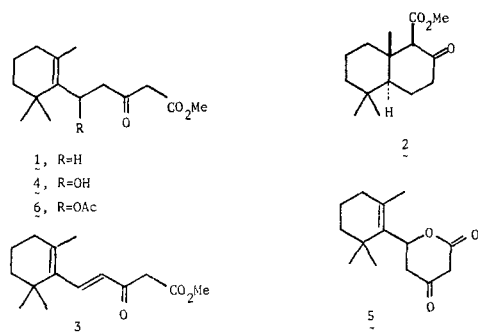


Photochemistry of Enolate Anions. Anion-Directed Photochemical Cyclization of a Dienone

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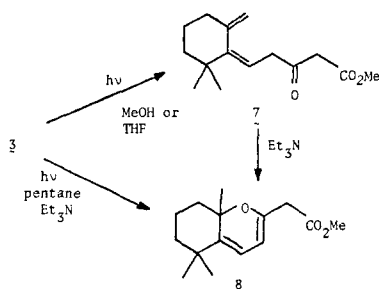
We recently reported that stannic chloride catalyzed cyclization of β -keto ester **1** leads in high yield to **2**, a versatile



intermediate for the synthesis of diterpenes.¹ In an attempt to extend the synthetic utility of keto esters of this type, we have investigated the photochemical behavior of dienone ester **3** and various enol and enolate derivatives, and have found that a sequence of discrete photochemical processes can be defined in this system which reveal a novel mechanistic dichotomy.

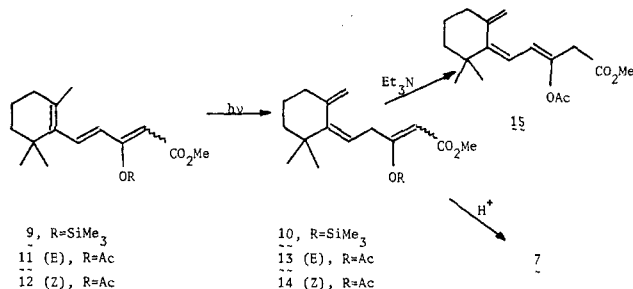
Condensation of the dianion of methyl acetoacetate² with β -cyclocitral³ gave the crystalline alcohol **4** (75%) which, however, could not be directly dehydrated since lactonization to **5** intervened. Instead, **4** was converted to its acetate **6** (acetyl chloride, pyridine- CH_2Cl_2) which, without isolation, was exposed to triethylamine to yield **3**.⁴ From its NMR spectrum (CDCl_3 , doublets, $J = 16$ Hz, at δ 6.14 and 7.32), this material was entirely the *E* isomer and contained ~15% of an enol tautomer.

Irradiation of a 0.01 M solution of **3** in methanol or in THF for 1 h with a 450-W lamp through Pyrex resulted in its conversion to **7**⁵ in 60% yield. On the other hand, when irradiation of **3** was carried out in pentane solution, the major product after several hours was the pyran derivative **8**. In this latter



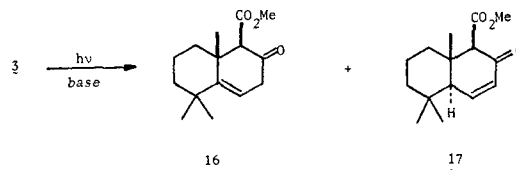
respect, the photochemical behavior of **3** is reminiscent of that of β -ionone, which was presumed to undergo an initial isomerization to cis dienone followed by thermal cyclization to a pyran.⁶ However, when a solution of **3** in pentane-methylene chloride containing 1 equiv of triethylamine was irradiated under the same conditions, a rapid (<1 h) and virtually quantitative conversion to **8** resulted. It was further found that the photoproduct **7** is transformed in a *dark* reaction with triethylamine to pyran **8**. This process occurred at a rate and with an efficiency that is compatible with **7** as an intermediate in the photochemical reaction in the presence of the amine.

The photoinitiated 1,5-hydrogen shift⁷ observed with **3** is also conspicuous in its enol derivatives. For example, silyl enol ether *E,Z*-**9** prepared from **3** by treatment with triethylamine and chlorotrimethylsilane, afforded a high yield of **10** (as a mixture of *E* and *Z* isomers) when irradiated with a 200-W sun lamp for 22 h. Mild acidic hydrolysis of **10** gave a 60% yield



of **7**. Acetylation of **3** (acetic anhydride, pyridine) furnished two enol acetates in the ratio 1.5:1, which were separated by chromatography and shown to be *E* and *Z* isomers **11** and **12**, respectively.⁸ These isomers in pentane were irradiated separately and gave identical mixtures of *E* (**13**) and *Z* (**14**) acetates in a ratio of 1.6:1.⁹ Cyclization of these systems to a pyran, as for **7**, is clearly precluded; instead, treatment of each isomer with triethylamine resulted in clean conversion to the crystalline, conjugated triene **15**, mp 80–82 °C.

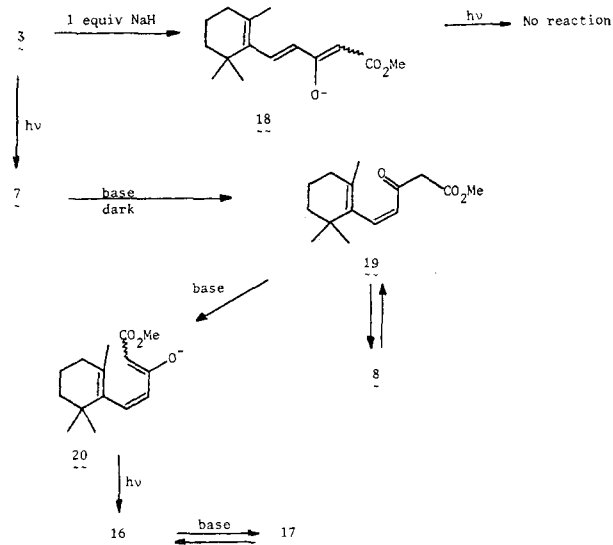
In contrast to the results with **3** and its enol derivatives **9**, **11**, and **12** in neutral solvents, irradiation of **3** in the presence of a base gave carbocyclic products, the yield of which depended on the amount of base present. For example, with 0.5 equiv of sodium hydride in THF, irradiation of **3** through Pyrex afforded a mixture of **16** and **17** in equal quantity. Optimum



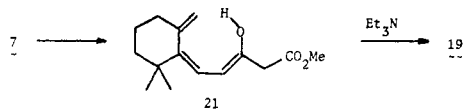
conditions for the formation of carbocyclic photoproducts required 2 equiv of methoxide in methanol, in which case a 1:1 equilibrium mixture of enones **16** and **17** was produced in 70% yield.¹⁰ However, when a full equivalent of sodium hydride in THF was used, the photochemistry of **3** was completely arrested and only starting material was recovered. The transformation of **3** to its enolate **18** is accompanied by a pronounced change in its UV spectrum (λ_{max} 323 nm ($\epsilon \sim 26,000$)) to a broad, very diffuse absorption ($\epsilon < 3000$) in the 300–400-nm range.

Divergent photochemical pathways of ketones and their enols¹¹ and enolates¹² have been noted previously, and the present example of **3** and its derivatives is a striking illustration

Scheme I



of this dichotomy.¹³ The partitioning of photoproducts from **3** between pyran **8** and ketone **16** apparently reflects the position of equilibrium of the 4,5-cis dienone **19** with its enolate **20**, the neutral species undergoing the well-precedented tautomerization to **8**,⁶ whereas for **20** a triene electrocyclization¹⁴ to **16** prevails (see Scheme I). Cis isomer **19** probably originates from **7** via a 1,7-prototropic shift of enol **21**;¹⁵ in any case, di-



rect photochemical trans \rightarrow cis isomerization of **3** (in polar solvents) as well as enolate **18** is excluded by these results. A consequence of the reversibility¹⁶ of the cis-dienone-pyran tautomerism in Scheme I is that access to **20**, and hence **16**, may also be gained via **8**.¹⁷ Thus, irradiation of **8** in methanolic sodium methoxide furnished a mixture of **16** and **17** similar in all respects, including yield, to that obtained from **3** under the same conditions. No enone was produced when **8** and sodium methoxide were mixed in the dark.

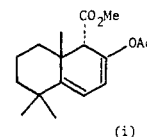
These results suggest that the photochemical behavior of conjugated enolates can be modulated in synthetically useful ways through pathways which differ significantly from those followed by the corresponding uncharged species.

Acknowledgments. We are grateful to the National Science Foundation and to the M. J. Murdock Charitable Trust for financial support. One of us (R.W.S) thanks the N. L. Tartar Research Fellowship Fund for financial support.

References and Notes

- (1) R. W. Skeean, G. L. Trammell, and J. D. White, *Tetrahedron Lett.*, 525 (1976).
- (2) S. N. Huckin and L. Weller, *J. Am. Chem. Soc.*, **96**, 1082 (1974).
- (3) (a) L. Colombi, A. Bosshard, H. Schinz, and C. F. Seidel, *Helv. Chim. Acta*, **34**, 265 (1951); (b) V. Prelog and H. Frick, *ibid.*, **31**, 417 (1948).
- (4) We have found that this compound can also be prepared directly from β -lonone by condensation with dimethyl carbonate in the presence of sodium hydride (N. Green and F. B. LaForge, *J. Am. Chem. Soc.*, **70**, 2287 (1948)).

- (5) The geometry of the exo trisubstituted double bond is assumed to be as shown on the basis of an intramolecular 1,5-hydrogen shift in **3**.
- (6) G. Büchi and N. C. Yang, *J. Am. Chem. Soc.*, **79**, 2318 (1957).
- (7) K. J. Crowley, *Proc. Chem. Soc.*, 17 (1964).
- (8) *E* isomer (CDCl_3): δ 5.55 (1 H, s), 6.60 (1 H, d, $J = 16$ Hz), 7.40 (1 H, d, $J = 16$ Hz). *Z* isomer (CDCl_3): δ 5.64 (1 H, s), 6.00 (1 H, d, $J = 16$ Hz). Assignment is based on the downfield shift ($\Delta\delta = 1.2$) of the C-4 vinyl proton due to the deshielding effect of the carbomethoxy group in the *E* isomer.
- (9) *E* isomer (CDCl_3): δ 3.76 (2 H, d, $J = 7$ Hz). *Z* isomer (CDCl_3): δ 3.14 (2 H, d of d, $J = 2.7$ Hz).
- (10) With >2.5 equiv of sodium methoxide the yields of **16** and **17** diminish owing to decomposition. An as yet unidentified yellow compound is one of the decomposition products. It was established that **17** arises from **16** through base-catalyzed isomerization.
- (11) A. Padwa and G. A. Lee, *J. Am. Chem. Soc.*, **96**, 1634 (1974).
- (12) E. E. van Tamelen, J. Schwartz, and J. I. Brauman, *J. Am. Chem. Soc.*, **92**, 5798 (1970).
- (13) In a related study, it has been reported (S. Isoe, *Abstr. Int. Congr. Pure Appl. Chem.*, 26th, 1977, 1108 (1977)) that **3** undergoes a photochemical cyclization to **17** in the presence of base. Although the quantity of base was not specified, the reaction is depicted as one involving a photochemical electrocyclicization of the 4,5-cis enolate of **3**, a pathway consistent with our observations. It was also reported that **12** undergoes an analogous carbocyclic closure, via the photochemically generated 4,5-cis isomer to **1**, a result which is difficult to reconcile with formation of **14** and **15** as major products in our hands.



- (14) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
- (15) This rearrangement is, of course, not accessible from enol derivatives **10**, **13**, and **14**, and may explain why an analogous isomerization of **9**, **11**, and **12** to their 4,5-cis counterparts is not observed.
- (16) E. N. Marvell, T. Chadwick, G. Caple, T. Gosink, and G. Zimmer, *J. Org. Chem.*, **37**, 2992 (1972).
- (17) We are indebted to a referee for suggesting this experiment and correctly predicting its outcome.
- (18) National Institutes of Health Research Career Development Awardee, 1976-1981.

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May 15, 1978

Book Reviews

Low Temperature X-Ray Diffraction Apparatus and Techniques. By REUBEN RUDMAN (Adelphi University). Plenum Press, New York, N.Y. 1976. xvi + 344 pp. \$35.00.

This book is a review and consolidation of all the techniques and apparatuses that have been used over the years to study low-temperature X-ray diffraction behavior of both polycrystalline and single crystal samples. The theory of the technique is discussed and a comparison of low temperature diffraction and room temperature diffraction is included. There are many detailed discussions and drawings of specific equipment and techniques, some of which are of historical interest.

The book covers such topics as temperature control, frost prevention, crystal stability, phase transitions, choice of adhesives, film properties, absorption, window materials, sample preparation, crystal growing techniques, and data collection and reduction. Discussion and drawings of low-temperature apparatus for powder cameras, single crystal cameras, and diffractometers are included. The Bibliography is extensive and included are a list of suppliers, an apparatus code number listing, and a techniques and applications code number listing to aid in the location of specific information.

William M. Butler, University of Michigan

Chemical Pharmacology of the Synapse. By D. J. TRIGGLE (State University of New York at Buffalo) and C. R. TRIGGLE (Memorial University of Newfoundland). Academic Press, New York, N.Y. 1976. ix + 654 pp. \$43.75.

This excellent book, with two chapters by both authors and the other three by only the one (D.J.T.), has some of the immediacy of a symposium proceeding together with the pedagogical qualities of a graduate-level textbook, an advanced one to be sure. Biochemists, pharmacologists, and physiologists, to cite only the broad classic divisions, cannot afford to be without this book. We recognize that a work of such wide appeal is difficult to aim for a consistent readership. Thus there are many simplistic diagrams of nerve endings to illustrate neurotransmitter synthesis, storage, and release, whereas the steric aspects of structure-activity relationships might have been improved by some introductory simplification. The chapter on ligand-receptor interaction contains a review of the formal models for cooperative behavior which is wide ranging. For example, not only are the well-known concerted and sequential models dealt with, but also reviewed are some nonequilibrium kinetic schemes which should generate cooperative behavior, as well as an example illustrating cooperativity generated by events other than those based on multiple binding site