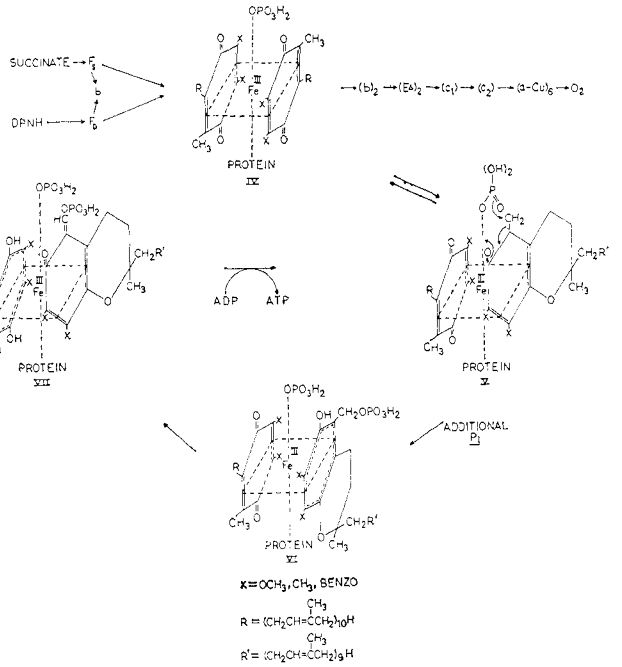


Fig. 1.—Macromolecular lipid–protein complex.

vitamin E and ascorbic acid than if given alone or with either vitamin separately.

Coenzyme Q_{10} was dissolved in glacial acetic acid containing an equimolar amount of ferric chloride and a fivefold excess of L-ascorbic acid. This solution was refluxed for approximately 1.5 hr. and then poured into water. The aqueous mixture was extracted with *n*-hexane. The hexane extract was washed several times with water, dried over anhydrous sodium sulfate, and then concentrated *in vacuo*, leaving a viscous yellow-brown oil. Thin layer chromatography on silica gel G (30% ether in *n*-hexane) showed only one Emmerie-Engel sensitive spot at $R_f = 0.44$. A sample of this material was further purified by preparative thin layer chromatography. The 60-Mc. n.m.r. spectrum of the 6-chromanol of CoQ_{10} in carbon tetrachloride is the best criterion of its identity; τ 4.88 (OH), 4.99 (CH=), 6.16 and 6.28 (CH_3O–), 7.48 triplet (—CH_2C=), and 8.01–9.1 (saturated alkyl groups). The infrared absorption spectrum of the product is nearly identical with the spectrum obtained from a sample of the chromanol of hexahydrocoenzyme Q_4. The major bands in the spectrum are 3480 (OH), 2900 (C–H stretching), 1450 (C–H deformation), and 1170 and 1190 cm.$^{-1}$ (C–O–CH_3).

Acknowledgment.—Appreciation is expressed to Dr. David E. Green of the University of Wisconsin for his continuing emphasis on the importance of nonheme iron in the chain.

STANFORD RESEARCH INSTITUTE HAROLD W. MOORE
MENLO PARK, CALIFORNIA KARL FOLKERS

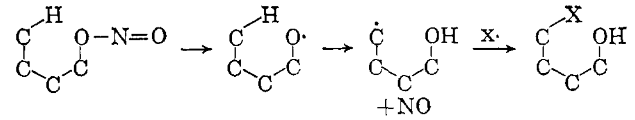
RECEIVED JUNE 4, 1964

Radical Exchange during Nitrite Photolysis[1]

Sir:

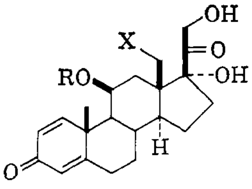
Recent examination of nitrite ester photolysis[2] with intramolecular hydrogen transfer has established[3] the mechanism (Scheme I) indicated below (X = NO).

SCHEME I

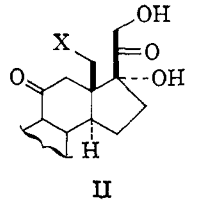


It seemed clear to us that other radicals (X·) could compete with NO and that radical transfer would also be possible. We now report examples of such radical-exchange reactions.

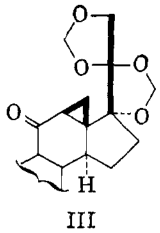
Photolysis[2] of prednisolone 21-acetate 11-nitrite[4] (Ia, R = NO, X = H) in benzene containing iodine (1.2 moles) gave 18-iodoprednisolone acetate (Ia, R = H, X = I; 28%), m.p. 131–134° dec., $[\alpha]_D$ +93° (all $[\alpha]_D$ *c* 1, chloroform), λ_{max}^{MeOH} 242 mμ (ε 15,300). Oxidation with chromic acid in acetone gave 18-iodoprednisone acetate (IIa, X = I), m.p. 172–176° dec., $[\alpha]_D$ +138°, λ_{max}^{MeOH} 239 mμ (ε 13,200). Similar photolysis of dexamethasone 21-acetate 11-nitrite[4] (Ib, R = NO, X = H) gave 18-iododexamethasone 21-acetate (Ib, R = H, X = I; 37%), m.p. 140–143° dec., $[\alpha]_D$ +89°, λ_{max}^{EtOH} 236 mμ (ε 12,600), oxidized as above to the 11-ketone IIb (X = I), m.p. 145–150° dec., $[\alpha]_D$ +125°, λ_{max}^{EtOH} 233 mμ (ε 15,000). Similar photolysis and oxidation of 17α,20;20,21-bismethylenedioxyprednisolone 11-nitrite (Ic, R = NO, X = H) gave 17α,20;20,21-bismethylenedioxy-18-iodoprednisone (IIc, X = I), m.p. 186–189° dec., $[\alpha]_D$ +40°, λ_{max}^{MeOH} 239 mμ (ε 16,200). Treatment of IIc (X = I) with potassium hydroxide in methanol gave the 12β,18-cyclopropyl ketone III,[5] m.p. 288–289°, $[\alpha]_D$ −21°, λ_{max}^{MeOH} 240 mμ (ε 16,400), which regenerated IIc (X = I) when treated with hydrogen iodide. Treatment of the initial photolysis product of Ic (R = NO, X = H) with methanolic potassium acetate gave the 11β,18-oxide IV (23%), m.p. 255–260°, $[\alpha]_D$ +5°, λ_{max}^{MeOH} 242 mμ (ε 16,200). Removal of the methylenedioxy groups and oxidation with sodium bismuthate gave 11β,18-oxidoandrosta-1,4-diene-3,17-dione, m.p. 168–170°, $[\alpha]_D$ +190°, λ_{max}^{MeOH} 242 mμ (ε 15,100), also obtained by photolysis of 11β-hydroxyandrosta-1,4-diene-3,17-dione nitrite[6] in the presence of iodine.



I

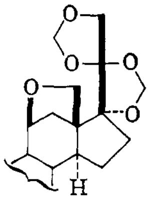


II

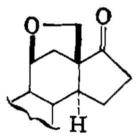


III

a, 21-acetate; b, 9α-fluoro-16α-methyl 21-acetate; c, 17α,20;20,-21-bismethylenedioxy



IV



V

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[1] Communication No. 31 from the Research Institute for Medicine and Chemistry.

[2] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960); **83**, 4076 (1961).

[3] M. Akhtar and M. M. Pechet, *ibid.*, **86**, 265 (1964).

[4] M. Akhtar, D. H. R. Barton, J. M. Beaton, and A. G. Hortmann, *ibid.*, **85**, 1512 (1963).

[5] *Cf.* J. F. Kerwin, M. E. Wolff, F. F. Owings, B. B. Lewis, B. Blank, A. Magnani, C. Karash, and V. Georgian, *J. Org. Chem.*, **27**, 3628 (1962).

[6] H. Reimann, A. S. Capomaggi, T. Strauss, E. P. Oliveto, and D. H. R. Barton, *J. Am. Chem. Soc.*, **83**, 4481 (1961).

Some examples of bromine insertion have also been observed. Photolysis of Ia (R = NO, X = H) in benzene containing excess CCl_3Br followed by oxidation of the product with chromium trioxide in acetone gave 18-bromoprednisone acetate (IIa, X = Br; 16%), m.p. 172–175° dec., $[\alpha]_D$ +179°, $\lambda_{\max}^{\text{MeOH}}$ 239 mμ (ε 16,300). Similar photolysis and oxidation of 11β-hydroxyandrosta-1,4-diene-3,17-dione nitrite[6] gave 18-bromoandrosta-1,4-diene-3,11,17-trione (18%), m.p. 183–186° dec., $[\alpha]_D$ +212°, $\lambda_{\max}^{\text{MeOH}}$ 239 mμ (ε 17,200).

The radical-exchange reaction has also been observed in the photolytic cleavage[7,8] of cyclic nitrites. Thus, photolysis of cyclopentanol nitrite gave 5-bromopentanal and 5-iodopentanal in the presence of CCl_3Br and of iodine, respectively.[9,10]

Acknowledgments.—We thank Dr. M. M. Pechet for his interest and encouragement and G. Berlinghieri, L. Salmansohn, and C. B. Pantuck for skillful technical assistance.

[7] P. Kabasakalian and E. R. Townley, *J. Org. Chem.*, **27**, 2918 (1962).

[8] M. Akhtar and D. H. R. Barton, *J. Am. Chem. Soc.*, **86**, 1528 (1964).

[9] Infrared and nuclear magnetic resonance spectra and microanalytical data in accord with the structures assigned have been obtained for all new compounds.

[10] For the photolytic rearrangement of iodohydrins formed *in situ* see K. Heusler and J. Kalvoda, *Helv. Chim. Acta*, **46**, 2732 (1963), and earlier papers there cited.

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RECEIVED JUNE 13, 1964

The Absolute Configuration of Menthyl Arenesulfinates[1]

Sir:

The ready availability of optically active sulfoxides by the Grignard synthesis[2–4] has sparked new interest in the question of the absolute configuration of the precursor menthyl arenesulfinates. Andersen[2] assigned the (*S*)-configuration to the asymmetric sulfur in (−)-menthyl (−)-*p*-toluenesulfinate [(−)-I][5] by comparing the rotation of (−)-I with that of (−)-menthyl (−)-*p*-iodobenzenesulfinate [(−)-II][5] at the D-line; Herbrandson and Cusano[6] had previously made a "tentative" assignment of the (*S*)-configuration to the asymmetric sulfur in (−)-II on the basis of kinetic and thermodynamic studies. Most recently, Andersen[7] has reversed himself and has claimed the (*R*)-configuration for (−)-I and (−)-II. We now present unequivocal evidence which forces a choice between these two assignments.

Crystals of (−)-II are monoclinic with the space group $P2_1$ and a density of 1.53 g./cm.³. The cell constants are a = 17.26 Å., b = 7.656 Å., c = 6.925 Å., and γ = 105.1°. This requires two molecules per unit cell. Three-dimensional intensity data were collected with Mo Kα radiation with Weissenberg geometry employing a scintillation counter for a detector. The 875 observed intensities were transformed to structure amplitudes without any correction for absorption. The structure was solved using the iodine as a heavy atom and refined with a full-matrix least-squares program.[8]

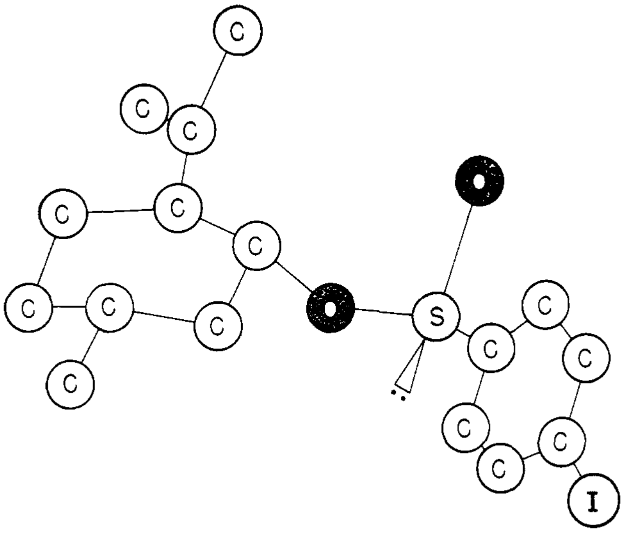

Figure 1.

The final disagreement factor, R, was 11%. The structure is shown in Fig. 1. The standard deviations of the bond distances are quite large (0.04 Å.); this is probably due to preferential absorption which was neglected in correcting the intensity data. The average for the benzene bond lengths is 1.38 Å., and for the carbon–carbon saturated bond lengths it is 1.53 Å.

The absolute configuration around the sulfur atom can be determined in this structure because the absolute configuration of the (−)-menthyl group is known.[9] As suggested by Mathieson,[10] the absolute configuration around an atom can be determined by ordinary X-ray techniques if an internal known asymmetric reference center is present in the molecule.[11] In the present case our internal reference is the (−)-menthyl group. *Using the above method the absolute configuration about the sulfur atom in (−)-II is (S).*

The configurations of I and II were correlated as follows. Reaction of *p*-toluenesulfinyl chloride and (−)-menthol at −78° in ether–pyridine afforded a diastereomeric mixture of (−)-menthyl *p*-toluenesulfinates, $[\alpha]_D$ −38.5° (Ia),[12] which was converted to *p*-tolyl butyl sulfoxide (IIIa), $[\alpha]_D$ −51°, by reaction with an excess of *n*-butylmagnesium bromide. Optically pure III, prepared from *n*-butylmagnesium bromide and diastereomerically pure (−)-I ($[\alpha]_D$ −206°), has $[\alpha]_D$ +187°. Therefore the ratio of enantiomers in IIIa is 36.4% (+)-III:63.6% (−)-III. This accurately reflects the ratio of diastereomers in precursor Ia (36.4% (−)-I:63.6% (+)-I), as shown by an ancillary experiment. A mixture ($[\alpha]_D$ −119°) of Ia (3.256 g.) and (−)-I (3.000 g.) was subjected to the Grignard

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[1] We gratefully acknowledge support by the National Science Foundation (grant GP-757) for the work conducted at New York University and by the Public Health Service (grant AM-5785) for the work conducted at the University of Chicago.

[2] K. K. Andersen, *Tetrahedron Letters*, **No. 3**, 93 (1962).

[3] K. Mislow, A. L. Ternay, Jr., and J. T. Melillo, *J. Am. Chem. Soc.*, **85**, 2329 (1963).

[4] C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).

[5] The diastereomers of I and II prepared from (−)-menthol have opposite signs of rotation at the D-line; the prefixes of I and II refer to these signs.

[6] H. F. Herbrandson and C. M. Cusano, *J. Am. Chem. Soc.*, **83**, 2124 (1961).

[7] K. K. Andersen, *J. Org. Chem.*, **29**, 1953 (1964).

[8] The observed structure amplitudes and the final coordinates for the structure are available upon request from E. B. F.

[9] V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953).

[10] A. M. Mathieson, *Acta Cryst.*, **9**, 317 (1956).

[11] A pertinent example of this technique is the establishment of the absolute configuration at sulfur in (+)-methylcysteine sulfoxide (R. Hine and D. Rogers, *Chem. Ind.* (London), 1428 (1956).

[12] Except for the *p*-toluenesulfinates, whose rotations were measured in nitrobenzene, all rotations refer to acetone solution.