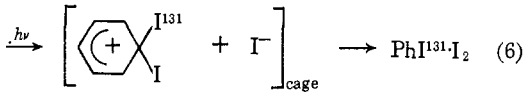
or



When the exchange quantum yield is calculated according to any of the above equations, 4, 5, or 6, taking into account the inner light filter effect of nonactive complexes ($PhI \cdot I_2$) and of PhI, the value $\gamma_e = 0.01 \pm 0.003$ is obtained (with $\sim 10^{-3}$ M I_2).

Preliminary observations indicate that similar reactions take place in the closely related $Ph^{131}I/Br_2$ and $CH_3(C_6H_4)I/^{131}II$ systems, but not with $PhCl/^{131}II$. Further work is in progress to elucidate the detailed CT exchange mechanism.

Acknowledgment. The authors are indebted to Mr. A. Naggar for his help in carrying out photochemical experiments.

A. Levy, D. Meyerstein
Nuclear Research Center
Negev, Israel

M. Ottolenghi
Department of Physical Chemistry
The Hebrew University, Jerusalem, Israel

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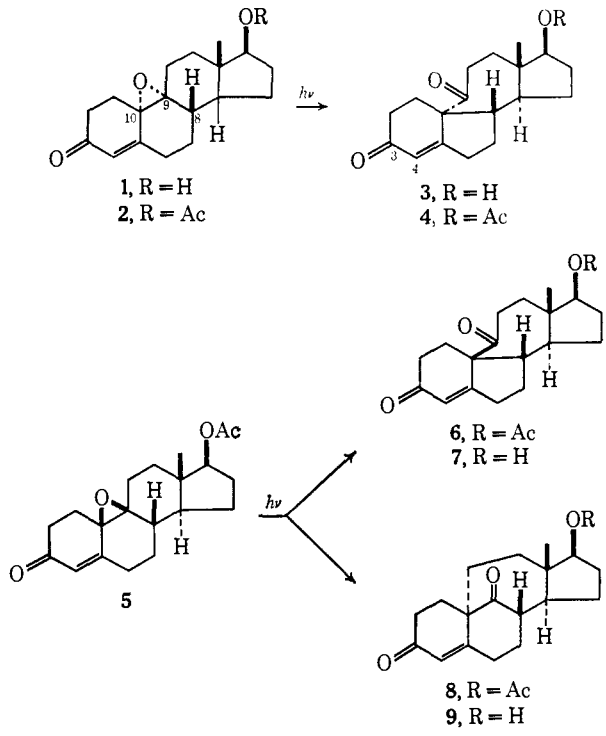
Photolysis of 9α,10α- and 9β,10β-Oxidoestr-4-en-3-ones[1]

Sir:

We wish to report the results of the photolyses of 9α,10α-oxido-17β-hydroxy- (**1**), 9α,10α-oxido-17β-acetoxy- (**2**), and 9β,10β-oxido-17β-acetoxyestr-4-en-3-ones (**5**) which resulted in the selective synthesis of the novel 8(9→10)*abeo*-10α- (from **1** and **2**) as well as the 8(9→10)*abeo*- and 11(9→10)*abeo*-10α-steroid nuclei (from **5**).[2,3]

Irradiation of **1** with 2537-Å ultraviolet light in *t*-butyl alcohol gave in 70% yield a new α,β-unsaturated ketone (**3**) having the following properties: mp 215–216°; $[\alpha]D$ −222° (*c* 1.15, $CHCl_3$); ir ($CHCl_3$) ν_{CO} 1660, 1685 cm^{-1}; uv (EtOH) λ_{max} 236 mμ (ε 13,350); nmr ($CDCl_3$) δ 0.90 (s, CH_3 -18), 5.72 (broadened s, CH-4).[4a] Of the two ketone bands in the infrared, the band at 1660 cm^{-1} (in $CHCl_3$) was readily assigned to the A-ring Δ^4-en-3-one chromophore on the basis of its nmr and uv properties. Moreover, this photoproduct was readily converted to a monoketal and a monoenol acetate, each retaining the 1685-cm^{-1} carbonyl band.[5] The latter carbonyl group was unaffected by attempted reduction of the ethylene ketal of **3** with lithium aluminum tri-*t*-butoxyhydride. These data suggest that the newly generated carbonyl function is considerably hindered.



Photoisomerization of **2** with 2537 Å in dioxane furnished in 80% yield of reacted starting material the product **4**, mp 181–182°, $[\alpha]D$ −204° (*c* 0.5, $CHCl_3$),[4b] which on hydrolysis gave compound **3**. The reaction **2** → **4** could also be effected on selective excitation of the n → π* absorption band, both in dioxane and in benzene solutions.[4c]

Irradiation of the 9β,10β-epoxyenone **5** with 2537-Å light in dioxane and in *t*-butyl alcohol gave a *ca.* 3:1 mixture of the two isomers **6** and **8**. Both compounds were obtained in amorphous form. **6** [ir ($CHCl_3$) ν_{CO} 1670, 1695, 1730 cm^{-1}; uv (EtOH) λ_{max} 240 nm (ε *ca.* 10,000); nmr ($CDCl_3$) δ 0.87 (s, CH_3-18), 5.95 (broadened s, CH-4)] formed a crystalline compound, **7**, on hydrolysis of the acetate function [mp 205–206°; $[\alpha]D$ +104° (*c* 0.41, $CHCl_3$); ir ($CHCl_3$) ν_{CO} 1670, 1690, ν_{OH} 3610 cm^{-1}; uv (EtOH) λ_{max} 237 mμ (ε *ca.* 10,000)]. Compound **8** exhibited the following spectral data: ir ($CHCl_3$) $\nu_{C=C}$ 1615, ν_{CO} 1670, 1715–1735 (broad), (CCl_4) ν_{COC} 1240, $\nu_{C=C}$ 1618, ν_{CO} 1680, 1712, 1740 cm^{-1}; uv (EtOH) max 242 mμ (ε *ca.* 10,000); nmr ($CDCl_3$) δ 0.90 (s, CH_3-18), 5.91 (broadened s, CH-4). Alkaline hydrolysis of **8** gave the amorphous 17-hydroxy derivative **9** [ir ($CHCl_3$) $\nu_{C=C}$ 1615, ν_{CO} 1668, 1710, ν_{OH} 3590 cm^{-1}; uv (EtOH) λ_{max} 243 mμ (ε *ca.* 10,000)].

(1) Part LVII of the E.T.H. series on Photochemical Reactions; for part LVI see S. Domb, G. Bozzato, J. A. Saboz, and K. Schaffner, *Helv. Chim. Acta*, **52**, in press. The photochemical results have been summarized in part by O. J.: Plenary Lecture, VIth International Symposium on the Chemistry of Natural Products, Mexico, April 1969; *cf.* O. Jeger and K. Schaffner, *Pure. Appl. Chem.*, in press.

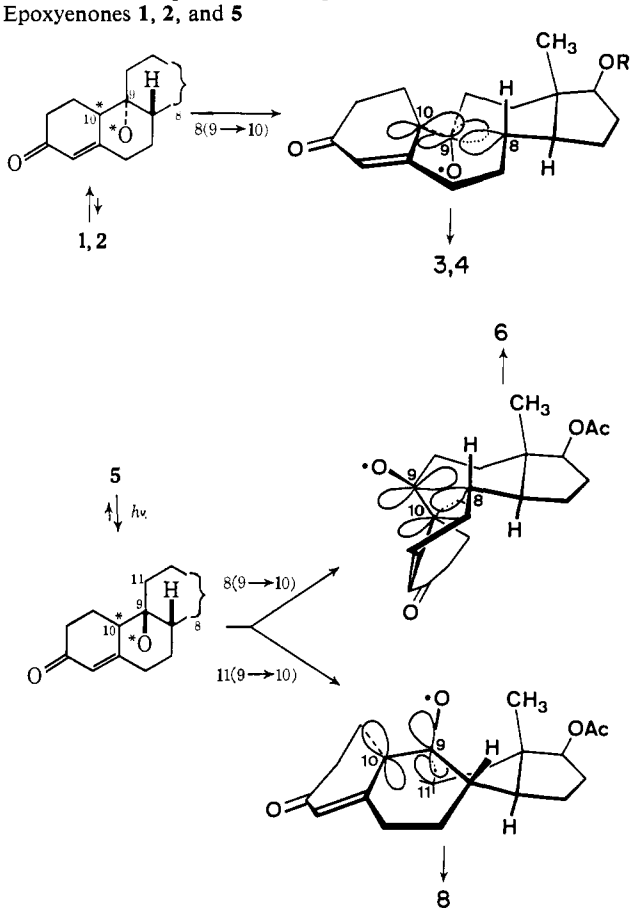
(2) (a) For a comprehensive review of epoxyketone photochemistry, see A. Padwa in "Organic Photochemistry," O. L. Chapman, Ed., Vol. I, Marcel Dekker, New York, N. Y., 1967, p 91; (b) H. Wehrli, C. Lehmann, P. Keller, J.-J. Bonet, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, 49, 2218 (1966); (c) O. Jeger, K. Schaffner, and H. Wehrli, *Pure Appl. Chem.*, **9**, 555 (1964).

(3) (a) For the preparation of **1** and **2**, see E. Farkas and J. M. Owen, *J. Med. Chem.*, 9, 510 (1966). (b) The preparation of 9β,10β-epoxide **5** will be described in a full paper.

(4) (a) A Rayonet chamber photochemical reactor (Southern New England Ultraviolet Co., Middletown, Conn.) equipped with 16-R.P.R. 2537-Å lamps was employed as the light source, using a quartz vessel and a stream of oxygen-free nitrogen at 40°; (b) irradiation by an NK 6/20 2537-Å lamp (Quarzlampen GmbH., Hanau) placed in a central quartz immersion well, with magnetic stirring at *ca.* 20°; (c) irradiation by a Q 81 high-pressure mercury lamp (Quarzlampen GmbH., Hanau) placed in a central Pyrex immersion well which was cooled by circulating an aqueous potassium hydrogen phthalate solution (wavelength cut-off at 3100 Å) through an outer jacket of 1-cm width, with magnetic stirring at *ca.* 20°.

(5) (a) B. E. Edwards and P. N. Rao, *J. Org. Chem.*, **31**, 324 (1966); the enolacetate of the photoproduct **3** had a uv absorption at 236 mμ (ε 15,500) and an nmr spectrum typical of a $\Delta^{3,5}$-diene structure; (b) exchange dioxolanation methods are extensively reviewed by J. Keana in "Steroid Reactions," C. Djerassi, Ed., Holden-Day, San Francisco, Calif., 1963, p 1.

Chart I. Stereospecific Rearrangement Pathways of Epoxyenones **1**, **2**, and **5**

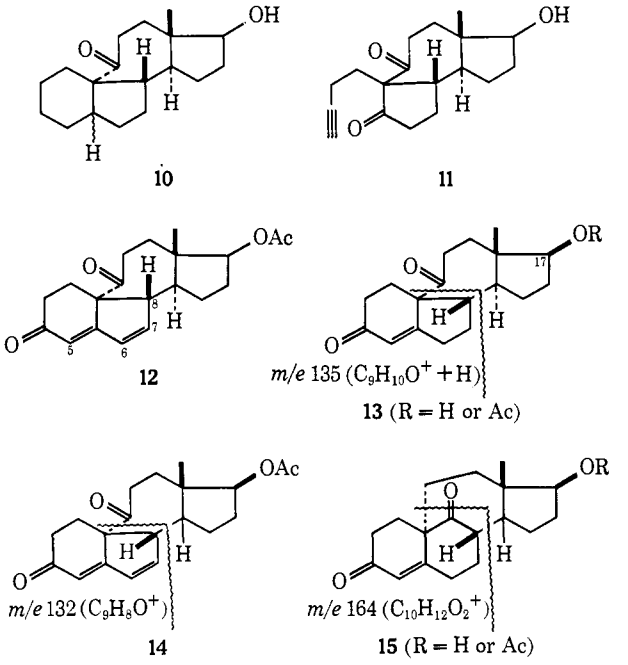


Separate experiments with **4** and **6** in dioxane show that they were not interconvertible photochemically.[4b]

Recent studies of the photorearrangement of the 6α,-7α-oxidoestr-4-en-3-ones[6] indicate that the well-defined mechanistic paths[7,8] operative in α,β-epoxy ketone photolyses apply directly. On this basis photolysis of **1** and **2** gives one likely structure, **3** and **4**, respectively.[2b,8] Alternatively, the two structures **6** and **8** may be expected as possible photoproducts from **5** on the same basis (see Chart I).

Hydrogenation (Pt, EtOH) of **3** gave the 3-deoxo derivative **10**, as well as the corresponding 3-hydroxy and 3-oxo compounds, all of which retained the 1685-cm^{-1} carbonyl absorption band.[9] After exhaustive deuterium exchange (CD_3OD, CD_3ONa, 48-hr reflux), the molecular ion in the high-resolution mass spectrum of **10** shifted from *m/e* 276 to 278. The δ 2.73 nmr signal attributable to the $-CH_2-CO-$ grouping in **10** disappeared upon dideuteration.

The size of ring B in **3** and **4** was confirmed by cleavage of ring A using the procedure recently reported by Eschenmoser and by Tanabe[10] and also by introduction



of a second double bond into conjugation with the enone system. The α,β-unsaturated ketone **3** with H_2O_2 gave the corresponding α,β-epoxy ketone, which reacted with *p*-toluenesulfonylhydrazine to give the acetylenic diketone **11**. The latter showed the presence of a new carbonyl group (ir: 1750 cm^{-1}), which is assigned to a five-membered ring. The mass spectrum of this product had the base peak at $M^+ - 52$ which corresponds to the facile loss of the elements of vinylacetylene from **11**.[11] Oxidation of **4** with DDQ reagent[12] furnished the dienone **12** [mp 187–188°; $[\alpha]D$ −360° (*c* 0.2, $CHCl_3$); ir ($CHCl_3$) $\nu_{C=C,CO}$ 1580, 1620, 1650, 1700, 1730 cm^{-1}; uv (EtOH) λ_{max} 288 mμ (ε 17,900)]. The nmr signals (in $CDCl_3$) of the olefinic protons of this compound appear as a singlet at δ 5.91 (CH-4) and as the AB part of an ABX system at δ 6.32 (J_{AB} = 5.5 cps, J_{BX} = 2 cps, CH-7) and 6.48 (J_{AX} = 1.5 cps, CH-6), respectively (cyclopentene *cis* double bond).[13]

The results of dideuteration of **10** and the data of products **11** and **12** support the assigned 8(9→10)*abeo* constitution of photoproducts **3** and **4** and eliminate bridged formulas of type **8** from further consideration. The mass spectra of **3** and **4** indicate that the favored fragmentation occurs as shown in **13**, since the base peak at *m/e* 135 ($C_9H_{11}O^+$) is independent of the substitution at C-17. Further support for this formulation may be derived from the mass spectrum of **12**, whose base peak is at *m/e* 132 ($C_9H_8O^+$) and is consistent with the fragmentation shown in **14**.

The stereoisomeric relationship of the photoproducts **4** and **6** is apparent from the similar spectral data (uv, ir, nmr) of the two compounds and of their respective 17-hydroxy derivatives **3** and **7**. The mass spectra of

(6) J. A. Saboz, T. Iizuka, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*. **51**, 1362 (1968).

(7) *I.e.*, rearrangement of the oxirane moiety to a $-CH_2-CO-$ grouping by way of fission of the allylic oxide bond and 1,2 migration of hydrogen.

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

(10) A. Eschenmoser, D. Felix, and G. Ohloff, *Helv. Chim. Acta*, **50**, 708 (1967); M. Tanabe, D. F. Crowe, R. L. Dehn, and G. Detre, *Tetrahedron Lett.*, 3739 (1967); M. Tanabe, D. F. Crowe, and R. L. Dehn, *ibid.*, 3943 (1967); J. Schreiber, D. Felix, A. Eschenmoser, M. Winter, F. Gautschi, K. H. Schulte-Elte, E. Sundt, G. Ohloff, J. Kalvoda, H. Kaufmann, P. Wieland, and G. Anner, *Helv. Chim. Acta*, **50**, 2101 (1968).

(11) Model studies showed that the mass spectra of acetylenic ketones similarly generated from 19-nortestosterone and testosterone also exhibit this mode of fragmentation with $M^+ - 52$ as a major fragment (favorably disposed toward McLafferty rearrangement).

(12) D. Burn, D. N. Kirk, and V. Petrow, *Proc. Chem. Soc.*, 14 (1960).

(13) B. Nann, D. Gravel, R. Schorta, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **46**, 2473 (1963); O. L. Chapman, *J. Amer. Chem. Soc.*, **85**, 2014 (1963); G. V. Smith and H. Kriloff, *ibid.*, **85**, 2016 (1963); P. Laszlo and P. von R. Schleyer, *ibid.*, **85**, 2017 (1963).

4 and **6** as well as of **3** and **7** show superimposable fragmentation patterns, with base peaks at *m/e* 135 (*cf.* **13**) in each case. Differences in peak intensities are negligible except for a stronger peak at *m/e* 302 in **6** and *m/e* 260 in **7**, both corresponding to $M^+ - 28$.

The expected stereochemistry of the photoproducts of **2** and **5**, based on mechanistic analogy with the photolysis products of α,β-epoxy ketones,[2b,8] is shown in structures **4**, **6**, and **8**. Work designed for detailed proofs of these structures is currently in progress.[14]

Acknowledgments. The authors from E. T. H. (D. B., T. I., K. S., and O. J.) gratefully acknowledge the financial support of the Schweiz. Nationalfonds zur Förderung der wissenschaftlichen Forschung, CIBA AG., Basel, and J. R. Geigy AG., Basel.

(14) Satisfactory elemental analyses and spectral data were obtained for all new crystalline compounds. The products **6**, **8**, **9**, and **11**, which could not be obtained in crystalline form, were carefully purified by column and preparative thin layer chromatography (2 mm, precoated Merck silica gel plates; one spot for each compound). The resulting samples gave satisfactory empirical formulas (high-resolution mass spectra) and spectral data.

Manuel Debono, R. Michael Molloy
The Lilly Research Laboratories
Eli Lilly and Company, Indianapolis, Indiana 46206

Daniel Bauer, Takeshi Iizuka
Kurt Schaffner, Oskar Jeger
Laboratorium für Organische Chemie
Eidg. Technische Hochschule, 8006 Zurich, Switzerland

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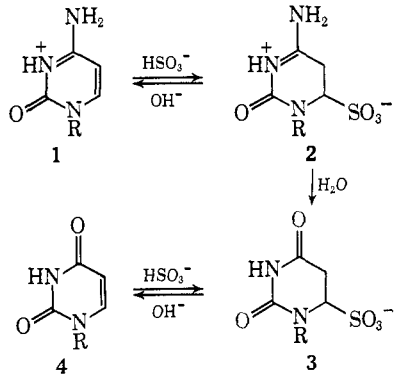
Reactions of Uracil and Cytosine Derivatives with Sodium Bisulfite. A Specific Deamination Method

Sir:

An important feature of the chemistry of uracil and cytosine is the susceptibility of their ring systems to nucleophilic attack at the 5,6 double bond. A number of synthetic transformations of uracil nucleosides have recently been shown to proceed through the intramolecular addition of a sugar substituent to that double bond.[1-4] It is believed that the transient addition of an external nucleophile is involved in deuterium exchange processes of uracil,[5] in the mechanism of cleavage of uracil by hydroxylamine,[6] and in the mode of action of thymidine synthetase.[7] We now wish to report that sodium bisulfite adds reversibly to the 5,6-double bond of uracil and its nucleosides, and that the favorable equilibrium with this reagent permits their complete conversion, under physiological conditions, to the dihydrouracil derivatives **3**. This reaction is reversed in basic solution. Cytosine derivatives react similarly and are converted by sodium bisulfite to saturated adducts of structure **2**. This conversion is analogous to the initial step of the reaction of the potent mutagen, hydroxylamine, with cytosine derivatives.[6] Unlike



a, R = β-D-2-deoxyribofuranosyl
b, R = β-D-ribofuranosyl
c, R = H

hydroxylamine, however, bisulfite does not react further to displace the amino group of the adduct. Rather, **2** deaminates upon standing in aqueous solution to give **3**. Adjustment of the pH of the solution to 10 converts **3** to the uracil derivative **4**. This sequence constitutes a method for the specific deamination of cytosine derivatives, under mild conditions, in the presence of the other common nucleic acid components. Adenosine and guanosine do not react with sodium bisulfite. The above reaction sequence is comparable to that involved in the hydrolytic deamination of cytidine by hot, aqueous, acidic buffer.[8-11] In that case, however, the equilibrium to the adduct corresponding to **2** is unfavorable, this adduct is present in very low concentration, and the conditions required by the reaction are too vigorous for it to be useful for preparative or mutagenic purposes.[12]

The ultraviolet absorbtion of uracil was rapidly lost after a sample was dissolved in a 1 *M* solution of $NaHSO_3$ at pH 7 ($t_{1/2}$ = 9.7 min at 24°). No ultraviolet-absorbing spots were observed when the reaction mixture was examined by thin layer chromatography on cellulose. After exposure of the plate to ammonia, however, a single ultraviolet-absorbing spot [R_f 0.33 in 2-propanol–water (70:30)] was detected. (When a portion of the reaction mixture was brought to pH 10 with ammonia, uracil was regenerated.) The product was isolated by crystallization from the reaction mixture and analyzed as a monohydrate of $C_4H_5N_2O_5SNa$. Its infrared spectrum (KBr) contained peaks at 8.20, 8.44, and 9.44 μ, which are attributed to a sulfonate group.[13] The nmr spectrum (D_2O) lacked the uracil low-field H-5 and H-6 absorbances, exhibiting instead multiplets at τ 5.55 (one proton) and 6.93 (two protons). This resembled the spectra of known 6-substituted dihydrouracils[14] and was consistent with structure **3** (R = H) for the product of the reaction. Cytosine derivatives showed a similar reactivity to sodium bisulfite. The unstable adducts **2** have not yet been isolated in pure

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(3) B. A. Otter, E. A. Falco, and J. J. Fox, *J. Org. Chem.*, **34**, 1390 (1969).
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