Preparation and Structure Investigations of Simple Bicyclo[1.1.0]butanones

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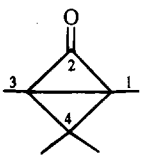
Abstract: Four 1,3-dialkyl-substituted bicyclo[1.1.0]butanones have been prepared. All have been completely characterized by ^1H and ^{13}C NMR spectroscopy, but ^{17}O NMR proved to be particularly diagnostic. The di-*t*-Bu **4** and di-*tert*-amyl **5** members can be obtained in the condensed phase by working quickly and at subambient temperatures, but attempts to obtain X-ray quality crystals have not been successful. The synthetic procedure involves a very rapid and efficient 1,3-elimination of two bromine atoms from 1,3-dibromocyclobutan-2-ones using the salt $PPN^+Cr(CO)_4NO^-$. This reaction is particularly well-suited for exploratory *in situ* low-temperature NMR experiments. Molecular orbital calculations show these ketones to have the typical bent bicyclobutane structure, but the central C1−C3 bond is very long and the carbonyl carbon is distinctly nonplanar. Both of these features can be attributed to a strong interaction of the C1−C3 "bond" with the carbonyl group, and several qualitative orbital interaction schemes are presented to show that bicyclobutanones have on one hand some oxyallyl character and, on the other, some similarities with the bonding in esters. Nucleophiles react with bicyclobutanones in a nonconcerted process to add across the C1−C3 bond.

Bicyclo[1.1.0]butanones (**1**) are the smallest bicyclic ketones. They combine the functionality of a cyclopropanone, a rather unstable class of organic molecules, and a bicyclo[1.1.0]butane skeleton, a well-studied ring system of considerable interest in its own right. In this paper we describe the synthesis, reactivity, and spectroscopic properties of several simple alkyl derivatives of (**1**).



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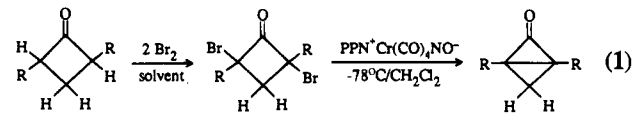
These ketones have been found in this work to be unstable in the condensed phase at room temperature, and although we have attempted to obtain crystals suitable for low-temperature X-ray analysis, this has not yet been successful. In the absence of this definitive structural information, MO computations have been carried out and the accessible experimental spectroscopic data (^1H, ^{13}C, and ^{17}O NMR chemical shifts, dynamic ^1H NMR results, and IR frequencies) have been quite successfully compared to the corresponding computed parameters. Some previous computations involving **1** have been published; in particular a recent study by Ichimura *et al.*[1] suggests that the parent compound **1** (C_4H_4O) may be one of the more stable cyclopropanones in that the corresponding oxyallyl valence-bond isomer, by way of which cyclopropanones commonly react, is computed to lie at 34 kcal/mol higher energy than **1**.

Results

Synthesis. A very simple methodology, previously successful for the preparation of other cyclopropanones,[2] was readily adapted to the bicyclo[1.1.0]butanone case, and ultimately four substituted systems (**2**−**5**) were prepared, as shown below:



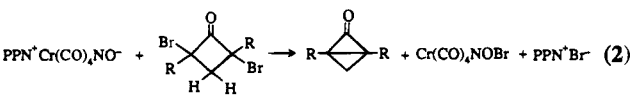
(**1**)

(*cis* or *trans* or mixtures)

10 R=CH_3	*6* R=CH_3 (*cis-trans* mixture)	*2* R=CH_3
11 R=iPr	*7* R=iPr (mainly trans)	*3* R=iPr
12 R=tBu	*8* R=tBu (cis)	*4* R=tBu
13 R=tAmyl	*9* R=tAmyl (cis)	*5* R=tAmyl

For several reasons, the preparation of the parent system (R = H) was not attempted: (1) previous negative results with debromination reactions on unhindered secondary−secondary dibromo ketones, (2) ketones **2**−**5** increase in stability with the bulkier substituents, making these better candidates for isolation, and (3) theoretical studies showing that the alkyl groups do not strongly alter the intrinsic structure of the bicyclo[1.1.0]butanone ring system.

In all cases, the final debromination reaction shown in eq 1 was first studied as a low-temperature NMR experiment, carrying out the reaction in the NMR tube at −78 °C and using CD_2Cl_2 solvent. In all cases, the reaction was virtually instantaneous at −78 °C and the *in situ* yield of the bicyclobutanone was good to essentially quantitative, as monitored by ^1H NMR spectroscopy. The complete stoichiometry of the reaction is shown in eq 2. The PPN^+Br^- byproduct, as



(**2**)

expected, shows only low-field aromatic ^1H NMR signals which do not interfere with the characterization. *In situ* ^{13}C NMR spectra were also obtained, and the PPN^+ signals are in an intermediate position which does not affect the high-field region

[⊗] Abstract published in *Advance ACS Abstracts,* April 1, 1995.

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

(2) Black, C.; Lario, P.; Masters, A. P.; Sorensen, T. S.; Sun, F. *Can. J. Chem.* **1993**, *71*, 1910.

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Table 1. ^1H and ^{13}C NMR[a] Results for Bicyclobutanones **2**–**5**

ketone	H4	^1H NMR of R group	^{13}C NMR (1,3)	^{13}C NMR (4)	^{13}C NMR (2)	^{13}C NMR (R)
2	2.175, 2.870 (1H each)	1.566 (6H)	67.57	36.15	185.12	9.38
3	2.290, 2.603 (1H each)	1.089, 1.052 (both d, $J = 7$, 6H each), 3.344 (hept, $J = 7$, 2H)	75.30	29.38	181.93	19.32, 19.63 (CH_3), 25.19 (CH)
4	2.386, 2.431 (1H each)	1.105 (18H)	81.53	30.10	180.55	27.24 (CH_3), 25.79 (Cq)
5	2.356, 2.419 (1H each)	1.096, 0.906 (6H each), 0.879 (t, $J = 7$, 6H), 1.48 (m, 4H, overlapping quart.)	81.03	33.23[b]	181.29	24.67, 23.63 (CH_3), 8.76 (CH_3 of ethyl), 26.13 (Cq), 34.40[b] (CH_2 of ethyl)

[a] DEPT spectra were obtained where necessary. [b] Assignment may be interchanged.

or the low-field carbonyl region of the ^{13}C spectrum. The $Cr(CO)_4NOBr$ byproduct shows a weak ^{13}C signal at 206.9 ppm.

After the NMR spectra had been measured at *ca.* −80 °C, the solutions were gradually warmed while their ^1H NMR spectra were continuously monitored, in order to get an approximate idea of the decomposition temperature and thus a measure of the particular low-temperature conditions which would then be needed for a more preparative scale workup.

In the case of ketone **2**, generalized decomposition set in at −50 to −60 °C. An attempt was made to isolate **2** by adding 5−10 volumes of liquid propane (−78 °C) to a similarly cooled solution of the ketone, prepared using $CHFCl_2$ (Freon 21) as solvent.[3] After a few minutes, the propane solution was decanted and evaporated to near dryness at *ca.* −78 °C. Addition of a phenyl sulfide solution gave some of the corresponding adduct (see later), showing that the residual material still consisted of **2**, but we were unsuccessful in obtaining crystals of **2** by cooling a fresh propane solution of this residue material. However, a number of diagnostic chemical reactions were performed on *in situ* solutions of **2**, and these will be discussed later, as well as a detailed discussion of the NMR spectra of **2**.

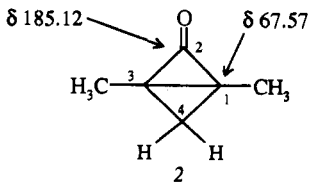
Solutions of ketone **3** were more stable; the rearrangement/decomposition was not rapid until the temperature reached −20 °C. However, ketones **4** and **5** were more stable yet, and so efforts to obtain suitable crystals for X-ray structure analysis were focused on these. Dilute solutions of **4** and **5** were reasonably stable at 20 °C for several hours.

Ketone **4** can be obtained as a white solid by using a workup similar to that described above for the attempted isolation of **2**, except that pentane was used as the diluent. This material can be kept at −78 °C for extended periods without change. We were initially hopeful that this ketone could be obtained in a crystalline form because recrystallization of **4** from pentane at −20 °C yielded small colorless needles. However, NMR and mass spectral analyses showed the material to be a dimer of **4** (see later). Cooling a pentane/CH_2Cl_2 solution of **4** to −78 °C led to the formation of a flocculent white solid, but this material had no obvious crystallinity, and on prolonged storage, the well-defined crystals which did form on the glass surface were again the dimer. Thus, as with many other reactive molecules, the dilute solution stability of **4** is misleading as applied to actually obtaining the pure compound.

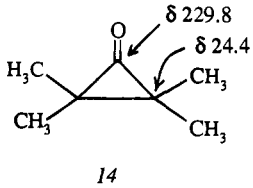
Ketone **5**, like **4**, could not be induced to form well-defined crystals at low temperature.

Assignment (Verification) of the Bicyclobutanone Structure. In accordance with the structure assignments for **2**–**5**, the NMR spectra show the expected C_s symmetry plane through the C2–C4 atoms, and given that these compounds are members of a previously unknown class of organic molecule, the respective ^1H and ^{13}C chemical shifts nevertheless appear in a reasonable position (see Table 1). However, these spectra obviously do not contain much informational complexity.

The C1–C3 ^{13}C peak in **2** is found at a considerably lower field than the similarly substituted carbon in cyclopropanone **14**[2] and the C2 carbonyl ^{13}C peak at a much higher field than that in **14**, as shown in the comparison below:



2



14

In the ^1H NMR spectra, the C4 methylene protons are nonequivalent, as is to be expected, but the chemical shift separation of these is dependent on the nature of the R group (Table 1). Unlike in the *cis*-dibromo precursors **6**, **8**, and **9**, there is no discernible geminal coupling between these C4 protons in any of the bicyclobutanones.

Recently, the tandem procedures of high-level MO calculations and NMR chemical shift computations[4] based on the resulting structure have been verified as a very useful structure proof tool. We were also interested in the MO results for their own sake, and so it was very expedient to carry out this procedure.

The geometry-optimized structure of **2** was obtained using two independent procedures, an MP2/6-31G* level study and the new hybrid density functional Becke 3LYP/6-31G* protocol.[5] Both resulting geometries were very similar, and the latter was used to compute NMR chemical shifts using the IGLO program.[6] As a reference case, we also calculated the structure and NMR shifts for cyclopropanone **14** at the same computational level. The molecular orbital results will be discussed in detail in a subsequent section; here we discuss only the IGLO results, which are presented in Table 2.

The ^{13}C chemical shift agreement (calculated *vs* experimental) for the reference cyclopropanone was quite good, and this lends credence to the method as applied to these very strained molecules. The ^{13}C results for **2** were not as good, but in part this depends on how one makes the comparisons. For example, the computed C1 result for **2** deviates by 7 ppm. However, the overall trends are reproduced reasonably well, i.e., the C2 carbon in **2** is computed to be at quite high field and the C1 carbon to be at abnormally low field, compared to the analogous carbons in **14**.

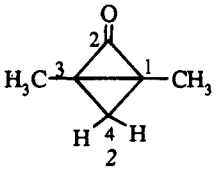
(3) The suitability of the low-boiling $CHFCl_2$ as a reaction solvent was tested by successfully preparing a solution of **2** at −117 °C (^1H NMR measured at −90 °C) using four parts of $CDFCl_2$ (used initially with the chromium salt) and one part of CD_2Cl_2 to dissolve the dibromide.

(4) Sieber, S.; Schleyer, P. von R.; Gauss, J. *J. Am. Chem. Soc.* **1993**, *115*, 6987. See ref 15 in this paper for a compilation of many previous papers by this group.

(5) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A., Gaussian, Inc., Pittsburgh, PA, 1992.

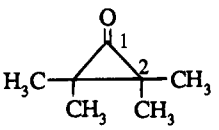
(6) (a) Schindler, M.; Kutzelnigg, W. *J. Chem. Phys.* **1982**, *76*, 1919. (b) Schindler, M. *J. Am. Chem. Soc.* **1987**, *109*, 1020.

Table 2. Comparison of Experimental and Computed NMR Chemical Shifts for Bicyclobutanone **2** and Reference Cyclopropanone **14**



2

	C1	C2	C4	CH_3
^{13}C (exptl)	67.57	185.12	36.15	9.38
^{13}C (calcd)	60.54	190.99	35.56	14.08
	H4 (inner)	H4 (outer)	CH_3	
^{1}H (exptl)[a]	1.99	2.95	1.566	
^{1}H (calcd)	2.175	2.870	1.82	
^{17}O (exptl)[b]	300[d]			
^{17}O (calcd)[c]	291			



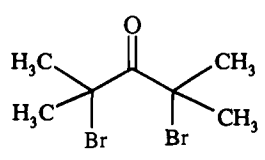
14

	C1	C2	CH_3
^{13}C (exptl)	229.8	24.4	16.6
^{13}C (calcd)	228.1	20.9	19.8
	CH_3		
^{1}H (exptl)	1.19		
^{1}H (calcd)	1.35		
^{17}O (exptl)[b]	512[e]		
^{17}O (calcd)[c]	515		

[a] The assignment of the individual H4 hydrogens has been made on a best fit basis with the calculations since the peaks themselves are otherwise unassignable. [b] Pure water was used as external reference. [c] Since bulk water is difficult to compute as a reference, the calculated values are based on acetone (δ 568) as a secondary reference, the calculations on acetone carried out at the same level as for **2** and **14**. [d] Estimated error limits ±5 ppm. At the measured temperature of −67 °C, the peak has a half-width at half-height of 1.4 kHz. [e] Measured at −30 °C ($\nu_{1/2}$ = *ca.* 250 Hz), −51 °C ($\nu_{1/2}$ = *ca.* 400 Hz) and −73 °C ($\nu_{1/2}$ = 1 kHz). The reported value is for −30 °C and has an estimated uncertainty of ±2 ppm.

Interestingly, the most useful result of the computations was a predicted ^{17}O shift for **2** of 291 ppm. Since normal ketones are usually found at about 550 ± 25 ppm, a value of 291 would be very diagnostic. This unusual result did not seem to be connected with the cyclopropanone functionality since the computed value for **14** was 515 ppm, just slightly higher field than the "normal" range for saturated ketones.

NMR spectra of the ^{17}O-enriched compounds were measured for both **2** and **14**, and for the respective starting materials for each of these, *trans*-dibromo ketone **6** and bromo ketone **15**.



15

Dibromo ketone **6** had δ (^{17}O) 524 ppm, while **15** had 540 ppm, both in the normal expected range. Cyclopropanone **14** had δ 512 ppm, quite close to the calculated value, while bicyclobutanone **2** had a measured value of 300 ppm, again quite close to the computed value and an experimental verification that the ^{17}O shift in bicyclobutanones really is uniquely different from that of other ketones.

Overall, we believe that these IGLO NMR computational results strongly support our bicyclobutanone assignment.

Table 3. Experimental and Computed[a] C=O Stretching Frequencies for Bicyclobutanones **2** and **4** and Cyclopropanone **14**

compound	calcd >C=O stretch (cm^{-1})	exptl >C=O stretch (cm^{-1})
2	1809.5	
4	1779.3	1762.6
14	1824.9	1839, 1820

[a] Frequencies obtained at the Becke 3LYP/6-31G* level, using a scaling factor of 0.95. Ketone **4** was computed using C_s symmetry, which corresponds to a very shallow transition state ($\nu_{imaginary}$ = 13.6 cm^{-1}). We feel that this factor should not materially affect the computed >C=O stretch for this molecule.

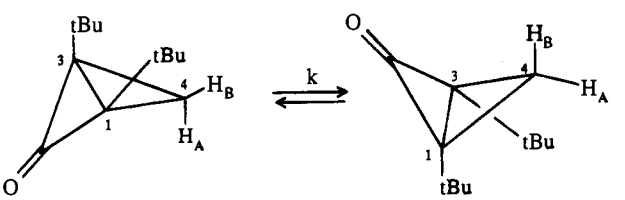
Infrared Spectra. The carbonyl stretching frequency for bicyclobutanones **4** and **5** was found at 1762−1763 cm^{-1}, which was surprising since cyclopropanones typically have values >1800 cm^{-1}; e.g., cyclopropanone **14** in methylene chloride has a double peak at 1839 and 1820 cm^{-1}.[2,7] Even the dibromo ketone precursor to bicyclobutanone **4** has a higher frequency C=O stretch (1782 cm^{-1}), in the normal range however for cyclobutanones.

In order to corroborate these lower than expected values, frequency calculations were carried out using the optimized geometries for ketones **2** and **4**, as well as for the reference cyclopropanone **14**. Using a scaling factor of 0.95, the calculated values are compared in Table 3 with experimental values. The calculated C=O stretching frequency for **4** is about 17 cm^{-1} too high, but the more important result is that this C=O stretch is 45.6 cm^{-1} lower than that calculated for **14**. The bicyclobutanone **2** is computed to have a considerably higher C=O stretch frequency than **4** but *in situ* IR experiments involving **2** are unreliable because of the strong NO and CO stretches of the $Cr(CO)_4NOBr$ byproduct and also possible interference from the phenyl rings of the PPN^+ cation.

Given that it is still difficult to compute frequencies which exactly match those of experiment (the latter are in solution as well), we feel that the IR results support the bicyclobutanone assignment.

Dynamic ^{1}H NMR Spectra of 4 and 5. A Low-Energy Ring Inversion Process. As mentioned, ketones **4** and **5** were stable enough in solution that they could be briefly warmed to 30 °C. At this temperature, the ^{1}H NMR spectra of both **4** and **5** show a broadened singlet for the two C4 hydrogens. By cooling the solution, one can observe decoalescence behavior and formation of the two separate peaks described previously (see Table 1). The process is reversible, indicating that the two C4 hydrogens are rapidly interconverting on the NMR time scale *at room temperature*. The *t*-Bu signal is unaffected.

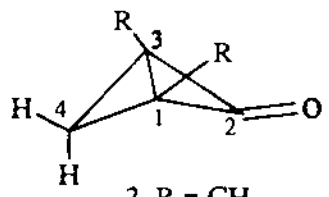
These results can be rationalized as a ring inversion process:

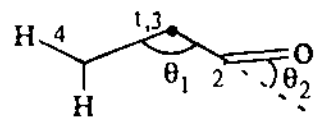


This mechanism is confirmed using bicyclobutanone **5**, where, besides the C4 hydrogen interconversion, one also sees concomitant line-broadening and coalescence of the diastereotopic methyl and methylene moieties of the *tert*-amyl group, but no change in the $-CH_2-CH_3$ signal. Unlike the C4 hydrogen interconversion alone, these "extra" observations directly require

(7) Turro, N. J. *Acc. Chem. Res.* **1969**, *2*, 25. Reported as 1843 and 1823 cm^{-1} in methylene chloride and 1825 cm^{-1} in pentane.

Table 4. Geometric Parameters for the Computed Structures of Bicyclobutanones **2** and **4**





2 R = CH_3
4 R = tBu

Bond Distances

	C1—C3	C=O	C1—C2[a]	C1—C4[a]	α-C of R on 1 to α-C of R on 3
2	1.665	1.213	1.451	1.499	3.750
4	1.674	1.219	1.450	1.505	4.070

Bond Angles

	θ_1 (deg)	θ_2 (deg)	∠(1−2−3) (deg)	∠(1−4−3) (deg)
2	134.6	14.8	70.0	67.4
4	132.4	13.3	70.5	67.6

[a] Ketone **2** has C_s symmetry. Ketone **4** was computed under C_s symmetry constraints because of the large size of the molecule. This geometry corresponds to a very shallow transition state ($\nu_{imaginary}$ = 13.6 cm^{-1}) involving rotations of the *t*-Bu group. In NMR experiments in solution the molecule would show effective C_s symmetry.

that there be inversion at the C1 and C3 centers, as of course does happen in the ring inversion shown above.

The rate for the ring inversion was determined by matching experimental and computed line shapes in the usual way, giving $\Delta G^{\ddagger}$ = 16.7 kcal/mol and $\Delta H^{\ddagger}$ = 16 ± 1 kcal/mol for **4**. Qualitatively, **5** appears to have an inversion barrier almost identical to that of **4**.

There has been considerable discussion[8] of the corresponding inversion process in bicyclobutanes.

Molecular Orbital Calculations. These have already been referred to in connection with the IR frequency and NMR chemical shift computations. In this section we present and discuss the computed structures and the nature of the orbital interactions. The structure of ketone **2** was optimized at both MP2/6-31G* and Becke 3LYP/6-31G* levels, and these produced very similar results. The much larger analog **4** was optimized using a C_s symmetry and the Becke 3LYP/6-31G* level. In most respects, the computed structures of **2** and **4** are quite similar, and the pertinent data are given in Table 4.

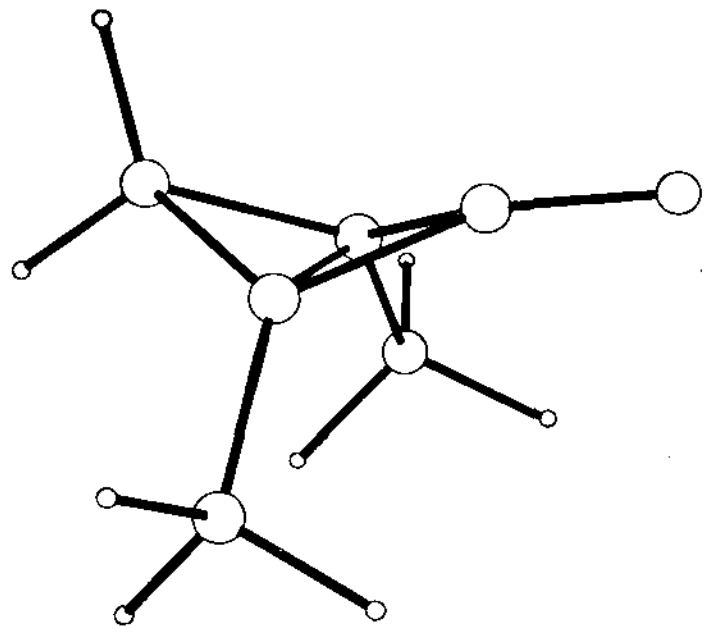
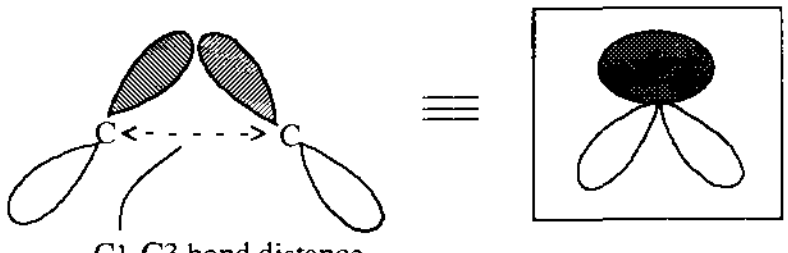


Figure 1. Optimized geometry of 1,3-dimethylbicyclobutanone (**2**) calculated as discussed in the text. Note the nonplanar carbonyl carbon.

There are a number of geometric-orbital interaction features in a bicyclo[1.1.0]butane ring *per se* which are quite unique, and these have been discussed a lot in the literature. For example, the bridgehead carbons can have all four bonds emanating from one hemisphere of space,[16] and this feature is also present in the computed structures of **2** and **4**. However, there are two major geometric features unique to our systems which are very noteworthy: (1) The computed C1—C3 bond distance of 1.665 and 1.674 Å in **2** and **4** respectively, is quite unusual for a bicyclo[1.1.0]butane ring, where this bond is often shorter than a normal C—C single bond distance.[17] (2) The >C=O is nonplanar, by 14.8° in **2** and 13.3° in **4**. Even more unusual is that the >C=O is bent *toward* the donor C1—C3 σ-bond.[24] The computed structure of **2** is shown in Figure 1.

The nonplanar >C=O and the long C—C central bond in **2** can be rationalized from an analysis of the orbital interactions. This central C1—C3 bond involves a nearly pure p—p-overlap[16] (banana bond), as sketched below:



C1-C3 bond distance ≡ treat as a single filled ($2e^-$) p-like orbital

Because these p-orbitals are partially π-like with respect to the

(8) The inversion barrier in the bicyclobutanones **4** and **5** is considerably lower than that for 1,3-diphenyl-2,4-dicarbomethoxybicyclu[1.1.0]butane ($\Delta H^{\ddagger}$ = 26 ± 2 kcal/mol).[9] For the parent hydrocarbon even higher barriers have been computed,[10,11,12] including a detailed picture of the molecular motions accompanying the inversion. For **4** and **5**, the nature of the inversion barrier transition state is presently in some doubt. Ichimura *et al.*[1] have computed the planar parent (C_4H_4O) singlet cyclobutyl oxyallyl, using a two configuration SCF procedure, and report this to be a local minimum structure lying 34 kcal/mol higher than the bicyclobutanone structure. We have carried out MP2/6-31G* and/or Becke 3LYP/6-31G* computations on this same planar species, and on the 1,3-dimethyl analog, and find them both to be transition states (one large imaginary frequency). The parent system was also computed at a two-configuration GVB/6-31G* level and was again a transition state. We recognize however that a multiconfiguration approach may be obligatory in this case, and we hope to use the CASPT2[13] procedure when frequencies become available at this level. A computation of the closed (nonplanar) and open (planar) forms of bicyclobutanedione has been reported,[14] and the energy difference is quite small, suggesting therefore that the inversion barrier in the closed form may be quite low. Since there are no C4 hydrogens in this molecule, a possible dynamic ^1H NMR study would require suitable substituents on the C1—C3 carbons. A higher level computational study of the planar dione has also been published.[15]

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(17) In bicyclo[1.1.0]butane the central bond is 1.497 Å,[18] reasonably similar to a computed value of 1.478 Å.[19] When a carbonyl group is present as a substituent on the C2 or C4 carbon, the C1—C3 bond length can decrease even further, and in a tricyclu[2.1.0.$0^{2,5}$]pentan-3-one derivative, this C1—C3 distance is an incredibly short 1.408 Å.[20] This C1—C3 distance has been strongly correlated with the dihedral angle between the two cyclopropane rings.[10,20-22] An MO analysis of the above tricyclic ketone has appeared,[23] and the very short bond is rationalized as the removal of C1—C3 antibonding interactions, akin to arguments used to explain short C_{α}—C_{α} bonds in cyclopropane carbonyl compounds. At the other extreme, bicyclo[1.1.0]butanedione has been computed[14] at a GVB MO level to have a C1—C3 bond distance of 1.888 Å.

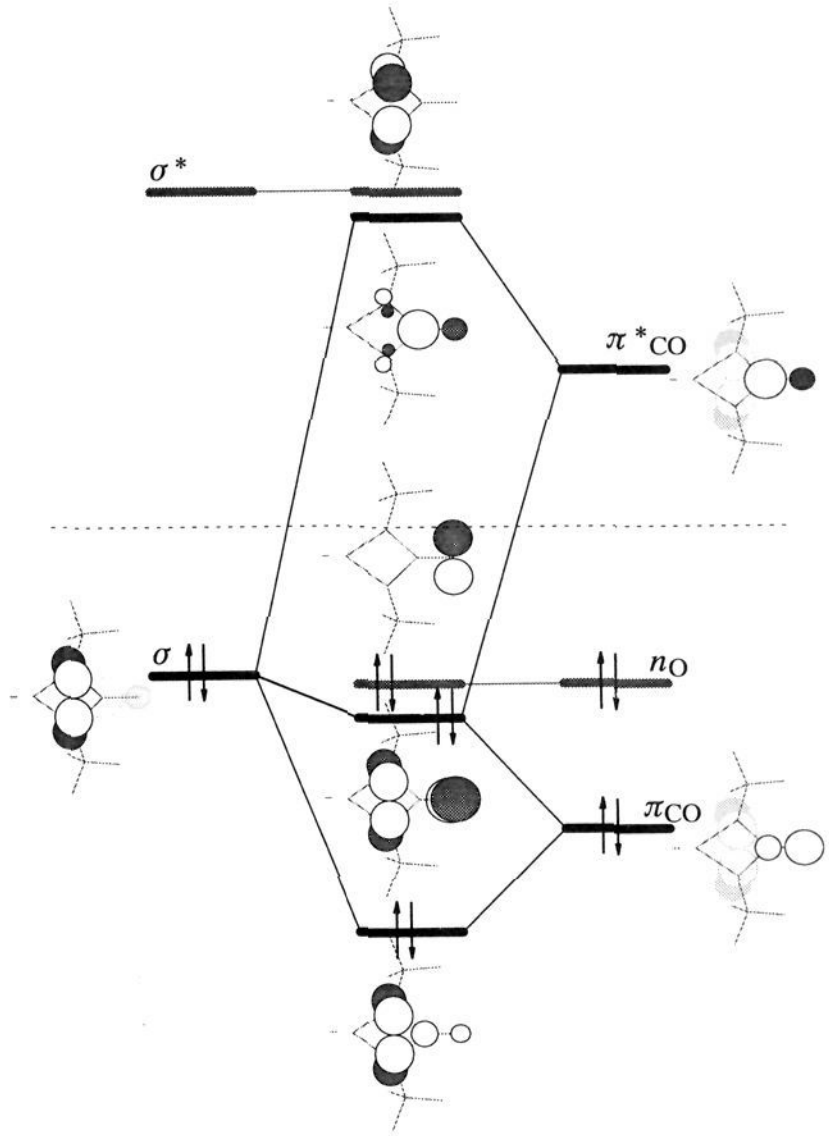


Figure 2. Interaction of the filled ($2e^-$) C1−C3 bonding orbital with the π- and π^*-orbitals of the carbonyl group.

carbonyl group and are close in space, there is predicted to be a strong interaction between them. In Figure 2 we show an orbital-interaction analysis in which the C1−C3 bond is treated as a filled ($2e^-$) p-like orbital interacting with the >C=O π- and π^*-orbitals (somewhat analogous to the interaction of the p_z lone pair electrons in the ether oxygen of an ester with the >C=O portion).

A related approach is to consider **2** to be a perturbed oxyallyl species, **16**. The four Hückel π MOs for this system and the n lone pair on oxygen are sketched in Figure 3b. Direct p−p overlap of the C1−C3 centers is probably significant in a cyclobutane ring but is not a strong interaction because of the distance involved. If the C1−C3 p-orbitals of the oxyallyl are now rotated toward each other by approximately 45° (disrotation) so that some σ-overlap occurs, then the HOMO orbitals are lowered, the LUMO is strongly raised, and the LUMO + 1 is essentially unaffected so that this now drops below the original LUMO in energy; i.e., the interaction diagram becomes identical to that shown in Figure 2. Using this approach, however, one

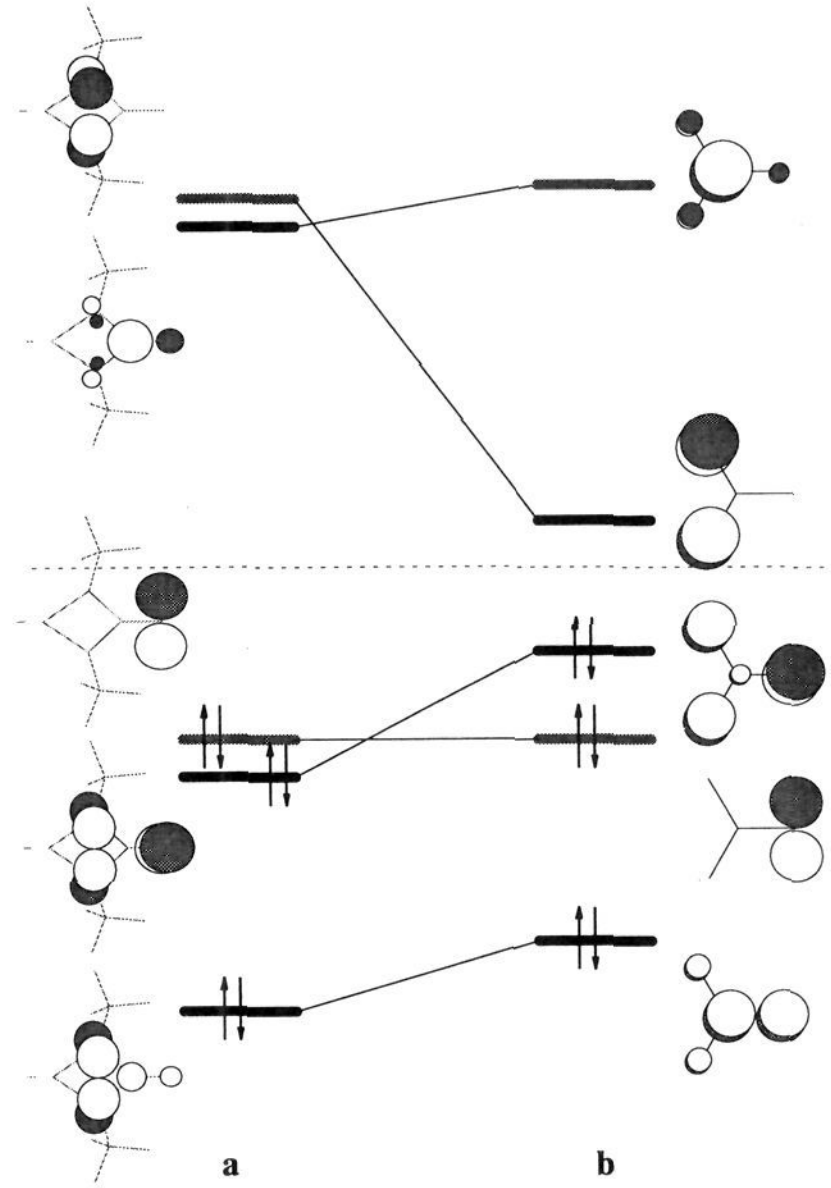
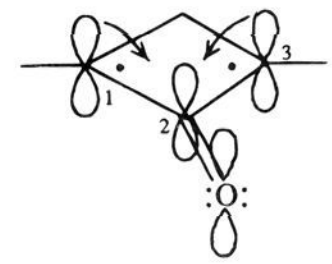


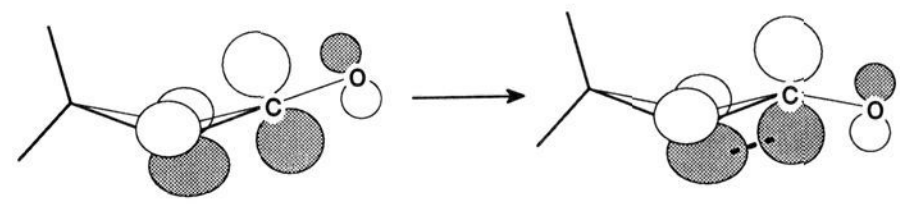
Figure 3. Correlation of the four π-orbitals in cyclobutyl oxyallyl (b) with those in a bicyclobutanone (a). The interconversion from right to left involves a partial disrotatory rotation of the oxyallyl terminal π orbitals.



16

can see more clearly that bicyclobutanone **2** has some cyclobutyl oxyallyl character.

The nonplanar carbonyl can be rationalized because the overlap angle of the carbonyl carbon and the p-orbitals on C1−C3 can be further improved by tipping the carbonyl carbon, as shown below:



This nonplanarity implies that the interaction is energetically favorable. Compared to the C1−C3 bond length in bicyclobutane, where no carbonyl is present, the net transfer of electron density from the C1−C3 bond as a consequence of mixing with the π- and π^*-orbitals results in a much longer bond (1.50 Å *vs* 1.665 Å).

In reality there are two opposing factors in determining this C1−C3 bond length, since a longer bond implies more p-character in the bond, which in turn results in better delocalization overlap with the carbonyl group. However, the σ-com-

(18) (a) Marlin, H. D.; Cox, K. *J. Am. Chem. Soc.* **1966**, *88*, 5049. (b) Cox, W. K.; Harmony, M. D.; Nelson, G.; Wiberg, K. B. *J. Chem. Phys.* **1969**, *50*, 1976.

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(22) Dowd, P.; Garner, P.; Schappert, R.; Irngartinger, H.; Goldman, A. *J. Org. Chem.* **1982**, *47*, 4240.

(23) Gleiter, R.; Haider, R.; Bischof, P.; Zefirov, N. S.; Boganov, A. M. *J. Org. Chem.* **1984**, *49*, 375.

(24) It is not unusual to find nonplanar carbonyl groups in the X-ray structures of complex carbonyl compounds. These situations correspond to an arrested nucleophilic attack by a rigidly positioned nitrogen atom, which is spatially close but which may be remote in terms of the bonding network. As expected, this interaction moves the carbonyl oxygen *away* from the nucleophilic center. Dunitz, J. D. *X-ray Analysis and the Sturcture of Organic Molecules*; Cornell University Press: Ithaca, NY, 1978; p 369.

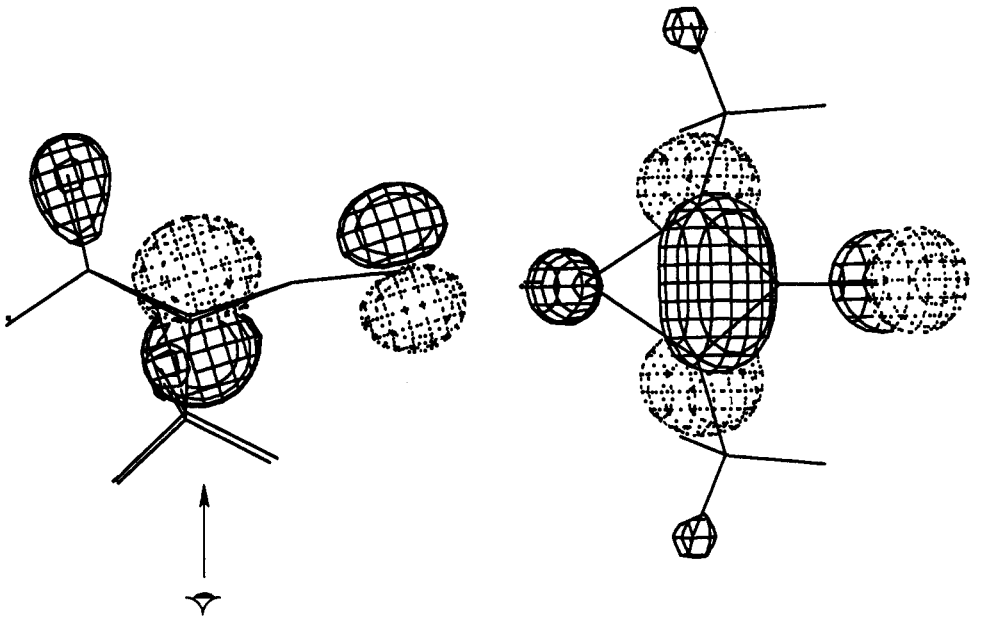
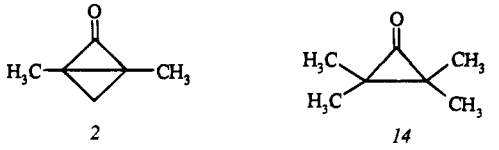


Figure 4. Two views of the HOMO-1 orbital in **2** as produced from the *ab initio* calculations and displayed as modified Salem–Jorgensen plots.[52] The view in (a) is through the C1–C3 bond, while in (b), the spatial character of the top and bottom lobes of the C1–C3 part of this overall orbital is emphasized. Although the interaction with the carbonyl π-system is nonbonding in this orbital, there is a lower lying orbital with in-phase overlap.

Table 5. Selected Orbital Energies for Bicyclobutanone **2** and Cyclopropanone **14** from *ab initio* Calculations[a]



LUMO + 1	σ^*	+0.031	LUMO + 1		+0.070
LUMO	π^*	+0.020	LUMO	π^*	-0.023
HOMO	n	-0.231	HOMO	n	-0.217
HOMO-1		-0.244	HOMO-1		-0.274

[a] Becke 3LYP/6-31G* level. Energies are in hartrees.

ponent is also favorable to the bond, and so a compromise between these mutually exclusive effects is reached.

The *ab initio* molecular orbitals resulting from the Becke 3LYP/6-31G* computation of **2** have the essential features shown in Figures 2 and 3. It is instructive however to show the HOMO-1 orbital plot (Figure 4, two views), which should correspond to the "sketched" HOMO-1 orbital in Figures 2 and 3, in order to visualize the "real" extent to which there is computed electron density in the region above the C1–C3 "bond". As can be seen in Figure 4, a view through the C1–C3 atoms does indeed look very p-orbital-like. In the *ab initio* results, the HOMO orbital is the n-orbital on oxygen. Just as in esters, the n → π^* transition in **2** should be shifted to shorter wavelengths, compared to a normal ketone (including simple cyclopropanones), because the π^* (LUMO) orbital in **2** has been significantly raised in energy (see Figure 2).

The n → π^* energy gap is an important factor in determining ^{17}O chemical shifts,[25] and one can speculate that the fact that ketone **2** has an ^{17}O chemical shift very similar to that of an ester carbonyl oxygen is a consequence of this increased n → π^* gap in both bicyclobutanones (proposed) and esters (a fact).

In Table 5, the orbital energies of the top two occupied and lowest two unoccupied orbitals are listed, along with those computed at the same level for tetramethylcyclopropanone **14**, which has a relatively normal ^{17}O chemical shift. In each case, the HOMO orbital is the n-orbital on oxygen and the LUMO is essentially a π^*-orbital. The gap is indeed significantly larger for the bicyclobutanone.[26]

Chemical Reactions of the Bicyclobutanones. These studies have focused on the reactions of simple X–H compounds (X = O, N, S) with the bicyclobutanones and on the outcome of thermal rearrangements or dimerization processes, which are of practical interest when trying to isolate these compounds.

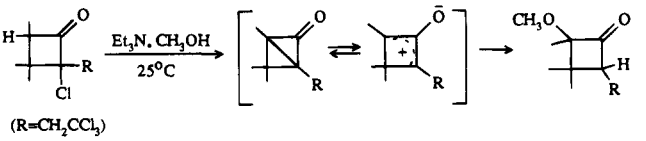
All of these addition reactions involve cleavage of the C1–C3 bond. In no case have we isolated a Favorski-type product (derivatives of 1,2-dialkylcyclopropanecarboxylic acid), which might be the expected end product of nucleophilic attack at the carbonyl group. This agrees with previous work[27] showing that the Favorski contraction of α-halocyclobutanones proceeds by the semi-benzylic mechanism, which does not involve a bicyclobutanone intermediate.[28]

(25) McFarlane, W.; McFarlane, H. C. E. in *Multinuclear NMR*; Mason, J., Ed.; Plenum Press: New York, 1987; Chapter 14.

(26) We are using this data in a qualitative way since the orbital energy differences in Table 5 do not directly represent the UV transition energies. It is well-known that an extensive CI procedure needs to be used to obtain reasonable estimates of these.

(27) (a) Conia, J. M.; Salaun, J. R. *Tetrahedron Lett.* **1963**, 1175. (b) Conia, J. M.; Salaun, J. R. *Bull. Soc. Chim. Fr.* **1964**, 1957. (c) Salaun, J. R.; Garnier, B.; Conia, J. M. *Tetrahedron* **1973**, *29*, 2895. (d) Rappe, C.; Knutsson, L. *Acta Chem. Scand.* **1967**, *21*, 163.

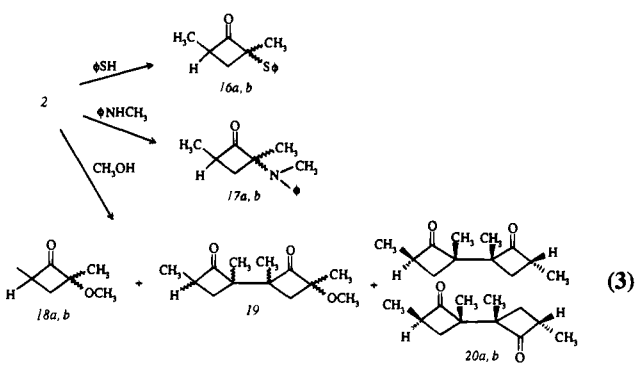
(28) A bicyclobutanone (and/or cyclobutyl oxyallyl) intermediate has however been postulated[29–33] in explaining the results of abnormal ("cine") nucleophilic substitution reactions in some α-halocyclobutanones (both mono and more complex cases). The following is representative:[32]



(R=CH_2CCl_3)

Our present work would favor a bicyclobutanone intermediate (see also ref 8 regarding the existence of a cyclobutyl oxyallyl).

The following reactions were carried out on solutions of **2**, as shown in eq 3. The additions are not stereospecific, which in turn suggests that the reaction is not concerted. The reactions

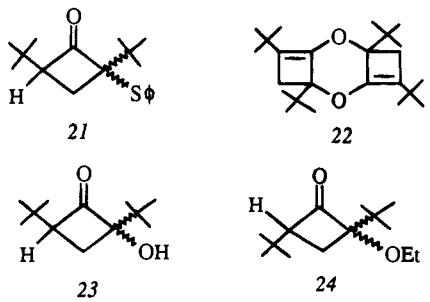


(3)

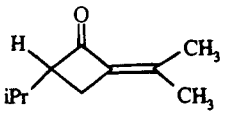
were carried out at −78 °C, and the solution was then warmed to room temperature, but since **2** itself decomposes at −50 to −60 °C, it seems likely that additions actually occur at the lower temperatures. The observation that the methanolysis reaction results in some dimer products[34] may be an indication that this reaction is not as fast as the other two. There is some indication that stereoisomers **20a,b** are formed in small amounts in the purely thermal decomposition of **2**.[35]

Ketone **4** also reacts with phenyl sulfide to give the 1,3-adducts **21**. The 1,3-addition of *N*-methylaniline to **2** suggests that a nucleophilic attack on C1(C3) initiates the reaction.[36] This is quite feasible from the molecular orbital D−A standpoint since the σ^*(C1−C3) and π^*(C=O) orbitals (LUMO + 1 and LUMO) are almost the same energy (Table 5).

Dimerization of 4. As described earlier, concentrated solutions of the bicyclobutanone **4**, intended for recrystallization, yield instead crystals of a dimer. The structure of this dimer **22** was easily solved because a closely-related species has been previously isolated[39a] from a dimethylcyclopentyl oxyallyl dimerization. The stereochemistry of **22** is not known. Dimer **22** is not very stable and reacts rapidly with moisture or ethanol to give the corresponding monomers **23** and **24**.



Rearrangement of 3. When the original −78 °C solution of **3** is warmed to about −20 °C, there is rapid loss of **3**, as monitored by ^{1}H NMR spectroscopy. In part, **3** has rearranged to the isomeric cyclobutanone **25**, and ^{1}H peaks for this can be detected in the crude solution. After workup, **25** was isolated and the spectra could be compared to the closely related *tert*-Bu derivative, a known compound.



25

The considerably increased solution stability of bicyclobutanones **4** and **5**, as compared to **3** (or **2**), seems to not be entirely a steric effect but is also a result of having no hydrogens on the α-carbon of the substituent, thus blocking the rearrangement pathway shown for **3** → **25**. A rearrangement similar to **3** → **25** has previously been noted[2] for a number of substituted cyclopropanones, and in these cases also, *t*-Bu groups "block" this rearrangement.

Discussion

Several bicyclobutanones have been shown in this work to be isolatable compounds, using a low-temperature synthesis and workup procedure. This somewhat fragile stability can be compared with that exhibited by a number of related structures, methylenebicyclo[1.1.0]butane,[40,41] dimethylenebicyclo[1.1.0]-butane,[42−44] methylenebicyclo[1.1.0]butanone,[15,42c] bicyclo-[2.1.0]pentan-5-ones,[1,39] and 5-methylenebicyclo[2.1.0]pentane.[1,45] Only in the second entry above has a closed structure form been detected; in the other cases either singlet or triplet diradicals are formed or proposed. In addition to these, the unknown bicyclobutanedione[14,15] system is a possible candidate for at least *in situ* solution synthesis, and may in fact be accessible using a methodology very similar to that employed in this work. There is also an expectation that the parent bicyclobutanone may be characterizable as a solution species if a suitable low-temperature synthetic procedure can be found, and it may eventually be possible to modify the present procedure to this end.

Experimental Section

Mass spectra and capillary GC were carried out on a Hewlett-Packard Model 5890 gas chromatograph equipped with a 5971 mass selective detector. NMR spectroscopy was carried out on a Bruker ACE-200, AMX2-300, or AM-400 (δ values for starting materials, etc., in $CDCl_3$, J in hertz). For ^{17}O studies, external H_2O was used as the reference (δ 0). For ^{1}H NMR, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. For $^{13}C\{^1H\}$ NMR, q = quaternary, the carbon multiplicities determined from DEPT 90 and 135 spectra. Infrared spectra were determined on a Mattson Model 4030 interfer-

(29) Harding, K. E.; Trotter, J. W.; May, L. M. *J. Org. Chem.* **1977**, *42*, 2715.
(30) Hassner, A.; Dillon, J. L.; Krepski, L. R.; Onan, K. D. *Tetrahedron Lett.* **1983**, *24*, 1135.
(31) Hassner, A.; Dillon, J. L.; Onan, K. D. *J. Org. Chem.* **1986**, *51*, 3315.
(32) Martin, P.; Greuter, H.; Riss, G.; Winkler, T.; Bellus, D. *Helv. Chim. Acta.* **1981**, *64*, 2571.
(33) Hassner, A.; Naidorf-Meir, S.; Gottlieb, H. E. *Tetrahed. Lett.* **1990**, *31*, 2181.
(34) A related dimer has been isolated in a nucleophilic reaction of an α-chlorocyclobutanone with H_2O−Et_3N.[33]
(35) It is by no means clear where the extra hydrogens in **20a,b** come from.
(36) The reaction chemistry of bicyclo[1.1.0]butane can also involve 1,3-addition of nucleophile−eletrophile, but these usually involve initial electrophile attack.[37] For example, iodination proceeds to give 1,3-diiodobutane isomers, but other reactions result in cyclopropylcarbinyl products or mixtures *via* the well-known cyclobutyl−cyclopropylcarbinyl carbocation rearrangement. Sulfides also readily add across the 1,3-bond, by means of a radical-chain reaction mechanism.[38]
(37) Wiberg, K. B. *Record Chem. Progr.* **1965**, *26*, 143.
(38) Szeimes, G.; Schlosser, A.; Philipp, F.; Dietz, P.; Mickler, W. *Chem. Ber.* **1978**, *111*, 1922.
(39) (a) Masters, A. P.; Parvez, M.; Sorensen, T. S.; Sun, F. *J. Am. Chem. Soc.* **1994**, *116*, 2804 and references therein. (b) Hirano, T.; Kumagai, T.; Miyashi, T.; Akiyama, K.; Ikegami, Y. *J. Org. Chem.* **1991**, *56*, 1907.
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(41) Lahti, P. M.; Berson, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 7011.
(42) (a) Snyder, G. J.; Dougherty, D. A. *J. Am. Chem. Soc.* **1989**, *111*, 3926. (b) Snyder, G. J.; Dougherty, D. A. *J. Am. Chem. Soc.* **1985**, *107*, 1774. (c) Dowd, P.; Paik, Y. H. *J. Am. Chem. Soc.* **1986**, *108*, 2788.
(43) Snyder, G. J.; Dougherty, D. A. *J. Am. Chem. Soc.* **1989**, *111*, 3942.
(44) Feller, D.; Davison, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1982**, *104*, 1216.
(45) (a) Platz, M. S.; McBride, J. M.; Little, R. D.; Harrison, J. J.; Shaw, A.; Potter, S. E.; Berson, J. A. *J. Am. Chem. Soc.*, **1976**, *98*, 5726. (b) Berson, J. A. In *Diradicals*; Borden, W. T., Ed.; Wiley: New York, 1982. (c) Chisholm, W. P.; Yu, H. L.; Murugesan, R.; Weissman, S. I.; Hilinski, E. F.; Berson, J. A. *J. Am. Chem. Soc.* **1984**, *106*, 4419.

ometer. Analytical mass spectra were obtained on a Kratos MS-80. Melting points and boiling points are uncorrected.

2,4-Dibromo-2,4-dimethylcyclobutanone (6). The ketone (*cis*–*trans* mixture[46]), 1.5 g (15 mmol) in 20 mL of CCl_4, was stirred overnight at room temperature with 2.5 mL of Br_2 (49 mmol) and 1 drop of 48% HBr. After workup, the residue was distilled, bp 87–90 °C (25 mm.Hg), to give 3.24 g (12.7 mmol, 83%) of a 77:23 *trans*–*cis* mixture of the title compound. ^{1}H NMR (400 MHz)(*trans-6*), δ 2.026 (s, 6H); 2.96 (s, 2H); (*cis-6*) δ 1.858 (s, 6H); 3.097 and 2.715 (both d, J = 14.8, 1H each). ^{13}C NMR: (*trans-6*) δ 28.05 (CH_3 × 2); 52.00 (CH_2); 62.41 (Cq × 2); 200.30 (C=O); (*cis-6*) 26.57 (CH_3 × 2); 51.92 (CH_2); 59.40 (Cq × 2); 201.51 (C=O). Gc–MS: nearly identical for *cis*- and *trans*-isomers, *m/e* 254, 256, 258 (M^+); 134, 136 (100). Anal. Calcd for $C_6H_8Br_2O$: C, 28.15; H, 3.15. Found: C, 28.04; H, 3.13.

2,4-Dibromo-2,4-diisopropylcyclobutanone (7). The ketone (*cis*–*trans* mixture[47]) was brominated as for **6**, except that the solution was heated to 60 °C for 5 h. After workup, the residue solidified in the freezer. This material was purified further by low-temperature (−20 °C) crystallization from hexane. The ^{1}H NMR shows that the *trans*-isomer is the major product, along with a minor amount of the *cis*-isomer. ^{1}H NMR: (*trans-7*) δ 1.05, 1.12 (both d, J = 7, 6H each); 2.197 (hept, J = 7, 2H); 2.87 (s, 2H). ^{13}C NMR: (*trans-7*) δ 18.21, 18.59 (2 × CH_3 each); 36.64 (CH_2); 47.09 (CH × 2); 75.57 (Cq × 2); 199.10 (C=O). MS: *m/e* 310, 312, 314 (M^+); 162, 164 (100); 147, 149 (60). IR: $\nu_{C=O}$ = 1760.7 cm^{-1}. Exact mass: calcd for $C_{10}H_{16}O^{79}Br^{81}Br$, 311.954 83; found, 311.9557.

***cis*-2,4-Dibromo-2,4-di-*tert*-butylcyclobutanone (8)** was prepared as described.[48] ^{1}H NMR (400 MHz): δ 1.17 (s, 18H); 2.63 and 3.05 (both d, J = 15.5, 1H each). ^{13}C NMR (100 MHz), δ 27.16 (CH_3 × 6); 37.71 (CH_2); 41.48 (Cq × 2); 77.32 (Cq × 2); 201.85 (C=O).

***cis*-2,4-Dibromo-2,4-bis(1,1-dimethylpropyl)cyclobutanone (9).** The hydrocarbon **13**, mainly *cis*, was prepared (0.27–6.7 mmol scale reactions) using a procedure identical to the literature[48] preparation of **12**, except that ethylmagnesium bromide was used. The reaction involves a two-step double-conjugate addition to 2,4-diisopropylidenecyclobutanone. The intermediates were verified by ^{1}H and ^{13}C NMR spectroscopy but were not further purified. ^{1}H NMR (400 MHz) (2-isopropylidene-4-(1,1-dimethylpropyl)cyclobutanone) δ 0.83 (t, J = 7.5, 3H); 0.86 (s, 3H); 0.96 (s, 3H); 1.25–1.45 (m, 2H); 1.743 (br s, 3H); 2.06 (t, J = 0.5, 3H); 2.28–2.38 (m, 1H); 2.45–2.55 (m, 1H); 2.91 (dd, J = 9.1, 6.5, 1H). ^{13}C NMR (100 MHz): δ 8.20 (CH_3); 20.93 (CH_3); 21.35 (CH_2); 23.11 (CH_3); 23.33 (CH_3); 23.99 (CH_3); 33.13 (CH_2); 35.16 (Cq); 64.32 (CH); 139.93 (Cq); 141.20 (Cq); 202.4 (C=O). MS: (2-isopropylidene-4-(1,1-dimethylpropyl)cyclobutanone) *m/e* 180 (M^+); 165 (25); 151 (60); 137 (60); 67 (100). ^{1}H NMR (400 MHz): (*cis*-2,4-bis(1,1-dimethylpropyl)cyclobutanone (**13**)), δ 0.815 (t, J = 7, 6H); 0.86 (s, 6H); 0.95 (s, 6H); 1.2–1.4 (m, 4H); 1.74 (td, J = 9.5, 10.5 1H); 1.95 (td, J = 10.5, 10.5, 1H); 2.94 (dd, J = 9.5, 10.5, 2H). ^{13}C NMR (100 MHz): (*cis*-2,4-bis(1,1-dimethylpropyl)-cyclobutanone (**13**)), δ 8.12 (CH_3 × 2); 15.57 (Cq × 2); 23.62 (CH_3 × 2); 24.24 (CH_3 × 2); 33.40 (CH_2); 34.85 (CH_2 × 2); 64.60 (CH × 2); 213.4 (C=O). Ms: (*cis*-2,4-*bis*(1,1-dimethylpropyl)cyclobutanone (**13**)), *m/e* 210 (M^+); 83 (100).

The title dibromide was prepared by reacting the crude **13** (6.7 mmol scale) with 3 equiv of Br_2 in CCl_4 (16 mL). This solution was sealed in a glass ampule and heated in an oven at 100 °C for 2 days. After workup, the residue could be recrystallized from 1:20 hexane–ethyl acetate to give pure **9**, white needles, mp 90–92 °C. ^{1}H NMR (200 MHz) δ 0.88 (t, J = 7.5, 6H); 1.08 (s, 6H); 1.14 (s, 6H); 1.4–1.8 (m, 4H); 3.16 and 2.66 (both d, J = 15.6, 1H each). ^{13}C NMR (100 MHz): δ 8.38 (CH_3 × 2); 22.72 (CH_3 × 2); 23.90 (CH_3 × 2); 31.62 (CH_2 × 2); 40.53 (Cq × 2); 42.24 (CH_2); 78.54 (Cq × 2); 202.12 (C=O). MS: *m/e* 190, 192 (75); 161, 163 (100). Anal. Calcd for $C_{14}H_{24}Br_2O$: C, 45.67; H, 6.57. Found: C, 46.48; H, 6.36.

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. The $PPN^+Cr(CO)_4NO^-$ [49] salt can be weighed and transferred to the Schlenk in air if one works quickly. After nitrogen purging and cooling the flask to −78 °C, methylene chloride was added to dissolve the salt (generally about 1 mL of CH_2Cl_2 for a 0.5 mmol scale). Another 1 mL of methylene chloride was used to dissolve the dibromo ketone. The deep-red color of $Cr(CO)_4NO^-$ disappears immediately, an indication that the reaction is essentially instantaneous. In most cases however a slight excess of the reagent was used to ensure that no starting material remained, and in these cases one does not observe the full color change. In the case of dibromo ketone **6** and bicyclobutanone **2**, the eq 1 reaction was also carried out using Freon 21 ($CFCl_2H$) as the solvent ($CFCl_2D$ for the NMR experiments). This was done in order to facilitate solvent removed at low temperature (under *ca.* 0.1 mmHg vacuum evaporation conditions). For bicyclobutanones **4** and **5**, prepared on a 0.3–0.45 mmol scale using a total volume of *ca.* 3 mL of CH_2Cl_2 solvent, pentane was slowly added to the −78 °C solution (10–15 mL) stirring was continued. After 5 min, the supernatant solvent was transferred by double-tip needle to a clean Schlenk tube and the solvents evaporated at *ca.* −30 °C to give a white solid. This material was thoroughly washed with 3 mL of cold pentane and the wash solution removed by double-tip needle and discarded. The residual wash solvent was again pumped off to give a dry solid residue which was stored at −78 °C when not being used. IR measurements on this material did not show appreciable $Cr(CO)_4NOBr$ to be present. Attempted recrystallization of **4** from hexane at −20 °C gave only crystals of a dimer.

***In Situ* NMR Experiments.** Bicyclobutanones **2**–**5** were initially characterized at *ca.* −80 °C by conducting the preparation in a septum-capped 5 mm NMR tube at −78 °C using CD_2Cl_2 (or $CFCl_2D$ in one case involving **2**). ^{1}H NMR spectra were referenced relative to $CHDCl_2$ (δ 5.33) and ^{13}C NMR relative to $^{13}CD_2Cl_2$ (δ 53.80). The *in situ* solution was gradually warmed to *ca.* −10 °C while ^{1}H NMR spectra were observed at intervals. At about 0 °C, the $Cr(CO)_4NOBr$ byproduct decarbonylates and the quality of the spectra markedly decreases (probable paramagnetic material present). For the ring inversion ^{1}H NMR studies of **4** and **5**, the isolated bicyclobutanones were used.

^{17}O NMR Experiments. Dibromo ketone **6**, 50 mg, was dissolved in 1.5 mL of THF, and 10 μL of water was added (60% $H_2{}^{16}O$, 20% $H_2{}^{17}O$, 20% $H_2{}^{18}O$, ISOTEC, Inc.). Gaseous HBr was occasionally bubbled through the solution with stirring at room temperature. After 5 days, the THF was evaporated, the residue redissolved in methylene chloride, and the solution dried over molecular sieves (4A), filtered, and evaporated to yield the labeled ketone. The mass spectrum showed a $^{81}Br^{81}Br^{18}O$ peak at *m/e* 260, indicating about 7% incorporation of ^{18}O, and therefore about 7% ^{17}O as well. NMR measurements of **6** at 40.69 MHz showed a strong peak at 524 ppm. Attempts to label dibromo ketone **15** using the same procedure (or even heating the solution) failed. However, when 2,4-dimethyl-3-pentanone (100 mg) in CCl_4 (0.3 mL), bromine (0.2 mL), and 10 μL of the enriched water was heated to 80 °C in a sealed tube, the resulting dibromo ketone was labeled to a similar extent as **6**. ^{17}O NMR gave a strong signal at 540 ppm. The ^{17}O NMR measurements of **2** and **14** were made on the *in situ*-generated compounds, as described earlier for the ^{1}H and ^{13}C NMR studies of **2**.

Computational Methods. Second-order Møller–Plesset (MP2), and density functional theoretical levels, used procedures implemented in the Gaussian 92/DFT system of programs.[5] In all cases the 6-31G* basis set was employed. In the case of the MP2 calculations, the frozen core approximation was used. For the DFT calculations, a hybrid approach based on Becke's[50] three-parameter functional was employed (Becke 3LYP).

Reactions of Bicyclobutanone 2. An *in situ* preparation of **2** at −78 °C was carried out as described earlier (0.3–0.6 mmol scale). After *ca.* 5 min, the second reagent was added by syringe as the pure liquid. The solution was allowed to warm to −30 to −20 °C over 0.5 h and then recooled to −78 °C, 10–15 mL of pentane was added, and the pentane was decanted and filtered through Celite or $MgSO_4$ and then evaporated to leave the products.

A. With Phenyl Sulfide. Compounds 16a,b. ^{1}H NMR and GLC indicate a *ca.* 85:15 ratio of two isomers, which were not separated. ^{1}H NMR (400 MHz): (major isomer) δ 0.93 (d, J = 7.4, 3H); 1.50 (s, 3H); 1.76 (dd, J = 11.5 and 7.5, 1H); 2.29 (dd, J = 10, 11.5, 1H);

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3.25 (m, 1H); 7.3−7.4 (m, 3H); 7.5−7.6 (m, 2H). MS: *m/e* 150 (100); 135. Exact mass: calcd for $C_{12}H_{14}OS$, 206.076 54; found, 206.0771.

B. With *N*-Methylaniline. Compounds 17a,b. From ^{1}H NMR, the product is a *ca.* 1:1 mixture of stereoisomers, which were not separated. Only the distinctive ^{1}H peaks are given (400 MHz): δ 1.24 and 1.20 (both d, $J = 7$, 3H each (two isomers)); 1.47 and 1.44 (s, 3H each, isomers); 3.02 and 2.98 (s, 3H each, isomers). All ^{13}C peaks are given but not assigned to individual isomers: δ 13.8, 14.2, 16.1, 18.1, 34.7, 35.0 (all CH_3); 36.8 and 37.0 (CH_2); 47.6 and 51.2 (CH); 77.5 and 79.2 (Cq); 117.3 and 118.6 (CH × 2); 118.75 and 119.6 (CH); 128.7 and 128.8 (CH × 2); 148.0 and 148.6 (Cq); 209.9 and 211.6 (C=O). IR: (mixture) $\nu = 1773$ cm^{-1} (C=O). MS: *m/e* 160 (100); 175, 105, 71, 56. Exact mass: calcd for $C_{13}H_{17}NO$, 203.131 01; found, 203.1306 (GC−MS).

C. With Methanol. Compounds 18a,b, 19, and 20a,b. A GC−MS analysis of the residual material showed that a complex mixture of monomeric and dimeric products was present. Small quantities of the major species were separated by preparative GC. The lowest retention products were two stereoisomers (**18a,b**), showing almost identical mass spectral fragmentation patterns, very weak M^+ at 128, but large *m/e* 100 and 85 (100) fragments. The two stereoisomers were assigned using NOE experiments in conjunction with COSY 2D spectra. ^{1}H NMR (400 MHz): (isomer **18a**, (2*RS*,4*RS*)-2,4-dimethyl-2-methoxycyclobutanone) δ 1.22 (d, $J = 7.5$, 3H); 1.38 (s, 3H); 1.59 (dd, $J = 11.8$ and 7.7, 1H); 2.50 (t, $J = 11.8$, 1H); 3.32 (s, 3H); 3.38 (m, 1H). ^{13}C NMR (100 MHz): δ 14.8 (CH_3); 18.7 (CH_3); 34.2 (CH_2); 49.9 (CH); 52.9 (CH_3); 92.7 (Cq); 213.2 (C=O). ^{1}H NMR (400 MHz): δ 1.19 (d, $J = 7.2$, 3H); 1.45 (d, $J = 0.8$, 3H); 1.86 (dd, $J = 11.0$ and 9.7, 1H); 2.18 (dd, $J = 11.0$, 11.0, 1H); 3.0−3.15 (m, 1H); 3.35 (s, 3H). ^{13}C NMR (100 MHz): (isomer **18b**, (2*RS*,4*SR*)-2,4-dimethyl-2-methoxycyclobutanone)13.1 (CH_3); 20.8 (CH_3); 32.0 (CH_2); 45.8 (CH); 52.6 (CH_3); 91.4 (Cq); 212.8 (C=O). IR: (isomer **18b**, (2*RS*,4*SR*)-2,4-dimethyl-2-methoxycyclobutanone) $\nu = 1775$ cm^{-1} (C=O). For dimer **19**, one main stereoisomer was obtained along with other minor products. MS: *m/e* 181 (100); 165 (40); 153 (60); 139 (95); 121 (60); 109 (80); 86 (65); 72 (80). IR: $\nu = 1767$ cm^{-1}. ^{1}H NMR (400 MHz): δ 1.16 (d, $J = 7.4$, 3H); 1.29 (s, 3H); 1.30 (s, 3H); 1.49 (s, 3H); 1.81 (d, $J = 12.1$, 1H); 1.98 (t, $J = 10.8$, 1H); 2.08 (dd, $J = 10.8$, 8.2, 1H); 2.59 (d, $J = 12.1$, 1H); 3.34 (m, 1H); 3.36 (s, 3H). ^{13}C NMR (100 MHz): δ 12.5 (CH_3); 19.0 (CH_3); 19.2 (CH_3); 20.6 (CH_3); 30.6 (CH_2); 37.6 (CH_2); 48.4 (CH); 52.8 (CH_3); 58.6 (Cq); 64.3 (Cq); 88.7 (Cq); 214.6 (C=O); 215.8 (C=O). Two stereoisomers of the reduced dimer **20** were obtained. Both show no symmetry element so they must be the two possible unsymmetrical isomers. ^{1}H NMR (400 MHz): (lowest retention isomer) δ 1.08 (d, $J = 7.3$, 3H); 1.15 (s, 3H); 1.22 (d, $J = 7.6$, 3H); 1.24 (s, 3H); 1.38 (dd, $J = 11.6$ and 6.7, 1H); 1.95 (d, $J = 8.1$, 1H); 1.95 (d, $J = 10.1$, H); 2.59 (dd, $J = 11.6$, 11.6, 1H); 3.17−3.27 (m, 1H); 3.27−3.38 (m, 1H). ^{13}C NMR (100 MHz): δ 12.5 (CH_3); 15.3 (CH_3); 18.1 (2 × CH_3); 30.4 (CH_2); 31.4 (CH_2); 48.4 (CH); 51.0 (CH) (no quaternary peaks located). MS: (lowest retention isomer) *m/e* 194 (M^+); 179 (50); 151 (30); 125 (75); 109 (90); 96 (80); 95 (100); 82 (90). ^{1}H NMR (400 MHz): δ 1.165 (d, $J = 7.4$, 3H); 1.19 (s, 3H); 1.20 (d, $J = 7.6$, 3H); 1.32 (s, 3H); 1.41 (dd, $J = 11.6$ and 6.9); 1.59 (dd, $J = 10.5$ and 7.9, 1H); 1.99 (dd, $J = 10.5$, 10.5, 1H); 2.18 (dd, $J = 11.6$, 11.6, 1H); 3.3−3.42 (m, 2H). ^{13}C NMR (100 MHz): (higher retention isomer) δ 12.5 (CH_3); 15.2 (CH_3); 18.6 (CH_3); 18.8 (CH_3); 30.8 (CH_2); 33.0 (CH_2); 48.3 (CH); 50.5 (CH); 64.2 (Cq); 65.0 (Cq) (too dilute to observe C=O). IR: $\nu = 1771$ cm^{-1} (C=O). MS: *m/e* 194 (M^+); 179 (40); 151 (25); 125 (65); 109 (100); 96 (80); 95 (95); 82 (75).

Dimer of 4. Compound 22. This compound forms as small colorless needles when one attempts to recrystallize **4**, mp 129−131 °C. ^{1}H NMR (400 MHz): δ 1.099 (s, 18H); 1.120 (s, 18H); 1.960 and 2.288 (both d, $J = 9.1$, 2H each). ^{13}C NMR (100 MHz): δ 27.14 (CH_3 × 6); 27.86 (CH_3 × 6); 31.94 (Cq × 2); 33.41 (CH_2 × 2); 38.59 (Cq × 2); 86.87 (Cq × 2); 128.13 (Cq × 2); 143.03 (Cq × 2). There is a NOESY interaction between the lowest field ^{1}H doublet and the highest field *t*-Bu group, suggesting that these groups are *cis* to one another. IR (CCl_4): $\nu = 1679.7$ cm^{-1} (enol ether). MS: *m/e* 360 (M^+); 345 (15); 57 (100). Exact mass: calcd for $C_{24}H_{40}O_2$, 360.30283; found, 360.3032.

Reaction of 4 with Phenyl Sulfide. Compound 21. The *in situ* preparation of **4** was carried out at −78 °C on a 0.29 mmol scale, and then 1.1 equiv (33 μL) of phenyl sulfide was added *via* syringe. Hexane was added and the solution allowed to warm to room temperature. The hexane solution was filtered and evaporated to yield a light yellow solid (73.2 mg) which could be recrystallized from hexane to give colorless crystals, mp 68−70 °C. ^{1}H NMR (400 MHz): δ 0.864 (s, 9H); 1.110 (s, 9H); 1.67 (dd, $J = 12$, 11, 1H); 2.135 (dd, $J = 12$, 10, 1H); 2.696 (dd, $J = 10$, 11, 1H); 7.3−7.5 (m, 3H); 7.54 (dd, $J = 6$, 1.7, 2H). ^{13}C NMR (100 MHz): δ 23.65 (CH_2); 26.82 (CH_3 × 3); 27.75 (CH_3 × 3); 32.19 (Cq); 36.65 (Cq); 66.28 (CH); 128.79 (CH × 2); 129.08 (CH); 136.54 (CH × 2); 207.65 (C=O); the ipso carbon not located. MS: *m/e* 290 (M^+); 192 (100); 135 (90). Exact mass: calcd for $C_{18}H_{26}OS$, 290.17044; found, 290.1697.

Reaction of 22 with Ethanol. Compound 24. Attempts to recrystallize **22** from ethanol produced the monomeric ethanolysis product **24** (oil) on removal of the excess solvent. One isomer is very dominant. ^{1}H NMR (200 MHz): δ 0.96 (s, 18H); 1.18 (t, $J = 7$, 3H); 1.9−2.2 (m, 2H); 3.10 (dd, $J = 11$, 12, 1H); 3.45−3.7 (m, 2H). ^{13}C NMR (50 MHz): δ 15.93 (CH_3); 24.22 (CH_3); 24.67 (Cq); 25.60 (CH_3 × 3); 32.48 (Cq); 62.89 (CH_2); 67.50 (CH); 99.47 (Cq); 212.3 (C=O).

Reaction of 22 (or 4) with Water. Compound 23. Both **22** and **4** are moisture sensitive, and on exposure to adventitious water there is ^{1}H NMR evidence for the formation of **23**. Deliberate exposure to water rapidly produces the same compound, 2,4-di-*tert*-butyl-2-hydroxycyclobutanone (**23**) (an oil), which appears to be a single stereoisomer. ^{1}H NMR (400 MHz): δ 0.975 (s, 9H); 1.005 (s, 9H); 1.855 (dd, $J = 12$, 12, 1H); 2.125 (dd, $J = 11$, 12, 1H); 2.22 (br s, 1H); 3.45 (dd, $J = 11$, 12, 1H). ^{13}C NMR (100 MHz): δ 24.63 (CH_3 × 3); 25.50 (CH_2); 27.60 (CH_3 × 3); 32.33 (Cq); 34.77 (Cq); 66.25 (CH); 93.67 (Cq); 212.2 (C=O). MS: *m/e* 198 (M^+); 183; 170; 113; 85.

2-Isopropyl-4-isopropylidenecyclobutanone (25). The *in situ* solution of the bicyclobutanone **3** was allowed to warm to *ca.* −10 °C and then recooled to −78 °C before adding pentane. The supernatant solvent was evaporated, and the ketone **25** was isolated from the residue by preparative GLC, as the dominant volatile product. ^{1}H NMR (400 MHz): δ 0.922 (d, $J = 6.5$, 3H); 1.044 (d, $J = 6.5$, 3H); 1.747 (br s, 3H); 1.892 (hept, $J = 6.5$, 1H); 2.069 (br s, 3H); 2.22 (d, $J = 14.5$, 1H); 2.58 (m, 1H); 2.678 (td, $J = 8.5$, 5.5, 1H). ^{13}C NMR (100 MHz): δ 20.17, 20.41, 20.98, 21.35 (all CH_3); 25.02 (CH); 29.43 (CH_2); 61.89 (CH); 139.9 (Cq); 142.0 (Cq); 202.18 (C=O). MS: *m/e* 152 (20); 137 (30); 109 (30); 82 (50); 67 (100). The compound has been previously reported[51] but only characterized by MS.

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