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(6) P. A. Grieco, M. Nishizawa, S. D. Burke, and N. Marinovic, *J. Am. Chem. Soc.*, **98**, 1612 (1976).
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(8) A. A. Petrov and K. B. Rall, *Zh. Obskck. Khim.*, **26**, 1588 (1956).
(9) (a) S. Danishefsky and T. Kitahara, *J. Am. Chem. Soc.*, **96**, 7807 (1974); (b) *J. Org. Chem.*, **40**, 538 (1975).
(10) In this thus far unoptimized reaction, ca. 20–40% of recovered **1** is obtained contaminated with varying degrees of methyl benzoate. Resubmission of accumulated low boiling fractions to the cycloaddition provides more of compound **3**.
(11) The structure and homogeneity of this product is supported by its infrared, NMR, and mass spectra.
(12) Cf. R. B. Woodward, F. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, 1 (1958).
(13) It is possible that the neighboring carboxyl also functions as a directing group (cf. S. A. Cerefice and E. K. Fields, *J. Org. Chem.*, **41**, 355 (1976)). However, this would probably only be possible in a high energy conformer in which the carboxy and hydroxy groups are 1,3-diaxial to the B-ring.
(14) R. Hirschmann, N. G. Steinberg, and R. Walker, *J. Am. Chem. Soc.*, **84**, 1270 (1962).
(15) R. A. Le Mahieu and R. W. Kierstead, *Tetrahedron Lett.*, 5111 (1970).
(16) While the formation of orthoesters from lactones with ethylene glycol has precedent,[15] the rapidity of the reaction in the case of **12** is unusual. In the absence of magnesium sulfate, disappearance of **12** is complete after 30 min. However, under these conditions, **13** is only obtained in ca. 20% yield. The preponderance of material is converted into water soluble products which have not been identified. The utilization of excess magnesium sulfates slows down the conversion of **12** → **13** but leads to a much higher yield of the latter. The nature of the role of the magnesium sulfate remains to be determined.
(17) The NMR spectrum of **14** suggests the presence of 10–20% of hemlacetal valence isomer.
(18) While the likely preferred conformation of **15** R = OH and R = OTHP can only be surmised on the basis of general considerations of conformational analysis, the fully resolved 250-MHz spectrum ($CDCl_3$) of its derived acetate, **15** (R = OAc), leaves little doubt that its preferred conformation is, in fact, **15e,e**. The crucial features are: (i) AcO–CH, δ 5.29 ppm, coupled to the adjacent AB system at C_9 by J = 9.6 and 7.5 Hz and (ii) a pronounced W coupling, J = 1.4 Hz, between the junction hydrogen (δ 2.28 ppm) at C_5 and the equatorial proton (δ 3.57 ppm) of the isolated AB methylene at C_1.
(19) For an excellent discussion of this principle see E. Eliel, "The Stereochemistry of Carbon Compounds", McGraw-Hill, New York, London, 1962.
(20) P. L. Creger, *J. Org. Chem.*, **37**, 1907 (1972).
(21) Under the strongly basic conditions, **15a** is certainly deprotonated. Conceivably trans-diaxial attack at position 7 of conformer **15a,a** (R = lithium counterion) is assisted by a Lewis acid effect of the proximate axial lithium counterion on the emerging alkoxide at position 6. Such an effect might account for the nonreactivity of the THP derivative of compound **15**. Clearly investigations of ring openings on a series of structurally varied epoxycyclohexanols is necessary before this reaction is understood.
(22) Merck F-254 precoated silica gel plates; 0.25 mm thickness.

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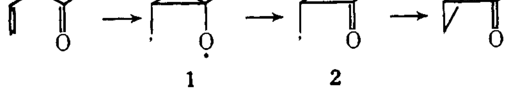
The "Methane Carbon" Stereochemistry of the Acyclic Oxadi-π-methane Photorearrangement[1]

Sir:

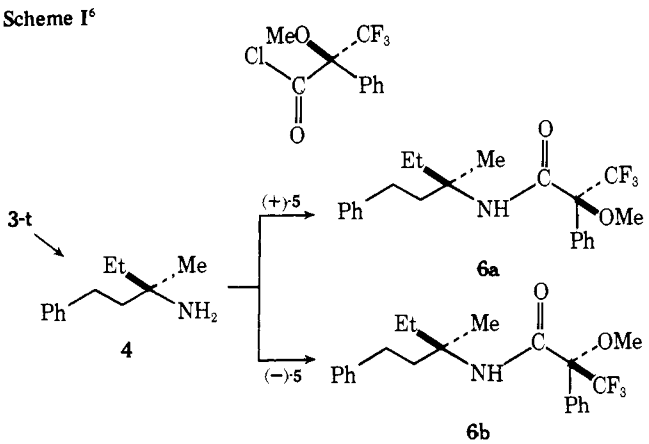
During the last 5 years, the oxadi-π-methane photorearrangement of β,γ-unsaturated ketones has been extensively investigated.[2] The possible mechanism of the reaction is pictured in qualitative valence bond terms in eq 1.[3] The diradicaloids **1** and **2** may be true intermediates in a stepwise process or may merely represent points on the energy hypersurface of a concerted $[_\pi 2 + _\sigma 2 + _\pi 2]$ or $[_\pi 2 + _\sigma 2]$ cycloaddition. To gain more insight into the mechanistic details, the reaction stereochemistries of many β,γ-unsaturated ketones have been investigated,[4] and it has been found that a high degree of asymmetry is preserved at the "methane carbon". Both retention and inversion of this carbon have been reported, and this dichotomy has been attributed to steric factors.[4] It has been concluded, however, that the results favored a concerted $[_\pi 2 + _\sigma 2]$ pathway.[4g]



(1)

1 **2**

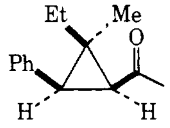
Scheme I[6]



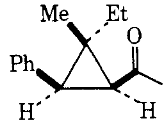
We have investigated the "methane carbon" stereochemistry of the oxadi-π-methane reaction of optically active *trans*-3-ethyl-3-methyl-5-phenyl-4-penten-2-one (**3-t**)[5] which, being acyclic, is free from all possible steric and conformational prejudices which were present in all previously studied compounds.

The degree of optical purity of the starting material **3-t** was established by the degradation of the ketone to the optically active amine **4** (hydrogenation, haloform reaction, Curtius degradation, and hydrolysis) followed by treatment with the optically active acid chlorides **5**[7] to yield the amides (Scheme I). The resulting diasteromeric amides **6a** and **6b** were found to be greater than 90% isomerically pure (NMR analysis), a result which indicates that the optical purity of **3-t** was at least 90%.

A benzene solution which was 0.01 M in optically active **3-t** and 0.01 M in chrysene[8] (E_t = 57 kcal/mol) was irradiated through a Nonex filter (10% T at 314 nm) with a 450-W medium-pressure Hanovia lamp for 48 h. The sensitizer chrysene absorbed greater than 99% of the light under these conditions. The major products (Scheme II), isolated by silica gel chromatography, were the oxadi-π-methane products **7-t,t** and **7-t,c**, the 1,3-acyl shift product **8**, and the cis isomer (**3-c**) of the starting material as well as a small amount of the starting material. Neither of the other two possible oxadi-π-methane products, **7-c,c** and **7-c,t**, was detected (<1%).



7-c,c

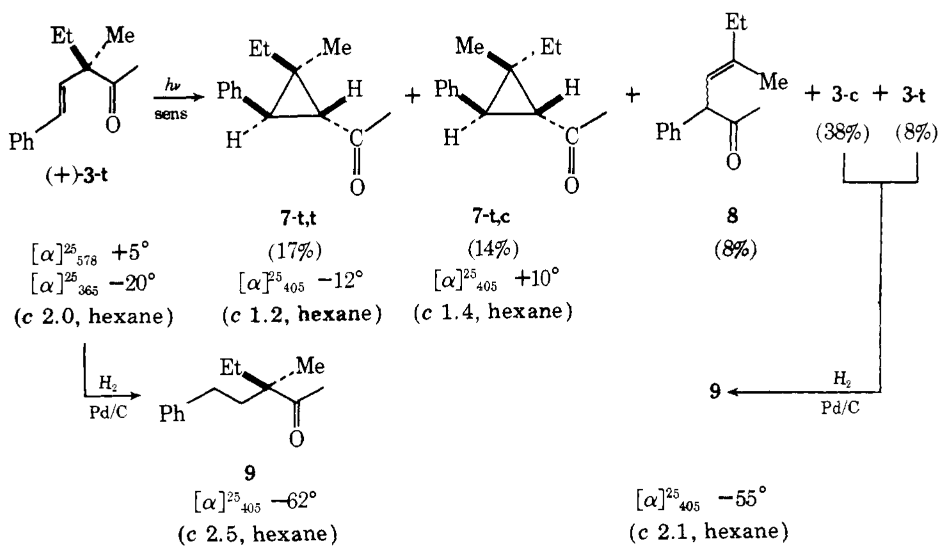


7-c,t

The cyclopropyl ketone isomers **7-t,t** and **7-t,c** were separated by high-pressure liquid chromatography (μ-porasil, 1% EtOAc–hexane) and were found to have small specific rotations, namely $[\alpha]^{25}{}_{405}$ −12° for **7-t,t** (99% purity by hplc, constant rotation) and $[\alpha]^{25}{}_{405}$ +10° for **7-t,c** (95% purity by HPLC). Independent synthesis of optically active **7-t,t**[9] ($[\alpha]^{25}{}_{405}$ −125 ± 3° (*c* 1.0, hexane)) indicated that the compound generated photochemically was *no more than 10% optically pure*.

Possible processes which could intervene in the production of largely racemized photoproducts **7-t,t** and **7-t,c** are: (a) photoracemization of starting enones; (b) formation and

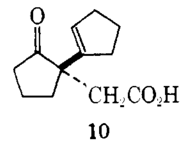
Scheme II



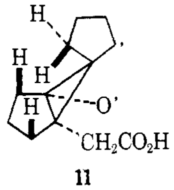
conversion of 1,3-shift product **8** to the observed oxadi-π-methane products; (c) photoracemization and/or photoepimerization of the isomeric trans photoproducts, themselves; and (d) photoepimerization of potential cis photoproducts **7-c,c** and **7-c,t**. All of these processes were ruled out by appropriate experiments: recovered starting enone showed less than 15% loss of optical activity (see Scheme II); 1,3-shift product **8**, optically active trans photoproduct **7-t,t**, and directly synthesized optically inactive cis ketone **7-c,c**[10] were stable to the photoreaction conditions for the full reaction time.[11]

In order for concerted, orbital symmetry allowed mechanisms to produce nearly racemic products, it requires the triplet of cis enone **3-c**[11] to follow one allowed pathway and the triplet of trans enone **3-t** to follow the other allowed pathway, i.e., $[_{\pi}2_{s} + {}_{\sigma}2_{s}]$ and $[_{\pi}2_{a} + {}_{\sigma}2_{a}]$, respectively. For these two processes to occur in about equal amounts is considered most unlikely. Thus, the transformation of **3-t** and/or **3-c** to nearly racemized products is best attributable to a stepwise mechanism which has at least one achiral intermediate, this being a diradicaloid species like **2** (or a loose radical pair).[12] The small amount of residual activity could be due to a small degree of asymmetric induction at the β-carbon in the formation of the species related to **1** or to competing concerted processes.

In view of the present results, the finding of greater than 90% inversion of the "methane carbon" stereochemistry in the case of the relatively sterically unhindered ketone **10**[4g] warrants comments. It may be that the reaction of **10** also follows a stepwise mechanism but that the diradicaloid intermediate **11**, which lies on the pathway for the *enantiomer* of the observed product, is energetically inaccessible because of the strong nonbonded hydrogen-hydrogen interactions shown. However,



10



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the likelihood that this steric effect is large enough to account for the reported high degree of stereoselectivity requires further evaluation. It is also possible that, as constraints are added to the β,γ-enone system, the mechanism becomes concerted and species like **2** are no longer intermediates. Additionally, it cannot be ruled out that the phenyl conjugation present in **3-t** (and **3-c**) stabilizes the benzylic diradical species to such an extent that the stepwise rearrangement competes successfully with a concerted process.

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References and Notes

(1) This work was supported by Grant No. AM-00709, National Institute of Arthritis, Metabolic and Digestive Diseases, U.S. Public Health Service and the Hoffmann-La Roche Foundation.

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(3) The di-π-methane rearrangement has been viewed in similar valence bond terms.[2a]

(4) (a) T. Matsuura and K. Ogura, *J. Am. Chem. Soc.*, **89**, 3850 (1967); (b)S. Domb and K. Schaffner, *Helv. Chim. Acta*, **53**, 677 (1970); (c) D. A. Plank and J. C. Floyd, *Tetrahedron Lett.*, 4811 (1971); (d) H. Sato, K. Nakanishi, J. Hayashi, and Y. Nakadaira, *Tetrahedron*, **29**, 275 (1973); (e) K. Schaffner, *Pure Appl. Chem.*, **33**, 329 (1973); (f) J. I. Seeman and H. Ziffer, *Tetrahedron Lett.*, 4409, 4413 (1973); (g) R. L. Coffin, R. S. Givens, and R. G. Carlson, *J. Am. Chem. Soc.*, **96**, 7554 (1974); (h) T. Akiyama, D. Pedder, J. V. Silverton, J. I. Seeman, and H. Ziffer, *J. Org. Chem.*, **40**, 3675 (1975).

(5) Ketone **3-t** was synthesized by reaction of lithium dimethylcuprate with the related acid chloride. The parent acid was prepared via the Reformatsky reaction with ethyl α-bromobutyrate followed by dehydration, methylation, and saponification. The acid was resolved into its enantiomers using (*R*)- and (*S*)-α-phenethylamine: the rotations of the resolved acids were $[\alpha]^{25}{}_{365}$ +61° (*c* 1.5, $CHCl_3$) and $[\alpha]^{25}{}_{365}$ −62° (*c* 1.3, $CHCl_3$), respectively.

(6) All absolute configurations shown were arbitrarily chosen. All new compounds reported gave satisfactory elemental analysis and ir, NMR, and mass spectra were consistent with assigned structures.

(7) (a) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969). (b) The optically pure acid chlorides were generously supplied by H. Rapoport and V. Lovell.

(8) Acetophenone sensitization of **3** also led to 7-**t,t** and **7-t,c** but the materials were unstable under the reaction conditions. The utilization of chrysene as sensitizer eliminated these further reactions. That chrysene functioned as a triplet, not a singlet, sensitizer is supported by the observation that direct irradiation of **3-t** gave 1,3-rearrangement product **8**; no **7** (<3% at 70% conversion) was observed. This latter result is in full agreement with previous reports, see *J. Am. Chem. Soc.*, **92**, 1786 (1970).

(9) Ketone **7-t,t** was prepared by treatment of the corresponding acid with methyllithium. The parent acid was synthesized by heating (*Z*)-2-methyl-1-phenyl-1-butene with ethyl diazoacetate, followed by saponification with 0.70 molar equiv of base. The acid was resolved with (−)-*N*,α-dimethylbenzylamine, the acid rotation was $[\alpha]^{25}{}_{365}$ −359° (*c* 1.1, $CHCl_3$). The starting olefin was obtained from the known (*E*)-2-ethyl-3-phenylpropenoic acid by reduction to the alcohol which was converted to the olefin by the SO_3·Py and LAH method of Corey.

(10) The optically inactive cis isomer was obtained from the ester residue from the limited hydrolysis in the above preparation by further controlled hydrolysis.

(11) The finding of only trans products suggests a sterically preferred orientation in the closing of the cyclopropane ring. Photoequilibration of **3-t** and **3-c** is much faster than the oxadi-π-methane rearrangement.

(12) Note Added in Proof. A similar conclusion has recently been published by B. Winter and K. Schaffner, *J. Am. Chem. Soc.*, **98**, 2022 (1976).

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