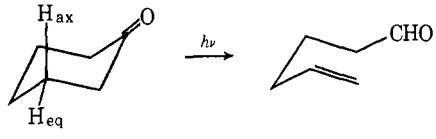
Specificity of Hydrogen Transfer in Photolysis of 3- and 4-Methylcyclohexanone

William C. Agosta*[1] and William L. Schreiber

Contribution from the Laboratories of The Rockefeller University, New York, New York 10021. *Received November 12, 1970*

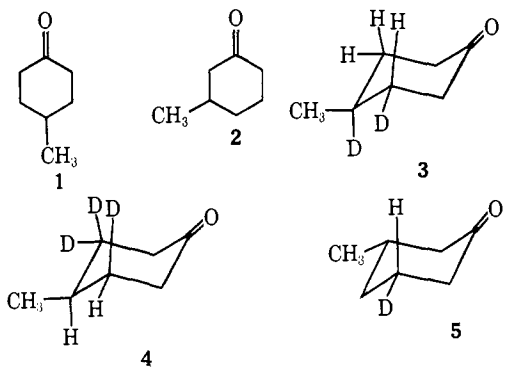
Abstract: Three deuterated 3- and 4-methylcyclohexanones, **3**, **4**, and **5**, have been prepared and photolyzed in methanol along with their unlabeled counterparts, **1** and **2**. Irradiation of **1** leads to aldehyde **22** and ester **23**; irradiation of **2** yields all four α-cleavage products, aldehydes **24** and **25** plus esters **26** and **27**. The deuterium distribution in **22** and **24** from **3**, **4**, and **5** indicates that approximately two-thirds of the aldehydic hydrogen was originally in an axial position and one-third was equatorial. The results support a biradical intermediate with virtually free rotation and involving intermediates **31** and **32**.

The photochemical rearrangement of cycloalkanones to ω-alkenals and ketenes has received extensive attention over the past several years.[2-8] There is now rather general agreement that a discrete biradical intermediate is involved,[3-5] although a concerted pathway was suggested[6,7] earlier, and the possibility of an oxycarbene precursor to the unsaturated aldehyde has been discussed[8] speculatively. In the formation of unsaturated aldehyde a hydrogen atom is transferred to the carbonyl carbon atom from a position β to the carbonyl group. We wish to focus attention here on the stereochemistry of this hydrogen transfer in the reaction leading from cyclohexanones to 5-hexenals. In cyclohexanones this transformation could be stereo-



specific, with either axial or equatorial hydrogen selectively migrating to the carbonyl carbon or alternatively the original distinction between axial and equatorial hydrogen at the β carbon could be partially or totally lost before hydrogen transfer occurs. We have investigated this question in the hope of determining the degree of stereospecificity in cyclohexanones and of reaching thereby a clearer picture of the rearrangement in general. The experiments discussed below concern photolysis of 4-methylcyclohexanone (**1**), 3-methylcyclohexanone (**2**), and the appropriately deuterated derivatives **3**, **4**, and **5**.

Preparation of Labeled Ketones. The deuterated compound **3** was conveniently prepared from *p*-methylanisole. Birch reduction of this aromatic ether furnished **6**,[9] which yielded ketal **7** on treatment with ethylene glycol in hot benzene containing oxalic acid. Reduction[10] of **7** using deuterium gas in benzene with tristriphenylphosphinerhodium(I) bromide as catalyst, followed by acid hydrolysis of the ketal, led to **3**. The other deuterated 4-methylcyclohexanone (**4**) was synthesized[11] starting with 4-benzoyloxycyclohexanone (**8**),[12] which was fully α-deuterated by successive treatments with potassium carbonate in deuterium oxide–ethanol-*d*. The resulting keto ester **9** was then converted to the methylcyclohexenol **10** following a modification of the reported[12] procedure. Reduction[10] of **10** with hydrogen gas in benzene containing tristriphenylphosphinerhodium(I) bromide gave a mixture of 4-methylcyclohexanols (**11**) which was oxidized with Jones reagent[13] to **4**. The deuterium labels introduced in these reactions are expected to be stereospecifically located as indicated in structures **3** and **4**, since the conditions adopted for the hydrogenation reactions are known[10,14] to favor cis addition and also to minimize extraneous hydrogen exchange and double bond isomerization. We have experimentally verified the expected labeling patterns of **3** and **4** by nmr measurements,[15] which



(1) Fellow of The Alfred P. Sloan Foundation.

(2) For reviews of this area see R. Srinivasan, *Advan. Photochem.*, **1**, 83 (1963); G. Quinkert, *Angew. Chem.*, 77, 229 (1965); R. B. Cundall and A. S. Davies, *Progr. Reaction Kinetics*, **4**, 149 (1967); and P. J. Wagner and G. S. Hammond, *Advan. Photochem.*, **5**, 21 (1968). For previous publications in this series, see W. C. Agosta and D. K. Herron, *J. Amer. Chem. Soc.*, **90**, 7025 (1968), and W. C. Agosta, D. K. Herron, and W. W. Lowrance, Jr., *Tetrahedron Lett.*, 4521 (1969).

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(4) J. A. Barltrop and J. D. Coyle, *Chem. Commun.*, 1081 (1969).

(5) P. J. Wagner and R. W. Spoerke, *J. Amer. Chem. Soc.*, **91**, 4437 (1969).

(6) R. Srinivasan, *ibid.*, **81**, 2601 (1959).

(7) R. Srinivasan and S. E. Cremer, *ibid.*, **87**, 1647 (1965).

(8) R. G. Shortridge, Jr., and E. K. C. Lee, *ibid.*, **92**, 2228 (1970).

(9) E. A. Braude, A. A. Webb, and M. U. S. Sultanbawa, *J. Chem. Soc.*, 3328 (1958), and references cited therein.

(10) J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc. A*, 1711 (1966).

(11) A conceptually similar preparation of *cis*- and *trans*-4-*tert*-butylcyclohexanol-3,5,5-d_3 was described by W. F. Trager, B. J. Nist, and A. C. Huitric, *J. Pharm. Sci.*, **56**, 698 (1967).

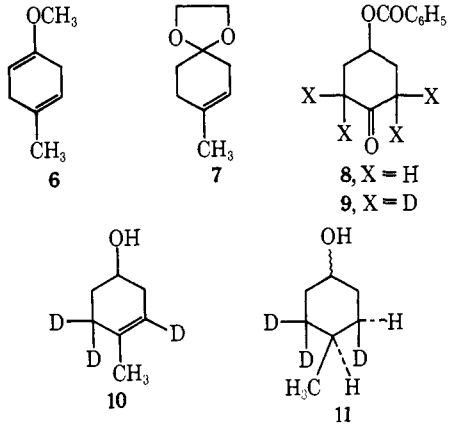
(12) E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 615 (1949).

(13) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *ibid.*, 2548 (1953), and C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

(14) R. L. Augustine and J. F. Van Peppen, *Chem. Commun.*, 495 (1970).

(15) The method is based on the observation that at 220 MHz the axial and equatorial protons at C(3) of **3** and **4** are separated and may be independently integrated.

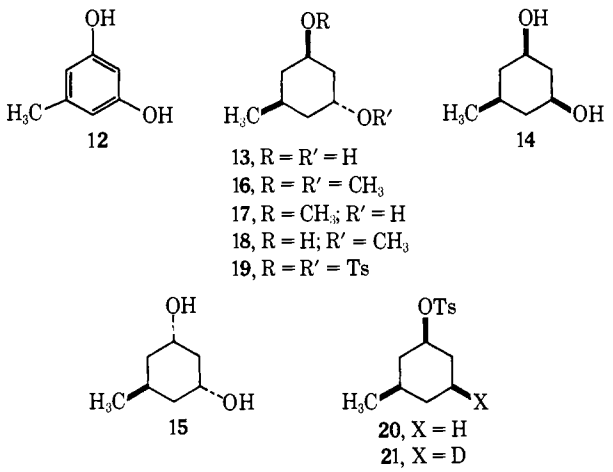
indicated for the equatorial position at C(3) (trans to C(4)–CH_3) 79% deuterium in **3** and 93% protium in **4**. These measurements further showed that no scrambling or exchange of hydrogen had occurred.



6 **7** **8**, X = H; **9**, X = D

10 **11**

Preparation of the labeled 3-methylcyclohexanone (**5**) began with orcinol (**12**). Hydrogenation of this phenol over rhodium on alumina in methanol gave a mixture of methylcyclohexanediols (**13**, **14**, and **15**), of which one isomer was readily separated and purified by fractional crystallization from acetone or ethyl acetate. The first indication that the isolated isomer was the *trans*-diol **13** came from its nmr spectrum in dry pyridine,[16] which showed two separate doublets for the hydroxyl protons. The other two isomers (**14** and **15**), each with *cis*-hydroxyl groups and an internal plane of symmetry, should show a single two-proton signal for these hydroxyl protons. Partial methylation of the isolated diol using methyl iodide and 1 equiv of sodium hydride in dimethyl sulfoxide provided proof that it was indeed the trans isomer **13**. This reaction yielded a mixture of three products, dimethyl ether **16** and two monomethyl ethers, **17** and **18**, which were separated by vapor phase chromatography (vpc). The formation of two monomethyl ethers demonstrates clearly that the diol in hand is the trans isomer, since there can exist only a single monoether from each of the *cis*-diols **14** and **15**.[17] Diol **13** was then esterified with *p*-toluenesulfonyl chloride in pyridine to furnish the beautifully crystalline, stable ditosylate **19**. Treatment of this derivative with lithium aluminum deuteride and lithium deuteride[18] led to selective, stereospecific reduction and formation of the deuterated monotosylate **21**. Selective attack of hydride, displacing the axial tosyloxy group of **19**, was expected[19] and could be easily confirmed experimentally, since reduction of axial sulfonate in **19** leads to a derivative of *cis*-3-methylcyclohexanol, while the alternative displacement of equatorial tosylate yields the isomeric *trans*-3-methylcyclohexyl series. The crude monotosylate **21** was cleaved by reaction[20] with sodium naphthalene anion radical to give *cis*-3-methylcyclohexanol contaminated with virtually none (<0.5%) of the trans isomer. Preparation of the deuterated ketone **5** was completed by oxidation of this alcohol with Jones reagent.[13] Alternatively, exposure of **21** to hot dimethyl sulfoxide containing sodium bicarbonate led directly to **5**.[21] Since hydride reduction of sulfonate esters and halides is known[22] to proceed with inversion, the replacement of the axial tosyloxy function of **19** should furnish **21** and **5** of the indicated stereochemistry (deuterium cis to methyl). This prediction was confirmed experimentally by nmr measurements and deuterium analysis on **5**.



12 **13**, R = R′ = H; **16**, R = R′ = CH_3; **17**, R = CH_3; R′ = H; **18**, R = H; R′ = CH_3; **19**, R = R′ = Ts **14**

15 **20**, X = H; **21**, X = D

Photolysis of Ketones. Irradiation of unlabeled 4-methylcyclohexanone (**1**) in methanol solution led to the expected[2-5] products of α-cleavage, aldehyde **22** and ester **23**. These were isolated and purified by preparative vpc and identified by ir and nmr spectroscopy, as well as elemental analysis of **23** and of the 2,4-dinitrophenylhydrazone of **22**. Similar irradiation of unlabeled 3-methylcyclohexanone (**2**) gave both possible aldehydes, **24** and **25**, and both esters, **26** and **27**. All four products were isolated, purified, and identified by the same procedures employed for **22** and **23**. These results with **2** must be contrasted with the two earlier reports[5,7] that photolysis of **2** leads specifically to 3-methyl-5-hexenal (**24**) with none of the isomeric 5-methyl-5-hexenal (**25**) being found. We have accordingly synthesized aldehyde **25** independently by reaction of the Grignard reagent from 5-chloro-2-methyl-1-pentene (**28**)[23] with methyl orthoformate, and subsequent hydrolysis of the product acetal **29**. Syn-

(16) A number of other solvents, particularly dimethyl sulfoxide, have been previously used to avoid exchange of hydroxyl protons. See L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon, Oxford, 1968, p 299, and references cited therein.

(17) The structure of each of these diastereomeric ethers (17 and 18) could be assigned from comparison of the nmr spectra of **16**, **17**, and **18**. Two principles must be satisfied: (a) equatorial protons appear downfield relative to their axial counterparts (see ref 16, p 238) and (b) conversion of hydroxyl to alkoxyl causes a slight upfield shift of the carbinyl proton (C*H*OR) (see ref 16, pp 176–179, and references cited therein). Application of these principles to the well-separated carbinyl proton signals in **16**, **17**, and **18** leads to unique structural assignments for **17** and **18**. The data and results are recorded in the Experimental Section. One of the *cis*-diols (**14** or **15**) was also obtained pure.

(18) J. E. Johnson, R. H. Blizzard, and H. W. Carhart, *J. Amer. Chem. Soc.*, **70**, 3664 (1948).

(19) From earlier studies the rate of displacement of axial tosylate is known to be much faster than that of equatorial tosylate: E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.*, **79**, 5995 (1957). Displacement of equatorial tosylate is further inhibited in **19** by the shielding to attack at this position provided by the axial tosyloxy substituent.

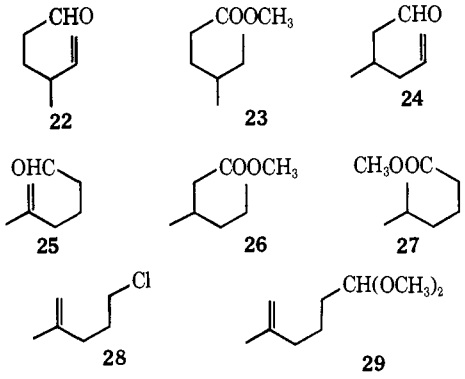
(20) W. D. Closson, P. Wriede, and S. Bank, *J. Amer. Chem. Soc.*, **88**, 1581 (1966).

(21) This is an extension to secondary tosylates of the aldehyde synthesis developed by N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Amer. Chem. Soc.*, **81**, 4113 (1959).

(22) E. L. Eliel, *ibid.*, 71, 3970 (1949); G. K. Helmkamp and B. F. Rickborn, *J. Org. Chem.*, 22, 479 (1957).

(23) G. Stork, H. J. E. Loewenthal, and P. C. Mukharji, *J. Amer. Chem. Soc.*, **78**, 501 (1956).

thetic **25** and the unexpected photoproduct were identical.[24]



Deuterated ketones **3**, **4**, and **5** were now irradiated, and the appropriate aldehyde (deuterated **22** from **3** and **4**, deuterated **24** from **5**) in each case was isolated and the deuterium labeling at C(1) (aldehydic proton) and C(5) (olefinic proton) was determined by nmr spectroscopy.[25] The results are recorded in Table I. Two

Table I. Labeling Patterns of Deuterated **22** and **24**

Compd and position	% protium
C(1) of **22** from **3**	85
C(5) of **22** from **3**	72
C(1) of **22** from **4**	18
C(5) of **22** from **4**	29
C(1) of **24**	65
C(5) of **24**	37

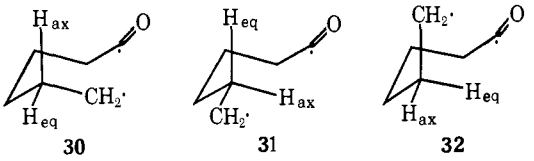
separate determinations of the specificity of hydrogen abstraction are possible for each labeled ketone, since the deuterium levels at C(1) and C(5) are independently measurable. From the labeling data we calculate the percentages of axial hydrogen transfer given in Table II. In these calculations appropriate allowance has

Table II. Percentage of Axial Hydrogen Transfer, Ketone → Aldehyde

	3 → **22**	**4** → **22**	**5** → **24**
Based on C(1)	64	63	68
Based on C(5)	74	64	68

been made for the symmetry properties of 4-methylcyclohexanone (**1**), and it is assumed that the distribution of conformational isomers in the excited state is unchanged from that of the ground state, that is 94% equatorial methyl group in **1** and 90% in **2**.[26] These data suggest slightly greater specificity in transferring the axial protium of **3** than the axial deuterium of **4**. This could be real and due to a kinetic isotope effect favoring protium abstraction, but the data are not sufficiently accurate to be conclusive[27] since the probable experimental error is approximately ±4% for both **3** and **4**. (For **5** the error is approximately ±2%.)

Our results then demonstrate that there is rather little stereospecificity in this reaction. Roughly two-thirds of the aldehydic hydrogens of **22** and **24** were originally in the axial position and one-third were equatorial. These observations are incompatible with any single concerted mechanism for the rearrangement. They could in principle reflect simultaneous operation of two competing concerted mechanisms, one for axial hydrogen and one for equatorial hydrogen, but Barltrop and Coyle have provided[4] kinetic evidence that makes this quite unlikely. The simplest interpretation of our experiments taken with previous information[2-8] is that there is a biradical intermediate (as **30**) with lifetime sufficient to permit free, or almost free, rotation about the C(4)–C(5) bond leading to chairlike intermediates[3] **31** and **32** from which abstraction occurs to give unsaturated aldehyde. The observed preference for transfer of axial hydrogen implies that **31** is favored over **32**. This is plausible since the energy content of **32** with its axial methylene group [C(6)] should be greater than that of **31** in which this group is equatorial.



In closing it should be pointed out that, although we have observed all four possible α-cleavage products from photolysis of 3-methylcyclohexanone (**2**), the directing effect discussed earlier by Wagner[5] is real. It was previously thought[5,7] that in 3-alkylcyclohexanones all α-cleavage leading to rearrangement was directed away from the substituted side of the ring, that is, that effective cleavage occurred only between C(6) and C(1). While this is not the case, we have found that the directing effect does operate, favoring C(6)–C(1) over C(2)–C(1) cleavage for *both* aldehyde (**24** and **25**) and ketene (**26** and **27**) products. The ratios **24**:**25** and **26**:**27** are both approximately 2:1.

Experimental Section

General. Vpc was carried out on Varian Aerograph Models A-90-P3, 700 Autoprep, or 600 Hi-Fi instruments using the following columns (with Chromosorb W support): A, 30% FFAP, 20 ft × 0.25 in. stainless steel; B, 30% QF-1, 10 ft × 3/8 in. aluminum; C, 30% PDEAS, 10 ft × 3/8 in. aluminum; D, 30%

(24) In our hands irradiation of **2** in benzene solution also gives both **24** and **25** in a ratio of approximately 2:1 (see below), although photolysis in benzene is roughly 20-fold slower than in methanol. The previous reports cited concern photolysis of the neat ketone (ref 7) and and of its benzene solution (ref 5). Aldehyde **25** is quite acid labile, much more so than **24**; possibly it escaped previous detection because of this.

(25) The C(5) proton is well separated from the terminal methylene protons at C(6); see A. A. Bothner-By, C. Naar-Colin, and H. Günther, *J. Amer. Chem. Soc.*, **84**, 2748 (1962).

(26) An excellent example of effective retention of ground-state conformation in a photoexcited state is given by J. E. Baldwin and S. M. Krueger, *ibid.*, **91**, 6444 (1969). Conformational distributions were calculated from the accepted conformational energy differences of the ketones (E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, Chapter 2) and the temperature of photolysis: 1.7 kcal/mol at 30° for 1 and 1.2 kcal/mol at 0° for 2.

(27) In an earlier investigation, J. Meinwald, R. A. Schneider, and A. F. Thomas [*J. Amer. Chem. Soc.*, **89**, 70 (1967)] found that photolytic conversion of rigid tricyclic carvonecamphor into the related methyl ester (*via* the ketene) occurs with stereospecific transfer of the *exo*-hydrogen atom. There was suggestive but inconclusive evidence of a kinetic isotope effect. In type II abstraction reactions of ketones isotope effects are observed: R. P. Borkowski and P. Ausloos, *J. Phys. Chem.*, **65**, 2257 (1961); D. R. Coulson and N. C. Yang, *J. Amer. Chem. Soc.*, **88**, 4511 (1966); A. Padwa and W. Bergmark, *Tetrahedron Lett.*, 5795 (1968); and N. C. Yang, S. P. Elliott, and B. Kim, *J. Amer. Chem. Soc.*, **91**, 7551 (1969).

Carbowax 20M, 10 ft × 3/8 in. aluminum; E, 30% DEGS, 10 ft × 3/8 in.; F, 5% FFAP, 20 ft × 1/8 in. stainless steel (Hi-Fi only, 30 ml/min flow rate). Temperatures in the range 110–190° and flow rates of 100–150 ml/min helium were employed.

Ir spectra were recorded on a Perkin-Elmer 237B grating spectrophotometer; nmr spectra were determined on Varian A-60 (60 MHz) and HR-220 (220 MHz) spectrometers; melting points are corrected. The petroleum ether used had bp 30–60°.

4-Methyl-3-cyclohexenone Ethylene Ketal (7). The Birch reduction of *p*-methylanisole (24.4 g, 0.200 mol) was carried out as described[9] and the intermediate enol ether **6** was extracted into benzene. The solution was concentrated to a volume of about 250 ml and ethylene glycol (12.3 ml, 0.220 mol) was added along with 1 g of oxalic acid. The mixture was refluxed through Linde 4A Molecular Sieves (Soxhlet extractor) for 3 hr. The reaction mixture was then washed with aqueous Na_2CO_3, dried over Na_2SO_4, and evaporated. Distillation of the residue provided 24.6 g (80%) of clear colorless liquid: bp 72–76° (aspirator); ir (CCl_4) 1160, 1115, 1065, 1055 cm^{-1}; nmr (60 MHz, CCl_4) δ 1.50–1.90 (m, 5 H), 1.90–2.30 (m, 4 H), 3.97 (s, 4 H), 5.21 (m, 1 H). An analytical sample was prepared by vpc on column B.

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.13; H, 9.10.

4-Methylcyclohexanone-*3,4-d*$_2$ (3). Ketal **7** (2.31 g, 15.0 mmol) was dissolved in 50 ml of benzene (degassed by boiling and cooling under N_2) and 0.12 g of tristriphenylphosphinerhodium(I) bromide was added. The solution was stirred overnight under deuterium gas at about 1 atm. The benzene solution was then stirred with 2 *M* HCl for 3 hr. The product was isolated by extracting with ether, washing with aqueous Na_2CO_3, and drying over Na_2SO_4. Evaporation of the solvent gave a dark red residue which was taken up in petroleum ether and filtered through grade III neutral alumina to remove the catalyst. Evaporation of the solvent gave a light yellow oil which was purified by vpc on column A to provide 0.943 g (56%) of colorless liquid: ir (CCl_4) 2960, 2200–2075 (w), 1745, 1275 cm^{-1} (m); nmr (220 MHz, CCl_4) δ 1.03 (broad s, 3 H), 1.29–1.54 (m, 2 H), 1.78–2.05 (m, 1.4 H), 2.19–2.32 (m, 4 H); nmr of undeuterated 4-methylcyclohexanone (>99% pure by vpc) (220 MHz, CCl_4) δ 0.99 (d, J = 6.5 Hz, 3 H), 1.21–1.50 (m, 2 H, axial C(3)-*H*), 1.70–2.02 (m, 3 H, equatorial C(3)-*H* and C(4)-*H*), 2.03–2.39 (m, 4 H).

4-Benzoyloxycyclohexanone-*2,2,6,6-d*$_4$ (9). A 10-g sample of 4-benzoyloxycyclohexanone[12] (**8**, 51.0 mmol) was dissolved in 15 ml of ethanol-*O-d* and 5 ml of D_2O. Anhydrous K_2CO_3 (0.10 g) was added and the mixture stirred overnight at room temperature. Solvents were removed at aspirator and then vacuum pump pressures, the residue being warmed to 50°. The above process was repeated twice using an additional 12 ml of ethanol-*O-d*, 5 ml of D_2O, and 0.10 g of K_2CO_3 each time. The final residue was taken up in ether, filtered, evaporated, and distilled to give 9.30 g (90%) of colorless oil, bp 115–130° (aspirator). The oil solidified to give material of mp 59–63° which was satisfactory for use in the next step: ir (CCl_4) 1750, 1270, 1110, 705 cm^{-1}; nmr (60 MHz, CCl_4) 2.18 (d, J = 4.7 Hz, 4 H), 5.17–5.57 (m, 1 H), 7.15–7.60 (m, 3 H), 7.85–8.20 (m, 2 H). The material could be recrystallized from ether to give mp 63–65° (lit.[12] mp for undeuterated compound 63°).

4-Methyl-3-cyclohexenol-*3,5,5-d*$_3$ (10). An ether solution of deuterated ketone **9** (8.00 g, 36.4 mmol) was stirred in an ice bath as a 25% excess of methylmagnesium bromide in ether was added dropwise. One hour after the addition was complete 7 ml of saturated aqueous NH_4Cl was added and the mixture was stirred at room temperature, then filtered and evaporated to give a viscous, dark yellow oil. The carbinol was dehydrated by distillation from 4 g of $KHSO_4$ to give 5.3 g of crude product which was directly saponified by boiling it overnight with 10% aqueous KOH and methanol. The alkaline mixture was diluted with brine and extracted with ether. The organic phase was dried over $MgSO_4$ and evaporated through a Vigreux column and then pumped out at aspirator pressure to give 2.16 g of an oil which was used directly in the next reaction: ir (neat) 3340, 3065 (w), 2925, 2040–2260 (w), 1650 (w), 1050 cm^{-1}. A sample was purified by vpc for nmr analysis which indicated the presence of less than 1% of an olefinic proton: nmr (60 MHz, CCl_4) δ 1.05–2.55 (m, 7 H), 3.46 (s, 1 H), 3.55–4.05 (m, 1 H).

4-Methylcyclohexanone-*3,3,5-d*$_3$ (4). Compound **10** (1.72 g, 15.3 mmol) was dissolved in 25 ml of benzene with 80 mg of tristriphenylphosphinerhodium(I) bromide. The solution was shaken overnight with H_2 at an initial pressure of 58 psig. The solvent was removed through a Vigreux column and the residue taken up in acetone and treated with excess Jones reagent.[13] The excess reagent was destroyed by adding a few drops of isopropyl alcohol and the mixture was filtered and evaporated. The residue was taken up in petroleum ether, dried over K_2CO_3, filtered, and evaporated to an orange oil. Distillation at aspirator pressure gave 0.90 g (52%) of clear colorless liquid which was suitable for irradiation (vpc); ir (CCl_4) 2955, 2030–2250 (w), 1750 cm^{-1}; nmr (220 MHz, CCl_4) δ 0.99 (d, J = 7 Hz, 3 H), 1.73–1.96 (m, 1.86 H), 2.20 (broad s, 4 H).

5-Methyl-*trans*-1,3-cyclohexanediol (13). A 30-g sample (0.211 mol) of orcinol hydrate (**12**, Eastman practical) in methanol was hydrogenated over 1 g of 5% Rh/Al_2O_3 in a Parr shaker overnight. The mixture was then filtered and evaporated to dryness. Recrystallization twice from acetone gave 9.30 g (34%) of colorless flakes, mp 139–143°, suitable for the next step. Fractional crystallization from ethyl acetate instead of acetone gave similar results but was more tedious. The above material could be recrystallized to give mp 144–145°: ir (KBr disk against KBr reference) 3325, 3225, 2940, 1355, 1040, 1017, 990 cm^{-1}; nmr (220 MHz, dry pyridine) δ 0.95 (d, J = 6 Hz), 1.05–1.34 (m), 4.50–4.61 (m), 4.61–4.77 (m), 5.93 (d, J = 3 Hz), 6.08 (d, J = 5 Hz).

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.57; H, 10.86.

From the mother liquors a second isomer (**14** or **15**) could be obtained by recrystallization from ethyl acetate: mp 95–96°; ir (KBr disk against KBr reference) 3340, 2940, 2925, 1350, 1090, 1025, 1010 cm^{-1}; nmr (220 MHz, dry pyridine) δ 0.91 (d, J = 6 Hz), 1.04–2.13 (m), 2.67–2.88 (m), 3.78–4.03 (m), 6.16 (d, J = 4.5 Hz).

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.83; H, 10.98.

Partial Methylation of Diol 13. A 550-mg sample (4.24 mmol) of diol **13** was added in 5 ml of dimethyl sulfoxide to a suspension of sodium hydride (225 mg, 53% in mineral oil, 4.97 mmol) in 5 ml of dimethyl sulfoxide. The mixture was stirred at room temperature until evolution of gas ceased at which time an excess of methyl iodide (0.33 ml) was added. After 2 hr the reaction was worked up by partitioning between water and ether. Evaporation of the organic layer and flash distillation of the residue afforded 318 mg of colorless oil which was separated into three major components by vpc on column D. The material first eluted was the predominant product, 5-methyl-*trans*-1,3-dimethoxycyclohexane (**16**): ir (CCl_4) 2945, 2920, 2865, 2815, 1455, 1125, 1100, 1085 cm^{-1}; nmr (220 MHz, CCl_4) δ 0.64–1.04 (m, 3 H), 0.93 (d, J = 6.5 Hz, 3 H), 1.64–2.30 (m, 4 H), 3.28 (s, 3 H), 3.30 (s, 3 H), 3.32–3.42 (m, 1 H, axial C*H*OCH_3), 3.57–3.64 (m, 1 H, equatorial C*H*-OCH_3).

Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.41; H, 11.49.

The second compound eluted from the column was *cis*-5-methyl-*trans*-3-methoxycyclohexanol (**18**): ir (CCl_4) 3625 (m), 3400 (m), 2925, 1085, 1015 cm^{-1}; nmr (220 MHz, CCl_4) δ 0.70–1.36 (m with d, J = 6 Hz, at 0.93, 6 H), 1.59–2.27 (m, 5 H), 3.28 (s, 3 H), 3.55–3.68 (m, 1 H, axial C*H*OH), 3.73–3.94 (m, 1 H, equatorial C*H*OCH_3).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.63; H, 11.21.

The third component, which was formed to a somewhat greater extent than the second, was *trans*-5-methyl-*trans*-3-methoxycyclohexanol (**17**): ir (CCl_4) 3625 (m), 3450 (m), 2925, 1095, 990 cm^{-1}; nmr (220 MHz, CCl_4) δ 0.66–1.28 (m, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 1.57–2.13 (m, 5 H), 3.32 (s, 3 H), 3.40–3.59 (m, 1 H, axial C*H*OCH_3), 4.17–4.26 (m, 1 H, equatorial C*H*OH).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.44; H, 11.32.

5-Methyl-*trans*-1,3-cyclohexanediol Bis-*p*-toluenesulfonate (19). Diol **13** (mp 139–143°, 9.30 g, 0.0715 mol) was dissolved in about 100 ml of pyridine along with 45 g (0.24 mol) of *p*-toluenesulfonyl chloride, and the mixture was kept at room temperature for 2 days. It was then poured into ice water, stirred, and seeded. After a few minutes the gum solidified and was filtered from the cold solution. The tan solid was washed well with water and dried *in vacuo*. Recrystallization from ether gave 26.4 g (84%) of large colorless crystals: mp 75–77°; ir (CCl_4) 1370, 1185, 1175; nmr (60 MHz, CCl_4) 0.89 (d, J = 6 Hz, 3 H), 1.05–2.27 (m, 7 H), 2.46 (s, 6 H), 4.26–4.97 (m, 2 H), 7.20–7.50 (m, 4 H), 7.58–7.87 (m, 4 H).

Anal. Calcd for $C_{21}H_{26}S_2O_6$: C, 57.53; H, 5.98. Found: C, 57.69; H, 6.10.

3-Methylcyclohexanone-*5-d* (5). Method A. Ditosylate **19** (35.3 g, 80.5 mmol) was treated with 0.530 g (12.6 mmol) of lithium

aluminum deuteride and 1.33 g (148 mmol) of lithium deuteride in refluxing ether for 40 hr. The mixture was then stirred in an ice bath as 3 ml of saturated aqueous NH_4Cl was added. After several minutes the reaction mixture was dried over Na_2SO_4, filtered, and evaporated. The residue was triturated with about 400 ml of petroleum ether and seeded with **19**. After crystallization appeared complete the mixture was refrigerated for several hours and then filtered to give 7.06 g of starting material, mp 74–75.5°. Solvent was evaporated from the mother liquor to give 11.3 g (65% based on unrecovered **19**) of oily tosylate **21**: nmr (60 MHz, CCl_4) δ 0.40–2.64 (m, 8 H), 0.89 (d, J = 5 Hz, 3 H), 2.43 (s, 3 H), 4.01–4.65 (m 1 H), 7.29 (d, J = 8 Hz, 2 H), 7.74 (d, J = 8 Hz, 2 H).

The above material was treated with sodium naphthalene anion radical in tetrahydrofuran as described.[20] Chromatography on grade I neutral alumina provided a convenient separation of the product from the excess of naphthalene. By comparison with authentic samples of *cis*- and *trans*-3-methylcyclohexanol (Chemical Samples Co.) it was shown (column F) that the product contained less than 0.5% *trans*-3-methylcyclohexanol based on the cis isomer. Treatment of this material in acetone with excess Jones reagent afforded the ketone **5**, 1.47 g (31% based on **21**) after distillation. Vpc on column B removed several minor impurities: ir (CCl_4) 2955 (m), 2240–2100 (w), 1720 cm^{-1}; nmr (220 MHz, CCl_4) δ 1.04 (d, J = 6 Hz, 3 H), 1.23–1.42 (m, 1 H), 1.54–1.74 (m, 1 H); for $C_7H_{11}DO$, calcd atom % excess D, 8.33; found (falling drop), 8.18, 8.25 ± 0.2; nmr of undeuterated 3-methylcyclohexanone (>99% pure by vpc) (220 MHz, CCl_4) 1.10 (d, J = 6 Hz, 3 H), 1.29–1.52 (m, 1 H, axial C(4 or 5)-*H*), 1.62–1.86 (m, 1 H, axial C(5 or 4)-*H*), 1.86–2.48 (m, 7 H).

Method B. Tosylate **21** (4.43 g, prepared as in method A) was dissolved in 25 ml of dimethyl sulfoxide and 5.0 g of $NaHCO_3$ was added. The mixture was stirred and heated in an oil bath at 150° for 6 min during which time considerable frothing occurred. The product was isolated by partitioning the reaction mixture between water and ether, drying the organic extracts over Na_2SO_4, and evaporating the solvent to provide 0.941 g of an orange oil. Purification of this material on column D yielded 369 mg (20%) of clear colorless oil. Although this material was homogeneous by vpc it had a sulfurous odor and was therefore repurified on column B before photolysis.

5-Chloro-2-methyl-1-pentene (28).[23] 4-Methyl-4-penten-1-ol (Chemical Samples Co., 5.00 g, 50.0 mmol) was dissolved in 50 ml of CCl_4 and 13.8 g (52.7 mmol) of triphenylphosphine was added.[28] After 1 hr at room temperature the solvent was distilled out through a Vigreux column. The residue was taken up in petroleum ether, filtered to remove triphenylphosphine oxide, and distilled to yield 3.03 g (51%) of clear colorless liquid: bp 44–47° (30 mm); ir (CCl_4) 3080 (m), 2955, 1655 (m), 1445, 885 cm^{-1}; nmr (60 MHz, CCl_4) δ 1.58–2.42 (m with broad s at 1.73, 7 H), 3.49 (t, J = 6 Hz, 2 H), 4.73 (m, 2 H).

5-Methyl-5-hexenal Dimethyl Acetal (29). Chloride **28** (3.03 g, 25.6 mmol) was converted to its Grignard reagent with 0.68 g (28 mg-atoms) of magnesium turnings in ether. Trimethyl orthoformate (2.85 g, 26.9 mmol) was added, and the mixture was stirred at reflux for several hours and at room temperature for 2 days. Aqueous ammonium formate was then added carefully, and the product was isolated by extraction with ether. The ether solution was dried over Na_2SO_4 and evaporated yielding 2.83 g (70%) of sweet-smelling, colorless liquid. Vpc on column D yielded an analytical sample: ir (CCl_4) 3075 (w), 2945, 1650 (m), 1125, 1070, 885 cm^{-1}; nmr (60 MHz, CCl_4) δ 1.17–2.26 (m, 6 H), 1.71 (barely resolved t, $J \sim 1$ Hz, 3 H), 3.20 (s, 6 H), 4.12–4.47 (m, 1 H), 4.67 (m, 2 H).

Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.74. Found: C, 68.38; H, 11.56.

5-Methyl-5-hexenal (25). Acetal **29** (1.00 g) was stirred with 6 ml of tetrahydrofuran and 3 ml of 0.1 *M* aqueous HCl. The unusual acid sensitivity of the product aldehyde **25** (see ref 24) required that the reaction be monitored by vpc (column D) and terminated long before hydrolysis of the acetal was complete. The reaction mixture was poured into aqueous Na_2CO_3 and extracted with ether. The organic phase was dried over Na_2SO_4, evaporated through a Vigreux column, and chromatographed on column D to give recovered acetal **29** and the aldehyde **25**, identical by ir and nmr spectral comparisons with the corresponding product from photolysis of 3-methylcyclohexanone.

It was found that a 2,4-dinitrophenylhydrazone of **25** could be obtained only in the cold. Once freed from acid it could be recrystallized without decomposition. Thus a cold methanol solution of the aldehyde was treated with 2,4-dinitrophenylhydrazine in 85% phosphoric acid. The derivative precipitated immediately. After a few minutes in an ice bath the solid was collected and washed with cold methanol. Recrystallization from methanol then gave orange crystals, mp 103–104° (lit.[29] mp 97–98°).

Anal. Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.71. Found: C, 53.37; H, 5.66; N, 19.32.

Photochemical Reactions. Ultraviolet light was provided by a 450-W medium-pressure mercury arc, Hanovia Type L-679A-36, contained in a water-cooled quartz immersion well. Solutions of the ketones (about 20 mg/ml) in methanol (distilled from magnesium methoxide) were irradiated through Pyrex in torodial vessels at ambient temperatures (unless otherwise noted). Prepurified nitrogen was bubbled through the solutions before and during irradiation. After irradiation the solutions were concentrated through a Vigreux column and the products isolated by vpc.

Photolysis of 4-Methylcyclohexanone (1). After a 6-hr irradiation of 1.65 g of **1**, two major products were isolated from column B. Each was further purified on column C. The compound first eluted (column B) was 4-methyl-5-hexenal (**22**): ir (CCl_4) 3080 (w), 2720 (w), 1735, 1640 (w), 990 (w), 910 cm^{-1} (m); nmr (60 MHz, CCl_4) δ 1.02 (d, J = 6 Hz, 3 H), 1.23–1.56 (m, 5 H), 4.70–5.20 (m, 2 H, $=CH_2$), 5.27–5.94 (m, 1 H, $=CH$), 9.67 (t, J = 1 Hz, 1 H). Material collected from column B gave a 2,4-dinitrophenylhydrazone, mp 90–91° (from methanol).

Anal. Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.28; H, 5.69; N, 19.38.

The other product was methyl 4-methylhexanoate (**23**): ir (CCl_4) 2965, 2930, 1745, 1190, 1170 cm^{-1}; nmr (60 MHz, CCl_4) δ 0.65–2.09 (m, 11 H), 2.09–1.48 (m, 2 H), 3.61 (s, 3 H).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.73; H, 11.36.

Photolysis of 3-Methylcyclohexanone (2). Irradiation of 1.65 g of **2** for 6 hr gave a mixture which was separated into two fractions (**24** plus **26**, and **25** plus **27**) on column C, each of which was separated into two components on column B. The major products were as follows.

3-Methyl-5-hexenal (24): ir (CCl_4) 3080 (w), 2965 (m), 2720 (m), 1735, 1640 (w), 990 (w–m), 910 (m); nmr (60 MHz, CCl_4) δ 0.97 (m, 3 H), 2.07–2.46 (m, 5 H), 4.77–5.20 (m, 2 H), 5.35–6.14 (m, 1 H), 9.67 (t, J = 1.5 Hz, 1 H); 2,4-dinitrophenylhydrazone (from methanol) mp 75.5–76°.

Anal. Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.30; H, 5.73; N, 19.34.

5-Methyl-5-hexenal (25, could also be isolated directly using column E): ir (CCl_4) 3080 (w), 2940 (m), 2715 (m), 1735, 1655 (w), 885 (m); nmr (60 MHz, CCl_4) δ 1.57–2.80 (m with broad s at 1.70, 9 H), 4.58 (m, 2 H), 9.67 (t, J = 1 Hz, 1 H).

Methyl 3-methylhexanoate (26): ir (CCl_4) 2960, 1745, 1190, 1170 cm^{-1}; nmr (60 MHz, CCl_4) δ 0.77–1.08 (m, 6 H), 1.08–2.05 (m, 5 H), 2.05–2.30 (m, 2 H), 3.60 (s, 3 H).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.43; H, 11.29.

Methyl 5-methylhexanoate (27): ir (CCl_4) 2965, 1745, 1165 cm^{-1}; nmr (60 MHz, CCl_4) δ 0.90 (d, J = 6 Hz, 6 H), 1.02–1.97 (m, 5 H), 2.03–2.40 (m, 2 H), 3.58 (s, 3 H).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.39; H, 11.16.

When 1.00 g of 3-methylcyclohexanone (**2**) was photolyzed in 50 ml of benzene for 12 hr, vpc (column C) indicated only about 25% conversion of starting ketone. After irradiation the solution was stirred for several minutes with aqeuous $NaHCO_3$ to remove ketenes and then concentrated through a Vigreux column. Two products with retention times (column C) corresponding to the aldehydes from photolysis in methanol were isolated; ir spectra confirmed that they were **24** and **25**.

Photolysis of Ketone 3. After irradiation of **3** (0.90 g) for 3 hr the aldehyde product was isolated by vpc on column B and further purified on column C: nmr (220 MHz, CCl_4) δ 4.91 (2.00 H defined), 5.54 (0.72 H), 9.67 (0.85 Hz).

Photolysis of Ketone 4. Compound **4** (0.90 g) was irradiated and the aldehyde isolated as for **3** above: nmr (220 MHz, CCl_4) δ 4.91 (2.00 H defined), 5.56 (0.29 H), 9.67 (0.18 H).

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To provide a standard for the above experiments the undeuterated ketone **1** was photolyzed and the aldehyde isolated as above: nmr (220 MHz, CCl_4) δ 4.91 (2.00 H defined), 4.54 (0.98 H), 9.67 (0.91 H).

Photolysis of Ketone 5. Ketone **5** (1.09 g) was irradiated for 3.5 hr during which time the apparatus was immersed in a circulating ice bath. The products were isolated by pouring the methanol solution into water and extracting with 1:1 ether–pentane. The extracts were dried over Na_2SO_4 and evaporated through a Vigreux column. The aldehyde corresponding to **24** was then isolated by vpc on column B: nmr (220 MHz, CD_3CN) δ 5.03 (2.00 H defined), 5.80 (0.37 H), 9.70 (0.65 H). A sample of aldehyde **24** was prepared in the same way from the undeuterated ketone (**2**): nmr (220 MHz, CD_3CN) δ 5.03 (2.00 H defined), 5.80 (0.98 H), 9.70 (0.96 H).

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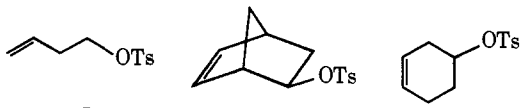
Enhanced Homoallylic Participation. Bicyclo[2.2.2]octyl Systems

Joseph B. Lambert*[1a] and Allen G. Holcomb[1b]

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. *Received November 19, 1970*

Abstract: The acetolysis of *cis-exo*-2,3-bicyclo[2.2.2]oct-5-enyl ditosylate (VI) proceeds 6850 times more rapidly than does acetolysis of its saturated analog, *cis*-2,3-bicyclo[2.2.2]octyl tosylate (VII). The corresponding monotosylate, *exo*-2-bicyclo[2.2.2]oct-5-enyl tosylate (VIII), acetolyzes only 63 times more rapidly than its saturated analog, 2-bicyclo[2.2.2]octyl tosylate (IX). The large acceleration in VI compared to VIII results from an enhanced requirement of the double bond to participate. As the first tosylate group solvolyzes, the double bond is called upon to provide greater charge dispersal because of the presence of the remaining electron-withdrawing tosylate group. This interpretation is reinforced by measurement of the solvolysis rate for *trans*-2,3-bicyclo[2.2.2]oct-5-enyl ditosylate (X). There is no evidence in any of these systems for loss of two tosylate groups to form a dicarbonium ion.

Homoallylic assistance in the solvolysis of arenesulfonate esters does not give rise to extremely large rate accelerations. Thus allylcarbinyl tosylate (I) formolyzes only 3.7 times more rapidly than *n*-butyl



I II III

tosylate,[2] *exo*-2-norborn-5-enyl tosylate (II) acetolyzes 3.37 times more slowly than *exo*-2-norbornyl tosylate,[3] and 3-cyclohexenyl tosylate (III) acetolyzes 1.26 times more slowly than cyclohexyl tosylate.[4] In the tabulation of Hanack and Schneider,[5] the largest value for k_{unsat}/k_{sat} in acetolysis is 350. The double bond in this system, (γ,γ-dimethylallyl)carbinyl tosylate, is trisubstituted. Although ions of varying symmetry have been suggested to describe double bond participation in these solvolyses,[5] we shall for simplicity utilize the term "homoallylic participation" to describe such interactions.[6] These relatively small rate accelerations, characteristic of systems with the double bond unsymmetrically disposed with respect to the leaving group, contrast with the factor of about 10^{11} in the solvolysis of *anti*-7-norbornenyl tosylate (IV),[7] in which the

IV V

symmetrical placement of the double bond permits formation of a bishomocyclopropenium ion.[7] The present studies concern only unsymmetrical (homoallylic) systems.

Recently, we reported that *cis-exo*-2,3-norborn-5-enyl ditosylate (V) acetolyzes 500 times more rapidly than its saturated analog,[3,8] in marked contrast with the unsaturated monotosylate II and other systems with disubstituted double bonds unsymmetrically positioned with respect to the leaving group.[3] We attributed this remarkable acceleration to an enhanced requirement of the double bond to participate.[8] More effective positive charge dispersal in the transition state can diminish the rate-retarding influence of the remaining electronegative substituent (the second tosylate group). The saturated analog of V apparently has little or no

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