 H, J = 8.4 Hz, H3), 7.49 (d, 1 H, J = 8.4 Hz, H4); EIMS, *m/e* (relative abundance) 200 (M^+, 56), 172 (75), 171 (100), 170 (12), 143 (12), 126 (25), 116 (10), 115 (55), 114 (14), 113 (11), 85 (12), 63 (19). Anal. Calcd for $C_{12}H_8O_3$: C, 72.00; H, 4.02. Found: C, 71.84; H, 4.34.

Method B. Quenching the dilithio derivative with dimethylformamide, as above, was then followed by stirring for 12–16 h at room temperature. The usual workup furnished **5a** in 21% yield and **7a** in 43% yield.

(17) Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356.

(18) Cook, J. W.; Lawrence, C. A. *J. Chem. Soc.* **1937**, 817.

(19) Berry, D.; Smith, D. C. C. *J. Chem. Soc., Perkin Trans. 1* **1972**, 699.

Preparation of 1-Hydroxy-8-(methylthio)naphthalene (5b) and 1-Hydroxy-2-(methylthio)naphthalene (6b). The dianion of **4** (2 mmol), generated as shown in the general procedure, was quenched with dimethyl disulfide (1 mL), dissolved in 1.5 mL of THP, and then stirred for 30 min. Standard extractive workup (ether) yielded a crude oily material, which was purified by chromatography on a short-path silica gel column (CH_2Cl_2–hexane) and then separated on preparative silica gel plates (CH_2Cl_2–hexane, 2:5), thus furnishing **5b**, **6b**, and **7b** in 50%, 19%, and 1% yield, respectively.

5b: yellow oil; bp 120 °C (10^{-3} mmHg); IR (film) 3380, 2930, 1565, 1255, 820, 760 cm^{-1}; ^1H NMR δ 7.84–7.00 (m, 7 H), 2.48 (s, 3 H); EIMS, *m/e* (relative abundance) 190 (M^+, 100), 175 (52), 147 (49), 115 (19), 102 (13), 69 (12). Anal. Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.29. Found: C, 69.85; H, 5.20.

6b: yellow oil; bp 70 °C (10^{-3} mmHg); IR (film) 3380, 2920, 1565, 1380, 1260, 1070, 880, 800 cm^{-1}; ^1H NMR δ 8.18 (m, 1 H, H8), 7.80–7.20 (m, 6 H), 2.33 (s, 3 H); EIMS, *m/e* (relative abundance) 190 (M^+, 100), 175 (69), 147 (32), 115 (24), 102 (15), 69 (17), 63 (20). Anal. Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.29. Found: C, 69.24; H, 5.19.

Attempted Preparation of 1-Hydroxy-8-methylnaphthalene (5c) and 1-Hydroxy-2-methylnaphthalene (6c). 1-Naphthol (**4**) (2 mmol) was first treated with *t*-BuLi as illustrated in the general procedure and then quenched with methyl iodide (1.84 g) dissolved in THP (3 mL). The usual extractive workup (ethyl acetate) furnished an unseparable mixture, which was shown (GC/MS) to contain two monomethyl derivatives and one dimethyl derivative, as well as starting material in a 2:10:1:7 ratio.

Preparation of 5-(Methylthio)-1,4-naphthoquinone (8b). A methanolic solution (9 mL) of **5b** (0.21 g) was added all at once to 10 mL of a buffered solution (pH 6) of Fremy's salt (0.6 g). The mixture was vigorously stirred for 15 min and then extracted with ethyl acetate (7 × 25 mL). The extracts were washed with brine and water and then dried over anhydrous Na_2SO_4. Removal of the solvent furnished crude **8b**, which gave crystals from methanol (89% yield): mp 200–201 °C; IR (KBr) 1655, 1640, 1600, 1565, 1325, 1285, 1135, 1075, 770 cm^{-1}; ^1H NMR δ 7.95–7.60 (m, 3 H), 6.95 (d, J = 10.2 Hz, 1 H), 6.92 (d, J = 10.2 Hz, 1 H), 2.51 (s, 3 H); EIMS, *m/e* (relative abundance) 204 (M^+, 60), 190 (34), 189 (76), 187 (34), 171 (19), 147 (14), 115 (29), 89 (17), 75 (29), 45 (17), 44 (100). Anal. Calcd for $C_{11}H_8O_2$: C, 64.69; H, 3.95; S, 15.69. Found: C, 64.58; H, 4.12; S, 15.86.

Preparation of 2-(Methylthio)-1,4-naphthoquinone (9b). A cooled (0 °C) solution of **6b** (0.105 g) in methanol (5 mL) was treated with 20 mL of a buffered solution of Fremy's salt (2.5 g), as above. The solution was left to stir for 60 min and then worked up as usual. The organic extracts (ethyl acetate), once washed with brine and water, were evaporated in vacuo, thus yielding 0.855 g (70%) of **9b**, which sublimed at 98 °C (10^{-3} mmHg): mp 185–186 °C (benzene–ethanol) (lit.[20] mp 185–186 °C); IR (KBr) 1660, 1635, 1580, 1545, 1290, 1290, 1120, 1090, 1070, 1020, 860, 800, 775 cm^{-1}; ^1H NMR δ 8.16–8.03 (m, 4 H), 6.57 (s, 1 H)8 2.38 (s, 3 H); EIMS, *m/e* (relative abundance) 204 (M^+, 100), 203 (31), 189 (80), 176 (31), 147 (12), 143 (13), 133 (18), 104 (29), 89 (40), 76 (65), 50 (45).

Preparation of 1-(Methylthio)anthrone (11) and 1-(Methylthio)-9,10-anthraquinone (12). Direct lithiation of commercial anthrone **10** (0.78 g, 4 mmol) was carried out as illustrated in the general procedure. The resulting paste was cooled to 0 °C and, subsequently, treated with dimethyl disulfide (0.75 g, 8 mmol). After 10 min the resulting mixture was worked up as usual. Column chromatography (silica gel, hexane–chloroform, 9:1) of the crude solid furnished 0.443 g of an easily oxidizable material, which on further chromatography provided 0.152 g of **11** and 0.100 g of **12**.

11: orange solid; mp 138–140 °C; IR (KBr) 1630, 1595, 1460, 1385, 1320, 1280, 930, 900, 810, 740, 710 cm^{-1}; ^1H NMR δ 2.46 (s, 3 H), 4.38 (s, 2 H), 7.10–7.60 (m, 6 H), 8.31 (m, 1 H, H8). An analytically pure sample of **11** could not be obtained.

12: orange solid; mp 196–8 °C; IR (KBr) 1660, 1560, 1410, 1330, 1310, 1260, 1230, 1155, 1130, 965, 950, 800 cm^{-1}; ^1H NMR (200 MHz) δ 2.53 (s, 3 H), 7.62 (dd, J = 8.2, 1.6 Hz, 1 H, H2), 7.70 (dd, J = 8.2, 7.2 Hz, 1 H, H3), 7.77 (ddd, J = 8.2, 7.2, 1.6 Hz, 1 H, H6), 7.79 (ddd, J = 8.2, 7.2, 1.6 Hz, 1 H, H7), 8.12 (dd, J = 7.2, 1.6 Hz, 1 H, H4), 8.24 ddd, J = 7.2, 1.6, 0.5 Hz, 1 H, H8), 8.32 (ddd, J = 7.2, 1.6, 0.5 Hz, 1 H, H5); EIMS, *m/e* (relative abundance) 254 (M^+, 54), 241 (6), 240 (15), 239 (100), 238 (9), 237 (45), 221 (14), 183 (5), 165 (7), 152 (7); exact mass calcd for $C_{15}H_{10}O_2S$ 254.0402 (M^+), found 254.0380.

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Registry No. 1, 135-19-3; **2a**, 581-71-5; **2b**, 116130-48-4; **2c**, 17324-04-8; **3**, 483-55-6; **4**, 90-15-3; **4** (dimethyl deriv), 40529-54-2; **5a**, 35689-26-0; **5b**, 116130-50-8; **5c**, 32849-41-5; **6b**, 90033-53-7; **6c**, 7469-77-4; **7a**, 116130-49-5; **7b**, 116130-51-9; **8b**, 116130-52-0; **9b**, 26037-60-5; **10**, 90-44-8; **11**, 116130-53-1; **12**, 2687-50-5; 1,3-$(OH)_2C_6H_4$, 108-46-3.

Epimerization and Stereoselectivity in the Diels–Alder Reaction of Monosubstituted Dienophiles

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Introduction

The Diels–Alder reaction between 1-substituted 1,3-butadiene and monosubstituted dienophiles can give two stereoisomers, endo and exo. Generally, the endo isomer is kinetically preferred and the exo isomer is thermodynamically more stable; however, exceptions to this generalization are known.[1] Epimerization is usually not observed under mild conditions for either the thermal or Lewis acid catalyzed reactions.[2-7] More vigorous reaction conditions in the presence of a strong base are needed to initiate conversion to the more stable exo stereoisomer.[2,3] In our investigation of the stereoselectivity in the Diels–Alder reaction between *trans*-1,3-pentadiene (piperylene) and acrolein, a rapid epimerization at room temperature was unexpectedly observed in the presence of a Lewis acid.[8] To understand the scope of this phenomenon, we initiated

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