Attempted Generation of an Observable Ethano-Bridged (Cyclopentyl) Oxyallyl. The Pericyclic Nature of an Oxyallyl–Oxyallyl Dimerization Reaction

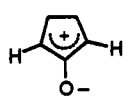
A. P. Masters, M. Parvez, T. S. Sorensen,* and F. Sun

Contribution from the Department of Chemistry, University of Calgary, Calgary, Alberta T2N 1N4, Canada

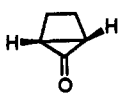
*Received November 29, 1993**

Abstract: An attempt is made to directly observe an ethano-bridged (cyclopentyl) oxyallyl using a synthetic methodolgy which employs aprotic solvents and homogeneous conditions involving a novel organometallic reagent and which can be carried out at very low temperatures. However, even with preparation temperatures of −120 °C, the 2,5-dimethylcyclopentyl oxyallyl is not observable by *in situ* NMR spectroscopy. Products corresponding to an oxyallyl + oxyallyl dimerization are observed instead. The major dimer is a *cis*-dioxane compound, and the formation of this suggests a process under pericyclic control. An analysis of the allowed molecular orbital overlaps is presented, and it is concluded that the mutual overlap involves all three terminal orbitals (overlap 2 in Figure 2), with preferential bond formation taking place between $carbon_A$–$oxygen_B$, $oxygen_A$–$carbon_B$, where A and B are the two oxyallyl monomers. The dioxane product represents only one of four possible double-connectivity ways in which two oxyallyl units can be joined (see Figure 1). The initially formed *cis*-dioxane product is quite labile and is easily transformed in a sequential and stereospecific manner into products representative of two of the other three connectivity modes. The formation of the parent cyclopentyl oxyallyl was also studied under the same reaction conditions. In this case one sees no dimeric products, but the formation of the oxyallyl is indicated because [4 + 3] diene adducts of the putative oxyallyl can be trapped, in accord with previous work in this area.

Recently, Ichimura *et al.*[1] have reported high level *ab initio* computational results on methano- and ethano-bridged oxyallyl (the four- and five-membered cyclic oxyallyls) and on the corresponding cyclopropanone structures (bicyclo[1.1.0]butan-2-one and bicyclo[2.1.0]pentan-5-one). The computations involving the ethano-bridged (cyclopentyl) system are especially interesting because the oxyallyl isomer **1**[2] is calculated to be



1



2

slightly more stable (ΔE) than the cyclopropanone **2**. By way of contrast, the methano-bridged (cyclobutyl) oxyallyl is computed to be considerably less stable than the corresponding cyclopropanone, and one can readily deduce that larger ring cyclic oxyallyls (cyclohexyl and larger[3]) will also be unstable relative to the corresponding cyclopropanone isomer; i.e., sterically these resemble simple acyclic oxyallyl systems which are known to be less stable than the cyclopropanones. Thus, the five-membered system **1** occupies an unique window of stability relative to the cyclopropanone **2**.

The tautomeric conversion (interconversion) of oxyallyls to cyclopropanones is an allowed disrotatory ring closure[4] which is predicted computationally to have a very small activation energy barrier. Therefore, for any reasonable hope of directly preparing an oxyallyl species, one requires a situation in which the oxyallyl is more stable than the cyclopropanone, and **1** *represents the simplest possible oxyallyl system in this regard.*[5]

Cyclopentyl oxyallyls have previously been proposed[7] as reactive intermediates in the photolysis of cross-conjugated dienones (a disrotatory ring closure). The emphasis in such work has focused on the rearrangement reactions of the putative oxyallyl in the presence of nucleophiles.

We have recently reported[3] a low-temperature synthetic route to cyclopropanones starting from α,α'-dibromo ketones and utilizing an organometallic reducing agent $Cr(CO)_4NO^-$, as the $(PPh_3)_2N^+(PPN^+)$ salt. The proposed mechanism of the cyclopropanone-forming reaction involves the initial *intermediacy* of an oxyallyl species, which was then postulated to rapidly ring-close to a cyclopropanone. It seemed quite possible therefore that, in the five-membered-ring systems, this oxyallyl, e.g. **1**, would be stable relative to **2** and this route would then constitute a chemical synthesis of an oxyallyl species. We even thought that a direct *in situ* NMR detection of the oxyallyl might be possible, since the reaction conditions generate the species in a reasonably inert environment, and on the basis of the cyclopropanone work, it seemed that very low temperatures could probably be employed. In any event, the synthesis would be expected to

* Abstract published in *Advance ACS Abstracts,* March 1, 1994.

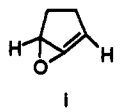
(1) Ichimura, A. S.; Lahti, P. M.; Matlin, A. R. *J. Am. Chem. Soc.* **1990**, *112*, 2868.

(2) Oxyallyls are shown in this paper in the traditional zwitterionic representation even though the calculations in ref 1 show the species to have some radical character.

(3) Recently verified in the case of seven- and eight-membered rings: Black, C.; Lario, P.; Masters, A. P.; Sorensen, T. S.; Sun, F. *Can. J. Chem.* **1993**, *71*, 1910.

(4) Schaad, L. J.; Hess, B. A., Jr.; Zahradnik, R. *J. Org. Chem.* **1981**, *46*, 1909.

(5) Allene oxides are a third species on this closely similar potential energy surface, and these can be converted to cyclopropanones *via* an oxyallyl intermediate.[6] Although Ichimura *et al.* did not include **1** in their computations, we have computed **2** and **1** (geometry optimization at the MP2/6-31G* basis set) and find that **1** is 34.6 kcal/mol higher in energy than **2**, and hence even higher yet when compared to **1**. Interestingly, in the geometry of **2**, the central bond is 1.66 Å, compared to the 1.59 Å reported by Ichimura *et al.* using their modified RHF/6-31G* basis set.



1

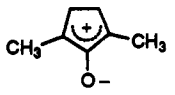
(6) Crandall, J. K.; Conover, W. W.; Komin, J. B.; Machleder, W. H. *J. Org. Chem.* **1974**, *39*, 1723.

(7) For a review see: Schaffer, K.; Demuth, M. M. In *Rearrangements in Ground and Excited States*; de Mayo, Ed.; Academic Press: New York, 1980; Vol. 3.

0002-7863/94/1516-2804$04.50/0

generate macroscopic amounts of the oxyallyl so that even in the absence of direct detection the reaction chemistry of this species could be explored.

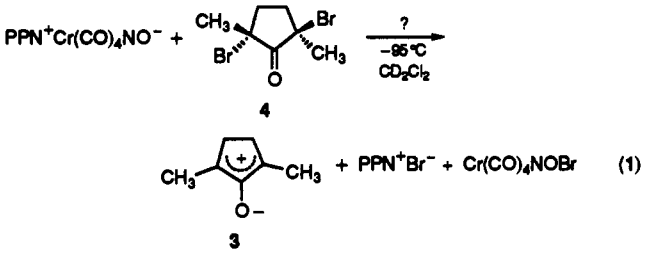
Because methyl groups should even further stabilize **1**, electronically and sterically, oxyallyl **3** was chosen for the initial study. Subsequently, the parent system **1** was also briefly investigated.



3

Results and Discussion

The reaction of *trans*-2,5-dibromo-2,5-dimethylcyclopentanone (**4**) with $PPN^+Cr(CO)_4NO^-$ was first attempted as an *in situ* NMR tube preparation using CD_2Cl_2 as solvent at a temperature of −95 °C (close to the freezing point of the solvent). The hypothetical reaction is shown in eq 1; the two byproducts are expected to be inert under these reaction conditions.



4

3 (1)

The chromium salt in CD_2Cl_2 in a 5-mm NMR tube protected with a septum cap was cooled in a liquid N_2–acetone slush bath (−95 °C) and the dibromide in a further amount of CD_2Cl_2 added with shaking via syringe. There was an immediate loss of the deep-red color of the chromium salt, an indication that the eq 1 reaction had already taken place. The NMR tube was then cooled to liquid N_2 temperature and placed in the precooled spectrometer at −95 °C. For **3**, one expects two ^1H peaks of 2:3 area, and in the ^{13}C NMR spectrum, four peaks. In fact, the ^1H NMR spectrum was dominated by a compound showing two strong singlets of equal area, and in the ^{13}C NMR, seven prominent peaks were observed. It was clear therefore that oxyallyl **3** was not being observed.

Even lower temperature experiments were then attempted using $CDFCl_2$ (mp −135 °C) as the NMR solvent, with preparation temperatures of −130 °C (pentane–N_2) and the NMR spectrometer precooled to *ca.* −120 °C. The initial spectra were poorly resolved at this temperature, but there was no indication that **3** was present, since warming the solution merely "sharpened" the existing peaks, with no sign that two of these rapidly disappeared. In fact even at −120 °C, the two peaks noted in the methylene chloride experiments were already present in the ^1H NMR spectrum, although they were not nearly as dominant as in the former case.

As shown in the next section, the actual products observed in these eq 1 reactions corresponded to dimers of **3**. It seemed clear therefore that oxyallyl **3** was an enormously reactive molecule, and further attempts to directly observe this species were abandoned. It should be emphasized however that the observation of these dimers (a second-order reaction) provides clear evidence that macroscopic quantities of oxyallyl **3** must have first formed in the eq 1 process. Since no previous study of such dimerization reactions has been reported, we next turned our efforts into characterizing this dimer product.

Dimerization Reaction

For studies of the dimerization of **3**, the reactions were conveniently carried out in CH_2Cl_2 or THF solution at −78 °C.

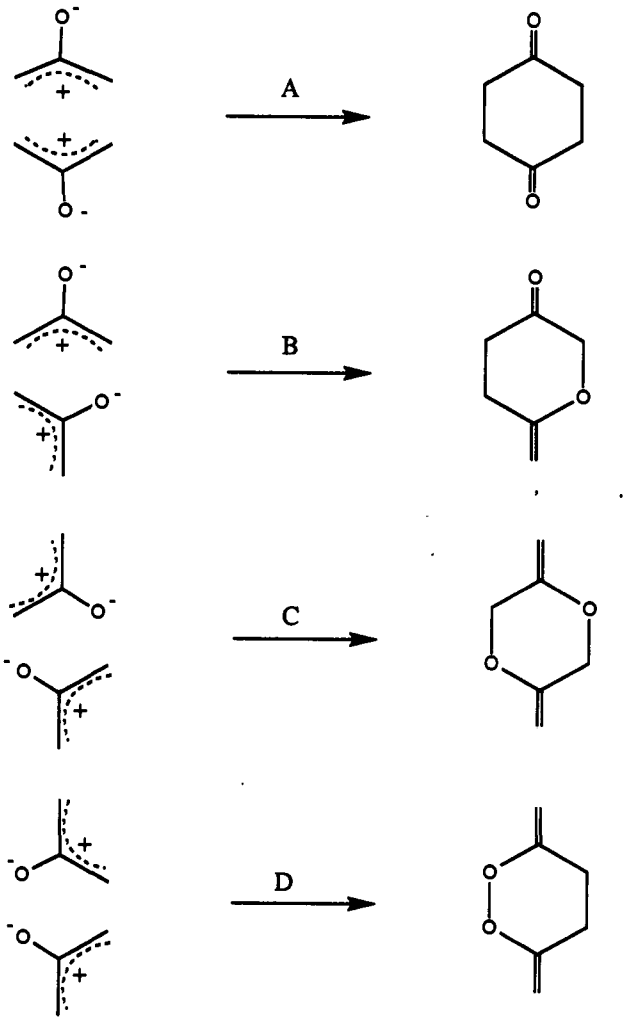
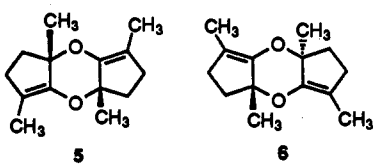


Figure 1. Four different double-connectivity modes for an oxyallyl + oxyallyl dimerization, with no regard for the "allowedness" of the orbital overlaps.

With careful workup and purification, a single major compound was isolated as a low-melting solid, and this had NMR properties corresponding to those referred to in the *in situ* NMR results discussed above. The ^1H NMR spectrum in $CDCl_3$ shows two "singlet" peaks for the four CH_3 groups, each 6H area, one at δ 1.594 and the other at δ 1.494 (doublet, J = 0.8 Hz). This observation strongly suggests a symmetry element whereby methyl pairs are chemically equivalent. The remaining protons form a complex series of peaks δ 1.85–2.15, 8H area. The ^{13}C NMR spectrum shows seven peaks (for fourteen carbons), again strongly suggesting a symmetry element. The seven peaks include a pair at δ 148.2 and 114.0, both quaternary, which can be assigned to an enol ether functionality. In the infrared spectrum, there is no strong >C=O stretching frequency, but a weak peak at 1704 cm^{-1} is appropriate for an enol ether.

These data are satisfied by either compound **5** or **6**, the corresponding cis and trans isomers of a bis-enol ether (dioxane).



5 **6**

Both **5** and **6** correspond to a dimer of **3** in which two bonds are made between the monomer units (double connectivity). However, the formation of **5** (or **6**) is only one of four possible double connectivities, as shown in Figure 1. The choice of which

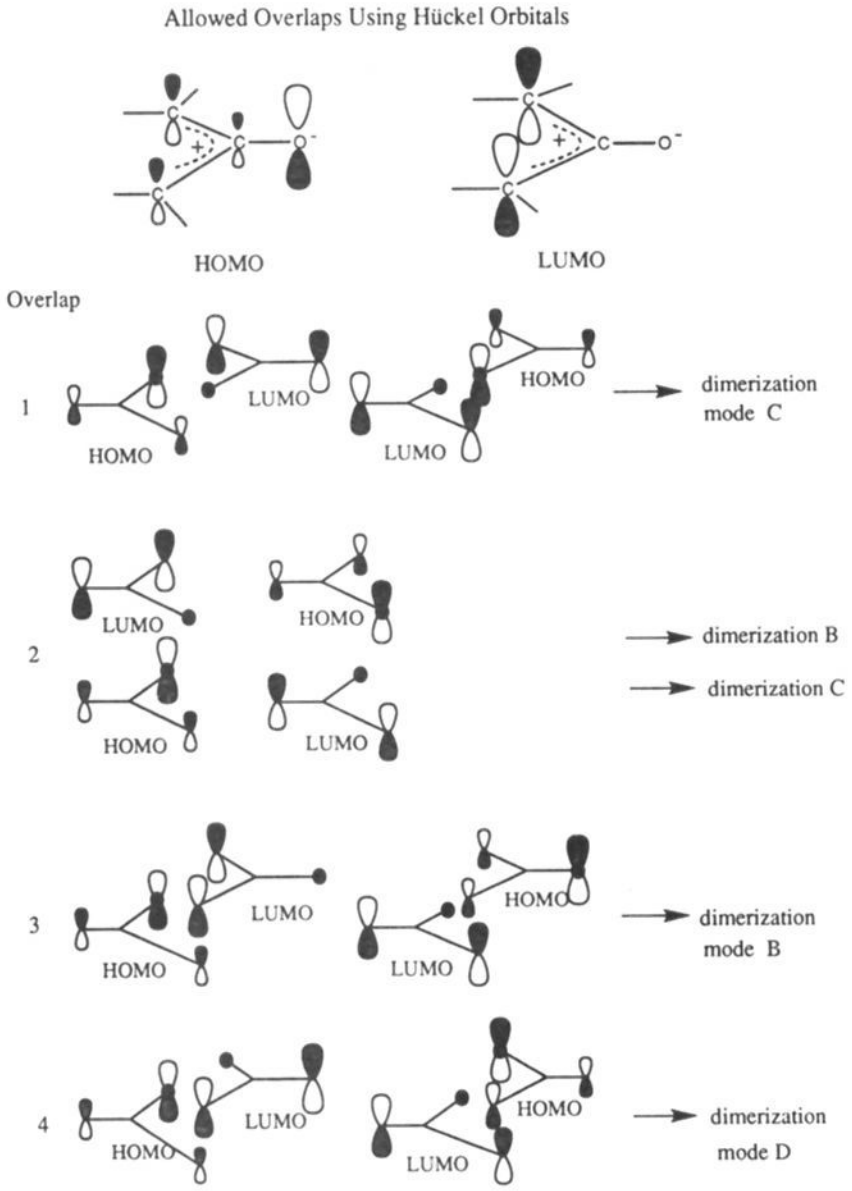


Figure 2. Allowed orbital overlaps for oxyallyl + oxyallyl dimerization using Hückel MO's. In the overlap diagrams, dotted lines, formal charges, bonds for carbon substituents, atom symbols, and the small orbital on the central carbon of the HOMO have all been removed in order to allow a clearer presentation. The oxygen atom is shown as a black dot.

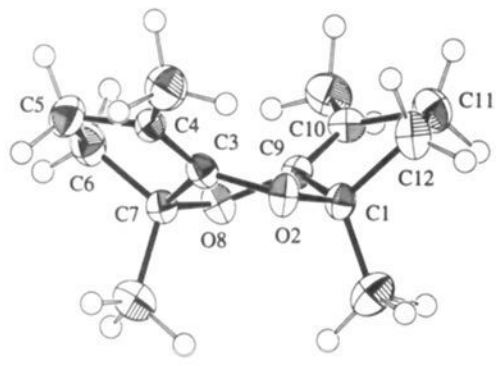


Figure 3. ORTEP structure of the *cis*-dioxane **5** from X-ray diffraction.

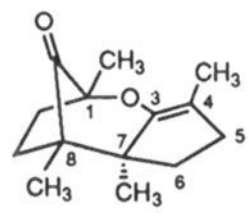
actual connectivity mode would be favored should be governed, at least in part, by the rules for a pericyclic cycloaddition process, i.e. a consideration of HOMO–LUMO orbital interactions, as shown in Figure 2.[8] A frontier orbital interaction analysis involves the LUMO of one oxyallyl with the HOMO of the other (or vise versa, since both species are identical). There is no allowed process corresponding to dimerization mode A. The mode D dimerization shown in Figure 2, overlap 4, is not allowed as a synchronous cycloaddition, since only the C–C overlap is positive. However it is not disallowed in the same sense as the mode A process. The mode D interaction would also involve a sizable Coulombic repulsion between the oxygen atoms.[9]

The isolation of a bis-enol ether in our reaction obviously corresponds to dimerization mode C (Figure 1). With a simple acyclic oxyallyl dimerization, one could not distinguish in the product between overlaps 1 or 2, as shown in Figure 2. However, in the case of a cyclopentyl oxyallyl an added stereochemical feature is produced when this dimerizes. Overlap 1 would lead to the trans bis-enol ether **6**, while overlap 2 would produce the cis isomer **5**. It thus became of importance to determine the stereochemistry of our bis-enol ether product.

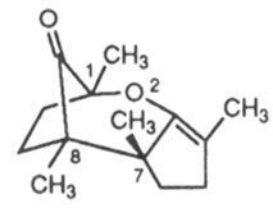
The cis bis-enol ether **5** is expected to have averaged C_2 symmetry and would exist as a racemic mixture, while the trans isomer **6** would have averaged S_2 symmetry (meso, no dipole moment). However, both these point groups lead to identical NMR equivalences, and since the two oxygen atoms effectively isolate both halves of the molecule from each other, there is no obvious NMR distinction between **5** and **6**. The use of a chiral NMR shift reagent would also not be definitive in this case.[10] The possibility of a chiral GC column resolution (or lack of) was frustrated by the thermal instability of the actual material in GC analyses.

The thermal reactivity (see later) of the isolated bis-enol ether compound suggested strongly that our material was the cis isomer **5**, and the matter was definitively settled by obtaining a single-crystal X-ray structure under low-temperature conditions.[11] The ORTEP structure is shown in Figure 3. The central 1,4-dioxane ring is necessarily a boat, and the preferred conformation places the oxygen and sp^3 carbons in the basal plane of the boat, with the alkene carbons at the prow positions.

As previously mentioned, the isolation of the cis isomer **5** in the dimerization reaction implies the orbital overlaps shown in 2 in Figure 2, with double O–C connectivity (mode C).[12] The alternative O–C, C–C connectivity (mode B) leads to tricyclic keto enol ether **7**. As described later, compound **7** can also be



7



8

isolated, and it may be noteworthy that a careful examination of the original *in situ* CD_2Cl_2 NMR spectrum shows this compound to be present in minor amounts in the initially formed mixture at –95 °C. Some of the stereoisomeric keto enol ether **8** is also present in this original mixture. Overall, however, both **7** and **8** are initially minor products in the dimerization reaction.

We thus conclude that the oxyallyl–oxyallyl dimerization takes place predominantly by way of overlap 2 in Figure 2 and that within this tripartite orbital overlap the major connectivity is O–C, C–O, which then leads to the *cis*-dioxane product **5**.

Solution Rearrangements of Dioxane 5

The initially formed dioxane **5**, from the dimerization of **3**, is an unstable molecule. If the original methylene chloride solution of mainly **5** is merely warmed to room temperature, **5** is slowly rearranged in a sequential manner to the keto–enol ethers **7** and **8**. Isomer **7** is initially the main rearrangement product, but eventually an equilibrium mixture in produced in which **8** is the major product, $K = \mathbf{8}/\mathbf{7}$ = ca. 10. The structures of **7** and **8**, both

(8) It might be argued that the formation of a dioxane is in fact a product of the most favorable Coulombic attractions. However, there are two problems with this: (a) On the basis of the computations of Ichimura *et al.*, the zwitterionic formulation traditionally used to represent an oxyallyl grossly overestimates the positive charge at the terminal carbons and (b) even assuming Coulombic attractions were involved, then a *trans*-dioxan would probably be the predicted major product, contrary to the actual results.

(9) The computed[1] charge on the oxygen of **1** is $q = -0.640$.

(10) Monocomplexation of a meso isomer destroys the internal symmetry.

(11) Crystal data: $C_{14}H_{20}O_2$; M 220.31; triclinic, space group $P\bar{1}$; a = 8.798(5) Å, b = 11.516(4) Å, c = 7.008(3) Å, α = 94.24(3)°, β = 112.58(3)°, γ = 74.25(4)°, V = 630.6(6) Å^3; Z = 2; D_{calcd} = 1.160 g cm^{-3}; Mo Kα radiation, λ = 0.71069 Å, μ = 0.075 mm^{-1}; 1198 observed reflections [$I > 3\sigma(I)$] collected on a Rigaku AFC6S diffractometer using a $\omega/2\theta$ scan method to a $2\theta_{max}$ = 50° at 200(1) K; the structure was solved by direct methods and refined by full-matrix least-squares calculations to a conventional R = 0.049 (R_w = 0.043).

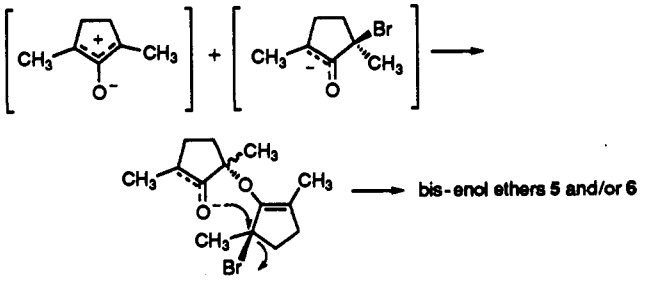
of which could be isolated in a pure form by flash chromatography, follow from a consideration of their ^1H and ^{13}C NMR (including COSY, HMQC, and COSYLR) spectra and IR spectra. The stereochemistry at C7 was assigned mainly on the basis of NOEDIFF and 2-D NOESY experiments.

Compounds **7** and **8**, as previously mentioned, correspond to the oxyallyl dimerization mode B in Figure 1, but they are clearly not formed to any great extent in the primary pericyclic reaction. While one cannot rule out a completely reversible oxyallyl + oxyallyl ⇄ dimer reaction, it seems more reasonable to postulate that the solution reactions **5** ⇄ **7** ⇄ **8** are the result of a reversible single C–O bond rupture in **5**, giving a zwitterionic intermediate which recloses a C–C bond, as shown in Scheme 1. The formation of **7** from **5** requires only a small rotation in the zwitterion and would be kinetically favored, whereas the ultimate formation of **8** from the zwitterion would involve a slightly more extensive reorganization. If these reactions are all reversible, one will of course eventually obtain the thermodynamic ratio of **7** and **8**.[15] Föhlisch[16] has postulated a related one-bond breakage to a zwitterion in solution rearrangements of oxyallyl–diene adducts.

The isolation of **7** and **8** in these rearrangement reactions further supports the idea that dioxane **5** is formed under pericyclic control, since **5** is clearly thermodynamically less stable than either **7** or **8** and computationally less stable than the *trans*-dioxane isomer **6**.[13]

In contrast to these solution rearrangements, the dioxane **5** also undergoes purely gas-phase thermal rearrangements, and under these conditions, only keto–enol ether **7** is a product of **5**, none of the isomeric **8** being observed (see next section).

(12) The preceding analysis is based on the assumption that *bis*-enol ether **5** is a product of direct oxyallyl–oxyallyl dimerization. An alternative to this might conceivably involve a reaction of the oxyallyl with a bromo enolate anion (a probable transient intermediate in the reduction of the dibromo ketone). Subsequent intramolecular displacement of bromine by the new enolate oxygen could then lead to **5** or **6**, as shown in the following equation.



This mechanism is not very likely because the predominant isolation of the cis isomer **5**, rather than the thermodynamic[13] product **6**, is typical of a pericyclic reaction (cf. endo products in Diels–Alder reactions). In the mechanism shown above it is certainly not obvious why only the cis product would be produced. There existed, however, a possible way of distinguishing between these two routes. The dibromo ketone **4** used as the starting material in this work can be shown by NMR analysis to have the trans configuration (C_2 point group) and hence exists as a racemic mixture. The dibromo ketone is itself very fragile and would be difficult to resolve, but dibromination of chiral 2,5-dimethylcyclopentanone (also C_2) might yield an enantiomerically enriched **4**, in which the major enantiomer, and the absoute configuration of this, would be dependent on the diastereomeric ratio present in the monobromo ketone intermediate. The *cis-bis*-enol ether **5** is chiral, but the oxyallyl **3** is achiral. A direct dimerization of **3** will yield racemic **5**, whereas a route involving an enantiomerically enriched bromo enolate could be expected to produce an enantiomerically enriched **5**. However, bromination of (2*R*,5*R*)-(–)-*trans*-2,5-dimethylcyclopentanone[14] gave essentially racemic **4**, thwarting this particular experiment. Inactive **4** could be the result of a 50:50 yield of monobromo diastereomers or it might be the result of a prior racemization of the starting ketone, which can occur *via* small populations of the achiral cis isomer (HBr, a plausible catalyst for this epimerization, is produced in the bromination reaction).

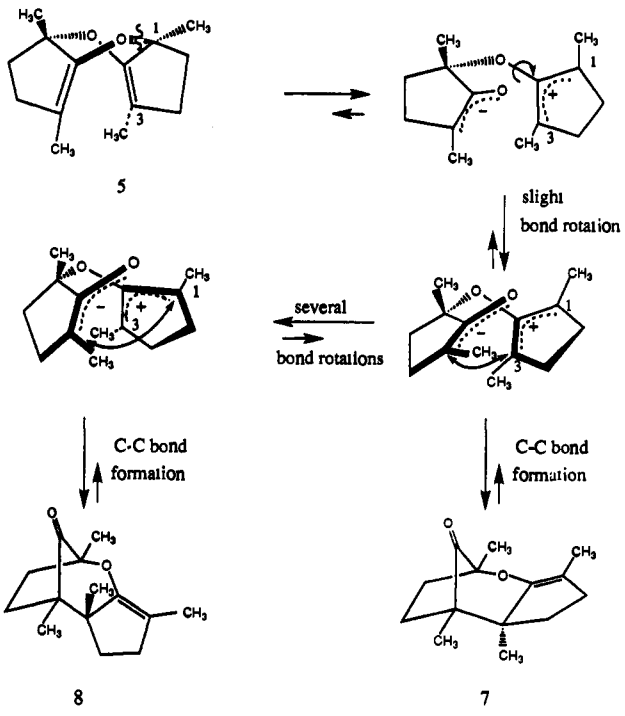
(13) An *ab initio* computation was carried out on **5** and **6** (structure optimized with the STO-3G basis set). The trans isomer **6** is computed to be 2.58 kcal/mol more stable than **5**.

(14) Gramain, J.-C.; Kergomard, A.; Renard, M. F.; Veschambre, H. *J. Org. Chem.* **1985**, *50*, 120.

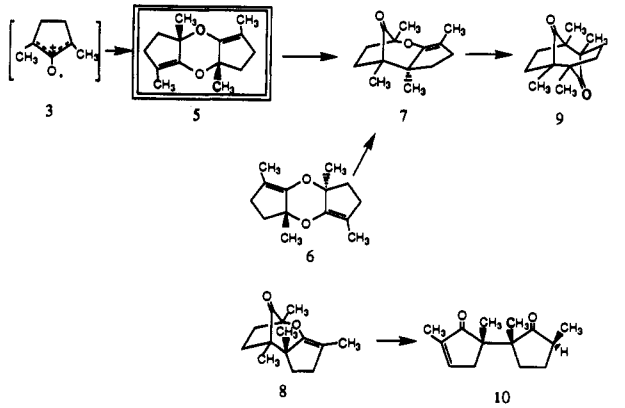
(15) Compound **8** is computed to be 3.8 kcal/mol more stable than **7** using the AM1 semiempirical method.

(16) Föhlisch, B.; Joachimi, R. *Chem. Ber.* **1987**, *120*, 1951.

Scheme 1



Scheme 2. Thermal Rearrangement Behavior of **5** and Related Compounds



Thermal Rearrangements

Dioxane **5** is also thermally labile, and initial attempts to use GC analysis on this material were confusing because of rearrangements in the injector and on the column (characteristic broad peaks). In fact, reasonable analyses for **5** were obtained only by using OV-1 540 μ columns with high carrier gas flow rates and low injection temperatures. Not only is **5** labile but the first rearrangement product is also quite thermally unstable. The overall thermal rearrangement reaction network is shown in Scheme 2. In terms of GC retention times, isomers **5** and **6** are well-separated from the longer retention **7** and **8**, which are in turn separated from the even longer retention time isomers **9** and **10**. In the latter two pairs, the individual isomers are also well-resolved.

In Scheme 2 we show rearrangement reactions involving the *trans*-dioxane isomer **6**. On flash chromatography of the original (mainly **5**) mixture, small amounts of a marginally earlier eluting material were obtained as a mixture with **5**, and this can be assigned to compound **6**. In capillary GC analysis, individual peaks for **5** and **6** can also be resolved, but under packed-column conditions, they coelute. Nevertheless, using packed-column preparative GC conditions (long retention times, high temperatures), small amounts of isomer **6** can be isolated as the lowest

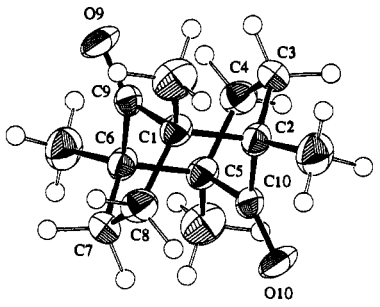


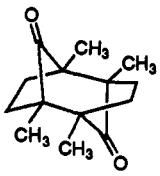
Figure 4. ORTEP structure of the diketone **9** from X-ray diffraction.

retention peak because all of the major dioxane isomer **5** has been completely rearranged (mostly on the column) to the higher retention isomers **7** and **9** (the *cis*-dioxane **5** rearranges stereospecifically to **7** in the temperature range 100–150 °C, and the further rearrangement of **7** to **9** requires only a slightly higher temperature).

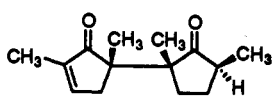
Using injector temperatures of 300–350 °C, one can also show that the *trans*-dioxane isomer **6** is rearranged stereospecifically into the *same* keto–enol ether **7**, and ultimately to **9**.

The other keto–enol ether **8** is not part of this thermal manifold, but even it is somewhat thermally labile and rearranges at 300–370 °C (injector temperature) into the diketone **10**.

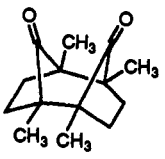
Diketone **9** was obtained pure by preparative GC collection. The ^1H and ^{13}C NMR spectra (three proton peaks, four ^{13}C peaks) do not unambiguously distinguish between diketone structures **9** and **11**, although the former is expected on mechanistic



9



10

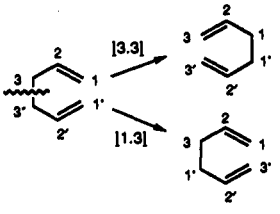


11

grounds (see following). A single-crystal X-ray diffraction was carried out to unambiguously verify the structure,[17] and the ORTEP diagram is shown in Figure 4.

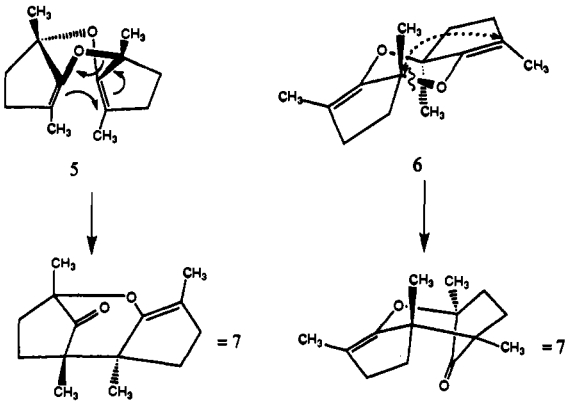
Diketone **10** could also be obtained by preparative GC and the gross structure established (one of four possible stereoisomers). Assuming that the C7–C8 stereochemistry in **8** is retained in **10** and that a hydrogen atom transfer would result in a *cis*-2,5-dimethylcyclopentanone substructure, the structure **10** was assigned.

The thermal rearrangements encountered in this work are a manifestation of the fact that *all* of the dimerization pathways shown in Figure 1 lead to products with 1,5-double bonds, two C=O bonds in the A case, two C=C bonds in C and D, and one C=C and one C=O bond in B. Because of the inherent weakness of the 3–3′ bond, such systems are prone to undergo either allowed



(17) Crystal data: $C_{14}H_{20}O_2$; M 220.31; orthorhombic, space group *Cmca*; α = 14.440(4) Å, b = 7.490(4) Å, c = 11.018(3) Å, V = 1191.8(7) Å^3; Z = 4; D_{calcd} = 1.228 g cm^{-3}; Mo Kα radiation, λ = 0.71069 Å, μ = 0.080 mm^{-1}; 257 observed reflections [$I > 3\sigma(I)$] collected on a Rigaku AFC6S diffractometer using a $\omega/2\theta$ scan method to a $2\theta_{max}$ = 50° at 250(1) K; the structure was solved by direct methods and refined by full-matrix least-squares calculations to a conventional R = 0.038 (R_w = 0.019).

Scheme 3



[3.3] sigmatropic rearrangements or [1.3] rearrangements. Given that a C=O bond is stronger than a C=C bond, the observed cascade **5** → **7** → **9** is expected on thermodynamic grounds. The interesting fact that both the *cis*- and *trans*-dioxanes **5** and **6** rearrange stereospecifically to the same keto–enol ether **7** is easily rationalized. Because of a favorable geometry, the cis isomer **5** undergoes an allowed [3.3] Claisen rearrangement which must produce only **7**, as shown in Scheme 3.

The trans isomer **6** must undergo the more difficult [1.3] sigmatropic rearrangement, since the [3.3] process is sterically impossible. However, this process is also stereospecific and would also lead to **7**, as shown in Scheme 3. In related work, Gajewski *et al.*[18] have shown that the degenerate thermal rearrangement of 1,4-dimethylenecyclohexane proceeds only by the allowed [3.3] sigmatropic process (Cope); i.e., a possible [1.3] rearrangement must have a considerably higher activation barrier.

The stereospecific transformation of **7** to **9** is also a [1.3] rearrangement (see **6** → **7** in the diagram for a very similar geometry change), and the stereochemistry in **9** (vs **11**) is easily predictable.

Finally, in the keto–enol ether **8**, a thermal process would be expected to begin with cleavage of the 1–2 bond as numbered in **8** (the 3–3′ bond in generic terms), but a [1.3] rearrangement would produce diketone **11**, which would have severe nonbonded methyl---methyl repulsions (a central boat with eclipsing methyl groups on both sides); so an alternative hydrogen atom transfer occurs instead, leading to diketone **10**.

An interesting aspect of these thermal rearrangements is that one has easy sequential access to three of the four possible dimers of the oxyallyl, *since the least stable system is the preferred pericyclic product*.[19] Indeed, the diketone **9** is not even an allowed pericyclic product, but this diketone can ultimately be made the major dimerization product under specific workup conditions.

There have been no previous studies of oxyallyl–oxyallyl dimerizations under controlled aprotic conditions. Föhlisch[20] has reported the isolation of a dioxane product related to **5** from what might be the dimerization of a cyano-substituted oxyallyl. Hoffmann[21] has reported a 2.5% yield of diketone **12** from a zinc reduction of dibromo ketone **13**. Berson[22] has studied the dimerization of the related cyclopentyl trimethylenemethane compounds, and this appears to be a particularly unselective reaction in that products are produced which correspond to at least three of the four possible dimerization modes. This result

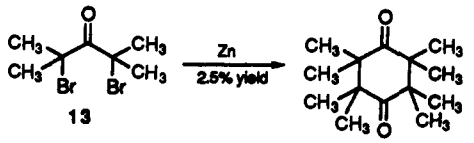
(18) Gajewski, J. J.; Hoffman, L. K.; Shih, C. N. *J. Am. Chem. Soc.* **1974**, *96*, 3705.

(19) The peroxy compounds from the mode D dimerization in Figure 1 are undoubtedly the least stable dimers, but there is no evidence that these are ever formed.

(20) Föhlisch, B.; Lutz, D.; Gottstein, W.; Dukek, U. *Liebigs Ann. Chem.* **1977**, 1847.

(21) Carpenter, B. K.; Rawson, D. I.; Hoffmann, H. M. R. *Chem. Ind.* **1975**, 886. Dibromo ketone **13**, under eq 1 reaction conditions, produces only the corresponding cyclopropanone, as implied in the Introduction.

(22) Siemionko, R. K.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 3870.

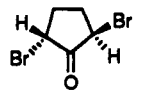


13 12

is consistent with calculations by Dixon *et al.*,[23] in that the five-membered ring trimethylenemethane is predicted to have a $^3B_2$ triplet ground state and, if so, the dimerization reactions may be less selective (more radical-like) than those involving the predicted singlet ($^1A_1$) oxyallyl species **3**.

Attempted Generation of the Parent Cyclopentyl Oxyallyl 1 or Dimerization Products of This

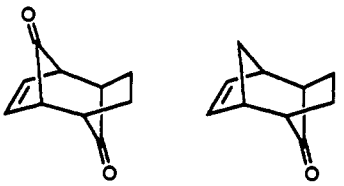
Previous experience in this laboratory has shown that disecondary, primary–secondary, or diprimary 1,3-dibromo ketones are not converted to cyclopropanones on reaction with $Cr(CO)_4NO^-$, in sharp contrast to the tertiary–tertiary or tertiary–secondary cases. It is also assumed, as explained previously, that an oxyallyl is initially produced in the reaction and that this is "instantly" transformed into a cyclopropanone if this process is thermodynamicaly favorable, which of course we assume is not the case with the cyclopentane system, as explained in the Introduction. Because *trans*-2,5-dibromocyclopentanone (**14**) is



14

a secondary–secondary dibromo ketone, we were apprehensive about whether this ketone would even react with $Cr(CO)_4NO^-$ to give an oxyallyl intermediate. Perhaps not surprisingly then, when **14** was treated at −78 °C with $Cr(CO)_4NO^-$, an immediate reaction ensued, but no volatile products were produced, i.e. no dimers corresponding to **5** etc.

However, if the reaction was carried out in the presence of excess furan or cyclopentadiene, reasonable yields of the known oxyallyl [4 + 3] adducts **15**[16] and **16**[24] were formed. The yields

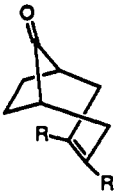


15 16

were best with the cyclic dienes, and using butadiene or 2,3-dimethylbutadiene, only poor yields of the adducts **17**[25] and **18** were obtained.

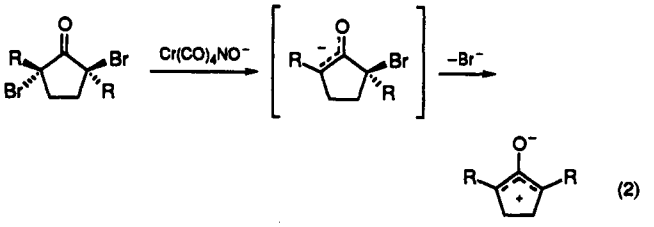
These experiments offer good evidence therefore that cyclopentyl oxyallyl[26] is being formed under these conditions but that it must be *immediately* trapped if one is to obtain simple products.

The most cogent explanation of the contrasting behavior of the disecondary bromide **14** and the ditertiary analog **4** comes from consideration of the oxyallyl-forming process as a two-step reaction



17: R = H
18: R = CH_3

(eq 2). If the rate of loss of Br^- in the bromo enolate intermediate



(2)

is much faster than the rate of formation of the bromo enolate, then a possible bimolecular reaction between oxyallyl and bromo enolate is unlikely. This we envisage to be the case with R = CH_3.[29] If Br^- loss is competitive with enolate formation, then it is possible that enolate and oxyallyl can react together,[31] although we have no specific evidence for this. However, it is reasonable that, in the presence of large amounts of a diene trap, this enolate–oxyallyl reaction could be sidetracked.

As evidence for the above suppositions, one can show by conducting these reactions at −78 °C in the presence of excess TMS-Cl in the solvent that the secondary bromo enolate is trappable to give **19**, whereas in the tertiary case, one sees no

19

TMS-trapped product and only the previously described oxyallyl–oxyallyl dimer products are produced.

Conclusions

The experimental results support the supposition that cyclopentyl oxyallyl is uniquely[32] more stable than the corresponding cyclopropanone, as predicted from the computations of Ichimura *et al.* The 2,5-dimethylcyclopentyl oxyallyl is not observable even at −120 °C, the $t_{1/2}$ for dimerization being <10 min at this temperature. The dimerization reaction gives a single major product, the *cis*-dioxane **5**, whose structure was definitively assigned by means of a single-crystal X-ray study. The formation of **5** can be rationalized as a pericyclic reaction where the two oxyallyl units are aligned as shown in overlap 2 of Figure 2. The *cis*-dioxane **5** is thermally labile and rearranges in a stereospecific fashion to provide compounds representative of two other dimerization connectivities. In particular, the "face-to-face" dimerization mode A (Figure 1), although not allowed (or observed) as a pericyclic product in the initial dimerization

(23) Dixon, D. A.; Dunning, T. H., Jr.; Eades, R. A.; Kleier, D. A. *J. Am. Chem. Soc.* **1981**, *103*, 2878.
(24) (a) Herter, R.; Föhlisch, B. *Synthesis* **1982**, 976. (b) Ernst, B.; Ganter, C. *Helv. Chim. Acta* **1978**, *61*, 1107.
(25) Onove, H.; Moritani, I.; Murahashi, S. I. *Tetrahedron Lett.* **1973**, 121.
(26) A number of oxyallyl-like intermediates have been used for [4 + 3] cycloaddition reactions, e.g. in the Noyori reaction[27] and from $ZnBr_2$-coordinated oxyallyls.[28] See also ref 16.
(27) For a review, see: Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61.
(28) For reviews, see: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819; **1984**, *23*, 1.
(29) In Favorski reactions, Bordwell[30] has shown that a tertiary bromo ketone is more reactive than a secondary one, and the former reaction is pictured as a simple S_N1 loss of Br^-.
(30) Bordwell, F. J.; Almy, J. *J. Org. Chem.* **1973**, *38*, 575 and earlier articles in this series.
(31) A polymerization reaction is possible *via* bromo enolate + oxyallyl → enolate dimer + oxyallyl → enolate trimer etc.
(32) There have been a number of Favorski rearrangement studies which have shown that cyclopentyl systems are clearly abnormal, and qualitatively this has been attributed to the instability of bicyclopropanone **2**. The computations of Ichimura *et al.* put this assumption on a much firmer theoretical basis. The present work makes it clear that an actual oxyallyl is the stable tautomer in this case.

reaction, can ultimately be made the major end product if one uses controlled workup conditions.

Experimental Section

Gas chromatography was performed on a Hewlett-Packard Model 5890A, with either a 10 m OV1 530 μ column (analytical) or a packed 3% OV17 (8′ × 4 mm i.d.) column (for the preparative collection, TC detector). Mass spectra and capillary GC were carried out on a Hewlett-Packard Model 5890 Gas Chromatograph equipped with a 5971A mass selective detector. Split injection was used employing a 12 m × 0.2 mm i.d. OV-101 column. Attempted GC separation of the enantiomers of **5** was carried out using a 25 m × 0.25 mm i.d. column coated with "chira-Metal" phase, CC and CC, Germany. NMR spectroscopy was carried out on a Bruker ACE-200 or AM-400 (δ values in $CDCl_3$, J in Hz). For ^1H NMR, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and b = broad. For $^{13}C\{^1H\}$ NMR, q = quaternary, and multiplicities were determined from DEPT 90 and 135 spectra. Infrared spectra were determined on a Nicolet 5-DX or a Mattson Model 4030, peaks being reported as very strong (vs), strong (s), medium (m), or weak (w). Analytical mass spectra were obtained on a Kratos MS-80. The X-ray equipment is described in refs 11 and 17. Optical rotations were determined on a Rudolph Autopol III polarimeter.

trans-2,5-Dibromocyclopentanone was prepared as described.[33] The preparation of 2,5-dimethylcyclopentanone, cis–trans mixture, followed a literature route.[34] The preparation of (2*R*,5*R*)-(−)-*trans*-2,5-dimethylcyclopentanone was carried out by a fungal reduction of 2,5-dimethylcyclopent-2-enone, as described.[14] *trans*-2,5-Dibromo-2,5-dimethylcyclopentanone was prepared as described.[35] The ^1H NMR spectrum (an AA′BB′ system) was simulated in order to definitively assign the stereochemistry, $\Delta\delta_{AB}$ = 20.8 Hz, $J_{AB} = J_{A'B'}$ = −5.6, $J_{AA'}$ = 6.2, $J_{BB'}$ = 0.40, $J_{AB'} = J_{A'B}$ = 2.5. The large difference in the AA′ and BB′ coupling constants is only consistent with a trans stereochemistry. ^1H NMR: 2.00 (s, 6H); 2.25–2.6 (m, 4H). ^{13}C NMR: 27.26 (CH_3); 38.51 (CH_2); 62.30 (q). The dark-red salt, PPN^+ $Cr(CO)_4NO^-$, was prepared from $Cr(CO)_6$ and $PPN^+NO_2^-$, as described by Mantell and Gladfelter,[36] and stored under nitrogen in the freezer.

General Conditions for Carrying Out the Eq 1 Reactions. Reactions were carried out in 10-mL oven-dried Schlenk tubes fitted with a septum and magnetic stirrer and generally cooled to −78 °C. The PPN^+ $Cr(CO)_4NO^-$ salt can be weighed and transferred to the Schlenk tube in air. After nitrogen purging, the solvent was added and stirring commenced. Generally for a 0.5-mmol scale, 1 mL of solvent (CH_2Cl_2 or THF) was used to dissolve the salt and another 1 mL used to dissolve the dibromo ketone, with proportionately larger amounts for larger scale reactions. The dibromo ketone solution was added by syringe over a period of several minutes. The deep-red color of $Cr(CO)_4NO^-$ disappears immediately, an indication that the reaction is essentially instantaneous. Pentane (5–8 mL) was then added slowly by syringe and the resulting heterogeneous mixture allowed to warm to 20 °C. The solution was filtered through Celite, the Celite washed with more pentane, and the pentane then evaporated to yield a nearly inorganic-free product (the PPN^+ Br^- is insoluble in pentane, while $Cr(CO)_4NOBr$ is thermally unstable at 20 °C and forms decomposition products which are also insoluble in pentane). This initial material was rich in dioxane **5**, which could be purified by preparative TLC (eluting with 9:1 hexane–ether). Alternatively, flash chromatography (methylene chloride) was used for separation, but under these conditions there is some rearrangement of **5** to keto–enols **7** and **8**. When the latter compounds were desired, the initial methylene chloride solution could be warmed to 20 °C before the pentane addition. Subsequent pentane addition and workup, as above, then yielded material much richer in compounds **7** and **8**. These two keto–enols were easily separated by flash chromatography on silica gel using methylene chloride as eluting solvent.

Trapping Reactions. These were carried out in the same way as described above, except that the solvent used to dissolve the chromium salt also contained the trapping compound. In the case of trimethylsilyl chloride, a threefold molar excess was used. In the case of the [4 + 3] cycloadditions, a 10–15% v/v of the diene was included in the methylene chloride solvent. The subsequent workup was similar to that described above.

***In Situ* NMR Experiments.** The requisite quantity of PPN^+ $Cr(CO)_4NO^-$ was added to a 5-mm NMR tube protected with a septum cap. The tube was flushed with nitrogen and ca. 0.3 mL of CD_2Cl_2 was added while cooling the tube at −78 °C. This tube was then transferred to an acetone–N_2 slush bath (ca. −95 °C), and the dibromo ketone in 0.2–0.3 mL of CD_2Cl_2 was rapidly added with shaking. The resulting mixture was cooled to liquid N_2 temperature and then placed in the precooled NMR spectrometer. Analogous experiments were done in which $CDFCl_2$[37] was used as the solvent, with mixing being done at −130 °C (pentane–N_2 slush) and the spectrometer precooled to −120 °C.

(1*RS*,7*RS*)-1,4,7,10-Tetramethyl-2,8-dioxatricyclo[7.3.0.0^{3,7}]dodeca-3,9-diene (5). Isolated as a solid, mp 53 °C (from pentane). IR: 1704 (w). ^1H NMR (400 MHz): δ 1.82–2.15 (m, 8H); 1.594 (6H); 1.494 (d, J = 0.8, 6H). ^{13}C NMR (100 MHz): 148.24 (q, C3 and C9); 114.03 (q, C4 and C10); 87.58 (q, C1 and C7); 38.05 (CH_2, C5 and C11); 29.77 (CH_2, C6 and C12); 23.88 (CH_3, CH_3 on C4 and C10); 11.56 (CH_3, CH_3 on C1 and C7). MS *m*/*z*: 220 (M^+); 111 (100); 110 (35). High-resolution MS: calcd for $C_{14}H_{20}O_2$, 220.14633; found, 220.1454.

(1*RS*,7*SR*)-1,4,7,10-Tetramethyl-2,8-dioxatricyclo[7.3.0.0^{3,7}]dodeca-3,9-diene (6). Obtained from flash chromatography as a 1:1 mixture with **5**. ^1H NMR (400 MHz): δ 1.300 (6H); 1.594 (overlaps with **5** signal). The CH_2 protons occupy a similar range to those of **5**.

(1*RS*,7*RS*,8*RS*)-1,4,7,8-Tetramethyl-2-oxatricyclo[6.2.1.0^{3,7}]undec-3-en-11-one (7). IR: 1752 (s); 1704 (w). ^1H NMR (400 MHz): 2.12–2.43 (m, 3H); 1.76–1.98 (m, 2H); 1.64–1.76 (m, 1H); 1.35–1.48 (m, 2H); 1.504 (poorly resolved quartet, 3H); 1.312 (3H); 1.156 (3H); 1.000 (3H). ^{13}C NMR (100 MHz): 213.90 (q, C=O); 151.11 (q, C3); 111.46 (q, C4); 82.08 (q, C1); 54.44 (q); 51.10 (q); 35.26 (CH_2); 32.44 (CH_2); 32.07 (CH_2); 28.04 (CH_2); 18.49 (CH_3); 17.17 (CH_3); 14.15 (CH_3); 11.39 (CH_3). MS *m*/*z*: 220 (M^+); 111 (100); 110 (57). High-resolution MS: calcd for $C_{14}H_{20}O_2$, 220.14633; found, 220.1463.

In benzene-d_6 solvent, a better resolution of the protons on C5, C6, C9, and C10 was obtained, allowing an assignment of all eight protons to be made via COSY, COSYLR, HMQC, and NOESY 2D spectra. In an NOEDIFF experiment, irradiation of the methyl at C7 gave positive NOE correlations with the endo proton on C9 and the endo proton on C6.

(1*RS*,7*SR*,8*RS*)-1,4,7,8-Tetramethyl-2-oxatricyclo[6.2.1.0^{3,7}]undec-3-en-11-one (8). Elutes in flash chromatography well behind **7**. IR: 1753 (s); 1704 (w). ^1H NMR (400 MHz): 2.33–2.46 (m, 1H); 2.19–2.27 (m, 1H); 2.13–2.19 (m, 1H); 1.91–1.99 (m, 1H); 1.8–1.9 (m, 1H); 1.6–1.7 (m, 1H); 1.34–1.46 (m, 2H); 1.614 (t, J = 1, 3H); 1.310 (3H); 0.995 (3H); 0.961 (3H). ^{13}C NMR (100 MHz): 215.95 (q, C=O); 150.64 (q, C3); 113.11 (q, C4); 81.02 (q, C1); 56.76 (q); 52.92 (q); 32.27 (CH_2); 29.62 (CH_2); 29.52 (CH_2); 27.77 (CH_2); 19.53 (CH_3); 17.36 (CH_3); 13.54 (CH_3); 11.43 (CH_3). MS m/z: 220 (M^+); 112 (21); 111 (100); 110 (36). High-resolution MS: calcd for $C_{14}H_{20}O_2$, 220.14633; found, 220.1462. From COSY, COSYLR, HMQC, and NOESY 2D spectra, it was possible to definitively assign the four protons on C5 and C6. Irradiation of the C7 methyl (0.995) produced an NOE enhancement at H6 (exo) (1.4–1.45).

(1*RS*,2*RS*,5*SR*,6*SR*)-1,2,5,6-Tetramethyltricyclo[4.2.1.1^{2,5}]decane-9,-10-dione (9). Under preparative GC collection conditions, either compound **5** or **7** is rearranged to **9** (injection temperature = 300 °C, initial temperature = 100 °C → 250 °C at 10 deg/min, retention time ca. 12–13 min). The product was recrystallized from hexane, white solid, mp 215–217 °C. IR: 1738 (s). ^1H NMR (400 MHz): 1.84–1.98 (m, 4H); 1.28–1.42 (m, 4H); 0.920 (s, 12H). ^{13}C NMR (100 MHz): 216.98 (q, C=O); 52.52 (q); 27.25 (CH_2); 13.50 (CH_3). MS *m*/*z*: 220 (M^+), 111 (100), 110 (62). High-resolution MS: calcd for $C_{14}H_{20}O_2$, 220.14633; found, 220.1460.

(5*RS*,2′*SR*,5′*RS*)-2,5-Dimethyl-5-(1′-oxo-(2′,5′-dimethylcyclopent-2′-yl)cyclopent-2-en-1-one (10). This compound was isolated by preparative GC in small amounts sufficient for structural confirmation by ^1H NMR. With an injector temperature of 370 °C, column temperature 100 → 250 °C at 10 deg/min, the injection of compound **8** led to the formation of a small amount of the longer retention **10** (ca. 14 min). There is a small tailing area on the high-retention side of the large **8** peak, indicating that some thermal conversion is occurring on the column, but most of the **8** → **10** reaction occurred in the injector port. ^1H NMR (400 MHz): 2.76 (bd, J = 18, 1H); 2.2–2.35 (m, 2H, one of these is a doublet of multiplets, J = 18); 2.07–2.13 (m, 1H); 1.68–1.8 (m, 2H); 1.33–1.48 (m, 1H); 1.77 (q, J = 1.5, 3H); 1.183 (s, 3H); 1.091 (d, J = 6.7, 3H); 1.035 (s, 3H). MS m/z: 220 (M^+), 112 (62), 111 (100), 110 (73).

(33) Hoffmann, H. M. R.; Vinter, J. G. *J. Org. Chem.* **1974**, *39*, 3921.
(34) Noyes, W. A.; Kyriakides, L. P. *J. Am. Chem. Soc.* **1910**, *32*, 1064.
(35) Fry, A. J.; O'Dea, J. J. *J. Org. Chem.* **1975**, *40*, 3625.
(36) Mantell, D. R.; Gladfelter, W. L. *J. Organomet. Chem.* **1988**, *347*, 333.
(37) Siegel, J. S.; Anet, F. A. L. *J. Org. Chem.* **1988**, *53*, 2629.

In the flash chromatography separations of **7** and **8**, there were minor amounts of slower eluting products seen, including a stereoisomer of **10** and an analogous dimer with the double bond as an exomethylene functionality. These may be formed by a minor proton-transfer pathway involving the zwitterions shown in Scheme 1.

[4 + 3]Adducts of 1 with Dienes. Cyclopentadiene–64% isolated yield of a 95:5 mixture of the known[24] **16** + isomer. Furan—the isolated yield was 40% of a single crystalline adduct.[16] Butadiene—8% isolated yield of the known adduct.[25] 2,3-Dimethylbuta-1,3-diene led to a ca. 3% yield of the corresponding adduct *3,4-dimethylbicyclo[4.2.1]non-3-en-9-one*. ^{1}H NMR (400 MHz): 2.28–2.46 (m, 4H); 2.14–2.24 (m, 2H); 1.95–2.02 (m, 2H); 1.57–1.65 (m, 2H); 1.765 (s, 6H). MS *m/z*: 164 (M^+, 100), 110 (48), 95 (45), 82 (47). High-resolution MS: calcd for $C_{11}H_{16}O$, 164.120115; found, 164.1188.

1-Bromo-2-(trimethylsiloxy)-2-cyclopentene (19). The trapping reaction was carried out at −78 °C on a 0.34-mmol scale by including a threefold molar excess of trimethylsilyl chloride along with the PPN^+ $Cr(CO)_4NO^-$ in 2 mL of methylene chloride solvent. The dibromide in 1 mL of methylene chloride was added by syringe over 4 min. Stirring was continued at −78 °C for 5 min, and then 10 mL of dry hexane was slowly added by syringe and the mixture left overnight in a freezer. A GC-MS analysis of this crude hexane solution showed two major peaks corresponding to the chloro and bromo silyl enol ethers. For the former, M^+ = 190 (21) and 192 (7), 175 (45), 155 (41), 154 (61), 93 (70), and 73 (100). For the latter, M^+ = 234 and 236 (11), 155 (81), 154 (75), 139 (80), and 73 (100). The supernatant liquid was removed by syringe, cooled to −78 °C, and filtered through Celite. Evaporation of the solvent produced 0.53 g of an oil (theoretical yield based on the bromo compound = 0.80 g). For the major bromo compound, distinctive ^{1}H NMR peaks (200 MHz) were seen at 4.94 (d, d, J = 2 and 2.5, 1H), 4.78 (an apparent doublet of triplets, J = 6.5 for doublet splitting, the triplet separation of 1.9 Hz may represent some virtual coupling phenomenon, 1H), and 0.26 (9H).

Acknowledgment. We thank the Natural Science and Engineering Research Council of Canada for generous financial support. We also thank Dr. A. Rauk for stimulating discussions concerning the orbital interactions involved in oxyallyl–oxyallyl dimerizations.

Supplementary Material Available: Complete X-ray data for compounds **5** and **9** (31 pages). Observed and calculated structure factors for 5 and 9 (12 pages). This material is contained in many 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.