a strong as (side-chain fragment from fission a) peak was present at m/e 183. The same set of peaks was also present in the acetate spectrum. These fragments are in full agreement with the side-chain structure indicated. The common ecdysones having partial structure **3** exhibit three prominent mass spectral peaks at m/e 363, 345, and 327 (bn) (nuclear fragment from fission b), but in ajugalactone the corresponding bn peaks appear at 14 higher mass units. Together with ir, uv, and CD data quoted above, this indicates that in contrast to the more than 30 ecdysones known to date,[12] an additional ketone group is present in the skeleton.

Similarity in the chemical shifts of protons attached to C-2, C-3, and C-5 in ajugalactone and the common ecdysones **3**, and the 9% increase in the 2-H peak intensity resulting from irradiation of 9α-H (due to intramolecular nuclear Overhauser effect, NOE)[13] in diacetate **2** establishes the configurations at C-2, C-3, and C-5, presence of the familiar 7-en-6-one moiety, and also indicates that ring A adopts a chair conformation (NOE).[13]

The extra ketone is six membered (ir of **2**) and therefore can only be at C-11 or C-12. Irradiation of the diacetate 3.67-ppm peak (9-H), which is coupled to the olefinic 7-H, converts a 2.61-ppm quartet (dd, J = 9.5 and 13 Hz, 11-H) to a doublet (J = 13 Hz); this shows that C-11 is a methylene having no adjacent protons other than the 9-H, *i.e.*, the ketone is at C-12. Two *tert*-hydroxyl groups are present. One is at C-14 as the splitting pattern of 7-H requires this carbon to be fully saturated, and also treatment of **1** with HCl–MeOH gives a compound absorbing at 294 nm, *i.e.*, presumably the 7,14-dien-6-one. The other hydroxyl group can only be at C-20. The side-chain structure is fully corroborated from nmr and other spectroscopic data.

The J value of the 22-H shows that the bond 20–22 is equatorially oriented with respect to the unsaturated δ-lactone. The absolute configuration shown in part structure **4** has been assigned to C-22 of a jaborasolactone A derivative[14] on the basis of its positive CD Cotton effect, $\Delta\epsilon$ +2.37 at 255 nm ($n \rightarrow \pi^*$);[15] this C-22 configuration is identical with that of withaferin A (part structure **5**) derived from X-ray analysis.[16] As mentioned above, ajugalactone (**1**) has a positive Cotton effect around 244 nm, its very strong positive value of $\Delta\epsilon$ +11.56 being due to the overlap of two positive Cotton effects. Thus, a C-22 configuration similar to **4**, *i.e.*, *R*, can be assigned to ajugalactone provided the C-20 hydroxyl group exerts no sign-reversing effect; this configuration is identical with that of ponasterone A and most other ecdysones.[17]

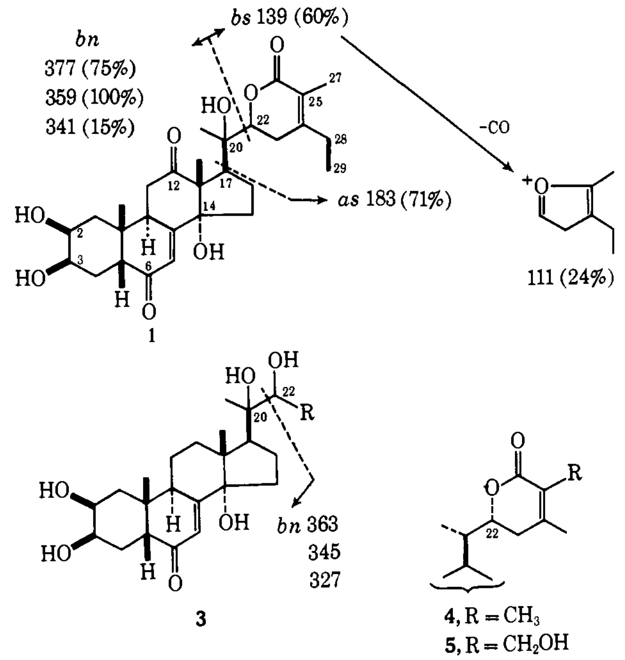

Figure 1. In structures **1** and **3**, bn, bs indicate, respectively, nuclear and side-chain fragments resulting from fission b [C(20)–C(22)] upon electron impact. Similarly an is the nuclear fragment resulting from fission a. Numerals denote mass units (m/e) of mass spectral peaks, while percentages in parentheses are intensities relative to base peak at m/e 359. The composition of all fragments indicated has been confirmed by exact mass measurements.

The 14-hydroxyl group has been assigned an α configuration on the basis of the isolation of ecdysones all having 14α-hydroxyls from the same plant. This is further supported by comparisons of chemical shifts of the 7-H (6.03 ppm in ajugalactone 2,3-diacetate, in CDCl$_3$) with an authentic 14β-hydroxy model. Thus, in $2\beta,3\beta,14\beta$-trihydroxy-23,24-bisnor-5α-chol-7-en-6-oic acid methyl ester 2,3-diacetate the 7-H peak appears at the low field of 6.57 ppm[18] due to near coplanarity of the hydroxyl group and the 7-H; in contrast, the 7-H in the 14α epimer is at 5.93 ppm (in CDCl$_3$).

[12] K. Nakanishi, *Pure Appl. Chem.*, in press.

[13] M. Koreeda, N. Harada, and K. Nakanishi, *Chem. Commun.*, 548 (1969).

[14] Compound IXa in R. Tschesche, H. Schwang, H.-W. Fehlhaber, and G. Snatzke, *Tetrahedron*, **22**, 1129 (1966).

[15] G. Snatzke, H. Schwang, and P. Welzel in "Some Newer Physical Methods in Structural Chemistry," R. Bounett and T. G. Davis, Ed., United Trade Press Ltd., London, 1967, p 159.

[16] S. M. Kupchan, R. W. Doskotch, P. Bollinger, A. T. McPhail, G. A. Sim, and J. A. S. Renauld, *J. Amer. Chem. Soc.*, **87**, 5805 (1965); D. Lavie, E. Glotter, and Y. Shvo, *J. Chem. Soc.*, 7517 (1965).

[17] The C-22 configuration has been chemically established as being *R* by correlation with C-2 of (−)-L-leucine: M. Koreeda, H. Hagiwara, and K. Nakanishi, unpublished. The only ecdysone of established side-chain configuration is ecdysone itself, based on X-ray studies: R. Huber, and W. Hoppe, *Chem. Ber.*, **98**, 2403 (1965).

[18] We acknowledge Dr. J. B. Siddall, Zoecon Corp., for nmr data of the two 14-epimers.

[19] Insect Hormones. XX. For part XIX see S. Imai, E. Murata, S. Fujioka, T. Matsuoka, M. Koreeda, and K. Nakanishi, *J. Amer. Chem. Soc.*, **92**, 7510 (1970).

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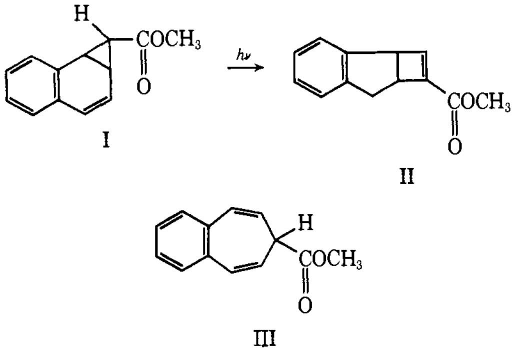
Deuterium Isotope Effect on Competing Hydrogen and Carbomethoxy Migration in Benzotropilidene Photochemistry

Sir:

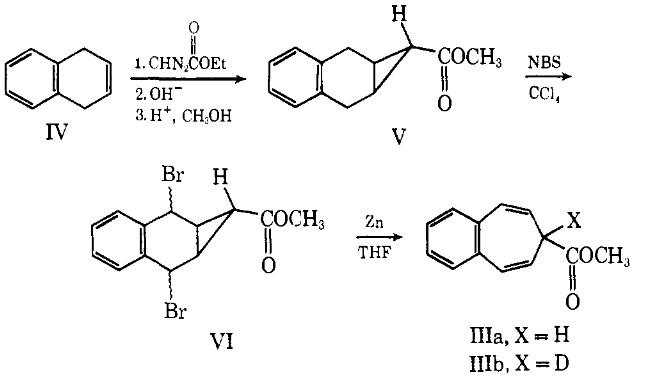
In an earlier report[1] we noted that photolysis of the benzonorcaradiene I yielded the rearranged isomer II in addition to fragmentation and hydrogen-shift

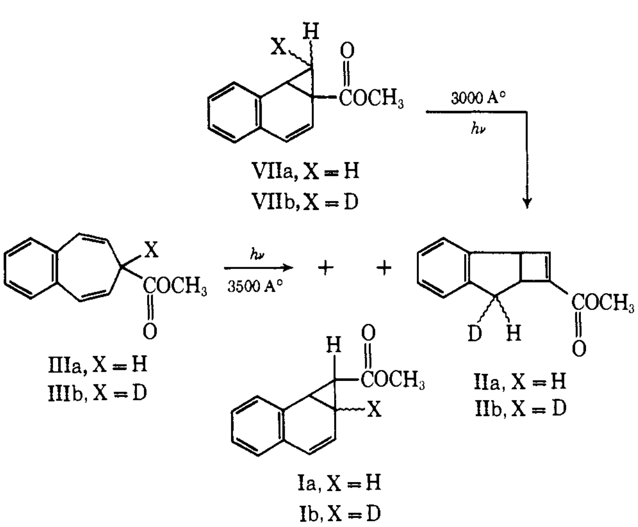
[1] J. S. Swenton and A. J. Krubsack, *J. Amer. Chem. Soc.*, **91**, 786 (1969).

products. Since the formation of II from I must involve either a carbomethoxy migration or a rearrangement of the carbon skeleton of I, III was considered as a plausible intermediate in the transformation. In view of the general interest in these photochemical systems[2] and the potential intermediacy of III in our earlier work, the photolysis of III has been studied in some detail. Here we wish to report an interesting photochemical example of competing hydrogen and carbomethoxy migration and the dramatic change in migratory aptitudes upon isotopic substitution.



The synthetic scheme outlined below afforded a convenient route not only to IIIa but also to its deuterated analog IIIb.[3] Photolysis of IIIa in cyclohexane at 3500 Å[4] yielded three products. Isolation of the photoproducts by preparative vapor phase chromatography resulted in the identification of two of these as I and II. The major photoproduct has been assigned as VII on the basis of its spectroscopic properties, the most conclusive being the nmr spectrum: aromatic hydrogens τ 2.5–2.9 (m, 4 H); vinyl hydrogens, AB quartet centered at τ 3.6 ($J = 9.5$ Hz, 2 H); methoxy resonance at τ 6.3 (s, 3 H), benzylic cyclopropyl hydrogen, quartet centered at τ 7.0 ($J = 6.5$, 10 Hz, 1 H); *exo*-cyclopropyl hydrogen, quartet centered at τ 7.9 ($J = 10$, 3 Hz, 1 H); and the *endo*-cyclopropyl hydrogen, quartet centered at τ 9.8 ($J = 6.5$, 3 Hz, 1 H).





Because of the complex photochemical interconversions noted in similar systems, we first sought to establish the primary products from photolysis of III. Careful monitoring of the photolysis by vpc indicated that the ratio of I:II:VII was invariant within experimental error from 20 to 95% conversion. This strongly suggests each of these products is formed in a one-photon step from excited III.[5] Furthermore, although photolysis of VIIa or VIIb at 3000 Å yields IIa or IIb in high yield,[5] irradiation of III at 3500 Å yields II *ca.* 8 times faster than its production from VII under identical conditions.[6]

While the formation of VII from III would arise by the hydrogen-shift mechanism of Pomeranz and Gruber,[2c] I could arise *via* two logical routes. One of these is the now commonplace di-π-methane–vinylcyclopropane reaction,[7] while the other involves a rather rare carbomethoxy migration.[8]

To establish the mechanism of the product formation,

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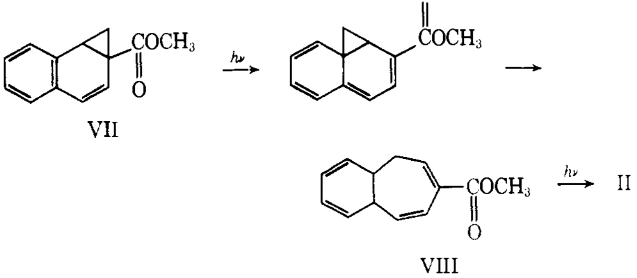
(2) M. Pomerantz and G. W. Gruber (a) *J. Amer. Chem. Soc.*, **89**, 6798 (1967); (b) *ibid.*, **89**, 6799 (1967); (c) G. W. Gruber and M. Pomerantz, *ibid.*, **92**, 4004 (1970); (d) R. K. Murray and H. Hart, *Tetrahedron Lett.*, 4995 (1968); (e) E. Ciganek, *J. Amer. Chem. Soc.*, **89**, 1458 (1967).

(3) The *exo*-methyl-3,4-benzobicyclo[4.1.0]heptane-7-carboxylate (V) was prepared in 40% overall yield and had mp 48.5–50.0°. The dibromide VI was obtained as a mixture of isomers from the reaction of 1 equiv of V and 2 equiv of *N*-bromosuccinimide in carbon tetrachloride. Fractional crystallization from chloroform yielded a crystalline isomer, mp 168–172° dec, of suitable purity for reaction to give III. The 7-carbomethoxy-3,4-benzotropilidene was prepared in 73% yield from VI by debromination with 1 equiv of zinc dust in tetrahydrofuran, mp 60–61°.

(4) In a typical irradiation, 0.323 g of III in 100 ml of cyclohexane was irradiated in a Pyrex vessel under nitrogen with a bank of sixteen RPR 3500-Å lamps for 6 hr. The final composition of the mixture was 14% II, 51% VII, and 35% I. The rate of reaction is not inhibited by 2.0 *M* piperylene; however, since the triplet energy of III is unknown the result must be considered inconclusive. Meaningful sensitization studies have been hindered thus far by the strong uv absorption of III.

(5) While the formation of IIa (IIb) from VIIa (VIIb) is in agreement with the Pomerantz–Gruber reactivity scheme, the data do not exclude the two-photon process shown below.



the deuterated compound IIIb was studied and the results obtained are shown in Table I. Compound VII showed by nmr integration the deuterium equally distributed in the exo and endo positions of the cyclopropane ring, thus confirming the hydrogen shift mechanism. On the other hand, I showed all of the deuterium located at the cyclopropyl-allylic position establishing carbomethoxy migration as the sole route to form I.[9] Even more surprising was the dramatic change in product ratio in the deuterated *vs.* the undeuterated III. While VII was the major product from IIa, I was the major product from IIb. Assuming a negligible secondary deuterium isotope effect, the change in product ratio indicates a minimum primary isotope effect of 3.7.[11]

Table I. Photolyses of IIIa, IIIb, and VIIb[a]

Starting material (% d_1)	% (d_1) I	VII	II
IIIa	35	51	14
IIIb (78)	64 (81)	31 (74)	6
IIIc (94)	67 (96)	27 (87)	5 (72)
VIIb (87)			90 (87)[b]

[a] The deuterium content was determined by nmr. [b] The 90% yield was that for VIIa as determined by vpc.

The effects of isotopic substitution noted here are particularly large and suggest that isotope effects may serve as a useful mechanistic probe for reactions other than those involving hydrogen abstraction. Furthermore, the discovery of competing hydrogen and carbomethoxy migrations in this system suggests that 7-substituted 3,4-benzotropilidenes may serve as a useful model for establishing photochemical migratory aptitudes for various functional groups. This point is under further study.

Acknowledgment. We gratefully acknowledge support from the Merck Company, Rahway, N. J.

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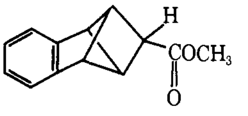
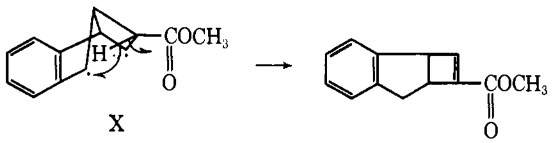
(6) Two pathways which can be envisioned for conversion of III to II involve hydrogen transfer in diradical X as depicted below. The diradical, X, could either be generated by 1,5 bonding in excited III or by thermolysis of IX formed in a photochemical step from III.



IX



X

II

(7) For leading references see H. E. Zimmerman and C. O. Bender, *J. Amer. Chem. Soc.*, **92**, 4366 (1970). The complete absence of the di-π-methanevinylcyclopropane route in the parent benzotropilidine suggests the hydrogen shifts in these systems must be of high efficiency.

(8) P. J. Kropp, *Tetrahedron Lett.*, 3647 (1964).

(9) One could consider the photochemistry of III as a competition between (a) hydrogen shift to give VII, (b) an oxa di-π-methane[10] rearrangement to give I, and (c) the unobserved carbo di-π-methane reaction. It is apparent then that the importance of the processes is in the order a > b ≫ c.

(10) (a) Reactions emanating from carbonyl–vinyl bridging[10b,c] have been recognized as general processes and termed the oxa di-π-methane rearrangement;[10d] (b) J. S. Swenton, *J. Chem. Educ.*, **46**, 217 (1969); (c) R. S. Givens and F. W. Oettle, *Chem. Commun.*, 1164 (1969); (d) W. G. Dauben, M. S. Kellogg, J. J. Seeman, and W. G. Spitzer, *J. Amer. Chem. Soc.*, **92**, 1787 (1970).

(11) For a brief discussion of the possible origin of isotope effects in photochemical systems, see D. R. Coulson and N. C. Yang, *ibid.*, **88**, 4511 (1966).

(12) NDEA Fellow, 1968–1969.

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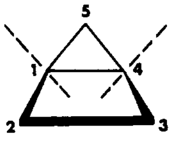
The Stereochemistry of Thermal Isomerizations of 2,3-Dimethylbicyclo[2.1.0]pentanes to 2,5-Heptadienes[1]

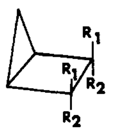
Sir:

To achieve conrotation in a concerted [$2_s + 2_a$] cycloreversion[2] to a butadiene, the two methylene carbon atoms of a cyclobutene each must turn through roughly 90°, so that the axes of the basis set atomic orbitals making up the breaking σ bond (C(3)–C(4)) rotate from an originally orthogonal to a finally parallel relationship to those making up the π bond (C(1)–C(2)). In simple cases, there are no major steric constraints, and the reaction is facile and highly stereospecific. This contrasts with the concerted [$2_s + 2_a$] cycloreversion of a cyclobutane to two ethylenes, where although two of the carbons destined to be π-bonded partners require little or no relative rotation, the other two require roughly 180°. The latter condition imposes severe distortion on the transition state, and convincing examples of this reaction are rare.[3,4]

Naively, one might expect that in a case where the geometric relationship of the axes of the reacting orbitals is intermediate between the extremes represented by cyclobutane and cyclobutene, it might be possible to observe the concerted [$2_s + 2_a$] cycloreversion, albeit with a conrotatory preference less than that of the cyclobutene reaction. The bicyclo[2.1.0]pentane molecule (**1**), in which the cyclopropane orbital axes (dashed lines) are canted with respect to the breaking C(2)–C(3) bond, provides a test of this notion. Pyrolyses of three stereochemically labeled derivatives of the system, *syn-cis-*, *anti-cis-*, and *trans*-2,3-dimethylbicyclo[2.1.0]pentane (**2**, **3**, and **4**) give

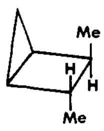


1



2: R_1 = Me, R_2 = H

3: R_1 = H, R_2 = Me



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(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We are also grateful for support given by AFOSR(SRC)-OAR, U. S. Air Force, through Grant No. AFOSR-66-1006A, and by the National Science Foundation through institutional Grant No. GU-3282.

(2) *Cf.* R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970, p 38 ff, and references cited therein.

(3) A. T. Cocks, H. M. Frey, and I. D. R. Stevens, *Chem. Commun.*, 458 (1969).

(4) J. E. Baldwin and P. W. Ford, *J. Amer. Chem. Soc.*, **91**, 7192 (1969).