Anal. Calcd for $C_6H_{12}N_2O_3$: C, 44.99; H, 7.55; N, 17.49. Found: C, 45.15; H, 7.49; N, 17.25.

Solvolysis of 4. In a vial were placed 1.0 g of **5**, 10 mL of HOAc, and 1.0 g of NaOAc; after sealing, the vial was heated at 60 °C for 6 h at which time the red solution was poured into 100 mL of CH_2Cl_2. The CH_2Cl_2 solution was then extracted repeatedly with saturated $NaHCO_3$. The neutral organic layer was then dried and stripped of solvent in vacuo leaving 357 mg (62%) of a dark red oil which was purified on a column of silica gel (Fisher grade 923) to give a pale yellow oil identical spectroscopically with **20**: $[\alpha]^{25}_D$ −9.729° (c 3.392 in ethanol).

Acknowledgments. We are grateful to the NSF (CHE 76-24095) and to NIH (1-RO1-CA22110) for their generous support.

Registry No. **1**, 66398-63-8; **2**, 66398-65-0; **3**, 66398-64-9; **4**, 70377-71-8; **5**, 3559-06-6; **6a**, 70377-73-0; **9**, 26921-68-6; **10**, 70377-74-1; **11**, 68292-94-4; **12**, 49807-74-1; **13**, 42055-15-2; **14**, 70415-59-7; **15**, 70377-75-2; **16**, 59724-61-7; **17**, 60915-12-0; **18**, 70377-76-3; **19**, 70377-77-4; **20**, 70377-78-5; *N*-methyl-2-hydroxyethylamine, 109-83-1; 2-pyrrolidinemethanol, 498-63-5; 3-hydroxypropylamine, 156-87-6; ethyl formate, 109-94-4; ethyl L-(+)-lactate, 687-47-8.

Stereochemistry of the Photoinduced and Michael Addition of Methanol to Seven- and Eight-Membered 2-Cycloalkenones. The Effect of Methyl Substituents

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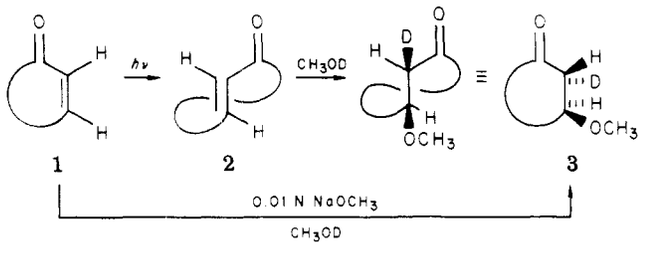
Irradiation of 2-methyl-2-cycloheptenone (**4**) or 2-methyl-2-cyclooctenone (**6**) in methanol gave only the corresponding *cis*-3-methoxy-2-methylcycloalkanones **5c** and **7c**, respectively, rationalized as a consequence of syn methanol addition to the trans enones. The isotope effect (CH_3OH/CH_3OD) for **4** was 2.0, appreciably less than the previously observed value for 2-cycloheptenone, suggesting that the 2-methyl substituent destabilizes the trans intermediate. Photoinduced methanol addition also occurred when the double bond had a methyl substitutent at C_3, but 2,3-dimethyl-2-cyclooctenone failed to add methanol photochemically. The base-catalyzed Michael addition of methanol to **4** and **6** gave a mixture of *cis*- and *trans*-3-methoxy-2-methylcycloalkanones, in contrast to the previously reported stereospecific additions to the unsubstituted 2-cycloalkenones. The acid-catalyzed addition of methanol to **4** gave a different cis-trans ratio than the base-catalyzed addition.

Strained trans seven- and eight-membered-ring 2-cycloalkenones, produced by irradiating the corresponding cis isomers,[1] react with alcohols and other nucleophiles to give Michael-type adducts.[2] By using CH_3OD as the nucleophile, we recently showed[3] that these reactions involve a regiospecific and stereospecific nucleophilic syn addition to the polarized, strained trans double bond (**2** → **3**). As part of a series of experiments designed to further probe the mechanistic details of this reaction, we also studied the base- and acid-catalyzed addition of CH_3OD to the cis ketones **1** and were surprised to find that the base-catalyzed Michael reaction is also stereospecific (i.e., **1** → **3**; **1** = 2-cycloheptenone, 2-cyclooctenone, and 2,3-benzo-2,6-cycloheptadienone).[3] Consistent with this observation, we found that the base-catalyzed deuterium exchange at C_2 in the corresponding 3-methoxycycloalkanones is also stereoselective, exchange being much faster for the proton trans to the methoxyl than for the corresponding cis proton. But the acid-catalyzed Michael addition, studied only with 2-cycloheptenone, was not stereoselective.



We decided that for at least two reasons it would be worthwhile to extend the above studies to cycloalkenones with methyl substituents on the carbon–carbon double bond. First, molecular models suggest that methyl substitution should, as a consequence of nonbonded interactions, increase the strain in the *trans*-2-cycloalkenones **2**. There is a question then of whether or not the trans isomers will be formed on irradiation and, if formed, whether they can be trapped. So far, there has been almost no systematic study of the effect of substitution on the stability and reactions of strained trans cycloalkenes. Second, it seemed important to determine whether the stereospecificity of the base-catalyzed Michael addition and deuterium exchange observed previously[3] is general. We report here our results on the effect which methyl substituents at C_2 and C_3 of 2-cycloheptenone and 2-cyclooctenone have on the outcome of the above reactions.

Results and Discussion

The Photoinduced Additions. Irradiation of 2-methyl-2-cycloheptenone (**4**) or 2-methyl-2-cyclooctenone (**6**) in methanol gave the *cis*-3-methoxy-2-methylcycloalkanones **5c** and **7c**, respectively. The cis stereochemistry

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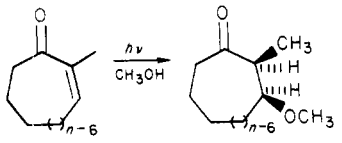
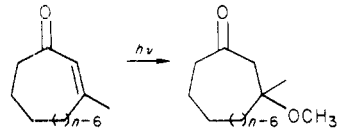


4, $n = 7$ **5c**, $n = 7$
6, $n = 8$ **7c**, $n = 8$

of **5c** and **7c** was assigned from the ^1H NMR spectra and by comparison with the corresponding trans isomers (vide infra). For example, the coupling constants $J(H_2,H_3)$ were only 1.0 and 3.5 Hz respectively in **5c** and **7c**, whereas in the trans isomers these coupling constants were appreciably larger. Previous studies[4,5] show that $J_{trans} > J_{cis}$ in such systems.

Irradiation of **4** in various CH_3OH/CH_3OD mixtures permitted the isotope effect for addition to be measured. The observed value was 2.0 at 25 °C, appreciably less than the value of 4.3 (29 °C) previously observed[3] for 2-cycloheptenone itself.

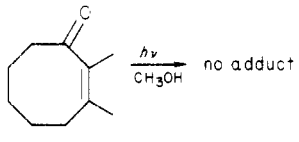
Irradiation of the 3-methyl-2-cycloalkenones **8** and **10**



8, $n = 7$ **9**, $n = 7$
10, $n = 8$ **11**, $n = 8$

was also briefly studied. With **10** the reaction proceeded cleanly to give a good yield of **11**, whose structure was clear from its NMR spectrum. With **8**, however, the reaction was complicated by the ease with which the addition product **9** eliminates methanol to give not only **8** but its Δ^3 isomer.

Finally, irradiation of 2,3-dimethyl-2-cyclooctenone (**12**)



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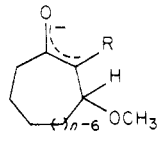
in methanol failed to give any adduct; prolonged irradiation led only to polymeric material.

Our results with **4** and **6** are consistent with earlier observations[3] that the photoinduced addition of nucleophiles to cis 2-cycloalkenones involves photoisomerization to the trans isomer followed by syn addition of the nucleophile. The substantial isotope effect is consistent with proton transfer being important in the rate-determining step. The smaller isotope effect observed with **4** rather than with 2-cycloheptenone can be rationalized if the methyl substituent causes the trans isomer to be more reactive and therefore less isotopically selective than in the unsubstituted compound. The reactions of **8** and **10** show that a methyl substituent at C_3 does not prevent the addition, even though the nucleophile must attack a tertiary center. However, methyl substitution at both positions, as in **12**, was sufficient to block methanol addition. It may be that the trans isomer in this case is so strained as a consequence of nonbonded interactions that it reverts to the cis isomer faster than it reacts with methanol.

The Base-Catalyzed Additions. Treatment of **4** with 0.01 N $NaOCH_3$ in CH_3OH at room temperature gave a mixture of **5c** and **5t** (the corresponding isomer with the methoxyl and methyl trans) in a 2:1 ratio. The same mixture was produced when pure **5c** (isolated from the photoinduced addition) was similarly treated with base, and experiments carried out for varying times show that it is the equilibrium mixture. Similar experiments with **6** gave a mixture of **6** (45%), **7c** (20%), and **7t** (35%). In the seven-membered ring series, addition is faster and more complete than in the eight-membered ring series. Furthermore, the cis isomer predominates at equilibrium in the former series, whereas in the latter it is the trans isomer which predominates. The energy differences are small, however, in either case.

The structures of **5t** and **7t** were assigned on the basis of their NMR spectra. In particular, the coupling constant $J(H_2,H_3)$ in **5t** was 6.9 Hz as compared with only 1.0 Hz in the cis isomer. In the spectrum of **7t**, it was not possible to discern this coupling constant directly because the chemical shifts of the methine protons H_2 and H_3 were nearly identical.[6] However, in a $Eu(fod)_3$ shifted spectrum it appeared that this coupling constant was approximately 6 Hz.

It seems likely that these base-catalyzed Michael additions and deuterium exchanges proceed through the enolate anion **13** (R = CH_3), which may be protonated to



13

give either the cis or trans product and in different ratios depending on the value of n. This result is more in line with expectation than the previous result[3] obtained when R = H, in which case protonation occurred exclusively trans to the methoxyl group. Either there is some special reason, not now clear, why the protonation of **13** is unique when R = H or there is a special, different mechanism involved for these reactions in the unsubstituted series. Lack of stereospecificity in the protonation, as observed

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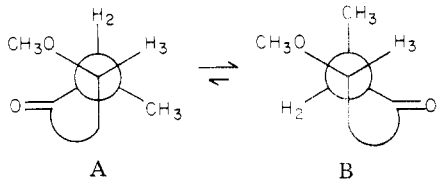
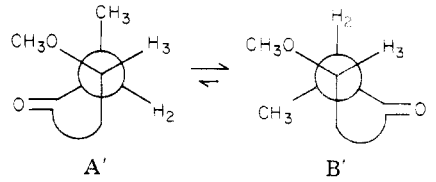
(5) Dunkelblum, E.; Hart, H. *J. Org. Chem.* **1977**, *42*, 3958.

(6) This near equivalence is apparently due to shielding of H_3, since the chemical shifts of H_2 in **5c**, **5t**, **7c**, and **7t** average δ 2.83 (2.80, 2.69, 2.90, 2.95, respectively), whereas the chemical shift of H_3 averages δ 3.56 (3.39, 3.26, 4.04) in the first three compounds but comes at abnormally high field (δ 2.95) in **7t**. The origin of this upfield shift is not certain but may be due to shielding of H_3 by the carbonyl group. A possible origin of this shielding can be seen from a crude conformational analysis of the system, assuming staggered conformations at the C_2–C_3 bond. In **7t**, a conformation approaching that of B will be preferred to that of A, placing



A B

H_3 in the proximity of the carbonyl group (note that in **5**, H_3 also appears at higher field in the trans isomer). In **7c**, on the other hand, a conformation approaching that of A′ may be preferred, since it places the largest group

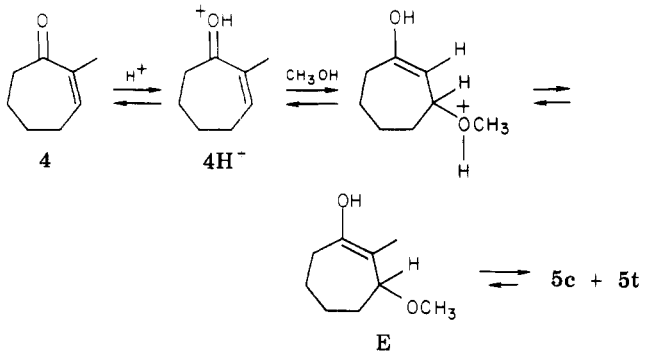


A′ B′

(CH_3) in the least crowded environment. This effect is likely to be most apparent in the larger ring (**7** > **5**).

in the present work, seems the more likely to be general.

The Acid-Catalyzed Addition. Treatment of **4** with 0.01 N H_2SO_4 in CH_3OH at room temperature gave a 1:1 mixture of **5c** and **5t**. However, treatment of **5c** with acid under the same conditions led to its complete recovery. Consequently, we conclude that the intermediate enol E is protonated equally from either side of the molecule but



that this protonation is essentially irreversible under the reaction conditions. The lack of stereospecificity in the acid-catalyzed Michael addition appears to hold whether or not the double bond of the cycloalkenone is methyl substituted.[3]

Synthesis. 2-Methylcycloheptenone **4** is previously known,[7] whereas its homologue **6** is new. These compounds were prepared from cycloheptanone and cyclooctanone, respectively, via their *N,N*-dimethylhydrazones,[8] which were alkylated according to the Corey procedure.[9] The 2-methylcycloalkanones obtained after hydrolysis were brominated[10] and dehydrobrominated[11] to give **4** and **6**.

3-Methylcycloheptenone (**8**)[12] was prepared by the method of Saegusa,[13] whereas its homologue **10** was obtained from 2-cyclooctenone[14] using the alkylative carbonyl transposition of Dauben.[15] Application of the latter method to **6** gave the previously unknown **12** in 30% yield (accompanied by a 27% yield of the epoxide of **12**). Although this method for the synthesis of **12** was only moderately successful, it was superior to the attempted bromination–dehydrobromination of 2,3-dimethylcyclooctanone, which gave only the exocyclic isomer, 3-methyl-2-methylenecyclooctanone.

Experimental Section

General Procedures. NMR spectra were measured in $CDCl_3$ against Me_4Si as an internal standard unless otherwise stated, using a Varian T-60 or Bruker WH-180 spectrometer. When necessary, Eu(fod)$_3$ (tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III)) was used to simplify the spectra. IR spectra were calibrated against a polystyrene film and were recorded on a Perkin-Elmer 237 grating spectrometer. UV spectra were obtained with a Unicam SP-800 spectrometer. Mass spectra were obtained at 70 eV using a Hitachi Perkin-Elmer RMU-6 spectrometer, or they were obtained through the courtesy of the NIH regional facility in the Biochemistry Department of Michigan State University. Melting points are uncorrected. Analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, Mich., or Clark Microanalytical Laboratory, Urbana, Ill. Gas chromatographic separations were carried out on a Varian Aerograph Model 1400 (flame ionization detector, analytical) or a Model 90P (thermal conductivity detector, preparative) instrument.

2-Methyl-2-cycloheptenone (4). The required starting material is 2-methylcycloheptanone. Although many routes for its preparation have been described,[16] we found that application of the Corey method[9] was most convenient. Because of the paucity of experimental procedures in the literature, we describe it in some detail. A mixture of cycloheptanone (44.8 g, 47.2 mL, 0.4 mol), anhydrous *unsym*-dimethylhydrazine (72 g, 91 mL, 1.2 mol), and 100 mL of absolute ethanol was refluxed overnight. Ethanol and excess dimethylhydrazine were removed (vacuum rotary evaporation, 50 °C), and the residue was distilled at 45–45.5 °C (1 torr) to give 52.5 g (85%) of cycloheptanone *N,N*-dimethylhydrazone: IR (neat) 2910, 1620, 1471, 1454, 972 cm^{-1}; NMR δ 1.4–1.68 and 2.4–2.75 (m, 12 H), 2.40 (s, 6 H, gem $(CH_3)_2$).

A mixture of diisopropylamine (21 mL, 0.15 mol) and 33 mL of anhydrous THF containing a few milligrams of triphenylmethane as indicator was cooled to 0 °C under N_2, and 58 mL of *n*-butyllithium (2.6 M in hexane) and 32 mL of hexane were added slowly, the temperature being kept below 5 °C. After addition, the solution should be a persistent orange-red. After being stirred at 0 °C for 4 h, a solution containing 20.6 g of cycloheptanone *N,N*-dimethylhydrazone in 16.7 mL of anhydrous THF was added slowly at 0 °C. After being stirred for 4 h more, 19.7 g of methyl iodide in 16.7 mL of THF was added (0 °C), and the mixture was stirred overnight. Workup by hydrolysis and extraction with methylene chloride gave a quantitative yield of crude 2-methylcycloheptanone-*N,N*-dimethylhydrazone. The crude product was hydrolyzed by overnight reflux with 100 mL of 10% sulfuric acid. Workup by ether extraction, drying ($MgSO_4$), and distillation at 39 °C (2.8 torr) gave 12.7 g (68%) of pure 2-methylcycloheptanone: IR (neat) 2940, 1702, 1455, 938 cm^{-1}; NMR δ 1.04 (d, 3 H, J = 6 Hz), 1.2–2.0 (m, 8 H), 2.3–2.72 (m, 3 H).

To a solution containing 5.13 g (40.7 mmol) of 2-methylcycloheptanone in 30 mL of ether was added dropwise at 0 °C 6.72 g (2.25 mL, 42 mmol) of bromine. A faint yellow color persisted for several minutes on completion of the reaction. After 15 min, 10 mL each of saturated sodium bicarbonate and sodium sulfite were added, and the product was extracted with ether (200 mL) to give, after washing with saturated $NaHCO_3$ and NaCl and drying ($MgSO_4$), 8.2 g of crude 2-bromo-2-methylcycloheptanone: NMR δ 1.80 (s, 3 H, CH_3) and multiplets at 1.4–2.0 and 2.3–2.75. The crude bromo ketone was refluxed with lithium carbonate (16.3 g) in anhydrous dimethylformamide (71 mL) under nitrogen for 5 h. Dilution with water and extraction with hexane gave 5.0 g of **4**, bp 45 °C (1.8 torr), which was purified by chromatography (silica gel): IR (neat) 1662 cm^{-1}; UV λ_{max} (cyclohexane) 232 nm (ϵ 12 500), 291 (110); NMR δ 1.2–1.98 and 2.20–2.78 (m, 8 H), 1.82 (d, 3 H, J = 1.2 Hz), 6.4–6.58 (m, 1 H); mass spectrum, m/e (rel intensity) 124 (61), 112 (18), 96 (18), 84 (27), 67 (100).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.43; H, 9.65.

2-Methyl-2-cyclooctenone (6). The procedures were analogous to those described for **4**. Cyclooctanone-*N,N*-dimethylhydrazone, bp 55 °C (0.5 torr), was obtained in quantitative yield: IR (neat) 2960 (s), 1630 (m), 1475 (m), 1455 (m), 1030 (m), 980 (m) cm^{-1}; NMR (CCl_4) δ 1.20–2.0 (br, 10 H), 2.26 (s, 6 H, gem $(CH_3)_2$), 2.0–2.5 (m, 4 H). The yield of 2-methylcyclooctanone *N,N*-dimethylhydrazone was also quantitative: IR (neat) 2960 (s), 1632 (m), 1475 (m), 1455 (m), 1380 (w), 1030 (m), 970 (m) cm^{-1}; NMR (CCl_4) δ 0.93 (d, 3 H, J = 7 Hz), 1.1–2.0 (m, 10 H), 2.0–2.4 (m, 3 H), 2.25 (s, 6 H, $N(CH_3)_2$). Hydrolysis gave 2-methylcyclooctanone in 95% yield, bp 38 °C (0.4 torr) or 72 °C (5 torr): IR (neat) 2950 (s), 1698 (s), 1470 (s), 1455 (m), 1380 (w) cm^{-1}; NMR (CCl_4) δ 0.98 (d, 3 H, J = 7 Hz), 1.1–2.05 (m, 10 H), 2.05–2.7 (m, 3 H). The crude 2-bromo-2-methylcyclooctanone had a methyl singlet at δ 1.75. Finally, dehydrobromination with Li_2CO_3 in DMF gave pure **6** in 66% yield, bp 73 °C (2.8 torr), which was

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(16) For example: Mueller, E.; Bauer, M., *Justus Liebigs Ann. Chem.* **1962**, *654*, 92. Conia, J. M.; Girard, C. *Tetrahedron Lett.* **1973**, 2767.

further purified by chromatography on silica gel using 3:1 chloroform/hexane as eluent: IR (neat) 2940 (s), 1685 (m), 1660 (s), 1450 (m), 1380 (m) cm^{-1}; UV λ_{max} (95% ethanol) 242 nm (ϵ 6800), 285 (750); NMR (CCl_4) δ 1.76 (d, 3 H, J = 1.5 Hz), 1.33–2.0 (m, 6 H), 2.0–2.66 (m, 4 H), 5.67–6.07 (t × q, 1 H, J = 7 and 1.5 Hz); mass spectrum, m/e (rel intensity) 138 (18), 123 (3), 110 (14), 96 (35), 95 (100), 81 (40), 67 (72), 54 (41).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.06; H, 10.10.

Irradiation of 4 in Methanol. All irradiations described in this paper were carried out with a Hanovia 450-W lamp. A degassed solution of **4** (106 mg, 0.855 mmol) in 10 mL of methanol was irradiated through Pyrex at 10 °C for 21 h. The rather slow reaction was followed by vapor-phase chromatography (VPC). The solvent was evaporated, and the residue was purified by preparative VPC (10% SE-30 on Chromosorb W, 125 °C) to give 5 mg (4.7%) of recovered **4** and 96 mg (72%) of the methanol adduct **5c**: IR (neat) $\nu_{C=O}$ 1702 cm^{-1}; NMR δ 1.20 (d, 3 H, J = 6.9 Hz, C_2 methyl), 1.40–1.90 (m, 6 H, C_4, C_5, and C_6 methylenes), 2.18–2.59 (m, 2 H, C_7 methylene), 2.80 (br q, 1 H, J = 7.0 Hz, C_2 methine), 3.28 (s, 3 H, methoxyl), 3.39 (br m, 1 H, C_3 methine). Irradiation at δ 2.80 collapsed the peak at δ 1.20 to a singlet; irradiation at δ 1.20 showed that the C_2 proton was only weakly coupled (J = 1.2 Hz) with the C_3 methine proton. Mass spectrum, m/e (rel intensity) 156 (10), 124 (17), 111 (14), 96 (17), 85 (22), 84 (100).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.94; H, 10.40.

When the irradiation of **4** was carried out in CH_3OD, the NMR spectrum of the product (isolated in 83% yield) was altered from that of **6** in the following ways. It had a broad singlet at δ 1.16 (C_2 methyl) and no peak at δ 2.80 (C_2 methine), and the peak at δ 3.36 (C_3 methine) was a doublet, J = 5 Hz, due to coupling with one of the C_4 methylene protons.

Isotope Effect Measurement. A solution containing 100 mg of **4** in a mixture of methanol (2 mL) and methanol-*d* (10 mL) was irradiated at 25 ± 1 °C for 20 h. The ratio of **5c** to **5c**-*d* (deuterium in place of hydrogen at C_2) was determined on both the crude and VPC collected product by integrating the areas of the doublet and singlet, respectively, for the C_2-methyl group. The value of the isotope effect was 2.1 ± 0.3. The analysis was repeated using 50 mg of **4** in the following solvent mixtures: 1 mL CH_3OH + 5 mL CH_3OD, 3 mL CH_3OH + 3 mL CH_3OD, and 4 mL CH_3OH + 2 mL CH_3OD with isotope effects respectively of 2.1 ± 0.3, 2.0 ± 0.3, 1.8 ± 0.3.

Irradiation of 6 in Methanol. A solution containing 139 mg (1 mmol) of **6** in 10 mL of methanol was flushed with nitrogen and irradiated through Pyrex at room temperature. The photolysis was followed by VPC (5 ft × 0.125 in. column, 5% SE 30 on Chromosorb G, 165 °C; retention times of starting material and product were 0.6 and 1.3 min, respectively). After 4 h, conversion was about 90% (longer times gave undesired products), and the product **7c** was formed in 80% (55% isolated) yield: IR (neat) 2940 (s), 1705 (s), 1470 (s), 1450 (s), 1384 (m), 1330 (m), 1095 (s), 950 (m), 910 (m) cm^{-1}; NMR (180 MHz) δ 1.09 (d, 3 H, J = 7.0 Hz, C_2 methyl), 1.25–2.07 (br m, 8 H, C_4–C_7 methylene), 2.24–2.76 (m, 2 H, C_8 methylene), 2.90 (d × q, 1 H, J = 3.5, 7.0 Hz, C_2 methine), 3.40 (s, 3 H, methoxyl), 4.04 (m, 1 H, C_3 methine). Irradiation at δ 1.09 caused the quartet of doublets at δ 2.90 to become a doublet, J = 3.5 Hz, and irradiation at δ 1.52 (which region contains the C_4 methylene) caused the multiplet at δ 4.04 to become a doublet, J = 3.5 Hz. Mass spectrum, m/e (rel intensity) 170 (6), 138 (24), 123 (7), 109 (25), 98 (25), 81 (26), 71 (100), 57 (71).

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.57; H, 10.57.

3-Methyl-2-cycloheptenone (8). 2-Methylcyclohexanone was converted to 2-(trimethylsilyloxy)-1-methylcyclohexene[17] which was cyclopropanated (Simmons–Smith) using the zinc dust–copper chloride procedure described by Rawson and Harrison.[18] The product was then converted to **8** as previously described;[13] IR and NMR data agreed with those reported.[13]

(17) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(18) Rawson, R. J.; Harrison, I. T. *ibid.* **1970**, *35*, 2057.

3-Methyl-2-cyclooctenone (10). Compound **10** was prepared according to the procedure recently described[15] but in only half the reported yield. Since the physical properties are not recorded, we give them here: IR (neat) 2940 (s), 1650 (s), 1450 (m), 1380 (m) 1340 (m) 1265 (m), 1145 (w), 885 (w), 845 (w) cm^{-1}; UV λ_{max} (95% EtOH) 245 nm (ϵ 7500); NMR (CCl_4) δ 1.35–2.1 (br m, 6 H), 1.84 (d, 3 H, J = 1.5 Hz, C_3 methyl), 2.2–2.8 (br m, 4 H), 5.78 (br m, 1 H); mass spectrum, m/e (rel intensity) 138 (20), 123 (7), 109 (6), 95 (100), 82 (34), 67 (34), 55 (18), 41 (23); high resolution, calcd for $C_9H_{14}O$ 138.10446, found 138.10384.

Irradiation of 8 in Methanol. A solution of **8** (200 mg, 1.61 mmol) in 20 mL of methanol was irradiated through Pyrex; the reaction was followed both by NMR and analytical VPC. In particular, the peaks at δ 1.91 and 5.80 due to the methyl and vinyl proton in **8** decreased in intensity as new peaks appeared at δ 1.18 and 3.10 due to the C_3-methyl and methoxyl groups in **9**. However, even after 48 h, reaction was incomplete; it was not possible to isolate a pure sample of **9**, due to facile elimination of methanol.

Irradiation of 10 in Methanol. A degassed solution of **10** (70 mg, 0.51 mmol) in 10 mL of methanol was irradiated through Pyrex. The reaction, followed by VPC (5 ft × 0.125 in. column, 5% FFAP on Chromosorb W, 180 °C), was essentially complete in 5 h. The major product, isolated in 72% yield, was 3-methoxy-3-methylcyclooctanone (**11**): IR (neat) 2940 (s), 1700 (s), 1470 (m), 1380 (w), 1310 (m), 1280 (w), 1220 (w), 1130 (m), 1080 (m) cm^{-1}; NMR (CCl_4) δ 1.16 (s, 3 H, C_3 methyl), 1.2–2.0 (br m, 8 H), 2.0–2.4 (br m, 2 H, C_8 methylene), 2.24 (d, 1 H, J = 11 Hz, C_2 proton trans to the methoxyl), 2.70 (d, 1 H, J = 11 Hz, C_2 proton cis to the methoxyl), 3.12 (s, 3 H, methoxyl); LIS slopes[5] for a 1:1 mol ratio of Eu(fod)$_3$:**11** were 17.4 (C_2 proton cis to the methoxyl), 12.3 (C_2 proton trans to the methoxyl), 6.9 (C_3 methyl), 11.6 (methoxyl), 8.3 (C_8 methylene); mass spectrum, m/e (rel intensity) 170 (3), 155 (5), 140 (7), 138 (7), 123 (3), 114 (18), 99 (22), 95 (31), 85 (77), 72 (100), 55 (45). Since the structure was clear from the method of synthesis and spectra, the compound was not analyzed.

2,3-Dimethyl-2-cyclooctenone (12). A solution of **6** (2.0 g, 14.5 mmol) in ether (50 mL) was treated under nitrogen with 10 mL of 1.7 M ethereal methyllithium (2 h at room temperature, 1 h reflux), hydrolyzed, and chromatographed (neutral alumina, 1:1 hexane/ether eluent) to give 0.70 g (35%) of recovered **6** and 1.20 g (83%) of 1,2-dimethyl-2-cycloocten-1-ol: IR (neat) 3410 (s), 2930 (s), 1450 (s), 1375 (m), 1035 (m), 950 (m), 885 (m), 850 (m) cm^{-1}; NMR (CCl_4) δ 1.06 (s, 1 H, hydroxyl), 1.23 (s, 3 H, C_1 methyl), 1.76 (br s, 3 H, C_2 methyl), 1.2–2.6 (br m, 10 H), 5.12 (m, 1 H, vinyl); mass spectrum, m/e (rel intensity) 154 (7), 136 (70), 121 (49), 107 (85), 93 (100), 91 (44), 79 (84), 67 (53). A solution containing 1.20 g (7.8 mmol) of this tertiary alcohol in 10 mL of methylene chloride was oxidized with 4.2 g (19.5 mmol) of pyridinium chlorochromate in 40 mL of methylene chloride at room temperature (3 h). Ether extracts were washed (10% NaOH, 10% HCl, saturated $NaHCO_3$), dried ($MgSO_4$), and chromatographed on neutral alumina (1:1 hexane/ether) to give 0.36 g (30%) of the desired **12** and 0.36 g (27%) of 2,3-dimethyl-2,3-epoxycyclooctanone. For **12**: IR (neat) 2930 (s), 1685 (s), 1650 (m), 1450 (m), 1380 (w), 1275 (w) cm^{-1}; UV λ_{max} (95% EtOH) 250 nm (ϵ 4360); NMR(CCl_4) δ 1.70 (s, 6 H, C_2 and C_3 methyls), 1.2–1.9 (br m, 6 H), 2.0–2.6 (br m, 4 H); mass spectrum, m/e (rel intensity) 152 (29), 147 (8), 137 (11), 123 (8), 109 (100), 96 (22), 81 (42), 67 (32). High resolution, calcd for $C_{10}H_{16}O$: 152.12012. Found: 152.12029. For **12** epoxide: IR (neat) 2940 (s), 1715 (s), 1465 (s), 1390 (m), 1110 (m), 1075 (m), 895 (m), 850 (m), 830 (m) cm^{-1}; NMR (CCl_4) δ 1.3 (s, 3 H, C_3 methyl), 1.43 (s, 3 H C_2 methyl), 1.0–2.0 (br m, 8 H), 2.1–2.8 (br m, 2 H); mass spectrum, m/e (rel intensity) 168 (11), 140 (10), 126 (83), 125 (100), 112 (22), 111 (62), 98 (23), 97 (63), 85 (39), 84 (57).

Irradiation of 12 in Methanol. A solution of **12** (46 mg) in 10 mL of methanol was flushed with nitrogen (15 min) and irradiated through Pyrex for 8 h. Gas chromatography did not indicate any new product and workup gave >90% recovered **12**.

Base-Catalyzed Addition of Methanol to 4. A solution of **4** (50 mg, 0.40 mmol) in 11 mL of 0.01 M sodium methoxide in methanol was stirred at room temperature for 53 h. The reaction, which was very slow, was followed by analytical VPC. It was quenched and worked up as previously indicated[3] to give 25 mg

(40%) of **5c** and 13 mg (21%) of **5t**: NMR δ 1.15 (d, 3 H, J = 6.9 Hz, C_2 methyl), 1.41–1.95 (m, 6 H, C_4–C_6 methylenes), 2.30–2.60 (m, 2 H, C_7 methylene), 2.69 (d × q, 1 H, J = 6.9, 6.9 Hz, C_2 methine), 3.22–3.70 (d, 1 H, C_3 methine), 3.29 (s, 3 H, methoxyl). Irradiation at δ 1.15 caused the peak at δ 2.69 to become a doublet, J = 6.9 Hz. Mass spectrum, m/e (rel intensity) 156 (9), 124 (18), 111 (19), 88 (35), 85 (26), 84 (100), 82 (35); high resolution, calcd for $C_9H_{16}O_2$ 156.11502, found 156.11540.

A similar reaction in CH_3OD for 48 h gave 30% recovered **4**, 26% of **5c**-d_3 and 14% of **5t**-d_3. The NMR spectra showed that the deuterium was at C_2 and C_7. For **5c**-d_3: NMR δ 1.15 (br s, 3 H, C_2 methyl), 1.4–1.62 (m, 6 H, C_4–C_6 methylenes), 3.23 (s, 3 H, methoxyl), 3.35 (d, 1 H, J = 5.5 Hz, C_3 methine coupled with a C_4 proton). For **5t**-d_3: NMR δ 1.17 (br s, 3 H, C_2 methyl), 1.21–1.83 (m, 6 H, C_4–C_6 methylenes), 3.20–3.24 (m, 1 H, C_3 methine), 3.31 (s, 3 H, methoxyl).

Base-Catalyzed Exchange of 5. A solution of **5c** (40 mg) in 0.01 M sodium methoxide in CH_3OD (5 mL) was stirred at room temperature for 22 h. Workup, including preparative VPC, of half the solution gave **5c**-d_3 (10 mg, 50%) and **5t**-d_3 (4 mg, 20%); after 44 h, the remainder of the solution gave **5c**-d_3 (9 mg, 45%) and **5t**-d_3 (4 mg, 20%). A similar experiment with 0.1 M sodium methoxide in CH_3OH gave, after 32 h, 21 mg (52%) of **5c** and 11 mg (27%) of **5t**.

Base-Catalyzed Addition of Methanol to 6. A solution of **6** (76 mg, 0.55 mmol) in 15 mL of 0.01 M methanolic sodium methoxide was stirred at room temperature, and the reaction was followed by VPC (5 ft × 0.125 in column, 5% SE30 on Chromosorb G, 170 °C). Only a small amount of product was formed in 24 h. The maximum yield was obtained in 192 h, at which time the mixture contained 45% **6**, 20% **7c** and 35% **7t**. The ratio did not change after 2 weeks. For **7t**: IR (CCl_4) 2940 (s), 1705 (s), 1465 (m), 1100 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.14 (d, 3 H, J = 6 Hz, C_2 methyl), 1.25–2.2 (br m, 8 H, C_4–C_7 methylenes), 2.35 (br m, 2 H), 2.95 (br m, 2 H), 3.28 (s, 3 H, methoxyl); mass spectrum, m/e (rel intensity) 170 (5), 138 (31), 123 (6), 109 (23), 98 (21), 81 (29), 71 (100).

LIS shift date were obtained on **7c** and **7t** using Eu(fod)$_3$. The values of Δ (ppm), the shift of each peak caused by adding 1 mol of shift reagent per mol of substrate, were: for **7c**, 10.4 (C_2 methine), 8.7 (C_2 methyl), 8.2 (C_8 methylene), 7.4 (C_3 methine), 4.4 (methoxyl); for **7t**, 4.9 (C_8 methylene), 4.6 (C_2 and C_3 methine), 3.2 (C_2 methyl), 1.4 (methoxyl).[19]

Base-Catalyzed Exchange of 7. A solution of **7c** (25 mg) in 5 mL of 0.01 N methanolic sodium methoxide was stirred at room temperature, and the reaction was followed by VPC. In 24 h, the composition was 45% **6**, 20% **7c**, and 35% **7t**, after which there was no further change.

Acid-Catalyzed Addition of Methanol to 4. A solution of **4** (60 mg) in 3 mL of 0.01 M sulfuric acid in methanol was kept at room temperature. After 29 h, very little **4** remained. The solution was neutralized with sodium bicarbonate, the methanol was removed in vacuo, and the aqueous solution was extracted with ether. NMR (180 MHz) on the crude product showed a 1:1 mixture of **5c** and **5t** (integration of the methyl and methoxyl signals). The ratio was the same after 49 h.

Isomerization Test on 5c with Acid. A solution of **5c** (30 mg) in 0.01 M sulfuric acid in methanol (1.5 mL) was kept at room temperature for 50 h. An NMR spectrum on the crude product, worked up as above, showed only recovered **5c**, no **5t**.

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Registry No. **4**, 65371-57-5; **5c**, 70527-90-1; **5c**-d, 70527-91-2; **5c**-d_3, 70527-92-3; **5t**, 70527-93-4; **5t**-d_3, 70527-94-5; **6**, 70527-95-6; **7c**, 70527-96-7; **7t**, 70527-97-8; **8**, 14525-83-8; **9**, 70527-98-9; **10**, 60934-87-4; **11**, 70527-99-0; **12**, 70528-00-6; **12** epoxide, 70528-01-7; cycloheptanone, 502-42-1; *unsym*-dimethylhydrazine, 57-14-7; cycloheptanone *N,N*-dimethylhydrazone, 39672-01-0; 2-methylcycloheptanone *N,N*-dimethylhydrazone, 70528-02-8; 2-methylcycloheptanone, 932-56-9; 2-bromo-2-methylcycloheptanone, 70528-03-9; cyclooctanone, 502-49-8; cyclooctanone *N,N*-dimethylhydrazone, 62461-18-1; 2-methylcyclooctanone *N,N*-dimethylhydrazone, 70528-04-0; 2-methylcyclooctanone, 10363-27-6; 2-bromo-2-methylcyclooctanone, 70528-05-1; 1,2-dimethyl-2-cycloocten-1-ol, 70528-06-2.

(19) Important differences between the two isomers are (a) generally larger Δ's for **7c** than for **7t**, (b) a larger difference between the C_2 and C_3 methine slopes for **7c** than for **7t**, and (c) a greater Δ for the C_2 methine than for the C_8 methylene protons in **7c** but not in **7t**. These data suggest coordination only at the carbonyl in **7t**, in a conformation in which both the C_2 methyl and C_3 methoxyl are pseudoequatorial, but some bidentate coordination[5] in **7c**, with the methoxyl and methyl pseudoaxial and equatorial, respectively.

Oxidation of Hydrocarbons. 9. The Oxidation of Alkynes by Potassium Permanganate

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A study of the oxidation of nonterminal alkynes by potassium permanganate has revealed that the reaction can be directed along any one of three different pathways: (i) In aqueous solutions, cleavage of the carbon–carbon triple bond, with formation of carboxylic acids, is the main reaction. (ii) In anhydrous methylene chloride solutions, the phase transfer assisted reaction leads to formation of α-diketones in good yields. (iii) In methylene chloride solutions in contact with aqueous permanganate, the phase transfer assisted reaction gives α-diketones plus cleavage products. In the last case, the cleavage reaction results in the loss of one carbon atom, indicating that it proceeds by way of an enol (RCOC(OH)=CHR') to an α-ketocarboxylic acid which subsequently undergoes an oxidative decarboxylation. The assumption that α-diketones are intermediates in the cleavage reactions was substantiated by a study of the oxidation of 8,9-hexadecanedione and 7,8-tetradecanedione under a variety of conditions.

There appears to be little agreement among various authors on the products to be expected from the oxidation of alkynes by potassium permanganate. For example, Freeman[1] states that "Neutral permanganate solution oxidizes carbon–carbon triple bonds to diketones in excellent yield", while Raphael[2] maintains that "the end products [are] two carboxylic acid molecules". This confusion is also reflected in the statements found in

(1) Freeman, F. *Rev. React. Species Chem. React.* **1973**, *2*, 179. This particular statement appears on p 197.

(2) Raphael, R. A. "Acetylenic Compounds in Organic Synthesis"; Academic Press: New York, 1955; p 31.

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