The Transannular Rearrangement of 5-Cyclodecynone

Michael F. Wempe and John R. Grunwell*

Department of Chemistry, Miami University, Oxford, Ohio 45056

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The acid-catalyzed rearrangement of 5-cyclodecynone (**1**) to bicyclo[4.4.0]-1(6)-decen-2-one (**5**) has been investigated via ^{13}C and deuterium labeling experiments, which showed that the transannular rearrangement proceeds by a mechanism not involving an enol of 5-cyclodecynone. Subjecting 5-cyclodecynone to NBS in ethyl ether resulted in the formation of a dibromooxetane **21** which arose from a bromo allylic alcohol **20** formed from 5-cyclodecynone and HBr. The chloro allylic alcohol **28** was formed from HCl and was subsequently converted to enone **5**. Pathways were investigated using AM1 calculations. As a result, a modified mechanism consistent with all the experimental data is proposed for the acid-catalyzed rearrangement of **1** to **5**.

Introduction

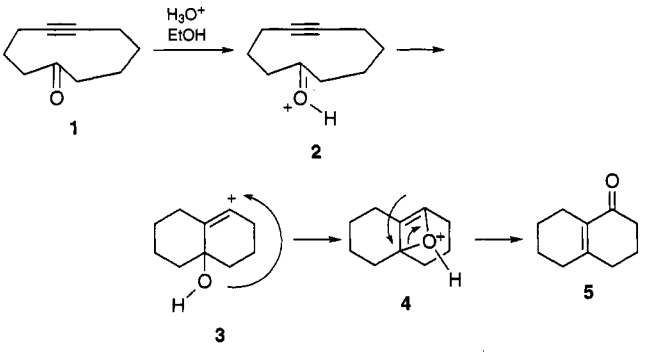
It is well known[1–3] that 5-cycloalkynones undergo a facile rearrangement with formation of a transannular carbon–carbon bond. Several pathways have been proposed for this reaction. The mechanism favored by Harding and co-workers[3,4] (Scheme 1) involves a highly strained anti-Bredt oxete **4**. An attractive alternative (Scheme 2), which avoids invoking this improbable intermediate, begins with the formation of an enol **6** that nucleophilically attacks the acetylene to form the requisite carbon–carbon bond. Previous work[5] showed three possible pathways from the enol. Two options feature the addition of the enol oxygen to the acetylene prior to the formation of the transannular carbon–carbon bond. These pathways included symmetrical anti-Bredt intermediates, which should not be as strained as the oxete intermediate.

Harding[4] presented evidence in support of the oxete mechanism by showing that 6-octyn-2-one rearranged in acid to 1-acetyl-2-methyl-1-cyclopentene and 2,3-dimethylcyclohexenone. The absence of 3-ethylcyclohexenone appears to rule out the enol mechanism. Nevertheless, models of **4** demonstrate that the double bond is horribly twisted with very little overlap between the two p-orbitals. We reported the results of a ^{13}C labeling experiment which was aimed at resolving this dilemma. A ^{13}C placed at the 5 position acetylenic carbon (C-NMR 83.3 ppm) of 5-cyclodecynone would distinguish among the three enol mechanisms and the oxete mechanism.

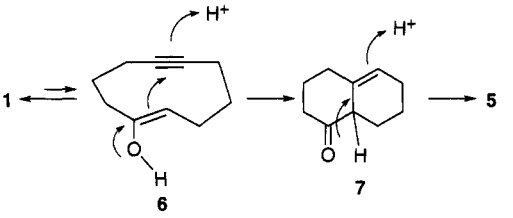
Results and Discussion

The synthesis of the required labeled 5-cyclodecynone was accomplished in nine steps (Scheme 3) according to the literature procedures,[3,6–8] starting from 3-bromo-1-phenylpropane (**8**) and ^{13}C-labeled potassium cyanide[9] in acetonitrile and 18-crown-6 ether.[10] Since the synthesis involved many steps, we decided to use 20% enrichment of ^{13}C. Throughout the synthesis (see Experimental Section), the position and quantity of the label were determined by ^{13}C-NMR and GC/MS, respectively. The [5-^{13}C]-5-cyclodecynone (**17**) was obtained in an overall yield of 7% and was >99% labeled at the 5 position.

Scheme 1



Scheme 2



The labeled [5-^{13}C]-5-cyclodecynone was subjected to four separate reaction conditions that have been shown in the past to induce the rearrangement (Table 1). In all cases we investigated, anhydrous or aqueous, virtually all of the labeled carbon was found at the carbonyl carbon of bicyclo[4.4.0]-1(6)-decen-2-one (**15**). This unequivocally ruled out the enol pathways because these mechanisms all require at least 50% of the ^{13}C to appear at the carbons comprising the double bond in the product. However, the result is consistent with the Harding oxete mechanism. According to Harding's ^{18}O study, the carbonyl oxygen in **1** is the same in **5**. Therefore, the issue was the timing of the oxygen migration with intramolecular carbon–carbon bond formation. In Harding's proposal, carbon–carbon bond formation preceded oxygen migration. Our

(1) Harding, C. E.; Hanack, M. *Tetrahedron Lett.* **1971**, 1253.
(2) Lange, G. L.; Hall, T. *J. Org. Chem.* **1974**, *39*, 3819.
(3) Harding, C. E.; Stanford, G. R., Jr. *J. Org. Chem.* **1989**, *54*, 3054.
(4) Harding, C. E.; King, S. L. *J. Org. Chem.* **1992**, *57*, 883.
(5) Grunwell, J. R.; Wempe, M. F.; Mitchell, J.; Grunwell, J. R. *Tetrahedron Lett.* **1993**, *34*, 7163.
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(7) House, H. O.; Thompson, H. W. *J. Org. Chem.* **1961**, *26*, 3729.
(8) Schreiber, J.; Felix, H.; Eschenmoser, A.; Winter, M.; Gautschi, F.; Schulte-Elte, K. H.; Sundt, E.; Ohloff, G.; Kalvoda, J.; Kaufmann, H.; Weiland, P.; Annen, G. *Helv. Chem. Acta* **1967**, *50*, 2101.
(9) Purchased from Aldrich Chemical Co., Lot no. 111H3759.
(10) Liotta, C. L.; Bowers, W.; Cook, F. L. *J. Org. Chem.* **1974**, *39*, 3416.

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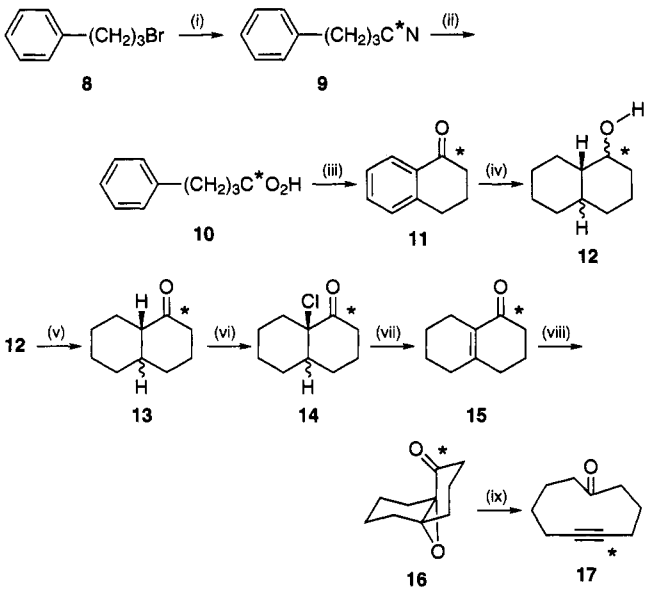
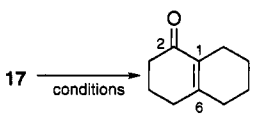
Scheme 3[a]



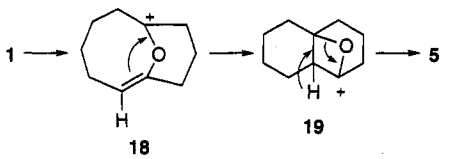
[a] (i) KCN, CH_3CN, 18-C-6; (ii) 12 N HCl; (iii) PPA; (iv) H_2, Rh/Al_2O_3; (v) CrO_3; (vi) SO_2Cl_2; (vii) LiCl, DMF; (viii) H_2O_2, HO^-; (ix) $TsNHNH_2$, CH_3CO_2H.

Table 1

experimental conditions	% 13C in product C1	C2	C6
alumina (neutral, activity I)	0	>99	0
1.5 N HCl, MeOH (anhydrous)	0	>99	0
4.0 N H_2SO_4, aqueous EtOH	0	>99	0
BF_3–Et_2O	0	>99	0



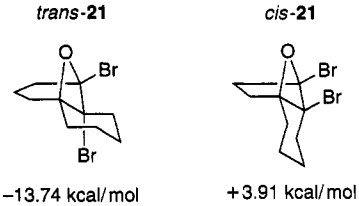
Scheme 4



initial proposal (Scheme 4) began with the formation of a bond between the carbonyl oxygen and carbon 5.

We continued the investigation by subjecting **1** and **5** to 4 N D_2SO_4. In the time it took to complete the rearrangement, some additional deuterium incorporation, roughly 5%, was observed in the rearrangement sample. This experiment further supports the notion that an enol mechanism is not occurring because one should at least expect to see a large M + 1 peak in the mass spectrum of **5** if the enol mechanism applies. In addition, any proposed mechanism should generally exclude deuterium incorporation from solvent.

When the acetylenic ketone **1** was dissolved in ethyl ether, followed by addition of 1.1 equiv of NBS, a reaction was observed. The GC/MS showed that slightly more than half of **1** had been consumed and that there was some rearrangement product **5**. It also showed two new products. The major product had a retention time (t_R) of 9.2–9.3 min (peak at 229 (M − 79)), and the minor product had a t_R of 7.8 min (peaks at 212 (M) and 214 (M + 2)). In order to completely consume **1**, 2.2 equiv of NBS was required. After treatment of the reaction mixture with water, dibromooxetane **21** was present at >95% by GC/MS analysis. As it was impossible to



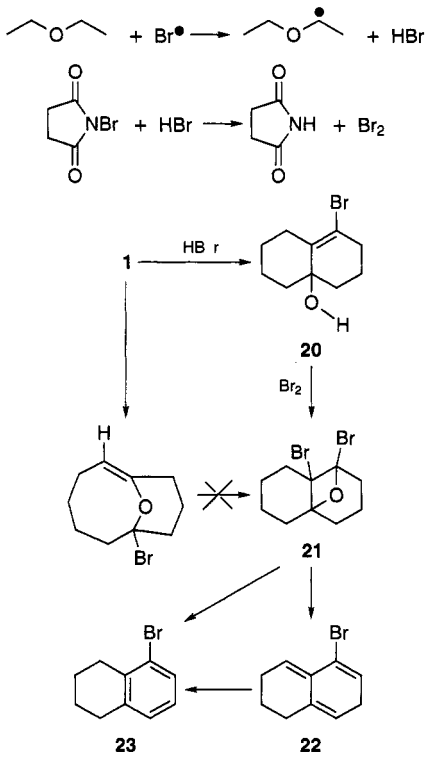
prepare an analytically pure sample of **21**, spectral and chemical data are offered as evidence that **21** is a dibromooxetane. The infrared spectrum showed no absorbances above 3000 cm^{-1} nor any between 2856 and 1451 cm^{-1}. The ^{1}H-NMR displayed two complex multiplets at 1.2–2.1 and 2.35–2.85 ppm which integrated for six and eight hydrogens, respectively. An electron impact (EI) mass spectrum showed a mass ion peak at (M − 79) 229 *m/z*. A broad band mass spectrum was obtained using FAB with glycerol as the matrix solvent. The mmH^+ was calculated to be 308.9 amu for $C_{10}H_{15}Br_2O$, and 308.8 amu was seen. A 1:2:1 pattern, consistent with a dibromo compound, was observed. Furthermore, the ^{13}C-NMR spectrum displayed 10 absorbances which were in the range of 19–76 ppm. According to DEPT experiments, seven of the absorbances between 19 and 43 ppm contain two hydrogens and those at 67.9, 69.9, and 75.8 ppm are quaternary carbons. These quaternary carbons comprise the carbons in the oxetane. We believe the stereochemistry of the ring junction to be *trans* because models suggest that the *cis* isomer would contain more repulsive interactions than the *trans* isomer and AM1 predicts that the *trans* isomer is more stable by 17.6 kcal/mol. Viewing Newmann projections, along the CBr–CBr axis, we found dihedral angles of 99.6 and 26.6° for the *trans* and *cis* isomers, respectively. Unfortunately, **21** was a liquid, and thus, an X-ray structure was not obtained.

When NBS was added to an ethereal solution containing **1** and exposed to light, the development of an intense yellow-orange color, due to the formation of bromine, was observed. We believe NBS under irradiation reacts with ether to produce HBr which reacts with NBS to form Br_2 (Scheme 5). Some of the HBr catalyzed the formation of the bromo allylic alcohol **20**, which reacts with Br_2 to form **21**. When the reaction was conducted with 1.1 equiv of NBS, the minor component was the dehydration product peak of **20**. This suggests that the formation of the bromo allylic alcohol **20** prior to the formation of **21** is a more probable pathway than the addition of Br_2 across Harding's oxete. The dibromooxetane **21** was also formed when **1** was added to an ethereal solution which contained 2 equiv of NBS and aqueous HBr.

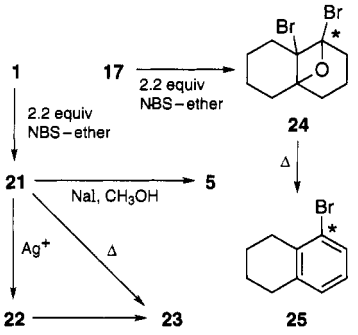
The dibromooxetane **21** was found to decompose on standing, although dilute solutions in deuteriochloroform were stable for 2–3 weeks. When **21** was allowed to decompose or stirred in ether containing excess $AgNO_3$, 5-bromotetralin **23** was formed in an overall yield of 56–62%. The ^{1}H-NMR spectrum for **23** was consistent with that found in the literature.[11] Under the $AgNO_3$ conditions, a major product—^{1}H-NMR 5.38–5.41 (m), 5.66–5.68 (m), 5.69–5.71 (m) and GC/MS (t_R 8.18 min) 210/

(11) Peyman, A.; Beckhaus, H.-D.; Kramer, D.; Peters, K.; von Schnering, H. G.; Ruchardt, C. *Chem. Ber.* **1991**, *124*, 1989.

Scheme 5



Scheme 6



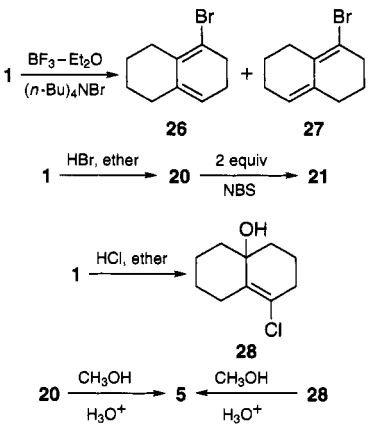
212 m/z—was initially formed. This slowly disappeared with time to give 5-bromotetralin **23**. This suggests that **21** decomposed to an alkene, probably **22,** which then isomerized to the aromatic 5-bromotetralin **23**.

When 5-cyclodecynone was treated with ethereal Br_2, a multitude of products could be seen by GC/MS analysis but **21** was not one of them. Attempts to form Harding's oxete from **21**, using Zn in refluxing methanol containing a catalytic amount of acetic acid, proved to be unsuccessful. But, according to GC/MS, bicyclic enone **5** was the major product (Scheme 6) when **21** was subjected to NaI in refluxing methanol. A sample of labeled ynone **17** was subjected to the NBS reaction conditions to afford dibromooxetane **24** labeled as indicated (Scheme 6). The decomposed product gave 5-bromotetralin **25** with the label located at the carbon bearing bromine (125 ppm). The location of the label in **25** supports the identification of dibromooxetane **24**.

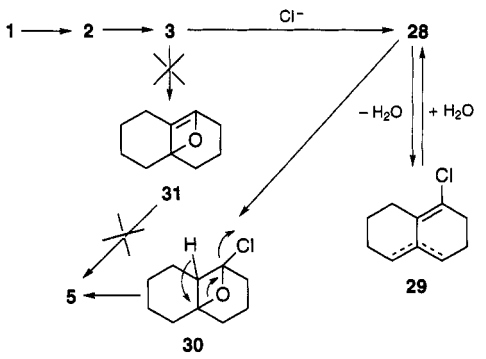
When **1** was subjected to conditions which Curran and co-workers[12] used to form bromo allylic alcohols, Scheme 7, the major products were a mixture of dehydration products **26** and **27** and a minor amount of enone **5** (9:1

(12) Balog, A.; Geib, S. V.; Curran, D. P. *J. Org. Chem.* **1995**, *60*, 337–352.

Scheme 7



Scheme 8



via GC/MS). The dehydration mixture peak was identical with the minor product peak found in the reaction of **1** with 1.1 equiv of NBS. When 1 drop of aqueous 48% HBr was added to an ethereal solution of **1** and allowed to stir for about 18 min (after which time all of **1** was consumed according to GC/MS analysis), the bromo allylic alcohol **20** was formed. After **20** was formed, 2 equiv of NBS was added to the solution. After 90 min, the initial yellow color disappeared, signaling completion of the reaction to afford the dibromooxetane **21**. This indicates that the bromo allylic alcohol **20** is an intermediate along the pathway toward the formation of **21**.

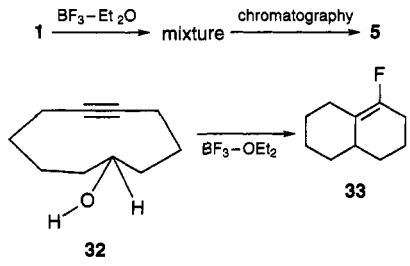
One drop of 12 N HCl was added to an ethereal solution of **1.** After 10 min, the chloro allylic alcohol **28** was isolated by the treatment of the ether solution with aqueous sodium bicarbonate, followed by drying over $MgSO_4$ and evaporation of the ether. The residue was characterized by IR and ^{1}H-NMR. When the isolated chloro allylic alcohol product was subjected to aqueous methanolic HCl, the α,β-unsaturated ketone **5** was afforded as the product. The chloro allylic alcohol dehydrates under the GC/MS conditions to give the dehydration product **29**, whose t_R (7.23–7.29 min) is very similar to that of **1** (t_R of **1**, 7.08–7.14 min). Within 10 min, **1** was completely consumed when it was subjected to aqueous DCl/CH_3OD (similar to Harding's[3] $H_2{}^{18}O$ reaction conditions), and according to GC/MS analysis, the major product was **29** (**28**) along with a minor amount of **5**. It took 4.5 h to completely convert **28** to enone **5**. These results clearly demonstrate that the chloro allylic alcohol **28** is formed fast and then converted to enone **5**.

The experimental evidence suggests that the HCl-catalyzed rearrangement begins with protonation of the carbonyl (Scheme 8), followed by attack of the transannular alkyne to give the vinyl cation **3** as is the original Hanack proposal.[1] This vinyl cation is trapped by a

Table 2

structure no.	AM1 (kcal/mol)	structure no.	AM1 (kcal/mol)
1 (−18.19)	**2** (+150.36)	**19** (+127.12)	*trans*-**21** (−13.74)
3 (+165.92)	**4** (+167.44)	*cis*-**21** (+3.91)	**28** (−75.37)
5 (−57.03)	**18** (+155.28)	**30** (−43.57)	**31** (+47.73)

Scheme 9



chloride ion. The chloro allylic alcohol intermediate **28** circumvents the highly energetic oxete **4** by acid-catalyzed ring closure to afford the chlorooxetane **30**, which could then ring open to produce the rearranged α,β-unsaturated ketone **5**. If roughly 5% of the halogenated allylic alcohol, **29**, were to dehydrate and then rehydrate under aqueous reaction conditions, this pathway could incorporate some deuterium and would be consistent with Harding's $H_2{}^{18}O$ and our ^{13}C experiments. The AM1 calculations[13] for the various pathways are found in Table 2. They suggest that the chlorooxetane intermediate **30** is lower in energy and more stable than **31**.

The acetylenic ketone **1** was subjected (Scheme 9) to boron trifluoride etherate, affording a dark green oil which we believe to be a mixture. Before column chromatography, the GC/MS showed the oil to be mostly enone **5** with a minor fluorinated product. However, the ^1H- and ^{13}C-NMR spectra of the oil were not consistent with **5**. The purification of this green oil by column chromatography gave, according to GC/MS, ^1H-NMR, and ^{13}C-NMR, the rearrangement product **5**. Pure enone **5** was subjected to the BF_3 conditions, and again a green oil was obtained. The GC/MS of this oil also corresponded to enone **5**; however, ^1H-NMR and ^{13}C-NMR did not match **5** nor did they correspond to the spectral data found for the oil from **1** and $BF_3{\cdot}OEt_2$.

When aqueous HF was added to an ethereal solution of **1**, no reaction was observed; however, when aqueous HBF_4 was added to an ethereal solution of **1**, a green color was observed and enone **5**, according to GC/MS, was the major product. The BF_3 results suggest that the rearrangement of **1** occurs by an initial BF_3 complex bound to the carbonyl of **1**, followed by transannular carbon−carbon bond making to form the vinyl cation as Harding[3] proposed. Fluoride ion could then trap the vinyl cation. Weiler et al.[14] have shown that, when cyclodecyn-6-ol (**32**) was subjected to $BF_3{\cdot}OEt_2$ in CH_2Cl_2, the volatile fluoroalkene **33** was formed. Presumably, diethyl ether contains enough H_2O to generate a sufficient amount of the strong acid $BF_3{\cdot}H_2O$[15] in order to catalyze the reaction. However, the ring closure and/or ring opening to afford enone **5**, under the $BF_3{\cdot}OEt_2$ reaction conditions, may occur during the gas or liquid chromatography processes.

(13) IBM, AM1, and RHF calculations.
(14) Balf, R. J.; Rao, B.; Weiler, L. *Can. J. Chem.* **1971**, *49*, 3135−3142.
(15) Gillespie, R. J.; Hartman, J. S. *Can. J. Chem.* **1967**, *45*, 859−863.

Conclusion

The transannular rearrangement of 5-cyclodecynone does not proceed by an enol intermediate. The formation and decomposition of the dibromooxetanes **21** and **24** along with ^{13}C-labeling experiments suggest that the rearrangement operates through a four-membered ring intermediate and that carbon−carbon bond formation occurs before carbon−oxygen bond formation as shown by the isolation of the chloro allylic alcohol and its subsequent conversion to enone **5**.

Experimental Section

The following compounds were obtained from Aldrich Chemical Co.: 1-bromo-3-phenylpropane, α-tetralone, KCN (99% ^{13}C), rhodium (5%) on alumina powder, CrO_3 resin, SO_2Cl_2, and H_2O_2 (30%). The GC/MS data were obtained using EI with a Hewlett-Packard model 5890 equipped with a high-performance capillary column, HP-1 cross-linked methyl silicone gum 25 m × 0.2 mm × 0.33 mm film thickness, and a HP 5971A mass-selective detector. The temperature parameters used included a 140 °C injector temperature and a 70 °C column temperature for 3 min, which was then ramped at 20 °C per minute and leveled off at 240 °C. Melting points were taken using a Gallencamp apparatus and are uncorrected.

[1-^{13}C]-4-Phenylbutyronitrile (9). Into a 250 mL round bottom flask were added 30.6 g (0.154 mol) of 1-bromo-3-phenylpropane (**8**), 1.0 g of 18-crown-6, 2.0 g (0.03 mol) of KCN (99% ^{13}C), and 50 mL of CH_3CN. The reaction mixture was refluxed under a drying tube for 24 h. Over 4 days, additional KCN (5.9, 6.5, 6.0, and 3.0 g) was added at intervals. The mixture was extracted with CH_2Cl_2 and washed with H_2O. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed by a rotary evaporator, affording 21.21 g (95%) of **9**: ^1H NMR 7.14−7.34 (5H, m), 2.71−2.78 (2H, t), 2.22−2.31 (2H, m, hydrogens α to the nitrile), 1.86−2.01 (2H, m); ^{13}C-NMR 16.33 (t) (carbon α to the nitrile), 26.90 (s), 34.34 (s), 119.57 (s, an asterisk (*) denotes the labeled carbon), 126.46 (s), 128.45 (s), 128.63 (s), 139.78 (s); GC/MS (t_R 6.76−6.87 min) M = 145, M + 1 = 146 (I = 35%); IR 2260 cm^{-1}.

[1-^{13}C]-4-Phenylbutyric Acid (10). The ^{13}C-enriched nitrile **9** was subjected to 150 mL of 12 N HCl and the vessel holding the mixture equipped with a Friedrick condenser. The mixture was refluxed for 8 h, allowed to cool, and extracted with 3 × 75 mL of CH_2Cl_2. The organic layer was dried over Na_2SO_4 and filtered, and the solvent was evaporated to afford 22.8 g (95%) of a light yellow solid: ^1H-NMR 11.8 (1H, s), 7.14−7.31 (5H, m), 2.68−2.61 (2H, t), 2.31−2.39 (2H, m, hydrogens α to the carbonyl), 1.91−2.09 (2H, m); ^{13}C-NMR 26.10 (s), 33.28 (t, carbon α to the carbonyl), 34.87 (s), 125.95 (s), 128.33 (s), 128.38 (s), 141.09 (s), 180.19 (s, ^{13}C-enriched carbon); IR (broad) 3400−2400 cm^{-1}; mp 49−52 °C.

[1-^{13}C]-α-Tetralone (3,4-Dihydo-1(2*H*)-naphthalenone) (11). The ^{13}C-enriched carboxylic acid **10** was heated until molten and subjected to 100 g of PPA at 90 °C for 3.5 min, followed by an additional 70 g of hot PPA and stirred for 5 min. Ice (120 g) was placed into the reaction flask, the flask allowed to cool, and then the mixture extracted with 3 × 150 mL of ether. The organic layer was washed with 2 × 100 mL of 5% NaOH, 2 × 100 mL of H_2O, 100 mL of 3% CH_3COOH, 100 mL of 5% $NaHCO_3$, and 100 mL of 5% NaCl. The aqueous layer upon acidification revealed no starting phenylbutyric acid. The organic layer was dried over $MgSO_4$, filtered, and evaporated to afford 19.0 g (94%) of **11**: ^1H-NMR 7.99−8.03 (1H, t), 7.40−7.44 (1H, t), 7.20−7.31 (2H, m), 2.90−2.96 (2H, t), 2.59−2.66 (2H, t), 2.07−2.16 (2H, m); ^{13}C-NMR 23.27 (s), 29.62 (s), 39.11 (t, carbon α to the carbonyl), 126.57 (s), 127.06 (s), 128.77 (s), 132.57 (s), 133.35 (s), 144.47 (s), 198.24 (s, an asterisk (*) denotes the labeled carbon); GC/MS (t_R 7.15−7.22 min) M = 146, M + 1 (I = 33%).

[1-^{13}C]-Decalol (Mixture) (12). The labeled α-tetralone (19.0 g, 0.130 mol) was placed into the hydrogenation apparatus. Five grams of catalyst and 150 mL of absolute ethanol were poured into the reaction vessel. Hydrogen

uptake was complete in 4 days, 50–25 psi with periodic checking via GC/MS. The Rh/Al_2O_3 was removed by filtration, and the organic solvent was removed. Recovered was 17.23 g (89.8%) of **12**: GC/MS (t_R 6.50–6.58, 6.82–6.92, and 6.96–7.04 min) M = 154 (weak), intense M = 136 (loss of H_2O); ^{1}H-NMR 1.10–1.90 (broad CH_2 peaks), 3.60–3.75 (m); ^{13}C-NMR (alcohol peaks) 74.93 (s), 73.48 (s), 70.60 (s), 68.72 (s) (all four were ^{13}C-enriched). IR (broad) 3550–3100 cm^{-1}.

[1-^{13}C]-*cis*- and -*trans*-1-Decalone ([1-^{13}C]-Decahydro-1-naphthalenone, (13). The ^{13}C-enriched alcohol mixture **12** (17.2 g, 0.117 mol) was placed into a 2000 mL round bottom flask containing 340 g of CrO_3 resin and 500 mL of toluene. The mixture was refluxed with a drying tube for a total of 12 h. The reaction vessel was allowed to cool, and then the resin was filtered. The organic layer was dried with $NaSO_4$, filtered, and concentrated via rotary evaporation. Recovered was 14.8 g (84.4%) of **13**: GC/MS (t_R 6.57–6.64 and 6.70–6.77 min) M = 152, M + 1 (I = 31%); ^{1}H-NMR (broad) 1.0–2.5; ^{13}C-NMR 212.72 (s), 213.57 (s) (both carbons were labeled).

[1-^{13}C]-*cis*- and -*trans*-9-Chloro-1-decalone (14). The ^{13}C-enriched ketone **13** (14.8 g, 0.0985 mol) was placed in a 500 mL three-neck round bottom flask containing 104 mL of CCl_4. The round bottom flask was connected to a condenser with a drying tube, a separatory funnel, and a glass stopper. The solution was cooled using an ice bath, and 17.8 g of SO_2Cl_2 in 56 mL of CCl_4 was added dropwise with stirring. The reaction mixture was stirred for 8 h. The organic layer was washed with 100 mL of H_2O, 2 × 100 mL of 5% $NaHCO_3$, and 100 mL of 5% NaCl, dried over $MgSO_4$, filtered, and evaporated to afford an organic oil which was distilled using a vacuum distillation apparatus consisting of a Vigreux column and a fraction collector (60–89 °C at 1.0 mmHg). The colorless material was a mixture of *cis* and *trans* products. Recovered after distillation was 10.5 g (57.1%) of **14**: ^{1}H-NMR (broad) 1.1–2.7, 2.9–3.3; ^{13}C-NMR 205.61 (s), 204.78 (s) (both carbons were ^{13}C-enriched). GC/MS (t_R 7.50–7.55 and 7.57–7.64 min) M = 186, M + 1 (I = 35%), M + 2 = 188 (I + 39%).

[2-^{13}C]Bicyclo[4.4.0]-1(6)-decen-2-one ([1-^{13}C]-$\Delta^{9,10}$-Octal-1-one) (15). The labeled chlorinated compound **14** (10.5 g, 0.0562 mol) was placed in a three-neck round bottom flask which contained 105 mL of DMF and 23.8 g of LiCl. The reaction mixture was heated to a sand bath temperature of 120–130 °C over 8 h under N_2. After the flask was cooled to room temperature, 100 mL of H_2O was added. The resulting solution was extracted with 4 × 100 mL of petroleum ether. The combined organic layers were washed with 100 mL of H_2O, dried over Na_2SO_4, filtered, and evaporated. The organic layer was then diluted with 200 mL of ether and washed with 3 × 100 mL of 6 M KOH (cold). The organic layer was dried over Na_2SO_4, filtered, and evaporated. Recovered was 7.0 g (82.9%) of **15**: ^{13}C-NMR 21.77 (s), 21.80 (s), 21.85 (s), 22.13 (s), 31.44 (s), 31.53 (s), 37.60 (t, CH_2 α to the carbonyl), 131.91 (t, carbon α to the carbonyl), 156.79 (s), 198.92 (s, an asterisk (*) denotes the labeled carbon); GC/MS (t_R 7.44–7.51 min) M = 150, M + 1 (I = 37%). The base wash when acidified, extracted with ether, dried, filtered, and concentrated gave 200 mg of [1-^{13}C]-5,6,7,8-tetrahydro-1-napthol.

[2-^{13}C]-1,6-Epoxybicyclo[5.3.0]decan-2-one (16). The ^{13}C-enriched α,β-unsaturated ketone **15** (7.0 g, 0.0466 mol) was added to a 300 mL three-neck round bottom flask containing 25.9 mL of CH_3OH and 4.8 mL of 6 M NaOH. The flask was connected to a condenser, a glass stopper, and a 125 mL separatory funnel. The mixture was cooled to 10–15 °C using an ice bath. Twelve milliliters of a 30% H_2O_2 solution was added dropwise. The reaction mixture was allowed to warm to room temperature and was stirred for 20 h. The flask was cooled to 15 °C, and 3.6 mL of 30% H_2O_2 was added. After warming to room temperature, the reaction mixture was stirred for an additional 15 h. CH_3OH was removed by rotary evaporation, diluted with 55 mL of H_2O, and extracted with 3 × 75 mL of ether. The combined organic layers were washed with 90 mL of H_2O, dried over $MgSO_4$, filtered, and evaporated. A short path vacuum distillation gave a colorless liquid (58–64 °C at 0.20 mmHg). Recovered after distillation was 3.0 g (38.8%) of **16**: ^{13}C-NMR 17.04 (s), 19.57 (s), 19.84 (s), 20.97 (s), 28.90 (s), 29.70 (s), 36.64 (s), 64.34 (s), 65.78 (s), 206.84 (s, an asterisk (*) denotes the labeled carbon); GC/MS (t_R 7.16–7.25 min) M = 166, M + 1 (I = 34%).

[5-^{13}C]-5-Cyclodecynone (17). The ^{13}C-labeled epoxy ketone **16** (3 g, 0.0181 mol) was diluted with 33 mL of both CH_3COOH and CH_2Cl_2. The solution with stirring was cooled to −23 °C. To the reaction mixture was added 3.7 g of *p*-toluenesulfonylhydrazine. The flask was kept at −23 °C for 30 min, at 0 °C for 2 h, and at room temperature for 3 h. The reaction mixture was neutralized by adding solid Na_2CO_3, and enough H_2O was added to dissolve any solid present. The two layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The organic portions were combined, washed with 70 mL of saturated $NaHCO_3$, dried over $MgSO_4$, and filtered, and the solvent was evaporated to afford an oil which was vacuum distilled as before (62–65 °C at 0.25 mmHg). Recovered after distillation was 1.587 g (58.4%) of **17**: ^{1}H-NMR 1.56–1.67 (2H, m), 1.78–1.90 (2H, m), 2.04–2.10 (6H, m), 2.32–2.39 (2H, m), 2.74–2.80 (2H, t); ^{13}C-NMR 18.18 (t, carbon α to the labeled acetylene), 19.28 (s), 21.75 (s), 25.64 (s), 26.87 (s), 42.56 (s), 42.64 (s), 83.33 (s, ^{13}C-enriched carbon), 85.67 (s), 210.72 (s); GC/MS (t_R 7.08–7.14 min) M − 1 = 149, M + 1 (I = 69%); ^{13}C-NMR (300 MHz) 17.91, 19.04, 21.46, 25.37, 26.63, 42.32, 42.45, 83.10* (an asterisk (*) denotes the labeled carbon), 85.46, 210.70.

1,6-Epoxybicyclo[5.3.0]decan-2-one. To a 300 mL three-neck round bottom flask was added 2.9 g (0.0193 mol) of the bicyclo[4.4.0]-1(6)-decen-2-one (**5**), and 13 mL of CH_3OH. A condenser, a glass stopper, and a separatory funnel were connected to the flask. Next, 2.0 mL of 6 M NaOH was added to the reaction solution which was cooled to 10–12 °C. Dropwise, 4.9 mL of 30% H_2O_2 was added. The reaction vessel was allowed to warm to room temperature while being stirred.

Another portion of 30% H_2O_2 (2.0 mL) was added 22 h later at 10–12 °C. The flask was allowed to warm to room temperature while being stirred for an additional 15 h. The mixture was diluted with 21 mL of H_2O. The reaction mixture was extracted with 3 × 75 mL of ether. The organic layer was dried over $MgSO_4$, filtered, and evaporated. A short path vacuum distillation gave a colorless liquid (60–70 °C at 0.3 mmHg). Recovered after distillation was 2.30 g (0.0139 mol, 72%) of the desired compound: ^{1}H-NMR 1.1–2.65; ^{13}C-NMR 17.62 (s), 19.77 (s), 20.04 (s), 21.19 (s), 29.11 (s), 29.91 (s), 36.63 (s), 64.46 (s), 65.92 (s), 207.05 (s); IR 1700 cm^{-1}; GC/MS (t_R 7.16–7.25 min) M = 166, M + 1 (I = 15%).

5-Cyclodecynone (1). Into a 300 mL round bottom flask were placed 2.3 g of the epoxy ketone, 26 mL of CH_2Cl_2, and 26 mL of CH_3COOH. The flask was cooled to −23 °C with dry ice and CCl_4. To the reaction mixture was added 2.83 g of *p*-toluenesulfonylhydrazine. The mixture was stirred at −23 °C for 30 min, at 0 °C for 2 h, and at room temperature for 3 h. The solution initially turned yellow and then became colorless at room temperature. Solid Na_2CO_3 was added until the mixture was neutralized, and then enough H_2O was added to dissolve any solid present. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The organic layers were combined, washed with 50 mL of saturated $NaHCO_3$, separated, dried over $MgSO_4$, and filtered, and the solvent was removed by rotary evaporation. The resulting oil was vacuum distilled using a short path distillation apparatus (65–70 °C at 0.5 mmHg). Recovered after distillation was 1.43 g (69%) of **1**: ^{1}H-NMR 1.60–1.71 (2H, m), 1.82–1.94 (2H, m), 2.07–2.14 (6H, m), 2.36–2.41 (2H, t), 2.77–2.83 (2H, t); ^{13}C-NMR 18.18 (s), 19.28 (s), 21.74 (s), 25.64 (s), 26.86 (s), 42.58 (s), 42.66 (s), 83.34 (s), 85.68 (s), 210.74 (s); GC/MS (t_R 7.08–7.14 min) M − 1 = 149, M + 1 (I = 42%); ^{1}H-NMR (300 MHz) 1.56–1.62 (m, 2H), 1.77–1.85 (m, 2H), 2.01–2.11(m, 6H), 2.30–2.33 (t, 2H), 2.71–2.75 (t, 2H).

[5-^{13}C]-5-Cyclodecynone rearrangement with Neutral Alumina. A 150 mg (9.99×10^{-1} mmol) sample of the ^{13}C-enriched 5-cyclodecynone **17** was placed on a column ($3^1/_2$ × $^1/_2$ in.) filled with neutral aluminum oxide. The column was eluted with 300 mL of hexane–ether (80:20). Evaporation of the solvent afforded 138 mg (4.33×10^{-1} mmol) of [2-^{13}C]-bicyclo[4.4.0]-1(6)-decen-2-one (**15**). The GC/MS was shown to be >95% pure: yield 92%; ^{13}C-NMR (the label to be located at the carbonyl, 198 ppm).

5-Cyclodecynone Rearrangement with 1.5 M HCl. Anhydrous HCl was bubbled into 25 mL of absolute CH_3OH until the concentration was 1.5 M, 1.38 g of HCl in 25 mL of alcohol. A 120 mg sample of 5-cyclodecynone was placed into a 50 mL round bottom flask. Seven milliliters of the methanolic HCl was added and the mixture stirred for 6 min. The HCl and CH_3OH were then removed under vacuum. Recovery of 106 mg of a yellow oil was shown by GC/MS to be **5**: yield 88%.

[5-^{13}C]-5-Cyclodecynone Rearrangement with 1.5 M HCl. A 120 mg sample of ^{13}C-enriched 5-cyclodecynone (**17**) was placed into a 50 mL round bottom flask. Eight milliliters of the 1.5 M HCl solution was added. The mixture was stirred for 6 min. The HCl and CH_3OH were removed under vacuum. The GC/MS showed the 98 mg of recovered product to be ketone **15**: yield 82%; ^{13}C-NMR (the labeled carbon was located at 198 ppm).

[5-^{13}C]-5-Cyclodecynone Rearrangement with 4 N H_2SO_4. A 160 mg (1.07 mmol) sample of ^{13}C-enriched 5-cyclodecynone (**17**) in 2 mL of 4 N H_2SO_4 and 2 mL of 95% ethanol was stirred at room temperature for 12 h. The solution was then poured into 10 mL of H_2O and extracted with ether. The organic layer was washed with saturated $NaHCO_3$ solution, followed by a brine wash. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was evaporated. The 147 mg (9.79×10^{-1} mmol, 91%) was **15**: ^{13}C-NMR (the labeled carbon was at 198 ppm).

Rearrangement of 5-Cyclodecynone with 4 N D_2SO_4. A 100 mg (6.67×10^{-1} mmol) sample of 5-cyclodecynone **1** and a 100 mg sample of bicyclo[4.4.0]-1(6)-decen-2-one (**5**) were both subjected to 2 mL of 4 N D_2SO_4 and 2 mL of ethanol-*O*-*d*. The solutions were allowed to stir at room temperature for 20 min. The mixtures were decanted using a Pasteur pipet into 5 mL of H_2O and extracted with 3 × 5 mL portions of ether. The organic layers were washed with 5 mL of saturated $NaHCO_3$ and 5 mL of brine solution. The ether layers were dried over $MgSO_4$, filtered, and evaporated to light yellow oils. The GC/MS's showed the rearrangement to have 12−15% deuterium incorporation, while the pure enone had essentially 5−8% incorporation.

Rearrangement of 1 in Aqueous DCl/CH_3OD. A 0.38 mL aliquot of 37% DCl/D_2O was diluted to 0.25 mL with D_2O. The solution was adjusted to a volume of 4.5 mL with CH_3OD. This solution was divided into two parts and added to 125 mg of **1** and 125 mg of **5**. The GC/MS of **1** (t_R 7.14 min) initially showed conversion to one product at 7.24 min, the dehydration peak. The solutions were allowed to stir for a total of 4.5 h, and the solvent was removed by reduced pressure. The residues were dissolved in ether and washed with sodium bicarbonate solution. The organic layers were dried over magnesium sulfate and concentrated.

***trans*-6,7-Dibromo-11-oxatricyclo[4.3.1.0^{1,6}]undecane (21).** NBS (140 mg, 0.778 mM) was added to 55 mg (0.367 mM) of **1** dissolved in 15 mL of ethyl ether. The mixture was irradiated for 3−5 min with sunlight and swirling until the liquid layer developed an intense yellow-orange color. The mixture was stirred for 2 h, and the liquid layer was colorless. The ethereal solution was augmented with 10 mL of ether, extracted with H_2O (3 × 20 mL), dried over $MgSO_4$, filtered, and evaporated to give 70 mg of **21** as a colorless liquid: yield 62%; GC/MS (t_R 9.28 min; mass peak at 229); ^{1}H-NMR (200 MHz, broad) 1.2−2.1 (mm, 6H) and 2.35−2.85 (mm, 8H); ^{13}C-NMR 19.47, 20.10, 21.86, 27.13, 28.25, 32.30, 42.62, 67.95, 69.55, 75.74; ^{13}C-NMR (300 MHz, DEPT 45 and 135) 19.43 (CH_2), 20.09 (CH_2), 21.83 (CH_2), 27.08 (CH_2), 28.21 (CH_2), 32.25 (CH_2), 42.58 (CH_2), 67.90 (C), 69.54 (C), 75.78 (C); IR 2938, 2863 cm^{-1}; broad band FABMS gave a calculated mmH^+ of 308.9484 amu for $C_{10}H_{15}Br_2O$; 308.8292 amu was found for $C_{10}H_{15}Br_2O$.

21 from NBS and HBr in Diethyl Ether. A 50 mg (0.333 mM) sample of **1** dissolved in 5 mL of ethyl ether was added dropwise to a stirred 10 mL solution which contained 121 mg (0.67 mM) of NBS and 1 drop of concentrated HBr. During the reaction, a minor product was observed at t_R 7.8 min (M (212) M + 2 (214)), the same minor product observed under 1.1 equiv of NBS, and the solution was allowed to stir for 90 min. The product after aqueous workup was 39 mg of **21**.

***trans*-[7-^{13}C]-6,7-Dibromo-11-oxatricyclo[4.3.1.0^{1,6}]-undecane (24).** NBS (130 mg, 0.723 mM) was added to 40 mg (0.267 mM) of **17** dissolved in 15 mL of ethyl ether. The mixture was irradiated for 3−5 min with sunlight and swirling until the liquid layer developed an intense yellow-orange color. The mixture was stirred for 2 h, and the liquid layer was colorless. The ethereal solution was augmented with 10 mL of ether, extracted with H_2O (3 × 20 mL), dried over $MgSO_4$, filtered, and evaporated to give 57 mg of **24** as a colorless liquid: yield 69%; GC/MS (t_R 9.28 min, mass peak at 229); ^{1}H-NMR (200 MHz, broad) 1.1−2.1 (6H, mm), 2.35−2.85 (8H, mm); ^{13}C-NMR 18.73, 19.37, 21.13, 26.39, 27.49, 31.55, 41.89, 67.20, 68.80, 75.03 (an asterisk (*) denotes the labeled carbon); IR 2937, 2856 cm^{-1}.

5-Bromotetralin (23). (A) A 52 mg (0.169 mM) sample of **21** was concentrated and allowed to stand for 3$^1/_2$ days. It formed a black solid and was placed onto a column that contained 1$^1/_2$ × $^1/_2$ in. of silica gel. The column was eluted with a 3:1 (hexane/chloroform) solvent mixture to afford, after concentration, 32 mg of a clear liquid which was **23**: yield after chromatography 90%; GC/MS (t_R 7.9 min) M (210), M + 2 (212); ^{1}H-NMR 1.74−1.84 (m, 4H), 2.70−2.79 (m, 4H), 6.87−7.06 (m, 2H), 7.34−7.38 (d, 1H); ^{13}C-NMR (300 MHz, DEPT 45 and 135) 22.65 (CH_2), 23.32 (CH_2), 30.13 (CH_2), 30.16 (CH_2), 125.87 (C), 126.53 (CH), 128.24 (CH), 129.65 (CH), 136.43 (C), 139.79 (C); IR 3030, 2980 cm^{-1}.

(B) A mixture of 65 mg (0.383 mM) of $AgNO_3$ and 41 mg (0.133 mM) of **21** dissolved in 20 mL of ethyl ether was allowed to stir at room temperature for 30 h. The organic layer was washed with H_2O (2 × 20 mL), dried over $MgSO_4$, filtered, and evaporated to afford 23 mg of **23**.

[5-^{13}C]-5-Bromotetralin (25). The sample of **24** (0.185 mM) was allowed to stand for 3$^1/_2$ days, formed a black solid, and was placed onto a column that contained 1$^1/_2$ × $^1/_2$ in. of silica gel. The column was eluted with a 3:1 (hexane/chloroform) solvent mixture to afford, after concentration, 32 mg (0.152 mM) of a clear liquid which was **25**: yield 82%. The label was located at 125.8 ppm.

5-Cyclodecynone (1) and Boron Trifluoride Etherate. A 100 mg (0.67 mM) sample of **1** dissolved in 2 mL of ethyl ether was placed into an NMR tube connected to a vacuum line. Boron trifluoride etherate, 0.2 mL, was added to the clear solution under a vacuum. The mixture formed two layers; the lower layer became a dark green color and was allowed to react for 15 min. The solvent was removed under vacuum to afford a dark green oil. A GC/MS of the crude oil had a major peak consistent with rearrangement product **5** and had a minor fluoronated product; however, ^{1}H- and ^{13}C-NMR were not consistent with the data of **5**. The oil was placed on a column which contained 2$^1/_2$ × $^1/_2$ in. of silica gel and was eluted with a 4:1 solvent (hexanes:ether) mixture. Concentration gave 80 mg of a clear liquid shown by GC/MS, ^{1}H-NMR, and ^{13}C-NMR to be **5**.

Enone 5 and Boron Trifluoride Etherate. BF_3·OEt_2 (0.12 mL) was added dropwise to 50 mg of enone **5** in 1 mL of ethyl ether. The mixture was stirred at room temperature for 15 min and also turned dark green. The solvent was removed, and GC/MS was consistent with the data of **5**. The ^{1}H-NMR and ^{13}C-NMR of the BF_3·**5** complex was different from the spectra obtained for the green oil derived from **1** with BF_3·OEt_2. After column chromatography, the recovered 32 mg was the α,β-unsaturated ketone **5**.

Enriched 5-Cyclodecynone (15) and Boron Trifluoride Etherate. A 100 mg (0.67 mM) sample of **17** was dissolved in 2 mL of ethyl ether and was stirred. BF_3·OEt_2 (0.25 mL) was added and the mixture allowed to stir for 15 min. The solvent was removed, and the green oil was placed on a column which contained 2$^1/_2$ × $^1/_2$ in. of silica gel and was eluted with a 4:1 solvent (hexanes:ether) mixture. Concentration gave 73 mg of a clear liquid shown by GC/MS, ^{1}H-NMR, and ^{13}C-NMR to be **15**. The label was located at 198 ppm.

5-Cyclodecynone (1) with Boron Trifluoride Etherate and Tetrabutylammonium Bromide (26 and 27).[12] A 47 mg (0.31 mM) sample of **1** was dissolved in 5 mL of CH_2Cl_2,

and 1.03 g (3.1 mM) of tetrabutylammonium bromide was added. The solution, under N_2 and with stirring, was cooled to 0 °C. Boron trifluoride etherate (0.33 mL) was slowly added, and the mixture was maintained at 0 °C for 1 h, and then allowed to warm to room temperature. The reaction mixture was slowly quenched with 5 mL of saturated $NaHCO_3$ and diluted with 8 mL of ether and 5 mL of H_2O. The mixture was extracted with 3 × 10 mL of ether. The combined organic layers were washed with 5 mL of a brine solution, dried with $MgSO_4$, and concentrated to an oil. Column chromatography on silica gel eluting with a 3:1 (hexanes:ethyl acetate) solvent mixture afforded 23 mg of a clear liquid. The liquid was an unseparated mixture of the two isomers **26** and **27**: GC/MS (t_R 7.78–7.89 min) 212/214 *m/z*; ^{1}H-NMR (had a doublet at 5.47 ppm (2H)); ^{13}C-NMR 22.61, 23.19, 24.53, 25.83, 29.36, 29.70, 30.27, 30.84, 37.42, 52.16, 52.26, 52.33, 52.51, 52.69, 52.73 ppm.

1 with HBr in Diethyl Ether (20). A 50 mg (0.33 mM) sample of **1** was dissolved in 15 mL of diethyl ether. One drop of 48% HBr was added and the mixture allowed to stir for 10 min. Magnesium sulfate was then added, and the solvent was filtered and removed by reduced pressure to afford 53 mg of the product: GC/MS (t_R 7.78–7.89 min) 212/214 (M − H_2O) 133 *m/z* (M − 97); IR (broad) 3480 cm^{-1}; ^{1}H-NMR 1.61–1.78 (m, 6H), 2.04–2.08 (m, 3H, 1 exchangeable in D_2O), 2.23–2.29 (t, 2H), 2.40–2.46 (t, 2H), 2.59–2.66 (t, 2H).

21 from 20 in Situ. A mixture of 20 mg of **1** and 6 mL of diethyl ether was stirred, and aqueous HBr was added. The solution was allowed to stir until **1** was consumed by GC/MS. To the solution was added 2 equiv of NBS (50 mg), and the solution was allowed to stir for 90 min. By GC/MS, the major product was **21** and the minor product was unreacted **20**.

1 with HCl in Diethyl Ether (28). One drop of 12 N HCl was added to 50 mg (0.333 mmol) of **1** dissolved in 15 mL of diethyl ether. The mixture was stirred for 10 min. The reaction mixture was neutralized with $NaHCO_3$, and the organic layer was dried with anhydrous $MgSO_4$. The solvent was evaporated after filtration to afford 32 mg of **28**: GC/MS (t_R 7.26 min) M − H_2O (168/170) M − 53 (133); IR (broad) 3380 cm^{-1}; ^{1}H-NMR (200 MHz) 1.62–1.72 (m, 2H), 1.82–1.94 (m, 2H), 2.05–2.24 (m, 7H, one exchangeable D_2O), 2.38–2.43 (t, 2H), 2.79–2.84 (t, 2H).

20 with Aqueous Methanolic HCl. A methanolic solution (5 mL of H_2O/10 mL of CH_3OH/2 mL of concentrated HCl) was added to 34 mg of **20**. The mixture was allowed to stir for 3 h, and by GC/MS, **20** was converted to enone **5**.

28 with Aqueous Methanolic HCl. A methanolic solution (5 mL of H_2O/10 mL of CH_3OH/2 mL of concentrated HCl) was added to 28 mg of **28**. The mixture was allowed to stir for 3 h, and by GC/MS, **28** was converted to enone **5**.

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Supplementary Material Available: AM1 calculations, the 300 MHz ^{13}C-NMR and DEPT spectra for the dibromooxetane (38 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any currect masthead page for ordering information.

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