Photoinduced Molecular Transformations. 157.[1] A New Stereo- and Regioselective Synthesis of 2,6-Diaryl-3,7-dioxabicyclo[3.3.0]octane Lignans Involving a β-Scission of Alkoxyl Radicals as the Key Step. New Total Syntheses of (±)-Sesamin, (±)-Eudesmin, and (±)-Yangambin[2]

Hiroshi Suginome,* Kazuhiko Orito, Kaoru Yorita, Masataka Ishikawa, Noriaki Shimoyama, and Takahiro Sasaki

Organic Synthesis Division, Faculty of Engineering, Hokkaido University, Sapporo 060, Japan

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New total syntheses of naturally occurring 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans, (±)-sesamin and (±)-eudesmin, and the first total synthesis of (±)-yangambin were achieved according to a general method devised by Suginome and colleagues for replacing the carbonyl group of the cyclopentanone ring with an oxygen atom to give a corresponding tetrahydrofuran ring involving a regioselective β-scission of alkoxyl radicals; arylation of dimethyl, diallyl, or dibenzyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarbonate (**18** and **19a,b**) with aryllead triacetate **9a–c**, followed by dealkoxycarbonylation of the resulting arylated product **20a–f**, gave 2,6-diaryl-3,7-dioxobicyclo-[3.3.0]octane **21a–c**. A regioselective Baeyer–Villiger oxidation of **21a–c** with *m*-CPBA–$NaHCO_3$ or $-K_2CO_3$ gave the corresponding δ-lactone **22a–c**, which was reduced with DIBAL to give the corresponding lactol **23a–c**. The irradiation of a solution of the hypoiodite of **23a–c**, generated *in situ* with mercury(II) oxide–iodine, in benzene with Pyrex-filtered light resulted in a regioselective β-scission of the corresponding alkoxyl radical to give iodo formate **24a–c**. Heating **24a–c** in MeOH with $NaBH_4$ gave (±)-sesamin (**25a**), (±)-eudesmin (**25b**), or (±)-yangambin (**25c**).

In previous papers, we have reported that a variety of molecules, including natural products, can be synthesized by several new reaction processes involving the selective β-scission of alkoxyl radicals generated by the photolysis of the corresponding hypoiodites as the key step.[3,4]

Among these new processes and their applications to syntheses, we have reported on new methods for useful transformations of cyclic alcohols and cyclic ketones into cyclic ethers and saturated N, S, Te, and Se heterocycles involving the regioselective β-scission of alkoxyl radicals generated from the corresponding hypoiodites as the key step.[4a]

Scheme 1 outlines the key reaction for transforming cyclic alcohols into corresponding cyclic ethers having the same ring size and pathway proven by our ^{18}O-labeling studies.[5] Thus, the irradiation of a solution of the hypoiodites of fused cyclic alcohols **1**, generated *in situ* in benzene containing mercury(II) oxide and iodine (each 3 molar equiv) with Pyrex-filtered light, gave iodo formates **2** as the principal products. The formation of the formates **2** involves the following sequence: (a) a selective β-scission of the alkoxyl radical **A** to a stabilized carbon-centered radical **B**, (b) a subsequent one-electron oxidation of radical **B** to the corresponding carbocation **C**, (c) its intramolecular combination with the formyl oxygen to form a cation **D**, (d) its reaction with diiodine oxide (I_2O) to generate a lactol hypoiodite **E**, and (e) a regioselective β-scission of the carbon–carbon bond of the alkoxyl radical generated from the hypoiodites, followed by the abstraction of an iodine from an iodine molecule by the resulting carbon-centered radical **F** to give the observed iodo formates **2**. These formates **2** can be readily transformed into the corresponding cyclic ethers **3** by treating them with a complex metal hydride or methyllithium. Formates **2** can also serve as valuable synthetic intermediates for obtaining saturated heterocycles.[4a] A β-scission of the alkoxyl radicals generated from the lactol hypoiodites **E** takes place so selectively that formates **2** are formed as exclusive products.

Our subsequent new method for a four-step substitution of a carbonyl group of cyclic ketones by an oxygen atom stemmed from the above-mentioned sequence of the reaction and is outlined in Scheme 2;[4a] a Baeyer–Villiger

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(3) For a review on synthetic applications of hypohalite photochemistry, see: Suginome, H. In *Handbook of Organic Photochemistry and Photobiology*; Song, P.-S., Horspool, W. H., Eds.; CRC Press: Boca Raton, FL, in press.

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(5) (a) Suginome, H.; Seki, Y.; Yamada, S.; Orito, K.; Miyaura, N. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1431. (b) Suginome, H.; Senboku, H. *Tetrahedron* **1994**, *50*, 13101.

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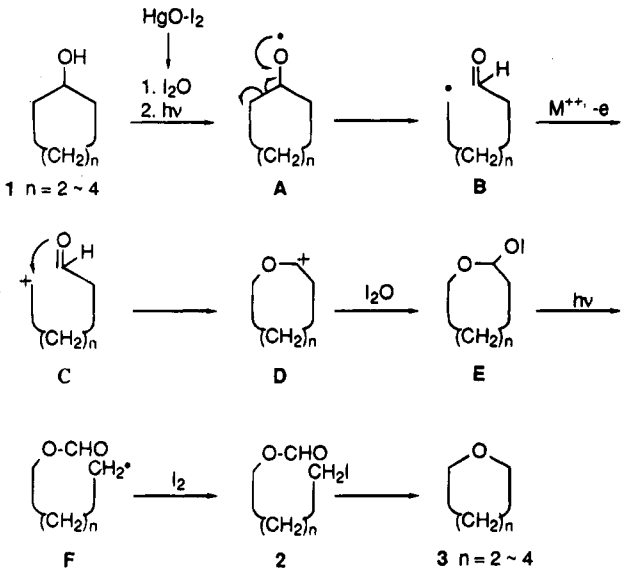
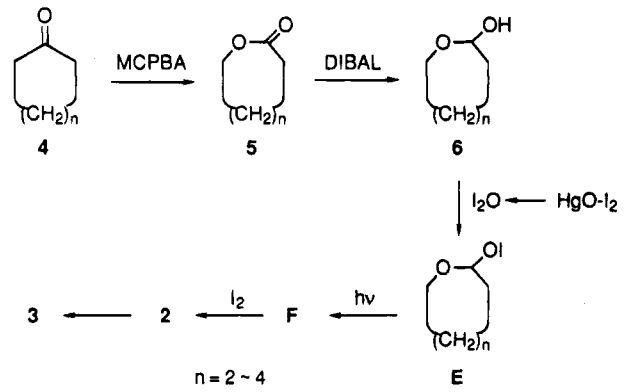
Scheme 1



Scheme 2

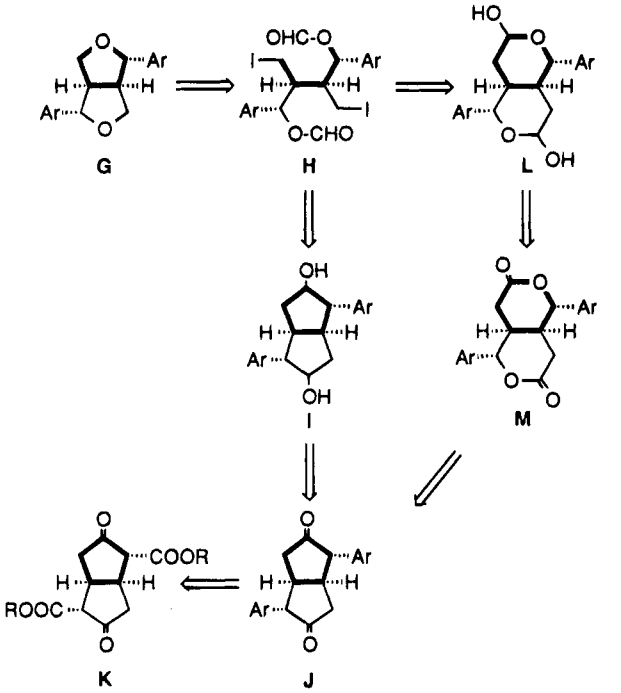


oxidation of a cyclic ketone **4** to lactone **5**, followed by its reduction with DIBAL, gives the corresponding lactol **6**, which is transformed *in situ* into the hypoiodite **E**, an assumed intermediate in the transformation outlined in Scheme 1, with mercury(II) oxide–iodine in benzene. Irradiation of this solution with Pyrex-filtered light gives iodo formate **2**. On the basis of this method, a number of steroidal cyclic ketones could be efficiently transformed into the corresponding oxasteroids.[4a]

The 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes comprise one of the largest groups of lignans,[6] to which many biologically active natural products belong.[7] Lignans possessing this skeletal structure have been synthesized by a variety of methods, including an approach *via* the oxidative coupling reactions of phenolic cinnamyl alcohol of cinnamic acid derivatives.[8] Their fused tetrahydrofuran structure seemed to us to be an attractive target for examining the versatility of the above-mentioned cyclic ketone–cyclic ether transfomation.

This article presents the full details concerning a successful application of our method to new total syntheses of two lignans, (±)-sesamin (**25a**)[9] and (±)-

Scheme 3



eudesmin (**25b**),[10] and the first total synthesis of another lignan, (±)-yangambin (**25c**).[11] The present synthesis, which utilizes a selective radical fragmentation as the key step, represents an entirely new approach to this class of molecules.

Results and Discussion

Our own approach to the total synthesis of 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans, which involves the aforementioned key reactions for transforming cyclic alcohols or cyclic ketones into corresponding cyclic ethers (Schemes 1 and 2), is based on retrosynthetic paths outlined in Scheme 3. This analysis suggested that we required alkyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate **K**, from which 2,6-diaryl-3,7-dioxobicyclo[3.3.0]-octanes **J** can be derived by arylation, followed by decarboxylation.

Either of the two synthetic routes can serve for transforming **J** into 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans **G**. The first route (**J** → **I** → **H** → **G**) has the advantage that it has less steps if the β-scission of alkoxyl radicals generated from fused cyclopentanol **I** takes place to give formate **H** in reasonable yields. It also has, however, the disadvantage that the stereochemical integrity of the carbon centers carrying the aryl groups will not be retained since the scission will take place to give stabilized benzyl radicals as the intermediates.

The second four-step route (**J** → **M** → **L** → **H** → **G**) has already been successfully applied to the synthesis of

(6) (a) For a review on the naturally occurring lignans until 1955, see: Hearon, W. M.; MacGregor, W. S. *Chem. Rev.* **1955**, *55*, 957. (b) For a review on lignans and neolignans until 1983, see: Whiting, D. A. *Nat. Prod. Rep.* **1985**, *2*, 191 and reviews cited therein.

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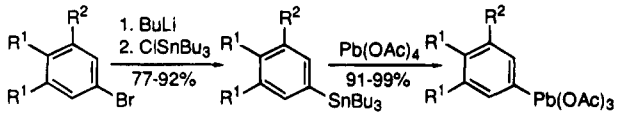
(10) Isolation of (−)-eudesmin: Maiden, J. H.; Smith, H. G. *Am. J. Pharm.* **1896**, 679.

(11) (a) Dickey, E. E. *J. Org. Chem.* **1958**, *23*, 179. (b) Hirose, M.; Satoh, Y.; Hagitani, A. *Nippon Kagaku Zasshi*, **1968**, *89*, 887, 889. (c) Kakisawa, H.; Chen Y. P.; Hsu, H. Y. *Phytochemistry* **1972**, *11*, 2289.

Scheme 4



7a R^1,R^1=OCH_2O; R^2=H **8a** R^1,R^1=OCH_2O; R^2=H **9a** R^1,R^1=OCH_2O; R^2=H
7b R^1=OMe; R^2=H **8b** R^1=OMe; R^2=H **9b** R^1=OMe; R^2=H
7c R^1= R^2=OMe **8c** R^1= R^2=OMe **9c** R^1= R^2=OMe

several oxasteroids.[4a] It has the advantage that the Baeyer–Villiger oxidation of **J** to **M** will take place regioselectively with the retention of the configurations at the carbon centers carrying the aryl groups.

Either of the synthetic routes use *cis*-alkyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate **18** as the starting material. It can be rather readily available by the partial removal of carbomethoxy groups[12a] from *cis*-tetramethyl 3,7-dioxobicyclo[3.3.0]octane-2,4,6,8-tetracarboxylate which is readily prepared from dimethyl β-ketoglutarate and glyoxal by Weiss' procedure.[12b]

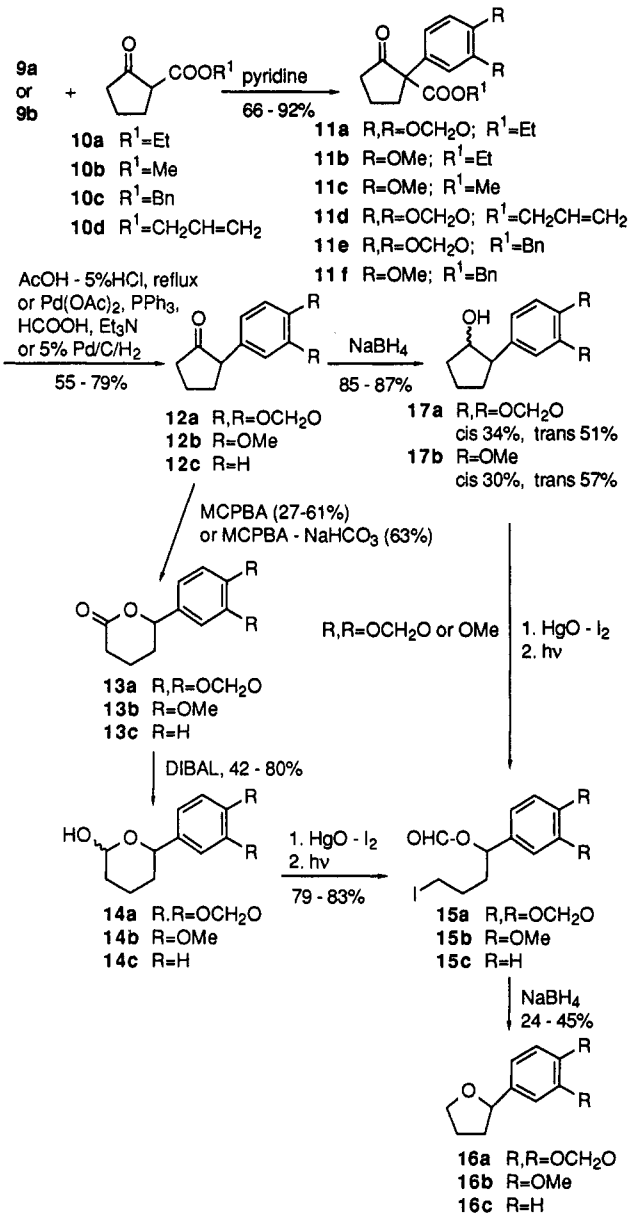
Thus, we first carried out some model transformations using monocyclic substrates **10** aimed at (a) finding an appropriate procedure for efficiently introducing an aryl group to the monocyclic cyclopentanone skeleton under mild conditions (**K** → **J**; bold lines), (b) the removal of the alkoxycarbonyl group under mild conditions, and (c) the transformation of the resulting 2-arylcyclopentanones into the corresponding 2-aryltetrahydrofurans **16** (**J** → **G**; bold lines) according to the sequence suggested by the retrosynthesis.

Transformations of 2-Oxocyclopentanecarboxylic Acid Esters 10a–d into 2-Aryltetrahydrofurans 16a–c (Schemes 4 and 5). (a) Introduction of an Aryl Group into the Monocyclic Cyclopentanones. Among several available methods[13] for introducing an aryl group to the α-position of cyclic ketones, a regioselective arylation of β-keto esters with an aryllead triacetate in the presence of pyridine, developed by Pinhey and collaborators,[13e] was most appropriate for the present purpose.

Three aryllead triacetates having 3,4-methylenedioxy, 3,4-dimethoxy, and 3,4,5-trimethoxy substituents on their phenyl groups, **9a, 9b, and 9c**, were thus prepared according to the sequence outlined in Scheme 4.

The lithiation of 4-bromo-1,2-(methylenedioxy)benzene (**7a**)[14] with butyllithium, followed by a reaction of the resulting lithio derivative with tributyltin chloride according to a procedure by Locksley and a collaborator,[15] gave 3,4-(methylenedioxy)(tributylstannyl)benzene (**8a**) in 52% yield. Treatment of **8a** with lead tetraacetate[19] in dichloromethane for 25 h at 46 °C under ultrasonication gave crystalline [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) in 94% yield. Similarly, starting with 4-bromo-1,2-dimethoxybenzene (**7b**)[17] and 4-bromo-1,2,3-trimethoxybenzene (**7c**)[18] gave **8b** and **8c**, respectively. Their treatment with lead tetraacetate yielded (3,4-dimethoxyphenyl)- and (3,4,5-trimethoxyphenyl)lead triacetates **9b and 9c**, respectively.

Scheme 5



Arylation of ethyl 2-oxocyclopentanecarboxylate (**10a**) with phenyllead triacetate (**9a**) in CH_2Cl_2 in the presence of pyridine gave crystalline ethyl 1-[3,4-(methylenedioxy)-phenyl]-2-oxocyclopentanecarboxylate (**11a**) in 66% yield. We found that ultrasonication in this arylation enhanced the yield of the arylated product **11a** to 86%. The reaction of **9b** with ethyl or methyl 2-oxocyclopentanecarboxylate, **10a** or **10b,** similarly gave ethyl or methyl 1-(3,4-dimethoxyphenyl)-2-oxocyclopentanecarboxylate (**11b** or **11c**) in 81–99% yield. In order to examine the removal of an alkoxycarbonyl group by hydrogenolysis, allyl and benzyl esters **11d–f** were also prepared. Thus,

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(14) Bruce, J. M. *J. Chem. Soc.* **1959**, 2366.

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(16) Kozyrod, R. P.; Pinhey, J. T. *Tetrahedron Lett.* **1983**, *24*, 1301.

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(18) Jung, M. E.; Lam, P. Y.-S.; Mansuri, M. M.; Speltz, L. M. *J. Org. Chem.* **1985**, *50*, 1087.

(19) Taber, D. F.; Amedio, J. C.; Patel, Y. K. *J. Org. Chem.* **1985**, *50*, 3618.

the arylation of allyl ester **10d**[20] with **9a** gave **11d** in 66% yield. The similar arylation of benzyl ester **10c** produced a 74% yield by a DMAP-catalyzed ester exchange of the ethyl ester **10a** according to a procedure of Taber and collaborators.[19] The arylation of **10c** with aryllead triacetates **9a** or **9b** yielded **11e**[21] in 42–67% yield.

(b) Decarbalkoxylation of Alkyl 2-Oxocyclopentanecarboxylates 11a–f. The removal of the alkoxycarbonyl group from alkyl, allyl, or benzyl esters **11a–f** was carried out under acidic, basic, and neutral (hydrogenolysis) conditions. The results are summarized as follows. Heating a solution of alkyl 1-aryl-1-oxocyclopentanecarboxylates **11a**, **11b**, or **11c** in 2:1 AcOH–5% HCl for 12 h under reflux afforded 2-aryl-1-cyclopentanone **12a** or **12b** in 55–79% yields. The lowest yield (55%) resulting from the decarbalkoxylation of **11a** was assumed to be due to the presence of an acid sensitive methylenedioxy group in **11a**.

The attempted decarbalkoxylation of alkyl esters **11a** or **11b** under basic conditions, on the other hand, resulted either in an intractable mixture (2 N NaOH, reflux) or in a recovery of the starting esters (LiCl–wet DMSO[22]).

Deallyloxycarbonylation of allyl ester **11d** by palladium-catalyzed reaction with ammonium formate[20] afforded 2-aryl-1-cyclopentanone[13a] in a much improved yield. Thus, the treatment of **11d** with palladium acetate–PPh_3 and the triethylamine salt of formic acid in THF at room temperature gave 2-aryl-1-cyclopentanone **12a** in 72% yield.

Finally, debenzyloxycarbonylation of benzyl esters **11e**[21] and **11f** in the presence of 10% Pd on carbon as a catalyst in an atmosphere of hydrogen afforded 2-arylcyclopentanones **12a** and **12b** in 53–72% yields.

(c) Transformation of 2-Arylcyclopentanones 12a, 12b, and 12c into the Corresponding 2-Aryltetrahydrofurans 16a, 16b, and 16c. The model experiments for transforming 2-arylcyclopentanones into 2-aryltetrahydrofurans were first carried out with 2-phenylcyclopentanone (**12c**).[13a] A Baeyer–Villiger oxidation of 2-phenylcyclopentanone (**12c**) with *m*-CPBA alone in CH_2Cl_2 for 2 days resulted in a regioselective oxidation to give the corresponding δ-lactone **13c**[23] in 61% yield. The reduction of lactone **13c** with DIBAL by the standard procedure gave the corresponding lactols **14c**[24] (a 1:1 mixture of the stereoisomers) in 56.3% yield. Lactols **14c** in benzene containing mercury(II) oxide–iodine (each 3 equiv) in a Pyrex vessel were irradiated for 1 h under nitrogen to give 4-iodo-1-phenylbutyl formate (**15c**) in 83% yield. Heating the formate **15c** in MeOH containing $NaBH_4$ under reflux gave crystalline 2-phenyltetrahydrofuran (**16c**)[25] in 45% yield.

Similarly, the substituted 2-arylcyclopentanones, **12a** and **12b**, were subjected to the four-step transformation into the corresponding 2-aryltetrahydrofurans **16a** and **16b**, respectively; in contrast to the case of **12c**, Baeyer–Villiger oxidation of **12a** with *m*-CPBA alone took place very slowly and gave a low yield of δ-lactone **13a**. The oxidation of **12b** with *m*-CPBA in the presence of a weak base such as $NaHCO_3$,[26] however, was completed within a much shorter time to give an appreciably improved yield (63%) of δ-lactone **13b.** We later found that the effects of the base were even more significant in the Baeyer–Villiger oxidation of 2,6-diaryl-3,7-dioxobicyclo[3.3.0]octanes **21a–c** *(vide infra)*.

The reduction of **13a** and **13b** to lactols **14a** and **14b**, respectively (42% and 80%, respectively), followed by the selective fragmentation, gave 4-iodo-1-arylbutyl formates **15a** and **15b**, respectively (79% and 65%, respectively). These formates were cyclized to give 2-aryltetrahydrofurans **16a** (40%) and **16b** (48%).

We also tested the direct transformation of 2-arylcyclopentanones, **12a** and **12b**, into iodo formates, **15a** and **15b** (**J** → **I** → **H** in Scheme 3). We found that the photolysis of the hypoiodites of 2-arylcyclopentanols **17a** (a 1:2 mixture of *cis* and *trans*) and **17b** (a 1:2 mixture of *cis* and *trans*), obtained by the reduction of 2-arylcyclopentanones with $NaBH_4$, gave **15a** (24%) and **15b** (65%), respectively, identical to those derived from a three-step route (**12** → **13** → **14** → **15**). Thus, this short-step procedure afforded greater overall yields of 2-aryltetrahydrofurans **16** in the monocyclic series. The results of this model study for the transformation of 2-oxocyclopentanecarboxylates into 2-aryltetrahydrofurans indicated that the method may well be applied to the stereoselective synthesis of 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans, and therefore, we proceeded to the total syntheses of (±)-sesamin (**25a**), (±)-eudesmin (**25b**), and (±)-yangambin (**25c**) as described below.

Total Synthesis of (±)-Sesamin (25a), (±)-Eudesmin (25b), and (±)-Yangambin (25c) (Scheme 6). Total synthesis of (±)-Sesamin (25a). Sesamin is one of the representative biologically active lignans and has been known since the end of the previous century.[9] The first syntheses[27] of this molecule were achieved by Beroza and by Freudenberg. An enantiocontrolled synthesis of (−)-sesamin has also been reported by Takano.[28]

According to the procedures set up by the above-mentioned model experiments, the arylation of dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarbonate (**18**)[12a] with [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) in dry dichloromethane under reflux for 12 h under ultrasonication afforded dimethyl 2,6-bis[3,4-(methylenedioxy)-phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20a**) in 73% yield. An NOE measurement established the *cis* disposition of the two aryl groups and the angular hydrogens attached to C(5) and C(8) of the bicyclo[3.3.0]-octane skeleton; irradiation of the signal at δ 3.44 (1α- and 5α-H) resulted in an enhancement of the signal areas at δ 2.88 (4α- and 8α-H) and the aromatic protons at δ 6.83 and 6.88 (2′- and 6′-H). In contrast to the monocyclic series, however, attempted decarbalkoxylation of dimethyl ester **20a** by heating it in AcOH–0.5% HCl gave no 2,6-diaryl-3,7-dioxobicyclo[3.3.0]octane **21a**. Compound **21a** was then successfully prepared by decar-

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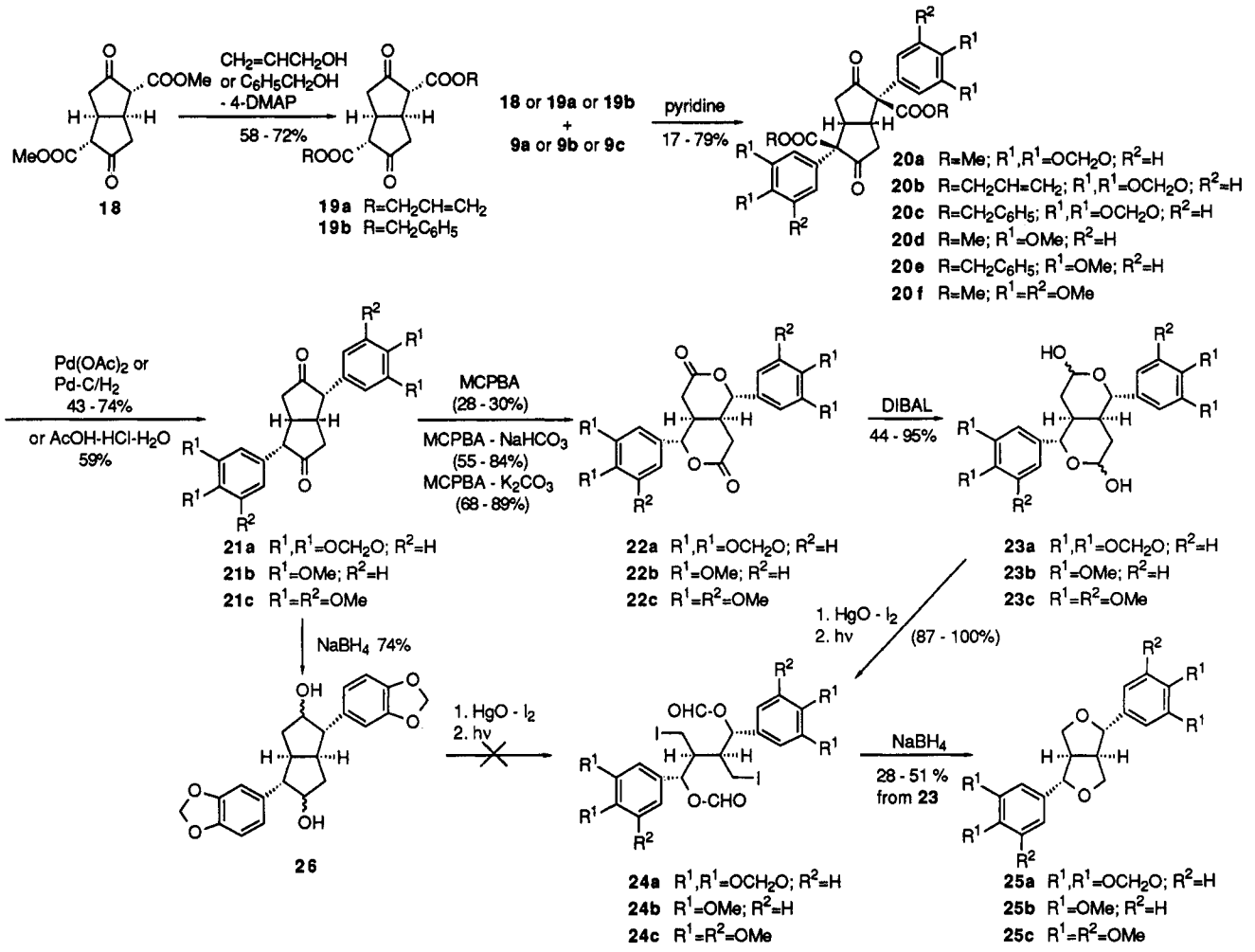
Scheme 6



balkoxylation of either diallyl or dibenzyl 2,6-diaryl-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate **20b** or **20c.** Diallyl and dibenzyl esters, **19a** and **19b**, were thus prepared in 55% yield by heating a solution of dimethyl ester **18**, excess allyl or benzyl alcohol, and a catalytic amount of DMAP in toluene under reflux. The arylation of diallyl ester **19a** with [3,4-(methylendioxy)phenyl]lead triacetate (**9a**) in the presence of pyridine in CH_2Cl_2 under ultrasonication gave diallyl 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate **20b** in 16.5% yield, while the similar arylation of dibenzyl ester **19b** with **9a** gave diarylated dibenzyl ester **20c** in 68.7% yield.

Treatment of diallyl ester **20b** with palladium acetate–PPh_3 and the triethylamine salt of formic acid in THF at room temperature gave 2,6-[bis[3,4-(methylenedioxy)-phenyl]-3,7-dioxobicyclo[3.3.0]octane (**21a**) in 43% yield. The hydrogenolysis of **20c** in the presence of a 10% palladium on carbon catalyst in methanol under hydrogen for 20 h also resulted in a spontaneous loss of CO_2 to give **21a** in 74% yield. An NOE measurement established the *cis* disposition of the two aryl groups and the angular hydrogens; irradiation of the signal at δ 3.11 (1α- and 5α-H) in the ^{1}H NMR spectrum resulted in an enhancement of the area of the signals at δ 2.72 (4α-H), 6.61 (6′-H), and 6.63 (2′-H).

As indicated by the experiments in the monocyclic series, while the selective Baeyer–Villiger oxidation of **21a** with *m*-CPBA alone for 10 days gave only 28% of 2,7-bis[3,4-(methylenedioxy)phenyl]-3,8-dioxabicyclo[4.4.0]-decane-4,9-dione (**22a**), the oxidation of **21a** with *m*-CPBA in the presence of $NaHCO_3$[29] was completed within a much shorter time (68 h) to give **22a** in appreciably higher yield (72%).

We then examined the oxidation with a variety of reagents such as *m*-CPBA–K_2CO_3,[29] $(MeSiO)_2$–$SnCl_4$,[30] $H_2S_2O_8$–AcOH,[31] $(CF_3CO)_2O$–H_2O_2,[32] or C_6H_5SeOH.[33] We thus found that the oxidation in the presence of K_2CO_3 gave an even better result than that obtained in the presence of $NaHCO_3$. The oxidation was completed within 1 h to give dilactone **22a** in 76% yield.

The reduction of **22a** with DIBAL in CH_2Cl_2 at −78 °C for 3.5 h gave a mixture of stereoisomers of 2,7-bis-[3,4-(methylenedioxy)phenyl]-3,8-dioxabicyclo[4.4.0]decane-4,9-diol (**23a**) in 44% yield. The dilactol **23a** in benzene was first treated with mercury(II) oxide and iodine (each 3 equiv) in benzene to form the hypoiodite. The solution was then irradiated with a 100 W high-pressure Hg arc through a Pyrex filter for 12 h at room temperature to give an oily iodo formate **24a**. The crude **24a** (obtained by the usual workup), which exhibited a formyloxy proton at δ 8.13 in the ^{1}H NMR spectrum, was immediately

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dissolved in MeOH containing $NaBH_4$. The solution was then heated under reflux for 12 h to give (±)-sesamin (**25a**) (28% from **23a**). Recrystallization from EtOH gave a pure sample, mp 129–130 °C. Its ^1H and ^{13}C NMR spectra were in agreement with those published in the literature.[34a]

The direct formation of **24a** from 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-3β,7β-diol (**26**) *via* the path outlined in Scheme 3 was also attempted. Thus, dione **21a** in MeOH–THF was treated with $NaBH_4$ at room temperture to give diol **26** in 74% yield. The ^1H NMR spectrum of **26** and NOE measurements (see Experimental Section) indicated that the OH and aryl groups in **26** are *trans*-oriented.

The diol **26** in benzene was subjected to β-scission under the conditions mentioned above. No iodo formate **24a**, however, was formed in this photolysis. The results thus differ from those of simpler model substrates, such as **17a** and **17b**.

(a) Total Synthesis of (±)-Eudesmin (25b) (Scheme 6). The success in synthesizing sesamin prompted us to carry out a total synthesis of its methoxyl analogue, (±)-eudesmin (**25b**), following the same series of reactions. Eudesmin is also a biologically active lignan, which was first isolated in its levorotatory form by Maiden and Smith[10] in 1895 from the kinos of Australian eucalyptus. Since then, (−)-eudesmin has been isolated from many plants.[35] The structure of eudesmin was established by Erdtman[36] who recognized it to be an antipode of pinoresinol dimethyl ether; the absolute configuration was established by an X-ray analysis by Vasquez *et al.*[37] The synthesis of racemic eudesmin was reported by Pelter and colleagues,[38] who obtained it by a four-step removal of the dilactone carbonyl groups from "dehydrodiferulic acid"[39] arising from the oxidative coupling of ferulic acid. An enantioselective synthesis of (−)-eudesmin involving an asymmetric 1,4-addition of the aryldithiane of 3,4-dimethoxybenzaldehyde to (5*S*)-(menthyloxy)-2(5*H*)-furanone was recently reported by Jansen and Feringa.[35]

The reaction of dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**18**)[27] with (3,4-dimethoxyphenyl)lead triacetate (**9b**) in the presence of pyridine in CH_2Cl_2 under the same conditions as for the preparation of the above-mentioned methylenedioxy analogue **20a** gave dimethyl 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo-[3.3.0]octane-2,6-dicarboxylate (**20d**) in 71% yield. The dealkoxycarbonylation of **20d** by heating the solution in AcOH–HCl under reflux for 15 h gave 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane (**21b**) in 68% yield; no reaction took place when **20d** in trifluoroacetic acid was heated under reflux.

Similarly, the arylation of dibenzyl ester **19b** with (3,4-dimethoxyphenyl)lead triacetate (**9b**) in the presence of pyridine gave the corresponding diarylated dibenzyl ester **20e** in 74% yield. Debenzyloxycarbonylation of **20e** was then carried out by either of two procedures: The hydrogenolysis of **20e** in ethyl acetate in the presence of 10% Pd–C in an atmosphere of hydrogen for 20 h gave **21b** in 68% yield. In contrast to methyl ester **20d** mentioned above, acidic hydrolysis of dibenzyl ester **20e** in trifluoroacetic acid by heating the solution under reflux for 2 h gave **21b** in 63% yield. Dealkoxycarbonylation of **20d** under acidic conditions thus gave a better yield of **21b**, since the methoxyl substituents of **20d** tolerate more acidic conditions.

The oxidation of **21b** with *m*-CPBA alone or in the presence of $NaHCO_3$ or K_2CO_3 gave the results similar to those of **21a**. Thus, while the oxidation of dione **21b** in CH_2Cl_2 with *m*-CPBA alone for 3 days at room temperature gave dilactone **22b** in only 32% yield, the oxidation in the presence of $NaHCO_3$ for 16 h gave **22b** in 84% yield. The oxidation in the presence of K_2CO_3 was completed within 1.5 h to give **22b** in 89% yield.

The reduction of **22b** with DIBAL as in the case of the methylenedioxy analogue **22a** gave crystalline dilactol **23b** in 94.6% yield. A solution of **23b** in benzene containing yellow mercury(II) oxide and iodine (each 6 molar equiv) was then irradiated with Pyrex-filtered light for 5 h to give an oily iodo formate **24b** (a singlet of the OCHO proton at δ 8.23) which was immediately dissolved in MeOH containing $NaBH_4$; the solution was then heated under reflux for 2 h to give (±)-eudesmin (**25b**)[36,38,40] (36% from dilactol **23b**). Recrystallization gave an analytical sample, mp 90–91 °C. Its ^1H NMR spectrum was in full agreement with the reported data[38] regarding eudesmin.

It has been known that the yellow form of mercury(II) oxide is generally more reactive.[41] We found that the reaction using yellow mercury(II) oxide in this radical fragmentation of **23b** was completed after 5 h to give 87% of **24b**, whereas the reaction using red mercury(II) oxide was completed after 23 h to give only a trace of **24b**. The poor yield was probably due to a secondary decomposition of the initially formed **24b**. A similar result was also found in the course of the synthesis of yangambin **25c** (described below).

(c) Total Synthesis of (±)-Yangambin (25c) (Scheme 6). (+)-Yangambin (**25c**) (lirioresinol-B dimethyl ether) was first isolated from yellow poplar, *Liriodendron tulipifera* L,[11a] and then from *Magnolia fargesii*.[11b,c] A total synthesis, to our knowledge, has not been reported. Following are the details concerning our total synthesis, which was carried out according to the same series of reactions as described above.

Arylation of dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**18**) with (3,4,5-trimethoxyphenyl)lead triacetate (**9c**) in CH_2Cl_2 in the presence of pyridine gave dimethyl 2,6-bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20f**) in 54% yield. Dealkoxycarbonylation of **20f** was then carried out under the same acidic conditions as mentioned for the preparation of 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo-[3.3.0]octane (**21b**); a solution of **20f** in 2:1 AcOH–5% HCl was heated under reflux for 27 h to give 2,6-bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane (**21c**) in 43% yield.

A regioselective oxidation of **21c** with *m*-CPBA in CH_2Cl_2 in the presence of K_2CO_3 for 2 h at room temperature

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gave 2,7-bis(3,4,5-trimethoxyphenyl)-3,8-dioxabicyclo-[4.4.0]decane-4,9-dione (**22c**) in 63% yield. The reduction of **22c** with DIBAL in CH_2Cl_2 at −78 °C for 2 h gave the corresponding crystalline dilactol **23c** in 83% yield. A solution of **23c** in CH_2Cl_2 containing yellow HgO and I_2 (each 6 mol equiv) was irradiated with Pyrex-filtered light for 8 h to give a nearly quantitative yield of a crude iodo formate **24c** (estimated by the OCHO proton as a singlet at δ 8.25). As in the case of the synthesis of eudesmin, the reaction using the red form of mercury-(II) oxide in this fragmentation took 24 h for completion and gave only a trace of **24c**. The heating of a solution of **24c** in MeOH containing $NaBH_4$ under reflux for 2 h gave (±)-yangambin (**25c**). It was purified by preparative TLC to give pure (±)-yangambin (**25c**) (mp 105.8−106.0 °C) in 51% yield. The ^{1}H NMR data of the synthetic lignan were in full agreement with those reported for (+)-yangambin.[11]

Conclusion. A number of elegant methods have been developed for synthesizing (±)-2,6-diaryl-3,7-dioxabicyclo-[3.3.0]octane lignans. The following principal steps are involved in these methods: (a) oxidative dimerization of cinnamic acid derivatives,[37,38,39a,42] (b) oxidative dimerization of β-keto esters with NaH and I_2,[27] (c) a stepwise construction of fused aryltetrahydrofurans from a four-carbon synthon with base,[43] (d) the formation of the tetrahydrofuran ring by intramolecular aldol reaction onto a γ-lactone,[44] (e) $TiCl_4$-catalyzed annelation of 2,5-bis(trimethylsiloxy)furan with aryl aldehydes,[45] (f) reaction of dimetalated succinamides with aryl aldehyde,[46] and (g) a stereocontrolled tandem Michael addition−aldol reaction.[47]

Enantiocontrolled synthesis of a lignan from diethyl L-tartarate involving intramolecular hetero Diels−Alder reaction,[28] the synthesis involving enantioselective Michael addition of the aryldithiane of aryl aldehydes to (5S)-(menthyloxy)-2(5*H*)-furanone,[35] and total synthesis of the naturally occurring 1-hydroxy derivative of 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes involving photocyclization[48a] or intramolecular ene reaction[48b] were also reported.

Among these syntheses, the methods involving the key steps a and b can only be applied to symmetrically substituted 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes. The oxidative dimerizations require a phenolic OH group at the *para* position of the starting cinnamic acids or the oxidative dimerization with thallium trifluoroacetate takes place vigorously with only moderate yields of fused γ-lactones.

The foregoing results concerning the total synthesis of three lignans **25a−c** may indicate that the method provides a versatile and relatively short synthesis of (±)-2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans from easily accessible starting material without using strong acid or base. The advantage of the method reported herein over some of the methods cited above is that a variety of substituents can be introduced to the C(2) and C(6) in 3,7-dioxabicyclo[3.3.0]octane skeleton; not only symmetrically substituted lignans but also unsymmetrically substituted ones[47] may be synthesized through a mixed arylation of 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylic acid esters **18** under mild conditions.

Experimental Section

General Methods. Melting points were recorded with a Yanaco micro melting point apparatus. IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrophotometer unless otherwise indicated. ^{1}H NMR spectra were determined with a Hitachi R-90H FT-NMR spectrometer (90 MHz), a JEOL JMN-EX270 FT high-resolution spectromter (270 MHz), or a JEOL JMN-EX400 FT high-resolution spectrometer (400 MHz) ($CDCl_3$, $SiMe_4$ as an internal standard). The high- and low-resolution mass spectra were determined with a JEOL JMS-HX110 or a JEOL JMS-DX303 spectrometer (70 eV). TLC was carried out on Merck Kiesel gel 60-PF_{254}. Combustion analysis was performed in the Laboraory for Microanalysis of the Faculty of Pharmaceutical Sciences, Hokkaido Universty. CH_2Cl_2, $CHCl_3$, CCl_4, $CHCl_2CHCl_2$, and toluene were dried over P_2O_5 and distilled under nitrogen. Diethyl ether was purified by distillation over natrium and benzophenone. Tributyltin chloride was distilled under reduced pressure. Light petroleum refers to the fraction of petroleum ether with a distillation range of 30−70 °C.

3,4-(Methylenedioxy)(tributylstannyl)benzene (8a). A solution of BuLi (1.5 M hexane solution, 33.8 mL, 50.7 mmol) was slowly added to a solution of 4-bromo-1,2-(methylenedioxy)benzene (**7a**)[17] (9.26 g, 46.1 mmol) in dry ether (50 mL) at −78 °C. The solution was stirred for 30 min and was allowed to warm to room temperature. To this solution was slowly added tributyltin chloride (13.8 mL, 50.7 mmol). The mixture was heated under reflux for 1 h, allowed to stand at room temperature overnight, washed with 1 N HCl solution (100 mL), 5% $NaHCO_3$ solution, water, and brine (100 mL) successively, and dried over anhydrous Na_2SO_4. The solvent was then evaporated to give an oily residue which was distilled under reduced pressure to give **8a** (14.55 g, 77%): bp 142−145 °C/0.1 Torr; ^{1}H NMR (90 MHz) δ 0.70−1.75 (27H, m), 5.90 (2H, s), 6.81 (1H, d, J = 7.5 Hz), 6.86 (1H, s), 6.90 (1H, d, J = 7.5 Hz). Anal. Calcd for $C_{19}H_{32}O_2Sn$: C, 55.50; H, 7.84. Found: C, 55.54; H, 8.07.

[3,4-(Methylenedioxy)phenyl]lead Triacetate (9a). A solution of 3,4-(methylenedioxy)(tributylstannyl)benzene (**8a**) (1.23 g, 3 mmol) and $Pb(OAc)_4$ (1.33 g, 3 mmol) in CH_2Cl_2 (10 mL) was warmed on an ultrasonic cleaner (Bronson 1200) at 46 °C for 2.5 h. The solution was concentrated to one-third by a rotary evaporator. The precipitate removed by filtration was washed with $CHCl_3$ (20 mL). The combined filtrate and washings were diluted with light petroleum (30 mL). The resulting precipitate was collected by suction filtration, washed with light petroleum (5 mL × 3), and dried in a vacuum dessicator to give **9a** (1.43 g, 94%): mp 117−118 °C; ^{1}H NMR (90 MHz) δ 2.10 (9H, s), 6.04 (2H, s), 6.98 and 7.19 (each 1H, AB q, J = 8.5 Hz), 7.18 (1H, s). Anal. Calcd for $C_{13}H_{14}O_8Pb$: C, 30.89; H, 2.72. Found: C, 30.77; H, 2.87. When the reaction was carried out without using the ultrasonic cleaner, the yield of the product was only 69%.

3,4-Dimethoxy(tributylstannyl)benzene (8b). A similar treatment of 4-bromo-1,2-dimethoxybenzene (**7b**)[20] (21.73 g, 100 mmol) in dry ether (106 mL) with BuLi in hexane (1.5 M, 71.7 mL, 108 mmol) at −78 °C, followed by the addition of tributyltin chloride (29.25 mL, 108 mmol) as mentioned above, gave a product. It was distilled under reduced pressure to give **8b** (38.87 g, 92%): bp 145−148 °C/0.1 Torr; IR (neat) 1582, 1507 cm^{-1}; ^{1}H NMR (90 MHz) δ 0.70−1.7 (27H, m), 3.87 and 3.88 (each 3H, s), 6.87 (1H, dd, J = 7.7 Hz), 6.96 (1H, s), 7.00 (1H, d, J = 7.7 Hz). Anal. Calcd for $C_{20}H_{36}O_2Sn$: C, 56.23; H, 8.49. Found: C, 56.22; H, 8.50.

(3,4-Dimethoxyphenyl)lead Triacetate (9b). A solution of 3,4-dimethoxy(tributylstannyl)benzene (1.28 g, 3 mmol) and $Pb(OAc)_4$ (1.33 g, 3 mmol) in CH_2Cl_2 (10 mL) was treated in an ultrasonic cleaner (Bronson) at 46 °C for 2.5 h, as described

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for the 3,4-methylenedioxy analogue to give **9b** (1.42 g, 91%): mp 138–145 °C; ^{1}H NMR (90 MHz) δ 2.12 (9H, s), 3.91 (6H, s), 7.01 and 7.18 (each 1H, AB q, J = 8.7 Hz), 7.18 (1H, s). Anal. Calcd for $C_{14}H_{18}O_8Pb$: C, 31.48; H, 3.48. Found: C, 31.60; H, 3.46.

(3,4,5-Trimethoxyphenyl)tributyltin (8c) was prepared similarly from 5-bromo-1,2,3-trimethoxybenzene (**7c**)[18](14.826 g, 60 mmol) to give a light yellow liquid (37.6 g) which was distilled under reduced pressure to give **8c** (24.05 g, 53 mmol, 88%) as a colorless oil: bp 152–157 °C/0.4 Torr; ^{1}H NMR (270 MHz) δ 0.7–1.7 (27H, m), 3.86 (3H, s), 3.88 (6H, s), 6.66 (2H, s); EIMS m/z (relative intensity) 457 (M^+, 0.14), 401 [(M − Bu)$^+$, 6.7], 345 [(M − 2Bu)$^+$, 5.8], 289 ($SnBu_3^+$, 6.8), 168 [$(MeO)_3C_6H_2^+$, 100]. Anal. Calcd for $C_{21}H_{38}O_3Sn$: C, 55.16; H, 8.38. Found: C, 54.87; H, 8.50.

(3,4,5-Trimethoxyphenyl)lead triacetate (9c) was obtained similarly from (3,4,5-trimethoxyphenyl)tributyltin (**8c**)-(6.43 g, 14 mmol) to give **9c** as light yellow crystals (7.65 g, 99%): mp >300 °C; ^{1}H NMR (270 MHz) δ 2.13 (9H, s), 3.87 (3H, s), 3.88 (6H, s), 7.26 (2H, s); EIMS m/z (relative intensity) 551 (M^+, 0.77), 492 [(M − Bu)$^+$, 6.7], 345 [(M − OAc)$^+$, 4.7], 432 [(M − 2OAc)$^+$, 19.0], 374 [(M − 3OAc)$^+$, 2.9], 267 ($PbOAc^+$, 100). Anal. Calcd for $C_{15}H_{20}O_9Pb$: C, 32.67; H, 3.66. Found: C, 32.40; H, 3.47.

Ethyl 1-[3,4-(Methylenedioxy)phenyl]-2-oxocyclopentanecarboxylate (11a). A mixture of ethyl 2-oxocyclopentanecarboxylate (**10a**) (0.14 g, 0.9 mmol), [3,4-(methylenedioxy)-phenyl]lead triacetate (**9a**) (0.5 g, 0.99 mmol), and pyridine (78 mg, 0.99 mmol) in dry CH_2Cl_2 (5 mL) was treated in an ultrasonic cleaner at 50–55 °C for 2.5 h. The solution was brought to room temperature, diluted with CH_2Cl_2 (30 mL), and washed with 3 N H_2SO_4 solution (30 mL). The aqueous layer was extracted with $CHCl_3$ (40 mL × 3). The organic layers were combined and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oil (228 mg) which was subjected to preparative TLC (2:1 hexane–ethyl acetate). The major fraction with R_f 0.7–0.8 was **11a** as a colorless oil which crystallized on standing (204 mg, 86%) (66% without using an ultrasonic cleaner): mp 59–61 °C; IR (neat) 1754, 1731, 1613, 1492 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.22 (3H, t, J = 7.0 Hz), 1.96 (2H, sex, J = 7.0 Hz), 2.25–2.56 (3H, m), 2.83 (1H, dt, J = 13.2, 6.6 Hz), 4.17 (2H, q, J = 7.0 Hz), 5.95 (2H, s), 6.77 (1H, d, J = 8.4 Hz), 6.84 (1H, dd, J = 8.4, 1.8 Hz), 6.94 (1H, d, J = 1.8 Hz); EIDIMS m/z (relative intensity) 276 (M^+, 100), 203 [(M − COOEt)$^+$, 62]; HRMS m/z calcd for $C_{15}H_{16}O_5$ 276.0998, found 276.0998.

Benzyl 2-Oxocyclopentanecarboxylate (10c). A solution of ethyl 2-oxocyclopentanecarboxylate (**10a**) (1.492 g, 9.6 mmol), DMAP (111 mg, 0.91 mmol), and benzyl alcohol (10 mL) in dry toluene (50 mL) was heated under reflux for 15 h. The solution was then brought to room temperature and diluted with Et_2O, washed successively with 1 N HCl solution (10 mL × 2), 5% $NaHCO_3$ solution (10 mL × 2), and brine (50 mL × 2), and dried over anhydrous Na_2SO_4. The solvent and excess benzyl alcohol were removed by distillation under reduced pressure (15–17 Torr). The resulting dark brown oil (2.433 g) was subjected to column chromatography on silica gel (30 g). Elution with CH_2Cl_2–hexane (2:1) gave **10c** (1.538 g, 74%): IR (neat) 1756, 1727 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.79–1.94 (1H, m), 2.06–2.21 (1H, m), 2.24–2.37 (4H, m), 3.21 (1H, t, J = 9.2 Hz), 5.18 (2H, s), 7.27–7.30 (5H, m); EIMS m/z (relative intensity) 218 (M,$^+$ 1.4), 190 [(M − CO)$^+$, 6.3], 127 [(M − $C_6H_5CH_2$)$^+$, 1.3), 91 ($C_6H_5CH_2^+$, 100); HRMS m/z calcd for $C_{13}H_{14}O_3$ 218.0942, found 218.0952.

Benzyl 1-[3,4-(Methylenedioxy)phenyl]-2-oxocyclopentanecarboxylate (11e). A solution of benzyl 2-oxocyclopentanecarboxylate (**10c**) (1.120 g, 5.14 mmol), [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) (2.816 g, 5.58 mmol), and dry pyridine (450 mg, 5.69 mmol) in dry CH_2Cl_2 (45 mL) was warmed in an ultrasonic cleaner at 50–55 °C for 12 h. The cooled solution was diluted with $CHCl_3$ (20 mL) and washed with 1 N H_2SO_4 solution (10 mL × 3). The precipitates were then removed by suction filtration. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were washed with 5% $NaHCO_3$ solution (10 mL × 3) and then water (100 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oil (1.363 g) which was subjected to column chromatography on silica gel (20 g). The major fractions obtained by elution with CH_2Cl_2–hexane (2:1) gave benzyl **11e** as a colorless oil (738 mg, 42%): IR (neat) 1755, 1722 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.90 (1H, dt, J = 2.6, 7.0 Hz, m), 1.95 (1H, dt, J = 1.4, 7.0 Hz), 2.26–2.54 (3H, m), 2.81 (1H, dt, J = 12.6, 7.0 Hz), 5.15 (2H, s), 5.98 (2H, s), 6.76 (1H, d, J = 8.1 Hz), 6.84 (1H, dd, J = 8.1, 1.8 Hz), 6.94 (1H, d, J = 1.8 Hz), 7.23–7.37 (5H, m); EIMS m/z (relative intensity) 338 (M^+, 20), 247 [(M − $CH_2C_6H_5$)$^+$, 8.2], 91 (C_6H_5-CH_2^+, 100); HRMS m/z (M^+) calcd for $C_{20}H_{18}O_5$ 338.1154, found 338.1148.

Allyl 1-(3,4-methylenedioxyphenyl)-2-oxocyclopentanecarboxylate (11d). A mixture of allyl 2-oxocyclopentanecarboxylate (**10d**) (727 mg, 4.33 mmol), [3,4-(methylenedioxy)-phenyl]lead triacetate (**9a**) (2.433 g, 4.82 mmol), and dry pyridine (391 mg, 4.95 mmol) in dry CH_2Cl_2 (25 mL) was stirred in an ultrasonic cleaner at 50–55 °C for 12 h. The solution was brought to room temperature, diluted with CH_2-Cl_2 (20 mL), and washed with 1 N H_2SO_4 (20 mL × 3). The precepitates were removed by suction filtration. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined aqueous layers were washed with water (50 mL × 4) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oil (1.131 mg) which was purified by preparative TLC (CH_2-Cl_2). A major fraction (R_f 0.45) was **11d** as a colorless oil (825 mg, 66%): IR (neat) 1737, 1721 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.86–2.08 (2H, m), 2.27–2.57 (3H, m), 2.84 (1H, dt, J = 13.2, 6.6 Hz), 4.61 (2H, dt, J = 5.5, 1.5 Hz, $COOCH_2$), 5.20 (1H, dq, J = 10.3, 1.5, 1.5 Hz, *cis* =CH), 5.25 (1H, dq, J = 17.2, 1.5 Hz, trans =CH), 5.95 and 5.96 (each 1H, AB type, J = 1.5 Hz), 6.77 (1H, d, J = 8.4 Hz), 6.84 (1H, dd, J = 8.4, 1.8 Hz), 6.96 (1H, d, J = 1.8 Hz); EIMS m/z (relative intensity) 288 (M^+, 100), 247 [(M − $CH_2CH{=}CH_2$)$^+$, 5.4]; HRMS m/z calcd for $C_{16}H_{16}O_5$ 288.0998, found 288.0995.

2-[3,4-(Methylenedioxy)phenyl]-1-cyclopentanone (12a). (a) Ethyl 1-[3,4-(methylenedioxy)phenyl]-2-oxocyclopentanecarboxylate (**11a**) (1.046 g, 3.79 mmol) was dissolved in 2:1 AcOH–5% HCl (6 mL). The solution was heated under reflux for 12 h. To the cooled reaction mixture was added water (20 mL). The solution was then extracted with CH_2Cl_2 (4 mL × 5). The combined organic layers were washed with 5% $NaHCO_3$ solution (5 mL) and water (10 mL × 2) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily residue (723 mg) which was subjected to preparative TLC (2:1 hexane–AcOEt). Extraction of a band (R_f 0.53) with ethyl acetate gave **12a** (424 mg, 54.8%) as a colorless oil: IR (neat) 1740, 1611, 1506, 1491 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.80–2.33 (4H, m), 2.39–2.52 (2H, m), 3.24 (1H, dd, J = 10.0, 9.2 Hz), 5.92 (2H, s), 6.64 (1H, dd, J = 7.7, 1.8 Hz), 6.67 (1H, d, J = 1.8 Hz), 6.77 (1H, d, J = 7.7 Hz); EIMS m/z (relative intensity) 204 (M^+, 66), 148 (M − $COCH_2CH_2$)$^+$, 100); HRMS m/z calcd for $C_{12}H_{12}O_3$ 204.0757, found 204.0759.

(b) To a stirred suspension of $Pd(OAc)_2$ (11 mg, 0.049 mmol) and PPh_3 (26 mg, 0.1 mmol) in dry THF (0.6 mL) were added a solution of HCOOH (43.9 mg, 0.95 mmol) and dry Et_3N (120 mg, 1.19 mmol) in dry THF (0.4 mL) and then a solution of allyl 1-[3,4-(methylenedioxy)phenyl]-2-oxocyclopentanecarboxylate (**11d**) (113 mg, 0.39 mmol) in dry THF (0.2 mL) under nitrogen. The mixture was stirred for 18 h, diluted with diethyl ether (20 mL), and washed successively with 5% $NaHCO_3$ solution (5 mL) and saturated brine (10 mL). The solution was then passed through a pad of silica gel (Merck No. 7734, 2.5 g) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oil (98.2 mg) which was subjected to preparative TLC (CH_2Cl_2) to give **12a** (57.4 mg, 72%, R_f 0.43).

(c) A solution of benzyl 1-[3,4-(methylenedioxy)phenyl]-2-oxocyclopentanecarboxylate (**11e**) (340 mg, 1.01 mmol) in ethyl acetate (20 mL) in the presence of 10% Pd–C (525 mg) was stirred under hydrogen at room temperature for 1 h. The catalyst was removed by filtration through a pad of Celite. The residue (200 mg) obtained by the removal of the solvent was purified by preparative TLC (CH_2Cl_2) in a manner as described above to give **12a** (109.3 mg, 53%, R_f 0.43).

6-(3,4-Dimethoxyphenyl)-2-oxotetrahydropyran (13b). To a solution of 2-arylcyclopentanone **12b** in CH_2Cl_2 (10 mL)

were added $NaHCO_3$ (66 mg, 0.786 mmol) and *m*-CPBA (136 mg, 0.786 mmol). The solution was stirred at room temperature for 113 h under nitrogen. The solution was filtered through Celite, and the filtrate was washed successively with 0.5% aqueous $Na_2S_2O_3$ solution, 5% $NaHCO_3$ solution, and water (each 10 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily product (166 mg) which was subjected to preparative TLC (2% MeOH–CH_2Cl_2) to give **13b** (90 mg, 63%): mp 90–92 °C (from EtOH); IR 1737, 1610, 1593, 1519 cm^{-1}; ^1H NMR (400 MHz) δ 1.83–2.18 (4H, m), 2.57 (1H, dt, J = 17.6, 7.8, 7.8 Hz), 2.70 (1H, dt, J = 18.1, 6.8, 6.8 Hz), 3.88, 3.89 (each 3H, s), 5.30 (1H, dd, J = 10.8, 3.4 Hz), 6.84–6.90 (3H, m); MS *m/z* (relative intensity) 236 (M^+, 78.8), 164 [$(M - C_2H_4COO)^+$, 100]. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.80; H, 6.83.

6-(3,4-Dimethoxyphenyl)-2-hydroxytetrahydropyran (14b). To a solution of 2-oxotetrahydropyran **13b** (59 mg, 0.25 mmol) in dry toluene (10 mL) was added dropwise a toluene solution of DIBAL (1.5 M, 0.25 mL, 0.315 mmol) at −78 °C under nitrogen. The solution was stirred at that temperature for 2 h. To the solution at room temperature was added water (10 mL), and the solution was filtered through Celite. The aqueous layer of the filtrate was extracted with benzene (20 mL). The benzene layer and the organic layer of the filtrate were combined, washed with brine (10 mL), and dried over anhydrous Na_2SO_4. Removal of the solvent gave a product (64.5 mg) which was subjected to preparative TLC (3% MeOH–CH_2Cl_2) to give **14b** (a mixture of 1:1 *cis* and *trans* forms, 47.5 mg, 80%): mp 79–83 °C (CH_2Cl_2–hexane); IR 3326, 1593, 1524, 1500 cm^{-1}; ^1H NMR (400 MHz) δ 1.6–2.2 (6H, m), 3.86 and 3.89 (each 3H, s), 4.43 (1H, dd, J = 11.2, 1.9 Hz), 4.88 (1H, d, J = 9.2 Hz), 4.97 (1H, dd, J = 11.2, 1.9 Hz), 5.44 (1H, br s), 6.83 (1H, d, J = 8.3 Hz), 6.88 and 6.89 (1H, each dd, J = 8.3, 1.9 Hz), 6.92 and 6.95 (1H, each d, J = 1.9 Hz); MS *m/z* (relative intensity) 238 (M^+, 34.5), 167 [$(M - CH_2CH_2CHO)^+$, 100]. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.47; H, 7.63.

2-(3,4-Dimethoxyphenyl)tetrahydrofuran (16b). *(a) From trans-2-(3,4-dimethoxyphenyl)cyclopentanol (**17b**).* To a solution of **17b** (55.6 mg, 0.25 mmol) in benzene (40 mL) in a Pyrex tube were added mercury(II) oxide (162.4 mg, 0.75 mmol) and iodine (190 mg, 0.75 mmol). The stirred solution was irradiated with light generated with a 100 W high-pressure Hg arc lamp for 3 h under nitrogen. The solution was then filtered through Celite. The filtrate was washed with 5% $Na_2S_2O_3$ solution (50 mL) and then water (50 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily product (136 mg) which was subjected to preparative TLC (2% MeOH–CH_2Cl_2) to give **15b** (59 mg, 65%): IR (neat) 1720, 1607, 1595, 1513 cm^{-1}; ^1H NMR (400 MHz) δ 1.70–2.12 (4H, m), 3.17 (2H, t, J = 6.8 Hz), 3.87 and 3.90 (each 3H, each s), 5.83 (1H, t, J = 6.8 Hz), 6.84 (1H, d, J = 8.3 Hz), 6.86 (1H, d, J = 1.9 Hz), 6.90 (1H, s); EIMS *m/z* (relative intensity) 364 (M^+, 100), 319 [$(M - OCHO)^+$, 35.3], 191 [$(M - HI - HOCHO)^+$, 44.1]; HRMS *m/z* calcd for $C_{13}H_{17}IO_4$ 364.0184, found 364.0172.

To a solution of formate **15b** (64 mg, 0.176 mmol) in MeOH (15 mL) was added $NaBH_4$ (6.6 mg, 0.176 mmol). The solution was heated under reflux for 3 h, and the MeOH was evaporated off. The residue was diluted with water (20 mL) and extracted with ether (5 mL × 2). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave a product which was subjected to preparative TLC (10:1 benzene–ether) to give **16b** (17.7 mg, 48.3%) as an oil: IR (neat) 1609, 1595, 1517 cm^{-1}; ^1H NMR (270 MHz) δ 1.72–2.35 (4H, m), 3.86 and 3.89 (each 3H, each s), 3.91 (1H, dt, J = 8.2,6.9 Hz), 4.10 (1H, dt, J = 8.2, 6.9 Hz), 4.82 (1H, t, J = 7.0 Hz), 6.8–6.92 (3H, m); EIMS *m/z* (relative intensity) 208 (M^+, 100), 193 [$(M - CH_3)^+$, 19.3], 177 [$(M - HCHO)^+$, 96.8]; HRMS *m/z* calcd for $C_{12}H_{16}IO_3$ 208.1071, found 208.1121.

*(b) From 6-Aryl-2-hydroxytetrahydropyran (**14b**).* Similar β-scission reaction of **14b** (95 mg, 0.4 mmol) in benzene (80 mL) in the presence of mercury(II) oxide (325 mg, 1.5 mmol) and iodine (380 mg, 1.5 mmol) for 8.5 h, followed by the workup as described above, gave an oily crude formate **15b** (126 mg). This crude product was dissolved in MeOH (29 mg). To the solution was added $NaBH_4$ (13 mg, 0.345 mmol), and the solution was heated under reflux for 3 h and worked up as described above to give an oily product. The product was subjected to preparative TLC (10:1 benzene–diethyl ether) to give **16b** (16.5 mg, 23%).

***cis*- and *trans*-2-[3,4-(Methylenedioxy)phenyl]-1-cyclopentanol (17a).** To a stirred solution of 2-[3,4-(methylenedioxy)phenyl]cyclopentan-1-one (**12a**) (115.6 mg, 0.57 mmol) in MeOH (20 mL) was added $NaBH_4$ (21.3 mg, 0.57 mmol) at room temperature. After 30 min, MeOH was evaporated off. To the residue were added water (20 mL) and CH_2Cl_2 (15 mL × 2). The combined organic layers were washed with water (20 mL), dried over anhydrous Na_2SO_4, and evaporated. The oily residue (112.0 mg) was subjected to preparatative TLC (CH_2Cl_2) to give two fractions. The more mobile fraction gave *cis* product **17a** (39.7 mg, 34%, R_f 0.54). A less mobile fraction gave a *trans* product **17a** (59.6 mg, 51%, R_f 0.31).

***cis* isomer:** IR 3358 cm^{-1}; ^1H NMR (270 MHz) δ 1.63–2.05 (6H, m), 2.95 (1H, m), 4.24 (1H, dt, J = 4.2, 1.5 Hz), 5.95 (2H, s), 6.76 (1H, dd, J = 8.1, 1.7 Hz), 6.79 (1H, dd, J = 8.1 Hz), 6.84 (1H, d, J = 1.5 Hz); EIMS *m/z* (relative intensity) 206 (M^+, 62), 135 [$(M - CH_2O_2C_6H_3CH_2)^+$, 100]; HRMS m/z calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0917.

***trans* isomer:** IR 3376 cm^{-1}; ^1H NMR (270 MHz) δ 1.60–1.92 (6H, m), 2.79 (1H, dt, J = 10.3, 7.8 Hz), 4.07 (1H, dd, J = 14.6, 7.3 Hz), 5.92 (2H, s), 6.71 (1H, dd, J = 7.8, 1.5 Hz), 6.75 (1H, d, J = 7.8 Hz), 6.76 (1H, d, J = 1.5 Hz); EIMS *m/z* (relative intensity) 206 (M^+, 62), 135 [$(M - CH_2O_2C_6H_3CH_2)^+$, 100]; HRMS *m/z* calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0934.

2-[3,4-(Methylenedioxy)phenyl]tetrahydrofuran (16a) from 17a. A stirred suspension of the above-mentioned *trans* alcohol **17a** (43.4 mg, 0.21 mmol), HgO (162 mg, 0.63 mmol), and I_2 (160.3 mg, 0.63 mmol) in dry benzene (30 mL) was irradiated with a 100 W high-pressure Hg arc under nitrogen for 3 h. After removal of the precipitate by suction filtration through a pad of Celite, followed by washing with benzene (20 mL), the filtrate was washed with 0.5% $Na_2S_2O_3$ (20 mL) and then water (20 mL × 2) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue (72.5 mg) which was dissolved in MeOH (10 mL). To this solution was added $NaBH_4$ (6.5 mg, 0.17 mmol). The mixture was heated under reflux for 3 h. Evaporation of the solvent gave a residue which was dissolved in water (30 mL) and CH_2Cl_2 (15 mL). The aqueous layer was further extracted with CH_2Cl_2 (14 mL × 3). The combined organic layers were washed with water (30 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue (31.6 mg) which was subjected to preparative TLC with 10:1 benzene–ether to give **16a** as a colorless oil (9.5 mg, 24% from **17a**).

2-(3,4-Dimethoxyphenyl)cyclopentanols (17b). To a solution of 2-arylcyclopentanone **12b** (166 mg, 0.75 mmol) in MeOH (27.6 mL) was added $NaBH_4$ (28.4 mg, 0.75 mmol) at room temperature. The solution was stirred for half an hour. Removal of MeOH gave a product which was shaken with water (10 mL) and CH_2Cl_2 (5 mL × 2). The organic layer was washed with water (10 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily **17b** (186 mg) which was subjected to preparative TLC (2% MeOH–CH_2Cl_2) to give a *cis*-**17b** (51 mg, 30.4%, R_f 0.62) and *trans*-**17b** (96 mg, 57.3%, R_f 0.34). *cis*-**17b**: IR (neat) 3522, 1607, 1590, 1516 cm^{-1}; ^1H NMR (400 MHz) δ 1.64–2.12 (6H, m), 2.97–3.04 (1H, m, 2-H), 3.87 and 3.88 (each 3H, s), 4.25 (1H, dt, J = 4.4, 1.0 Hz), 6.83 (1H, br s), 6.85 (2H, d, J = 1.0 Hz); EIMS *m/z* (relative intensity) 222 (M^+, 65.9), 151 [$(M - (CH_2)_2CHOH)^+$, 100]; HRMS *m/z* calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1256. *trans*-**17b**: IR (neat) 3382, 2836, 1608, 1592, 1516 cm^{-1}; ^1H NMR (400 MHz) δ 1.62–1.92 (4H, m), 2.06–2.18 (2H, m), 2.83 (1H, dt, J = 10.2, 7.8 Hz), 3.86 and 3.88 (each 3H, s), 4.11 (1H, dd, J = 14.6, 7.3 Hz), 6.80 (1H, dd, J = 6.8, 1.9 Hz), 6.82 (1H, d, J = 1.9 Hz), 6.83 (1H, d, J = 6.8 Hz); MS *m/z* (relative intensity) 222 (M^+, 48.9), 151 [$(M - (CH_2)_2CHOH)^+$, 100]; HRMS *m/z* calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1255.

Dimethyl 2,6-Bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20a). Freshly

prepared powdered [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) (2.520 g, 4.99 mmol) was suspended in a solution of dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**18**) (574 mg, 2.26 mmol) and dry pyridine (394 mg, 4.98 mmol) in dry CH_2Cl_2 (40 mL). The solution was heated under reflux for 12 h under nitrogen in an ultrasonic cleaner (Branson 1200). The cooled mixture was diluted with CH_2Cl_2 (40 mL). Precipitates were removed by suction filtration. The filtrate was diluted with CH_2Cl_2 (100 mL), washed with 3 N H_2SO_4 solution (20 mL × 5) and water (50 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a brown oily residue (1.8 g) which was recrystallized from CH_2Cl_2–light petroleum to give **20a** as colorless crystals (816 mg, 73%): mp 215–216 °C; IR 1762, 1719 cm^{-1}; ^1H NMR (270 MHz) δ 2.33 (2H, dd, J = 20.2, 9.2 Hz), 2.88 (2H, ddd, J = 20.2, 7.3, 2.9 Hz), 3.45 (2H, ddd, J = 9.2, 7.3, 2.9 Hz), 3.65 (6H, s), 6.00 and 6.02 (each 1H, AB q, J = 1.5 Hz), 6.83 (2H, d, J = 1.5 Hz), 6.83 (2H, d, J = 1.1 Hz), 6.88 (2H, dd, J = 1.5, 1.1 Hz). Irradiation of the signal of the bridgehead protons at δ 3.45 resulted in an enhancement of the signal areas of 4α-H and 8α-H (δ 2.88) and the aromatic protons at positions 2′ and 6′ (δ 6.83 and 6.88). EIMS m/z (relative intensity) 494 (M^+, 75), 435 [$(M - COOMe)^+$, 100], 375 [$(M - C_6H_3OCH_2O)^+$, 26]. Anal. Calcd for $C_{26}H_{22}O_{10}$: C, 63.15; H, 4.49. Found: C, 63.25; H, 4.51.

Diallyl 3,7-Dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (19a). A solution of dimethyl 3,7-dioxobicyclo[3.3.0]-octane-2,6-dicarboxylate (**18**) (1.27 g, 5.0 mmol), DMAP (122 mg, 0.1 mmol), and allyl alcohol (5.8 g, 100 mmol) in dry toluene (25 mL) was heated under reflux for 15 h. The cooled solution was diluted with benzene (30 mL), washed with 2 N HCl (2 mL × 2) and then brine (2 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent and allyl alcohol gave a crystalline solid (1.549 g) which was recrystallized from EtOH to give **19a** (838 mg, 55%): mp 106–108 °C; IR 1673, 1640 cm^{-1}; ^1H NMR (270 MHz) δ 2.45–3.10 (6H, m), 3.50–3.58 (2H, m), 4.60–4.76 (4H, m), 5.23–5.40 (4H, m), 5.95 (2H, ddt, J = 18.0, 10.4, 5.5 Hz); EIMS m/z (relative intensity) 306 (M^+, 5.4), 265 [$(M - CH_2{=}CHCH_2)^+$, 0.8], 41 ($CH_2{=}CHCH_2^+$, 100). Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.69; H, 5.95.

Diallyl 2,6-Bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20b). A mixture of the diallyl ester **19a** (522 mg, 1.71 mmol), [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) (1.922 g, 3.81 mmol), and dry pyridine (303 mg, 3.88 mmol) in CH_2Cl_2 (30 mL) was heated under reflux for 15 h under nitrogen in an ultrasonic cleaner (Branson 1200). To the cooled dark brown reaction mixture were added CH_2Cl_2 (50 mL) and 1 N H_2SO_4 solution (50 mL), and the mixture was shaken. After the precipitates were removed by suction filtration, the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic layers were washed with 5% $NaHCO_3$ (10 mL × 2) and water (100 mL × 2) and dried over anhydrous Na_2SO_4. Removal of the solvent gave a dark brown oil (910 mg) which was subjected to preparative TLC (0.5% MeOH–CH_2Cl_2) to give a crude **20b** as colorless crystals (154 mg, R_f 0.25, 16.5%) mp 176–181 °C. Recrystallization from CH_2Cl_2–ether gave an analytical sample (100.4 mg): mp 181–183 °C; IR 1750, 1730 cm^{-1}; ^1H NMR (270 MHz) δ 2.35 (2H, dd, J = 19.8, 9.2 Hz), 2.86 (2H, ddd, J = 19.8, 9.2, 2.9 Hz), 3.47 (2H, dt, J = 2.9, 9.2 Hz), 4.55 and 4.56 (each 2H, dt, J = 5.8, 1.5 Hz), 5.18 (2H, dq, J = 10.3, 1.5 Hz), 5.20 (2H, dq, J = 10.3, 1.5 Hz), 5.78 (2H, ddt, J = 17.2, 10.3, 5.8 Hz), 6.85 (2H, d, J = 0.7 Hz), 6.85 (2H, d, J = 1.8 Hz), 6.91 (2H, dd, J = 1.8, 0.7 Hz); EIMS m/z (relative intensity) 546 (M^+, 8.5), 41 ($CH_2CH{=}CH_2^+$, 100). Anal. Calcd for $C_{30}H_{26}O_{10}$: C, 65.93; H, 4.80. Found: C, 65.92; H, 4.81.

Dibenzyl 3,7-Dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (19b). A solution of dimethyl 3,7-dioxobicyclo[3.3.0]-octane-2,6-dicarboxylate (**18**) (5.191 g, 20.4 mmol), DMAP (500 mg, 4.1 mmol), and benzyl alcohol (44 g, 41 mmol) in dry toluene (200 mL) was heated under reflux for 16 h. The cooled solution was diluted with Et_2O (100 mL), washed successively with 1 N H_2SO_4 solution (50 mL), 5% $NaHCO_3$ solution (50 mL), and brine (100 mL), and dried over anhydrous Na_2SO_4. Removal of the solvents and excess benzyl alcohol by distillation under reduced pressure (15 Torr) gave a brown crystalline solid (6.827 g) which was recrystallized from MeOH to give **19b** (5.962 mg, 72%): mp 104–106 °C; IR 1658, 1621 cm^{-1}; ^1H NMR (270 MHz) δ 2.40–3.70 (6H, m), 3.50–3.58 (2H, m), 5.18 and 5.25 (each 2H, AB q, J = 8.8 Hz), 7.36 (10 H, s); EIMS m/z (relative intensity) 406 (M^+, 0.35), 315 [$(M - C_6H_5CH_2)^+$, 0.5], 91 ($C_6H_5CH_2^+$, 100). Anal. Calcd for $C_{24}H_{22}O_6$: C, 70.93; H, 5.46. Found: C, 70.86; H, 5.50.

Dibenzyl 2,6-Bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20c). A mixture of dibenzyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**19b**) (3.40 g, 8.4 mmol), [3,4-(methylenedioxy)phenyl]lead triacetate (**9a**) (8.56 g, 17.0 mmol), and dry pyridine (1.36 mL, 17.0 mmol) in dry CH_2Cl_2 (140 mL) was heated under reflux for 24 h under nitrogen in an ultrasonic cleaner (Branson 1200). The resulting dark brown reaction mixture was washed successively with 1 N H_2SO_4 solution (10 mL × 3), 5% $NaHCO_3$ solution (10 mL × 2), and water (100 mL × 2) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oil (6.28 g), to which CH_2Cl_2–Et_2O was added to give a colorless crystalline **20c** (3.731 g, 68.7%), mp 153–155 °C. The mother liquor (2.397 g) was subjected to column chromatography on silica gel (50 g). A main fraction (625 mg) eluted with 5% MeOH–CH_2Cl_2 was crystallized from CH_2Cl_2–Et_2O to give an additional amount of the product (563 mg, 10.3%): mp 153–155°C; IR 1763, 1738 cm^{-1}; ^1H NMR (270 MHz) δ 2.26 (2H, dd, J = 20.2, 9.2 Hz), 2.72 (2H, ddd, J = 20.2, 7.7, 2.9 Hz), 3.45 (2H, ddd, J = 9.2, 7.7, 2.9 Hz), 5.04 and 5.11 (each 2H, AB q, J = 12.5 Hz), 5.98 and 6.00 (each 2H, AB q, J = 1.1 Hz), 6.81 (2H, d, J = 0.7 Hz), 6.81 (2H, d, J = 1.5 Hz), 6.85 (2H, dd, J = 1.5, 0.7 Hz), 7.16–7.30 (10 H, m). Irradiation of the signal due to the bridgehead protons at δ 3.45 resulted in an enhancement of the signal areas of 4α-H and 8α-H (δ 2.72) and the aromatic protons at positions 2′ and 6′ (δ 6.81): EIMS m/z (relative intensity) 646 (M^+, 3.4), 555 [$(M - CH_2C_6H_5)^+$, 1.0], 511 [$(M - COOCH_2C_6H_5)^+$, 2.7], 91 ($C_6H_5CH_2^+$, 100). Anal. Calcd for $C_{36}H_{26}O_{10}$: C, 70.68; H, 4.68. Found: C, 70.74; H, 4.84.

2,6-Bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo-[3.3.0]octane (21a). (a) Decarbomethoxylation of dimethyl 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20a**) by boiling in 2:1 AcOH–5% HCl solution failed to give **21a**.

(b) To a stirred suspension of $Pd(OAc)_2$ (14.5 mg, 0.065 mmol) and PPh_3 (34.8 mg, 0.13 mmol) in dry THF (0.8 mL) was added a solution of HCOOH (58.6 mg, 1.27 mmol) and dry Et_3N (160 mg, 1.58 mmol) in dry THF (0.5 mL). To this mixture was added a solution of diallyl 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20b**) (142 mg, 0.26 mmol) in dry THF (1.5 mL) with vigorous stirring. The solution was stirred for 24 h, and the mixture was diluted with ether (20 mL) and washed with 5% $NaHCO_3$ solution (5 mL) and brine (10 mL × 2). Insoluble materials were removed by suction filtration through a pad of silica gel (Merck No. 7734, 2.5 g). The filtrate was then dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the crude product (102.3 mg) which was purified by preparative TLC on silica gel (0.5% MeOH–CH_2Cl_2) to give **21a** (42.5 mg, 43%).

(c) A suspension of dibenzyl 2,6-bis[3,4-(methylenedioxy)-phenyl]-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20c**) (1.938 g, 3.0 mmol) and 10% Pd–C (310 mg) in MeOH (134 mL) was stirred under hydrogen for 20 h at room temperature. Removal of the catalyst and solvent gave a yellow oil (1.132 g) which was recrystallized from CH_2Cl_2–Et_2O to give **21a** (843 mg, 74%): mp 215–217 °C; IR 1748, 1731 cm^{-1}; ^1H NMR (270 MHz) δ 2.62 (2H, d, J = 19.5 Hz), 2.72 (2H, dd, J = 19.5, 4.4 Hz), 3.11 (2H, d, J = 4.4 Hz), 3.12 (2H, s), 5.97 (4H, s), 6.61 (2H, dd, J = 7.8, 1.9 Hz), 6.63 (2H, d, J = 1.9 Hz), 6.81 (2H, d, J = 7.8 Hz). Irradiation of the signals at δ 3.11 or 3.12 resulted in an enhancement of the signal areas at δ 2.72 (4α-H and 8α-H), 6.61 (6′-H) and 6.63 (2′-H). EIMS m/z (relative intensity) 378 (M^+, 100), 216 [$(M - CH_2O_2C_6H_3CH{=}C{=}O)^+$, 9.3]. Anal. Calcd for $C_{22}H_{18}O_6$: C, 69.83; H, 4.79. Found: C, 69.69; H, 4.67.

2,7-Bis[3,4-(methylenedioxy)phenyl]-3,8-dioxabicyclo-[4.4.0]decane-4,9-dione (22a). (a) With *m*-CPBA. A solution of 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo-[3.3.0]octane (**21a**) (27.8 mg, 0.1 mmol) and *m*-CPBA (138 mg, 0.8 mmol) in CH_2Cl_2 (4 mL) was stirred at room temperature for 10 days. The mixture was diluted with CH_2Cl_2 (20 mL), washed successively with 5% $Na_2S_2O_3$ solution (14 mL), 5% Na_2CO_3 solution (14 mL), and water (20 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily product (14.1 mg) which was purified by preparative TLC on silica gel (4:1 benzene–ether) to give crystalline **22a** (11.3 mg, R_f 0.54, 28%): mp >300 °C; IR 1734 cm^{-1}; ^1H NMR (270 MHz) δ 2.24 (2H, dd, J = 15.2, 6.2 Hz) and 2.35 (2H, dd, J = 15.2, 10.9 Hz), 2.66 (2H, m), 4.94 (2H, d, J = 10.3 Hz), 6.02 (4H, s), 6.79 (2H, dd, J = 8.1, 1.5 Hz), 6.85–6.90 (4H, m). Irradiation of the signals at δ 2.66 resulted in an enhancement of the signal areas at δ 2.24 (5α-H and 10α-H), 6.79 (6′-H) and 6.85 (2′-H). EIMS *m/z* (relative intensity) 410 (M^+, 100), 260 [(M − $CH_2O_2C_6H_3CHO)^+$, 56.5], 232 [(M − $CH_2O_2C_6H_3$-$CHOCO)^+$, 13.7], 218 ($CH_2O_2C_6H_3CHOCOC_5H_5O_2^+$, 60.8). Anal. Calcd for $C_{22}H_{18}O_6$: C, 64.39; H, 4.42. Found: C, 64.65; H, 4.39.

(b) With *m*-CPBA–$NaHCO_3$. A solution of 2,6-bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo[3.3.0]octane (**21a**) (18.9 mg, 0.05 mmol), *m*-CPBA (80%, 56 mg, 0.26 mmol), and $NaHCO_3$ (21.8 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) was stirred for 68 h at room temperature. To the mixture was added a further amount of *m*-CPBA (28.0 mg) and $NaHCO_3$ (10.9 mg). The solution was stirred for another 23 h and then filtered through a Celite pad. The filtrate was worked up as described above. Evaporation of the solvent gave a brown-colored oil (26.8 mg) which crystallized on addition of MeOH to give **22a** (14.8 mg, 72%).

(c) With *m*-CPBA–K_2CO_3. A suspension of dioxobicyclo-[3.3.0]octane **21a** (68 mg, 0.18 mmol), *m*-CPBA (80%, 310.6 mg, 1.44 mmol), and K_2CO_3 (248.8 mg, 1.8 mmol) in dry CH_2Cl_2 (18 mL) was stirred for 1 h at room temperature. The mixture was then worked up as mentioned above to give a colorless oil. It was crystallized by the addition of EtOH to give **22a** (56.1 mg, 76.0%).

2,6-Bis[3,4-(methylenedioxy)phenyl]-3,7-dioxobicyclo-[3.3.0]octane-3β,7β-diol (26). To a stirred solution of 2,6-bis[3,4-(methylenedioxy)phenyl]bicyclo[3.3.0]octane-3,7-dione (**21a**) (19 mg, 0.05 mmol) in MeOH (2 mL) and THF (3 mL) was added $NaBH_4$ (5 mg, 0.13 mmol). After the mixture was stirred for 30 min at room temperature, the solvent was evaporated. The residue was dissolved in water (5 mL), extracted with CH_2Cl_2 (3 mL × 2), washed with water (5 mL), and dried over anhydrous Na_2SO_4. The product **26** (19 mg) was purified by preparative TLC on silica gel (3:2 benzene–ether) and extracted with 2:1 CH_2Cl_2–MeOH. The product was recrystallized from MeOH to give **26** (14 mg, 74%) as colorless crystals: mp 209–213 °C; IR 3266 cm^{-1}; ^1H NMR (270 MHz) δ 1.59 (2H, ddd, J = 12.5, 9.5, 7.0 Hz), 1.76 (2H, br s, disappeared by addition of D_2O), 2.31 (2H, ddd, J = 12.5, 8.0, 6.6 Hz), 2.48 (2H, dddd, J = 9.5, 8.0, 7.0, 2.6 Hz), 2.73 (2H, t, J = 9.5 Hz), 4.11 (2H, dt, J = 9.5, 6.6 Hz), 5.94 (4H, s), 6.72 (2H, dd, J = 8.1, 1.8 Hz), 6.77 (2H, d, J = 1.8 Hz), 6.78 (2H, d, J = 8.1 Hz). Irradiation of signals due to 2β-H (6β-H) at δ 2.73 resulted in an enhancement of the signal areas of 4β-H, 2′-H and 6′-H. Irradiation of signals due to 3α-H (7α-H) at δ 4.11 resulted in an enhancement of the signal areas of 4α-H (8α-H), 2′-H, and 6′-H. Irradiation of signals due to the aromatic protons, 2′-H and 6′-H, at δ 6.72 and 6.77, respectively, enhanced the signal areas of 1-H (5-H), 2-H (6-H), and 3α-H (7α-H). EIMS *m/z* (relative intensity) 382 (M^+, 5), [(M − $H_2O)^+$, 27], 346 [(M − 2 $H_2O)^+$, 15]. Anal. Calcd for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 69.22; H, 5.84.

2,7-Bis[3,4-(methylenedioxy)phenyl]-3,8-dioxabicyclo-[4.4.0]decane-4,9-diol (23a). To a stirred solution of dilactone **22a** (52 mg, 0.13 mmol) in dry CH_2Cl_2 (15 mL) at −78 °C was added DIBAL (0.22 mL, 1.6 M, 0.35 mmol), and the mixture was stirred for 3.5 h at that temperature. To the solution at room temperature was added water (20 mL). The precipitates were removed by suction filtration and washed with CH_2Cl_2 (20 mL). The filtrate was washed with water (20 mL × 2) and dried over anhydrous Na_2SO_4. Purification of the residue (61.9 mg) by preparative TLC (4:1 benzene–ether) gave **23a** (23.3 mg, R_f 0.38, 44%): mp 200–203 °C; IR 3372 cm^{-1}; EIMS *m/z* (relative intensity) 414 (M^+, 4.0), 396 [(M − $H_2O)^+$, 2.7], 378 [(M − 2$H_2O)^+$, 2.0], 246 [(M − $CH_2O_2C_6H_3$-CHO − $H_2O)^+$, 33.8], 228 [(M − $CH_2O_2C_6H_3CHO$ − 2$H_2O)^+$, 37.1], 151 ($CH_2O_2C_6H_3CHOH^+$, 100). Anal. Calcd for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.52; H, 5.29.

3a,4,6,6a-Tetrahydro-1,4-bis[3,4-(methylenedioxy)-phenyl]-1*H*,3*H*-furo[3,4-*c*]furan: (±)-Sesamin (25a). A stirred mixture of the dilactol **23a** (6.3 mg, 0.015 mmol), red HgO (20.3 mg, 0.09 mmol), and I_2 (25.5 mg, 0.09 mmol) in dry benzene in a Pyrex test tube was irradiated under nitrogen with a 100 W high-pressure Hg arc at room temperature for 5 h until most of **23a** was consumed (TLC analysis). Precipitates were removed by suction filtration. The filtrate was diluted with benzene (20 mL), washed with 0.5% $Na_2S_2O_3$ solution (22 mL) and then water (20 mL), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily product **24a** (12.5 mg) whose ^1H NMR spectra exhibited the signal of the O–CHO proton at δ 8.13. To the formate **24a** dissolved in MeOH (10 mL) was added $NaBH_4$ (5.2 mg, 0.14 mmol). The mixture was then heated under reflux for 2 h, and the solvent was evaporated to dryness. The residue was dissolved in CH_2Cl_2 (10 mL), washed with water (10 mL), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the crude product which was purified by preparative TLC on silica gel (5:1 benzene–ether) to give a crystalline solid of (±)-sesamin (**25a**) (1.5 mg, R_f 0.5, 28% from **23a**), mp 120–124 °C. Recrystallization from EtOH gave a pure sample of sesamin: mp 129–130 °C (lit.[26] mp 126 °C); ^1H NMR (270 MHz) δ 3.05 (2H, ddd, J = 7.3, 4.4, 3.9 Hz), 3.87 (2H, dd, J = 9.3, 3.9 Hz), 4.23 (2H, dd, J = 9.3, 7.3 Hz), 4.72 (2H, d, J = 4.4 Hz), 5.95 (4H, s), 6.79 (2H, d, J = 7.8 Hz), 6.80 (2H, dd, J = 7.8, 1.5 Hz), 6.85 (2H, d, J = 1.5 Hz).

Dimethyl 2,6-Bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20d). A mixture of freshly prepared (3,4-dimethoxyphenyl)lead triacetate (**9b**) (8.60 g, 16.5 mmol), dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**18**) (1.27 g, 5.0 mmol), and dry pyridine (1.303 g, 16.5 mmol) in dry CH_2Cl_2 (125 mL) was heated under reflux for 3 h under nitrogen in an ultrasonic cleaner (Branson 1200). Precipitates were removed by suction filtration. The filtrate was diluted with CH_2Cl_2 (100 mL), washed with 3 N H_2SO_4 solution (50 mL) and then H_2O (100 mL × 3), and dried over anhydrous Na_2SO_4. Removal of the solvent gave a brown oily residue (2.783 g). Addition of EtOH afforded **20d** as colorless crystals (1.865 g, 71%), mp 170–171 °C. An analytical sample, recrystallized from the same solvent, melted at 172–173 °C. IR 1762, 1719 cm^{-1}; ^1H NMR (400 MHz) δ 2.38 (2H, dd, J = 19.5, 9.3 Hz), 2.87 (2H, ddd, J = 19.5, 7.3, 2.9 Hz), 3.53 (2H, ddd, J = 9.3, 7.3, 2.9 Hz), 3.65 (6H, s), 3.78 and 3.90 (each 6H, s), 6.87 (2H, d, J = 8.3 Hz), 6.92 (2H, d, J = 2.4 Hz), 6.94 (2H, dd, J = 8.3, 2.4 Hz), 7.14–7.28 (10H, m). Irradiation of the bridgehead protons at δ 3.53 resulted in an enhancement of the signal areas of 4α-H and 8α-H (δ 2.87) and the aromatic protons at positions 2′ and 6′ (δ 6.92 and 6.94): EIMS *m/z* (relative intensity) 526 (M^+, 100), 494 [(M − MeOH)$^+$, 44], 467 [(M − COOMe)$^+$, 91]. Anal. Calcd for $C_{28}H_{30}O_{10}$: C, 63.87; H, 5.74. Found: C, 63.65; H, 5.75.

Dibenzyl 2,6-Bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20e). A mixture of dibenzyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**19b**)-(816 mg, 2 mmol), freshly prepared (3,4-dimethoxyphenyl)lead triacetate (**9b**) (3.42 g, 6.6 mmol), and dry pyridine (522 mg, 6.6 mmol) in dry CH_2Cl_2 (50 mL) was heated under reflux for 6.5 h under nitrogen in an ultrasonic cleaner (Branson 1200). The resulting dark brown mixture was diluted with CH_2Cl_2 (50 mL), washed successively with 3 N H_2SO_4 (180 mL × 3), 5% $NaHCO_3$ solution (30 mL × 2), and water (100 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oil (1.477 g) to which CH_2Cl_2–Et_2O was added to give **20e** (998 g, 74%) as colorless crystals: mp 185.5–187 °C; IR 1760, 1708 cm^{-1}; ^1H NMR (400 MHz) δ 2.33 (2H, dd, J = 20.0, 9.3 Hz), 2.75 (2H, ddd, J = 20.0, 7.6, 2.9 Hz), 3.51 (2H, ddd, J = 9.3, 7.6, 2.9 Hz), 3.75 and 3.89 (each 6H, s), 5.06 and 5.10

(each 2H, AB q, J = 12.6 Hz), 6.85 (2H, d, J = 2.0 Hz), 6.86 (2H, d, J = 8.3 Hz), 6.91 (2H, dd, J = 8.3, 2.0 Hz), 7.14–7.28 (10H, m). Irradiation of the signals of the bridgehead protons at δ 3.51 resulted in an enhancement of the signal areas of 4α-H and 8α-H (δ 2.75) and aromatic protons at positions 2′ and 6′ (δ 6.85 and 6.91): EIMS m/z (relative intensity) 678 (M^+, 8.3), 587 [$(M^+ - CH_2C_6H_5)^+$, 1.7], 543 [$(M - COOCH_2C_6H_5)^+$, 3.2], 91 ($C_6H_5CH_2^+$, 100). Anal. Calcd for $C_{40}H_{38}O_{10}$: C, 70.78; H, 5.64. Found: C, 70.67; H, 5.62.

2,6-Bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]-octane (21b). (a) By AcOH–HCl-Catalyzed Decarboxylation. A solution of dimethyl 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20d**) (2.104 g, 4.0 mmol) in AcOH–5% HCl (2:1, 60 mL) was heated under reflux for 15 h, and the cooled mixture was diluted with water (100 mL) and extracted with CH_2Cl_2 (30 mL × 3). The combined CH_2Cl_2 layers were washed with 5% Na_2CO_3 (30 mL × 3) and water (50 mL × 3) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue (1.731 g) which was crystallized by the addition of MeOH–Et_2O to give **21b** (1.121 g, 68%), mp 188–191 °C. Recrystallization from CH_2Cl_2–Et_2O gave an analytical sample: mp 188–189 °C; IR 1737 cm^{-1}; ^1H NMR (400 MHz) δ 2.66 (2H, d, J = 19.5 Hz), 2.76 (2H, ddd, J = 19.5, 3.4, 2.9 Hz), 3.17 (2H, d, J = 2.9 Hz), 3.18 (2H, br s), 3.88 and 3.89 (each 6H, each s), 6.66 (2H, d, J = 2.0 Hz), 6.71 (2H, dd, J = 8.3, 2.0 Hz), 6.88 (2H, d, J = 8.3 Hz). Irradiation of the signals at δ 3.17 resulted in an enhancement of the signals at δ 2.76 (4α-H and 8α-H) and aromatic protons at C-2′ and 6′ (δ 6.66 and 6.71): EIMS m/z (relative intensity) 410 (M^+, 100). Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.39. Found: C, 69.97; H, 6.33.

The dione was also obtained when dibenzyl 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20e**) (20.3 mg, 0.03 mmol) in AcOH (8 mL) and 5% HCl (4 mL) was heated under reflux for 17 h and worked up as described above. Purification of the oily residue (19 mg) by preparative TLC (2% MeOH–CH_2Cl_2) gave an oil (8.6 mg) which was crystallized from CH_2Cl_2–ether to give **21b** (7.4 mg, 60%), mp 184–185 °C.

(b) By Hydrogenolysis. A suspension of dibenzyl 2,6-bis-(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20e**) (1.017 mg, 1.5 mmol) and 10% Pd–C (155 mg) in ethyl acetate (200 mg) was vigorously stirred for 20 h under hydrogen. Removal of the catalyst through a Celite pad, followed by evaporation of the solvent, gave a yellow oil (576 mg), which was heated for 30 min in a mixture of AcOH (100 mL) and 5% HCl (50 mL) at 80 °C. The cooled mixture was diluted with water (100 mL) and extracted with CH_2Cl_2 (30 mL × 3). The combined extracts were washed with 5% $NaHCO_3$ solution (50 mL) and water (50 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and crystallization of the oily residue (480 mg) gave **21b** (312 mg, 51%).

(c) By CF_3CO_2H-Catalyzed Decarboxylation. A solution of dibenzyl ester **20e** (38.9 mg, 0.05 mmol) in trifluoroacetic acid (0.7 mL) was heated under reflux under nitrogen for 2 h. Removal of the solvent gave a residue which was dissolved in CH_2Cl_2 (5 mL). The solution was washed with 5% $NaHCO_3$ solution (5 mL) and then water (5 mL × 2) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oil (22.4 mg). Addition of CH_2Cl_2–EtOH gave **21b** (13 mg, 63%). Heating of dimethyl ester **20d** (36.8 mg, 0.07 mmol) in CF_3-COOH (1 mL) for 2 days failed to give **21b**. Crude **20d** (43 mg) was recovered unchanged.

2,7-Bis(3,4-dimethoxyphenyl)-3,8-dioxabicyclo[4.4.0]-decane-4,9-dione (22b). (a) With *m*-CPBA. A solution of 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane (**21b**)-(410 mg, 1 mmol) and *m*-CPBA (1.38 g, 8 mmol) in CH_2Cl_2 (50 mL) was stirred at room temperature for 3 days. The mixture was then diluted with CH_2Cl_2 (20 mL), washed successively with 5% $Na_2S_2O_3$ solution (30 mL), 5% Na_2CO_3 solution (20 mL × 2), and water (30 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily product (458 mg) which was subjected to preparative TLC on silica gel (2% MeOH–CH_2Cl_2) to give a crystalline solid (222 mg). Its recrystallization from EtOH gave **22b** (141 mg, 32%): mp >300 °C; IR 1734 cm^{-1}; ^1H NMR (400 MHz) δ 2.23 (2H, dd, J = 15.1, 5.9 Hz) and 2.38 (2H, dd, J = 15.1, 11.2 Hz), 2.72 (2H, ddd, J = 11.2, 9.8, 5.9 Hz), 3.91 (12H, s), 4.99 (2H, d, J = 9.8 Hz), 6.79 (2H, dd, J = 8.1, 1.5 Hz), 6.85–6.90 (4H, m). Irradiation of the signals at δ 2.72 resulted in an enhancement of the signal areas at δ 2.23 (5α-H and 10α-H) and part of the aromatic protons at δ 6.85–6.90: EIMS m/z (relative intensity) 442 (M^+, 100), 276 [$(M - MeO_2C_6H_3CHO)^+$, 37]. Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92. Found: C, 64.88; H, 5.71.

(b) With *m*-CPBA and $NaHCO_3$. To a stirred solution of 2,6-bis(3,4-dimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane (**21b**) (20.5 mg, 0.05 mmol) and *m*-CPBA (44.8 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) was added powdered $NaHCO_3$ (21.8 mg, 0.26 mmol). The suspended solution was stirred for 16 h at room temperature, diluted with CH_2Cl_2 (2 mL), washed successively with 5% $Na_2S_2O_3$ solution (2 mL), 5% Na_2CO_3 solution (2 mL × 2), and H_2O (5 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a colorless solid (23.4 mg). Recrystallization of the solid from CH_2Cl_2–EtOH gave **22b** (18.5 mg, 84%).

(c) With *m*-CPBA and K_2CO_3. A solution of dioxobicyclo-[3.3.0]octane **21b** (12.3 mg, 0.03 mmol), *m*-CPBA (80%, 51.8 mg, 0.24 mmol), and K_2CO_3 (41.5 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) was stirred for 1.5 h at room temperature. The solution was then worked up by the procedure described above to give a crude **22b** (12.9 mg) which was recrystallized from CH_2Cl_2–EtOH to give pure **22b** (11.8 mg, 89%).

2,7-Bis(3,4-dimethoxyphenyl)-3,8-dioxabicyclo[4.4.0]-decane-4,9-diol (23b). To a stirred solution of dilactone **22b** (22.1 mg, 0.05 mmol) in dry CH_2Cl_2 (8 mL) at −78 °C was added DIBAL (1.5 M, 0.15 mL, 0.2 mmol). The mixture was stirred at this temperature for 4 h. The cooling bath was removed, and water (10 mL) was added. The precipitates were removed by suction filtration and washed with CH_2Cl_2 (10 mL). The filtrate was washed with water (10 mL × 2) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a solid (21.5 mg) which was crystallized from MeOH to give **23b** (21.1 mg, 94.6%): mp 218–223 °C; IR 3342 cm^{-1}; EIMS m/z (relative intensity) 446 (M^+, 6.6), 428 [$(M - H_2O)^+$, 5.7], 410 [$(M - 2H_2O)^+$, 1.9], 280 [$(M - MeO_2C_6H_3CHO)^+$, 4.4], 244 [$(M - MeO_2C_6H_3CHO - 2H_2O)^+$, 51.7], 167 ($MeO_2C_6H_3CHOH^+$, 100). Anal. Calcd for $C_{24}H_{30}O_8$: C, 64.56; H, 6.77. Found: C, 64.37; H, 6.75.

3a,4,6,6a-Tetrahydro-1,4-bis(3,4-dimethoxyphenyl)-1*H*,3*H*-furo[3,4-*c*]furan: (±)-Eudesmin (25b). A stirred mixture of dilactol **23b** (18 mg, 0.04 mmol), yellow HgO (52 mg, 0.24 mmol), and I_2 (61 mg, 0.24 mmol) in dry CH_2Cl_2 in a Pyrex test tube was irradiated in an atmosphere of nitrogen with a 100 W high-pressure Hg arc for 5 h at room temperature until most of the dilactol was consumed (TLC analysis). Precipitates (HgO and HgI_2) were removed by suction filtration. The filtrate was washed with 0.5% $Na_2S_2O_3$ solution (8 mL) and then water (20 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily formate **24b** (69 mg) whose ^1H NMR spectra exhibited the signals of the OCHO proton as a singlet at δ 8.23. This residue was dissolved in MeOH (10 mL), and $NaBH_4$ (4 mg, 0.10 mmol) was added to the solution. After stirring at room temperature for 10 min, the mixture was heated under reflux for 2 h. Removal of the solvent gave a residue which was dissolved in CH_2Cl_2 (10 mL), washed with water (20 mL), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a crude product (14 mg) which was purified by preparative TLC on silica gel (1% MeOH–CH_2Cl_2) to give a crystalline solid of the crude (±)-eudesmin (**25b**) (5.6 mg, R_f 0.4, 36% from dilactol **23b**), mp 89–90 °C. Recrystallization from EtOH gave a pure sample: mp 90–91 °C (lit.[36] mp 90–93 °C, lit.[40] mp 91–92 °C; ^1H NMR (270 MHz) δ 3.12 (2H, ddd, J = 7.3, 4.4, 3.9 Hz), 3.88 and 3.90 (each 6H, each s), 3.91 (2H, dd, J = 9.5, 3.9 Hz), 4.26 (2H, dd, J = 9.5, 7.3 Hz), 4.76 (2H, d, J = 4.4 Hz), 6.84 (2H, d, J = 8.3 Hz), 6.88 (2H, dd, J = 8.3, 2.0 Hz), 6.91 (2H, d, J = 2.0 Hz).

Dimethyl 2,6-Bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (20f). A solution of freshly prepared (3,4,5-trimethoxyphenyl)lead triacetate (**9c**) (16.99 g, 30.8 mmol), dimethyl 3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**18**) (3.56 g, 14.0 mmol), and dry pyridine (2.44 g, 30.8 mmol) in dry CH_2Cl_2 (350 mL) was heated under

reflux for 3 h under nitrogen in an ultrasonic cleaner (Branson 1200). Precipitates in the cooled reaction mixture were removed by suction filtration. The filtrate was diluted with CH_2Cl_2 (200 mL), washed with 3 N H_2SO_4 (100 mL) and water (200 mL × 3), and dried over anhydrous Na_2SO_4. The resulting brown oily product (8.179 g) was crystallized by the addition of EtOH to give **20f** as colorless crystals (4.405 g, 54%): mp 190–191 °C; IR 1748, 1720 cm^{-1}; ^1H NMR (270 MHz) δ 2.38 (2H, dd, J = 20.1, 9.3 Hz), 2.90 (2H, ddd, J = 20.1, 7.9, 2.3 Hz), 3.50 (2H, ddd, J = 9.3, 7.9, 2.3 Hz), 3.68 (6H, s), 3.83 (12H, s), 3.86 (6H, s), 6.60 (4H, s); EIMS *m/z* (relative intensity) 586 (M^+, 52), 527 [$(M - COOMe)^+$, 26]. Anal. Calcd for $C_{30}H_{34}O_{12}$: C, 61.43; H, 5.84. Found: C, 61.18; H, 5.83.

2,6-Bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]-octane (21c). A solution of dimethyl 2,6-bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane-2,6-dicarboxylate (**20f**) (586.6 mg, 1 mmol) in 2:1 AcOH–5% HCl (12 mL) was heated under reflux for 27 h. The cooled mixture was diluted with water (30 mL) and extracted with CH_2Cl_2 (10 mL × 3). The CH_2Cl_2 layers were washed with 5% $NaHCO_3$ (10 mL) and then H_2O (20 mL × 3) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily product (526.9 mg) which was recrystallized from EtOH to give **21c** (201.3 mg, 43%): mp 200–201 °C; IR 1735 cm^{-1}; ^1H NMR (270 MHz) δ 2.69 (2H, d, J = 19.8 Hz), 2.80 (2H, dd, J = 19.8, 5.6 Hz), 3.12 (2H, d, J = 5.6 Hz), 3.15 (2H, br s), 3.85 (6H, s), 3.87 (12H, s), 6.34 (4H, s); EIMS *m/z* (relative intensity) 470 (M^+, 100). Anal. Calcd for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.64; H, 6.39.

2,7-Bis(3,4,5-trimethoxyphenyl)-3,8-dioxabicyclo[4.4.0]-decane-4,9-dione (22c). To a solution of 2,6-bis(3,4,5-trimethoxyphenyl)-3,7-dioxobicyclo[3.3.0]octane (**21c**) (47.1 mg, 0.1 mmol) and *m*-CPBA (80%, 172.6 mg, 0.8 mmol) in CH_2Cl_2 (10 mL) was added powdered K_2CO_3 (138.2 mg, 1.0 mmol). The suspension was stirred at room temperature for 2 h, and precipitates were removed by suction filtration through a Celite pad. The filtrate was diluted with CH_2Cl_2 (5 mL), washed successively with 5% $Na_2S_2O_3$ solution (10 mL), 5% $NaHCO_3$ solution (1 mL), and H_2O (20 mL × 2), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a colorless solid **22c** (50.4 mg). Recrystallization from CH_2Cl_2–EtOH gave **22c** (31.8 mg, 63%): mp >300 °C; IR 1728 cm^{-1}; ^1H NMR (270 MHz) δ 2.29 (2H, dd, J = 15.0, 6.3 Hz), 2.42 (2H, dd, J = 15.0, 10.9 Hz), 2.71 (2H, ddd, J = 10.9, 9.9, 6.3 Hz), 3.87 (6H, s), 3.89 (12H, s), 4.97 (2H, d, J = 9.9 Hz), 6.56 (4H, s); EIMS *m/z* (relative intensity) 502 (M^+, 100), 306 [$(M - (MeO)_3C_6H_3CHO)^+$, 9]. Anal. Calcd for $C_{26}H_{30}O_{10}$: C, 62.14; H, 6.02. Found: C, 61.88; H, 5.81.

2,7-Bis(3,4,5-trimethoxyphenyl)-3,8-dioxabicyclo[4.4.0]-decane-4,9-diol (23c). To a stirred solution of dilactone **22c** (50.3 mg, 0.1 mmol) in dry CH_2Cl_2 (16 mL) at −78 °C was added DIBAL (1.5 M, 0.33 mL, 0.5 mmol), and the mixture was stirred at that temperature for 2 h. After the solution was allowed to warm to room temperature, water (20 mL) was added. The precipitates were removed by suction filtration and washed with CH_2Cl_2 (20 mL). The filtrate was washed with water (20 mL × 2) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a solid (43.7 mg), which was recrystallized from MeOH to give **23c** (41.8 mg, 83%): mp 218–223 °C; IR 3354 cm^{-1}; EIMS *m/z* (relative intensity) 506 (M^+, 3.8), 488 [$(M - H_2O)^+$, 6.0], 470 [$(M - 2H_2O)^+$, 2.7], 274 [$(M - (MeO)_3C_6H_3CHO)^+$, 20.0], 197 [$(MeO)_3C_6H_3CHOH^+$, 64.2]. Anal. Calcd for $C_{26}H_{34}O_{10}$: C, 61.65; H, 6.77. Found: C, 61.54; H, 6.86.

3a,4,6,6a-Tetrahydro-1,4-bis(3,4,5-trimethoxyphenyl)-1*H*,3*H*-furo[3,4-*c*]furan: (±)-Yangambin (25c). A stirred solution of dilactol **23c** (25.3 mg, 0.05 mmol), yellow HgO (65 mg, 0.30 mmol), and I_2 (76 mg, 0.30 mmol) in dry CH_2Cl_2 in a Pyrex test tube was irradiated under nitrogen with a 100 W high-pressure Hg arc for 5 h at room temperature until most of **23c** was consumed (TLC analysis). Precipitates were removed by suction filtration. The filtrate was washed with 0.5% $Na_2S_2O_3$ solution (10 mL) and then water (20 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue (35.1 mg) whose ^1H NMR spectrum exhibited a signal of the OCHO proton as a singlet at δ 8.25. To the formate dissolved in MeOH (11 mL) was added $NaBH_4$ (4 mg, 0.10 mmol). After stirring at room temperature for 10 min, the solution was heated under reflux for 2 h. Evaporation of the solvent gave a residue which was dissolved in CH_2Cl_2 (10 mL), washed with water (20 mL), and dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude product (18.3 mg) which was purified by preparative TLC on silica gel (2% MeOH–CH_2Cl_2) to give a crystalline solid of (±)-yangambin (**25c**) (7.7 mg, R_f 0.5, 51% from **23c**): mp 105.8–106.0 °C; ^1H NMR (270 MHz) δ 3.11 (2H, ddd, J = 6.9, 4.3, 3.6 Hz), 3.84 (6H, s), 3.88 (12H, s), 3.94 (2H, dd, J = 9.1, 3.6 Hz), 4.31 (2H, dd, J = 9.1, 6.9 Hz), 4.75 (2H, d, J = 4.3 Hz), 6.57 (4H, s). Anal. Calcd for $C_{24}H_{30}O_8$: C, 64.56; H, 6.78. Found; C, 64.68, H, 6.78.

Supplementary Material Available: Experimental details for the preparation of **11b, 11c, 11f, 12b, 13c–16c, and 13a–16a** and ^1H NMR peak assignments of all the synthetic intermediates described in this paper (17 pages). 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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