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Concise Synthesis of Novel Oxa-Bridged Compounds

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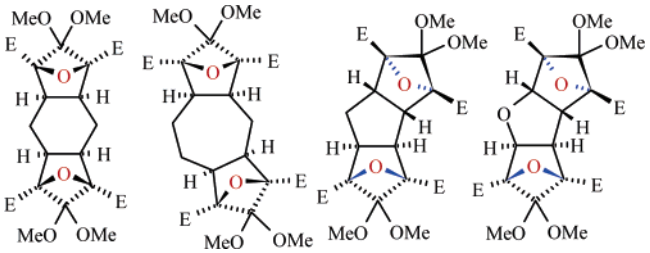

A stereoselective strategy for the replacement of the 1,2-dihaloalkene bridge of tetrahalonorbornyl derivatives by an oxygen bridge involving stepwise controlled oxidation, cleavage of the dione thus formed, and reiterative intramolecular S_N2 displacement of two bridgehead halogens is devised. The synthesis of four highly strained pentacyclic bis-oxa-bridged derivatives **10**, **27**, **28**, and **29** with interesting structural variations is presented. The two oxa bridges are syn to each other, separated by central cyclohexane and cycloheptane rings in **10** and **27**, while they are anti to each other and are separated by central cyclopentane and furan rings in **28** and **29**. In the case of the highly symmetric bis-oxa-bridged derivative **10** the two syn oxa bridges constrain the central cyclohexane ring into the boat form. The endo,anti,endo 2:1 bis adducts of 1,2,3,4-tetrahalo-5,5-dimethoxycyclopenta-1,3-diene with cyclopentadiene were prepared for the first time, while the reactivites of previously unexplored bis adducts derived from furan and cycloheptatriene were revealed.

Introduction

The rational design of strained polycylic heterocycles has been exhilarating and fascinating but, nevertheless, a difficult synthetic task to accomplish.[1] Synthesis of target molecules with unusual geometries and marvelous structural architecture and the exploration of their physicochemical properties has been one of the challenging research activities of contemporary chemists.[2] In this particular area much attention has been devoted to the synthesis of a wide class of strained polycarbocyclic caged compounds.[2,3] The tetrachloronorbornyl derivatives[4] have played a pivotal role in the synthesis of highly complex, aesthetically pleasing, unnatural molecules, such as cubane (tetraprismane),[3a] homopentaprismane,[3b,c] hexaprismane,[3d] heptaprismane,[3e] pagodane,[3f] and dodecahedrane.[3g,h] The synthesis of rigid heterocyclic caged molecules is relatively less explored[1] and is particularly interesting due to the useful properties exhibited by the heteroatoms such as oxygen, nitrogen, or sulfur as promising metal binders.

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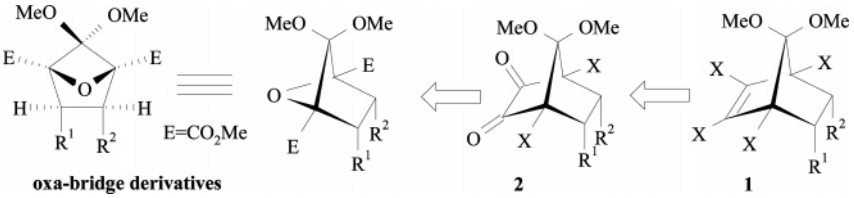
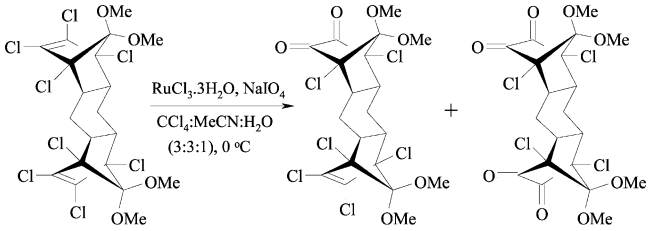
SCHEME 1. Replacement of the Dihaloalkene Bridge by an Oxygen Bridge via the Diketones



As part of an ongoing investigation on selective exploitation of halogens[5−8] of easily accessible Diels−Alder adducts of 1,2,3,4-tetrahalo-5,5-dimethoxycyclopenta-1,3-diene,[4] we developed a novel, facile, and extremely efficient method for their smooth transformation to the synthetically useful norbornyl α-diketones employing catalytic $RuCl_3 \cdot 3H_2O$ and $NaIO_4$ as a stoichiometric cooxidant.[6] The norbornyl α-diketones[8] were elaborated to obtain highly functionalized novel cyclopentane possessing bis(α-chloroester) groups[6] or potential bridged bicyclic lactones,[6,7] which are inaccessible via the existing methods. We recently reported the preliminary results on the synthesis of a highly symmetric, strained bis-oxa-bridged compound **10**[9] from a 2:1 bis adduct of 1,2,3,4-tetracholoro-5,5-dimethoxycyclopenta-1,3-diene and cyclohexa-1,4-diene, an interesting example of extracting the fullest advantage of geometric constraints on the reactivity of the molecule. Herein, we present a detailed illustration of the synthesis of the highly oxygenated derivative **10** and further elaboration of the synthetic technology of orchestration of selective utilization of the two sets of chlorines toward previously unexplored 2:1 bis adducts of 1,2,3,4-tetracholoro-5,5-dimethoxycyclopenta-1,3-diene to generate novel highly strained pentacycles. The one-pot synthesis of a highly oxygenated strained bis-oxa-bridged compound from the bis-α-diketone was generalized to other tetrahalonorbornyl derivatives, thus demonstrating that the process could be efficiently applied to replace the 1,2-dihaloalkene bridge of tetrahalonorbornyl derivatives **1** with an oxygen bridge via the diketones **2**, as depicted in Scheme 1.

Although Akhtar and co-workers[10] had observed the formation of an oxa-bridged compound during $KMnO_4$-mediated oxidation of 1,2-dichloroalkene present in the bicyclo[2.2.2] framework of a polycyclic compound possessing intramolecularly displaceable bridgehead chlorines, like in **1**, this remained an isolated example for over three decades. Further, Favorskii ring contraction of α-choloro ketones derived from hydrolysis of **1** (X = Cl) is a convenient and well-established tool for the synthesis of polycyclic caged systems.[2] Depending on the substrate structure and the reaction conditions, Haller−Bauer cleavage products were obtained as unwanted side products, which in a few cases underwent an intramolecular bridgehead chlorine displacement reaction to furnish a lactone or a different type of oxa-bridged compound with an oxa-bicyclo[2.2.1]heptane framework via a second bridgehead chlorine displacement.[11] However, in the present work, unlike the few examples reported in the literature, a general and efficient strategy to the oxa-bridged compounds in which the bridge is part of an oxa-bicyclo[2.1.1]hexane framework is described.

SCHEME 2. Ruthenium-Catalyzed Oxidation of Bis Adduct 3



	4	5
1) 9% $RuCl_3.3H_2O$; 1.6 equiv $NaIO_4$; 10 h	42%	10%
2) 11% $RuCl_3.3H_2O$; 2.2 equiv $NaIO_4$; 12 h (slow addition of substrate to $RuCl_3$+$NaIO_4$)	7%	59%
3) 11% $RuCl_3.3H_2O$; 2.2 equiv $NaIO_4$; 12 h (slow addition of $NaIO_4$ to substrate and $RuCl_3$)	14%	41%
4) 11% $RuCl_3.3H_2O$; 2.5 equiv $NaIO_4$; 12 h	—	97%
5) 0.6% Ru-LDH; 2.5 equiv $NaIO_4$; 12 h	—	96%

Results and Discussion

Synthesis of the Symmetric Bis-Oxa-Bridged Compound. Recently, we have demonstrated the versatility of the ruthenium-catalyzed oxidation by a near quantitative conversion of the bis adduct **3** to bis-α-diketone **5** (Scheme 2).[6,9] The adduct **3** was obtained from the Diels−Alder reaction between 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and 1,4-cyclohexadiene following the literature procedure.[12] After numerous surveys of different combinations of the catalysts, $RuCl_3 \cdot 3H_2O$ and cooxidant $NaIO_4$, the initially formed diketone **4** in the reaction medium was allowed to get completely converted to **5** under the reaction conditions to obtain quantitative yield (Scheme 2). When the bis adduct **3** was subjected with 9 mol % ruthenium catalyst and 1.6 equiv of $NaIO_4$ in $MeCN/CCl_4$ (1:1) at 0 °C for 10 h, a mixture of monodiketone **4** and bis-diketone **5** were obtained in a ratio of 4:1 in 52% isolated yield (Scheme 2). The major product **4** (which was isolated in 42% yield) and the minor product **5** (10%), a highly crystalline and sparingly soluble

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compound, were characterized as mono- and bis-diketones, respectively, based on ^{1}H and ^{13}C NMR analysis. The symmetrical nature of **5** was evident from a 7-line ^{13}C NMR spectrum, while compound **4** showed a 13-line ^{13}C NMR spectrum. When the substrate **3** in MeCN/CCl_4 (1:1) was added slowly over 10 h to a solution of 11% $RuCl_3$ and 2.2 equiv of $NaIO_4$ in aqueous MeCN and CCl_4 at 0 °C, a mixture of products was isolated in 66% yield with **5** as the major product (Scheme 2). On the other hand, slow addition (10 h) of an aqueous solution of 2.2 equiv of $NaIO_4$ to a mixture of substrate and 11% $RuCl_3$ also did not improve the yield. In both cases, catalyst deactivation after 12 h, as evidenced by the dark-green color of the solution, was observed. The best optimized condition to prepare exclusively bis-diketone **5** was found to be the addition of an aqueous solution of 11% $RuCl_3$ and 2.5 equiv of $NaIO_4$ in one portion to the substrate in MeCN/CCl_4 at 0 °C. The isolation of this yellow, highly crystalline, and sparingly soluble bis-diketone **5** was straightforward and involved the filtration of the reaction mixture through a small pad of silica gel and subsequent washing with a ca. 1:1 mixture of CH_2Cl_2 and EtOAc, to afford the bis-diketone **5** in 97% yield (Scheme 2).

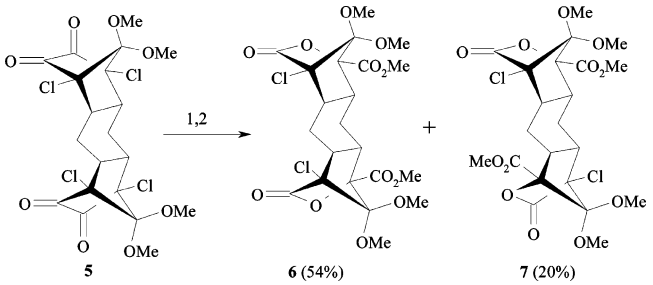
To make the process environmentally benign and inexpensive, we recently developed recyclable ruthenium-based supported catalysts employing layered double hydroxide (Ru-LDH) or MgO (Ru−MgO) as supports.[13] With the employment of just 0.6 mol % of the Ru-LDH ($RuCl_3 \cdot 3H_2O$ immobilized onto layered double hydroxide, LDH, 3.9% ruthenium loading),[13] an excellent yield of the required bis-dione **5** was obtained (entry 5, Scheme 2).

Driven by the curiosity to know what would be the fate of the tetracarboxylate intermediate that would be generated under the α-dione cleavage conditions, especially because of the availability of at least two intramolecularly displaceable halides for each carboxylate, we subjected the bis-diketone **5** to cleavage reaction using alkaline H_2O_2, an efficient method we have recently demonstrated for the cleavage of other norbornyl α-diketones.[6,9] The products formed in this reaction upon subsequent treatment with diazomethane were isolated, characterized, and assigned the regioisomeric pentacyclic lactone structures **6** and **7** (Scheme 3).

A detailed analysis of the possible pathways available for the in situ generated tetracarboxylate intermediate **8** is presented in Scheme 4. Path A or A′ would lead to bridged lactones **6** and **7**, by intramolecular displacement of the halide by the carboxylate, while path B or B′ would lead to caged lactones via transannular displacement. Interestingly, both pairs of lactones (bridged and caged) have the potential to undergo one more iteration of S_N2 displacement, under basic conditions, this time utilizing the last surviving out of the initial four halides, leading either to caged compound **9** or oxa-bridged compound **10** as shown in Scheme 4.

Interestingly, our results revealed that intermediate **8** leads exclusively to a separable mixture of two bridged

SCHEME 3. Cleavage Reaction of Bis-α-diketone 5[a]



[a] (1) 30% H_2O_2, 6 N NaOH, MeOH/THF (1:1), rt, 1 h, H_3O^+; (2) CH_2N_2, Et_2O/MeOH (1:1), 0 °C.

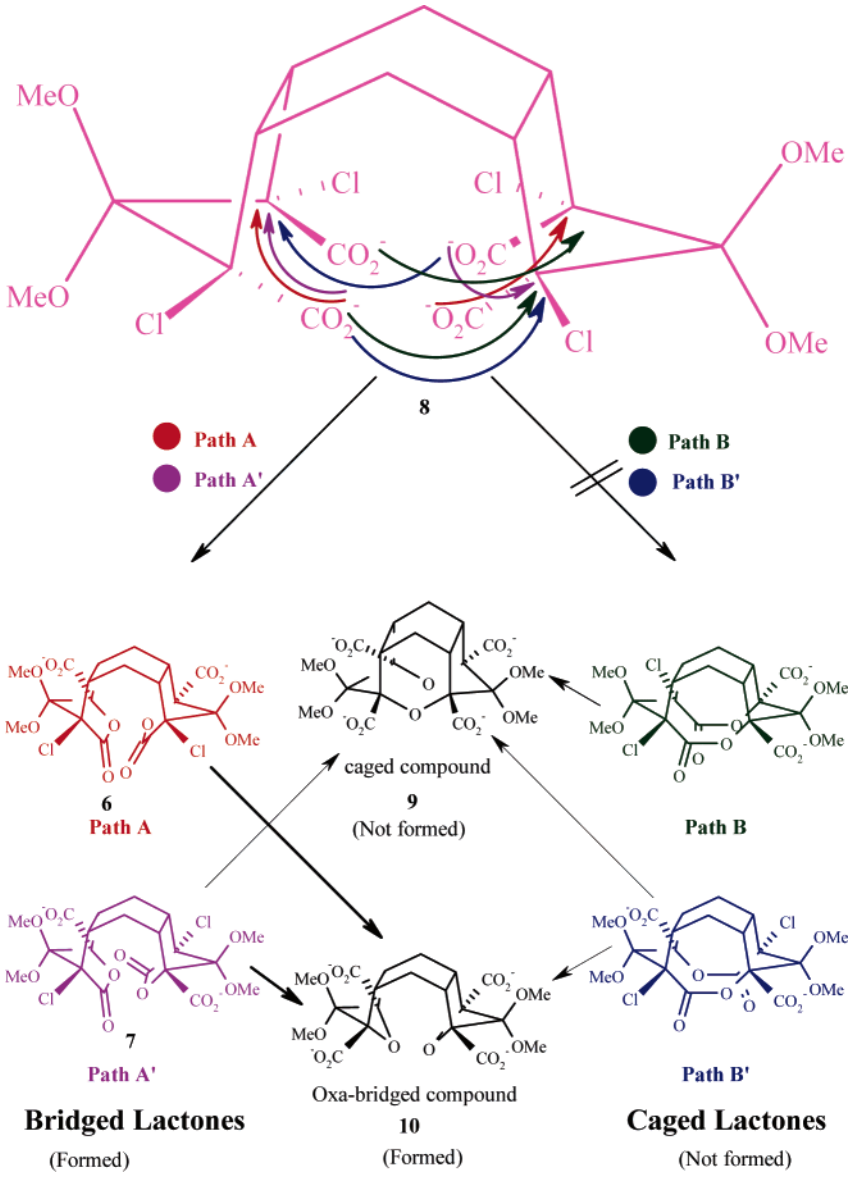
lactones (**6** + **7**) in 74% yield, (following path A or A′) in a ratio of 73:27 (Scheme 3). The peaks in the ^{1}H NMR spectra revealed that **6** is less symmetric than **7**. In the ^{13}C NMR spectra, the major compound **6** (54%) showed a 12-line spectrum, while the minor compound **7** (20%) showed an 11-line spectrum. Based on the degree of symmetry shown in the ^{13}C NMR spectra, the major compound was unambiguously assigned the *σ*-symmetric pentacyclic bis-lactone structure **6**. The minor lactone, which is more symmetric, was assigned C_2-symmetric pentacyclic bis-lactone **7**.

A careful observation of the structural morphology of the minor C_2-symmetric pentacyclic bis-lactone **7** revealed that the intermediate **11**, which would be generated upon treatment of **7** with NaOH (Scheme 5), possesses suitably disposed alkoxide moieties that are expected to undergo intramolecular face-to-face S_N2 cyclization resulting in cage compound **9**. On the other hand, a relatively strained bis-oxa-bridged compound **10** would result if the alkoxide moieties displace the respective chlorine atoms present in the same ring. To check the feasibility of this plan, the minor bridged lactone (path A′) was refluxed with NaOH in aqueous MeOH for 24 h in anticipation of the formation of caged compound **9**. However, to our surprise, the esterification of the crude product with diazomethane gave oxa-bridged derivative **10** in 52% yield via **12** (Scheme 5) through a reiterative process, which is selectively undergoing intramolecular S_N2 displacement within each cyclopentane ring as depicted in Scheme 5. It is intriguing that a reaction pathway leading to a strained oxygen-bridged compound **10** was favored over the alternative that would have led to a less-strained cage compound **9**. Both ^{1}H and ^{13}C NMR spectra of **10** reveal a highly symmetrical structure. The four ester groups appeared as a singlet at 3.80 ppm, while two sets of peaks at 3.44 and 3.31 ppm were assigned for the four OMe groups. In the ^{13}C NMR spectrum, a single peak was seen at 166.5 ppm for the carbonyl of all the ester groups. The four carbons bearing the oxygen bridge as well as the ester groups appeared at 91.6 ppm. Since it was not possible to explicitly rule out structure **9** based on ^{1}H, ^{13}C NMR, IR, or CHN, a single-crystal X-ray analysis of the product was carried out to prove the strained, but highly symmetric, structure **10** unambiguously.[6]

Further, it is clear from the proposed pathway leading to oxa-bridged compound **10** that the major bridged lactone **6** (path A, Scheme 4), which is not a suitable precursor for caged compound, could in principle furnish

(13) Khan, F. A.; Sahu, N. *J. Catal.* **2005**, *231*, 438−442. No effort has been made to recover the catalyst in the case of highly insoluble bis adducts leading to the corresponding insoluble bis-diones where a solvent system consisting of MeCN/CCl_4/H_2O (3:3:1) has been used. In all other cases where solubility is not a constraint, a MeCN/H_2O (6:1) solvent system was used, and the catalyst was recovered as well as reused.

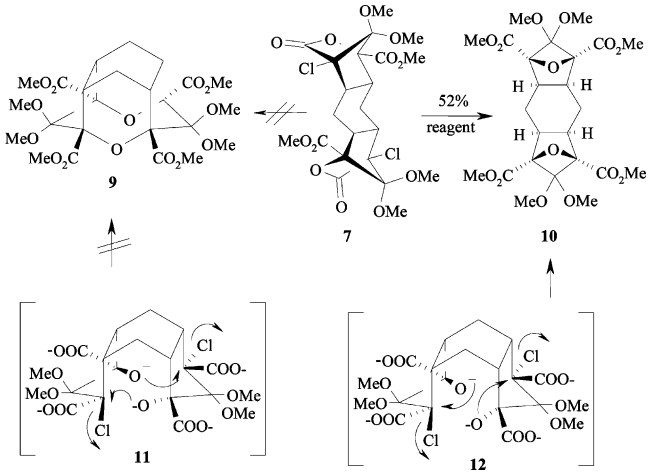
SCHEME 4. Possible Pathways of the in Situ Generated Tetracarboxylate Intermediate 8



oxa-bridged derivative **10**, thus furnishing a "chemical" proof for the structural assignment and proposed mechanism. Indeed, when **6** was subjected to aqueous alkaline conditions followed by esterification, **10** was obtained in 46% yield (Scheme 6). The entire process essentially amounts to converting two hydrocarbons, i.e., benzene and cyclopentadiene, to highly symmetric pentacyclic bis-oxa-bridged compound **10** by adding as many as 14 oxygen atoms (Scheme 6), since cyclohexadiene and 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene were prepared from benzene and cyclopentadiene, respectively.

At this point we thought of generalizing the methodology to obtain a variety of mono-oxa-bridged derivatives. The Diels–Alder adducts of cycloalkenes (five- to eight-membered) with 1,2,3,4-tetrahalo-5,5-dimethoxycyclopenta-1,3-dienes were smoothly converted to the corresponding diketones **13a–d** and **14a–c**, respectively, using our old protocol.[14] The alkaline H_2O_2 cleavage of

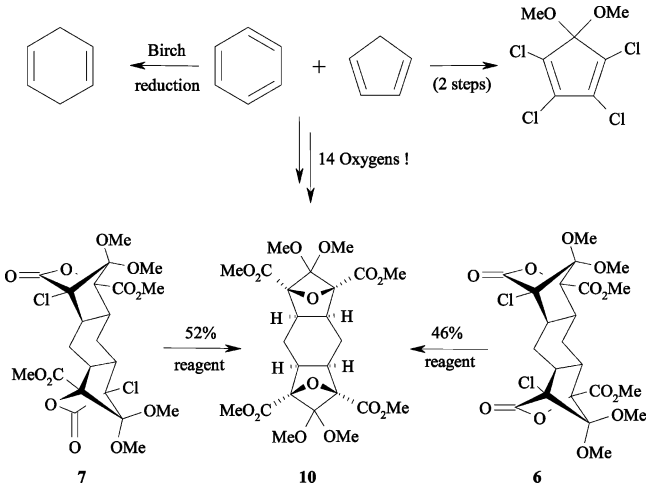
SCHEME 5. Synthesis of the Novel Bis-Oxa-Bridged Compound 10[a]



[a] Reagents: (1) aq NaOH/MeOH, 24 h reflux, H_3O^+; (2) CH_2N_2, Et_2O, 0 °C.

(14) For the old protocol, see ref 6; we currently use our new protocol (ref 13) for these transformations.

SCHEME 6. Synthesis of Bis-Oxa-Bridged Derivative 10[a]



[a] Reagents: (1) aq NaOH/MeOH, 24 h reflux, H_3O^+; (2) CH_2N_2, Et_2O, 0 °C.

SCHEME 7. Synthesis of Tricyclic Oxa-Bridged Derivatives 17a−d

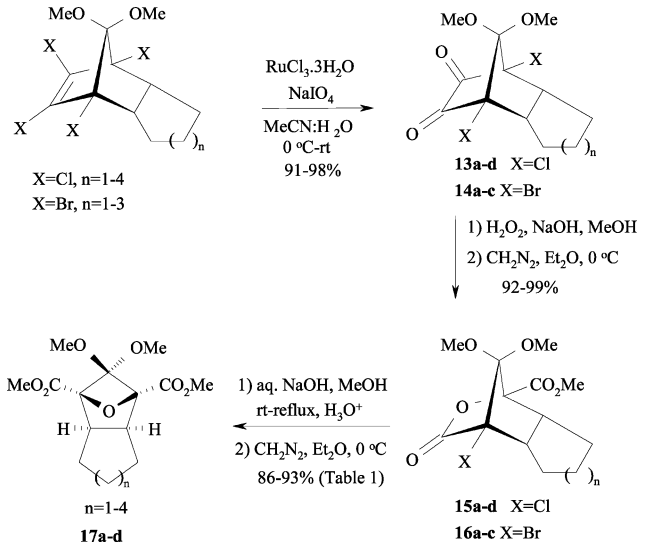
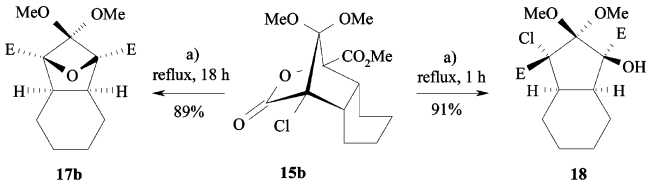


TABLE 1. Preparation of Oxa-Bridge Derivatives 17a−d from Bridged Lactones 15, 16

entry	substrate, X, *n*	temp, time	yield (%)	product
1	**15a**, Cl, 1	reflux, 16 h	86	**17a**
2	**16a**, Br, 1	rt, 28 h	88	
3	**15b**, Cl, 2	reflux, 18 h	89	**17b**
4	**16b**, Br, 2	rt, 24 h	90	
5	**15c**, Cl, 3	reflux, 18 h	88	**17c**
6	**16c**, Br, 3	rt, 24 h	93	
7	**15d**, Cl, 4	reflux, 20 h	92	**17d**

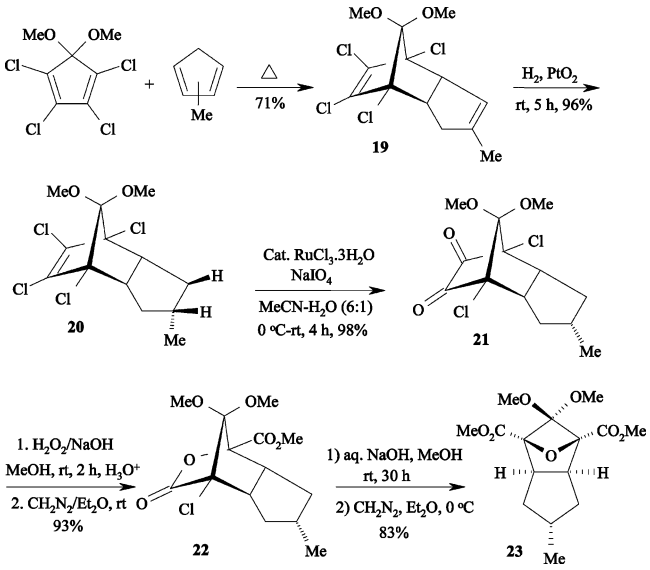
the these α-diketones furnished the tricyclic bridged lactones **15a−d** and **16a−c** (Scheme 7). When the lactone **15b** was refluxed with aqueous NaOH in MeOH for 18 h, the corresponding oxabridged derivative **17b** was formed in 89% yield (entry 3, Table 1). The methodology was generalized for a number of tricyclic lactones **15a−d** and **16a−c** employing chloro and bromo derivatives to obtain the oxa-bridged compounds **17a−d** in high yield

SCHEME 8. Synthesis of α-Hydroxy Ester Derivative 18[a]



[a] Reagents: (1) aq NaOH/MeOH, 24 h reflux, H_3O^+; (2) CH_2N_2, Et_2O, 0 °C.

SCHEME 9. Synthesis of Oxa-Bridged Derivative 23

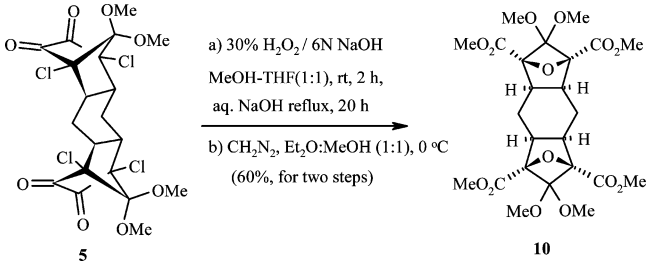


(Scheme 7, Table 1). The reaction conditions for bromo lactones **16a−c** were optimized at room temperature to furnish the corresponding oxa-bridged derivatives in excellent yields (Table 1, entries 2, 4, 6). The ^{1}H NMR spectrum of the oxa-bridged derivatives **17a−d** showed three singlets, two for OMe and one for both the methyl esters (3.81−3.82 ppm). In the ^{13}C NMR spectra of **17a−d**, a single peak at ∼167 ppm was observed for the ester carbonyl, while the oxa-bridge-bearing carbons showed a diagnostic peak in the range of 91.1−93.7 ppm.

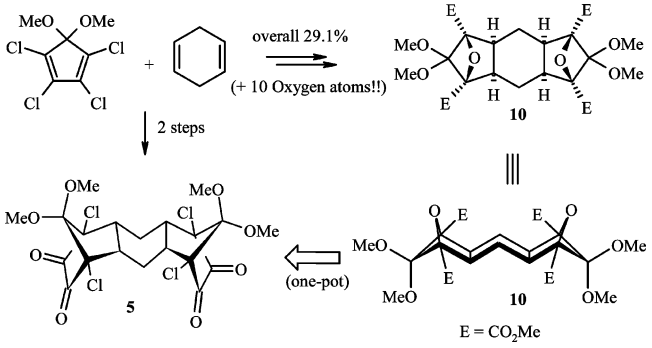
However, giving less reaction time, i.e., refluxing for 1 h, the chloro lactone **15b** was stereoselectively transformed to the α-hydroxy ester derivative **18** in 91% yield (Scheme 8). So depending on reaction time, either the α-hydroxy ester derivative or the oxa-bridged compound could be synthesized.

The oxa-bridged derivative **23** with a substituent on the cyclic dienophile part could be easily derived starting from the methyl cyclopentadiene adduct **19** (Scheme 9). We prepared the methyl cyclopentadiene adduct **19** because of our current interest to develop a quick access to diquinanes and triquinanes using this adduct employing our methodology. The adduct **19** was stirred at room temperature with catalytic PtO_2 in ethyl acetate under hydrogen atmosphere to furnish the hydrogenated product **20** in 96% yield. As anticipated, the hydrogenation took place on the sterically more open convex face. Both the carbons bearing bridgehead chlorines appeared at 78.1 ppm, and a 9-line ^{13}C NMR spectrum indicated the symmetrical nature of the product **20**. The oxa-bridge

SCHEME 10. One-Pot Synthesis of the Oxa-Bridged Compound 10



SCHEME 11. Two Syn Oxa Bridges Fixed the Cental Cyclohexane Ring into the Boat Form

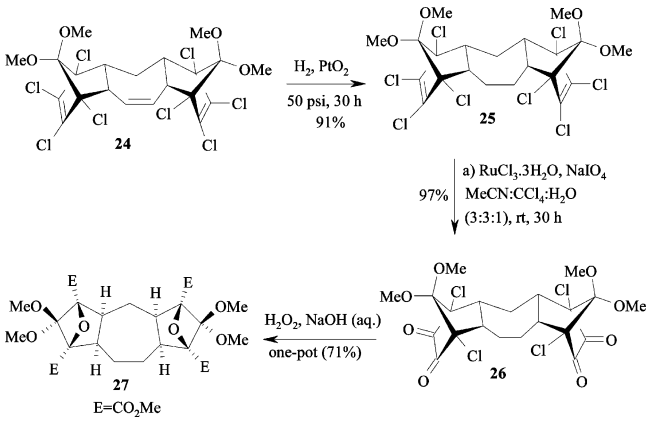


derivative **23** was prepared from the α-dione **21** via the bridged lactone **22**. The symmetrical nature of **23** was evident from a 10-line ^{13}C NMR spectrum.

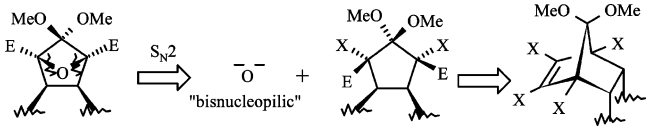
One-Pot Synthesis of Oxa-Bridged Derivatives. After successfully demonstrating the smooth transformation of bridged bicyclic lactones to the oxygen-bridged compounds, the next logical step was to develop a one-pot sequence directly from the diketone without the isolation of the intermediate bridged lactones. We started with the bis-diketone **5**, which is the precursor for both **6** and **7**. Treatment of **5** with aqueous alkaline H_2O_2 in MeOH/THF, initially at room temperature, and then at reflux temperature, followed by esterification, furnished the product **10** in 60% overall yield (Scheme 10). Thus, **10** was prepared in just three steps with an overall yield of 29.1% starting from 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and 1,4-cyclohexadiene (Scheme 11). The two syn oxa bridges in **10** constrain the central cyclohexane ring into the boat form.

The presence of hydroazulene ring systems in biologically active, synthetically challenging natural products such as dilatriol, rameswarilide, phorbol, and guanacastepene A, which stimulated the development of new methodologies,[15] also attracted our attention to study the 2:1 adduct **24** (Scheme 12). The endo,syn,endo bis adduct **24** between 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and cycloheptatriene was prepared according to the literature procedure.[16] To our knowledge, this adduct has not been used so far for any synthetic application. The adduct **24** was hydrogenated to obtain **25** which was subsequently subjected with 11 mol % of $RuCl_3 \cdot 3H_2O$, 2.5 equiv of $NaIO_4$ in 3:3:1 MeCN/CCl_4/H_2O

SCHEME 12. Synthesis of Bis-Oxa-Bridged Derivative 27 from Cycloheptatriene Bis Adduct 24



SCHEME 13. Schematic Representation of Incorporation of Formal "Bisnucleopilic" (Hypothetical) Oxygen Leading to Oxa-Bridged Derivatives



at room temperature for 30 h to furnish a near quantitative yield of yellow crystalline bis-α-diketone **26** (Scheme 12). One-pot transformation of bis-diketone **26** to bis-oxa-bridged derivative **27** was achieved in 71% yield. In the case of the highly symmetric bis-oxa-bridged derivative **10**, the four methyl ester groups appeared as a singlet at 3.80 ppm, while two singlets at 3.80 and 3.78 ppm were seen for the substrate **27** in the ^1H NMR spectrum in accordance with the reduced level of symmetry in the latter. The two sets of peaks at 3.46 and 3.30 ppm were assigned for the four OMe groups of **27**. Similarly, in the ^{13}C NMR spectrum, a single peak was observed at 166.5 ppm for all the ester groups for **10**, while the compound **27** exhibits two peaks at 166.6 and 166.4 ppm. The diagnostic four carbons bearing the oxygen bridge as well as the ester groups for **27** appeared as two sets at 92.9 and 92.1 ppm, whereas a single peak was seen at 91.6 ppm for **10**. The molecule contains a core made of a cis,syn,cis-5-7-5-ring system, and the oxygen bridges are syn to each other.

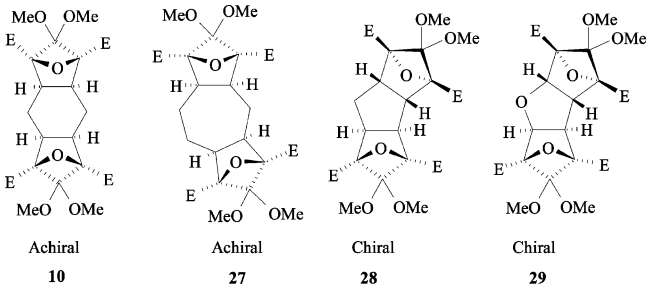
The synthetic sequence leading to oxa-bridged derivatives depicts a beautiful orchestration of selective utilization of the two sets of chlorines along with an illustration of an unprecedented example of extracting the fullest advantage of geometric constraints on the reactivity of the molecule. In contrast to all the applications known so far of tetrachloro norbornyl derivatives[4] where complete dechlorination is invariably followed, the availability of "retained" bridgehead chlorines by our method facilitates the smooth incorporation of oxa bridges in a stepwise manner through a formal "bisnucleophilic" oxygen as shown in Scheme 13. This demonstrates that the 1,2-dihaloalkene bridge of tetrahalonorbornyl derivatives is a useful surrogate for the oxygen bridge via the α-diketone.

The establishment of an elegant and stereoselective strategy to replace the 1,2-dihaloalkene bridge by the

(15) (a) Trost, B. M.; Shen, H. C. *Angew. Chem., Int. Ed.* **2001**, *40*, 2313. (b) Nguyen, T. M.; Seifert, R. J.; Mowrey, D. R.; Lee, D. *Org. Lett.* **2002**, *4*, 3959.

(16) Bratby, D. M.; Fray. G. I. *J. Chem. Soc., Perkin Trans. 1* **1972**, 195.

CHART 1. Design of Novel Molecular Scaffolds



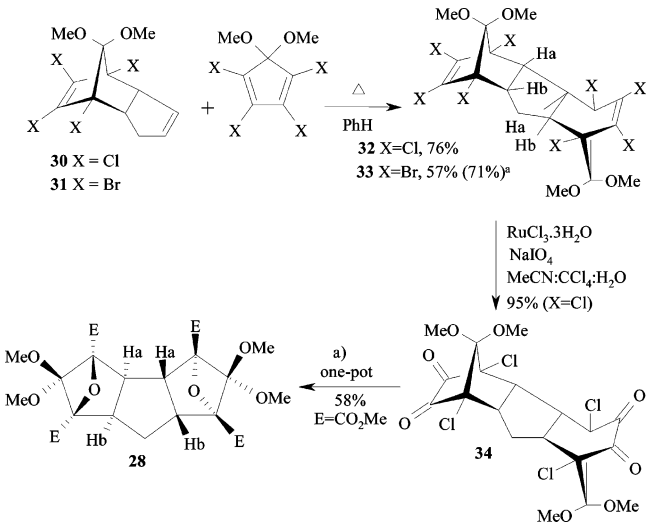
oxygen bridge encouraged us to design some rigid molecular scaffolds which could act as multifunctional molecules upon suitable elaboration (Chart 1). We could incorporate interesting variations in the structure of rigid molecular scaffolds; not only can we have highly symmetric molecules**10** and **27** with both the oxygen atoms on one side but also a "kinked structure" such as **28** with oxygen bridges on the opposite face, separated by a central cyclopentane ring. Further, replacing the methylene of the central five-membered ring by an oxygen atom would provide molecule **29**, with a perfect crown component of three oxygen atoms separated by two ethylene bridges predisposed in a well-defined structure.

The first molecule **10** is highly symmetric, thus achiral; the second molecule **27**, although not as symmetric as the first one, is, however, still achiral because of the σ-plane passing through it. The anti-oxa-bridge nature of the third and fourth molecules **28** and **29** has important consequences with regard to their structure and properties, e.g., now these molecules, although C_2-symmetric, are chiral (only one enantiomer is shown for the sake of convenience; all chiral compounds in the present study are racemic). Both the molecule possesses handedness, and we believe this will open up a newer avenue, e.g., to design chiral catalysts such as crown ethers for phase transfer catalysis, which are docked on rigid molecular scaffolds.

2:1 Adduct of 1,2,3,4-Tetrachloro-5,5-dimethoxycyclopenta-1,3-diene with Cyclopentadiene. We for the first time prepared and studied the 2:1 adduct of 1,2,3,4-tetrahalo-5,5-dimethoxycyclopenta-1,3-diene with cyclopentadiene (Scheme 14). The initially formed mono adducts **30** and **31** were further treated with 1 equiv of the corresponding 1,2,3,4-tetrahalo-5,5-dimethoxycyclopenta-1,3-diene in benzene in a sealed tube for 48 h to furnish the endo,anti,endo adducts **32** and **33**, unlike the bis adducts of the same diene with cyclohexadiene and cycloheptatriene.

In the ^{1}H NMR spectrum of adducts **32**, **33**, two singlets appeared for four OMe groups and two sets of equivalent peaks were observed for four methine protons. Two methine protons (H_a) gave a doublet at 2.99 and 3.17 ppm, the other two methine protons (H_b) showed a doublet of a doublet at 3.13 and 3.25 ppm, and the two methylene protons appeared as a triplet at 1.77 and 1.88 ppm for the chloro and bromo derivatives, respectively. Similarly in the ^{13}C NMR spectra, two sets of bridgehead carbons appeared at 77.9 and 77.1 ppm for chloro adduct **32** and at 71.4 and 71.1 ppm for bromo analogue **33**. The chloro adduct **32** was smoothly transformed to the corresponding bis-diketone **34** in 95% yield. The one-pot procedure was generalized for the pentacyclic bis-diketone **34** to achieve the strained anti-oxa-bridged derivative **28** (Scheme 14). The structures of the endo,anti,endo adducts **32**, **33** and the anti-oxa-bridged derivative **28** were unambiguously established by the X-ray crystal structure of compound **28** (Figure 1).

SCHEME 14. Synthesis of anti-Oxa-Bridged Derivative 28[a]



[a] Based on recovered starting material. Reagents: (1) H_2O_2, NaOH (aq), H_3O^+, THF/MeOH (1:1); (2) CH_2N_2, Et_2O, 0 °C.

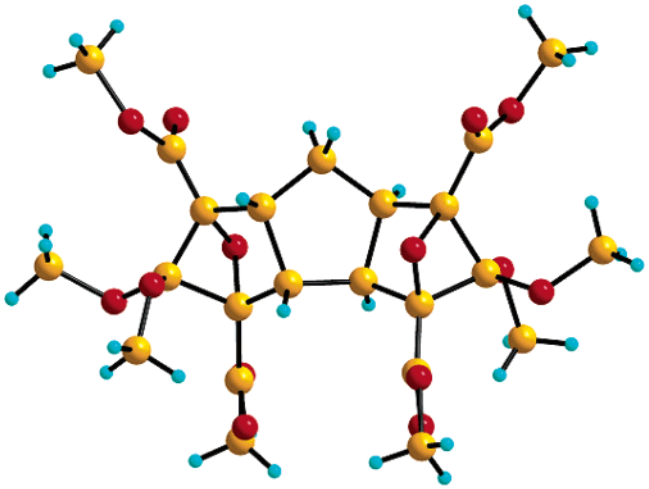


FIGURE 1. X-ray picture of anti-oxa-bridged derivative **28**: gold, carbon; red, oxygen; cyan, hydrogen.

Fascinated by the number of theoretically possible pentacyclic lactones that would be obtained from the unsymmetrical bis-diketone **34** and also the utility of the resulting endo,anti,endo pentacyclic bis-lactones as prospective building blocks for the cis:anti:cis triquinanes, the cleavage reaction of **34** was carried out. Interestingly, out of the three theoretically possible isomers **35**, **36**, and **37**, only one, i.e., **37**, was predominantly formed and isolated in 80% yield (Scheme 15).

From the extensive ^{1}H and ^{13}C NMR studies we concluded that the major lactone could be either **36** or **37**, clearly ruling out structure **35**. It was not possible, at this stage, for us to figure out which was which, i.e., whether the isolated product was **36** or **37**. Both the structures are configurationally quite alike for an easy

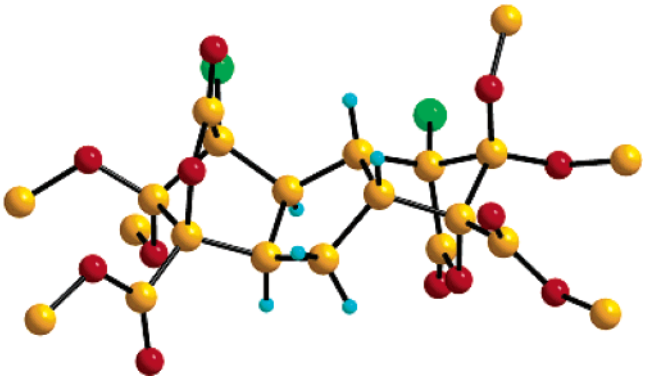
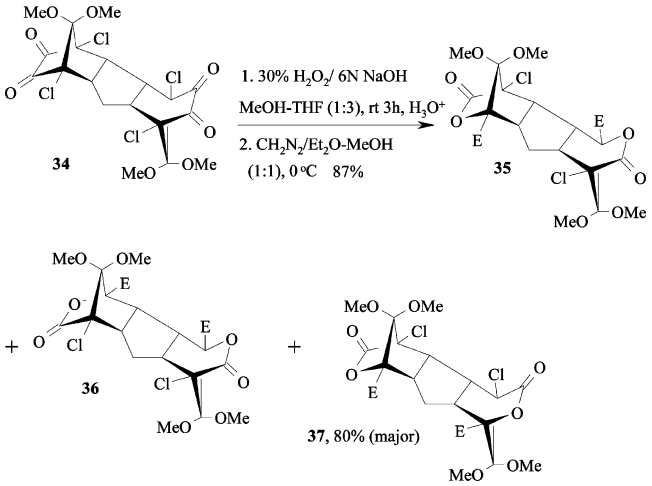


FIGURE 2. X-ray diagram of endo,anti,endo pentacyclic bis-lactone **37**. Hydrogen atoms with the exception of those on the central cyclopentane ring are excluded for clarity: gold, carbon; red, oxygen; cyan, hydrogen.

SCHEME 15. Cleavage Reaction of Bis-α-diketone 34



distinction by routine NMR; e.g., both the chlorine atoms are present on the same side as that of the carbonyl of the lactone bridge and both the ester groups are present on the same side as the oxygen of the bridged lactone, in both cases. The only difference between the two structures of **36** and **37** is the location of the methylene of the central cyclopentane ring; i.e., whether it is located on the ester side or the chlorine side. The isolated compound clearly showed lactone and ester peaks in the IR spectrum at 1800 and 1740 cm^{-1}, respectively. The compound exhibited three singlets, one at 3.83 ppm for both the ester groups, two at 3.58 and 3.69 ppm for two pairs of OMe groups in the ^1H NMR spectrum. The two sets of methine protons appeared at 3.70 ppm as a doublet of a doublet and at 2.99 ppm as a doublet. The methylene protons appeared at 1.92 ppm as a triplet. The bridgehead carbons, two bearing chlorines and the other two bearing ester groups, appeared at 75.0 and 86.3 ppm, respectively, in the ^{13}C NMR spectrum. A comparison of H_a, H_b, and H_c values of **28**, **32**, **34**, and **37** is listed in Chart 2, which suggests that the two H_a protons of **37** are more toward the chlorine side (compared with those of adduct **32**) and the two H_b's are toward the ester side (compared with those of the oxa-bridge compound **28**).

However, a single-crystal X-ray analysis was carried out to unambiguously prove the structure of the bridged

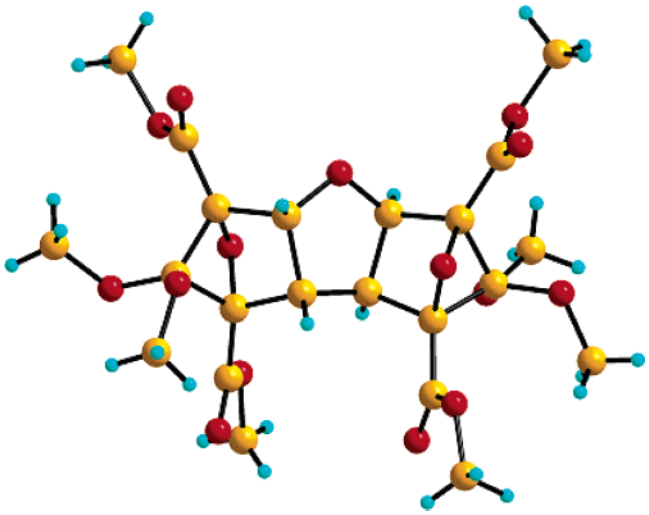
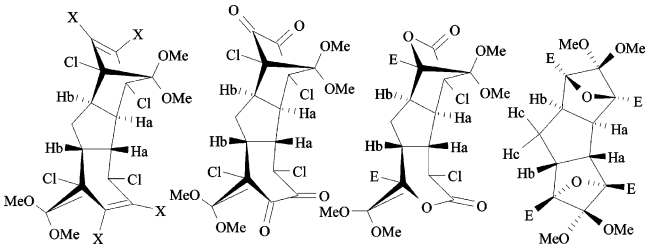


FIGURE 3. X-ray picture depicting anti-oxa-bridged derivative **29**: gold, carbon; red, oxygen; cyan, hydrogen.

CHART 2. Comparison of H_a, H_b, and H_c Values



	32	**34**	**37**	**28**
H_a	2.99	2.89	2.99	3.04
H_b	3.13	3.19	3.70	3.46
H_c	1.77	1.66	1.92	1.72

H_a, H_b, H_c values are in ppm; E=CO_2Me

lactone, which is shown in Figure 2, and which clearly indicates that the methylene of the central cyclopentane ring is on the side of esters, i.e., **37** was exclusively formed in a highly regio- and stereoselective manner. However, the crude reaction mixture of the lactones, which presumably contained traces of **36**, was treated to furnish the oxa-bridge compound **28** in 63% yield.

2:1 Adduct of 1,2,3,4-Tetrachloro-5,5-dimethoxycyclopenta-1,3-diene with Furan. We also studied the previously overlooked 2:1 adduct **38** between 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene with furan.[17] The adduct was prepared by heating a mixture of diene and furan in benzene at 130−140 °C for 48 h in a sealed tube. The oxidation of adduct **38** furnished bis-α-diketone **39** in near quantitative yield. Subjecting **39** to the one-pot reaction conditions smoothly transformed it into the novel C_2-symmetric pentacycle **29** (Scheme 16). Figure 3 presents the X-ray structure of the molecule **29**.

The anti-oxa-bridged compound **29** could function as a multifunctional molecule which possesses three important substructures as shown in Chart 3. It contains a

(17) *Chem. Abstr.* **1956**, 10013. Except mp, no spectral data and stereochemistry were known.

SCHEME 16. Synthesis of anti-Oxa-Bridged Derivative 29 from the Furan Bis Adduct 38

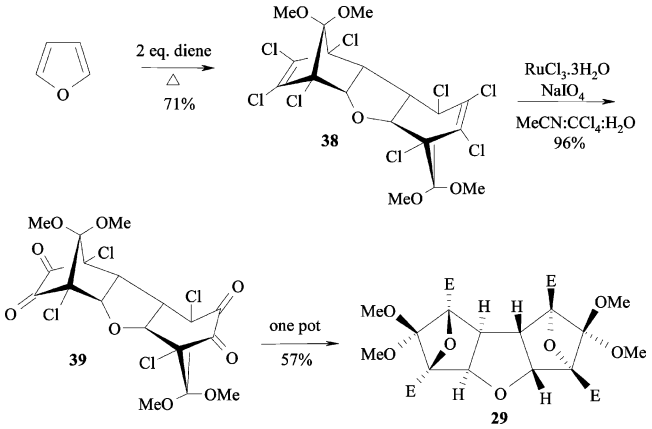
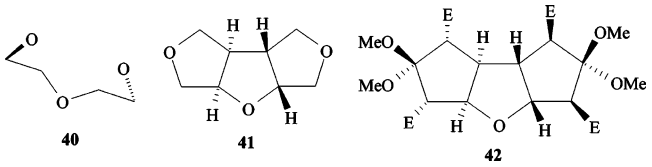


CHART 3. Substructures Embedded in anti-Oxa-Bridged Compound 29



perfect crown component **40** with three oxygen atoms separated by two ethylene bridges, and the central oxygen is equidistant to the other two oxygen atoms on opposite faces. The synthesis of structurally organized polyethers that have a preexisting disposition for strong metal ion binding continues to be the focus of much research.[18] The molecule **29** comprises a cis:anti:cis fused tris-THF core **41**. The POV ray diagram for the cis:anti:cis fused tris-THF core of **41** is shown in Figure 4. The polyethers containing five or three THF rings are known to exhibit ionophoric functions and cytotoxicities.[19] Finally, molecule **29** also includes a highly functionalized cis:anti:cis oxa-triquinane substructure **42**, which receives current interest and attention. While a number of methods have been developed for the synthesis of triquinanes, only few methods are known for oxa-triquinanes or other hetero analogues of triquinane.[20]

The anti-oxa-bridged compounds **28** and **29** exhibited two sets of singlet peaks for four methyl esters and two sets of singlets for the four OMe groups, similar to syn-oxa-bridge derivative **27**. In the ^{13}C NMR spectrum, the four diagnostic carbons bearing the oxygen bridge as well as the ester groups appeared as two sets, similar to **27** at 92.7, 90.9 ppm for **28** and 91.7, 90.9 ppm for **29**.

Dioxabicyclo[3.3.0]octane Core of Lignans. Natural lignans display a wide range of potent biological activities such as antitumor activity, platelet-activating factor (PAF) antagonists, and inhibitory effects on microsomal monooxygenase in insects.[21] The diverse array of these potentially useful characteristics make them attractive targets for synthesis.[22] The 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes (Chart 4) constitute one of the largest groups of lignans and comprise a large group of natural products exhibiting biological activities.[22] Fused bis-ethers of type **A** were found as constituents in the Chinese drug "shin-i" and in Nigerian bark extracts. The presence of bis-THF rings in naturally occurring lignans (Chart 4) encouraged us to successfully transform one of our easily accessible starting materials, the oxa-diketone **43**, to the corresponding oxygen-bridged compound **44** (Scheme 17). Once again the one-pot transformation using alkaline H_2O_2 conditions gave the optimal result. The tricyclic compound **44** was obtained in 53% yield and possess the dioxabicyclo[3.3.0]octane core of naturally occurring lignans.

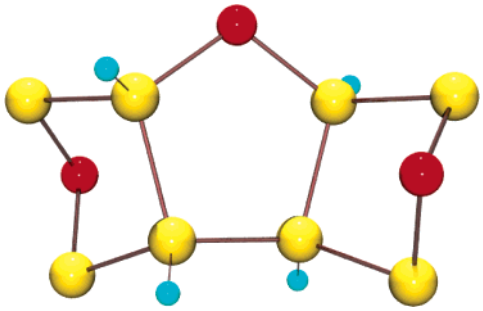
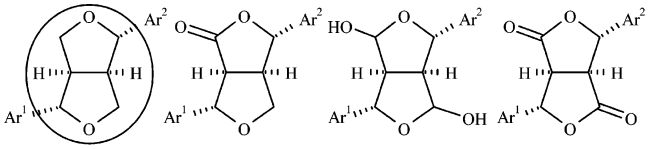
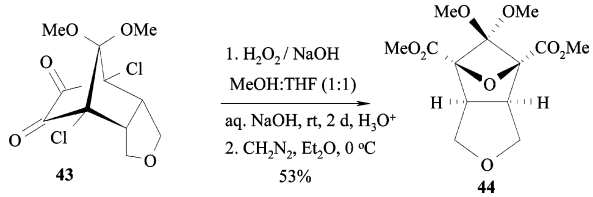


FIGURE 4. POV ray diagram for the cis:anti:cis fused tris-THF core **41** of anti-oxa-bridged compound **29**: gold, carbon; red, oxygen; cyan, hydrogen.

CHART 4. Naturally Occurring 2,6-Diaryl-3,7-dioxabicyclo[3.3.0]octane Lignans



SCHEME 17. Novel Tricycle 44 Containing a *cis*-Bis-tetrahydrofuran Core



Bridged Oxetane Derivatives from Monosubstituted α-Diketones. Further, the methodology was not restricted to only norbornyl α-diketones derived from cyclic dienophiles; bridged oxetane derivatives with any substituent pattern could be prepared. The one-pot procedure was extended to monosubstituted α-diketones **45a**,**b** to afford the oxa-bridged products **46a**,**b** (Scheme

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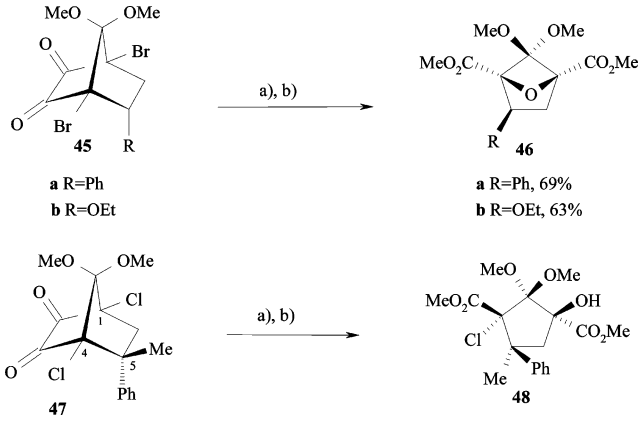
(19) (a) Morimoto, Y.; Takaishi, M.; Iwai, Toshiyuki, Kinoshita, T.; Jacobs, H. *Tetrahedron Lett.* **2002**, *43*, 5849. (b) Bellenie, B. R.; Goodman, J. M. *Tetrahedron Lett.* **2001**, *42*, 7477.

(20) (a) Singh, V.; Alam, S. Q. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2517. (b) Toyota M.; Nishikawa, Y.; Motoki, K.; Yoshida, N.; Fukumoto, K.; *Tetrahedron* **1993**, *49*, 11189.

(21) (a) Ward, R. S. *Chem. Soc. Rev.* **1982**, *11*, 75. (b) Ward, R. S. *Tetrahedron* **1990**, *46*, 5029.

(22) Pelter, A.; Ward, R. S.; Collins, P.; Venkateswarlu, R.; Kay, I. T. *J. Chem. Soc., Perkin Trans I* **1985**, 587. (b) Chan, T. H.; Brownbridge, P. *Tetrahedron Lett.* **1980**, *21*, 3427. (c) Till, C. P.; Whiting, D. A. *J. Chem. Soc., Chem. Commun.* **1984**, 590 and references therein.

SCHEME 18. One-Pot Synthesis of Oxa-Bridged Compound 46 and α-Hydroxy Ester 48[a]



[a] Reagents and conditions: (a) 30% H_2O_2/6 N NaOH, MeOH, rt 2 h aq NaOH, reflux 3 h, H_3O^+; (b) CH_2N_2, Et_2O, 0 °C, Et_2O/MeOH (1:1).

18). The only limitation appears to be for compounds with steric encumbrance in the α-position (C-5), for example, the dione **47** failed to furnish the oxa-bridged derivative. The reaction stopped at the α-hydroxy ester stage (see Scheme 8) resulting in five-membered carbocycle **48** with an α-hydroxy ester and an α-halo ester with well-defined stereochemistry (Scheme 18).

Conclusion. The 2:1 adduct of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and 1,4-cyclohexadiene was transformed to a novel bis-oxa-bridge derivative **10** by involving stepwise-controlled oxidation and intramolecular S_N2 displacements, eventually adding up to as many as 10 oxygen atoms. The versatility and broad potential in further systems is revealed by the one-pot transformation of a variety of norbornyl α-diketones to the corresponding strained oxa-bridged compounds. A novel and stereoselective strategy for the replacement of the 1,2-dihaloalkene bridge of tetrahalonorbornyl derivatives by an oxygen bridge is developed. The methodology was successfully extended not only to norbornyl α-diketones derived from cyclic dienophiles but also to the synthesis of the bridged oxetane derivatives with any substituent pattern. The fused bis-ether motif found in naturally occurring lignans was efficiently synthesized. The endo,anti,endo 2:1 bis adducts of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene with cyclopentadiene and furan could serve as prospective building blocks for cis:anti:cis triquinanes and oxatriquinanes.

Experimental Section

General Information. Melting points are uncorrected. IR spectra were recorded as KBr pellets (solids) or thin films (liquids). ^1H NMR and proton-decoupled ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q =q uartet, m = multiplet; integration; coupling constant(s) in Hz; assignment). Samples for NMR were made in $CDCl_3$, and insoluble compounds were made to dissolve by adding 3−4 drops of DMSO-d_6 into the $CDCl_3$ solution. Tetramethylsilane was used as the internal standard. Column chromatography was performed using silica gel (100−200 mesh), and ethyl acetate/hexane was used as eluant. Acetonitrile and CCl_4 were distilled over P_2O_5. Distilled water was used for the reactions.

General Procedure for the Synthesis of α-Diketones. To a vigorously stirred solution of the substrate (0.5 mmol) in acetonitrile (6 mL) at 0−5 °C (ice−water bath) was added a solution of $RuCl_3 \cdot 3H_2O$ (0.035 mmol) and $NaIO_4$ (0.75 mmol) in water (1 mL). The mixture was stirred for the specified time and continuously monitored by TLC. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (15 mL). Concentration of the filtrate followed by silica gel column chromatography gave the pure yellow-colored diketones.

General Procedure for the Cleavage of α-Diketones. To a stirred solution of diketone (1 mmol) in methanol (5 mL) was added 30% H_2O_2 (0.75 mL) followed by slow addition of 6 N NaOH solution (0.3 mL). After stirring at room temperature (∼20 °C) for 1−3 h, 5% HCl (10 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether/methanol (1:1) at 0 °C. After quenching the excess diazomethane with acetic acid, the solution was concentrated, and silica gel column chromatography afforded the pure products.

Preparation of Bis-α-diketone 5: **A. General Procedure.** The bis adduct **3** (57 mg, 0.093 mmol) was subjected to the ruthenium-catalyzed oxidation conditions, where 9% $RuCl_3$ (2 mg, 0.0083 mmol) and 1.6 equiv of $NaIO_4$ (32 mg, 0.15 mmol) in 0.2 mL of water was added to the substrate in 2 mL of MeCN/CCl_4 (1:1) at 0 °C. The mixture was stirred for 10 h and continuously monitored by TLC. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (30 mL). Concentration of the filtrate followed by silica gel column chromatography furnishes mono-α-diketone **4** (24 mg, 42%) and bis-diketone **5** (5 mg, 10%).

B. Slow Addition of the Substrate to the Reagent System. With the assumption that slow addition of the substrate to the increasing amount of the reagent system would improve the yield of **5**, a solution of the substrate **3** (45 mg, 0.074 mmol) in 2 mL of MeCN/CCl_4 (1:1) was added slowly (10 h) to a solution of 11% $RuCl_3$ (2 mg, 0.0083 mmol) and 2.2 equiv of $NaIO_4$ (36 mg, 0.167 mmol) in 0.25 mL of water at 0 °C. After 12 h the catalyst got deactivated, which was evident from the dark-green color of the solution, and two products were isolated in 66% overall yield. The bis-diketone **5** was the major product isolated in 59% yield (23 mg), while the mono-diketone **4** was isolated in 7% yield (3 mg).

C. Increasing the Catalyst. To a vigorously stirred solution of the bis adduct **3** (608 mg, 1 mmol) in acetonitrile (6 mL) and CCl_4 (6 mL) at 0 °C (ice−water bath) was added a solution of $RuCl_3 \cdot 3H_2O$ (29 mg, 0.11 mmol) and $NaIO_4$ (535 mg, 2.5 mmol) in water (2 mL). The mixture was stirred for 12 h and continuously monitored by TLC. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with CH_2Cl_2 and ethyl acetate (40 mL, 1:1). Concentration of the filtrate followed by washing the resulting yellow crystalline product in hexane (10 mL) gave the pure bis-diketone **5** (512 mg, 97%).

Mono-α-diketone 4. Yield, 42%; yellow crystals (dichloromethane/hexane); mp 210−212 °C; ^1H NMR δ 3.73 (s, 3H), 3.57 (s, 3H), 3.56 (s, 3H), 3.52 (s, 3H), 2.77 (m, 2H), 2.58 (m, 2H), 1.94 (m, 2H), 0.35 (m, 2H); ^{13}C NMR δ 187.7, 129.2, 112.3, 102.5, 79.4, 77.8, 52.8 (2C's), 52.1, 51.6, 45.6, 41.7, 18.6 (CH_2); IR (KBr) 2900, 1790, 1760, 1600 cm^{-1}. Anal. Calcd. for $C_{20}H_{20}Cl_6O_6$: C, 42.21; H, 3.54. Found: C, 42.04; H, 3.54.

Bis-α-diketone 5. Yield, 97%; yellow crystals; mp 308−310 °C (dec); ^1H NMR ($CDCl_3$/ DMSO-d_6, 1:1) δ 3.08 (s, 6H), 2.89 (s, 6H), 2.33 (m, 4H), 1.21 (m, 2H), −0.4 (m, 2H); ^{13}C NMR δ 187.2, 101.7, 78.8, 52.1, 51.6, 40.4, 18.0; IR (KBr) 2900, 1790, 1760 cm^{-1}. Anal. Calcd. for $C_{20}H_{20}Cl_4O_8$: C, 45.31; H, 3.80. Found: C, 45.88; H, 3.80.

Cleavage Reaction of Bis-α-diketone 5. To a stirred solution of diketone (90 mg, 0.17 mmol) in THF (2 mL) and methanol (2 mL) was added 30% H_2O_2 (0.22 mL) followed by slow addition of 6 N NaOH solution (0.1 mL). After stirring at room temperature (~20 °C) for 1 h, 5% HCl (2 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether/methanol (1:1) at 0 °C. After quenching the excess diazomethane with acetic acid, the solution was concentrated, and silica gel column chromatography afforded the pure products **6** and **7** in the specified yields given below (Scheme 3).

***σ*-Symmetric Pentacyclic Bis-lactone 6.** Yield, 54%; colorless solid; mp 256−258 °C; ^{1}H NMR δ 3.86 (s, 6H), 3.61 (s, 6H), 3.38 (s, 6H), 3.14 (ddd, 2H, J = 13.4, 10.9, 4.9 Hz), 2.62 (ddd, 2H, J = 14.1, 10.5, 4.9 Hz), 2.06 (td, 1H, J = 13.4, 4.9 Hz), 1.45 (m, 1H), 1.30 (td, 1H, J = 13.2, 4.9 Hz), 0.70 (m, 1H); ^{13}C NMR δ 166.5 (2C), 165.6 (2C), 108.6 (2C), 86.3 (2C), 75.5 (2C), 53.4 (2C), 51.9 (2C), 51.8 (2C), 40.9 (2C), 39.5 (2C), 19.8, 15.3; IR (KBr): 2900, 1800, 1730 cm^{-1}. Anal. Calcd. for $C_{22}H_{26}Cl_2O_{12}$: C, 47.75; H, 4.73. Found: C, 47.87; H, 4.54.

***C*$_2$-Symmetric Pentacyclic Bis-lactone 7.** Yield, 20%; colorless solid; mp 314−318 °C; ^{1}H NMR δ 3.86 (s, 6H), 3.61 (s, 6H), 3.39 (s, 6H), 3.15−3.08 (m, 2H), 2.68−2.61 (m, 2H), 1.71−1.66 (m, 2H), 1.12−1.02 (m, 2H); ^{13}C NMR δ 166.9, 165.5, 108.7, 86.4, 75.7, 53.4, 51.9, 51.8, 40.8, 39.7, 17.5; IR (KBr) 2900, 1800, 1720 cm^{-1}. Anal. Calcd. for $C_{22}H_{26}Cl_2O_{12}$: C, 47.75; H, 4.73. Found: C, 47.52; H, 4.46.

Bis-Oxa-Bridged Compound 10. To a solution of the minor bis-lactone **7** (15 mg, 0.027 mmol) in MeOH (0.5 mL) was added a solution of NaOH (108 mg, 2.7 mmol) in H_2O (1 mL). The mixture was refluxed for 24 h. Then, 5% HCl (10 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether/methanol (1:1) at 0 °C. After quenching the excess diazomethane with acetic acid, the solution was concentrated, and silica gel column chromatography (50% ethyl acetate/hexane) afforded the pure product. Yield, 52%; colorless flakes; mp 250 °C; ^{1}H NMR δ 3.80 (s, 12H), 3.43 (s, 6H), 3.31 (s, 6H), 2.76−2.73 (m, 4H), 1.44−1.36 (m, 4H); ^{13}C NMR δ 166.5 (4C), 110.2 (2C), 91.6 (4C), 52.6 (4C), 52.0 (2C), 51.7 (2C), 40.1 (4C), 16.8 (2C); IR (KBr) 2900, 1730, 1420 cm^{-1}. Anal. Calcd. for $C_{24}H_{32}O_{14}$: C, 52.94; H, 5.92. Found: C, 52.85; H, 5.89.

A similar experiment was performed with the pentacyclic lactone **6** (38 mg, 0.069 mmol) using aqueous NaOH (3.75 mmol, 150 mg in 1 mL of water) in 3 mL of MeOH to achieve this highly strained molecule **10** (17.6 mg) in 46% yield in two steps (Scheme 6).

Diketone 13a. Yield, 98%; yellow solid; mp 88−89 °C; ^{1}H NMR δ 3.74 (s, 3H), 3.54 (s, 3H), 3.25−3.24 (m, 2H), 1.75−1.68 (m, 3H), 1.58−1.53 (m, 2H), 1.17−1.08 (m, 1H); ^{13}C NMR δ 189.0 (2C), 104.3, 80.1 (2C), 52.5, 52.1, 50.6 (2C), 26.2, 26.1 (2C); IR (KBr) 2900, 1760, 1440, 1300, 1220 cm^{-1}. Anal. Calcd. for $C_{12}H_{14}Cl_2O_4$: C, 49.17; H, 4.81. Found: C, 49.20; H, 4.83.

Diketone 14a. Yield, 92%; yellow solid; mp 129−130 °C; ^{1}H NMR δ 3.78 (s, 3H), 3.59 (s, 3H), 3.32−3.30 (m, 2H), 1.80−1.64 (m, 3H), 1.57−1.50 (m, 2H), 1.18−1.05 (m, 1H); ^{13}C NMR δ 188.2 (2C, −C=O), 104.6, 72.7 (2C), 52.6, 52.1, 51.9 (2C), 26.4 (2C), 25.7; IR (KBr) 2900, 1760, 1440, 1300, 1220 cm^{-1}. Anal. Calcd. for $C_{12}H_{14}Br_2O_4$: C, 37.73; H, 3.69. Found: C, 37.70; H, 3.67.

Diketone 13c. Yield, 97%; yellow crystals (CH_2Cl_2/hexane); mp 140−142 °C; ^{1}H NMR δ 3.74 (s, 3H), 3.56 (s, 3H), 2.87−2.79 (m, 2H), 2.05−1.89 (m, 4H), 1.83−1.80 (m, 1H), 1.18−1.03 (m, 3H), 0.88−0.79 (m, 2H); ^{13}C NMR δ 188.3 (2C), 102.0, 80.6 (2C), 52.5, 52.0, 47.8 (2C), 30.2, 28.8 (2C), 25.1 (2C); IR (KBr) 2850, 1780, 1430, 1360, 1340 cm^{-1}. Anal. Calcd. for $C_{14}H_{18}Cl_2O_4$: C, 52.35; H, 5.65. Found: C, 52.40; H, 5.67.

Diketone 14c. Yield, 91%; yellow crystals (CH_2Cl_2/hexane); mp 170−172 °C; ^{1}H NMR δ 3.79 (s, 3H), 3.60 (s, 3H), 2.87−2.79 (m, 2H), 2.05−1.96 (m, 4H), 1.81−1.78 (m, 1H), 1.18−1.05 (m, 3H), 0.90−0.79 (m, 2H); ^{13}C NMR δ 187.6 (2C), 102.2, 74.4 (2C), 52.8, 52.2, 49.0 (2C), 30.1, 28.9 (2C), 25.7 (2C); IR (KBr) 2900, 1780, 1440, 1300, 1280, 1200 cm^{-1}. Anal. Calcd. for $C_{14}H_{18}Br_2O_4$: C, 41.00; H, 4.42. Found: C, 41.04; H, 4.40.

Tricyclic Lactone 15a. Yield, 95%; colorless solid; ^{1}H NMR δ 3.77 (s, 3H), 3.52 (s, 3H), 3.43−3.33 (m, 1H), 3.27 (s, 3H), 3.03−2.97 (m, 1H), 1.74−1.65 (m, 1H), 1.63−1.53 (m, 4H), 1.51−1.45 (m, 1H); ^{13}C NMR δ 168.1, 166.0, 111.4, 86.4, 75.6, 53.0, 51.46, 51.41, 48.3, 48.0, 26.5, 25.9, 24.8; IR (KBr) 2900, 1800, 1730, 1460 cm^{-1}. Anal. Calcd. for $C_{13}H_{17}ClO_6$: C, 51.24; H, 5.62. Found: C, 51.27; H, 5.64.

Tricyclic Lactone 16a. Yield, 98%; colorless solid; mp 120−122 °C; ^{1}H NMR δ 3.87 (s, 3H), 3.65 (s, 3H), 3.50−3.48 (m, 1H), 3.38 (s, 3H), 3.18−3.12 (m, 1H), 1.83−1.54 (m, 6H); ^{13}C NMR δ 168.0, 166.3, 111.8, 86.8, 67.7, 53.1, 51.7, 51.5, 49.3, 49.0, 26.5, 26.4, 24.9; IR (KBr) 2900, 1800, 1730, 1460 cm^{-1}. Anal. Calcd. for $C_{13}H_{17}BrO_6$: C, 44.72; H, 4.91. Found: C, 44.75; H, 4.94.

Tricyclic Lactone 15b. Yield, 92%; colorless solid (dichloromethane/hexane); mp 135−136 °C; ^{1}H NMR δ 3.80 (s, 3H), 3.61 (s, 3H), 3.33 (s, 3H), 3.03−2.96 (m, 1H), 2.57−2.50 (m, 1H), 1.70−1.63 (m, 3H), 1.41−1.27 (m, 4H), 1.12−1.02 (m, 1H); ^{13}C NMR δ 168.0, 166.0, 108.5, 87.0, 76.5, 53.0, 51.7, 51.6, 42.1, 40.6, 18.9, 18.3, 18.2, 16.4; IR (KBr) 2900, 1800, 1740, 1440, 1150 cm $^{-1}$. Anal. Calcd for $C_{14}H_{19}ClO_6$: C, 52.75; H, 6.01. Found: C, 52.99; H, 5.97.

Tricyclic Lactone 16b. Yield, 99%; colorless solid; mp 120−121 °C; ^{1}H NMR δ 3.86 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H), 3.09−3.02 (m, 1H), 2.61 (ddd, 1H, J = 13.1, 11.0, 5.4 Hz), 1.76−1.70 (m, 3H), 1.48−1.34 (m, 4H), 1.17−1.07 (m, 1H); ^{13}C NMR δ 167.8, 166.1, 108.6, 87.2, 68.7, 53.1, 51.8, 51.5, 43.1, 41.4, 19.3, 18.4, 18.3, 16.5; IR (KBr) 2850, 1780, 1740, 1420, 1300 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}BrO_6$: C, 46.30; H, 5.27. Found: C, 46.21; H, 5.46.

Tricyclic Lactone 15c. Yield, 92%; colorless solid; mp 124 °C; ^{1}H NMR δ 3.86 (s, 3H), 3.63 (s, 3H), 3.37 (s, 3H), 3.15 (ddd, 1H, J = 12.7, 10.9, 3.8 Hz), 2.70−2.63 (m, 1H), 2.02−1.95 (m, 3H), 1.83−1.82 (m, 1H), 1.53−1.40 (m, 2H), 1.22−1.01 (m, 4H); ^{13}C NMR δ 167.7, 166.1, 108.4, 87.8, 76.8, 53.1, 51.61, 51.55, 47.6, 46.2, 30.6, 28.7 (2C), 25.4, 24.7; IR (KBr) 2900, 1800, 1740, 1420, 1300, 1200 cm^{-1}. Anal. Calcd. for $C_{15}H_{21}ClO_6$: C, 54.14; H, 6.36. Found: C, 54.19; H, 6.39.

Tricyclic Lactone 16c. Yield, 97%; colorless solid; mp 138−140 °C; ^{1}H NMR δ 3.86 (s, 3H), 3.67 (s, 3H), 3.37 (s, 3H), 3.16 (ddd, 1H, J = 12.3, 10.6, 3.5 Hz), 2.68 (dt, 1H, J = 11.8, 2.4 Hz), 2.04−1.95 (m, 3H), 1.83−1.81 (m, 1H), 1.57−1.40 (m, 2H), 1.25−1.04 (m, 4H); ^{13}C NMR δ 167.5, 166.2, 108.4, 88.2, 69.7, 53.1, 51.61, 51.58, 48.3, 46.8, 30.5, 28.8 (2C), 26.1, 24.7; IR (KBr) 2900, 1800, 1740, 1430, 1300, 1190 cm^{-1}. Anal. Calcd. for $C_{15}H_{21}BrO_6$: C, 47.76; H, 5.61. Found: C, 47.80; H, 5.64.

Tricyclic Lactone 15d. Yield, 19%; colorless solid; mp 86−87 °C; ^{1}H NMR δ 3.87 (s, 3H), 3.63 (s, 3H), 3.36 (s, 3H), 3.00 (t, 1H, J = 10.5 Hz), 2.50 (t, 1H, J = 10.5 Hz), 1.88−1.84 (m, 1H), 1.72−1.53 (m, 3H), 1.42−1.25 (m, 8H); ^{13}C NMR δ 167.6, 166.3, 107.5, 88.8, 77.2, 53.2, 51.7, 51.6, 45.8, 45.5, 29.9, 29.85, 25.7, 25.6, 22.7, 21.8; IR (KBr) 2800, 1780, 1720, 1420, 1160 cm^{-1}. Anal. Calcd. for $C_{16}H_{23}ClO_6$: C, 55.41; H, 6.68. Found: C, 55.47; H, 6.72.

General Procedure for the Preparation of Oxa-Bridged Derivatives 17a−d from Bridged Lactones 15a−d and 16a−c. To a solution of the lactones (0.2 mmol) in MeOH (2 mL) was added a solution of NaOH (6 mmol) in H_2O (1 mL). The mixture was refluxed for the specified time. Then, 5% HCl (10 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate

layer was treated with excess diazomethane in ether/methanol (1:1) at 0 °C. After quenching the excess diazomethane with acetic acid, the solution was concentrated, and silica gel column chromatography (ethyl acetate−hexane) afforded the pure product.

Oxa-bridged Derivarive 17a. Yield, 88%; colorless solid; mp 48−50 °C (dec); ^{1}H NMR δ 3.78 (s, 6H), 3.40 (s, 3H), 3.28 (s, 3H), 3.09 (br s, 2H), 1.79−1.78 (m, 1H), 1.70 (m, 2H), 1.48−1.37 (m, 1H), 1.29 (m, 2H); ^{13}C NMR δ 167.0 (2C), 113.9, 91.1 (2C), 52.3 (2C), 51.7, 51.6, 49.0 (2C), 28.5, 25.8 (2C); IR (KBr) 2900, 1720, 1440 cm^{-1}. Anal. Calcd. for $C_{14}H_{20}O_7$: C, 55.99; H, 6.71. Found: C, 55.53; H, 6.78.

Oxa-bridged Derivarive 17b. Yield, 90%; colorless solid; mp 58−60 °C (dec); ^{1}H NMR δ 3.81 (s, 6H), 3.46 (s, 3H), 3.33 (s, 3H), 2.72−2.70 (m, 2H), 1.69 (m, 2H), 1.40−1.36 (m, 6H); ^{13}C NMR δ 167.0 (2C), 110.2, 92.2 (2C), 52.3 (2C), 51.9, 51.6, 41.7 (2C), 17.9 (2C), 17.6 (2C); IR (KBr) 2850, 1700, 1430 cm^{-1}. Anal. Calcd. for $C_{15}H_{22}O_7$: C, 57.32; H, 7.05. Found: C, 57.53; H, 7.14.

Oxa-bridged Derivarive 17c. Yield, 93%; colorless solid; mp 98−100 °C; ^{1}H NMR δ 3.81 (s, 6H), 3.47 (s, 3H), 3.32 (s, 3H), 2.84−2.81 (m, 2H), 1.93 (br s, 2H), 1.80−1.73 (m, 1H), 1.60−1.45 (m, 4H), 1.22−1.18 (m, 3H); ^{13}C NMR δ 166.9 (2C), 110.3, 92.5 (2C), 52.2 (2C), 51.7, 51.6, 47.9 (2C), 31.0, 28.9 (2C), 25.8 (2C); IR (KBr) 2850, 1700, 1430 cm^{-1}. Anal. Calcd. for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.56; H, 7.40.

Oxa-bridged Derivarive 17d. Refluxing the bicyclic lactone **15d** (96 mg, 0.28 mmol) with NaOH (331 mg, 8.28 mmol in 1 mL water) in MeOH for 20 h and treatment of the resulting crude carboxylic acid in CH_2N_2, as described above, furnished the oxa-bridged compound **17d** (87 mg). Yield, 92%; colorless solid; mp 119−121 °C; ^{1}H NMR δ 3.82 (s, 6H), 3.48 (s, 3H), 3.30 (s, 3H), 2.69−2.67 (m, 2H), 1.72−1.62 (m, 4H), 1.45−1.34 (m, 8H); ^{13}C NMR δ 167.2 (2C), 109.5, 93.7 (2C), 52.3 (2C), 51.9, 51.7 (2C), 46.7 (2C), 29.8 (2C), 25.9 (2C), 23.2 (2C); IR (KBr) 2850, 1710, 1430, 1100 cm^{-1}. Anal. Calcd. for $C_{17}H_{26}O_7$: C, 59.64; H, 7.66. Found: C, 59.73; H, 7.51.

α-Hydroxy Ester Derivative 18. Yield, 91% (75% conversion); colorless solid; mp 68−69 °C; ^{1}H NMR δ 3.83 (s, 3H), 3.79 (s, 3H), 3.77 (br s, 1H, OH, D_2O exchangeable), 3.53 (s, 3H), 3.49 (s, 3H), 3.36 (m, 1H), 2.24−2.36 (m, 1H), 1.93−1.90 (m, 1H), 1.76−1.60 (m, 4H), 1.49−1.39 (m, 2H), 1.17−1.08 (m, 1H); ^{13}C NMR δ 175.4, 168.3, 112.3, 90.5, 79.3, 53.8, 53.6, 53.1, 52.8, 51.5, 37.8, 24.8, 23.4, 22.7; IR (KBr) 3400, 2800, 1700, 1420, 1200 cm^{-1}. Anal. Calcd. for $C_{15}H_{23}ClO_7$: C, 51.36; H, 6.61. Found: C, 51.22; H, 6.25.

Methyl Cyclopentadiene Adduct 19. To a stirred solution of 6.24 g of freshly cracked methyl cyclopentadiene was slowly added a mixture of 7 g of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and a catalytic hudroquinone in 4 mL of toluene at room temperature. After 1 h of stirring at room temperature, the mixture was then refluxed for 1 h (until the completion of the starting material). The toluene and excess methyl cyclopentadiene were distilled off under reduced pressur,e and the residue was subjected to silica gel column chromatography with 20:1 hexane/EtOAc which furnished the adduct **19** (6.35 g, 71%). Yield, 71%; colorless solid; mp 96 °C; ^{1}H NMR δ 5.17 (s, 1H), 3.63−3.61 (m, 1H), 3.60 (s, 3H), 3.54 (s, 3H), 3.22 (dt, 1H, J = 9.0, 3.4 Hz), 2.30 (d of 1/2 of AB quartet, 1H, J = 17.7, 9.5 Hz), 2.15 (1/2 of AB quartet, 1H, J = 17.7 Hz), 1.67 (s, 3H); ^{13}C NMR δ 145.6, 129.6, 127.1, 119.8, 113.5, 78.5, 78.0, 61.2, 52.4, 51.5, 49.4, 35.9, 16.7; IR (KBr) 2900, 1600, 1440 cm^{-1}. Anal. Calcd. for $C_{13}H_{14}Cl_4O_2$: C, 45.38; H, 4.10. Found: C, 45.45; H, 4.04.

Tetrachloro Derivative 20. A mixture of the adduct **19** (550 mg, 1.59 mmol) and PtO_2 (4 mg) was stirred under an atmosphere of hydrogen (a balloon) until the absorption of hydrogen ceased. Filtration of the reaction mixture through a small pad of silica gel column afforded the pure product (531 mg, 96%). Yield, 96%; colorless solid; mp 50 °C; ^{1}H NMR δ 3.58 (s, 3H), 3.54 (s, 3H), 3.09−3.02 (m, 2H), 1.94−1.84 (m, 3H), 0.96 (d, 3H, J = 5.8 Hz), 0.78−0.70 (m, 2H); ^{13}C NMR δ 129.7 (2C), 115.5, 78.1 (2C, bridgehead), 53.8 (2C), 52.4, 51.5, 36.6, 34.3 (2C), 18.9; IR (KBr) 2850, 1600, 1440 cm^1. Anal. Calcd. for $C_{13}H_{16}Cl_4O_2$: C, 45.12; H, 4.66. Found: C, 45.37; H, 4.58.

α-Diketone 21. This was prepared following the general procedure. Yield, 98%; yellow solid (directly crystallized without a column); mp 123−124 °C; ^{1}H NMR δ 3.73 (s, 3H), 3.55 (s, 3H), 3.23−3.19 (m, 2H), 2.03−1.95 (m, 3H), 0.95 (d, 3H, J = 5.8 Hz), 0.61−0.56 (m, 2H); ^{13}C NMR δ 188.9 (2C), 105.7, 79.4 (2C), 52.4, 52.0, 48.8 (2C), 36.7, 35.0 (2C), 18.2; IR (KBr) 2850, 1750, 1440, 1210 cm^{-1}. Anal. Calcd. for $C_{13}H_{16}Cl_2O_4$: C, 50.83; H, 5.25. Found: C, 50.93; H, 5.30.

Bridged Lactone 22. Yield, 93%; colorless solid; mp 124−126 °C; ^{1}H NMR δ 3.85 (s, 3H), 3.61 (s, 3H), 3.46 (q, 1H, J = 10 Hz), 3.38 (s, 3H), 3.04 (q, 1H, J = 10 Hz), 2.02−1.95 (m, 2H), 1.80−1.74 (m, 1H), 1.21−1.12 (m, 1H), 1.00 (d, 3H, J = 4.9 Hz), 0.88−0.79 (m, 1H); ^{13}C NMR δ 168.0, 166.2, 111.9, 85.6, 76.3, 53.1, 51.64, 51.61, 48.6, 47.6, 36.9, 35.2, 31.7, 18.4; IR (KBr) 2900, 1800, 1730, 1460, 1300 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}ClO_6$: C, 52.75; H, 6.01. Found: C, 52.80; H, 5.98.

Oxa-Bridged Derivative 23. Yield, 83%; ^{1}H NMR δ 3.81 (s, 6H), 3.44 (s, 3H), 3.33 (s, 3H), 3.16−3.09 (m, 2H), 1.98−1.84 (m, 1H), 1.81−1.75 (m, 2H), 1.00 (d, 3H, J = 6.4 Hz), 0.98−0.92 (m, 2H); ^{13}C NMR δ 167.2 (2C), 113.8, 90.6 (2C), 52.4 (2C), 51.9, 51.8, 49.2, 37.5, 33.7, 18.5; IR (KBr) 2850, 1700, 1430 cm^{-1}. Anal. Calcd. for $C_{15}H_{22}O_7$: C, 57.32; H, 7.05. Found: C, 57.56; H, 7.08.

Bis Adduct 24. This was prepared using the literature procedure.[16] Yield, 77%; colorless solid; mp 212 °C; ^{1}H NMR δ 5.55 (s, 2H), 3.60 (s, 6H), 3.54 (s, 6H), 3.39 (d, 2H, J = 11.2 Hz), 2.74−2.67 (m, 2H), 2.03 (dt, 1H, J = 13.1, 2.0 Hz), 0.74 (q, 1H, J = 12.8 Hz); ^{13}C NMR δ 129.2 (2C), 129.0 (2C), 125.8 (2C), 111.4 (2C), 78.7 (2C), 77.7 (2C), 52.7 (2C), 51.6 (2C), 49.1 (2C), 48.6 (2C), 20.9; IR (KBr) 2900, 1600, 1440 cm^{-1}.

Compound 25. A mixture of the bis adduct **24** (550 mg, 0.89 mmol) in dry ethyl acetate (5 mL) was shaken in a Parr hydrogenation apparatus over PtO_2 (6 mg) at a hydrogen pressure of 50 psi. for 30 h. The catalyst was filtered off, and the solvent was removed to furnish the pure product **25** (537 mg). Yield, 97%; colorless solid; mp 190−192 °C; ^{1}H NMR δ 3.58 (s, 6H), 3.53 (s, 6H), 2.77−2.69 (m, 4H), 2.05 (d, 1H, J = 13.9 Hz), 1.77−1.72 (m, 2H), 1.57−1.49 (m, 2H), 1.00−0.85 (m, 1H); ^{13}C NMR δ 129.1 (2C), 128.9 (2C), 111.4 (2C), 79.5 (2C), 79.1 (2C), 52.7 (2C), 51.6 (2C), 50.4 (2C), 46.8 (2C), 22.6 (2C), 21.3; IR (KBr) 2900, 1600, 1440 cm^{-1}. Anal. Calcd. for $C_{21}H_{22}Cl_8O_4$: C, 40.55; H, 3.57. Found: C, 40.67; H, 3.63.

Bis-α-diketone 26. To a vigorously stirred solution of the substrate **25** (311 mg, 0.5 mmol) in acetonitrile (6 mL) and CCl_4 (6 mL) at 0 °C (ice−water bath) was added a solution of $RuCl_3 \cdot 3H_2O$ (15.7 mg, 0.06 mmol) and $NaIO_4$ (299.6 mg, 1.4 mmol) in water (1 mL). The mixture was stirred for 30 h and continuously monitored by TLC. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with CH_2Cl_2 and ethyl acetate (40 mL, 1:1). Concentration of the filtrate followed by washing the resulting yellow crystalline product in hexane (10 mL) afforded the yellow crystalline bis-diketone **26** (264 mg, 97%). Yield, 97%; yellow solid; mp 260 °C; ^{1}H NMR δ 3.73 (s, 6H), 3.54 (s, 6H), 2.93−2.85 (m, 4H), 2.06−2.02 (m, 1H), 1.84−1.79 (m, 2H), 1.28−1.24 (m, 2H), 0.72−0.62 (m, 1H); ^{13}C NMR δ 187.4 (2C), 187.3 (2C), 101.6 (2C), 80.2 (2C), 79.5 (2C), 52.8 (2C), 52.1 (2C), 46.2 (2C), 42.2 (2C), 22.0 (2C), 20.7; IR (KBr) 2900, 1750, 1450 cm^{-1}. Anal. Calcd. for $C_{21}H_{22}Cl_4O_8$: C, 46.35; H, 4.08. Found: C, 46.43; H, 4.11.

Bis-Oxa-Bridged Derivative 27. Yield, 71%; colorless solid; mp 128−130 °C; ^{1}H NMR δ 3.80 (s, 6H), 3.78 (s, 6H), 3.46 (s, 6H), 3.30 (s, 6H), 2.99−2.95 (m, 4H), 1.87−1.78 (m, 2H), 1.67−1.63 (m, 2H); 1.30−1.26 (m, 2H); ^{13}C NMR δ 166.6 (2C), 166.4 (2C), 109.9 (2C), 92.9 (2C), 92.1 (2C), 52.4 (2C), 52.3 (2C), 51.8 (2C), 51.7 (2C), 46.1 (2C), 42.6 (2C), 22.9 (2C), 21.9; IR (KBr) 2900, 1720, 1420, 1220 cm^{-1}. Anal. Calcd. for $C_{25}H_{34}O_{14}$: C, 53.76; H, 6.14. Found: C, 53.88; H, 6.20.

Preparation of 2:1 Adducts 32, 33. The monoadducts **30** and **31** were further treated with 1 equiv of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene and 1,2,3,4-tetrabromo-5,5-dimethoxycyclopenta-1,3-diene, respectively, in benzene in a sealed tube for 48 h to furnish the endo,anti,endo adducts **32** and **33**.

Bis Adduct 32. Yield, 76%; colorless solid; mp 232−234 °C; ^{1}H NMR δ 3.57 (s, 6H), 3.51 (s, 6H), 3.13 (dd, 2H, J = 15.6, 7.8 Hz), 2.99 (d, 2H, J = 7.8 Hz), 1.77 (t, 2H, J = 7.8 Hz); ^{13}C NMR δ 130.0 (2C), 129.2 (2C), 114.5 (2C), 77.9 (2C), 77.1 (2C), 56.3 (2C), 54.6 (2C), 52.5 (2C), 51.6 (2C), 24.4; IR (KBr) 2900, 1600, 1420 cm^{-1}. Anal. Calcd. for $C_{19}H_{18}Cl_8O_4$: C, 38.42; H, 3.06. Found: C, 38.50; H, 3.11.

Bis Adduct 33. Yield, 71% (based on recovered starting material); colorless solid; mp 248−250 °C (dec); ^{1}H NMR δ 3.60 (s, 6H), 3.56 (s, 6H), 3.25 (dd, 2H, J = 15.5, 7.8 Hz), 3.17 (d, 2H, J = 7.8 Hz), 1.88 (t, 2H, J = 7.6 Hz); ^{13}C NMR δ 126.0 (2C), 125.2(2C), 114.5 (2C), 71.4 (2C), 71.1 (2C), 57.7 (2C), 55.8 (2C), 52.8 (2C), 51.6(2C), 24.6; IR (KBr) 2900, 1580, 1420, 1330, 1280, 1260 cm^{-1}. Anal. Calcd. for $C_{19}H_{18}Br_8O_4$: C, 24.03; H, 1.91. Found: C, 24.12; H. 1.93.

Bis-α-diketone 34. Yield, 95%; yellow solid; mp 258−260 °C; ^{1}H NMR δ 3.68 (s, 6H), 3.54 (s, 6H), 3.19 (dd, 2H, J = 16.4, 10.7 Hz), 2.89 (d, 2H, J = 10.7 Hz), 1.66 (t, 2H, J = 8.2 Hz); ^{13}C NMR δ 188.1 (2C), 187.7 (2C), 104.3 (2C), 79.2 (2C), 78.3 (2C), 52.7 (2C), 52.3 (2C), 50.5 (2C), 50.4 (2C), 25.2; IR (KBr) 2900, 1740, 1440 cm^{-1}. Anal. Calcd. for $C_{19}H_{18}Cl_4O_8$: C, 44.21; H, 3.52. Found: C, 44.33; H, 3.62.

Anti-Oxa-Bridged Derivative 28. Yield, 58%; colorless crystals (EtOAC); mp 127 °C; ^{1}H NMR δ 3.85 (s, 6H), 3.81 (s, 6H), 3.46 (dd, 2H (H_b), J = 14.2, 6.8 Hz), 3.38 (s, 6H), 3.29 (s, 6H), 3.04 (d, 2H (H_a), J = 6.6 Hz), 1.72 (t, 2H (H_c), J = 7.2 Hz); ^{13}C NMR δ 166.4 (2C), 166.2 (2C), 113.0 (2C), 92.7 (2C), 90.9 (2C), 52.9 (2C), 52.6 (2C), 52.5 (2C), 51.9 (2C), 51.8 (2C), 51.7 (2C), 26.3; IR (KBr) 2900, 1720, 1440, 1380 cm^{-1}. Anal. Calcd. for $C_{23}H_{30}O_{14}$: C, 52.08; H, 5.70. Found: C, 52.10; H, 5.72.

Pentacyclic Bis-lactone 37. To a stirred solution of diketone **35** (100 mg, 0.194 mmol) in THF (2 mL) and methanol (2 mL) was added 30% H_2O_2 (0.22 mL) followed by slow addition of 6 N NaOH solution (0.1 mL). After stirring at room temperature (∼20 °C) for 1 h, 5% HCl (2 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether/methanol (1:1) at 0 °C. After quenching the excess diazomethane with acetic acid, the solution was concentrated, and silica gel column chromatography afforded the pure product. Yield, 80%; colorless crystals (EtOAc); mp 216−218 °C; ^{1}H NMR δ 3.83 (s, 6H), 3.70 (dd, 2H, J = 16.7, 8.7 Hz), 3.58 (s, 6H), 3.37 (s, 6H), 2.99 (d, 2H, J = 11.7), 1.92 (t, 2H, J = 8.1 Hz); ^{13}C NMR δ 167.2 (2C), 165.2 (2C), 111.0 (2C), 86.3 (2C), 75.0 (2C), 53.4 (2C), 51.9 (2C), 51.8 (2C), 50.5 (2C), 49.7 (2C), 22.4; IR (KBr) 2900, 1800, 1740, 1440 cm^{-1}. Anal. Calcd. for $C_{21}H_{24}O_{12}Cl_2$: C, 46.77; H, 4.49. Found: C, 46.79; H, 4.52.

Bis Adduct 38. The 1,2,3,4-tetrachloro-5,5-dimethoxycyclopenta-1,3-diene (4 mmol, 1.056 g) was treated with 2 g of furan in 0.5 mL of benzene in a sealed tube for 48 h to furnish 846 mg of endo,anti,endo adduct **38**. The reaction mixture was a solid, which was washed with hexane to furnish the pure product. Yield, 71% (ref 17, 55%); colorless solid; mp 222−224 °C (ref 17, 243 °C); ^{1}H NMR δ 4.70 (d, 2H, J = 6.3 Hz), 3.56 (s, 6H), 3.52 (s, 6H), 3.10 (d, 2H, J = 6.3 Hz); ^{13}C NMR δ 130.1 (2C), 128.4(2C), 114.1 (2C), 93.7 (2C), 78.0 (2C), 76.0 (2C), 53.1 (2C), 52.6 (2C), 51.7 (2C); IR (KBr) 2900, 1600, 1420, 1330 cm^{-1}. Anal. Calcd. for $C_{18}H_{16}Cl_8O_5$: C, 36.28; H, 2.71. Found: C, 36.15; H, 2.63.

Bis-α-diketone 39. Yield, 96%; yellow solid; mp 245−247 °C (dec); ^{1}H NMR δ 4.61 (d, 2H, J = 8.1 Hz), 3.68 (s, 6H), 3.52 (s, 6H), 3.21 (d, 2H, J = 8.1 Hz); ^{13}C NMR δ 187.3 (2C), 183.6 (2C), 104.5 (2C), 88.9 (2C), 78.9 (2C), 76.8 (2C), 52.9 (2C), 52.4 (2C), 49.9 (2C); IR (KBr) 2900, 1760, 1440 cm^{-1}. Anal. Calcd. for $C_{18}H_{16}Cl_4O_9$: C, 41.72; H, 3.11. Found: C, 41.52; H, 3.19.

Anti-Oxa-Bridged Derivative 29. Yield, 57%; colorless crystals (EtOAC); mp 175 °C; ^{1}H NMR δ 5.28 (d, 2H, J = 5.1 Hz), 3. 87 (s, 6H), 3.84 (s, 6H), 3.37 (s, 6H), 3.30 (s, 6H), 3.19 (d, 2H, J = 5.1 Hz); ^{13}C NMR δ 165.4 (2C), 164.9 (2C), 113.6 (2C), 91.7 (2C), 90.9 (2C), 89.7 (2C), 52.8 (2C), 52.7 (2C), 51.9 (4C), 50.1 (2C); IR (KBr) 2900, 1740, 1420 cm^{-1}. Anal. Calcd. for $C_{22}H_{28}O_{15}$: C, 49.63; H, 5.30. Found: C, 49,73; H, 5.41.

Tricyclic Oxa-Bridged Derivative 44. Yield, 53%; colorless solid; mp 86−88 °C; ^{1}H NMR δ 3.96−3.93 (m, 2H), 3.84 (s, 6H), 3.54−3.47 (m, 4H), 3.46 (s, 3H), 3.35 (s, 3H); ^{13}C NMR δ 166.0 (2C), 114.9, 90.3 (2C), 67.3 (2C), 52.8 (2C), 52.0, 51.9, 50.0 (2C); IR (KBr) 2900, 1710, 1430, 1360 cm^{-1}; Anal. Calcd. for $C_{13}H_{18}O_8$: C, 51.66; H, 6.00. Found: C, 51.45; H, 6. 43.

Oxa-Bridged Derivative 46a. Yield, 69%, colorless solid; mp 98−100 °C; ^{1}H NMR δ 7.40−7.20 (m, 5H), 3.93 (dd, 1H, J = 8.5, 4.3 Hz), 3.87 (s, 3H), 3.56 (s, 3H), 3.54 (s, 3H), 3.37 (s, 3H), 2.98 (dd, 1H, J = 11.7, 8.5 Hz), 2.20 (dd, 1H, J = 11.7, 4.2 Hz); ^{13}C NMR δ 166.9, 166.1, 139.0, 128.7 (2C), 128.3 (2C), 127.3, 111.1, 93.4, 88.6, 52.6, 52.2, 52.0, 51.7, 47.4, 39.9; IR (neat) 2946, 1728, 1497, 1458, 1454 cm^{-1}. Anal. Calcd. for $C_{17}H_{20}O_7$: C, 60.71; H, 5.99. Found: C, 60.64; H, 6.03.

Oxa-Bridged Derivative 46b. Yield, 63%; colorless viscous liquid; ^{1}H NMR δ 4.55 (dd, 1H, J = 6.6, 1.2 Hz), 3.86 (s, 3H), 3.83 (s, 3H), 3.60−3.52 (m, 1H), 3.51−3.46 (m, 1H), 3.43 (s, 3H), 3.33 (s, 3H), 2.77 (dd, 1H, J = 11.7, 6.6 Hz), 1.94(dd, 1H, J = 12.0, 1.2 Hz), 1.17 (t, 3H, J = 6.8 Hz); ^{13}C NMR δ 166.4, 166.1, 111.3, 91.7, 88.7, 80.2, 65.6, 52.52, 52.48, 51.9, 51.6, 39.4, 15.1; IR (neat) 2952, 1735, 1436 cm^{-1}. Anal. Calcd. for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63. Found: C, 51.53; H, 6.54.

α-Hydroxy Ester 48. Yield, 61%; colorless solid; mp 89−90 °C; ^{1}H NMR δ 7.37−7.10 (m, 5H), 4.44 (s, 1H, D_2O exchangeable), 3.73 (s, 3H), 3.56 (s, 3H), 3.55 (s, 3H), 3.37 (d, 1H, J = 14.4 Hz), 3.31 (s, 3H), 2.85 (d, 1H, J = 14.4 Hz), 1.57 (s, 3H); ^{13}C NMR δ 171.8, 171.6, 145.4, 128.1 (2C), 126.6, 125.5 (2C), 110.7, 88.8, 85.1, 54.0, 53.41, 53.37, 52.6, 49.8, 49.3, 28.8; IR (KBr) 3400, 2950, 1700, 1600, 1420 cm^{-1}. Anal. Calcd. for $C_{18}H_{23}ClO_7$: C, 61.71; H, 6.33. Found: C, 61.80; H, 6.51.

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Supporting Information Available: Crystallographic information files (CIF) for **28**, **29**, and **37**. This material is available free of charge via the Internet at http://pubs.acs.org.

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