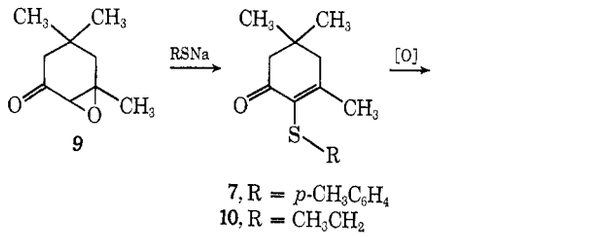
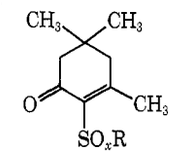
SCHEME II

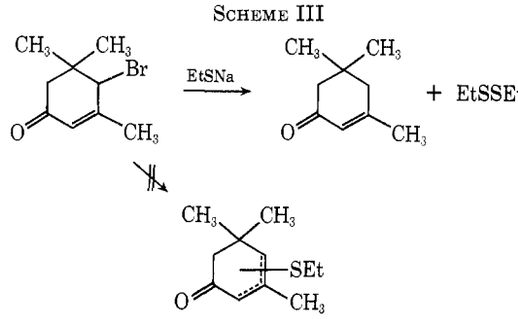


7, R = p-$CH_3C_6H_4$
10, R = CH_3CH_2



8, x = 2; R = p-$CH_3C_6H_4$
11, x = 1; R = CH_3CH_2
12, x = 2; R = CH_3CH_2

SCHEME III



supports the observations made by Marx, Carnrick, Cox[1] suggesting that nucleophilic reactions on 4-bromoisophorone take place in an SN2′ fashion with formation of 2-substituted derivatives and not in an SN2 reaction as earlier proposed.[2]

Experimental Section[6]

Preparation of 2-p-Toluenethioisophorone (7). Method A.—In 50 ml of EtOH was dissolved 2.3 g (0.10 mol) of sodium metal and to the solution was added 13.8 g (0.10 mol) of 90% p-toluenethiol. The sodium thiolate solution was then added to a solution of 21.7 g (0.10 mol) of 4-bromoisophorone dissolved in 100 ml of EtOH. After stirring for 5 hr, the precipitated NaBr was filtered and the filtrate was diluted with 100 ml of H_2O and extracted with CH_2Cl_2. The organic layer was reduced *in vacuo*, leaving 26 g of product, an oily liquid. A portion of the product was purified by distillation: bp 140–142° (0.07 mm); nmr ($CDCl_3$) δ 1.03 (s, 6, 5-$(CH_3)_2$–), 2.25 (s, 3, 3-CH_3), 2.25 (s, 3, $CH_3C_6H_4$–), 2.38 (s, 2, 6-CH_2–), 2.45 (s, 2, 4-CH_2–), 7.05 (s, 4, aromatic). This material was oxidized as given below to 2-p-toluenesulfonylisophorone (8).

Method B.—In 200 ml of EtOH was dissolved 10.1 g (0.44 mol) of sodium metal. To the solution was added 61 g (0.44 mol) of 90% p-toluenethiol and then 17 g (0.11 mol) of 2,3-isophorone oxide.[4] The solution was stirred for 12 hr and then diluted with 500 ml of H_2O. Extraction with CH_2Cl_2 and washing with H_2O and 0.1 N NaOH afforded 29 g of product upon removal of solvent *in vacuo*. A portion of the product was distilled, bp 142–144° (0.05 mm).

Anal. Calcd for $C_{16}H_{20}OS$: C, 73.80; H, 7.74; S, 12.32. Found: C, 73.48; H, 7.81; S, 12.34.

This material was shown by ir and nmr to be identical with that prepared by method A.

(6) All melting points are uncorrected. Infrared spectra data were obtained on a Perkin-Elmer Infracord spectrophotometer as Nujol mulls or neat. All nmr spectra were obtained on a Varian A-60 spectrometer in deuteriochloroform using TMS as the internal standard. Elemental analyses were obtained from the Analytical Services Laboratory of The Dow Chemical Co.

Preparation of 2-p-Toluenesulfonylisophorone (8). Method A.—To 10.8 g (0.05 mol) of 4-bromoisophorone[2] dissolved in 50 ml of DMF was added 8.9 g (0.05 mol) of sodium p-toluenesulfinate. The mixture was heated on a steam bath for 13 hr with precipitation of NaBr. The reaction mixture was then diluted with 200 ml of H_2O and extracted with CH_2Cl_2. The organic layer was washed with H_2O and reduced *in vacuo*, leaving 9.5 g (65% yield) of product which was recrystallized (EtOH): mp 147–149°; nmr ($CDCl_3$) δ 0.93 (s, 6, 5-$(CH_3)_2$–), 2.18 (s, 2, 6-CH_2–), 2.37 (s, 3, 3-CH_3), 2.52 (s, 2, 4-CH_2–), 2.58 (s, 3, CH_3-C_6H_4–), 7.25 and 7.83 (m, 4, J = 8.0 Hz, aromatic).

Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.72; H, 6.89; S, 10.97. Found: C, 65.46; H, 6.89; S, 11.18.

Method B.—To 18.8 g (0.072 mol) of 2-p-toluenethioisophorone prepared *via* displacement of sodium p-toluenethiolate as shown above dissolved in 140 ml of $CHCl_3$ was added 30.4 g (0.15 mol) of 85% m-chloroperbenzoic acid dissolved in 350 ml of $CHCl_3$. The reaction mixture was stirred for 4 hr and then washed with saturated $NaHCO_3$. The solvent was removed *in vacuo*, leaving 22 g (quantitative yield) of product which was recrystallized from acetone, mp 146–149°. This material was shown by ir and nmr to be identical with that synthesized by method A.

Preparation of 2-Ethylthioisophorone (10).—In 250 ml of EtOH was dissolved 16.5 g (0.72 mol) of sodium metal. To the solution was added 46.5 g (0.75 mol) of ethanethiol and then 28 g (0.18 mol) of 2,3-isophorone oxide.[4] After stirring for 12 hr, the reaction mixture was diluted with 500 ml of H_2O and extracted with CH_2Cl_2. The organic layer was reduced *in vacuo*, leaving 36 g (quantitative yield) of product which was purified by distillation: bp 128–131° (4.0 mm); lit.[5] mp 34–37.5°; nmr ($CDCl_3$) δ 1.03 (s, 6, 5-$(CH_3)_2$–), 1.15 (t, 3, CH_3CH_2S–), 2.24 (s, 2, 4-CH_2–), 2.25 (s, 3, 3-CH_3–), 2.37 (s, 2, 6-CH_2–), 2.72 (q, 2, CH_3CH_2S–).

Preparation of 2-Ethylsulfinylisophorone (11).—To 10 g (0.050 mol) of 2-ethylthioisophorone dissolved in 50 ml of glacial AcOH was added 5.72 g (0.051 mol) of 30% hydrogen peroxide. The mixture was stirred for 3 weeks at room temperature and then extracted with CH_2Cl_2. The organic layer was washed with 10% Na_2CO_3 and reduced *in vacuo*, leaving the product which was recrystallized (cyclohexane): mp 72.5–75°; nmr ($CDCl_3$) δ 1.05 (s, 6, 5-$(CH_3)_2$–), 1.28 (t, 3, CH_3CH_2SO–), 2.33 (s, 2, 6-CH_2–), 2.37 (s, 3, 3-CH_3–), 2.42 (s, 2, 4-CH_2–), 3.13 (q, 2, CH_3CH_2SO–).

Anal. Calcd for $C_{11}H_{18}O_2S$: C, 61.64; H, 8.47; S, 14.96. Found: C, 61.53; H, 8.56; S, 15.40.

Preparation of 2-Ethylsulfonylisophorone (12).—To 10 g (0.050 mol) of 2-ethylthioisophorone dissolved in 50 ml of glacial AcOH was added 11.5 g (0.10 mol) of 30% hydrogen peroxide. After stirring for 16 days, the reaction mixture was worked up by adding 200 ml of H_2O and extracting with CH_2Cl_2. The CH_2Cl_2 layer was washed with saturated Na_2CO_3 and reduced *in vacuo*, leaving 10.7 g (92% yield) of product which was recrystallized (cyclohexane): mp 71–73°; nmr ($CDCl_3$) δ 1.07 (s, 6, 5-$(CH_3)_2$–), 1.27 (t, 3, $CH_3CH_2SO_2$–), 2.38 (s, 2, 6-CH_2–), 2.48 (s, 3, 3-CH_3–), 2.55 (s, 2, 4-CH_2–), 3.38 (q, 2, $CH_3CH_2SO_2$–).

Anal. Calcd for $C_{11}H_{18}O_3S$: C, 57.36; H, 7.88, S, 13.92. Found: C, 57.36; H, 7.50; S, 14.21.

Registry No.—1, 16004-91-4; 7, 40919-40-2; 8, 40919-41-3; 9, 10276-21-8; 10, 17304-83-5; 11, 40919-43-5; 12, 40919-44-6; p-toluenethiol, 106-45-6; sodium p-toluenesulfinate, 824-79-3; sodium p-toluenethiolate, 10486-08-5; ethanethiol, 75-08-1.

Preparation and Photochemistry of Hexamethyl-2,5-cyclohexadienone Epoxides

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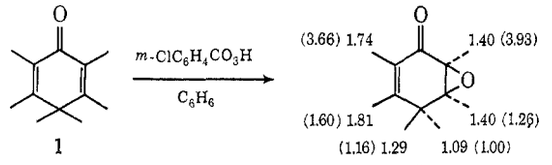
Received May 3, 1973

"The reaction of α,β-unsaturated ketones with peracids usually does not lead to epoxidation of the double

bond." [1] Instead, the carbonyl group is usually attacked. Although exceptions to this generality are known,[2] they are not common. We wish to report that the title dienone **1**[3] is readily epoxidized with *m*-chloroperbenzoic acid, whereas it is recovered unchanged from the usual alkaline peroxide[4] or peroxide–tungstate[5] treatments. We also describe the photoisomerization of the resulting epoxy ketone.

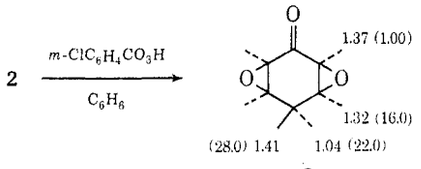
Treatment of **1** with *m*-chloroperbenzoic acid in benzene afforded the monoepoxide **2**. Its structure is



1 2

based on spectral data and further chemical transformations. The ir and uv spectra of **2** are consistent for an α,β-unsaturated cyclohexenone. The nmr spectrum[6] (see structure) is also reasonable. Epoxide prepared from **1** in which the C-3 and C-5 methyls were replaced by CD_3 groups[3] lacked the peak at δ 1.81, and the peak at δ 1.40 integrated for only three protons. Assuming that shift reagent coordinates at the carbonyl group but preferentially at the epoxide "face," the methyl group at δ 1.29 ,which has the larger europium shift and occurs at lowest field, is assigned as cis to the epoxide ring.

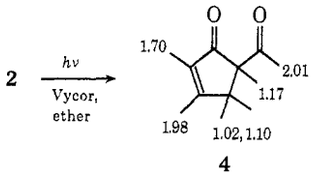
Further treatment of **2** with *m*-chloroperbenzoic acid gave the *cis*-diepoxide **3**. The crude reaction product



3

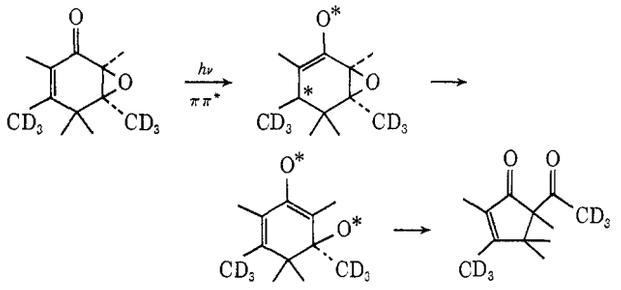
contained no nmr peaks in addition to those observed for pure **3**; thus there is no evidence for the presence of the trans isomer. The nmr spectrum,[6] which shows two different three-proton singlets for the *gem*-dimethyl group, requires the cis geometry. Diepoxide prepared from **1** in which the C-3 and C-5 methyls were replaced by CD_3 groups[3] lacked the singlet at δ 1.32. The europium shift data for **3** are curious in that coordination appears to occur remote from the carbonyl group.

Irradiation of **2** through a Vycor filter gave a single photoisomer, formulated as **4**. Ir, uv, and nmr data

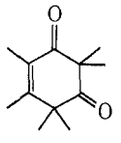


4

were consistent with the cyclopentenone and β-diketone moieties. When **4** was obtained from **2** labeled with CD_3 groups at C-3 and C-5, the nmr signals at δ 1.98 and 2.01 were absent. This is consistent with the following mechanism.



Ring contraction in the final step, rather than methyl migration to give **5**, is consistent with earlier results



5

on the irradiation of α,β-epoxy ketones.[7] Irradiation of **2** through Pyrex, in ether or acetone solution, caused no photoreaction, suggesting that the observed photoisomerization proceeds *via* $\pi\pi^*$ singlet excitation. It is interesting that the mass spectra of **2** and **4** are nearly identical, suggesting that a similar rearrangement may occur on electron impact.

Irradiation of **3** under a variety of conditions led only to recovered starting material.

Experimental Section

2,3-Epoxy-2,3,4,4,5,6-hexamethyl-2,5-cyclohexadienone (2).—A solution of 1.98 g (0.013 mol) of *m*-chloroperbenzoic acid in 50 ml of benzene was cooled to 0°. To this solution was added, slowly, a solution of 1.78 g (0.010 mol) of 2,3,4,4,5,6-hexamethyl-2,5-cyclohexadienone (**1**) in 10 ml of benzene. The mixture was stirred at 5° for 1 hr, then at room temperature for 14 hr. The benzene solution was washed successively with dilute sodium carbonate and saturated sodium chloride and dried ($MgSO_4$). Removal of the solvent (rotary evaporator) left a white residue (1.84 g) which was chromatographed over alumina (80–200 mesh) with benzene–carbon tetrachloride eluent (1:10). The first fraction was the desired monoepoxide **2**, 1.30 g (69%), mp 48–48.5°. The second fraction was unconverted dienone; no diepoxide **3** was formed under these conditions. The monoepoxide **2** had the following properties: ir (CCl_4) 1700 (w), 1655 (s), 1625 (m), 1470 (m), 1380 (s), 1365 (m), 1345 (m), 1280 (w), 1240 (w), 1205 (w), 1135 (m), 1105 (s), 1075 (m), 1025 (m), 1000 (w), 965 (w), 940 (m), 865 (s), 690 cm^{-1} (m); uv (cyclohexane) 323 nm (ϵ 86), 246 (8330); mass spectrum (70 eV) *m/e* (rel intensity)[8] 194 (3), 179 (8), 178 (4), 164 (4), 163 (6), 152 (100), 137 (86), 123 (34), 109 (12), 81 (45); nmr, see structure.

Anal.[9] Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.93; H, 9.29.

***cis*-2,3:5,6-Diepoxy-2,3,4,4,5,6-hexamethyl-2,5-cyclohexadienone (3).**—To a cooled (ice) solution of 1.92 g (0.01 mol) of *m*-chloroperbenzoic acid in 30 ml of benzene was added slowly a solution of the monoepoxide **2** (0.97 g, 0.005 mol) in 10 ml of benzene. The mixture was allowed to warm to room temperature and stirred for 18 hr. The benzene solution was washed with dilute sodium carbonate and saturated sodium chloride, and dried ($MgSO_4$). Evaporation of the solvent and recrystalliza-

(1) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 306.

(2) Flavoindogenides (α-arylidene flavones) are an example: D. D. Keane, W. I. O'Sullivan, E. M. Philbin, R. M. Simons, and P. C. Teague, *Tetrahedron*, **26**, 2533 (1970).

(3) H. Hart and D. W. Swatton, *J. Amer. Chem. Soc.*, **89**, 1874 (1967).

(4) R. L. Wasson and H. O. House, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 522.

(5) G. B. Payne and P. H. Williams, *J. Org. Chem.*, **24**, 54 (1959).

(6) Determined in CCl_4 with TMS as internal reference; chemical shifts are in δ units, and values in parentheses are the relative slopes of the chemical shift differences as a consequence of adding the shift reagent Eu(fod)$_3$.

(7) C. S. Markos and W. H. Reusch, *J. Amer. Chem. Soc.*, **89**, 3363 (1967); for a review, see A. Padwa, *Org. Photochem.*, **1**, 91 (1967).

(8) Determined on a Hitachi Perkin-Elmer RMU-6 instrument.

(9) Spang Microanalytical Laboratory, Ann Arbor, Mich.

tion of the residue from hexane or methanol afforded 0.97 g (93%) of the diepoxide **3**, mp 80–81°. The same product could be obtained directly from **1** using an excess (two to threefold) of oxidant. Mixtures of **2** and **3** are difficult to resolve by column chromatography, though they can be separated by gas chromatography (10 ft × 0.25 in. column, 20% DEGS on 60/80 Chromosorb W, 150°): ir (CCl_4) 1685 (s), 1660 (w), 1630 (w), 1475 (m), 1455 (w), 1415 (m), 1380 (m), 1375 (w), 1340 (w), 1290 (w), 1255 (s), 1220 (w), 1165 (w), 1155 (w), 1120 (s), 1070 (m), 1030 (m), 940 (w), 875 (s), 700 cm^{-1} (m); uv (cyclohexane) 240 nm (ϵ 607), 217 (1960); mass spectrum (70 eV) *m/e* (rel intensity) 210 (2), 195 (3), 194 (0.5), 178 (4), 167 (20), 153 (32), 139 (100), 125 (37), 121 (33), 97 (43), 81 (49), 69 (40), 57 (46), 55 (91), 53 (64); nmr, see structure.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.39; H, 8.59.

Irradiation of 2.—A solution of 0.6 g of **2** in 30 ml of anhydrous ether was irradiated through Vycor with a 450-W Hanovia lamp. The photolysis was followed by vpc using a 5 ft × 0.25 in. column, 20% SE-30 on 60/80 Chromosorb W, 144°, He carrier gas flow 150 ml/min. As the reaction proceeded, the peak with a retention time of 9.5 min (starting material) decreased in area and a product peak appeared at 7.5 min. After 10 hr the reaction was complete and the product, **5-acetyl-2,3,4,4,5-pentamethyl-2-cyclopentenone** (**4**) was collected by preparative vpc: ir (CCl_4) 1690 and 1700 (broad, s) 1647 (m), 1385 (m), 1355 (m), 1325 (m), 1020 cm^{-1} (m); uv (cyclohexane) 233 nm (ϵ 14,750); mass spectrum (70 eV) *m/e* (rel intensity) 194 (20), 179 (3), 152 (100), 137 (90), 123 (19), 109 (33), 81 (24); nmr, see structure.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.23; H, 9.33.

Irradiation of ether or acetone solutions of **2** as above but through Pyrex gave only unchanged starting material.

Irradiation of 3.—Irradiation of a 1% solution of **3** in ether through quartz, or in acetone through Pyrex for 9–16 hr with a 450-W Hanovia lamp, gave only unchanged starting material.

Acknowledgment.—We are indebted to the National Science Foundation and the National Institutes of Health for financial support of this research.

Registry No.—**1**, 14790-04-6; **2**, 40940-60-1; **3**, 40940-61-2; **4**, 40940-46-3.

Photochemical Reactions of Nucleic Acid Constituents. Peroxide-Initiated Reactions of Purines with Alcohols

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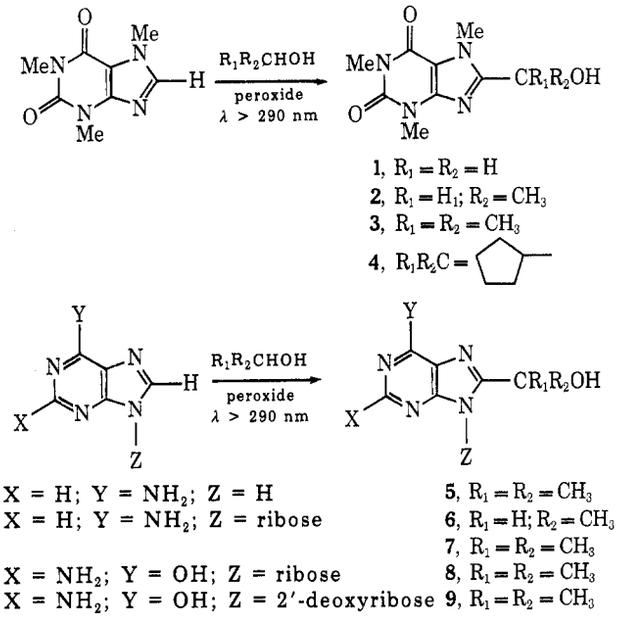
Received March 20, 1973

The photoalkylation of purines with alcohols has been described in recent years.[2] Most of these reactions led to the substitution of a hydroxyalkyl group for the C-8 hydrogen atom in the purine nucleus. The reactions were initiated either directly by ultraviolet light ($\lambda > 260$ nm), or through photosensitization with acetone ($\lambda > 290$ nm). We now report the light-induced reactions of purines with alcohols initiated with peroxides which lead to nearly quantitative yields of the appropriate C-8 hydroxyalkyl purines (with quantum yields of up to 0.05). A variety of peroxides, such as di-*tert*-butyl peroxide (DBP) and dicumyl peroxide (DCP), were employed in these reactions, all leading to high yields of the purine alcohol photoproduct. Light of $\lambda > 290$ nm or sunlight was used for the initiation of these reactions, which can be summarized as shown in Scheme I.

SCHEME I



The photoproducts were generally isolated by column chromatography and characterized through their physical properties, as well as by comparison with authentic samples.[2c,e] In some cases (*e.g.*, adenosine and 2-propanol), chromatography could be omitted in the work-up procedure, and the photoproduct was obtained by direct crystallization from the bulk of the reaction mixture. The reactions studied and the photoproducts isolated are summarized in Table I.

Traces ($\leq 1\%$) of 8-alkylpurines, the alkyl side chain of which depended on the alcohol employed, were sometimes found as by-products of the reactions. For example, 8-isopropyladenine was detected in the reaction of adenine with 2-propanol. A product (**10**)[2e] resulting from the alkylation both at the C-8 position and at the N-7 methyl group of caffeine could be isolated in minute amounts ($\leq 1\%$) from the caffeine–2-propanol reaction (see Experimental Section).

Spectral measurements indicated that most of the incident light is absorbed by the peroxide (*ca.* 90% with DBP). It is, therefore, suggested that the initiation of the reaction results from the light-induced fragmentation of the peroxide into free radicals, which abstract a hydrogen atom from the solvent, thus generating alcohol free radicals. The latter are scavenged by a purine molecule to yield, subsequently, the appropriate photoproduct.[2e]

To conclude, the reported reactions present a simple method for the synthesis of 8-hydroxyalkyl purines in high yields. The broad choice of alcohols in these reactions makes our method very versatile

(1) In partial fulfillment of the requirements for a Ph.D. thesis to be submitted to the Feinberg Graduate School.

(2) (a) H. Linschitz and J. S. Connolly, *J. Amer. Chem. Soc.*, **90**, 297 (1968); (b) D. Elad, I. Rosenthal, and H. Steinmaus, *Chem. Commun.*, 305 (1969); (c) H. Steinmaus, I. Rosenthal, and D. Elad, *J. Amer. Chem. Soc.*, **91**, 4921 (1969); (d) B. Evans and R. Wolfenden, *ibid.*, **92**, 4751 (1970); (e) H. Steinmaus, I. Rosenthal, and D. Elad, *J. Org. Chem.*, **36**, 3594 (1971); (f) Y. Yawazoa, M. Maeda, and K. Nushi, *Chem. Pharm. Bull.*, **20**, 1341 (1972).