A One-Pot Condensation of Pyrones and Enals. Synthesis of 1*H*,7*H*-5a,6,8,9-Tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyrans

Duy H. Hua,* Yi Chen, Hong-Sig Sin, Maria J. Maroto, Paul D. Robinson,[1] Steven W. Newell,[2] Elisabeth M. Perchellet,[2] James B. Ladesich,[2] Jonathan A. Freeman,[2] Jean-Pierre Perchellet,[2] and Peter K. Chiang[3]

Department of Chemistry, Kansas State University, Manhattan, Kansas 66506

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Condensation of various 6-substituted 4-hydroxypyrones **1** with 1-cyclohexenecarboxaldehydes in the presence of L-proline in ethyl acetate gave high yields of substituted 1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyrans. The reaction presumably occurs via the 1,2-addition of the pyrone with the aldehyde followed by dehydration and then cyclization through a 6Π electrocyclic process. A remarkable asymmetric induction was obtained from a stereogenic center (C4) of the cyclohexenecarboxaldehyde [such as (*S*)-perillaldehyde] to provide only the C5a,7-*trans* tricyclic pyrone products. On the other hand, condensation of 3-(formyloxy)- or 3-hydroxy-2-methyl-1-cyclohexenecarboxaldehydes with pyrones **1** gave mixtures of C5a,6−*cis* and -*trans* products. Several of the tricyclic pyrones strongly inhibit acetylcholinesterase activity, DNA synthesis, and tumor cell growth *in vitro*.

I. Introduction

Condensation reactions of 4-hydroxy-6-methyl-2-pyrone (**1A**)[4] and 4-hydroxycoumarin[5] with acyclic α,β-unsaturated enones and enals provided 1,4-addition products (Michael adducts; attack from C3 of pyrones) as the predominant[4] or sole[5] products; 1,2-addition products were formed as the minor products in few of the reactions.[4a,b] Acetic acid and piperidine in ethanol[4] or pyridine[5] were used as reagents and solvent in these reactions. Reaction with cyclic enals has not been reported. In our studies of the synthesis of biologically active compounds and studies toward total synthesis of natural products such as pyripyropenes[6] and arisugacin,[7] various substituted tricyclic pyrones were synthesized via the condensation of 6-substituted 4-hydroxy-2-pyrones **1** with substituted 1-cyclohexenecarboxaldehydes **2**−**5** in the presence of an amino acid (such as L-proline). These tricyclic pyrones were formed presumably through 1,2-addition reaction followed by *in situ* ring closure. In the ring closure reactions, asymmetric induction was observed from a stereogenic center (C4) in the carboxaldehyde. These tricyclic compounds have not been previously reported and possess a variety of important biological activities. Herein, the condensation reactions are reported and some of the biological testing results are summarized.

II. Results and Discussion

Despite the finding that the 1,4-adducts were the predominant products in the condensation of pyrone **1A** with (*E*)-2-butenal and cinnamaldehyde,[4b] treatment of 1-cyclohexenecarboxaldehyde (**2**) with 1 equiv of **1A** and 0.5 equiv of L-proline in ethyl acetate at 70 °C for 24 h provided a 76% yield of tricyclic pyrone **6A** (Scheme 1). Presumably, **6A** was formed through the 1,2-addition of the pyrone onto the enal followed by dehydration and ring closure via the 6Π electrocyclic process (i.e., **7**; in which the catalyst, L-proline, is not involved).[8] The structure of **6A** was firmly established by a single-crystal X-ray analysis (Figure 1).[9] The crystal has a centric space group, triclinic $P\bar{1}$, and is racemic (the optical rotation of **6A** is zero). Although no intermediate was detected when the reaction was followed by ^{1}H NMR spectroscopy, the formation of a racemic product suggests that a

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(1) Department of Geology, Southern Illinois University at Carbondale, Carbondale, IL 62901. Author to whom correspondence concerning the X-ray crystal structure determination should be addressed.

(2) Anti-Cancer Drug Laboratory, Department of Biology, Ackert Hall, Kansas State University, Manhattan, KS 66506-4901.

(3) Department of Applied Biochemistry, Walter Reed Army Institute of Research, Washington DC 20307-5100.

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(9) The asymmetric unit contains two nearly identical molecules with $a = 8.8552(16)$ Å, $b = 18.977(4)$ Å, $c = 6.7869(11)$ Å, and R factor = 0.0450. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

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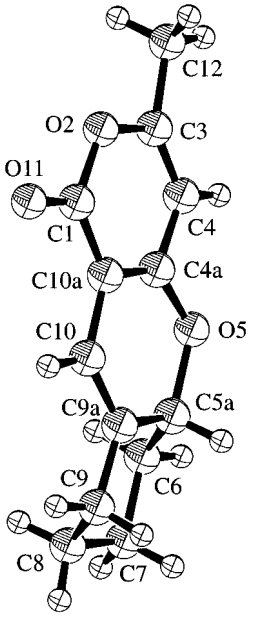
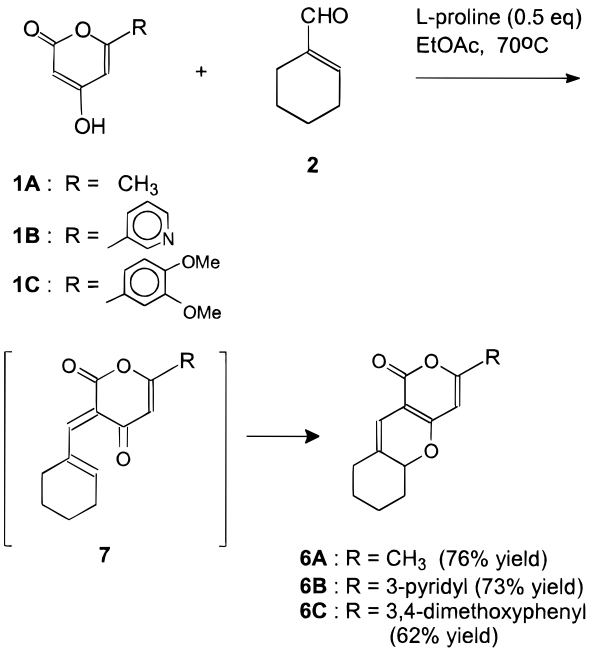


Figure 1. ORTEP drawing of X-ray crystallographically determined structure of **6A**. Displacement ellipsoids are shown at the 30% probability level.

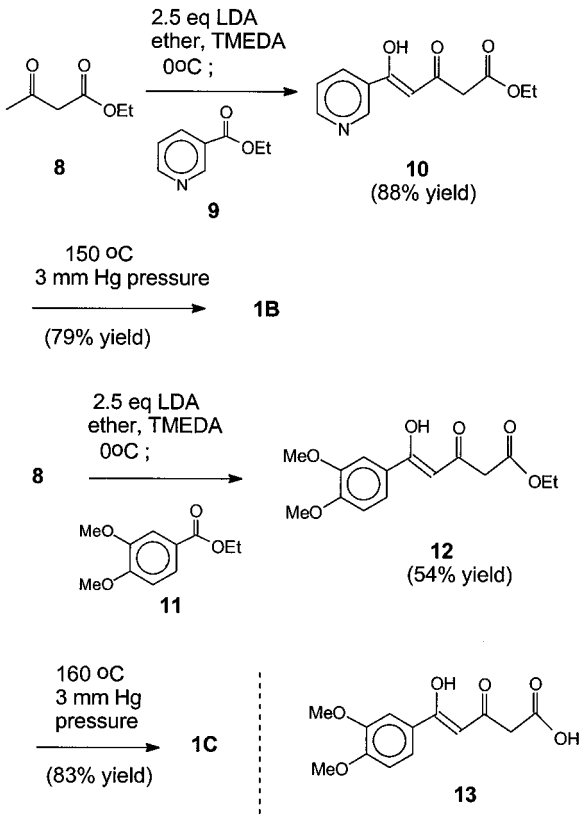
Scheme 1



dienone intermediate, **7**, is involved. Other catalysts, such as L-phenylalanine, (1*S*)-(+)-camphorsulfonic acid, (+)-quinidine, (*S*)-2-pyrrolidinemethanol, *d*-camphoric acid, and acetic acid−piperidine, were also used in the condensation reaction, but L-proline provided the highest yield. In all cases, racemic **6A** was formed. Other pyrones, such as **1B** and **1C**, also underwent the condensation reaction. For example, coupling of aldehyde **2** with pyrones **1B** and **1C** separately in the presence of 0.5 equiv of L-proline in ethyl acetate at 70 °C generated pyranobenzopyrans **6B** and **6C** in 73% and 62% yields, respectively (Scheme 1).

Scheme 2 outlines the preparation of pyrones **1B** and **1C** via a small modification of a procedure which reported **1B**.[10a] Treatment of ethyl acetoacetate (**8**) in diethyl ether with 2.5 equiv of lithium diisopropylamide (LDA)

Scheme 2



at 0 °C for 1 h followed by 1 equiv of ethyl nicotinate (**9**) gave an 88% yield of triketone **10** (as its enol). Cyclization of **10** at 150 °C under reduced presure (3 mmHg) for 0.5 h gave a 79% yield of pyrone **1B**. Similarly, pyrone **1C** was synthesized from ethyl 3,4-dimethoxybenzoate (**11**). Hence, triketone **12** was obtained in 54% yield from the Claisen condensation of **8** and **11** under similar reaction conditions as those of **10**. However, during workup of this reaction, if acetic acid was not added to neutralize the excess of base before filtration of the crystalline product **12**, the lithium salt of carboxylic acid **13** was obtained which, upon acidification and methylation with diazomethane in methylene chloride and diethyl ether, afforded a 56% yield of the methyl ester derivative **12A**. Intramolecular cyclization of **12** or **12A** gave an ~83% yield of **1C**. Attempted cyclization of acid **13** under similar conditions gave only the decarboxylation product, 1-(3,4-dimethoxyphenyl)-1,3-butadione.

Unexpectedly, a remarkable asymmetric induction was observed from a C-4 stereogenic center in the carboxaldehyde, such as (*S*)-(−)-perillaldehyde (**3**) in this case. Thus, treatment of (*S*)-**3** with pyrones **1A**, **1B**, and **1C** separately gave single diastereomers **14** (78% yield), **15** (65% yield), and **16** (63% yield), respectively (Scheme 3). On the bases of ^{1}H NMR, the structures were assigned as 5a*S* and 7*S*: the C5a proton (for example, in **14**) resonates at δ 5.15 as a doublet of doublets with $J = 11.2$ and 5.2 Hz (axial−axial and axial−equatorial couplings), indicative of an axial hydrogen (at C5a). The *cis* isomers were not detected in these reactions.

Other substituted carboxaldehydes such as **4** and **5** were synthesized and subjected to the condensation reaction. Thus, pyrone **1A** condensed with carboxalde-

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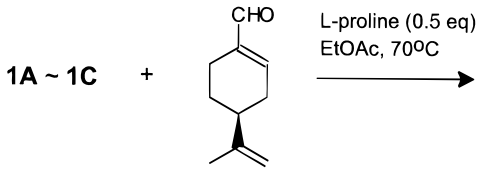
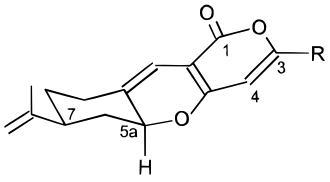
Scheme 3



(*S*)- 3



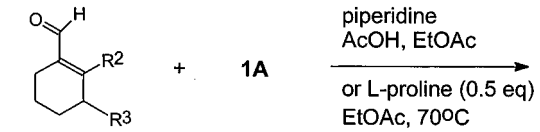
(a single isomer)

14 : R = Me (78% yield)
15 : R= 3-pyridyl (65% yield)
16 : R= 3,4-dimethoxyphenyl (63% yield)

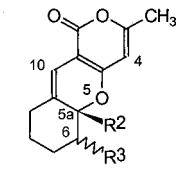
hydes **4** and **5** separately in the presence of 0.5 equiv of L-proline or a catalytic amount of piperidine and acetic acid in ethyl acetate at 60−80 °C to give a 72% yield of a mixture of **17A** and **17B** (in a ratio of 1.6:1; determined by ^{1}H NMR) and a 62% yield of a mixture of **18A** and **18B** (in a ratio of 3:1), respectively (Scheme 4). Although compounds **17A** and **17B** were not separately isolated, oxidation of this mixture with 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one[11] in CH_2Cl_2 at room temperature gave the corresponding C-6 ketone **19**. Reduction of this ketone with diisobutylaluminum hydride (Dibal-H) in THF provided pure *cis* alcohol **17A** in 87% yield and **17B** in 9% yield. Pyranobenzopyrans **18A** and **18B** were separated by column chromatography, and the structure of the *cis* isomer **18A** was unequivocally determined by single-crystal X-ray analysis. Basic hydrolysis of pure **18A** with K_2CO_3 in MeOH at room temperature gave pure alcohol **17A** (Scheme 4).

Aldehydes **4** and **5** were synthesized by a modification of the procedure reported by Corey and Erickson[12] (Scheme 5). Bromination of 2-methylcyclohexanone (**20**) with 1 equiv of *N*-bromosuccinimide[13] in refluxing CCl_4 for 12 h quantitatively yielded 2-bromo-2-methylcyclohexanone which underwent dehydrobromination when treated with 3 equiv of Li_2CO_3 and 3 equiv of LiBr in *N*,*N*-dimethylformamide (DMF)[14] at 130 °C for 3 h to provide a 72% yield of 2-methyl-2-cyclohexen-1-one (**21**).[15] 1,2-Addition reaction of **21** with 1.5 equiv of lithiated 1,3-dithiane [generated from 1,3-dithiane (**22**) treated with *n*-BuLi in THF] in THF at −10 °C gave a 96% yield of the 1,2-adduct **23**. Rearrangement of **23** with 1% sulfuric acid in *p*-dioxane (58% yield) followed by removal of the dithiane protecting group of the resulting alcohol (**24**) with *N*-chlorosuccinimide (NCS) and silver nitrate in acetonitrile−water gave aldehyde **4** (50% yield). Aldehyde **4** decomposes at room temperature in a few days. A more stable aldehyde, **5**, was synthesized in better yield from the rearrangement reaction of **23** in formic acid−THF in the presence of a catalytic amount of *p*-toluenesulfonic acid (70% yield) followed by removal of the dithiane moiety with NCS−$AgNO_3$ (59% yield) (Scheme 5). Formic acid rearrangement leads to the desired product, 1-[2-(1,3-dithianyl)]-3-(formyloxy)-2-methyl-1-

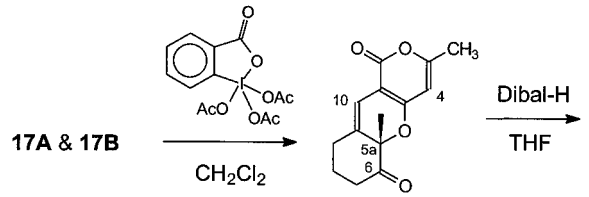
Scheme 4



4 : $R^2 = CH_3$; R^3 = OH
5 : $R^2 = CH_3$; R^3 = OCHO



17A : $R^2 = CH_3$; R^3 = β–OH (major)
17B : $R^2 = CH_3$; R^3 = α–OH (minor)
(72% yield)
18A : $R^2 = CH_3$; R^3 = β–OCHO (major)
18B : $R^2 = CH_3$; R^3 = α–OCHO (minor)
(62% yield)



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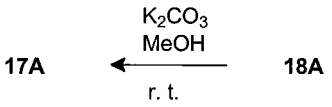
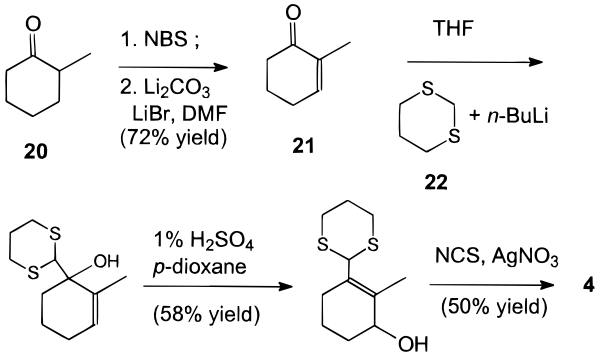
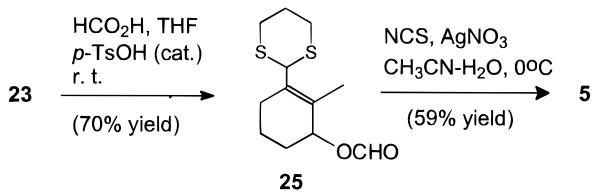


β = ◀ α = ⋯

Scheme 5





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(12) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553−3560.
(13) Rinne, W. W.; Deutsch, H. R.; Bowman, M. I.; Joffe, I. B. *J. Am. Chem. Soc.* **1950**, *72*, 5759−5760.
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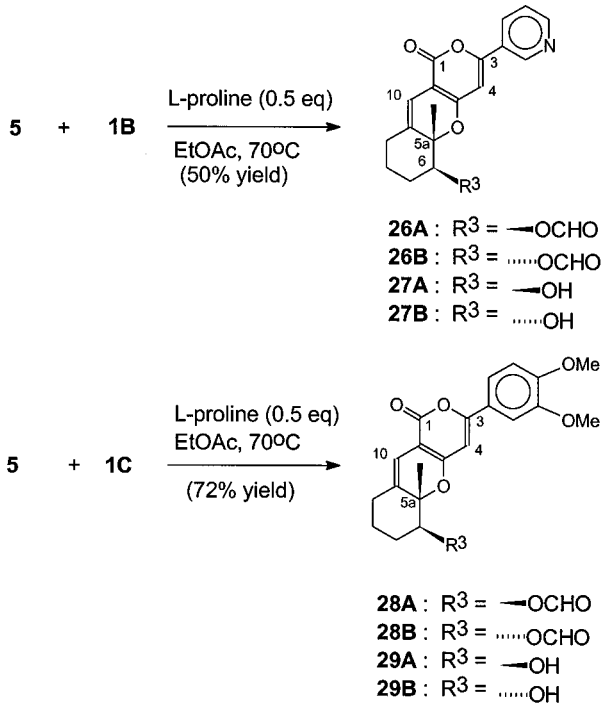
(15) Enone **21** had been synthesized from the chlorination followed by dehydrochlorination of **20**: Warnhoff, E. W.; Martin, D. G.; Johnson, W. S. *Organic Syntheses*; New York, 1963; Collect. Vol. 4, pp 162−166.

Scheme 6



cyclohexene (**25**) as well as 3-[2-(1,3-dithianyl)]-2-methyl-2-cyclohexen-1-ol (**24**), isolated in 9% yield.

In the condensation of formyloxy aldehyde **5** with pyrones **1B** and **1C**, some of the formyloxy groups were hydrolyzed, leading to the corresponding alcohols (Scheme 6). Hence, treatment of aldehyde **5** with pyrone **1B** and 0.5 equiv of L-proline in ethyl acetate at 70 °C afforded a 39% yield of formates **26A** and **26B** (in a ratio of 2:1) and an 11% yield of alcohols **27A** and **27B** (ratio of 2:1). Similarly, condensation of **5** with pyrone **1C** gave a 48% yield of **28A** and **28B** (2:1) and a 24% yield of **29A** and **29B** (2:1). However, when the condensation reactions were carried out under anhydrous conditions (adding 3 Å molecular sieves), the alcohol isomers such as **29A** and **29B** were not found and a 4.8:1 ratio of **28A** and **28B** was obtained. These *cis* and *trans* isomers (e.g., **26A** and **26B**, etc.) were separated by silica gel column chromatography. Condensation of alcohol **4** with pyrone **1C** also provided a mixture of the *cis* and *trans* adducts **29A** and **29B** (2:1). The lack of stereoselectivity in the electrocyclic ring closure reactions of these 2-methyl-3-hydroxy- and 3-(formyloxy)cyclohexenecarboxaldehydes (**4** and **5**) may be attributed to the presence of the 2-methyl substituent. In the ^{1}H NMR spectra, similar to that of **18A**, the C6 protons of **26A**, **27A**, **28A**, and **29A** appear as a doublet of doublets with $J = 11-12$ and $4-5$ Hz (axial−axial and axial−equatorial couplings), indicative of a axial hydrogen (at C6).

Some biological activities of the tricyclic pyrones have been evaluated, including their ability to inhibit acetylcholinesterase (AChE) activity, DNA synthesis, and tumor cell growth. At 50 μM, four tricyclic pyrones, **6B**, **6C**, **28A**, and **29A**, remarkably inhibit DNA synthesis and tumor cell growth in the murine L1210 system *in vitro*.[16] Among these four compounds, **6C** is the most effective against DNA synthesis ($IC_{50} = 8.5$ μM) whereas **6B** is the most effective against leukemic cell growth ($IC_{50} = 1.1$ μM). Interestingly, **6B** is an inhibitor of L1210 cell growth and is almost as potent as the known S phase-specific anticancer drug cytosine β-D-arabionofuranoside, which was used for comparison.[17] In contrast, trideacetylpyripyropene A has no inhibitory activity under similar bioassay conditions. The competitive inhibitions[18] of various tricyclic pyrones with acetylthiocholine using electric eel AChE and fetal bovine serum AChE were studied. The AChE inhibition constants K_i for **6A**, **18A**, **27A**, and **29A** are 7, 5, 8, and 4 μM, respectively (K_i of tacrine is 1 nM and was used for comparison).[19]

(16) Perchellet, J. P.; Newell, S. W.; Ladesich, J. B.; Perchellet, E. M.; Chen, Y.; Hua, D. H. *Proc. Am. Assoc. Cancer Res.* **1997**, *38*, 610−611.

III. Conclusions

A high-yielding one-pot condensation of 6-substituted 4-hydroxy-2-pyrones with substituted 1-cyclohexenecarboxaldehydes has been developed. A 1,2-addition reaction followed by dehydration and then ring closure via a 6Π electrocyclic process is proposed. Stereoselective ring-closure reactions are observed when (*S*)-4-isopropenyl-1-cyclohexenecarboxaldehyde (perillaldehyde) is used; 2-substitution (such as with methyl) of cyclohexenecarboxaldehydes decreases the selectivity in the electrocyclic reaction. Application of this method in the construction of (+)-pyripyropenes and arisugacin is being studied. Several of the tricyclic pyrones strongly inhibit AChE activity, DNA synthesis, and tumor cell growth *in vitro*. Many biologically active tricyclic compouds, such as analogs with nitrogen and sulfur at the 2 and 5 positions, should be synthesized by this method, and we plan to undertake that study in the future.

IV. Experimental Section

General Methods. Nuclear magnetic resonance spectra were obtained at 400 MHz for ^{1}H and 100 MHz for ^{13}C in deuteriochloroform, unless otherwise indicated. Infrared spectra are reported in wavenumbers (cm^{-1}). Mass spectra were taken from a Hewlett-Packard 5890 Series II GC-HPLC-MS. FAB spectra were taken by using Xe beam (8 KV) and *m*-nitrobenzyl alcohol as matrix. 4-Hydroxy-6-methyl-2-pyrone (**1A**), ethyl nicotinate (**9**), ethyl 3,4-dimethoxybenzoate (**11**), ethyl acetoacetate (**8**), (*S*)-perillaldehyde (**3**), 2-methylcyclohexanone (**20**), 1,3-dithiane (**22**), and L-proline were purchased from Aldrich Chemical Co. Davisil silica gel, grade 643 (200−425 mesh), was used for the flash column chromatographic separation. THF and diethyl ether were distilled over sodium and benzophenone before used. Methylene chloride was distilled over CaH_2, and toluene and benzene were distilled over $LiAlH_4$. Ethyl acetate was dried over $CaCl_2$, filtered, and distilled under argon atmosphere.

General Procedure for the Condensation of Pyrone and Enal. The following reaction procedure is representative:

3-Methyl-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyran (6A). A solution of 0.100 g (0.91 mmol) of cyclohexenecarboxaldehyde (**2**), 0.115 g (0.91 mmol) of 4-hydroxy-6-methyl-2-pyrone (**1A**), and 0.052 g (0.455 mmol) of L-proline in 5 mL of ethyl acetate was heated at 70 °C under an argon atmosphere for 24 h. The mixture was cooled to room temperature, diluted with 100 mL of methylene chloride, washed twice with 30 mL portion of a saturated aqueous $NaHCO_3$ solution, with 60 mL of water, and then with 60 mL

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(19) Details of the biological studies along with acyl-CoA:cholesterol acyltransferase (ACAT) inhibitory activities of various pyrone derivatives will be reported in separate manuscripts in due course.

of brine, dried ($MgSO_4$), filtered, and concentrated to give 0.200 g of crude product. Column chromatography on silica gel of the crude product using a gradient mixture of hexane:ether as eluant gave 0.150 g (76% yield) of **6A** and 6 mg (5% recovery) of **1A**. Compound **6A**: mp 110−112 °C; X-ray analysis was carried out on a single crystal obtained from the recrystallization from ether−hexane: IR (Nujol) ν 1710 (s, C=O), 1630 (C=C), 1560. ^{1}H NMR δ 6.07 (s, 1 H, C10H), 5.7 (s, 1 H, C4H), 5.02 (dd, J = 11, 5 Hz, 1 H, C5aH), 2.41 (m, 1 H, C9H), 2.18 (s, 3 H, Me), 2.13 (m, 1 H), 2.02−1.88 (m, 2 H), 1.8−1.7 (m, 2 H), 1.5−1.4 (m, 2 H); ^{13}C NMR δ 174.0 (s, C=O), 163.2 (s, C3), 161.4 (s, C4a), 133.1 (s, C10a), 109.2 (d, C10), 99.8 (d, C4), 97.3 (s, C9a), 79.7 (s, C5a), 35.2 (t), 33.1 (t), 26.9 (t), 24.5 (t), 20.1 (q, Me); MS (CI) m/z 219 (M + 1). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.39; H, 6.53.

Ethyl 5-(3-Pyridyl)-3,5-dioxopentanoate (10). To a cold (−10 °C) solution of 13.45 mL (96.2 mmol) of diisopropylamine in 150 mL of diethyl ether under argon was added 42.36 mL (96.2 mmol; 2.27 M solution in hexanes) of *n*-BuLi via syringe, and the solution was stirred for 1 h. In a separate flask, 5 g (38.5 mmol) of freshly distilled ethyl acetoacetate (**8**) and 60 mL of diethyl ether were added and the solution was cooled to −78 °C. To this solution was added the LDA solution (above) via cannula followed by 5.8 mL (38.5 mmol) of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (distilled from $LiAlH_4$) via syringe, and the solution was stirred at 0 °C for 3 h. To this dianion solution was added a solution of 5.81 g (38.5 mmol) of ethyl nicotinate (**9**; freshly distilled) in 60 mL of diethyl ether via cannula, and the reaction solution was warmed to room temperature and stirred for 30 h. After 5.5 mL of acetic acid was added and the solution was stirred for 10 min, it was filtered through a fritted funnel and the solid (desired product; exists as a protonated salt) was washed with 200 mL of diethyl ether. The filtrate was concentrated to give 1.691 g of material, and the NMR spectrum indicated that it is a mixture of starting material and some unidentified components. The solid was dissolved in 160 mL of distilled water, to it, 60 mL of 1 *N* HCl was added, and the solution was extracted three times with a 120 mL portion of methylene chloride. The combined extracts were washed with 100 mL of brine, dried ($MgSO_4$), and concentrated to give 7.921 g (88% yield) of the desired product **10**. The ^{1}H NMR spectrum of this material indicated it was sufficiently pure and to be used in the next reaction without purification: mp 38.5−39 °C; ^{1}H NMR δ 9.07 (s, 1 H, C-2′ H, pyr), 8.74 (d, J = 4.6 Hz, 1 H, C6′ H, pyr), 8.16 (d, J = 8 Hz, C4′ H), 7.41 (dd, J = 8 Hz, 4.6 Hz, C5′ H), 6.32 (s, 1 H, =CH of enol; the compound exists completely in its C4 enolic form), 4.22 (q, J = 7.2 Hz, 2 H, OCH_2), 3.5 (s, 2 H, CH_2), 1.3 (t, J = 7.2 Hz, 3 H, Me); ^{13}C NMR δ 189.9 (s, C=O, C3), 180.0 (s, O−C=, C5), 167.1 (s, C=O ester), 152.7 (d, C2′), 148.1 (d, C6′), 134.3 (d, C4′), 129.7 (s, C3′), 123.4 (d, C5′), 97.2 (d, =CH, C4), 61.4 (t, OCH_2), 45.7 (t, CH_2), 13.9 (q, Me); MS FAB, m/z 236 (M + 1), 235 (M^+).

4-Hydroxy-6-(3-pyridyl)-2-pyrone (1B). To a flask equipped with an adaptor connected to a manifold and maintained under argon was added 0.594 g (2.53 mmol) of ester **10**. The flask was then connected to a vacuum set at 3 mmHg pressure and heated over an oil bath at 150 °C. It was kept at this temperature for 0.5 h, and then cooled to room temperature. Diethyl ether was added to the reaction mixture which was then filtered and the solid residue was washed with diethyl ether. The solid was dried *in vacuo*; 0.380 g (79% yield) of **1B**. The filtrate was concentrated and column chromatographed to give 0.065 g (10.9% recovery) of starting ester **10**. Compound **1B**: recrystallization from *p*-dioxane−hexane (1:1) gave yellow solids; mp 205−207 °C dec; lit.[10a] mp 207−209 °C; ^{1}H NMR ($CDCl_3$ and DMSO-d_6) δ 9.03 (s, 1 H, C2′ H), 8.67 (d, J = 5.2 Hz, 1 H, C6′ H, pyr ring), 8.13 (d, J = 8 Hz, 1 H, C4′ H), 7.41 (dd, J = 8 Hz, 5.2 Hz, 1 H, C5′ H), 6.56 (d, J = 1.6 Hz, 1 H, C5 H), 5.62 (d, J = 1.6 Hz, 1 H, C3 H); ^{13}C NMR (DMSO-d_6) δ 170.3 (s, C2), 162.7 (s, C4), 157.9 (s, C6), 151.3 (d, C2′), 146.6 (d, C6′), 133.0 (d, C4′), 127.1 (s, C1′), 123.9 (d, C5′), 99.6 (d, C3), 90.2 (d, C5); MS FAB, m/z 190 (M + 1), 189 (M^+).

Ethyl 5-(3,4-Dimethoxyphenyl)-3,5-dioxopentanoate (12) and Methyl 5-(3,4-Dimethoxyphenyl)-3,5-dioxopentanoate (12A). To a cold (−20 °C) solution of 8.9 mL (63.7 mmol) of diisopropylamine in 100 mL of diethyl ether under argon was added 28.1 mL (63.7 mmol; 2.27 M solution in hexanes) of *n*-BuLi via syringe, and the solution was stirred at 0 °C for 45 min. In a separate flask, 3.32 g (25.5 mmol) of freshly distilled ethyl acetoacetate (**8**) and 50 mL of diethyl ether were added and the solution was cooled to −78 °C. To this solution was added the LDA solution (above) via cannula followed by addition of 3.84 mL (25.5 mmol) of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (distilled from $LiAlH_4$) via syringe, and the solution was stirred at 0 °C for 3 h. To this dianion solution was added a solution of 5.0 g (25.5 mmol) of methyl 3,4-dimethoxybenzoate (**11**) in 50 mL of diethyl ether via cannula, and the reaction solution was warmed to room temperature and stirred for 40 h. Acetic acid (4 mL) was added, and the mixture was stirred for 10 min. The reaction mixture was filtered through a fritted funnel, washed with 70 mL of ether, and the solid (desired product) was set aside. The organic filtrate from the above filtration was washed with 100 mL of 0.5 N HCl and then with 80 mL of brine, dried ($MgSO_4$), and concentrated to give ethyl ester **12** and starting material **11**. The solid that was set aside was then dissolved in 100 mL of 1 N HCl and extracted three times with a 50 mL portion of methylene chloride. The combined methylene chloride extracts were washed with 80 mL of brine, dried ($MgSO_4$), and concentrated to give additional product **12**. The combined crude products were column chromatographed on silica gel using a gradient mixture of hexane and ethyl acetate as eluant to give 4.053 g (54% yield) of pure **12** and 1.370 g (28% recovery) of **11**. **12**: ^{1}H NMR δ 7.51 (dd, J = 8.5 Hz, 2 Hz, 1 H, C5′ H, Ar), 7.44 (d, J = 2 Hz, 1 H, C2′ H), 6.89 (d, J = 8.5 Hz, 1 H, C6′ H), 6.25 (s, 1 H, =CH of enol at C4 and 5), 4.22 (q, J = 7 Hz, 2 H, OCH_2), 3.93 (s, 6 H, 2 OMe), 3.45 (s, 2 H, CH_2), 1.30 (t, J = 7 Hz, 3 H, Me); ^{13}C NMR δ 186.3 (s, C3), 184.1 (s, C5), 167.8 (s, C1), 153.1 (s, C4′ Ar), 149.1 (s, C3′), 127.1 (s, C1′), 121.5 (d, C2′), 110.5 (d, C5′), 109.6 (d, C6′), 96.1 (d, C4), 61.5 (t, OCH_2), 56.1 (q, OMe), 56.0 (q, OMe), 45.2 (t, CH_2), 14.2 (q, Me); MS FAB, m/z 295 (M + 1), 294 (M^+).

If acetic acid was not added before the reaction mixture was filtered in the workup procedure, 5-(3,4-dimethoxyphenyl)-3,5-dioxopentanoic acid (**13**) was produced. Similar aqueous treatment, followed by methylation of the combined carboxylic acid products (dissolved in 50 mL of CH_2Cl_2) with a solution of diazomethane in diethyl ether, concentration on rotary evaporator, and then column chromatographic separation on silica gel using a gradient mixture of hexane and ethyl acetate as eluant gave 3.798 g (56% yield) of pure methyl ester **12A**: ^{1}H NMR δ 7.51 (dd, J = 8.5 Hz, 2 Hz, 1 H, C5′ H, Ar), 7.45 (d, J = 2 Hz, 1 H, C2′ H), 6.9 (d, J = 8.5 Hz, 1 H, C6′ H), 6.24 (s, 1 H, =CH of enol at C4 and 5), 3.95 (s, 6 H, 2 OMe on Ar ring), 3.77 (s, 3 H, MeO), 3.47 (s, 2 H, CH_2); ^{13}C NMR δ 186.2 (s, C3 C=O), 184.1 (s, C5 =C−O), 168.2 (s, C=O ester), 153.2 (s, C4′), 149.1 (s, C3′), 127.0 (s, C1′), 121.5 (d, C2′), 110.6 (d, C5′), 109.7 (d, C6′), 96.2 (d, C4), 56.1 (q, OMe), 56.0 (q, OMe), 52.3 (q, OMe of ester), 44.9 (t, CH_2); MS FAB, m/z 281 (M + 1), 280 (M^+).

4-Hydroxy-6-(3,4-dimethoxyphenyl)-2-pyrone (1C). A flask containing the methyl ester **12A** (1.56 g; 5.57 mmol) was connected into a vacuum system to provide ∼3 mmHg pressure and heated in an oil bath to 160 °C over a 1 hour period. The reaction was kept at this temperature for another hour, cooled to room temperature, diluted with a small amount of ether, and filtered to collect the yellow solids, which were washed with ether and dried under vacuum to give 0.56 g of pyrone **1C**. The filtrate was concentrated to give 0.921 g of starting ester **12A**. This starting material was subjected to the same procedure as described above to give a total of 1.144 g (83% yield) of pyrone **1C**. Compound **1C**: mp 210−212 °C; ^{1}H NMR δ 7.40 (dd, J = 8.3 Hz, 2 Hz, 1 H, C6′ of the phenyl ring), 7.33 (d, J = 2 Hz, 1 H, C2′ of Ph ring), 6.91 (d, J = 8.3 Hz, 1 H, C5′), 6.40 (s, C5 H), 5.55 (s, 1 H, C3 H), 3.95 (s, 3 H, OMe), 3.94 (s, 3 H, OMe); ^{13}C NMR (DMSO-d_6) δ 170.7 (s, C2), 163.1 (s, C4), 160.3 (s, C6), 151.2 (s, C4′), 148.9 (s, C3′), 123.5 (s, C1′), 118.8 (d, C3), 111.7 (d, C2′), 108.5 (d, C5′), 97.0 (d, C6′), 88.7 (d, C5), 55.7 (q, OMe), 55.6 (q, OMe); MS FAB, m/z 249

(M + 1), 248 (M^+). Under similar reaction conditions, ethyl ester **12** provided a similar yield (84% yield) of the ring closure product **1C**.

3-(3-Pyridyl)-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-b][1]benzopyran (6B). From 0.344 g (1.82 mmol) of pyrone **1B** and 0.2 g (1.82 mmol) of aldehyde **2**, 0.373 g (73% yield) of **6B** was obtained after column chromatographic separation: IR (Nujol) ν 3070, 1690, 1620, 1540, 1200, 1060, 1020; ^{1}H NMR δ 8.99 (d, J = 2 Hz, 1 H, C2′ H, pyr), 8.65 (dd, J = 4.9 Hz, 2 Hz, 1 H, C6′H), 8.1 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.38 (dd, J = 8 Hz, 4.9 Hz, 1 H, C5′H), 6.44 (s, 1 H, C10 H), 6.14 (s, 1 H, C4 H), 5.14 (dd, J = 11 Hz, 5 Hz, 1 H, C5a H), 2.47 (m, 1 H, C9 H), 2.19 (m, 1 H, C9 H), 2.03 (m, 1 H), 1.94 (m, 1 H), 1.86−1.76 (m, 2 H), 1.5 (dt, J = 13 Hz, 3.4 Hz, 1 H), 1.37 (dt, J = 13 Hz, 3.4 Hz, 1 H); ^{13}C NMR δ 162.6 (s, C1), 161.4 (s, C4a), 156.5 (s, C3), 151.2 (d, C2′), 146.7 (d, C6′), 134.9 (s, C1′), 132.8 (d, C4′), 127.6 (s, C10a), 123.7 (d, C5′), 109.2 (d, C10), 99.8 (s, C9a), 98.6 (d, C4), 80.1 (d, C5a), 35.3 (t), 33.4 (t), 27.0 (t), 24.6 (t); MS FAB, m/z 282 (M + 1, 100%), 281 (M^+), 252, 202, 148, 136, 106. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37. Found: C, 72.33; H, 5.42.

3-(3,4-Dimethoxyphenyl)-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1] benzopyran (6C). From 0.200 g (0.81 mmol) of **1C** and 0.135 g (0.81 mmol) of aldehyde **2**, 0.200 g (62% yield) of **6C** was obtained after column chromatographic separation: mp 137−138 °C; IR (Nujol) ν 3010, 3050, 1700, 1650, 1630, 1560, 1520, 1280, 1240, 1150; ^{1}H NMR δ 7.37 (dd, J = 8.5 Hz, 2 Hz, 1 H, C6′ H, Ph ring), 7.28 (d, J = 2 Hz, 1 H, C2′ H), 6.9 (d, J = 8.5 Hz, 1 H, C5′ H), 6.29 (s, 1 H, C10 H), 6.14 (s, 1 H, C4 H), 5.07 (dd, J = 11.4 Hz, 5.2 Hz, 1 H, C5a H), 3.94 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 2.45 (d, J = 14 Hz, 1 H, C9 H), 2.18 (m, 1 H), 2.02 (m, 1 H), 1.92 (m, 1 H), 1.78 (m, 2 H), 1.54−1.34 (m, 2 H); ^{13}C NMR δ 163.4 (s, C1), 162.0 (s, C4a), 159.3 (s, C3), 151.3 (s, C4′), 149.2 (s, C3′), 133.6 (s, C1′), 124.1 (s, C10a), 118.9 (d, C2′), 111.1 (d, C5′), 109.4 (d, C10), 108.1 (d, C6′), 98.1 (s, C9a), 96.1 (d, C4), 79.8 (d, C5a), 56.1 (q, OMe), 56.0 (q, OMe), 35.3 (t), 33.3 (t), 27.0 (t), 24.6 (t); MS FAB, m/z 341 (M + 1, 100%), 340 (M^+), 307, 289, 261, 235, 219. Anal. Calcd for $C_{20}H_{20}O_5$: C, 70.58; H, 5.92. Found: C, 70.31; H, 6.11.

(5a*S*,7*S*)-7-Isopropenyl-3-methyl-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1] benzopyran (14). From 1.000 g (7.93 mmol) of **1A** and 1.191 g (7.93 mmol) of aldehyde (*S*)-**3**, 1.596 g (78% yield) of **14** was obtained after column chromatographic separation: yellow solids, mp 140−141 °C; $[\alpha]^{22}_D$ = +31.9° (*c* 0.75, $CHCl_3$); ^{1}H NMR δ 6.1 (s, 1 H, C10 H), 5.72 (s, 1 H, C4 H), 5.1 (dd, J = 11 Hz, 5 Hz, 1 H, C5a H), 4.75 (m, 1 H, =CH), 4.73 (m, 1 H, =CH), 2.48 (ddd, J = 14 Hz, 4 Hz, 2.4 Hz, 1 H), 2.22−2.02 (series of m, 3 H), 2.19 (s, 3 H, C4-Me), 1.88−1.72 (series of m, 2 H), 1.74 (s, 3 H, MeC=), 1.31 (ddd, J = 25 Hz, 12.8 Hz, 4 Hz, 1 H); ^{13}C NMR δ 163.4 (s, C=O), 162.6 (s, C3), 161.7 (s, C4a), 147.9 (s, C10a), 132.3 (s, =C), 109.8 (d, C10), 109.6 (t, $=CH_2$), 99.9 (d, C4), 97.5 (s, C9a), 79.4 (s, C5a), 43.6 (d, C7), 40.0 (t), 32.5 (t), 32.1 (t), 20.9 (q, Me), 20.3 (q, Me); MS FAB, m/z 259 (M+1; 70%), 258, 257, 215, 189, 139 (100%). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.17; H, 7.33.

(5a*S*,7*S*)-7-Isopropenyl-3-(3-pyridyl)-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyran (15). From 0.200 g (1.06 mmol) of **1B** and 0.160 g (1.06 mmol) of aldehyde (*S*)-**3**, 0.221 g (65% yield) of **15** was obtained after column chromatographic separation; yellow solids, mp 99−100 °C; $[\alpha]^{22}_D$ = +100.6° (*c* 0.77, CH_2Cl_2); ^{1}H NMR δ 8.98 (d, J = 2 Hz, 1 H, C2′ H, pyr), 8.65 (dd, J = 4.8 Hz, 2 Hz, 1 H, C6′H), 8.07 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.38 (dd, J = 8 Hz, 4.8 Hz, 1 H, C5′H), 6.44 (s, 1 H, C10 H), 6.15 (s, 1 H, C4 H), 5.17 (dd, J = 11.6 Hz, 5.2 Hz, 1 H, C5a H), 4.74 (m, 2 H, $=CH_2$), 2.52 (m, 1 H), 2.26−1.75 (a series of m, 5 H), 1.75 (s, 3 H, Me), 1.3 (m, 1 H); ^{13}C NMR δ 162.5 (s, C1), 161.3 (s, C4a), 156.6 (s, C3), 151.2 (d, C2′), 147.6 (d, C6′), 146.7 (s, C=), 133.9 (s, C3′), 132.7 (d, C4′), 127.4 (s, C10a), 123.7 (d, C5′), 109.9 (d, C10), 109.4 (t, $=CH_2$), 99.8 (s, C9a), 98.4 (d, C4), 79.6 (d, C5a), 43.4 (d, C7), 39.9 (t), 32.5 (t), 31.9 (t), 20.8 (q, Me); MS FAB, m/z 322 (M+1, 100%), 278 (M^+), 252, 202, 148, 106. Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96. Found: C, 74.48; H, 6.12.

(5a*S*,7*S*)-7-Isopropenyl-3-(3,4-dimethoxyphenyl)-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]-benzopyran (16). From 0.200 g (0.81 mmol) of **1B** and 0.121 g (0.81 mmol) of aldehyde (*S*)-**3**, 0.193 g (63% yield) of **16** was obtained after column chromatographic separation: yellow solids, mp 119−120 °C; $[\alpha]^{22}_D$ = +90.4° (*c* 0.76, $CHCl_3$); ^{1}H NMR δ 7.37 (dd, J = 8.8 Hz, 2.4 Hz, 1 H, C6′ H, Ph ring), 7.28 (d, J = 2.4 Hz, 1 H, C2′ H), 6.89 (d, J = 8.8 Hz, 1 H, C5′ H), 6.29 (s, 1 H, C10 H), 6.17 (s, 1 H, C4 H), 5.15 (dd, J = 11 Hz, 5 Hz, 1 H, C5a H), 4.75 (m, 2 H, $=CH_2$), 3.94 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 2.52 (ddd, J = 13 Hz, 6 Hz, 3.6 Hz, 1 H), 2.26−2.24 (a series of m, 3 H), 1.88−1.76 (m, 2 H), 1.75 (s, 3 H, Me), 1.34 (m, 1 H); ^{13}C NMR δ 163.6 (s, C1), 162.1 (s, C4a), 159.7 (s, C3), 151.6 (s, C4′), 149.4 (s, C3′), 148.0 (s, =C), 132.8 (s, C1′), 124.3 (s, C10a), 119.1 (d, C2′), 111.3 (d, C5′), 109.9 (d, $=CH_2$), 109.9 (d, C10), 108.4 (d, C6′), 98.3 (s, C9a), 96.2 (d, C4), 79.5 (d, C5a), 56.3 (q, OMe), 56.2 (q, OMe), 43.6 (d, C7), 40.1 (t), 32.6 (t), 32.1 (t), 20.9 (q, Me); MS FAB, m/z 381 (M+1, 100%), 380 (M^+). Anal. Calcd for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36. Found: C, 72.43; H, 6.17.

Preparation of 2-Methyl-2-cyclohexen-1-one (21). A solution of 15.00 g (0.134 mol) of 2-methyl-1-cyclohexanone (**20**) and 23.84 g (0.134 mol) of *N*-bromosuccinimide in 150 mL of carbon tetrachloride was stirred and heated to reflux for 12 h under argon. The mixture was cooled to room temperature and filtered through Celite to remove succinimide, and the filter cake was washed with 150 mL of ether. The filtrate was concentrated to give 25.60 g (100% yield) of 2-bromo-2-methyl-1-cyclohexanone: ^{1}H NMR δ 3.21 (td, J = 16 Hz, 8 Hz, 1 H, CH−CO), 2.36 (m, 2 H), 2.06 (m, 2 H), 1.82 (s, 3 H, Me), 1.77 (m, 2 H), 1.62 (m, 1 H). This material was used in the following step without further purification.

A mixture of 25.60 g (0.134 mol) of 2-bromo-2-methylcyclohexanone (above), 29.70 g (0.4 mol) of Li_2CO_3, and 34.90 g (0.4 mol) of LiBr in 300 mL of DMF was heated at 130 °C under argon for 3 h. The reaction mixture was cooled to room temperature, diluted with 400 mL of water, and extracted three times with ether (300 mL × 2 and 200 mL). The combined extract was dried ($MgSO_4$) and concentrated on a rotary evaporator to give 12.96 g of crude product which was vacuum distilled to give 10.6 g (72% yield) of **21**, bp 90−95 °C/45 mmHg; lit.[13] 93−97 °C/25 mmHg; ^{1}H NMR δ 6.75 (broad s, 1 H, =CH), 2.42 (dd, J = 5.6 Hz, 5 Hz, 2 H), 2.33 (m, 2 H), 1.95 (pent, J = 8 Hz, 2 H), 1.78 (q, J = 2 Hz, 3 H, Me); ^{13}C NMR δ 199.9 (s, C=O), 145.6 (d, =CH), 135.7 (s, =C), 38.3 (t), 26.0 (t), 23.3 (t), 16.0 (q).

1-[2-(1,3-Dithianyl)]-2-methyl-2-cyclohexen-1-ol (23). To a cold (−10 °C) solution of 6.71 g (55.9 mmol) of 1,3-dithiane (**22**) in 50 mL of THF under argon was added 24.6 mL (55.9 mmol; from a 2.27 M solution in hexane) of *n*-BuLi dropwise via syringe over 35 min, and the resulting solution was stirred for 2 h. In a separate flask, a solution of 4.10 g (37.7 mmol) of **21** in 25 mL of THF was prepared and added via cannula into the above dithiane anion solution. The solution was stirred at −10 °C for 1 h and kept in the refrigerator for 18 h, diluted with 100 mL of water, stirred for 10 min, and extracted three times with diethyl ether (100, 75, and 50 mL). The combined extracts were washed twice with 100 mL portion of brine, dried ($MgSO_4$), filtered, and concentrated to give 13.15 g of crude product. Column chromatographic separation on silica gel using a gradient mixture of hexane:ether as eluant gave 8.21 g (96% yield) of **23** as an oil: ^{1}H NMR δ 5.74 (t, J = 4 Hz, 1 H, =CH), 4.42 (s, 1 H, CH−S), 3.0−2.8 (m, 4 H, CH_2S), 2.28 (s, 1 H, OH), 2.16−1.6 (series of m, 8 H), 1.82 (broad s, 3 H, Me); ^{13}C NMR δ 133.8 (s, =C), 130.3 (d, =CH), 74.0 (s, CO), 59.1 (d, CH-S), 33.9 (t, CH_2S), 31.8 (t, CH_2S), 31.3 (t, CH_2), 26.4 (t, CH_2), 25.6 (t, CH_2), 18.7 (t, CH_2), 17.8 (q, Me); MS (EI) m/z 230 (M^+).

3-[2-(1,3-Dithianyl)]-2-methyl-2-cyclohexen-1-ol (24). A solution of 1.031 g (4.48 mmol) of alcohol **23** in 50 mL of *p*-dioxane and 75 mL of 1% aqueous solution of H_2SO_4 was stirred at 25 °C for 5.5 h and extracted three times with a 100 mL portion of diethyl ether. The combined extracts were washed with 80 mL of saturated aqueous $NaHCO_3$, twice with 80 mL portions of water, and 80 mL of brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluant to

give 0.533 g (58% yield based on recovered starting material **23**) of **24** as an oil and 0.110 g (11% recovery) of **23**. Compound **24**: ^{1}H NMR δ 5.09 (s, 1 H, CHS), 3.97 (broad s, 1 H, CHO), 3.04−2.95 (m, 2 H, CH_2S), 2.87−2.81 (m, 2 H, CH_2S), 2.32−2.24 (m, 1 H), 2.16−2.07 (m, 2 H), 1.91 (t, J = 4 Hz, 3 H, Me), 1.89−1.58 (a series of m, 5 H); ^{13}C NMR δ 132.9 (s, C=), 131.9 (s, =C), 69.6 (d, CO), 51.1 (d, CHS), 31.8 (t), 31.4 (2 C, t, CH_2S), 26.6 (t), 25.5 (t), 18.5 (t), 16.4 (q, Me); MS (EI) m/z 230 (M^+). Anal. Calcd for $C_{11}H_{18}OS_2$: C, 57.35; H, 7.87. Found: C, 57.56; H, 8.10.

3-Hydroxy-2-methyl-1-cyclohexene-1-carboxaldehyde (4). To 0.197 g (1.16 mmol) of $AgNO_3$ and 0.139 g (1.04 mmol) of *N*-chlorosuccinimide (NCS) under argon were added 6 mL of CH_3CN and 2.5 mL of H_2O. The solution was stirred and cooled in an ice−water bath, and a solution of 0.059 g (0.26 mmol) of **24** in 5 mL of acetonitrile was added dropwise via cannula. The solution was stirred at 0 °C for 45 min, and 1 mL each of saturated aqueous Na_2SO_3 and Na_2CO_3 were added at 1-min intervals followed by 20 mL of a 1:1 mixture of CH_2Cl_2−petroleum ether was also added. The resulting mixture was filtered through Celite and the solid carefully washed with 120 mL of 1:1 mixture of CH_2Cl_2 and petroleum ether. The filtrate was transferred into a separatory funnel, and the water layer was removed. The organic layer was washed with 10 mL of saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated to give 32 mg of the crude aldehyde **4**. This material can be used directly in the next reaction without further purification. For characterization, the mixture was separated by silica gel column chromatography and provided 18 mg (50% yield) of pure **4**. Aldehyde **4** is unstable; elemental analysis was not performed. **4**: ^{1}H NMR δ 10.18 (s, 1 H, CHO), 4.16 (broad s, 1 H, CH−O), 2.27 (s, 3 H, Me), 2.31−1.6 (a series of m, 6 H); ^{13}C NMR δ 192.4 (s, C=O), 154.2 (s, C=), 135.0 (s, C=), 70.3 (d, C-O), 31.8 (t), 22.7 (t), 17.9 (t), 14.9 (q, Me); MS FAB m/z 141 (M+1, 100%), 140 (M^+).

3-(Formyloxy)-2-methyl-1-cyclohexene-1-carboxaldehyde (5). A solution of 0.494 g (2.15 mmol) of alcohol **23** and three crystals of *p*-toluenesulfonic acid (anhydrous) in 2.43 mL of formic acid and 15 mL of THF was stirred under argon at 25 °C for 16 h. The solution was diluted with 100 mL of diethyl ether, washed with 40 mL of saturated aqueous $NaHCO_3$ and 50 mL of brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluant to give 0.388 g (70% yield) of 1-[2-(1,3-dithanyl)]-3-(formyloxy)-2-methyl-1-cyclohexene (**25**) and 0.048 g (9% yield) of alcohol **24**. Compound **25**: ^{1}H NMR δ 8.12 (s, 1 H, CHO), 5.36 (broad s, 1 H, CH−O), 5.1 (s, 1 H, CHS), 3.05−2.95 (m, 2 H, CH_2S), 2.9−2.8 (m, 2 H, CH_2S), 2.4−2.3 (m, 1 H), 2.2−2.05 (m, 2 H), 1.94−1.6 (m, 5 H), 1.78 (s, 3 H, Me); ^{13}C NMR δ 161.0 (s, C=O), 135.2 (s, C=), 128.4 (s, C=), 71.7 (d, C−O), 51.0 (d, CS), 31.3 (t, 2 C, CS), 28.7 (t), 26.4 (t), 25.4 (t), 18.6 (t), 16.3 (q, Me); MS FAB m/z 259 (M + 1), 258 (M^+).

To a dried 100 mL round-bottomed flask were added 1.19 g (7 mmol) of $AgNO_3$, 0.828 g (6.2 mmol) of NCS, 40 mL of CH_3CN, and 16 mL of H_2O under argon, the solution was stirred and cooled in an ice−water bath, and a solution of 0.4 g (1.55 mmol) of **25** in 10 mL of CH_3CN was added dropwise over 30 min. To this solution were added 2 mL of a saturated aqueous solution of Na_2SO_3 and Na_2CO_3, 2 mL of a saturated aqueous NaCl solution, and 20 mL of a 1:1 mixture of CH_2Cl_2−petroleum ether sequentially at 1-min intervals. The whole mixture was then filtered through Celite and washed with 100 mL of CH_2Cl_2 and petroleum ether. The filtrate was transferred into a separatory funnel, and the aqueous layer was separated and extracted with 40 mL of CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered, concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluant to give 0.154 g (59% yield) of pure **5**: IR (neat) ν 2750, 1720, 1680 (C=O); ^{1}H NMR δ 10.2 (s, 1 H, CHO), 8.18 (d, J = 0.8 Hz, 1 H, formyloxy CH), 5.53 (t, J = 4.8 Hz, 1 H, CH−O), 2.39−2.3 (m, 1 H), 2.14 (s, 3 H, Me), 2.17−2.08, (m, 1 H), 1.94−1.6 (a series of m, 4 H); ^{13}C NMR δ 191.6 (s, C=O aldehyde), 160.7 (s, C=O of formyloxy), 148.7 (s, C=), 137.4 (s, C=), 71.7 (d, CH-O), 28.6 (t), 22.5 (t), 17.9 (t), 14.8 (q, Me); MS FAB m/z 169 (M + 1), 168 (M^+). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.98; H, 7.31.

General Procedure for the Condensation of Pyrones with Aldehydes 4 and 5. *cis*- and *trans*-3,5a-Dimethyl-6-(formyloxy)-1*H*,7*H*-5a,6,8,9-tetrahydro-1−oxopyrano[4,3-*b*][1]benzopyran (18A and 18B). A solution of 0.1470 g (0.88 mmol) of aldehyde **5**, 0.11 g (0.88 mmol) of pyrone **1A**, and 0.05 g (0.4 mmol) of L-proline in 10 mL of ethyl acetate was stirred under argon at 25 °C for 1 day, 40 °C (bath temperature) for 3 days, and 60 °C for 1 day. The mixture was diluted with 120 mL of methylene chloride, washed with 50 mL of saturated aqueous $NaHCO_3$ and then with 50 mL of brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluant to give 0.1133 g (46.5% yield) of **18A** and 0.0378 g (15.5% yield) of **18B**. Compound **18A**: mp 138−140 °C; IR (Nujol) ν 2980, 1720, 1690, 1630, 1550, 1110; ^{1}H NMR δ 8.14 (d, J = 1 Hz, 1 H, CHO), 6.18 (d, J = 2.2 Hz, 1 H, C10 H), 5.73 (s, 1 H, C4 H), 5.31 (dd, J = 11.6 Hz, 4.4 Hz, 1 H, C6 H, axial H), 2.39−2.33 (m, 1 H), 2.29−2.23 (m, 1 H), 2.19 (d, J = 0.44 Hz, 3 H, Me), 2.12−2.05 (m, 1 H), 1.88−1.8 (m, 1 H), 1.7−1.5 (m, 2 H), 1.54 (s, 3 H, Me); ^{13}C NMR δ 162.4 (s, C=O), 162.3 (s), 160.4 (s, 2 C), 132.7 (s, C10a), 112.5 (d, C10), 100.1 (d, C4), 97.7 (s, C9a), 84.4 (s, C5a), 76.5 (d, C6), 31.3 (t), 29.3 (t), 23.1 (t), 20.3 (q, Me), 18.9 (q, Me); MS FAB, m/z 277 (M + 1, 100%), 230, 139, 91. Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.47; H, 5.61. Single crystals were obtained from the recrystallization in ether, and the structure was unequivocally determined by an X-ray analysis.

Compound 18B: ^{1}H NMR δ 8.11 (d, J = 0.92 Hz, 1 H, CHO), 6.23 (d, J = 1.6 Hz, 1 H, C10 H), 5.72 (s, 1 H, C4 H), 2.44−2.28 (m, 2 H), 2.19 (d, J = 0.6 Hz, 3 H, Me), 2.1−2.0 (m, 1 H), 1.9−1.64 (a series of m, 3 H), 1.57 (s, 3 H, Me); ^{13}C NMR δ 162.5 (s, C=O), 161.9 (s), 160.1 (s, 2 C), 131.6 (s, C10a), 112.2 (d, C10), 99.7 (d, C4), 97.1 (s, C9a), 82.9 (s, C5a), 74.3 (d, C6), 31.0 (t), 27.9 (t), 23.7 (t), 20.6 (q, Me), 20.1 (q, Me); MS FAB, m/z 277 (M + 1, 100%). Basic hydrolysis of **18B** with K_2CO_3 in MeOH gave the corresponding C6 alcohol having exactly the same NMR as the *trans*-alcohol obtained from the condensation of pyrone **1A** and aldehyde **4**.

***cis*- and *trans*-3,5a-Dimethyl-6-hydroxy-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyran (17A and 17B).** From 24.0 mg (0.188 mmol) of aldehyde **4** and 23.7 mg (0.188 mmol) of pyrone **1A**, heating with 3 mL of ethyl acetate and 3 drops (~15 mg) of piperidine and 3 drops of acetic acid at 80 °C for 18 h, 33.0 mg (72% yield) of a mixture of **17A** and **17B** in a ratio of 1.6:1 (determined from ^{1}H NMR spectrum) was obtained. Compound **17A**: ^{1}H NMR δ 6.13 (d, J = 2 Hz, 1 H, C10 H), 5.77 (s, 1 H, C4 H), 4.07 (dd, J = 8.4 Hz, 3.4 Hz, 1 H, C6 H), 2.36−2.16 (a series of m, 2 H), 2.21 (s, 3 H, C3 Me), 2.14 (broad s, 1 H, OH), 1.98−2.04 (m, 1 H), 1.83−1.76 (m, 1 H), 1.56−1.42 (m, 2 H), 1.47 (s, 3 H, C5a Me); ^{13}C NMR δ 162.4 (s, C1), 162.1 (s, C4a), 158 (s, C3), 134.2 (s, C10a), 111.7 (d, C10), 100.1 (d, C4), 98.1 (s, C9a), 87.1 (s, C5a), 76.2 (d, C6), 31.6 (t), 30.9 (t), 23.2 (t), 20.4 (q, Me), 17.5 (q, Me); MS FAB, m/z 249 (M + 1), 248 (M^+). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.67; H, 6.72.

Compound 17B: ^{1}H NMR δ 6.23 (d, J = 3 Hz, 1 H, C10 H), 5.80 (s, 1 H, C4 H), 3.87 (t, J = 1 Hz, 1 H, C6 H), 2.21 (s, 3 H, C3 Me), 1.44 (s, 3 H, C5a Me), 2.4−1.5 (a series of m, 6 H); ^{13}C NMR δ 162.1 (s, C1), 161.7 (s, C4a), 156.2 (s, C3), 133.4 (s, C10a), 112.5 (d, C10), 99.9 (d, C4), 98.5 (s, C9a), 85.6 (s, C5a), 73.0 (d, C6), 31.1 (t), 29.0 (t), 22.5 (t), 20.1 (q, Me), 19.5 (q, Me); MS FAB, m/z 249 (M + 1), 248 (M^+). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.49; H, 6.57.

***cis*- and *trans*-3-(3-Pyridyl)-5a-methyl-6-(formyloxy)-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]-benzopyran (26A and 26B) and *cis*- and *trans*-3-(3-Pyridyl)-5a-methyl-6-hydroxy-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-*b*][1]benzopyran (27A and 27B).** After condensation of 73 mg (0.39 mmol) of pyrone **1B** and 65 mg (0.39 mmol) of aldehyde **5** in the presence of 23 mg (0.19 mmol) of L-proline in 5 mL of ethyl acetate under argon at 70 °C for 3 days, 3 mL of DMF was added and the reaction mixture was heated at the same temperature for another 3 days. After

aqueous workup as described in the general procedure, 131 mg of crude product was obtained. Column chromatographic separation of this material afforded a 39% yield of formates **26A** and **26B** (in a ratio of 2:1) and an 11% yield of alcohols **27A** and **27B** (ratio of 2:1). Compounds **26A** and **26B** and **27A** and **27B** were separated by a careful silica gel column chromatography to give 34 mg (26% yield) of **26A**, 17 mg (13% yield) of **26B**, 9 mg (7.3% yield) of **27A**, and 4 mg (3.7% yield) of **27B**. Compounds **27A** and **27B** were probably formed from the hydrolytic reaction with the H_2O formed from the reaction. Compound **26A**: mp 160−161 °C; ^{1}H NMR δ 9.0 (d, J = 2 Hz, 1 H, C2′ H, pyr), 8.66 (dd, J = 5 Hz, 2 Hz, 1 H, C6′H), 8.18 (s, 1 H, CHO), 8.09 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.39 (dd, J = 8 Hz, 5 Hz, 1 H, C5′H), 6.46 (s, 1 H, C10H), 6.26 (s, 1 H, C4H), 5.38 (dd, J = 12 Hz, 5 Hz, 1 H, C6H), 2.42 (m, 1 H, C9H), 2.3 (m, 1 H, C9H), 2.12 (m, 1 H), 1.88 (m, 1 H), 1.7−1.52 (m, 2 H), 1.60 (s, 3 H, Me); ^{13}C NMR δ 161.5 (s, C1), 160.1 (d, s, 2 C, CHO & C4a), 157.1 (s, C3), 151.3 (d, C2′, pyr), 146.7 (d, C4′), 134.2 (s, C1′), 132.8 (d, C6′), 127.3 (s, C10a), 123.6 (d, C5′), 112.3 (d, C10), 99.8 (s, C9a), 98.5 (d, C4), 84.6 (s, C5a), 76.2 (d, C6), 31.3 (t), 29.1 (t), 22.9 (t), 18.9 (q, Me); MS FAB, m/z 340 (M+1, 100%), 293, 278, 266, 240, 202, 173. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05. Found: C, 67.07; H, 5.29.

Compound 26B: ^{1}H NMR δ 9.0 (d, J = 2 Hz, 1 H, C2′ H, pyr), 8.66 (dd, J = 5 Hz, 2 Hz, 1 H, C6′H), 8.14 (s, 1 H, CHO), 8.10 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.39 (dd, J = 8 Hz, 5 Hz, 1 H, C5′H), 6.45 (s, 1 H, C10H), 6.31 (s, 1 H, C4H), 5.28 (broad s, 1 H, C6H), 2.46−1.5 (a series of m, 6 H), 1.64 (s, 3 H, Me); ^{13}C NMR δ 161.9 (s, C1), 160.3 (d, s, 2 C, CHO & C4a), 157.3 (s, C3), 151.5 (d, C2′, pyr), 147.2 (d, C4′), 133.6 (s, C1′), 133.1 (d, C6′), 127.6 (s, C10a), 123.9 (d, C5′), 112.5 (d, C10), 100.1 (s, C9a), 98.8 (d, C4), 83.5 (s, C5a), 74.5 (d, C6), 31.5 (t), 28.1 (t), 24.0 (t), 20.8 (q, Me); MS FAB, m/z 340 (M+1, 100%). Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05. Found: C, 66.97; H, 5.12.

Compound 27A: ^{1}H NMR δ 9.0 (d, J = 2 Hz, 1 H, C2′H, pyr), 8.66 (d, J = 4 Hz, 1 H, C6′ H), 8.10 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.39 (dd, J = 8 Hz, 4 Hz, 1 H, C5′H), 6.51 (s, 1 H, C10H), 6.20 (d, J = 2 Hz, 1 H, C4H), 4.14 (dd, J = 12 Hz, 4.4 Hz, 1 H, C6H), 2.42−1.4 (a series of m, 6 H), 1.54 (s, 3 H, Me); ^{13}C NMR [from a mixture of **27A** (*c*) and **27B** (*t*)] δ 161.7 (s, C1), 160.3 (s, C4a), 157.3 (s, C3), 151.5 (d, C2′), 147.2 (d, C4′), 135.9 (s, C1′, *c*), 135.5 (s, C1′, *t*), 133.0 (d, C6′), 127.6 (s, C10a), 123.9 (d, C5′), 112.6 (d, C10, *t*), 111.7 (d, C10, *c*), 100.0 (s, C9a), 98.8 (d, C4, *c*), 94.0 (s, C5a, *t*), 87.5 (d, C4, *t*), 86.3 (s, C5a, *c*), 76.2 (d, C6, *c*), 73.3 (d, C6, *t*), 31.8 (t, C9, *c*), 31.5 (t, C9, *t*), 31.1 (t, C7, *c*), 29.9 (t, C7, *t*), 29.3 (t, C8, *c*), 23.2 (t, C8, *t*), 23.0 (q, Me, *c*), 19.8 (q, Me, *t*). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50. Found: C, 69.17; H, 5.21.

Compound 27B: ^{1}H NMR δ 9.0 (d, J = 2 Hz, 1 H, C2′H, pyr), 8.66 (d, J = 4 Hz, 1 H, C6′ H), 8.10 (dt, J = 8 Hz, 2 Hz, 1 H, C4′H), 7.39 (dd, J = 8 Hz, 4 Hz, 1 H, C5′H), 6.32 (s, 1 H, C10H), 6.20 (d, J = 2 Hz, 1 H, C4H), 3.94 (broad s, 1 H, C6H), 2.42−1.4 (a series of m, 6 H), 1.51 (s, 3 H, Me); MS FAB, m/z 312 (M+1, 100%).

***cis*- and *trans*-3-(3,4-Dimethoxyphenyl)-5a-methyl-6-hydroxy-1*H*,7*H*-5a,7,8,9-tetrahydro-1-oxopyrano[4,3-*b*]-[1]benzopyran (29A and 29B).** Condensation of 0.103 g (0.41 mmol) of pyrone **1C** and 0.058 g (0.41 mmol) of hydroxy aldehyde **4** gave a 68% yield of **29A** and **29B** in a ratio of 2:1. Column chromatographic separation gave pure **29A** and **29B**. Compound **29A**: ^{1}H NMR δ 7.39 (dd, J = 8 Hz, 2 Hz, 1 H, C6′, Ph), 7.29 (d, J = 2 Hz, C2′H), 6.9 (d, J = 8 Hz, 1 H, C5′H), 6.37 (s, 1 H, C10H), 6.2 (d, J = 2 Hz, 1 H, C4H), 4.12 (dd, J = 12 Hz, 5 Hz, 1 H, C6H), 3.94 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 2.36 (m, 1 H), 2.26 (m, 1 H), 2.04 (m, 1 H), 1.82 (m, 1 H), 1.6−1.46 (m, 2 H), 1.51 (s, 3 H, Me); ^{13}C NMR δ 162.5 (s, C1), 161.6 (s, C4a), 158.6 (s, C3), 151.6 (s, C4′, Ph), 149.2 (s, C3′), 134.4 (s, C1′), 124.1 (s, C10a), 119.2 (d, C2′), 112.0 (d, C5′), 111.1 (d, C10), 108.2 (d, C6′), 98.5 (s, C9a), 96.2 (d, C4), 86.9 (s, C5a), 76.3 (d, C6), 56.3 (q, OMe), 53.6 (q, OMe), 31.7 (t), 31.1 (t), 23.3 (t), 17.6 (q, Me); MS FAB, m/z 371 (M+1, 100%), 370 (M$^+$), 355, 325, 307, 261, 219, 207. Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 67.89; H, 5.73.

Compound 29B: ^{1}H NMR δ 7.38 (dd, J = 8 Hz, 2 Hz, 1 H, C6′, Ph), 7.29 (d, J = 2 Hz, C2′H), 6.9 (d, J = 8 Hz, 1 H, C5′H), 6.37 (s, 1 H, C10H), 6.31 (d, J = 2 Hz, 1 H, C4H), 3.92 (m, 1 H, C6H), 3.94 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 2.53 (broad s, 1 H, OH), 2.42 (m, 1 H), 2.3 (m, 1 H), 2.08 (m, 1 H), 1.88 (m, 1 H), 1.77 (m, 1 H), 1.58 (m, 1 H), 1.49 (s, 3 H, Me); ^{13}C NMR δ 162.3 (s, C1), 161.6 (s, C4a), 159.5 (s, C3), 151.4 (s, C4′), 149.2 (s, C3′), 133.9 (s, C1′), 124.0 (s, C10a), 118.9 (d, C2′), 112.7 (d, C5′), 111.0 (d, C10), 108.2 (d, C6′), 99.1 (s, C9a), 96.2 (d, C4), 85.6 (s, C5a), 73.1 (d, C6), 56.1 (q, OMe), 56.0 (q, OMe), 31.2 (t), 29.0 (t), 22.6 (t), 19.6 (q, Me); MS FAB, m/z 371 (M + 1, 100%), 370 (M$^+$). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 68.02; H, 5.65.

***cis*- and *trans*-3-(3,4-Dimethoxyphenyl)-6-(formyloxy)-5a-methyl-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3-b][1]benzopyran (28A and 28B).** From 62 mg (0.25 mmol) of pyrone **1C** and 42 mg (0.25 mmol) of aldehyde **5**, 48 mg (48% yield) of a 2:1 mixture of formyloxy derivatives **28A** and **28B** and 22 mg (24% yield) of a 2:1 mixture of alcohol **29A** and **29B** were obtained after column chromatographic separation.

Compound 28A: IR (Nujol) ν 3080, 1690 (s, C═O), 1640, 1610, 1595, 1310, 1255, 1170, 1130, 1010; ^{1}H NMR δ 8.20 (s, 1 H, CHO), 7.40 (dd, J = 8 Hz, 2 Hz, 1 H, C6′H, Ph), 7.27 (d, J = 2 Hz, 1 H, C2′H), 6.90 (d, J = 8 Hz, 1 H, C5′H), 6.32 (s, 1 H, C10H), 6.24 (d, J = 2 Hz, 1 H, C4H), 5.34 (dd, J = 12 Hz, 4.6 Hz, 1 H, C6H), 3.94 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 2.4−1.5 (a series of m, 6 H), 1.58 (q, Me); ^{13}C NMR δ [from a 2:1 ratio of a mixture of **28A** (*c*) and **28B** (*t*)] 162.3 (C1, *t*), 162.1 (C1, *c*), 161.3 (C4a, *t*), 161.2 (C4a, *c*), 160.1 (CHO, *c*), 160.0 (CHO, *t*), 159.7 (C3, *c*), 159.4 (C3, *t*), 151.2 (C4′, *c*), 151.1 (C4′, *t*), 148.9 (C3′, *c* & *t*), 132.7 (C1′, *c*), 131.8 (C1′, *t*), 123.7 (C10a, *c* & *t*), 118.8 (C2′, *c*), 118.7 (C2′, *t*), 112.2 (C5′, *c*), 112.1 (C5′, *t*), 110.8 (C10, *c* & *t*), 107.8 (C6′, *c*), 107.8 (C6′, *t*), 97.9 (C9a, *c*), 97.5 (C9a, *t*), 95.9 (C4, *c*), 95.7 (C4, *t*), 84.0 (C5a, *c*), 82.7 (C5a, *t*), 76.2 (C6, *c*), 74.0 (C6, *t*), 56.8 (OMe, *c* & *t*), 55.7 (OMe, *c* and *t*), 30.9 (C9, *c*), 30.8 (C9, *t*), 28.8 (C7, *c*), 27.7 (C7, *t*), 22.7 (C8, *c*), 20.4 (C8, *t*), 18.5 (Me, *c* and *t*); MS FAB, m/z 399 (M+1, 80%), 398 (M$^+$), 352 (90%), 261, 165 (100%), 136. Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.09; H, 5.31.

Compound 28B (pure): ^{1}H NMR δ 8.15 (s, 1 H, CHO), 7.40 (dd, J = 8 Hz, 2 Hz, 1 H, C6′H, Ph), 7.27 (d, J = 2 Hz, 1 H, C2′H), 6.90 (d, J = 8 Hz, 1 H, C5′H), 6.32 (s, 1 H, C10H), 6.29 (s, 1 H, C4H), 5.28 (s, 1 H, C6H), 3.94 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 2.4−1.5 (a series of m, 6 H), 1.62 (q, Me); MS FAB, m/z 399 (M + 1, 80%), 398 (M$^+$).

Addition of 3 Å Molecular Sieves. Condensation of 11 mg (0.065 mmol) of aldehyde **5**, 20 mg (0.08 mmol) of pyrone **1C**, 0.10 g of 3 Å molecular sieves, and 4 mg of L-proline in 2 mL of ethyl acetate at 65 °C for 2 days gave 7.5 mg (29% yield) of **28A**, 1.6 mg (6% yield) of **28B**, 5.5 mg (50% recovery) of **5**, and 12 mg of pyrone **1C**.

3,5a-Dimethyl-6-oxo-1*H*,7*H*-5a,6,8,9-tetrahydro-1-oxopyrano[4,3*b*][1]-benzopyran (19). To a solution of 17 mg (0.069 mmol) of a mixture of **17A** and **17B** in 2 mL of CH_2Cl_2 under argon was added 58 mg (0.14 mmol) of 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one.[11] After being stirred at 25 °C for 24 h, the reaction mixture was diluted with 50 mL of diethyl ether, filtered through Celite, washed with 10 mL of saturated aqueous $NaHCO_3$, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel using hexane:ether (1:1) as eluant to give 14.8 mg (87% yield) of **19**; ^{1}H NMR δ 6.28 (s, 1 H, C10 H), 5.97 (s, 1 H, C4 H), 2.68−2.56 (m, 4 H), 2.22 (s, 3 H, C3-Me), 2.1 (m, 1 H), 1.7 (m,1 H), 1.64 (s, 3 H, Me); MS FAB, m/z 247 (M + 1), 246 (M$^+$). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.01; H, 6.02.

Condensation of pyrone **1A** with 2-methyl-3-oxo-1-cyclohexenecarboxaldehyde and 0.5 equiv of L-proline in ethyl acetate at 50 °C gave a 70% yield of ketone **19**, and the spectral data are identical with those obtained from the above oxidation reaction.

Reduction of 19 with Dibal-H. Formation of Alcohol **17A.** To a cold (−60 °C) solution of 13 mg (0.053 mmol) of ketone **19** in 2 mL of THF under argon was added 42 μL (0.063 mmol) of Dibal-H (1.5 M in toluene). After being stirred at −60 °C for 1 h and 0 °C for 4 h, the solution was diluted with 10 mL of water and extracted twice with CH_2Cl_2, and the combined CH_2Cl_2 was dried ($MgSO_4$), concentrated, and column chro-

matographed on silica gel to give 11.3 mg (87% yield) of **17A** and 1.2 mg (9% yield) of **17B**.

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Supporting Information Available: ORTEP drawing of X-ray crystallographically determined structure of **18A** (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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