1,7- and 1,8-Directed Lithiations of 1-Indanol and 1-Tetralol

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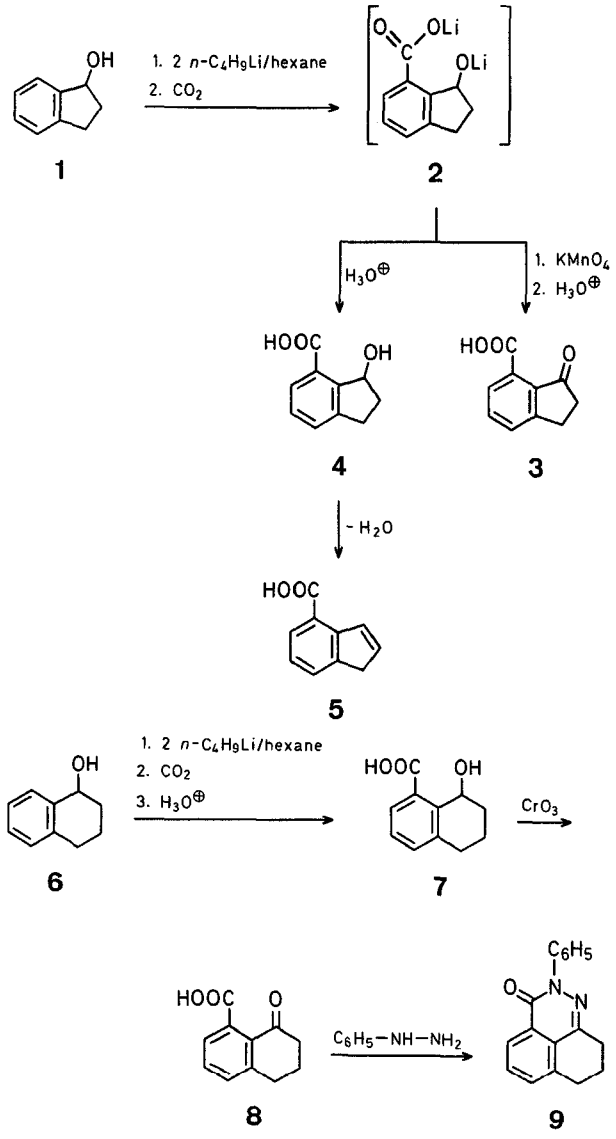
Lithiations at positions α or β to heteroatoms have been known for almost fifty years and a review has been published recently on the work of the second half of this period[1]. Among metalations directed by oxygen atoms, those which occur α or β to ethers are very common and those β to alcohols are relatively rare[2]. Lithiations directed to positions ω to a hydroxy moiety are unknown, as far as the authors can determine, except for a few examples which involve a neighboring methoxy group[3] in addition to the alcohol.

We report here a facile and direct method for the lithiation of 1-indanol (**1**) and 1-tetralol (**6**) at the 7- or 8-positions (see **4** and **7**) in good yield. Since neither product has been reported in the literature, verification of their structures was necessary. 1-Indanol-7-carboxylic acid (**4**) was unstable in all but basic media: readily dehydrating to 1-indene-7-carboxylic acid (**5**). It was best to convert it (as the lithium salt, **2**) to the known 1-indanone-7-carboxylic acid[4] (**3**). 1-Tetralol-8-carboxylic acid (**7**) was oxidized to the ketocarboxylic acid, **8**, which formed a cyclic pyridazone derivative, **9**, on reaction with phenylhydrazine.



The Lithiation of 1-Indanol (1):

To a refluxing solution of 1-indanol (**1**; 12.88 g, 96 mmol) in dry hexane (300 ml) under a slow stream of argon gas is added dropwise during a 5 min period, a 2.5 molar solution of *n*-butyllithium in hexane (80.6 ml, 201.6 mmol) which is diluted with dry hexane (120 ml). The reaction mixture changes to a yellow then a deep red color and, finally, a yellow precipitate separates. After being heated to the reflux temperature for 90 min, the stirred mixture is cooled to 10 °C and dry carbon dioxide is bubbled through for 8 h, during which time the yellow precipitate changes to white. The reaction mixture is then stored at ambient temperature for about 16 h, after which it is diluted with water (200 ml) and extracted with ethyl acetate (3 × 50 ml). The organic extracts are combined and washed with water (6 × 80 ml or until the ethyl acetate/hexane solution becomes clear) and all of the aqueous portions (which contain the lithium salt, **2**) are pooled and used for either procedure A or B below. The ethyl acetate/hexane solution is dried with molecular sieves (4A) and the solvents removed by distillation under reduced pressure. On cooling, the oily residue crystallizes to a solid mass of recoved 1-indanol (**1**); yield: 5.84 g (45%); m.p. 53–54 °C (Ref.[5], m.p. 54 °C). This product is homogeneous on T.L.C. analysis (silica gel 60 plates, 16:3:1 benzene/ethyl acetate/acetic acid).

Procedure A; 1-Indanone-7-carboxylic Acid (3):

The aqueous solution of the lithium salt of 1-indanol-7-carboxylic acid (**2**) from above (assumed, from the amount of unrecovered 1-indanol, to contain 0.0525 mol of product) is cooled to 5 °C and then diluted with a solution of sodium hydroxide (1.83 g, 0.046 mol) in water (15.2 ml). The resultant solution is stirred and maintained below 10 °C while a solution of potassium permanganate (20.74 g, 0.131 mol) in water (387 ml) is added dropwise during a 30 min period. After further stirring for 3 h in an ice-water bath, the mixture is filtered through a cake of Celite. The filtrate is adjusted to pH 2.0 with 6 normal sulfuric acid and a yellow solid which precipitates is collected by filtration. This filtrate is extracted with ethyl acetate (5 × 70 ml), the organic phase is washed with water, dried, and the solvent removed by distillation under reduced pressure. The residual oil crystallizes during storage at room temperature. This product is combined with that obtained by filtration to give 1-indanone-7-carboxylic acid (**3**); total yield: 5.76 g (62% from **2**); m.p. 159–161 °C (Ref.[4], m.p. 159.5–161.5 °C).

$C_{10}H_8O_3$	calc.	C 68.17	H 4.58
(176.2)	found	67.89	4.61

I.R. (Nujol): ν = 2500 (bonded OH); 1700 (ketone); 1640 (carboxyl); 1280; 760 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 3.05 (m, 2H, CH_2); 3.3 (m, 2H, CH_2—C=O); 7.8 (m, 3H$_{arom}$); 8.35 ppm (m, 1H, COOH).

^{13}C-N.M.R. ($CDCl_3$): δ = 26.3 (C-3); 36.1 (C-2); 129.7–133.3 (C-4, 5, 6, 9); 136.0 (C-7); 158.4 (C-8); 164.7 (COOH); 212.3 ppm (C-1).

Procedure B; 1-Indanol-7-carboxylic Acid (4) and 1-Indene-7-carboxylic Acid (5):

The aqueous solution of **2** from the lithiation of 1-indanol (see above) is assumed, from the amount of unrecovered 1-indanol, to contain 0.0525 mol of **2**. It is adjusted to pH 2.0 with 6 normal hydrochloric acid while being stirred in an ice-water bath. A solid precipitates which is recrystallized from dichloromethane and identified as 1-indene-7-carboxylic acid (**5**); yield: 4.32 g (51% from **2**); m.p. 156–157 °C.

$C_{10}H_8O_2$	calc.	C 74.98	H 5.03
(160.2)	found	74.17	5.08

I.R. (Nujol): ν = 2500–3300 (OH and CH); 1690 (C=O); 1250; 760 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 3.6 (d, 2H, CH_2); 7.0–8.0 (m, 5H, CH=CH and H$_{arom}$); 10.3 ppm (br s, 1H, COOH).

^{13}C-N.M.R. ($CDCl_3$): δ = 38.5 (CH_2); 122.2–146.7 (CH=CH and C$_{arom}$); 169.0 ppm (COOH).

The filtrate left from the isolation of product **5**, above, is extracted with ethyl acetate (3 × 20 ml), and the pooled organic solutions are washed and dried, and the solvent removed by distillation under reduced pressure. The residual viscous oil (1.23 g) is homogeneous by T.L.C. (silica gel 60 plates, 16:3:1 benzene/ethyl acetate/acetic acid) and crystallizes during storage of a dichloromethane solution to give 1-indanol-7-carboxylic acid (**4**); yield: 1.23 g (13% from **2**); m.p. 128.0–128.5 °C.

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$C_{10}H_{10}O_3$	calc.	C 67.40	H 5.66
(178.2)	found	66.99	5.57

I.R. (Nujol): ν = 3300 (OH); 2600 (OH bonded); 1650 (C=O), 1260, 760 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 2.3 (m, 2H, CH_2); 3.0 (m, CH_2); 5.6 (t, 1H, CH—OH); 7.3–8.1 (m, 3H$_{arom}$); 11.3 ppm (br, 1H, OH).

^{13}C-N.M.R. ($CDCl_3$): δ = 30.2 (C-3); 32.4 (C-2); 75.4 (C-1); 125.8–130.5 (C-4, 5, 6, 9); 145.4 (C-7); 146.8 (C-8); 171.8 ppm (COOH).

The Lithiation of 1-Tetralol (6); 1-Tetralol-8-carboxylic Acid (7):

A solution of 1-tetralol (**6**; 14.23 g, 96 mmol) in dry hexane (300 ml) is heated to the reflux temperature while a slow stream of argon gas is passed through the apparatus. A dropping funnel is charged with tetramethylethylenediamine (22.33 g, 192 mmol), dry hexane (30 ml), and a 2.4 molar solution of *n*-butyllithium in hexane (80 ml, 192 mmol). The resultant yellow mixture is added dropwise during a 4 min period to the refluxing tetralol solution. An orange-red precipitate separates and heating is continued for 2 h following the addition. The mixture is then stirred and cooled in an ice bath while dry carbon dioxide is bubbled through for 8 h. The reaction mixture is stored at room temperature for 16 h, after which it is diluted with water (200 ml), cooled in an ice bath, and adjusted to pH 2.0 with 1 normal hydrochloric acid. The aqueous layer is extracted with ethyl acetate (6 × 100 ml) and the pooled organic solutions (ethyl acetate and hexane) are extracted with 1 normal sodium hydrogen carbonate solution (6 × 80 ml). The organic phase is washed with water, dried with molecular sieves (4 A), and the solvents removed by distillation under reduced pressure. The residual oil is homogeneous by T.L.C. (silica gel 60 plates, benzene) and the R_f is identical with that of 1-tetralol (**6**); yield: 5.03 g (35% recovery).

The basic aqueous solution from above is stirred in an ice bath and adjusted to pH 2.0 with 1 normal hydrochloric acid. A pale yellow solid precipitates (6.15 g) and is collected by filtration. The filtrate is extracted with ethyl acetate (4 × 50 ml), the organic extract is washed, dried, and the solvent removed by distillation in vacuo. The residual oil (3.76 g) crystallizes on cooling. Both crystalline products are identical and homogeneous by T.L.C. (silica gel 60 plates, 70:29:1 hexane/ethyl acetate/acetic acid) and identified as 1-tetralol-8-carboxylic acid (**7**); total yield: 9.91 g (83% based on **6** reacted); m.p. 133–134 °C.

$C_{11}H_{12}O_3 \cdot 0.5\,H_2O$	calc.	C 65.65	H 6.51
(402.4)	found	65.76	6.50

I.R. (Nujol): ν = 3420 (free OH); 3200 and 2640 (bonded OH); 1680 (COOH); 1275; 1145; 965 cm^{-1}.

^{1}H-N.M.R. (CD_3COCD_3): δ = 2.0 (m, 4H, CH_2CH_2); 2.85 (m, 2H, CH_2); 5.05 (m, 1H, CH—OH); 5.7 (br, 1H, OH); 7.2–7.9 ppm (m, 3H$_{arom}$).

^{13}C-N.M.R. (CD_3SOCD_3): δ = 17.5 (C-3); 29.7 (C-4); 31.6 (C-2); 62.7 (C-1); 126.7, 127.4, 132.3 (C-5, 6, 7); 133.1, 137.8, 138.7 (C-8, 9, 10); 170.6 ppm (COOH).

1-Tetralone-8-carboxylic Acid (8):

A solution of 1-tetralol-8-carboxylic acid (**7**; 1.0 g, 5.2 mmol) in glacial acetic acid (10 ml) is obtained by heating the stirred mixture to 35 °C. A second solution of chromic acid anhydride (0.52 g, 5.2 mmol), water (5 ml), and glacial acetic acid (20 ml), is added dropwise to the first during a 10 min period while the temperature is maintained below 50 °C. The resultant mixture is stirred for 3.5 h at 45 °C after which most of the water and acetic acid are removed by distillation in vacuo. The concentrate is then diluted with water (50 ml) and extracted with ethyl acetate (4 × 50 ml). The organic phase is washed, dried, and the solvent removed by rectification under reduced pressure. The residual oil (0.7 g) crystallizes during storage at room temperature and is recrystallized from dichloromethane to give **8** homogeneous by T.L.C. (silica gel 60 plates, 16:3:1 benzene/ethyl acetate/acetic acid); yield: 0.57 g (58%); m.p. 168–170 °C.

$C_{11}H_{10}O_3$	calc.	C 69.46	H 5.30
(190.2)	found	69.00	5.23

I.R. (Nujol): ν = 2560 and 2650 (OH); 1680 (carboxyl C=O); 1700 (ketone C=O); 1590; 1190 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 2.1 (m, 2H, CH_2); 2.7 (m, 2H, CH_2); 3.0 (t, 2H, CH_2—C=O); 7.4 (m, 3H$_{arom}$); 11.2 ppm (br, 1H, COOH).

^{13}C-N.M.R. ($CDCl_3$): δ = 22.8 (C-3); 29.9 (C-4); 39.0 (C-2); 126.4, 130.6, 132.8 (C-5, 6, 7); 130.0, 134.0, 145.3 (C-8, 9, 10); 175.0 (COOH); 197.8 ppm (C=O).

If the oxidation of **7** is attempted under alkaline conditions (4.0 mmol sodium hydroxide in 15 ml water) using 11.2 mmol of potassium permanganate (4–20 °C reaction temperature; 45 min reaction period), it proceeds further than with chromium trioxide and produces a product whose structure is assumed to be that of *2-hydroxy-1-tetralone-8-carboxylic acid*; yield: 39%; m.p. 183–185 °C (from ethyl acetate).

$C_{11}H_{10}O_4$	calc.	C 64.07	H 4.89
(206.2)	found	63.90	5.12

I.R. (Nujol): ν = 3500 (OH); 2620, 2685 (bonded OH); 1700 (ketone C=O); 1680 (carboxyl C=O); 1580, 1260 cm^{-1}.

^{1}H-N.M.R. (CD_3SOCD_3): δ = 2.1–3.1 (br m, 4H, CH_2CH_2); 5.5 (t, 1H, CH—OH); 7.4–8.1 ppm (m, 3H$_{arom}$).

^{13}C-N.M.R. (CD_3SOCD_3): δ = 30.0, 33.0 (C-3, 4); 61.8 (C-2); 127.9, 129.1, 134.6 (C-5, 6, 7); 132.1, 132.7, 144.7 (C-8, 9, 10); 169.0 (COOH); 197.2 ppm (C=O).

3-Oxo-2-phenyl-2,3,8,9-tetrahydro-7*H*-benzo[*d,e*]cinnoline (9):

The procedure described here is that used for the preparation of the pyridazone of xanthone-1-carboxylic acid[6]. A mixture of **8** (0.1 g, 0.52 mmol), phenylhydrazine (1.0 ml), and pyridine (5.0 ml) is heated to the reflux temperature for 15 min. The reaction mixture is then poured into water (50 ml) and stirred for 15 min. A yellow precipitate separates and is collected by filtration: yield: 0.13 g (94%). It is recrystallized from 1:1 ethanol/petroleum ether (b.p. 30–60 °C); m.p. 138–139 °C.

$C_{17}H_{14}N_2O$	calc.	C 77.84	H 5.38	N 10.68
(262.3)	found	77.38	5.30	10.71

I.R. (Nujol): ν = 1660 (C=O); 1610 (C=N); 1310; 760 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 2.1, 2.9 (m, 6H, $CH_2CH_2CH_2$); 7.6 ppm (m, 8H$_{arom}$).

^{13}C-N.M.R. ($CDCl_3$): δ = 23.0 (C-8); 29.2, 30.5 (C-7, 9); 125.1–171.6 (at least 10 aromatic peaks); 181.0 (C=O); 217.0 ppm (C=N).

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[1] H. W. Gshwend, H. R. Rodriguez, *Org. React.* **26**, 1 (1979).

[2] For some examples see: N. Meyer, D. Seebach, *Angew. Chem.* **90**, 563 (1978); *Angew. Chem. Int. Ed. Engl.* **17**, 521 (1978).
D. W. Slocum, D. I. Sugarman, *Adv. Chem. Ser.* **130**, 222 (1974).

[3] H. O. House, C. B. Hudson, E. J. Racah, *J. Org. Chem.* **37**, 989 (1972).
M. Uemura, S. Tokuzama, T. Sakan, *Chem. Lett.* **1975**, 1195.

[4] R. H. Callighan, M. F. Tarker, Jr., M. H. Wilt, *J. Org. Chem.* **27**, 765 (1962).

[5] R. Weissberger, *Ber. Dtsch. Chem. Ges.* **44**, 1436 (1911).

[6] N. Campbell, S. R. McCallum, D. J. Mackenzie, *J. Chem. Soc.* **1957**, 1922.