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Supplementary Material Available: Further details of the preparation of and/or spectroscopic data for compounds **11**, **13**, **15–18**, **19b,c**, **20b,c**, **21b,c**, **22a–c**, **23a–c**, **24a–c**, **25a–c**, **26a–c**, **27b,c**, **36**, **38–41**, **42a,b**, **43a**, **44a,b**, **45a,b**, **46–57**, **58a,c,d**, **60–62**, **69b–d**, **70b–d**, **71b–d**, **72–74**, **78**, **80**, **and 81** (16 pages) Ordering information is given on any current masthead page.

Syntheses of 5-, 7-, and 8-Methoxy-3-methyl-2-tetralone

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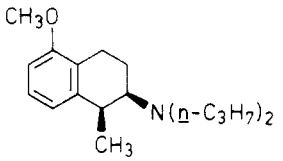
Two efficient syntheses of 5-methoxy- and 8-methoxy-3-methyl-2-tetralone and the synthesis of the 7-methoxy isomer via a different route are described. Also reported is the synthesis of 8-methoxy-3,3-dimethyl-2-tetralone. The regioselectivity of lithium carbanion formation in 1,6-, 1,7-, and 2,7-dihydroxynaphthalene is discussed. The latter compound undergoes dimetalation more easily than the other isomers.

Several 2-aminotetralin derivatives possess potent and selective dopamine- or 5-hydroxytryptamine-receptor-stimulating abilities.[1,2] Recently, it has been demonstrated that the introduction of methyl substituents, in the C1 or C2 positions of certain 2-aminotetralins changes the pharmacological profile.[3] Notably, (1*S*,2*R*)-5-methoxy-1-methyl-2-(di-*n*-propylamino)tetralin (**1**) appears to be



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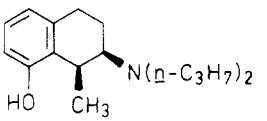

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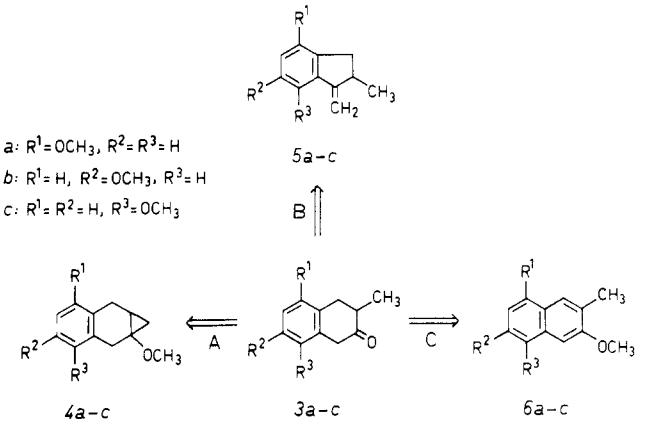
a dopamine-receptor antagonist with selectivity for dopamine autoreceptors[3a,4] and (1*S*,2*R*)-8-hydroxy-1-methyl-2-(di-*n*-propylamino)tetralin (**2**) is a highly potent 5-hydroxytryptamine-receptor agonist.[5] These interesting results provide impetus for the synthesis of C3-methyl-substituted 2-aminotetralin analogues. Access to the corresponding 3-methyl-2-tetralones would enable the preparation of the desired 2-amino-3-methyltetralins.[6]

Scheme I



At least four synthetic routes to C3-alkyl-substituted 2-tetralones have been reported previously: (a) 2-Tetralones can be carboxylated regiospecifically in the C3 position by use of magnesium methoxy carbonate.[7] Alkylation of the resulting β-keto esters followed by hydrolysis of the ester function and, finally, decarboxylation gives the target compounds. This strategy has been used by Cannon et al.[8] in their synthesis of some *trans*-6,7-dihydroxy-1,2,3,4,4a,5,10,10b-octahydrobenzo[*g*]quinolines. However, the carboxylation procedure and the removal of the carboxyl group are only moderately efficient reactions, thus making this approach less appealing. (b) Protection

(1) For recent review on dopamine-receptor agonists, see: Kaiser, C.; Tikam, J. *Med. Res. Rev.* **1985**, *5*, 145–229. Cannon, J. G. *Prog. Drug Res.* **1985**, *29*, 303–414.

(2) For recent reviews on 5-hydroxytryptamine-receptor agonists, see: Arvidsson, L.-E.; Hacksell, U.; Glennon, R. A. *Prog. Drug Res.*, in press. Glennon, R. A. In *CRC Handbook of Stereoisomers: Drugs in Psychopharmacology*; Smith, D. F., Ed.; CRC: Boca Raton, FL, 1984; pp 327–368.

(3) (a) Johansson, A. M.; Arvidsson, L.-E.; Hacksell, U.; Nilsson, J. L. G.; Svensson, K.; Hjorth, S.; Clark, D.; Carlsson, A.; Sanchez, D.; Andersson, B.; Wikström, H. *J. Med. Chem.* **1985**, *28*, 1049–1053. (b) Hacksell, U.; Arvidsson, L.-E.; Johansson, A. M.; Nilsson, J. L. G.; Sanchez, D.; Andersson, B.; Lindberg, P.; Wikström, H.; Hjorth, S.; Svensson, K.; Carlsson, A. *Acta Pharm. Suec.* **1985**, *22*, 65–74.

(4) (a) Svensson, K.; Hjorth, S.; Clark, D.; Carlsson, A.; Wikström, H.; Andersson, B.; Sanchez, D.; Johansson, A. M.; Arvidsson, L.-E.; Hacksell, U.; Nilsson, J. L. G. *J. Neural Transm.* **1986**, *65*, 1–27. (b) Svensson, K.; Carlsson, A.; Johansson, A. M.; Arvidsson, L.-E.; Nilsson, J. L. G. *J. Neural Transm.* **1986**, *65*, 29–38. (c) Svensson, K.; Johansson, A. M.; Magnusson, T.; Carlsson, A. *Naunyn-Schmiedeberg's Arch. Pharmacol.*, in press.

(5) Arvidsson, L.-E. *Acta Univ. Ups., Abstr. Uppsala Diss., Fac. Pharm.* **1985**, *109*, 1–70.

(6) 2-Aminotetralins are available from 2-tetralones by a variety of synthetic methods. See, for example: Hacksell, U.; Svensson, U.; Nilsson, J. L. G.; Hjorth, S.; Carlsson, A.; Wikström, H.; Lindberg, P.; Sanchez, D. *J. Med. Chem.* **1979**, *22*, 1469–1475.

(7) (a) Pelletier, S. W.; Parthasarathy, P. C. *Tetrahedron Lett.* **1964**, 103–106. (b) Pelletier, S. W.; Chappel, R. L.; Parthasarathy, P. C.; Lewin, N. *J. Org. Chem.* **1965**, *31*, 1747–1752. (c) Beres, J. A.; Cannon, J. G. *Synthetic Commun.* **1979**, *9*, 819–824.

(8) Cannon, J. G.; Lee, T.; Beres, J. A.; Goldman, H. D. *J. Heterocyclic Chem.* **1980**, *17*, 1633–1636.

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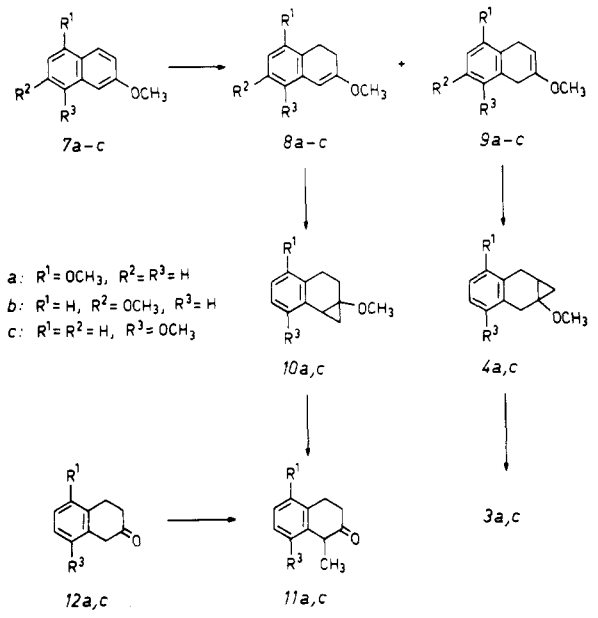
Scheme II



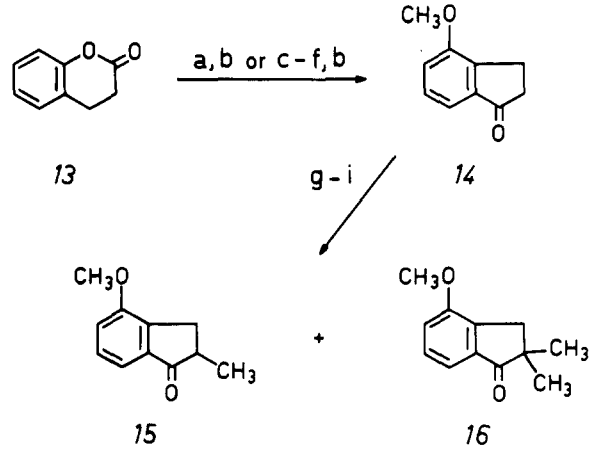
of the reactive benzylic methylene group of a 2-tetralone permits selective alkylation at the less acidic C3-position. This approach was recently used by Nordmann and Petcher[9] in their synthesis of some novel octahydrobenzo[*g*]quinolines. The introduction (82% yield) and the removal (71% yield) of the protective group (diphenyl dithioketal) do, however, decrease the total yield in the reaction sequence. (c) Formation of the dianion of a 1-methoxycarbonyl-2-tetralone permits alkylation in the C3 position.[10] This reaction was recently used for facile introduction of a C3-allyl substituent in 2-tetralone and 5-methoxy-2-tetralone.[10] (d) Condensation of 2-(phenylsulfonylmethyl)benzyl bromide derivatives with the anion of monoalkyl-substituted malonic ester proceeds regioselectively to give C3-substituted 2-tetralones.[11]

A retrosynthetic analysis devising three alternative synthetic routes (A–C) to C3-methylated 2-tetralones is shown in Scheme I. Route A is based on a regioselective sodium reduction of a 2-methoxy-substituted naphthalene followed by cyclopropanation of the resulting enol ether and acid-catalyzed ring opening. Recently, this approach was reported to provide 5-methoxy-3-methyl-2-tetralone (**3a**) in more than 50% yield from 1,6-dihydroxynaphthalene.[12] Routes B and C represent synthetic approaches to C3-methyl-substituted 2-tetralones, which, to the best of our knowledge, have not been evaluated. In the present report we discuss the evaluation of routes A–C, which has resulted in facile synthetic methods for 5-methoxy-, 7-methoxy-, and 8-methoxy-3-methyl-2-tetralone (compounds **3a**, **3b**, and **3c**, respectively).

Results and Discussion

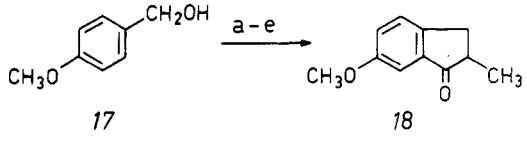
Route A. This sequence consists of four synthetic steps: Dimethoxynaphthalenes, readily obtained in 90–95% yield, by base-promoted methylation (dimethyl sulfate or methyl iodide) of the corresponding commercially available dihydroxynaphthalenes, are converted to dihydro derivatives via dissolved metal reduction. The resulting nonconjugated enol ethers are cyclopropanated, and acid-catalyzed

Scheme III[a]



[a] (a) $AlCl_3$/NaCl, Δ; (b) $(CH_3)_2SO_4$, K_2CO_3; (c) NaOH, PhCOCl; (d) $SOCl_2$; (e) $AlCl_3$, CH_2Cl_2; (f) NaOH; (g) pyrrolidine, H^+; (h) CH_3I; (i) H^+, H_2O.

Scheme IV[a]



[a] (a) $SOCl_2$; (b) $CH_3CH(COOC_2H_5)_2$, $NaOC_2H_5$; (c) KOH, Δ; (d) $SOCl_2$; (e) $AlCl_3$.

ring opening affords the desired 3-methyl-2-tetralones (Scheme II). The key step is the regioselective formation of compounds **9a–c**. The initially formed enol ethers are readily isomerized by base catalysis to the conjugated isomers **8a–c**.[12] However, the regioselective formation of **9a** was accomplished by careful choice of the reaction conditions; use of granulated sodium in 2-propanol produced **9a** in high yield and high isomeric purity.[12] Reduction of **7c** using these reaction conditions proved less consistent; isomeric ratios of **9c** to **8c** varied from 90:10 to 80:20. Sodium reduction of **7b** produced **9b** and **8b** in a 88:12 ratio when 2-propanol was used as solvent. Use of ethanol in this latter reaction resulted in overreduced products and a smaller isomeric ratio of **9b** to **8b**. No attempt was made to prepare **3b** by route A.

To establish unambiguously the structures of the enol ethers and the cyclopropanated derivatives, mixtures of **8** and **9** were converted to isomerically pure **8** by treatment with potassium hydride in tetrahydrofuran. ^1H NMR spectra of regioisomers **8** and **9** differ considerably when recorded in deuterochloroform. The vinylic protons of **9** appear 0.7 ppm upfield of the resonances due to the vinylic protons of **8**.[12] These differences were utilized when calculating relative amounts of **8** and **9** from ^1H NMR spectra of crude product mixtures.

Simmons–Smith reaction[13] of **8a** and **9a** using a heterogeneous procedure (diiodomethane and a zinc–copper couple[14]) afforded only moderate yields of cyclopropanated derivatives **10a** and **4a**, respectively. However, use of a homogeneous modification[15] (diiodomethane and diethylzinc in benzene) considerably improved the cyclopropanation reaction; for example, enol ether **9a** was

(9) Nordmann, R.; Petcher, T. J. *J. Med. Chem.* **1985**, *28*, 367–375.
(10) Aristoff, P. A.; Johnson, P. D.; Harrison, A. W. *J. Am. Chem. Soc.* **1985**, *107*, 7967–7974.
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(14) Le Goff, E. *J. Org. Chem.* **1964**, *29*, 2048–2050.
(15) Ito, Y.; Fujii, S.; Nakatsuka, M.; Kawamoto, F.; Saegusa, T. *Org. Synth.* **1979**, *59*, 113–122.

Table I. Product Distributions in Methylations of Dimethoxynaphthalene Anions[a]

dimethoxynaphthalene	additive	temp,[b] °C	reaction time,[b] h	products (yield,[c] %)		
7a	TMEDA[d]	25	12	**6a** (80)	**19a** (19)	
7a	–	25	4	**6a** (48)	**19a** (14)	
7a	–	−15	12	**6a** (84)	**19a** (12)	
7b	–	25	12	**6b** (73)	**19b** (15)	**20** (3)
7b	*e*	25	12	**6b** + **19b** (22)		**20** (72)
7c	TMEDA	25	12	**6c** (98)		
7c	–	25	12	**6c** (98)		

[a] Reactions were performed as described in the Experimental Section. [b] Conditions used for formation of carbanions. [c] Determined from ^{1}H NMR spectra and GC of crude reaction products. Isolated yields are reported in Experimental Section. [d] Tetramethylethylenediamine. [e] Four equivalents of butyllithium were used.

converted to **4a** in 94% yield. The availability of regioisomers **4** and **10** allowed unambiguous assignments of their structures.

Acid-catalyzed ring opening[16] of compounds **4a** and **4c** gave the target compounds **3a** and **3c** in high yields. Ring opening of the isomeric cyclopropane derivatives **10a** and **10c** gave the 1-methyl-2-tetralones **11a** and **11c**, which have been previously prepared by enamine alkylation of 2-tetralones **12a** and **12c**, respectively (Scheme I).[17,18]

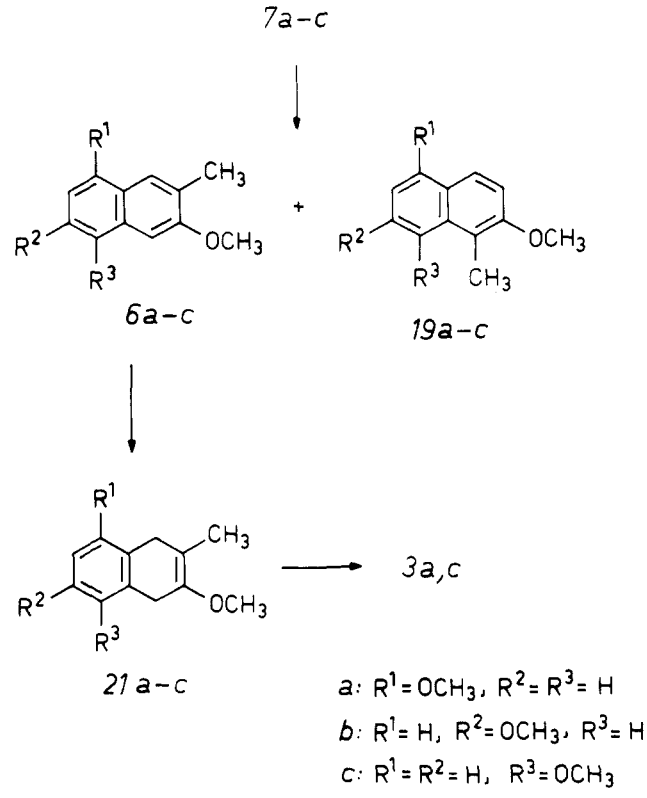
Route B. The thallium(III)-promoted ring expansion of cyclic aralkyl ketones, which was developed by Taylor et al.,[19] forms the basis for route B. The required 2-methyl-1-indanones **15** and **18** were prepared as shown in Schemes III and IV, respectively; 4-methoxy-1-indanone (**14**) is available from dihydrocoumarin (**13**) in approximately 60% yield using either a two-step[20] or a five-step synthetic procedure,[21] the latter being more convenient for large-scale experiments. Formation of the pyrrolidine enamine of **14** was accomplished by azeotropic water removal. The subsequent methylation resulted in formation of the dimethylated **16** in addition to the desired monomethylated **15**.[22] Separation of **15** from unchanged starting material and from byproduct **16** proved difficult and pure **15** was obtained in only 22% yield as calculated from **14** (Scheme III). The synthesis of 6-methoxy-2-methyl-1-indanone (**18**) was more facile (Scheme IV); the yield of **18** from 4-methoxybenzyl alcohol was 70%.

Indanones **15** and **18** were converted to exocyclic methylene derivatives **5a** and **5b** in more than 90% yield by reaction with triphenylphosphonium methylide in dimethyl sulfoxide. However, the subsequent thallium-mediated ring expansion consistently proceeded in less than 60% yield. No attempt was made to prepare **3c** by route B.

Route C. The third sequence, which consists of four synthetic steps, involves (a) regioselective methylation of a dimethoxynaphthalene, (b) dissolved-metal reduction, and (c) hydrolysis of the enol ether thus formed (Scheme V).

Previously, **6c** has been prepared in 52–72% yield from the lithium anion of **7c** (generated at 36 °C with butyllithium in diethyl ether)[23] and reaction of the lithium anion

Scheme V



of **7a** (generated with butyllithium and tetramethylethylenediamine in tetrahydrofuran at 25 °C) with carbon dioxide, has been reported to produce 75% of 3,8-dimethoxynaphthalene-2-carboxylic acid and two minor unidentified isomers.[24,25]

Table I summarizes the results obtained after methylation of lithium anions of dimethoxynaphthalenes **7a–c**. The presence of tetramethylethylenediamine does not appear to affect the regiochemistry of the reaction. Ortho lithiation of **7c** seems to be regiospecific; treatment of the lithium anion of **7c** with iodomethane, consistently produced isomerically pure **6c**. Anion formation in **7a** and **7b** was found to be less regioselective; isomers **19a** and **19b** were always produced in addition to the dominating isomers **6a** and **6b**. Although excess butyllithium was used, no dimethylated byproducts were detected in the methylations of **7a** and **7c**. However, in the reactions of **7b**, a small amount of dimethylated product(s) was formed in the absence of excess butyllithium. Treatment of **7b** with

(16) (a) Wenkert, E.; Berges, D. A. *J. Am. Chem. Soc.* **1967**, *89*, 2507–2509. (b) Wenkert, E.; Mueller, R. A.; Reardon, E. J., Jr.; Sathe, S. S.; Scharf, D. J.; Tosi, G. *Ibid.* **1970**, *92*, 7428–7436.

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(19) Taylor, E. C.; Chiang, C.-S.; McKillop, A. *Tetrahedron Lett.* **1977**, 1827–1830.

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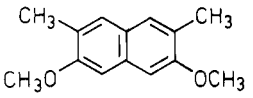
(22) Dialkylated products have been observed previously in enamine alkylations. See: House, H. O. *Modern Synthetic Reactions*; Benjamin: Menlo Park, CA, 1972, p 576.

(23) Barnes, R. A.; Bush, W. M. *J. Am. Chem. Soc.* **1959**, *81*, 4705–4709.

(24) Mander, L. N.; Pyne, S. P. *Aust. J. Chem.* **1981**, *34*, 1899–1911.

(25) For a discussion of ortho lithiations in anisoles and methoxynaphthalenes, see: Shirley, D. A.; Harmon, T. E.; Cheng, C. F. *J. Organomet. Chem.* **1974**, *69*, 327–344.

4 equiv of butyllithium followed by excess iodomethane allowed the isolation of 2,7-dimethoxy-3,6-dimethylnaphthalene (**20**). In contrast, **7c** did not produce dimethylated products under similar reaction conditions.



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The structural assignment of **6a** was based on the appearance of a singlet at δ 7.98 (due to C4–H) in its ^{1}H NMR spectrum;[26] in the spectrum of **7a** (1,6-dimethoxynaphthalene), the resonance due to the C8–H appears as a doublet at δ 8.20. The other methylated dimethoxynaphthalenes (**6b**, **6c**, **19a**, and **19b**) gave ^{1}H NMR spectra with complicated aromatic regions. Therefore, the structures of these compounds were assigned by use of ^{13}C NMR spectroscopy; calculated chemical shifts, based on well-established substituent-induced ^{13}C NMR chemical shifts,[27] were obtained for possible isomers and compared with experimental data. In addition, the structures of **6a** and **6c** were determined unambiguously by chemical correlation (vide infra).

Sodium reduction of **6a** and **6c** in ethanol produced the more substituted enol ethers **21a** and **21c** in high yields and the subsequent hydrolysis gave tetralones **3a** and **3c**, respectively (Scheme V). The facile access to enol ether **21c** was utilized for the preparation of 8-methoxy-3,3-dimethyl-2-tetralone (**23**, Scheme VI).

^{1}H NMR studies of crude reaction mixtures resulting from sodium reductions of **6b** indicated the presence of **21b** and 1,4-dihydro-6-methyl-2,7-dimethoxynaphthalene in a 2:3 ratio, and also overreduced products. These compounds were never isolated and no attempt was made to prepare **3b** by route C.

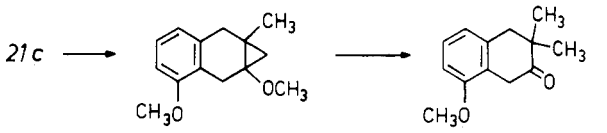
In conclusion, the pronounced stereoselectivity of the ortho lithiation of **7c** makes it possible to produce multigram quantities of **3c** in high yields (77%) from 1,7-dihydroxynaphthalene. Preparation of **3a** by route C also proceeds fairly well but synthesis of **3a** via route A (80% overall yield) is superior.

Experimental Section

General Comments. Dry THF was distilled from Na metal in the presence of benzophenone under dry argon. Pure KH was obtained by washing a 20% KH–oil suspension with several portions of pentane and finally drying the hydride in a stream of dry N_2. All other chemicals were used as received. Solutions were dried with $MgSO_4$. Melting points (uncorrected) were determined in open glass capillaries on a Thomas-Hoover apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL FX 90Q spectrometer at 25 °C, using $CDCl_3$ solutions referenced to internal Me_4Si. IR spectra were recorded on a Perkin-Elmer 157G spectrophotometer. Mass spectra were recorded at 70 eV on a LKB 9000 spectrometer using a direct insertion probe. GC was performed on a Varian 2700 instrument with a flame ionization detector. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F_{254} (0.2 mm), E. Merck. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden.

General Procedure for the Preparation of Dimethoxynaphthalene Derivatives. 1,7-Dimethoxynaphthalene (7c).[28]

Scheme VI



22 *23*

1,7-Dihydroxynaphthalene (97%; 200 g, 1.21 mol) was added to a 2 M NaOH solution (1800 mL, 3.6 mol) which had been previously purged with N_2. Dimethyl sulfate (528 g, 4.2 mol) was carefully added to the resulting, vigorously stirred, solution. After 1 h, additional portions of 5 M NaOH (600 mL) and dimethyl sulfate (188 g, 1.5 mol) were added. Throughout, the reaction temperature was kept between 17 and 21 °C by adjusting the rate of dimethyl sulfate addition and, when necessary, by use of an ice bath. After 1 h at room temperature, the reaction mixture was heated to reflux for 1 h. The cooled mixture was extracted with ether. The combined ether layers were washed with 5 M NaOH and with water. The ether extract was dried, filtered, and concentrated. Distillation afforded 219.2 g (96%) of pure **7c**: bp 102–105 °C/0.2 mmHg (lit.[28] 123–130 °C/0.4 mmHg).

1,6-Dimethoxynaphthalene (7a)[29] and **2,7-dimethoxynaphthalene (7b)**[30] were prepared by the same procedure.

Sodium Reduction of 7c To Yield 1,4-Dihydro-2,8-dimethoxynaphthalene (9c). To a vigorously stirred solution of **7c** (20 g, 106 mmol) in dry 2-PrOH (2000 mL) kept at gentle reflux under N_2 was rapidly added granulated Na[31] (56 g, 2.43 mol). After 35 min, heating was interrupted, and water (200 mL) and NH_4Cl (130 g, 2.43 mol) were added. The 2-PrOH was evaporated in vacuo. To the semisolid residue were added water and ether. The ether layer was separated, dried, filtered, and concentrated to give 19.73 g of a mixture of **9c** (90%) and **8c** (10%) which was used in further reactions without any purification.

9c: R_f 0.52 (ether/light petroleum 1:19); ^{1}H NMR δ 7.22–6.55 (m, 3 H), 4.82–4.69 (m, C3–H), 3.80, 3.60 (s's, OMe's), 3.58–3.20 (m, 4 H); ^{13}C NMR δ 156.92, 153.46 (C2, C8), 135.33, 122.73 (C4a, C8a), 126.31 (C6), 120.17 (C5), 106.73 (C7), 89.96 (C3), 55.03, 53.86 (OMe's), 29.59, 28.97 (C1, C4).

Sodium Reduction of 7a To Yield 1,4-Dihydro-2,5-dimethoxynaphthalene (9a). Compound **7a** (25.0 g, 0.13 mol) was reduced by the above procedure.[12] ^{1}H NMR indicated that the crude product (24.5 g) consisted of **8a** (9%) and **9a** (91%).

9a: R_f 0.51 (CH_2Cl_2); ^{1}H NMR δ 7.25–6.55 (m, 3 H), 4.78 (narrow m, C3–H), 3.75, 3.56 (s's, OMe's), 3.39 (narrow m, 4 H); ^{13}C NMR δ 156.89, 152.63 (C2, C5), 134.96 (C8a), 126.44 (C7), 123.16 (C4a), 120.51 (C8), 106.86 (C6), 90.37 (C3), 54.97, 53.80 (OMe's), 31.87, 24.34 (C1, C4).

Sodium Reduction of 7b To Yield 1,2-Dihydro-3,6-dimethoxynaphthalene (8b) and 1,4-Dihydro-2,7-dimethoxynaphthalene (9b). Compound **7b** (1.0 g, 5.3 mmol) was reduced by the above procedure. ^{1}H NMR indicated that the crude reaction mixture (0.95 g) consisted of **8b** (10%), **9b** [75%; ^{1}H NMR δ 7.10–6.82 (m, 1 H), 6.78–6.40 (m, 2 H), 4.80 (broad s, C3–H), 3.75, 3.59 (s's, OMe's), 3.40 (apparent s, 4 H)], and **1,2,3,4-tetrahydro-2,7-dimethoxynaphthalene** (15%).

Isomerization of a Mixture of 8c and 9c. Preparation of 1,2-Dihydro-3,5-dimethoxynaphthalene (8c). A solution of 5.5 g of a mixture of **9c** (53%, 15.3 mmol) and **8c** (47%, 13.6 mmol) in dry THF was carefully added to a suspension of KH (0.8 g, 20 mmol) in dry THF (100 mL) kept under N_2. The mixture was stirred at room temperature for 2 days and then quenched by dropwise addition of MeOH (5 mL) and then a saturated NH_4Cl solution (100 mL). The organic solvent was evaporated in vacuo. The residue was partitioned between water and ether. The ether layer was dried, filtered, and concentrated. Distillation of the residue gave 5.1 g (93%) of pure **8c**: bp 132–136 °C/2 mmHg; R_f 0.45 (ether/light petroleum 1:19); ^{1}H NMR δ 7.20–6.55 (m, 3

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H), 5.88 (broad s, C4–H), 3.81, 3.71 (s's, OMe's), 3.05–2.65 (m, 2 H), 2.50–2.20 (m, 2 H); ^{13}C NMR δ 159.76, 153.71 (C3, C5), 133.29, 126.16 (C4a, C8a), 124.68 (C7), 119.86 (C8), 108.68 (C6), 90.06 (C4), 55.41, 54.76 (OMe's), 28.94, 27.24 (C1, C2); mass spectrum, *m/z* (relative intensity) 190 (100, M$^+$), 175 (52), 160 (31). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.8 H, 7.4. Found: C, 76.1 H, 7.6.

1,2-Dihydro-3,8-dimethoxynaphthalene (8a).[12] A mixture (5.00 g) of **7a** (10%), **8a** (22%), and **9a** (68%) was subjected to the same procedure:[12] yield 2.09 g (42%); ^{1}H NMR δ 7.22–6.55 (m, 3 H), 5.50 (broad s, C4–H), 3.81, 3.69 (s's, OMe's), 3.05–2.78 (m, 2 H), 2.50–2.25 (m, 2 H); ^{13}C NMR δ 160.44, 156.12 (C3, C8), 136.82 (C4a), 126.90 (C6), 119.49 (C8a), 117.95 (C5), 107.29 (C7), 95.99 (C4), 55.37, 54.70 (OMe's), 26.75, 20.97 (C1, C2).

1,2,3,4-Tetrahydro-2,3-methano-2,8-dimethoxynaphthalene (4c). A solution of crude **9c** [19.73 g; consisting of 90% of **9c** (93.3 mmol) and 10% of **8c** (10.4 mmol)], in dry benzene (150 mL), was prepared in a dry three-necked flask kept under N_2, and then a 15% solution of diethylzinc in hexane (114.5 mL, 103.8 mmol) was added at once with a syringe; CH_2I_2 (12.5 mL, 155.2 mmol) was added dropwise to the rapidly stirred mixture. Two more 12.5-mL portions of CH_2I_2 were added during the next 48 h. A precooled saturated NH_4Cl solution (100 mL) was carefully added, and the resulting mixture was diluted with ether. The organic layer was separated, washed several times with water, dried, filtered, and concentrated. Repetitive flash chromatography of the residue using ether/light petroleum 1:19 as eluant gave 12.75 g (67%) of pure **9c**: bp 80 °C/0.2 mmHg; R_f 0.29 (ether/light petroleum 1:19); ^{1}H NMR δ 7.25–6.97 (m, 1 H), 6.68–6.56 (m, 2 H), 3.81, 3.39 (s's, OMe's), 3.20–2.65 (m, 4 H), 1.65–1.36 (m, 1 H), 0.82–0.57 (m, 1 H), 0.47–0.27 (m, 1 H); ^{13}C NMR δ 157.14 (C8), 135.15, 123.16 (C4a, C8a), 126.62 (C6), 121.37 (C5), 107.54 (C7), 61.64 (C2), 55.16, 53.86 (OMe's), 18.79 (C3), 30.51, 24.46, 11.12 (C1, C4, cyclopropane –CH_2–); mass spectrum, *m/z* (relative intensity) 204 (52, M$^+$), 189 (73), 173 (53). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.4 H, 7.9. Found: C, 76.3 H, 7.9.

1,2,3,4-Tetrahydro-2,3-methano-2,5-dimethoxynaphthalene (4a).[12] Crude **9a** [22.28 g; consisting of 91% of **9a** (107 mmol) and 9% of **8a** (11 mmol)] was cyclopropanated by the above procedure. The crude product was purified by repetitive flash chromatography using ether/light petroleum 1:19 as eluant to afford 0.2 g of an impure fraction and 20.62 g (94%) of pure **4a**: bp 94 °C/0.05 mmHg; R_f 0.43 (ether/light petroleum 1:19); ^{1}H NMR δ 7.25–6.63 (m, 3 H), 3.77, 3.37 (s's, OMe's), 3.30–2.66 (m, 4 H), 1.63–1.40 (m, 1 H), 0.79–0.61 (m, 1 H), 0.48–0.31 (m, 1 H); ^{13}C NMR δ 157.38 (C5), 136.14 (C4a), 123.35 (C7), 122.39 (C8a), 121.40 (C8), 107.91 (C6), 61.67 (C2), 55.28, 53.95 (OMe's), 18.22 (C3), 31.93, 23.00, 11.12 (C1, C4, cyclopropane –CH_2–).

1,2,3,4-Tetrahydro-1,2-methano-2,8-dimethoxynaphthalene (10c). Compound **8c** (5.1 g, 26.8 mmol) was cyclopropanated by the above procedure: yield 4.1 g (74%); bp 117–119 °C/0.8 mmHg; R_f 0.30 (ether/light petroleum 1:19); ^{1}H NMR δ 7.11–6.88 (m, 1 H), 6.78–6.55 (m, 2 H), 3.82, 3.35 (s's, OMe's), 2.75–1.90 (m, 4 H), 1.38–0.98 (m, 3 H); ^{13}C NMR δ 157.04 (C8), 134.74, 126.62 (C4a, C8a), 125.26 (C6), 120.69 (C5), 108.25 (C7), 64.83 (C2), 55.50, 54.05 (OMe's), 27.33, 21.43 (C3, C4), 17.26 (C1), 16.52 (cyclopropane –CH_2–); mass spectrum, *m/z* (relative intensity) 204 (64, M$^+$), 189 (19), 173 (100). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.4 H, 7.9. Found: C, 76.4 H, 7.7.

1,2,3,4-Tetrahydro-1,2-methano-2,5-dimethoxynaphthalene (10a). The preparation of **10a** from **8a** has been previously described:[12] ^{1}H NMR δ 7.24–6.59 (m, 3 H), 3.77, 3.37 (s's, OMe's), 3.28–2.90 (m, 1 H), 2.45–1.85 (m, 4 H), 1.29–1.09 (m, 2 H); ^{13}C NMR δ 156.55 (C5), 139.75 (C8a), 126.47 (C7), 121.40 (C4a), 120.38 (C8), 107.26 (C6), 65.50 (C2), 55.31, 56.26 (OMe's), 24.05 (C1), 20.91, 19.46, 17.08 (C3, C4, cyclopropane –CH_2–).

Solvolysis of 4c. Preparation of 8-Methoxy-3-methyl-2-tetralone (3c). A solution of **4c** (10.3 g, 50.4 mmol), 12 M HCl (105 mL), and MeOH (300 mL) was heated to reflux under N_2. After 20 h, the volatiles were evaporated, and the residue was extracted with ether. The ether layer was dried, filtered, and concentrated to give 8.74 g of crude **3c**. Distillation gave 7.95 g (83%) of analytically pure **3c**: bp 83–86 °C/0.1 mmHg; R_f 0.20 (ether/light petroleum 1:4); ^{1}H NMR δ 7.29–6.65 (m, 3 H), 3.80 (s, OMe), 3.50 (apparent d, *J* = 9 Hz, 2 H), 3.26–2.40 (m, 3 H), 1.18 (d, *J* = 6.3 Hz, C3–Me); ^{13}C NMR δ 211.89 (C2), 156.70 (C8), 137.03, 122.18 (C4a, C8a), 127.21 (C6), 120.05 (C5), 108.00 (C7), 55.34 (OMe), 42.62 (C3), 37.80, 37.34 (C1, C4), 14.48 (C3–Me); mass spectrum, *m/z* (relative intensity) 190 (100, M$^+$), 134 (83); IR (KBr): 1710 cm^{-1} (ν C=O). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.8 H, 7.4. Found: C, 76.0 H, 7.6.

Solvolysis of 4a To Yield 5-Methoxy-3-methyl-2-tetralone (3a).[12] Compound **4a** (26.28 g, 129 mmol) was solvolyzed by the same procedure: yield 24.0 g (98%, no recrystallization); ^{1}H NMR δ 7.26–6.66 (m, 3 H), 3.85 (s, OMe), 3.59 (narrow m, 2 H), 3.45–3.20 (m, 1 H), 2.70–2.35 (m, 2 H), 1.21 (d, *J* = 6.2 Hz, C3–Me); ^{13}C NMR δ 212.08 (C2), 156.46 (C5), 135.18 (C8a), 127.43 (C7), 124.52 (C4a), 120.29 (C8), 108.22 (C6), 55.54 (OMe), 43.82 (C1), 42.06 (C3), 29.83 (C4), 14.82 (C3–Me).

Solvolysis of 8c To Yield 8-Methoxy-1-methyl-2-tetralone (11c).[5,18] Compound **8c** (4.0 g, 19.6 mmol) was solvolyzed by the same procedure. Distillation of the crude product gave 2.9 g (77%) of **11c**: bp 90 °C/0.03 mmHg; R_f 0.43 (ether/light petroleum 1:4); ^{1}H NMR δ 7.20–6.91 (m, 1 H), 6.80–6.58 (m, 2 H), 3.71 (s, OMe), 3.13–2.02 (m, 5 H), 1.28 (d, *J* = 7.4 Hz, C1–Me); ^{13}C NMR δ 212.60 (C2), 156.83 (C8), 136.91, 127.61 (C4a, C8a), 127.33 (C6), 120.32 (C5), 108.62 (C7), 55.16 (OMe), 41.85 (C1), 37.93, 27.86 (C3, C4), 18.13 (C1–Me).

Solvolysis of 8a To Yield 5-Methoxy-1-methyl-2-tetralone (11a).[17,32] Compound **8a** was solvolyzed by the same procedure:[12] ^{1}H NMR δ 7.29–7.10 (m, 1 H), 6.85–6.70 (m, 2 H), 3.82 (s, OMe), 3.60–2.40 (m, 5 H), 1.44 (d, *J* = 7.2 Hz, C1–Me); ^{13}C NMR δ 212.63 (C2), 156.12 (C5), 140.00 (C8a), 127.58 (C7), 124.86 (C4a), 118.69 (C8), 108.37 (C6), 55.47 (OMe), 47.28 (C1), 36.69 (C3), 20.45 (C4), 15.44 (C1–Me).

4-Methoxy-2-methylindan-1-one (15). A solution of 4-methoxyindan-1-one (**14**)[20,21] (5.0 g, 31 mmol), pyrrolidine (8.8 g, 124 mmol), and *p*-toluenesulfonic acid monohydrate (0.005 g, 0.02 mmol) in 250 mL of dry benzene was refluxed for 6 days in a Dean–Stark apparatus under N_2. The benzene and excess pyrrolidine were evaporated and the residue was distilled affording 4.15 g (63 %) of the air-sensitive pyrrolidine enamine of **14** [bp 121–125 °C/0.01 mmHg; ^{1}H NMR δ 7.35–7.10 (m, 2 H), 6.82–6.60 (m, 1 H), 5.07 (apparent t, C2–H), 3.86 (s, OMe), 3.55–3.20 (m, 6 H), 2.05–1.80 (m, 4 H)].

To a solution of the above enamine (4.15 g, 18 mmol) in dioxane (40 mL) was added CH_3I (10 mL, 124 mmol). The solution was heated at 50 °C for 3 days under N_2. During this period, two 5-mL portions of CH_3I were added (on the second and third day, respectively). Evaporation of the volatiles gave a residue to which were added MeOH (20 mL), water (10 mL), and 12 M HCl (10 mL). The resulting homogeneous solution was heated under reflux for 12 h, the volatiles were evaporated, and the brownish residue was partitioned between CH_2Cl_2 and water. Drying, filtration, and concentration of the organic layer gave a residue which was purified using repetitive flash chromatography with ether/light petroleum 1:4 as eluant to give 0.3 g of **5-methoxy-2,2-dimethylindan-1-one** (**16**) as an oil, 0.5 g of recovered **14**, 0.6 g of impure fractions containing mainly **15**, and 1.05 g (22% based on recovered **14**) of pure **15**. An analytical sample of **15** was prepared by recrystallization from ether.

15: mp 72–73 °C; R_f 0.42 (ether/petroleum ether 1:4); ^{1}H NMR δ 7.42–6.95 (m, 3 H), 3.90 (s, OMe), 3.55–3.10 (m, 1 H), 2.90–2.45 (m, 2 H), 1.30 (d, *J* = 7.3 Hz, C2–Me); ^{13}C NMR δ 209.61 (C1), 156.95 (C4), 142.34, 137.83 (C7a, C3a), 128.88 (C6), 115.54, 114.83 (C7, C5), 55.41 (OMe), 41.82 (C2), 31.56 (C3), 16.37 (C2–Me); mass spectrum, *m/z* (relative intensity) 176 (69, M$^+$), 161 (100). Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.0 H, 6.9. Found: C, 74.9 H, 6.9.

16: R_f 0.48 (ether/light petroleum 1:4); ^{1}H NMR δ 7.42–6.95 (m, 3 H), 3.89 (s, OMe), 2.90 (s, C3–H's), 1.23 (s, C2–Me's); ^{13}C NMR δ 211.43 (C1), 157.01 (C4), 141.02, 136.82 (C7a, C3a), 128.91 (C6), 115.94, 114.95 (C7, C5), 55.34 (OMe), 45.28 (C2), 39.47 (C3), 25.26 (C2–Me's); mass spectrum, *m/z* (relative intensity) 190 (45, M$^+$), 175 (100). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.8 H, 7.4. Found: C, 75.3 H, 7.6.

6-Methoxy-2-methylindan-1-one (18).[32] 4-Methoxybenzyl chloride (prepared in 90% yield from 4-methoxybenzyl alcohol) was alkylated with diethyl methylmalonate anion. Hydrolysis of the ester functions followed by decarboxylation gave *p*-meth-

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oxy-α-methylhydrocinnamic acid[33] in 94% yield.

Indanone **18** was prepared in analogy with a literature method[34] for cyclization of acyl chlorides: $AlCl_3$ (45 g, 0.34 mol) was added in portions to a stirred solution of *p*-methoxy-α-methylhydrocinnamoyl chloride (59 g, 0.28 mol) in CH_2Cl_2 (1500 mL) kept at 5 °C under N_2. After 2 h at room temperature, the mixture was poured into ice water and extracted with ether. The ether extract was washed with water, aqueous NaOH, and brine. Drying, filtration, and concentration of the ether layer gave an oily residue which was distilled to afford 42 g (86%; 69% as calculated from 4-methoxybenzyl alcohol) of pure **18**: bp 95 °C/0.4 mmHg (lit[32] bp 148 °C/10 mmHg); R_f 0.33 (ether/light petroleum 1:4); ^{1}H NMR δ 7.39–7.09 (m, 3 H), 3.82 (s, OMe), 3.53–2.51 (m, 3 H), 1.30 (d, J = 7.2 Hz, C2–Me); ^{13}C NMR δ 209.21 (C1), 159.30 (C6), 146.14 (C7a), 137.31 (C3a), 127.18 (C4), 123.84 (C5), 105.07 (C7), 55.37 (OMe), 42.68 (C2), 34.19 (C3), 16.28 (C2–Me); mass spectrum, m/z (relative intensity) 176 (61, M^+), 161 (100).

Ring Expansion of 15. Alternative Preparation of 3a. A suspension of 204 mg (6.8 mmol) of 80% NaH in 1.5 mL of dry Me_2SO under N_2 was heated at 75 °C for 40 min. After addition of 1.25 mL of dry Me_2SO 2.43 g (6.8 mmol) of methyltriphenylphosphonium bromide was added in portions. Stirring for 15 min, addition of a solution of 600 mg (3.4 mmol) of **15** in 2 mL of dry Me_2SO, and heating of the mixture at 65 °C for 8 h completed the reaction. The reaction mixture was poured into a mixture of 120 mL of ice water and 20 mL of hexane. Precipitated triphenylphosphine oxide was filtered, and the organic layer was washed with water. Drying, filtration, and concentration of the organic layer gave 510 mg (86%) of crude **4-methoxy-2-methyl-1-methyleneindan (5a)**: ^{1}H NMR δ 7.35–6.60 (m, 3 H), 5.44 (d, J = 2 Hz, 1 H), 4.96 (d, J = 2 Hz, 1 H), 3.80 (s, OMe), 3.35–2.30 (m, 3 H), 1.24 (d, J = 7 Hz, C2–Me).

A solution of 50 mg (0.29 mmol) of crude **5a** in 1 mL of MeOH was added in one portion to a freshly prepared solution of thallium(III) nitrate trihydrate (127 mg, 0.29 mmol) in 1 mL of MeOH. The mixture was stirred vigorously for 1 min and 3 mL of $CHCl_3$ was added. The resulting suspension was filtered and more $CHCl_3$ was added. The solution was washed with a saturated $NaHCO_3$ solution and with water. Drying, filtration, and concentration of the organic layer gave a yellow residue which was recrystallized from ether/hexane to give 29 mg (53 %) of **3a**, identical (^{1}H and ^{13}C NMR, mp) with the product obtained by solvolysis of **4a**.

Ring Expansion of 18. Preparation of 7-Methoxy-3-methyl-2-tetralone (3b). Compound **3b** was prepared from **18** by a small modification of the procedure used for the preparation of **3a** from **15**: the MeOH solution of the intermediate **6-methoxy-2-methyl-1-methyleneindan [5b**: ^{1}H NMR δ 7.35–6.73 (m, 3 H), 5.42 (d, J = 2 Hz, 1 H), 4.97 (d, J = 2 Hz, 1 H), 3.80 (s, 3 H), 3.3–2.3 (m, 3 H), 1.24 (d, J = 7 Hz, C2–Me)] was added to a cold (−30 °C) solution of thallium(III) nitrate trihydrate in MeOH: yield of **3a** 2.9 g (54% as calculated from **18**); mp 66–67 °C (hexane/ether); R_f 0.25 (ether/light petroleum 1:4); ^{1}H NMR δ 7.16–6.66 (m, 3 H), 3.78 (s, OMe), 3.56 (s, 2 H), 3.10–2.38 (m, 3 H), 1.18 (d, J = 6.6 Hz, C3–Me); ^{13}C NMR δ 211.74 (C2), 158.40 (C7), 134.59 (C8a), 128.60 (C5), 128.11 (C4a), 113.16 (C8), 112.20 (C6), 55.16 (OMe), 44.16 (C1), 42.62 (C3), 35.92 (C4), 14.92 (C3–Me); mass spectrum, m/z (relative intensity) 190 (45, M^+), 134 (100); IR (KBr) 1710 cm^{-1} (ν C=O). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.8 H, 7.4. Found: C, 75.9 H, 7.4.

Methylation of Lithium Anions of Dimethoxynaphthalene Derivatives. Below are given representative examples of the reactions listed in Table I. All reactions were followed by GC analyses of aliquots of the reaction mixture that had been quenched by addition of excess CH_3I.

Methylation of 7c. Preparation of 3,5-Dimethoxy-2-methylnaphthalene (6c).[23] To a stirred solution of **7c** (20.0 g, 0.11 mol) in dry THF (200 mL) kept at −10 °C under N_2, was added a 1.5 M solution of butyllithium in hexane (79 mL, 0.12 mol) followed by tetramethylethylenediamine (25.7 g, 0.22 mol). After being stirred at room temperature for 20 h, the mixture was cooled to −70 °C, and CH_3I (6.9 mL, 0.11 mol) was added. After 1 h, a saturated solution of NH_4Cl (150 mL) was added to the cold reaction mixture. Ether was added, and the organic layer was separated and concentrated. The residue was diluted with ether and extracted with 2 M HCl. The ether layer was dried, filtered, and concentrated to afford 24.1 g (98%) of **6c** which was pure according to GC. Recrystallization from light petroleum gave colorless needles, mp 73–74.5 °C, (lit.[23] 72–73 °C); R_f 0.48 (ether/light petroleum 1:19); ^{1}H NMR δ 7.51–7.40 (m, 2 H), 7.35–7.05 (m, 2 H), 6.78–6.61 (m, 1 H), 3.93, 3.91 (s's, OMe's), 2.35 (s, C2–Me); ^{13}C NMR δ 156.55, 154.39 (C3, C5), 129.77, 128.69, 125.11 (C2, C4a, C8a), 128.54 (C1), 123.26 (C7), 119.37 (C8), 103.46 (C6), 98.98 (C4), 55.28 (OMe's), 16.77 (C2–Me); mass spectrum, m/z (relative intensity) 202 (100, M^+), 187 (81).

Methylation of 7a. Preparation of 2,5-Dimethoxy-3-methylnaphthalene (6a). A solution of butyllithium in hexane (187 mL, 0.23 mol) was added to a stirred solution of **7a** (40 g, 0.21 mol) in dry THF kept under N_2 at −65 °C. The solution was stirred at −15 °C overnight. CH_3I (18 mL, 0.29 mol) was added, and the mixture was stirred at room temperature overnight. An additional portion of CH_3I (5 mL, 0.08 mol) was added. After 1 h, excess NH_4Cl was added, the volatiles were evaporated, and the residue was partitioned between water and ether. The ether layer was extracted with 1 M HCl, dried, filtered, and concentrated to give, according to ^{1}H NMR, a mixture of **6a** (84%), **2,5-dimethoxy-1-methylnaphthalene (19a)** (12%) and unchanged **7a** (4%). Pure **6a** (22.5 g, 52%) was obtained by repeated recrystallization from light petroleum. Pure **19a** was obtained by recrystallization from the combined mother liquors.

6a: mp 75–76 °C; R_f 0.53 (ether/light petroleum 1:19); ^{1}H NMR δ 7.98 (C4–H), 7.30–7.01 (m, 3 H), 6.74–6.54 (m, 1 H), 3.94, 3.90 (s's, OMe's), 2.37 (d, $J \approx 0.8$ Hz, C3–Me); ^{13}C NMR δ 157.19, 155.00 (C2, C5), 134.65 (C8a), 127.36 (C3), 125.48 (C7), 122.94 (C4), 120.38 (C4a), 118.93 (C8), 104.23 (C1), 101.85 (C6), 55.19, 55.03 (OMe's), 17.01 (C3–Me); mass spectrum, m/z (relative intensity) 202 (100, M^+), 187 (16), 159 (48). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.2 H, 7.0. Found: C, 77.2 H, 6.9.

19a: mp 79–80 °C (lit.[35] mp 84–85 °C); R_f 0.44 (ether/light petroleum 1:19); ^{1}H NMR δ 8.16 (d, J = 9.3 Hz, C4–H), 7.57–7.17 (m, 3 H), 6.75–6.60 (m, 1 H), 3.97, 3.93 (s's, OMe's), 2.52 (s, C1–Me); ^{13}C NMR δ 155.87, 154.91 (C2,C5), 134.90 (C8a), 126.25 (C7), 121.10 (C4), 118.93 (C4a), 115.91 (C3), 112.32 (C8), 101.39 (C6), 56.52, 55.44 (OMe's), 10.87 (C1–Me); mass spectrum, m/z (relative intensity) 202 (100, M^+), 187 (13), 159 (50).

Monomethylation of 7b. Preparation of 3,6-Dimethoxy-2-methylnaphthalene (6b). Compound **7b** (4.0 g, 21.3 mmol) was subjected to the above procedure. GC, ^{1}H-, and ^{13}C NMR indicated that the crude reaction product (4.2 g) consisted of **6b** and **2,7-dimethoxy-1-methylnaphthalene (19b)** in a 4:1 ratio. In addition, trace amounts of unchanged **7b** and dimethylated product(s) were observed. Flash chromatography of the mixture with ether/light petroleum as eluant followed by recrystallization of partially purified fractions from MeOH gave pure **6b** (2.1 g, 50%), mp 97–100 °C; R_f 0.36 (ether/light petroleum 1:19); ^{1}H NMR δ 7.62–7.30 (m, 2 H), 7.05–6.83 (m, 3 H), 3.91, 3.88 (s's, OMe's), 2.32 (s, C2–Me); ^{13}C NMR δ 157.45, 157.35 (C3, C6), 134.50 (C4a), 128.54, 128.32 (C1, C8), 125.73, 124.06 (C2, C8a), 115.67 (C7), 105.07, 103.80 (C4, C5), 55.19 (OMe's), 16.65 (C2–Me); mass spectrum, m/z (relative intensity) 202 (100, M^+), 187 (11), 159 (54). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.2 H, 6.98. Found: C, 77.0 H, 7.25.

19b[36] was never completely purified, but the following NMR characteristics of **19b** were obtained from a mixture of **6b** and **19b**: ^{1}H NMR δ 7.65–7.48 (m, 2 H), 7.18–7.02 (m, 3 H), 3.95, 3.92 (s's, OMe's), 2.50 (s, C1–Me); ^{13}C NMR δ 158.00, 154.94 (C2, C7), 134.87 (C8a), 129.90, 126.84 (C4, C5), 126.46 (C4a), 117.98 (C1), 115.81, 110.90 (C3, C6), 101.89 (C8), 56.46, 55.13 (OMe's), 10.69 (C1–Me).

Dimethylation of 7b. Preparation of 2,7-Dimethoxy-3,6-dimethylnaphthalene (20). Dimethylation of **7b** (3.0 g, 16 mmol) was performed by the same procedure (4 equiv of butyllithium, room temperature for 5 h, 5 equiv of CH_3I). GC indicated that the crude product (3.2 g) consisted of unchanged **7b** (6%), monomethylated products (22%), and **20** (72%). Recrystallization

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from MeOH gave 1.1 g (32% of pure **20**, mp 167–169 °C; R_f 0.41 (ether/light petroleum 1:19); ^{1}H NMR δ 7.32 (s, 2 H), 6.92 (s, 2 H), 3.83 (s, OMe's), 2.30 (s, C3- and C6-Me's); ^{13}C NMR δ 156.58 (C2, C7), 133.10 (C8a), 127.83 (C4, C5), 125.33 (C_3, C_6), 123.87 (C4a), 103.58 (C1, C8), 55.07 (OMe's), 16.65 (C3- and C6-Me's); mass spectrum, m/z (relative intensity) 216 (100, M^+), 201 (18), 173 (55). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.7 H, 7.5. Found: C, 77.7 H, 7.5.

Sodium Reduction of 6c. Preparation of 1,4-Dihydro-3,5-dimethoxy-2-methylnaphthalene (21c). To a vigorously stirred solution of **6c** (30.0 g, 148.3 mmol) in dry EtOH (500 mL), kept at gentle reflux under N_2, were added thin slices of Na (56 g, 2.44 mol) during 2.5 h. The heating was interrupted, and water (200 mL) and NH_4Cl (130 g, 2.44 mol) were added. After evaporation of the EtOH, water and ether were added to the semisolid residue. The ether layer was separated, dried, filtered, and concentrated to give 28.4 g (94%) of white crystals, mp 58–61 °C (*n*-pentane); R_f 0.35 (ether/light petroleum 1:19); ^{1}H NMR δ 7.23–7.02 (m, 1 H), 6.80–6.58 (m, 2 H), 3.82, 3.62 (s's, OMe's), 3.38 (broad s, 4 H), 1.74 (s, C2-Me); ^{13}C NMR δ 156.83 (C5), 145.46 (C3), 135.15, 122.89 (C4a, C8a), 126.44 (C7), 119.95 (C8), 110.72 (C2), 106.64 (C6), 56.24, 55.07 (OMe's), 35.89, 24.27 (C1, C4), 14.79 (C2-Me); mass spectrum, m/z (relative intensity) 204 (63, M^+), 189 (100). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.4 H, 7.9. Found: C, 76.5 H, 8.0.

Sodium Reduction of 6a To Yield 1,4-Dihydro-2,5-dimethoxy-3-methylnaphthalene (21a). Compound **6a** (10.0 g, 49.4 mmol) was subjected to the same procedure. NMR spectral analysis of the crude reaction products indicated the presence of unchanged **6a** (3.5%) and **21a** [96.5%; ^{1}H NMR δ 7.21–7.04 (m, 1 H), 6.77–6.61 (m, 2 H), 3.80, 3.58 (s's, OMe's), 3.55–3.15 (m, 4 H), 1.77 (broad s, C3-Me); ^{13}C NMR δ 156.67 (C5), 144.75 (C2), 135.27 (C8a), 126.44 (C7), 122.98 (C4a), 120.42 (C8), 111.74 (C3), 106.92 (C6), 56.49, 55.22 (OMe's), 30.64, 29.31 (C1, C4), 15.07 (C3-Me)].

Sodium Reduction of 6b. Compound **6b** (0.40 g, 2 mmol) was reduced by the same procedure. ^{1}H NMR indicated that the crude reaction mixture consisted of **1,4-dihydro-2,7-dimethoxy-6-methylnaphthalene** [30%; ^{1}H NMR δ 4.78 (broad s, C3-H), 2.17 (s, C6-Me)], **1,2-dihydro-3,6-dimethoxy-7-methylnaphthalene** [10%; ^{1}H NMR δ 5.48 (broad s, C4-H), 2.17 (s, C7-Me)], **1,4-dihydro-3,6-dimethoxy-2-methylnaphthalene** [**21b**; 45%; ^{1}H NMR δ 1.74 (s, C2-Me)], and **1,2,3,4-tetrahydro-2,7-dimethoxy-6-methylnaphthalene** [15%, ^{1}H NMR δ 2.17 (s, C6-Me)].

Solvolysis of 21a. Alternative Preparation of 3a. A solution of **21a** (18.8 g, 92 mmol), 12 M HCl (66 mL), and MeOH (290 mL) was heated to reflux under N_2 for 3 h. The volatiles were evaporated, and the residue was partitioned between water and ether. The ether layer was dried, filtered, and concentrated to give 17.2 g (98%) of **3a** which was identical with a sample prepared from **4a**.

Solvolysis of 21c. Alternative Preparation of 3c. Compound **3c** was prepared from **21c** (14.0 g, 68.5 mmol) by the same procedure. Distillation gave 11.4 g (87%) of pure **3c**.

1,2,3,4-Tetrahydro-2,3-methano-3,5-dimethoxy-2-methylnaphthalene (22). A 15% solution of diethylzinc in hexane (71.2 mL, 64.6 mmol) was added at once, with a syringe, to a solution of **21c** (13.2 g, 64.6 mmol) in dry benzene (100 mL), kept under N_2. After 5 min, CH_2Cl_2 (7.8 mL, 96.9 mmol) was added dropwise to the rapidly stirred reaction mixture. Ten days later a precooled saturated NH_4Cl solution (80 mL) was added carefully. The resulting solution was diluted with ether. The organic layer was separated, washed several times with water, dried, filtered, and concentrated. Flash chromatography of the residue using ether/light petroleum 1:19 as eluant gave 5.55 g (39%) of pure **22**; mp 44.5–45.0 °C; R_f 0.31 (ether/light petroleum 1:19); ^{1}H NMR δ 7.10–6.95 (m, 1 H), 6.75–6.55 (m, 2 H), 3.81, 3.42 (s's, OMe's), 3.18–2.60 (m, 4 H), 2.34 (s, C2-Me), 0.51–0.28 (m, 2 H); ^{13}C NMR δ 156.95 (C5), 136.60, 123.63 (C4a, C8a), 126.50 (C7), 120.91 (C8), 107.51 (C6), 65.10 (C3), 55.22, 54.51 (OMe's), 38.11, 24.77 (C1, C4), 22.82 (C2), 18.87 (C2-Me), 16.09 (cyclopropane $-CH_2-$); mass spectrum, m/z (relative intensity) 218 (100, M^+). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.0 H, 8.3. Found: C, 77.3 H, 8.2.

8-Methoxy-3,3-dimethyl-2-tetralone (23). A solution of **22** (5.55 g, 25.4 mmol) in 12 M HCl (20 mL) and MeOH (80 mL) was heated to reflux under N_2. After 5 h, the MeOH was evaporated in vacuo, and the residue was extracted with ether. The ether layer was dried, filtered, and evaporated. Distillation gave 3.2 g (62%) of analytically pure **23**: bp 80–82 °C/0.03 mmHg; R_f 0.52 (ether/light petroleum 1:4); ^{1}H NMR δ 7.30–7.06 (m, 1 H), 6.84–6.65 (m, 2 H), 3.83 (s, OMe), 3.53 (s, 2 H), 2.88 (s, 2 H), 1.11 (s, 6 H); ^{13}C NMR δ 213.71 (C2), 156.18 (C8), 136.17 (C4a), 127.24 (C6), 121.44 (C8a), 120.50 (C_5), 107.88 (C7), 55.13 (OMe), 43.58, 43.21, 36.44 (C1, C3, C4), 24.09 (C3-Me's); mass spectrum, m/z (relative intensity) 204 (96, M^+), 161 (100). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.4 H, 7.9. Found: C, 76.7 H, 7.8.

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Registry No. **3a**, 105372-20-1; **3b**, 105372-40-5; **3c**, 105372-21-2; **4a**, 105372-16-5; **4c**, 105372-17-6; **5a**, 105372-26-7; **5b**, 105372-27-8; **6a**, 105372-28-9; **6b**, 105372-30-3; **6c**, 105372-31-4; **7a**, 3900-49-0; **7a** (diol), 575-44-0; **7b**, 3469-26-9; **7b** (diol), 582-17-2; **7c**, 5309-18-2; **7c** (diol), 575-38-2; **8a**, 16291-62-6; **8b**, 65472-35-7; **8c**, 65472-37-9; **9a**, 32940-13-9; **9b**, 60683-71-8; **9c**, 60683-72-9; **10a**, 105372-18-7; **10c**, 105372-19-8; **11a**, 42263-75-2; **11c**, 65565-29-9; **14**, 13336-31-7; **14** (pyrrolidine enamine), 105372-22-3; **15**, 105372-23-4; **16**, 99545-62-7; **17**, 105-13-5; **17** (benzyl chloride), 824-94-2; **18**, 60848-62-6; **19a**, 105372-29-0; **19b**, 89229-22-1; **20**, 99309-20-3; **21a**, 105372-32-5; **21b**, 105372-33-6; **21c**, 105372-34-7; **22**, 105372-37-0; **23**, 105372-38-1; *p*-$MeOC_6H_4CH_2C(CH_3)(CO_2Et)_2$, 105372-24-5; *p*-$MeOC_6H_4CH_2C(CH_3)(CO_2H)_2$, 105372-25-6; *p*-$MeOC_6H_4CH_2CH(CH_3)CO_2H$, 52427-11-9; *p*-$MeOC_6H_4CH_2CH(CH_3)COCl$, 56935-39-8; diethyl methylmalonate, 609-08-5; 1,4-dihydro-2,7-dimethoxy-6-methylnaphthalene, 105372-35-8; 1,2-dihydro-3,6-dimethoxy-7-methylnaphthalene, 105372-36-9; 1,2,3,4-tetrahydro-2,7-dimethoxynaphthalene, 105372-39-2; 1,2,3,4-tetrahydro-2,7-dimethoxy-6-methylnaphthalene, 105372-41-6.