an important bearing on the current controversy concerning the nature of bridged carbonium ions.

Experimental Section

Mass spectra were measured on an Atlas CH-4 apparatus; temperature of source 275°, temperature of introducton 150°, ionizing voltage 70 ev. Gas–liquid partition chromatography was carried out at 200° using a column of 15% Carbowax on Chromosorb W.

endo-α-**Deuteriocamphor (8).** A solution of 250 mg of α,α-dideuteriocamphor[13] (97% d_2), five drops of 40% sodium hydroxide solution, and 10 ml of 50% aqueous dioxane was heated for 15 min on a steam bath and then allowed to stand overnight. Pentane was added, and the solution was washed with water and evaporated, giving crude **8**, which after purification by glpc contained 21% d_2, 64% d_1, and 15% d_0.

endo-α-**Deuterioisoborneol (9).** To 50 mg of lithium aluminum hydride in 25 ml of dry ether was added 200 mg of *endo*-α-deuteriocamphor (**8**). After 3 hr at room temperature 1 ml of water was added to decompose excess hydride. Filtration and concentration left the crude alcohol (**9**), which was purified by glpc.

endo-α-**Deuterio-*endo*-isofenchyl Compounds.** *endo*-α-Deuterioisofenchone, *endo*-α-deuterio-*endo*-isofenchol (**12**), and *endo*-α-deuterio-*endo*-isofenchyl acetate were prepared, starting with isofenchone, by the same procedures used to prepare the corresponding isobornyl compounds. After purification by glpc, **11** contained 7% d_2, 78% d_1, and 15% d_0.

exo-α-**Deuteriocarvonecamphor (13).** A pellet of sodium about 1 mm in diameter was dissolved in a solution of 5 ml of deuterium oxide and 5 ml of dry, peroxide-free dioxane; then 250 mg of carvonecamphor was added. The mixture was allowed to stand overnight and then was extracted with pentane. The pentane was washed twice with 2 ml of deuterium oxide, then with water, and then evaporated. The residue was treated with excess potassium permanganate solution in the presence of Dry Ice chips, and then sodium oxalate solution was added and the *exo*-α-deuteriocarvonecamphor was separated by steam distillation. It was found to be pure by glpc analysis, and contained 95% d_1 and 4% d_0.

endo-α-**Deuteriocarbonecamphor (14).** This compound was prepared by the same procedure described for *endo*-α-deuteriocamphor, starting with α,α-dideuteriocarvonecamphor prepared as described previously.[14] The product contained 87% d_1 and 13% d_0.

Acknowledgment. We gratefully acknowledge the assistance of Dr. K. H. Schulte-Elte in the preparation of carvonecamphor and Dr. B. Willhalm for assistance with the mass spectra.

(13) D. S. Weinberg and C. Djerassi, *J. Org. Chem.*, **31**, 115 (1966).

(14) J. Meinwald and R. A. Schneider, *J. Am. Chem. Soc.*, **87**, 5218 (1965).

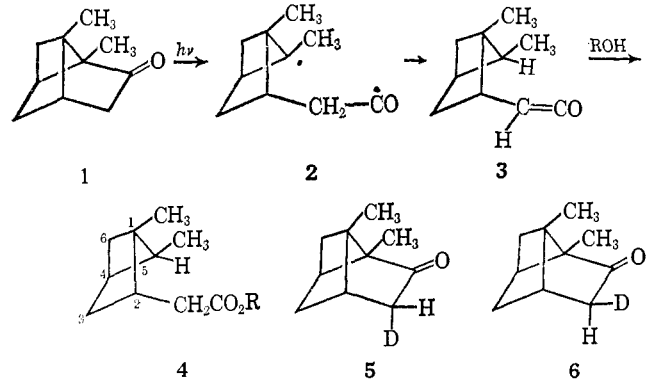
Stereospecific Hydrogen Transfer in the Photolysis of Carvonecamphor[1]

Jerrold Meinwald, Ronald A. Schneider,[2] and Alan F. Thomas

Contribution from the Department of Chemistry, Cornell University, Ithaca, New York 14850, and the Laboratoires de Recherches, Firmenich & Cie, Geneva, Switzerland. *Received August 29, 1966*

Abstract: *endo*-α-Deuteriocarvonecamphor (**5**) is transformed into the deuterated ester **7**; this change corresponds to transfer of the *exo*-α-proton upon irradiation in methanol solution. The *exo*-α-deuterated isomer **6** gives chiefly ester **9**, *via* deuteron transfer, under similar conditions. The stereospecific transfer of the *exo*-hydrogen atom α to the carbonyl group is thus established. The mass spectra of a variety of deuterated products encountered in this work are presented, and the mechanistic implications of the stereospecific photolytic reaction are explored briefly.

The photolysis of carvonecamphor (**1** → **4**) provides a particularly clean example of the well-known photolytic conversion of cyclic ketones into carboxylic acids or their derivatives.[3] A sizeable body of evidence supports the general mechanism in which an excited ketone molecule suffers homolytic cleavage to give a diradical, which is then transformed into a ketene *via* an intramolecular hydrogen atom transfer.[4] Addition of nucleophilic solvent to the ketene gives rise to the usual products. Consideration of this mechanism, pictured below for the case of carvonecamphor, raises the question of whether the hydrogen atom transfer step (**2** → **3**) would show any appreciable degree of stereospecificity with respect to which of the hydrogen atoms on the donor carbon atom would be transferred.



Since the photochemical formation of **4** is almost free of competing processes, this reaction provides an attrac-

(1) The partial support of this work by a research grant (GP 4128), from the National Science Foundation is acknowledged with pleasure.

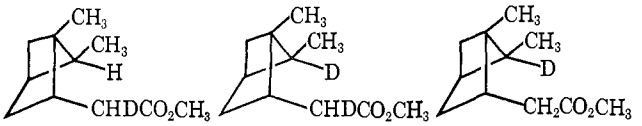
(2) National Science Foundation Cooperative Graduate Fellow, 1962–1965; National Institutes of Health Fellow, 1965–1966.

(3) J. Meinwald and R. A. Schneider, *J. Am. Chem. Soc.*, **87**, 5218 (1965); see also T. Gibson and W. F. Erman, *J. Org. Chem.*, **31**, 3028 (1966).

(4) For recent reviews of this group of reactions, see G. Quinkert, *Angew. Chem.*, **77**, 229 (1965), and G. Quinkert in "International Symposium on Organic Photochemistry," Butterworth & Co. (Publishers) Ltd., London, 1964 (*Pure Appl. Chem.*, **9**, 607 (1964). See also ref 3, and J. Iriarte, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **47**, 1255 (1964).

tive opportunity to examine this previously unexplored stereochemical point. Toward this end we have prepared both *endo-* and *exo-α*-deuteriocarvonecamphor (**5** and **6**),[5] and we now wish to report the results of irradiating methanolic solutions of these labeled, bridged ketones.

Photolysis of 5 and 6. *endo-α*-Deuteriocarvonecamphor (**5**) was irradiated in methanol and the resultant methyl ester isolated in the usual way. The infrared, nmr, and mass spectra of this ester proved to be essentially identical with those of the monodeuterated methyl ester **7** obtained previously[3] by diazomethane esterification of the acid formed *via* irradiation of unlabeled **1** in dioxane–deuterium oxide.[6] The presence of one deuterium atom α to the methoxycarbonyl group was reflected in the nmr integration (τ 7.5–8.5).



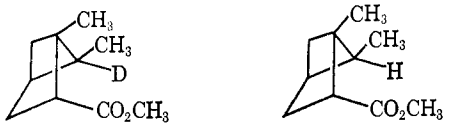
7 **8** **9**

The absence of any significant amount of deuterium from C_5 was clearly shown in the nmr spectrum by the appearance of the C_5-methyl group as a *doublet* (τ 8.95, J = 6 cps), exactly as it appears in unlabeled **4** (R = CH_3), with no trace of the essentially unsplit C_5-methyl resonance previously observed to be characteristic of the C_5-deuterated ester **8**.[3]

This experiment indicated a clear preference for transfer of the *exo-α*-proton in **5** rather than the *endo-α*-deuteron. This preference might be interpreted either as an isotope effect or as a steric effect. The former possibility can be ruled out as the dominant one by the results obtained with *exo-α*-deuteriocarvonecamphor (**6**).

When a methanolic solution of **6** was irradiated, the resultant ester showed a sharp C_5-methyl group *singlet* at τ 8.97 in its nmr spectrum, flanked by two small peaks analogous to the C_5-methyl doublet of unlabeled **4** (R = CH_3). It follows that **6** suffered nearly complete transfer of its *exo* α-deuteron to C_5, giving **9** as the major product.

In order to determine more precisely the extent of deuterium transfer to C_5, the photolysis product **9** was



10 **11**

converted into the next lower homolog, **10**, by means of a Barbier–Wieland degradation. The nondeuterated Barbier–Wieland product **11** showed a C_5-methyl doublet centered at τ 8.94 (J = 6 cps). The deuterated ester **10** showed a singlet at τ 8.94 and a small peak at 8.89 which represented the only half of the doublet which would have been observable. The area of the doublet peak indicated that H was present at C_5 to the extent of about 10–20%.[7]

Mass Spectra. To confirm these observations mass spectra were obtained of **4** (R = CH_3), **7**, **8**, and **9**, as well as of **10** and **11**.

The two samples of **7**, prepared in the different ways referrred to above, gave mass spectra which were identical.[6] This identity verifies the conclusion drawn from nmr evidence that, in the case of *endo-α*-deuteriocarvonecamphor, the radical abstraction is very nearly stereospecific.

The product **9** derived from **6** retained the same degree of monodeuteration (94–96%) that characterized the starting *exo-α*-deuteriocarvonecamphor. The lower homolog, **10**, appeared to contain 90–95% of monodeuteriated species as calculated by comparing the relative abundances of its M^+ and $(M - 1)^+$ fragments (at 20 ev) with those of the nondeuterated **11**. However, since the $(M - 1)^+$ fragment is almost one-third as abundant as the M^+ fragment, and since the M^+ fragment is very small, this calculation may not be very accurate, and a more reliable fragment ought to be $(M - 15)^+$, which is roughly ten times as abundant and with respect to which the nondeuterated fragment of one lower mass number is negligible.

The mass spectral data are presented in Table I. The relationship between **4**, **7**, **8**, and **9** is evident from the fragments listed.

Table I. Principal Mass Spectral Fragments

Compd	4	7	9	8	11	10
Base fragment	108	108	108	108	109	110
			109	109	108	109
Other fragments in order of decreasing abundance	93	93	94	94	55	56
			93	85	67	68
	41	85	85	110	93	94
	55	55	110	93	41	41
	85	41	107	107	127	128
			41	41	139	139
	67	67	68	68	153	154
			59	59	168	169
	122	123	123	124		
	153	154	142	154		
	141	142	153	143		
	167	168	168	169		
	182	183	183	184		

In all of the fragments above *m/e* 120 arising from each of the six compounds all the deuterium is completely retained except for the fragment which is $(M - 29)^+$ if an H atom is at C-5 (**4**, **7**, and **11**) and $(M - 30)^+$ if a D atom is at C-5 (**8**, **9**, and **10**). This fragment must accordingly arise from loss of the C-5 carbon atom accompanied by its substituents and an additional hydrogen atom.

(5) A. F. Thomas, R. A. Schneider, and J. Meinwald, *J. Am. Chem. Soc.*, **89**, 68 (1967).

(6) It might be noted that the samples of 7 prepared in the two different ways may actually be stereoisomers, since one arises from the reaction of the ketene **3** with deuterium oxide and the other from the reaction of the deuterated ketene with ordinary methanol. If protonation were stereoselective, different stereoisomers would result. In fact, the infrared and mass spectra of the two samples appear to be identical, while the nmr spectra show subtle differences in the region τ 7.5–8.5, the real significance of which is uncertain. Although these results are ambiguous, this point is not relevant to the major problem under consideration in this work.

(7) This evidence might now suggest that an isotope effect is operating to make the transfer in the case of **6** (where D is transferred in preference to H) less selective than in the case of **5** (where H is transferred in preference to D), but the precision of our measurements is not sufficient to allow one to make a meaningful statement. This problem is now being examined in other cases by Dr. Alfred Courtin at Cornell University.

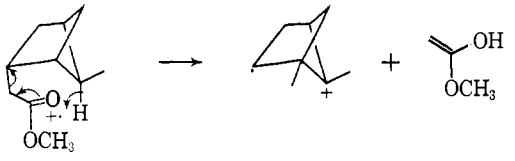
The position of the deuterium in **7** has been proved, as previously reported,[3] by the fact that the mass spectral fragments of **7** are identical with those of the nondeuterated **4** between *m/e* 25 and 120 (all principal fragments in that range were concluded to derive from loss of the side chain at C-2), while above 120 they are identical except that every fragment in the spectrum of **4** is shifted to one higher mass number in the spectrum of **7**. This same statement can be made for **9** and **8**, establishing that **9** and **8** are related in the same way.

The mass spectra of **7** and **9**, while not being related so simply, are in fact surprisingly similar. The base fragment, 108, is the same for each. Table II indicates the relative abundances of the fragments from *m/e* 107 to 110 for **4**, **7**, **8**, and **9**.

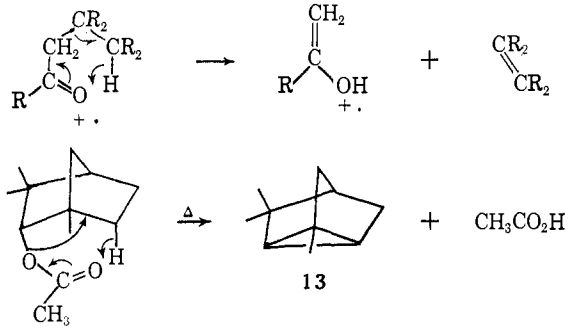
Table II. Relative Abundances of Fragments in the Mass Spectra of Photolysis Products

Compd	Abundance at *m/e* 107	108	109	110
4	40	100	39	3
7	24	100	32	8
8	39	100	99	40
9	33	100	79	36

The base fragment, 108, of **4** and **7** arises from loss of the side chain and hydrogen transfer.[3] For **9** and **8**, the fragment at 108 has been only partially displaced to 109, but the fragment at 109 (in which, presumably, the side chain is lost but no hydrogen is transferred) is apparently displaced to 110. The behavior of **9** and **8** makes it clear that the majority of the hydrogen transferred in this fragmentation comes from the C-5 position by a rearrangement such as that shown.



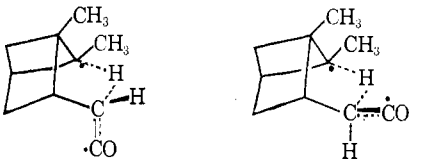
This rearrangement is a seven-membered analog of the now familiar one first proposed by McLafferty[8] in which β cleavage occurs accompanied by migration of a γ-hydrogen atom to the carbonyl oxygen (in which case most of the charge usually remains with the oxygen, whereas in our case none does). It is also reminiscent of the pyrolysis of *endo*-fenchyl acetate (**12** → **13**).[9]



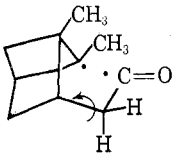
12 **13**

Curiously, the fragmentation of the lower homologs, **10** and **11**, takes place with much less hydrogen transfer; the base fragments are at *m/e* 110 and 109. Although McLafferty rearrangements involving seven- or eight-membered rings have been reported,[10] the present instance appears to be the first in which this rearrangement preferentially occurs through a seven-membered ring, but not through the six-membered ring homolog, no doubt because in the latter the distance between the hydrogen and the oxygen is more than 2 A, in which case the rearrangement becomes impossible.[11]

Mechanistic Implications. The selective transfer of an *exo*-α-hydrogen atom in the photolysis of carvonecamphor may be rationalized in several ways. One attractive possibility would be simply that the transition state for *exo*-hydrogen transfer, represented by formula **14**, is preferred over that for *endo*-hydrogen transfer, **15**, because it suffers fewer nonbonded repulsions. Alternatively, if hydrogen transfer takes place very quickly after excitation of the ketone, the stereoselectivity might reflect the tendency of the carbonyl group to rotate away from the two methyl groups (as shown in formula **16**), bringing the *exo* hydrogen into a reactive conformation, rather than in the opposite direction. In the extreme, this could amount to the hydrogen transfer merging with the carbon–carbon bond cleavage, a mechanism which might reveal itself by giving rise to a kinetic isotope effect. At the present time there is no basis for choosing one of these possibilities, although it may become possible to make more detailed statements in the future.



14 **15**



16

Experimental Section[12]

1-*exo*-5-Dimethyl-*syn*-2-methoxycarbonylmethylbicyclo[2.1.1]-hexane-5-*d* (9). A solution of 175 mg of *exo*-α-deuteriocarvonecamphor (**6**)[13] was dissolved in 80 ml of methanol and irradiated with black light for 5 days, whereupon glpc analysis (Carbowax) revealed only one peak, that of the product **9**. The methanol was removed at reduced pressure and the product was distilled to give 67 mg of the methyl ester; nmr spectrum (τ), methyl singlets at 9.10, 8.97, and 6.44. Traces of impurities giving peaks in the region 7.5–8.5 prevented an accurate integration of that region.

1-*exo*-5-Dimethyl-*syn*-2-methoxycarbonylmethyl-*d*-bicyclo[2.1.1]-hexane (7). *endo*-α-Deuteriocarvonecamphor (**5**)[13] was irradiated, as was the *exo* compound. The methanol was removed by distillation and the residue was purified by glpc (15% silicone, 125°;

(8) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).
(9) W. Hückel and H.-J. Kern, *Ann.*, **687**, 40 (1965).
(10) N. C. Rol, *Rec. Trav. Chim.*, **84**, 413 (1965).
(11) C. Djerassi and L. Tökes, *J. Am. Chem. Soc.*, **88**, 536 (1966).
(12) For details of apparatus and procedure, see ref 3. Mass spectra were measured on an Atlas CH-4 apparatus; temperature of source, 275°, temperature of introduction, 150°, ionizing voltage, 70 ev unless otherwise specified.
(13) Prepared as described in ref 5.

retention time, 20–28 min). The nmr spectrum was essentially the same as that of the monodeuterated compound obtained upon irradiation of carvonecamphor in deuterium oxide followed by treatment with diazomethane. If the methoxyl group is taken as 3.0 protons, the region from τ 7.4 to 8.36 contains 6.3 protons (compared to 7.0 for **4**), while the total number of protons appears as 17.1 (16 is theoretical). No trace of any peak appears between the doublet peaks at τ 8.90 and 9.00, indicating the nearly complete absence of deuterium atoms at C-5.

Barbier–Wieland Degradations. Degradations of the methyl esters **4** and **9** were carried out as described by Lane and Wallis.[14]

(14) J. L. Lane and E. S. Wallis, *J. Am. Chem. Soc.*, **63**, 1674 (1941).

1-*exo*-5-Dimethyl-*syn*-2-methoxycarbonylbicyclo[2.1.1]hexane (11) was produced in 45% over-all yield; bp 54° (5 mm); nmr spectrum (τ), a singlet at 6.43 (3 H), a series of peaks between 7.3 and 8.4 (5 H), and a series of peaks between 8.6 and 9.2 (8 H) including two peaks at 8.89 and 8.99 interpreted as a singlet at 8.99 (3 H) and a doublet at 8.94 (3 H, J = 6 cps); $\lambda_{max}^{CCl_4}$ 5.76 (s), 6.90 (m), 6.99 (m), 7.24 (w), 7.38 (m), 7.81 (m), 8.40 (s), 8.51 (s), 8.60 (s), 9.40 (m), and 10.85 (m) μ.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.61; H, 9.57.

1-*exo*-5-Dimethyl-*syn*-2-methoxycarbonylbicyclo[2.1.1]hexane-5-*d* (10). The nmr spectrum is identical with that of **11** for τ values <8.6. Between 8.6 and 9.3 (7 H) lies predominantly one major singlet at 8.98 which has a second singlet on its side at 8.94 and a small peak at 8.89 appearing as a shoulder near the base.

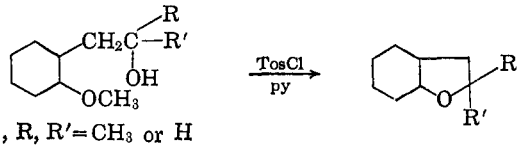
Stereochemical Consequences of Methoxyl Participation. The Stereochemistry of the Cyclization of 5-Methoxy-2-pentyl Brosylate to 2-Methyltetrahydrofuran[1]

Ernest R. Novak[2] and D. Stanley Tarbell

Contribution from the Department of Chemistry, University of Rochester, Rochester, New York 14627. *Received August 11, 1966*

Abstract: 5-Methoxy-2-pentanol has been resolved and its configuration correlated with that of 1-penten-4-ol, 4-methoxy-1-pentene, 2-methoxypentane, 1,4-pentanediol, and 2-methyltetrahydrofuran. Treatment of 5-methoxy-2-pentyl brosylate with lithium chloride in pyridine gives about 4% of 2-methyltetrahydrofuran, with complete inversion of configuration; an optically active mixture consisting of 80% 2-chloro-5-methoxypentane and 20% of 5-chloro-2-methoxypentane was also formed. Use of lithium bromide on the brosylate yields the tetrahydrofuran, formed with 50% inversion, and a mixture of optically inactive bromomethoxypentanes. The mechanism proposed to account for these observations involves the formation of a methoxonium ion with inversion, followed by attack of nucleophiles on this at the methyl group, at C-2 and at C-5. An open carbonium ion is considered unlikely; lack of optical activity in the bromomethoxypentanes must be due to direct displacement by bromide ion and reversibility of most steps in the scheme.

During structural elucidation of the antibiotic fumagillin,[3] we observed several examples of the formation of a perhydrobenzofuran ring, from a cyclohexane containing a hydroxyl group in the side chain and a methoxyl group on the cyclohexane ring adjacent to the side chains. A study of simpler compounds,[4] of type **1**, where the hydroxyl was primary, secondary, or tertiary and the substituents on the cyclohexane ring were either *cis* or *trans*, showed that the reaction was a general one, and gave some information concerning the reaction mechanism.



1, R, R′ = CH_3 or H

It was shown by O^{18}-tracer studies that the oxygen lost in the cyclization was that in the hydroxyl group;[4] it was obviously significant, for the general problem of methoxyl participation, and for the specific problem of syntheses in the fumagillin series,[5] to define the stereochemistry of the cyclization with respect to the carbon carrying the hydroxyl group.

Compound **1** contains two asymmetric carbon atoms, in addition to the one carrying the hydroxyl, when R = CH_3 and R′ = H. It was therefore experimentally much more feasible to study the problem in a compound containing a single asymmetric carbon. In the present paper, we have shown that the transformation of 5-methoxy-2-pentyl brosylate (**3b**) to 2-methyltetrahydrofuran (**4**) takes place with 100% inversion of configuration. Further results allow a correlation of the absolute configurations of a number of open-chain compounds with 2-methyltetrahydrofuran. The results, therefore, give some insight into the stereochemistry of methoxyl participation.

Racemic 5-methoxy-2-pentyl brosylate in pyridine with lithium chloride gave a few per cent of **4**, as was anticipated from earlier work,[3,4,6] in addition to a mixture of halomethoxypentanes.

5-Methoxy-2-pentanol was therefore resolved;[7]

(1) Aided by Grant AI-06328 from the National Institutes of Health.
(2) National Science Foundation Summer Teaching Fellow, 1966.
(3) D. S. Tarbell, *et al.*, *J. Am. Chem. Soc.*, **83**, 3096 (1961).
(4) S. E. Cantor and D. S. Tarbell, *ibid.*, **86**, 2902 (1964).
(5) S. T. Young, J. R. Turner, and D. S. Tarbell, *J. Org. Chem.*, **28**, 928 (1963); D. P. Brust, D. S. Tarbell, S. M. Hecht, E. C. Hayward, and L. D. Colebrook, *ibid.*, **31**, 2192 (1966).
(6) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958); E. L. Allred, Ph.D. Dissertation, University of California, Los Angeles, 1959 (private communication from Professor Winstein).
(7) General method of R. H. Pickard and W. O. Littlebury, *J. Chem. Soc.*, **91**, 1973 (1907).