Chemistry of Oxaziridines. 16.[1] A Short, Highly Enantioselective Synthesis of the AB-Ring Segments of γ-Rhodomycinone and α-Citromycinone Using (+)-[(8,8-Dimethoxycamphoryl)sulfonyl]oxaziridine

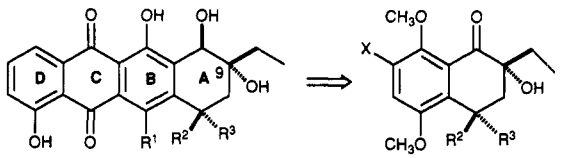
Franklin A. Davis,* Anil Kumar, and Bang-Chi Chen

Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104

Received July 3, 1990

A highly efficient procedure for the preparation of rhodomycinone 1 AB synthons (−)-**2a** and (+)-**2b** in high enantiomeric purity (93–4% ee) and good yield is described. This method involves asymmetric oxidation of the lithium enolate of 2-ethyl-5,8-dimethoxy-1-tetralone (**4**) with (+)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine (**5c**), a new enantiomerically pure, aprotic oxidizing reagent. Lower stereoselectivities were observed with this reagent for the enantioselective oxidation of 2-substituted 1-tetralone enolates **8** lacking the 8-methoxy group.

The development of an efficient methodology for the synthesis of the anthracycline antibiotics in enantiomerically pure form continues to be of interest because of the remarkable antitumor activity exhibited by these compounds.[2,3] Although numerous asymmetric syntheses of the anthracyclones[3] have been described, there are only a few reports on enantioselective syntheses of the rhodomycinones **1**.[4-6] The rhodomycinones are the principal aglycons of rhodomycins and the recently isolated potent antitumor anthracycline antibiotics betaclamycin A[7] and distrisarubicin B.[8] The main challenge in the synthesis of **1**, or for that matter the anthracyclinones in general, is introduction of the C-9 stereocenter with the desired stereochemistry.[3]

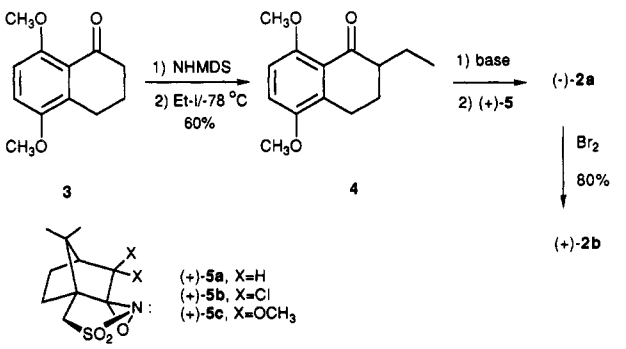


1a, R^1,= OH, R^2, R^3=H
b, R^1, R^3= OH, R^2=H
c, R^1= R^2=H, R^3=OH

(-)-**2a**, X=H, R^1,R^2=H
(+)-**2b**, X=Br, R^1,R^2=H
c, X=Br, R^2=H, R^3=OH
d, X=Br, R^2=OH, R^3=H

One strategy used in the synthesis of these compounds involves the convergent, regioselective coupling of an enantiomerically pure AB building block **2** to produce the tetracyclic skeleton. Indeed AB synthon (−)-**2a** was recently used in the first total synthesis of (−)-γ-rhodomycinone (**1a**).[4] However, the reported preparations of (−)-**2a** employing (2*S*,3*S*)-1,4-dimethoxy-2,2-butanediol as a chiral auxiliary[4b] or incorporating a "chiral pool" fragment such as α-D-isosaccharino-1,4-lactone[5] are multistep and proceed in low overall yield. In this context we describe a short, highly efficient enantioselective synthesis of AB synthons

Scheme I



(−)-**2a** and (+)-**2b** using our asymmetric enolate oxidation protocol.[9] This study is part of our continuing efforts in the development of new and more effective chiral oxidizing reagents by synthesizing architecturally interesting molecules having the α-hydroxycarbonyl structural unit.

The synthesis of (−)-**2a** begins with inverse addition of the sodium enolate of 5,8-dimethoxy-1-tetralone (**3**),[10] prepared by treating 1.5 mmol of **3** with 0.66 equiv of sodium bis(trimethylsilyl)amide to excess iodoethane (Scheme I). These measures, which largely avoid dialkylation, afforded 2-ethyl-5,8-dimethoxy-1-tetralone (**4**) in 60% yield following flash chromatography. We next envisioned that the lone stereocenter in **2a** could be introduced stereospecifically via the enantioselective hydroxylation of the enolate of **4** using (+)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine (**5b**).[11] Very high asymmetric induction, 90 to ≥95% ee, for oxidation of the sodium enolates of related 2-substituted 1-tetralones to the corresponding α-hydroxytetralones has been observed with this reagent.

Typically asymmetric enolate oxidations were carried out by addition of 1.6 equiv of oxaziridine **5** to the preformed enolate of **4** at −78 °C and warming to 0 °C in the case of the lithium enolates. When the oxidation was complete, as determined by TLC analysis (usually 0.5 h), the reaction was quenched by addition of NH_4Cl solution. Preparative TLC or flash chromatography afforded (−)-**2a** in 55–72% isolated yield. The enantiomeric purity was determined by comparison of its optical rotation with reported values[4b] and by using the chiral shift reagent Eu(hfc)$_3$ on the acetate of (−)-**2a**. The results of these oxi-

(1) Davis, F. A.; Thimma Reddy, R.; McCauley, J. P. Jr.; Przeslawski, R. M.; Harakal, M. E.; Carroll, P. J. *J. Org. Chem.* **1991**, *56*, 809.

(2) (a) El Khadem, E., Ed. *Anthracycline Antibiotics*; Academic Press: New York, 1982. (b) Arcamone, F. *Doxrubicin Anticancer Antibiotics*; Academic Press: New York, 1982.

(3) For excellent reviews on the total synthesis of the anthracyclinones see: Krohn, K. *Fortsch. Chem. Org. Naturst.* **1989**, *55*, 37. Krohn, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 790. Broadhurst, M.; Hassall, C. H.; Thomas, G. J. *Chem. Ind. (London)* **1985**, 106.

(4) (a) Fujioka, H.; Yamamoto, H.; Kondo, H.; Annoura, H.; Kita, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 1509. (b) Fujioka, H.; Kondo, H.; Annoura, H.; Yamamoto, H.; Ko, T.; Kita, Y.; Tamura, Y.; Aoe, K. *Chem. Pharm. Bull.* **1989**, *37*, 1488.

(5) Genot, A.; Florent, J.-C.; Monneret, C. *Tetrahedron Lett.* **1989**, *30*, 711.

(6) Krohn, K.; Muller, U. *Tetrahedron* **1986**, *42*, 6635.

(7) Yoshimoto, A.; Matsuzawa, Y.; Ishikura, T.; Sawa, T.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1984**, *37*, 920.

(8) Kunimoto, S.; Takahashi, Y.; Uchida, T.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1988**, *41*, 655.

(9) For a review on the chemistry of *N*-sulfonyloxaziridines which includes a section on enolate oxidations by these reagents, see: Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.

(10) Moore, J. A.; Rahm, M. *J. Org. Chem.* **1961**, *26*, 1109.

(11) Davis, F. A., Weismiller, M. E. *J. Org. Chem.* **1990**, *55*, 3715.

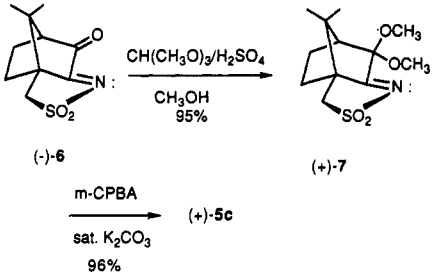
(12) Davis, F. A.; Sheppard, A. C.; Chen, B. C.; Haque, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6679.

0022-3263/91/1956-1143$02.50/0

dations are summarized in Table I.

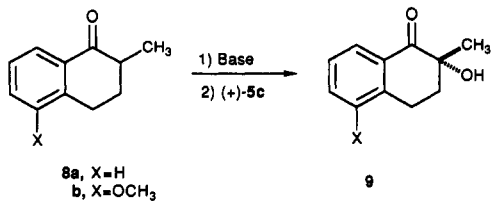
Unexpectedly, oxidation of the sodium enolate of **4** with oxaziridine (+)-**5a** gave (−)-**2a** in higher ee than did (+)-**5b**, 83 vs 68% (Table I, entries 1 and 3). In our recent studies of the oxidation of related tetralone enolates, we speculated that the much higher ee's observed with (+)-**5b** compared to (+)-**5a** (90–95% vs 15–70% ee) were due to stereoelectronic and metal chelation effects.[11] In an effort to improve the ee's of (−)-**2a**, (+)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine (**5c**) was employed because of the presence of the more potent chelating methoxy groups.

Oxaziridine (+)-**5c** was prepared from imine **6**[13] by refluxing with trimethyl orthoformate to give (+)-**7** in 95% yield. Oxidation of (+)-**7**, as previously described,[11] with 1.5 equiv of >95% *m*-chloroperbenzoic acid (*m*-CPBA) in the presence of potassium carbonate afforded (+)-**5c** in 96% isolated yield.



Significantly, oxidation of the lithium enolate of **4** with (+)-**5c** gave (−)-**2a** in 94% ee and 66% isolated yield. It is noteworthy that the better chelating lithium enolate gave higher ee's than did the sodium enolate (94 vs 60% ee) despite the fact that the temperature of oxidation in the former is higher (Table I, compare entries 5 and 6). While it is attractive to attribute the higher ee's to more effective chelation between (+)-**5c** and the enolate as a consequence of the methoxy groups, this can be only part of the answer. The reason is that the presence of the 8-methoxy group in tetralone **4** is a necessary requirement for high enantioselectivities with this reagent.

As summarized in Table II, the ee's observed with (+)-**5c** for the oxidation of 2-substituted 1-tetralone enolates lacking an 8-methoxy group were inferior to those obtained with (+)-**5b**.[11] For example, oxidation of the sodium enolates of **8a** and **8b** with (+)-**5b** gave (+)-(*R*)-**9** in ≥95% ee[11] whereas (+)-**5c** gave (+)-(*R*)-**9** in 36% and 5% ee, respectively. Similar results were observed for the acyclic enolate of propiophenone (Table II, entries 5 and 6). Undoubtedly these results are related to the fact that these enolates have different structures in solution. Our inability to relate enolate solution structure with reactivity accounts for the difficulty in predicting enolate oxidation stereoselectivities with these reagents.[12]



Swenton and co-workers, in pioneering studies, demonstrated the application of racemic (±)-**2c** in the synthesis of the (±)-α-citromycinone **1c**.[14,15] The cis C-7 oxygen was introduced by treatment of (±)-**2b** with O_2 and base while (±)-**2c** was transformed into (±)-**2d** with trifluoroacetic acid.[14] The preparation of (+)-**2b** was readily accomplished in greater than 80% yield and 93% ee by treatment of (−)-**2a** with bromine (Scheme I).

Attempts to prepare (+)-**2b** by asymmetric oxidation of the lithium enolate of 7-bromo-2-ethyl-5,8-dimethoxy-1-tetralone[14] with (+)-**5c** proved disappointing. While **2b** was obtained, both the asymmetric induction (11% ee) and yield (30–35%) were low. The poor yield may be related to instability of the enolate as evidenced by the fact that less than 47% of the starting material was recovered, in addition to resinous polar material, after 40 min on quenching in the absence of the oxidant.

In conclusion, the lithium enolate of **4** on oxidation with oxaziridine (+)-**5c** affords rhodomycinone AB synthon (−)-**2a** in high enantiomeric purity and good yield. Synthon (+)-**2b** is prepared from (−)-**2a** by bromination. The availability of these synthons should make the enantioselective synthesis of the rhodomycinones (**1**) and their derivatives more convenient. Finally, the apparent complementary nature of oxaziridines **5b** and **5c** for the asymmetric oxidation of 2-substituted 1-tetralone enolates is expected to find application in the stereoselective synthesis of biologically active natural products.

Experimental Section

Details concerning the recording of spectra, the analytical instruments used, the determination of melting points and elemental analyses, and the purification of solvents (freshly distilled) have been previously described.[11] Enolate oxidations were performed in flame-dried flasks equipped with rubber septa under a dry argon atmosphere. Lithium diisopropylamide (LDA) was freshly prepared and sodium bis(trimethylsilylamide) (NHMDS), 1.0 M solution in THF, was purchased from Aldrich Chemical Co. (Camphorylsulfonyl)oxaziridines (+)-**5a**[16] and (+)-**5b**[11] were prepared as previously described. Tetralone **8b** was prepared as previously described.[11]

(−)-3-Oxocamphorsulfonyl Imine (6). This imine was prepared as previously described using a modified procedure.[13] To a solution of 21.3 g (0.1 mol) of (−)-camphorylsulfonyl imine[16] in 750 mL of acetic acid was added 15 g of selenium dioxide. The reaction mixture was heated at refluxed for 20 h, the solution was filtered to remove the precipitate selenium, and 1000 mL of H_2O and 500 mL of CH_2Cl_2 were added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 500 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed to give 16.2 g (72%) yield of (−)-**6** of sufficient purity for the next step.

(+)-3,3-Dimethoxycamphorsulfonyl Imine (7). A solution of 2.27 g (10 mmol) of (−)-**6**[13] in 25 mL of trimethyl orthoformate, 5 mL of methanol, 0.5 mL of concentrated H_2SO_4, and 0.5 g of Amberlist-15 ion-exchange resin were stirred and refluxed overnight. The room temperature solution was filtered, 20 mL of H_2O was added, and the mixture was extracted with CH_2Cl_2 (3 × 30 mL); the combined extracts were washed with 30 mL of H_2O and dried ($MgSO_4$). Removal of the solvent afford a white solid which was purified by crystallization from absolute EtOH to give 2.6 g (95%) of **6**: mp 186–7 °C; $[\alpha]^{20}_D$ +7.2° (*c* 3.6 $CHCl_3$); IR (KBr), 1620, 1340, 1160, cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.46 (s, 3 H), 3.38 (s, 3 H), 3.09 (AB quartet, 2 H, J_{AB} = 12 Hz), 2.38–1.80 (m, 5 H), 1.10 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 188.6, 102.9, 64.2, 52.0, 50.5, 48.8, 46.0, 29.2, 20.6, 20.5, 20.4. Anal. Calcd for $C_{12}H_{19}NO_4S$: C, 52.73; H, 7.01. Found: C, 52.60; H, 7.00.

(+)-[(Dimethoxycamphoryl)sulfonyl]oxaziridine (5c). In a 250-mL three-necked Morton-flask equipped with mechanical

(13) Glashsl, G.; Hermann, R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1753.

(14) Coburn, C. E.; Anderson, D. K.; Swenton, J. S. *J. Org. Chem.* **1983**, *48*, 1455.

(15) Swenton, J. S.; Anderson, D. K.; Coburn, C. E.; Haag, A. P. *Tetrahedron* **1984**, *40*, 4633.

(16) Davis, F. A.; Towson, J. C.; Weismiller, M. C.; Lal, S. G.; Carroll, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 8477. Towson, J. C.; Weismiller, M. C., Lal, G. S.; Sheppard, A. C.; Davis, F. A. *Org. Synth.* **1990**, *69*, 158.

Table I. Enantioselective Oxidation of the Enolate of 4 Using Oxaziridines 5 in THF

entry	oxaziridine	conditions base/temp, °C	% ee (config)	% isolated yield	$[\alpha]^{20}_D$ ($CHCl_3$)
1	(+)-**5a**	NHMDS/−78	83 (*R*)	72	−21.8° (*c* = 4.0)
2		LDA/0	61 (*R*)	66	−15.9° (*c* = 3.5)
3	(+)-**5b**	NHMDS/−78	68 (*R*)	70	−17.8° (*c* = 4.0)
4		LDA/−78	73 (*R*)	55	−19.0° (*c* = 2.6)
5	(+)-**5c**	NHMDS/−78	60 (*R*)	58	−15.6° (*c* = 3.5)
6		LDA/0	94 (*R*)	66	−24.5° (*c* = 4.0)

Table II. Asymmetric Oxidation of 2-Methyl-1-tetralone (8) and Propiophenone Enolates 8 Using (+)-5c

entry	enolate	conditions base (temp, °C)	% ee [% ee[b] (config)[a]]	% isolated yield
1	**8a** (X = H)	NHMDS (−78)	36 (*R*) [≥95 (*R*)]	66
2		LDA (0)	2 (*R*) [≥95 (*R*)]	67
3	**8b** (X = OMe)	NHMDS (−78)	5 (*R*) [≥95 (*R*)]	62
4		LDA (0)	19 (*R*) [≥95 (*R*)]	66
5	propiophenone	NHMDS (−78)	79 (*S*) [≥95 (*S*)]	73
6		LDA (0)	75 (*S*)	70

[a] Determined using Eu(hfc)$_3$. [b] Using (+)-**5b** as reported in ref 11.

stirrer was placed 1.37 g (5 mmol) of (+)-**7**, 1.36 g (7.5 mmol) of >95% *m*-chloroperoxybenzoic acid in 50 mL of CH_2Cl_2, and 50 mL of saturated K_2CO_3 solution. After the reaction mixture was rigorously stirred for 8 h, the organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed with saturated $Na_2S_2O_3$ (30 mL) and H_2O (30 mL) and dried ($MgSO_4$). Removal of the solvent afforded a white solid which was crystallized from absolute EtOH to give 1.4 g (96%) of (+)-**5c**: mp 189 °C dec; $[\alpha]^{20}_D$ 91.3° (*c* 3.39, $CHCl_3$); IR (KBr) 1356, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 3.28 (s, 2 H), 3.20 (AB quartet 2 H, J_{AB} = 12 Hz), 2.30–1.75 (m, 5 H), 1.32 (s, H), 1.05 (s, H); ^{13}C NMR ($CDCl_3$) δ 102.7, 97.6, 54.6, 52.9, 50.8, 50.6, 47.5, 45.2, 45.2, 28.2, 21.7, 20.6. Anal. Calcd for $C_{12}H_{19}NO_5S$: C, 49.81; H, 6.62. Found: C, 49.90; H, 6.61.

2-Ethyl-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-one (4). A 1 M solution (1.0 mL, 1 mmol) of NHMDS was stirred magnetically and cooled to 0 °C (ice bath) under argon, and a solution of 309 mg (1.5 mmol) of tetralone **3**[10] in 2 mL of tetrahydrofuran (THF) was added dropwise. After being stirred for 30 min the reaction mixture was added via cannula tube (inverse addition) to a solution of 1.56 g (10 mmol) of iodoethane in 10 mL of THF which was stirred and cooled at −78 °C (dry ice–acetone bath) under argon. After the addition was complete the reaction mixture was warmed to room temperature and quenched after 12 h by adding 24 mL of saturated aqueous NH_4Cl. The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic extracts were washed with H_2O (50 mL) and brine (50 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give 280 mg of crude **4**, which was purified by flash chromatography (ether/pentane, 3:7) to give 150 mg (60%) of **4** and 90 mg (30%) of recovered **3**. Compound **4** had the following properties: mp 55–6 °C; IR (KBr) 1671 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94–1.0 (t, *J* = 7.45 Hz, 3 H) 1.39–1.65 (m, 1 H), 1.71–2.01 (m, 2 H), 2.13–2.24 (m, 1 H), 2.33–2.44 (m, 1 H), 2.65–2.79 (m, 1 H), 2.99–310 (m, 1 H), 3.81 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 6.78 and 6.95 (AB q, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 199.7, 153.2, 149.7, 133.9, 122.9, 114.3, 109.7, 56.0, 55.5, 49.7, 26.7, 22.3, 11.3; MS *m/e* (relative intensity) 234 (M, 100), 206 (75), 205 (70), 178 (88), 149 (36), 121 (68), 77 (56). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.79; H, 7.69. Found: C, 71.41; H, 7.70.

(−)-(*R*)-2-Ethyl-5,8-dimethoxy-2-hydroxy-1,2,3,4-tetrahydronaphthalen-1-one (2a). A solution of 58.5 mg (0.25 mmol) of tetralone **4** in 2 mL of THF was added dropwise to a stirred and cooled −78 °C solution of 0.3 mL (0.30 mmol) of a 1 M solution of LDA in 2 mL of THF. After the mixture was stirred at −78 °C for 30 min a solution of 116 mg (0.4 mmol) of (+)-**5c** in 5 mL of THF was added dropwise. The reaction was monitored by TLC, warmed to 0 °C as required, and quenched by the addition of 3 mL of saturated aqueous NH_4Cl after 0.5–1 h. The reaction mixture was extracted with diethyl ether (3 × 25 mL), and the combined organic extracts were washed with H_2O (20 mL) and brine (20 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give a white solid (170 mg), which was purified by preparative TLC (eluant pentane/ether/CH_2Cl_2, 3:1:1, R_f = 0.3) to give 40.6 mg (66%) of **2a**: mp 74–5 °C (lit.[4b] colorless oil); $[\alpha]^{20}_D$ −24.5° (*c* = 4.0, $CHCl_3$) [lit.[3b] $[\alpha]^{20}_D$ −26.0° (*c* 0.65, $CHCl_3$)]; IR and NMR spectral data are consistent with reported values.[4b] Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.20; H, 7.20. Found: C, 67.09; H, 7.22.

General Procedure for Oxidation of Enolates 8 by (+)-5c. Enolates were generated and oxidized as described above and the α-hydroxytetralones **9** were isolated as previously described.[11]

2-Acetoxy-2-ethyl-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-one. A solution of 40 mg (0.16 mmol) of **2a**, 10 mg of 4-(*N*,*N*-dimethylamino)pyridine, and 3 mL of triethylamine in 5 mL of CH_2Cl_2 was cooled to 0 °C, and a solution of 65.3 mg (0.64 mmole) of acetic anhydride in 1 mL of CH_2Cl_2 was slowly added. The reaction mixture was warmed to room temperature, stirred for 12 h, and quenched by slow addition of 5 mL of methanol. After removal of the solvent under reduced pressure the residue was dissolved in 40 mL of ether, washed with cold 1.0 N HCl (10 mL), H_2O (20 mL), saturated $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (20 mL), and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a solid which was purified by preparative TLC (silica gel) eluting with 1:1:3 CH_2Cl_2/ether/*n*-pentane (R_f = 0.45) to give 39 mg (74%) of the acetate: mp 153–154 °C; $[\alpha]^{20}_D$ +9.9° (*c* = 0.91, $CHCl_3$); IR (KBr) 1743 (CO_2Me), 1692 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79–0.85 (t, *J* = 7.36 Hz, CH_3), 1.55–1.98 (m, 4 H), 2.05 (s, 3 H, $C(O)CH_3$), 2.59–2.74 (m, 1 H), 3.0–3.1 (m, 1 H), 3.69 (s, 3 H, OMe), 3.77 (s, 3 H, OMe), 6.76 and 6.92 (AB quartet, *J* = 9 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 193.8, 169.6, 154.4, 149.8, 132.7, 121.8, 115.0, 110.5, 83.5, 56.5, 55.9, 28.9, 26.8, 21.3, 20.5, 7.6; MS, *m/e* (relative intensity) 292 (M, 9.4), 249 (16), 232 (42), 203 (22), 178 (20), 121 (13), 57 (100).

(+)-(*R*)-7-Bromo-2-ethyl-2-hydroxy-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-one (2b). A solution of 102 mg (0.64 mmol, 1.2 equiv of Br_2 in 2 mL of CH_2Cl_2 was added dropwise to a solution of 133 mg (0.53 mmol) of hydroxytetralone **2a** in 5 mL of CH_2Cl_2. After being stirred at room temperature for 30 h the reaction mixture was quenched by the addition of 3 mL of 10% $Na_2S_2O_3$, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with 5% $NaHCO_3$, H_2O, and brine and dried ($MgSO_4$). Removal of the solvent gave a white solid which was purified by preparative TLC (eluant pentane/ether/CH_2Cl_2, 8:1:1, R_f = 0.5) to give 141 mg (80%) of **2b**: mp 118–119 °C (lit.[15] mp 119–120 °C); $[\alpha]^{20}_D$ +4.5° (*c* = 0.7, $CHCl_3$); IR and NMR spectral data are consistent with reported values.[15]

2-Acetoxy-7-bromo-2-ethyl-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-one. The procedure described above for the preparation of the acetate of **2a** was followed: yield 67%; mp 104–105 °C; $[\alpha]^{20}_D$ +25.91° (*c* = 1.3, $CHCl_3$); IR (KBr) 1734 (CO_2Me), 1696 (C=O), 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96–1.02 (t, 3 H, *J* = 7.49 Hz), 1.79–2.12 (m, 4 H), 2.05 (s, 3 H), 2.59–3.04 (m, 2 H), 3.82 (s, 3 H), 3.84 (s, 3 H), 7.14 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 193, 169.6, 152.5, 150.8, 131.9, 127, 118.4, 116.8, 83.5, 61.7, 56.0, 29.0, 26.7, 21.2, 20.4, 7.4; MS *m/e* (relative intensity) 373 (M + 2, 10.4), 371 (M^+, 11.2), 327 (14.2), 329 (15.01), 312 (33.4), 310 (35.5), 57 (100).

Acknowledgment. We thank Professor John Swenton (Ohio State University) for helpful discussions and gratefully acknowledge the financial support of the National Institutes of Health (Institute of General Medical Sciences) through Grant GM 34014.