**Registry No.** 2, 101652-40-8; $C_6H_5CO_2Na$, 532-32-1; $C_6H_5CH_2OH$, 100-51-6; $C_6H_5CHO$, 100-52-7; $C_6H_5COCH_3$, 98-86-2; plumbagin, 481-42-5; cyclopentanone, 120-92-3; 2-butylcyclopentanone, 934-42-9; 2-hexylcyclopentanone, 13074-65-2.

## Synthesis of 5,8-Dimethoxy-1-naphthoic Acid and 1,4-Dimethoxy-7,12-dimethylbenz[*a*]anthracene[1]

Melvin S. Newman* and Vinod K. Khanna[2]

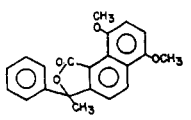
*Department of Chemistry, The Ohio State University, Columbus, Ohio 43210*

*Received July 15, 1985*

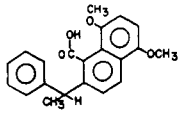
This work was undertaken as part of a program to synthesize possible metabolites of 7,12-dimethylbenz[*a*]-anthracene. Our first goal, to develop a good synthesis of 5,8-dimethoxy-1-naphthoic acid, **5**, was achieved as shown in Scheme I.

The Diels–Alder reaction of ethyl 2,4-pentadienoate,[3] **1**, with benzoquinone yielded ethyl 5,8-diketo-1,4,5,8-tetrahydro-1-naphthoate, **2**, which was immediately methylated[4] to ethyl 1,4-dihydro-5,8-dimethoxy-1-naphthoate, **3**, from which ethyl 5,8-dimethoxy-1-naphthoate, **4**, was obtained in a 53% overall yield from **2** by heating with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ).

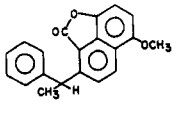
The acid, **5**, obtained by hydrolysis of **4** was converted via its acid chloride into *N,N*-diethyl-5,8-dimethoxy-1-naphthamide,[5] **6**. On lithiation followed by reaction with acetophenone and acid hydrolysis there was obtained 5,8-dimethoxy-2-(α-hydroxy-α-methylbenzyl)-1-naphthoic acid lactone, **7**, which was reduced to 5,8-dimethoxy-2-(α-methylbenzyl)-1-naphthoic acid, **8**.



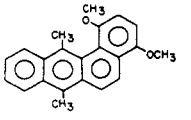
**7**



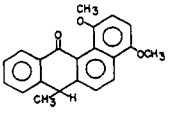
**8**



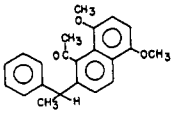
**9**



**11**



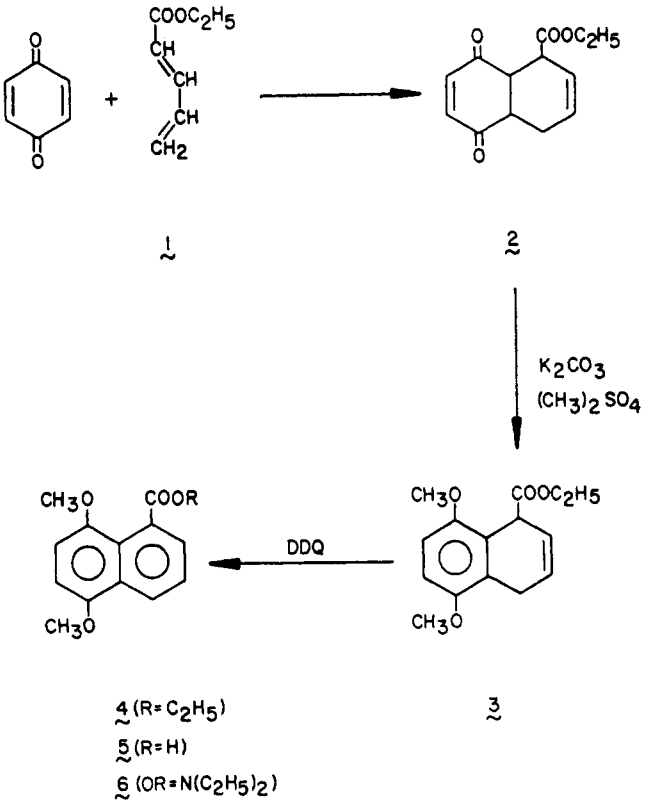
**10**



**12**

In an attempt to cyclize **8** to 7,12-dihydro-1,4-dimethoxy-7-methyl-12-benz[*a*]anthracenone, **10**, or its enol acetate by heating with acetic anhydride–$ZnCl_2$ reagent there was obtained mainly the lactone of 8-hydroxy-5-methoxy-2-(α-methylbenzyl)-1-naphthoic acid, **9**. Cyclization of **8** to **10** was accomplished in 90% yield by a 1-h treatment with anhydrous HF.[6] Reaction of **10** with methyllithium yielded 1,4-dimethoxy-7,12-dimethylbenz-[*a*]anthracene, **11**. On treatment of the acid chloride of **8** with lithium dimethylcuprate,[7] 1-aceto-5,8-dimethoxy-2-(α-methylbenzyl)naphthalene, **12**, was obtained. However, attempts to cyclize **12** by heating with PPA or trifluoroacetic acid yielded 5,8-dimethoxy-2-(α-methylbenzyl)naphthalene, **13**, the product resulting from loss of the acetyl group.

**Scheme I**




## Experimental Section[6]

**Ethyl 1,4-Dihydro-5,8-dimethoxynaphthoate, 3.** A solution of 27.0 g (0.25 mol) of *p*-benzoquinone and 31.5 g (0.25 mol) of ethyl 2,4-pentadienoate, **1**, in 500 mL of benzene was refluxed for 2 days. After rotary evaporation of the benzene the residue was washed with 50–100 mL of hexane (discarded) and taken into $CH_2Cl_2$. After being washed with saturated salt solution, the solvent was removed. As the crude Diels–Alder product was sensitive it was dissolved in 1 L of deaerated acetone ($N_2$) containing 138 g of $K_2CO_3$ and treated with 69 g (0.55 mol) of dimethyl sulfate at reflux for 1 day.[4] Most of the acetone was removed and water added. The resulting solid was collected, washed with a little pentane, and dried. The solid was then extracted with 600–700 mL of hot hexane. Cooling yielded 37.4 g (57%) of **3**: mp 91–92 °C; IR (KBr) 1728 $cm^{-1}$ (CO); NMR ($CDCl_3$) 1.23 (t, 3, $CH_3$), 3.22–3.48 (m, 2, $CH_2$), 3.74 (s, 3, $OCH_3$), 3.79 (s, 3, $OCH_3$), 4.14 (q, 2, $OCH_2$), 4.37–4.55 (m, 1, CH), 5.91–6.06 (m, 2, CH=CH), 6.69 (s, 2-ArH); MS, $M^+$ 262.1213, calcd for $C_{15}H_{18}O_4$ 262.3083. Anal.[8] Calcd for $C_{15}H_{18}O_4$: C, 68.7; H, 6.9. Found: C, 68.6; H, 6.7.

A small part of the crude adduct was crystallized from hexane to yield pale yellow prisms of ethyl 5,8-diketo-1,4,4a,5,8,8a-hexahydro-1-naphthoate: mp 90–91 °C; IR 1720, 1685 $cm^{-1}$; NMR 1.28 (t, 3, $CH_3$), 2.12–2.42 (m, 2, $CH_2$), 3.08–3.43 (m, 2, 4a,8aH), 4.02 (t, 1, 1 H), 4.25 (q, 2-$OCH_2$), 5.12–5.87 (m, 1, =CH), 6.15–6.35

(1) This work was supported by Grant CA-07394 of The National Cancer Institute, Department of Health, Education and Welfare, and by Grant 2 507 RR07074-19 of Biomedical Research of the DHHS, PHS, NIH Division of Research Resources.
(2) Postdoctoral Research Associate.
(3) Idoux, J. P.; Ghane, H. *J. Chem. Eng. Data* **1979**, *24*, 157.
(4) Chang, D. S. C.; Filipescu, N. *J. Am. Chem. Soc.* **1972**, *94*, 4170.
(5) Beak, P.; Brown, R. A. *J. Org. Chem.* **1979**, *44*, 4463.
(6) Fieser, L. F.; Hershberg, E. B. *J. Am. Chem. Soc.* **1939**, *61*, 1272.
(7) Posner, G. H.; Whitten, C. E. *Tetrahedron Lett.* **1970**, 4647.
(8) Microanalyses by the Galbraith Laboratories, Knoxville, TN. The term "worked up as usual" means that an ether–benzene solution of the product was washed with dilute acid and/or alkali and then saturated brine and filtered through anhydrous $MgSO_4$. The solvent was then removed on a rotary evaporator. All melting points are uncorrected. All NMR are done in $CDCl_3$. Mass spectra by Mr. R. Weisenberger.

0022-3263/86/1951-1921$01.50/0 

(mofd, 1, =CH) 6.63–6.82 (m, 2, =CH). We thank Dr. A. Kumar[2] for this work.

**Ethyl 5,8-Dimethoxy-1-naphthoate, 4.** A well-stirred mixture of 29.4 g (0.112 mol) of **3** and 17.9 g (0.123 mol) of DDQ in 500 mL of benzene was held at reflux for 5 h. The $DDQH_2$ was filtered and washed with hot benzene. The filtrate and washings were concentrated and passed over a column of basic alumina. The benzene was removed and the residue was crystallized from hexane to yield 27.1 g (93%) of colorless prisms of **4**: mp 86–87 °C; NMR 1.36 (t, 3, $CH_3$), 3.74 (s, 3, $OCH_3$), 3.87 (s, 3, $OCH_3$), 4.26–4.51 (q, 2, $CH_2$), 6.70 (s, 2, ArH), 7.42–7.57 (d, 2, ArH), 8.25–8.36 (t, 1, ArH). Anal.[8] Calcd for $C_{15}H_{16}O_4$: C, 69.3; H, 6.2. Found: C, 69.7; H, 6.2.

**5,8-Dimethoxy-1-naphthoic Acid, 5.** A mixture of 57.5 g of **4** in 500 mL of alcohol containing 500 mL of 20% KOH was held at reflux for 1 day. After much of the alcohol was removed by rotary evaporation, any unreacted ester was extracted with ether–benzene and the acid liberated by acidification to yield 51.3 g (93%) of **5**: mp 208–209 °C as colorless prisms from benzene–methanol; NMR 3.8 (2 close s, 6, $OCH_3$), 6.9 (s, 2, ArH), 7.6 (m, 2, ArH), 8.3 (m, 1, ArH). Anal.[8] Calcd for $C_{13}H_{12}O_4$: C, 67.2; H, 5.2. Found: C, 67.3; H, 5.4.

***N,N*-Diethyl-5,8-dimethoxy-1-naphthamide, 6.** A mixture of 59.16 g of **5**, 56 g of $PCl_5$, and 100 mL of $CH_2Cl$ was held at reflux for 1 h while no more HCl was evolved. After rotary evaporation, the acid chloride was added dropwise to a solution of 58 g of diethylamine in 250 mL of $CH_2Cl_2$ at 0 °C. After standing overnight at ambient temperature, the mixture was washed with cold water and 10% $NaHCO_3$ and worked up as usual. On distillation 68.1 g (93%) of **6**, bp 195–199 °C at 1 mm, was obtained. Crystallizations from hexane yield colorless prisms, mp 90–91 °C. Anal.[8] Calcd for $C_{17}H_{21}NO_3$: C, 71.1; H, 7.4; N, 4.9. Found: C, 71.2; H, 7.5; N, 4.6.

**5,8-Dimethoxy-2-(α-methylbenzyl)-1-naphthoic Acid, 8.** To a stirred solution at −78 °C of 17.22 g of **6** in 450 mL of ether and 150 mL of THF containing 9 g of tetramethylethylenediamine (TMEDA) was added dropwise a solution of 1.25 M *sec*-butyllithium (Aldrich) in cyclohexane. After 1 h a solution of 12 g of acetophenone in 100 mL of ether was added in 30 min. After 2 h at −78 °C the mixture was allowed to come to room temperature overnight. After treatment with dilute HCl, the product was worked up as usual and gave a product which was heated with 600 mL of 4 M HCl for 4 h. The product was chromatographed over silica gel and eluted with 3:1 benzene/ethyl acetate to yield 15 g of a noncrystalline lactone, **7**; IR 1760 $cm^{-1}$, one spot on TLC. A stirred mixture of this lactone, 90 g of activated zinc dust (3-min treatment with 180 mL of water and 20 mL of concentrated HCl, and then 100 mL of 5% $CuSO_4$), 800 mL of 10% KOH, and 60 mL of pyridine was refluxed for 1 day. The acid product isolated as usual was crystallized from benzene–hexane to yield 10.9 g (72%) of **8**, mp 204–205 °C. Anal.[8] Calcd for $C_{21}H_{20}O_4$: C, 75.0; H, 6.0. Found: C, 74.8; H, 5.9.

**8-Hydroxy-5-methoxy-2-(α-methylbenzyl)-1-naphthoic Acid Lactone, 9.** From the neutral fraction of the products resulting from heating 1.0 g of **8** with 5 mL each of acetic acid and acetic anhydride containing 0.1 g of $Cl_2$ for 3 h was obtained 200 mg of pure **9**: mp 130–131 °C, as pale yellow prisms; IR 1760 $cm^{-1}$; MS 304.1088, calcd for $C_{20}H_{26}O_3$ 304.1099. The acid portion yielded 0.3 g of **8**.

**7,12-Dihydro-1,4-dimethoxy-7-methyl-12-benz[*a*]anthracenone, 10.** To 60 mL of HF[6] in a polyethylene bottle was added 2.70 g of finely powdered **8** with swirling. After 1 h the mixture was poured on ice and worked up as usual to yield 2.30 g of pale yellow prisms of **10**, mp 144–146 °C. Anal.[8] Calcd for $C_{21}H_{18}O_3$: C, 79.2; H, 5.7. Found: C, 78.8; H, 5.6.

**1,4-Dimethoxy-7,12-dimethylbenz[*a*]anthracene, 11.** To a stirred solution of 1.70 g of **10** in 200 mL of ether under $N_2$ was added 10 mL of 1.7 M methyllithium in ether (Aldrich). After 1 day the mixture was worked up as usual and the crude product was chromatographed over basic alumina to yield 48% of pale yellow prisms of **11**: mp 105–106 °C; NMR 2.83 (s, 3, $CH_3$), 3.01 (s, 3, $CH_3$), 3.92 (s, 3, $OCH_3$), 4.00 (s, 3, $OCH_3$), 6.96 (q, 2, ArH), 7.55 (m, 2, ArH), 7.90 (m, 2, ArH), 8.26 (, 2, ArH). Anal.[8] Calcd for $C_{22}H_{18}O_2$: C, 83.5; H, 6.4. Found: C, 83.1; H, 6.3.

An attempt to convert 5,8-dimethoxy-2-(α-methylbenzyl)-1-acetonaphthalene, **12**, readily prepared in 80% yield from **8**, by heating at 90–100 °C for 1 h with PPA resulted in cleavage of the acetyl group to yield 5,8-dimethoxy-2-(α-methylbenzyl)-naphthalene, *m/e* 292.

**Registry No.** **1**, 13038-12-5; **2**, 101671-02-7; **3**, 101671-03-8; **4**, 101671-04-9; **5**, 101671-05-0; **6**, 101671-06-1; **7**, 101671-07-2; **8**, 101671-08-3; **9**, 101671-09-4; **10**, 101671-10-7; **11**, 101671-11-8; **12**, 101671-12-9; *p*-benzoquinone, 106-51-4; acetophenone, 98-86-2; 5,8-dimethoxy-2-(α-methylbenzyl)naphthalene, 101671-13-0.

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## Procedure for the Catalytic Asymmetric Epoxidation of Allylic Alcohols in the Presence of Molecular Sieves†

Robert M. Hanson and K. Barry Sharpless*

*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139*

*Received January 17, 1986*

In the original report[1] on the titanium-catalyzed asymmetric epoxidation of allylic alcohols, the general procedure called for a stoichiometric amount of the titanium tartrate "catalyst". That report also mentioned that 10% catalyst sufficed for reactive substrates, and a recent procedure[2] for the asymmetric epoxidation of (*E*)-2-hexen-1-ol prescribed 50% catalyst. Nevertheless, the numerous applications of the asymmetric epoxidation to date have been carried out almost exclusively by using stoichiometric or near-stoichiometric amounts of the titanium–tartrate catalyst.[3]

We now report the first *general* procedure for the asymmetric epoxidation of allylic alcohols employing *tert*-butyl hydroperoxide (TBHP) and *catalytic* (i.e., <10%) amounts of titanium(IV) isopropoxide and diethyl tartrate. The key element of this modification is the presence of 3A or 4A molecular sieves (zeolites) during the reaction. The advantages of using a catalytic amount of titanium include economy, mildness of conditions, ease of isolation, increased yields, and the potential for in situ derivatization of the product. In the absence of molecular sieves, reactions employing only 5 mol % titanium(IV) isopropoxide often yield product of low optical purity (39–80% ee), proceed slowly, and generally stop after achieving only 50–60% conversion. In contrast, our new procedure enables the reaction to be carried out by using only 5–10 mol % titanium(IV) isopropoxide and only 6–13 mol % of tartrate ester, giving product of high enantioselectivity (90–95% ee) at rates similar to those of the stoichiometric system. The two procedures presented below (one for disubstituted allylic alcohols and one for trisubstituted allylic alchols) are very similar and differ only in minor details of the reaction conditions and isolation technique.

Undecenol was chosen as a representative *trans*-disubstituted allylic alcohol. Decenol and hexenol have been studied also, and their reactions are quite similar, reacting completely in 1–3 h and giving products of >90% ee. In one respect undecenol is unrepresentative of its class: Optimal temperatures for *trans*-disubstituted allylic alcohols are in the range of −20 to −25 °C. However, the epoxide of undecenol is insoluble in dichloromethane below about −15 °C. Although this would not necessarily be a limitation, precipitation of the epoxide does appear to hinder further reaction, and therefore the reaction must be run at −15 °C to −10 °C.

† Dedicated to the memory of Lawrence A. Reed, III.

0022-3263/86/1951-1922$01.50/0 