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EPOXIDATION OF RETINOL AND THE STRUCTURE OF "CHROMOGEN 574"

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Abstract—Epoxidation of retinol (vitamin A alcohol, 1) with freshly prepared and standardized *mono*-perphthalic acid in ether affords a product which Karrer named "*chromogen* 574" in 1945. Repetition of this peracid oxidation of retinol (1) with several peracids (*m*-PPA, *m*-CPBA, or CH_3CO_3H) with or without a buffer ($NaHCO_3$ or Na_2HPO_4) produces dihydropyran alcohol 4 as characterized by spectroscopy and subsequent chemical transformations. Thus the structures proposed for "*chromogen* 574" by Karrer in 1945–47 and Troitskii in 1948 are now revised to correspond to cyclic alcohol 4.

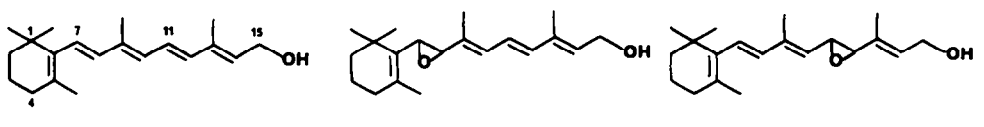
The *mono*-perphthalic acid oxidation of vitamin A alcohol (retinol, 1, Fig. 1) was first described by Karrer and Jucker in 1945.[1] The principal product of this reaction was assigned as 5,6-epoxyretinol which they named "*chromogen* 574" after its characteristic UV absorbance in the Carr-Price reaction ($SbCl_3$ in $CHCl_3$). After considering the UV spectrum of this oxidation product [UV max (EtOH) 272–275 nm, ϵ 13,600] Karrer and Jucker in 1947[2] revised their original structural assignment to correspond to 7,8-epoxyretinol (2) which should have an absorption near 264 nm (calcd)[3] as compared to 294 nm (calcd)[3] for 5,6-epoxyretinol. In 1948 Triotskii revised Karrer and Jucker's structural assignment to 11,12-epoxyretinol (3, UV 269 nm, calcd)[3] again based upon the UV spectrum which suggests the presence of a β-ionylidine unit (alkenes C-5 to C-10).[4] More recently 11,12-epoxyretinol (3) has been claimed as a major product resulting from the cobalt-catalyzed auto-oxidation of retinol (1).[5]

In an attempt to prepare epoxides of vitamin A for screening as possible epithelial cancer "chemopreventative"[6] agents, we had an occasion to re-examine this peracid oxidation of retinol (1). In this paper we wish to present evidence which establishes dihydropyran alcohol 4[7] (Fig. 2) as the structure of "*chromogen* 574."

Following the procedure of Karrer and Jucker,[1,2] treatment of alcohol 1 with freshly prepared and standardized[8] *mono*-perphthalic acid (*m*-PPA) in anhydrous diethyl ether for 20 hr at room termperature affords cyclic ether alcohol 4, (Fig. 2) as the major product. Careful chromatography on either neutral alumina (activity IV) or silica gel gives pure alcohol 4 as a pale yellow oil. The UV spectral data [UV max (EtOH) 272–274 nm, ϵ 13,000; UV max ($SbCl_3 + CHCl_3$, Carr-Price reaction) 570 nm] confirms the identity of alcohol 4 with "*chromogen* 574."

An examination of the 100 MHz H^1 NMR spectral data of compound 4 (Fig. 2) clearly reveals the presence of a secondary OH functional group and the β-ionylidine unit.[9] These conclusions were verified further by preparation of acetate **5a** (Ac_2O/pyr.), 3,5-dinitrobenzoate **5b** (3,5-DNBzCl/pyr.), and phenyl urethane **5c** (PhNCO/pet-ether, 45°). The NMR spectra of alcohol 4 and acetate **5a** are very similar except that only one oxymethine proton (CH–O) moves to lower field in acetate **5a** (br m, δ4.99) compared to alcohol 4 (br m, δ3.62). The protons at C-15 in alcohol 4 appear as a coupled AB quartet[10] at δ3.84 with $J_{AB} = 13$ Hz, $J_{eq',C-4} = 1.7$ Hz, $J_{ax',C-14} = 2.4$ Hz which also suggests a cyclic structure as opposed to an open chain compound like epoxide 3.

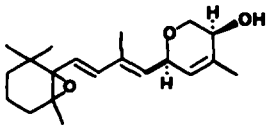
Further proof for a cyclic structure was provided by oxidation of alcohol 4 (CrO_3-Pyr_2/CH_2Cl) to produce pyranenone 6. The NMR spectral data of enone 6 are summarized in Fig. 2. The β-ionylidine moiety remains essentially the same in enone 6 as in alcohol 4; however, the methine proton at C-11 in alcohol 4 (doublet of quartets at δ4.81) moves to lower field in enone 6 (doublet of quartets δ5.16). More dramatically the vinyl proton on C-12 in alcohol 4 (multiplet, δ5.42) moves to very low field in enone 6 (m, δ6.66) strongly suggesting a β-vinyl proton on an α,β-unsaturated ketone. The UV spectrum [238 nm (ϵ 23,000), 267 nm (ϵ 13,000)] and the IR spectrum (1695 cm^{-1}) also support structure 6 for this oxidation product. Establishment of the structure and stereochemistry of dihydropyran alcohol 4 can be made by examination of the europium induced proton nuclear magnetic resonance shifts utilizing $Eu(DPM)_3$.[11] The slopes calculated from the $Eu(DPM)_3$ shift analysis of alcohol 4 are listed in Fig. 2. The salient features of these europium induced shifts are: (1) the oxymethine proton at C-14 displays the largest shift (slope = 4.83), thus



1 2 3

Fig. 1.

confirming the close proximity of europium species to the OH moiety; (2) the equatorial-like proton at C-15 shows the second largest shift (slope = 3.13) and the axial-like proton at C-15 exhibits the third largest shift (slope = 1.88) which indicates a closer relationship between the equatorial-like proton at C-15; and 3) the protons at C-10 (slope = 1.20), C-11 (slope = 1.25), and C-12 (slope = 1.45) are much further removed from the europium coordinated OH moiety as indicated by the respective slopes of each. All of these europium induced PMR shifts are in complete agreement structure **4**. This is convincing evidence for the assignment of structure **4** and not epoxide **3** for "*chromogen* 574."



7ab

In proposing a mechanistic pathway leading to the formation of dihydropyran alcohol **4** from retinol (**1**) one must account for three key features: (1) the selectivity of the peracid for the 13, 14-alkene bond, (2) epoxide ring opening and (3) the formation of dihydropyran alcohol **4**.

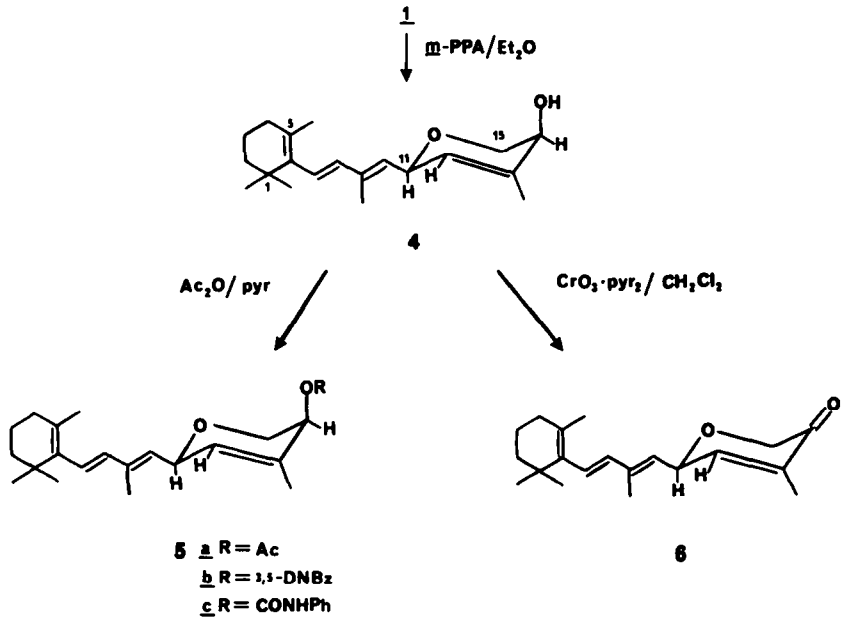


Fig. 2. 100 MHz NMR spectral data.

Figure II (Cont.)

100 MHz NMR Spectral Data ($CDCl_3$)

Protons	Slope*	4	5a	6
C-1 $(CH_3)_2$	0.08	s, 1.00	s, 1.00	s, 1.00
C-5 CH_3	0.08	s, 1.66	s, 1.66	s, 1.68
C-9 CH_3	0.68	t, 1.83; J=1.7 Hz	t, 1.75; J=1.7 Hz	t, 1.84; J=1.7 Hz
C-10 H	1.20	d, 5.34; J=8.5 Hz	d, 5.41; 8.5 Hz	d, 5.47; J= 8 Hz
C-11 H	1.25	d of q, 4.81; J=8.5 Hz J=1.7 Hz	d of q, 4.81; J=8.5Hz J=1.8 Hz	d of q, 5.16; J=8 Hz J=1.7 Hz
C-12 H	1.45	m, 5.42	m, 561	m, 6.66
C-13 CH_3	1.71	d, 1.88; J=1 Hz	d, 1.88; J=1.2 Hz	d, 1.94; J=1.2 Hz
C-14 H	4.83	br m, 362	brm, 4.99	-----
C-14 OH or OAc	----	d, 2.55; J=9 Hz	s, 2.11	-----
C-15 CH_2		coupled AB, 3.84	coupled AB, 3.88	coupled AB, 4.22
		J_{AB} = 13 Hz	J_{AB} = 13 Hz	J_{AB} = 16 Hz
eq' (low field)	3.13	$J_{eq',C-14}$ = 1.7 Hz	$J_{eq',C-14}$ = 1.3 Hz	$J_{eq',C-14}$ = 0 Hz
ax' (high field)	1.88	$J_{ax',C-14}$ = 2.4 Hz	$J_{ax',C-14}$ = 2.5 Hz	$J_{ax',C-12}$ = 1.6 Hz

*These slopes are calculated from the $Eu(DPM)_3$ NMR shift analysis of alcohol **4** in δ(ppm) vs $[Eu(DPM)_3]/[4]$.

The proposed mechanistic pathway given in Fig. 3, provides for these three criteria.

The electronically favored position of attack of peracids in retinol (1) should be the 5,6-alkene since it is tetrasubstituted.[12] This is demonstrated by the fact that retinyl acetate[13] and methyl retinoate[14] undergo exclusive epoxidation at the 5,6-position with *mono*-perphthalic as well as *meta*-chloroperbenzoic[15] (*m*-CPBA) acids. However, intermolecular H-bonding is a well known phenomenon for providing regioselectivity and stereoselectivity in the peracid epoxidations of alkenes with a OH group in close proximity.[16] Thus intermolecular H-bonding of retinol (1) to the peracid followed by epoxidation is expected to produce intermediate epoxy alcohol 8. However, under these reaction conditions, epoxy alcohol 8 is susceptible to proton mediated ring opening followed by allylic rearrangement and ring closure to afford dihydropyran alcohol 4. In practice, however, the reaction is more conveniently carried out using 1.5 equivalents of peracid to consume all of the retinol (1) which is extremely difficult to separate from alcohol 4. Under these conditions epoxides **7ab** can be isolated also in 6% and 11% yields, respectively. The use of other peracids such as *m*-CPBA or peracetic acid with or without a buffer ($NaHCO_3$ or Na_2HPO_4) in ether give cyclic alcohol 4 as the major isolatable product. In a 1973 account of the peracetic acid oxidation of retinol (1) Ogata *et al.* claim regioselective epoxidation of the 11,12-position.[17] The major product utilizing excess peracetic acid is claimed to be 11,12-epoxyretinal. We, however, have not been able to verify this observation even after repeated attempts to do so.

The *cis*-stereochemical relationship between the β-ionylidine unit (R) and the OH group in structure 4 can be rationalized by examination of Dreiding stereomodels of intermediate carbonium ion 9. A model of structure 9 which represents ring closure to produce the *trans*-isomer shows the C-13 methyl and C-14 OH substitutents are eclipsed (dihedral angle ~0°); however, a model of structure 9 that affords *cis*-isomer 4 displays a dihedral angle of ~120° between the C-13 Me and C-14 OH groups in the dihydropyran forming cyclization step. All attempts to buffer ($NaHCO_3$ or Na_2HPO_4) this reaction (with various peracids, *m*-PPA, *m*-CPBA, CH_3CO_3H) have failed to thwart this epoxide ring opening and cyclization. In every case cyclic alcohol 4 was obtained as the major isolatable product.

EXPERIMENTAL

Materials and techniques. M.ps were determined on a Büchi m.p. apparatus and are uncorrected. Analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI, 49951. Silica gel 60, F-254 (E. Merck No. 5765), Silica gel 60 (E. Merck No. 7734, 70–230 Mesh) and Aluminum oxide 90, active neutral (E. Merck No. 1077, 70–230 mesh) available from Brinkmann Instruments were used for thin layer and column chromatography, respectively. UV spectra were recorded on a Cary-14 spectrometer in 95% ethanol. IR spectra were recorded on a Perkin–Elmer 237B spectrometer in spectroquality CCl_4 soln using 0.10 mm NaCl cells. NMR spectra were measured on Varian Associates Model T-60 (Experimental) and/or Model XL-100 (Fig. 2) spectrometers. High resolution mass spectra (HRMS) were measured on a Dupont Flash CEC 21-110B spectrometer at 70 eV and low resolution mass spectra (LRMS) were recorded on a Finnigan 3000 spectrometer at 25 eV. Retinyl acetate was obtained from Hoffmann–LaRoche, Inc., Nutley, NJ 07110. For all reactions performed under an atmosphere of dry N_2 the equipment was dried in an oven at 120° for several hr, then allowed to cool in an atmosphere of dry N_2. All liquid transfers were made with N_2 filled syringes. The term "pet-ether" refers to Baker "Analyzed Reagent" b.p. 30–60°. The term "dry-ether" refers to the purification of commercial anhyd diethyl ether by distillation from LAH under N_2. "Dry pyridine" was obtained by distillation of commercial material from calcium hydride (−40 mesh) under N_2. "Dry dichloromethane" was obtained by distillation of commercial material from P_2O_5. The nomenclature utilized is that preferred by Chemical Abstracts.[18]

The mono-*perphthalic acid oxidation of retinol* (1)

(±) - [2*α*(1E,3E), 3*α*] - 3,6 - *Dihydro* - 4 - *methyl* - 2 - [2 - *methyl* - 4 - (2,6,6 - *trimethyl* - 1 - *cyclohexene* - 1 - *yl*) - 1,3 - *butadienyl*] 2H - *pyran* - 3 - *ol*(4). To vitamin A acetate (656 mg, 2.0 mmol) in dry ether (25 ml) at −15° (ice-MeOH bath) under N_2 was added an ethereal soln of MeLi (4.2 mL, 5.0 mmol, 1.2 M, Aldrich Cat. No. 18,620-1). After 2 hr the mixture was quenched with sat. $NaHCO_3$aq and partitioned between ether (150 mL) and sat. $NaHCO_3$aq (50 mL). The ethereal soln was washed further with sat. $NaHCO_3$aq (2 × 50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give 600 mg of crude 1 as a pale yellow oil. To this material dissolved in dry ether (30 mL) was added freshly prepared and standardized ethereal *mono*-perphthalic acid soln (13.4 mL, 3.0 mmol, 0.225 M)[8] at room temp under N_2. After 20 hr at room temp the mixture was diluted with ether (100 mL) and extracted with sat. $NaHCO_3$aq (2 × 30 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Column chromatography

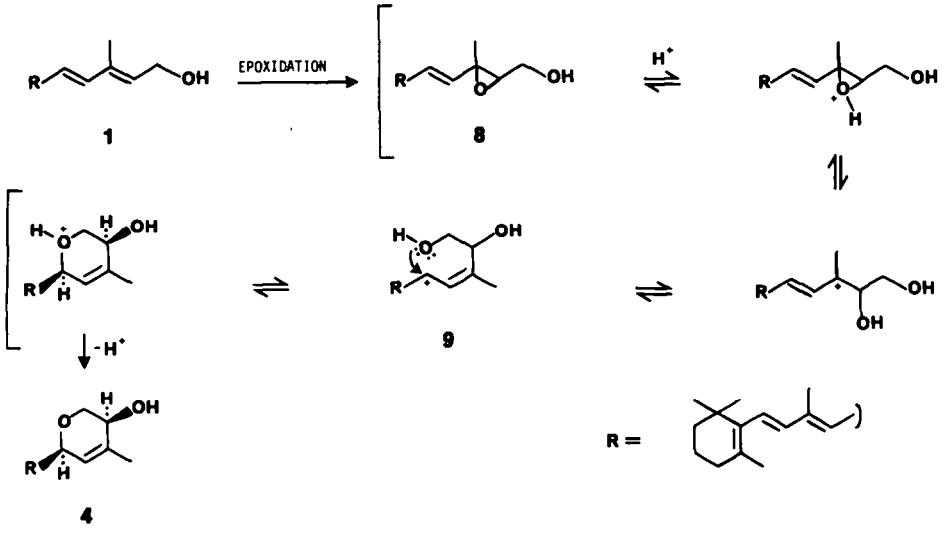


Fig. 3.

over neutral Al_2O_3 (activity IV) eluting with 30% ether/pet-ether afforded 158 mg (26%) of cyclic **4** as a pale yellow oil: UV max (95% EtOH) 272–274 nm (ε 13,000) [lit.[1,2] 272–275 nm (ε 13,600)]; IR(CCl_4) 3400 (br) cm^{-1}; NMR (100 MHz-see Fig. 2). Further elution gave isomeric compounds **7a** and **7b**. The faster moving isomer **7a** (37.1 mg, 5.9%) displays the following spectral data: UV max (95% EtOH) 240 nm (ε 22,000); IR(CCl_4) 3450 cm^{-1}; NMR ($CDCl_3$) δ0.93 (s, 3H), 1.08 (s, 3H), 1.14 (s, 3H), 1.84 (m, 8H), 2.4 (brs, 1H,–OH), 3.62 (brs, 1H), 3.66 (d of d, 1H, J = 13 Hz and 2 Hz), 4.02 (d of d, 1H, J = 13 Hz and 2 Hz), 4.77 (brd, 1H, J = 8 Hz), 5.3–5.5 (m, 2H), 5.80 (d, 1H, J = 16 Hz), 6.21 (d, 1H, J = 16 Hz). The slower moving isomer **7b** (67.2 mg, 11%) exhibited the following spectral data: UV max (95% EtOH) 240 nm (ε 22,000); IR(CCl_4) 3440 cm^{-1}; NMR ($CDCl_3$) δ0.92 (s, 3H), 1.06 (s, 3H), 1.10 (s, 3H), 1.84 (br s, 8H), 2.4 (br s, 1H,–OH), 3.63 (d of d, 1H, J = 12 and 2 Hz), 3.65 (br s, 1H), 4.00 (d of d, 1H, J = 12 Hz and 2 Hz), 4.78 (br d, 1H, J = 8 Hz), 5.41 (m, 2H), 5.80 (d, 1H, J = 16 Hz), 6.20 (d, 1H, J = 16 Hz). (Found: (isomer **7a**) C, 75.15; H, 9.32; (isomer **7b**) C, 75.19; H, 9.36. Calcd for $C_{20}H_{30}O_3$: C, 75.43, H, 9.50%).

Derivatization of cyclic alcohol **4**

(a) (±)-{2α(1E, 3E), 3α] - 3, 6 - *Dihydro* - 4 - *methyl* - 2 - [2 - *methyl* - 4 - (2, 6, 6 - *trimethyl* - 1 - *cyclohexen* - 1 - *yl*) - 1, 3 - *butadienyl*] - 2*H* - *pyran* - 3 - *ol acetate* (**5a**). To cyclic **4** (208 mg, 0.69 mmol) dissolved in dry pyridine (5 mL) was added Ac_2O (0.40 mL, 4.0 mmol). After 20 hr at room temp the mixture was diluted with ether (150 ml) and extracted with 5% HClaq (3 × 25 mL) and sat. $NaHCO_3$aq (1 × 25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography on silica gel using 10% ether/pet-ether as an eluant afforded 177 mg (75%) of **5a** as a pale yellow oil: UV (95% CHOH) 245 nm (ε 10,000), 270 (ε 10,000); IR (CCl_4) 1740 cm^{-1}; NMR (100 MHz-See Fig. 2); mass spectrum (LRMS), m/z (rel intensity) 344 (m^+, 26), 284 (12), 269 (29), 213 (54), 187 (52), 161 (52), 149 (58), 119 (55), 105 (53), 95 (100). (Found: C, 76.51; H, 9.20; Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36%. Found: 344.2346 (MS), 1.1 ppm error (by HRMS) Calcd for $C_{22}H_{32}O_3$: 344.2351).

(b) 3, 5-*Dinitrobenzoate* **5b**. Cyclic **4** (154 mg, 0.51 mmol) dissolved in dry pyridine (15 mL) was added to 3,5-dinitrobenzoyl chloride at room temp. After 20 hr at room temp the mixture was then diluted with ether (100 mL) and extracted with 5% HClaq (2 × 25 mL) and sat. $NaHCO_3$aq (1 × 25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography on silica gel using 20% ether/pet-ether as an eluant followed by crystallization (same solvent) gave 138 mg (55%) of 3, 5-dinitrobenzoate **5b**: m.p. 100.5° (dec); IR (CCl_4) 1730 cm^{-1}, NMR ($CDCl_3$) δ1.02 (s, 6H), 1.4–1.8 (m, 4H), 1.70 (s, 3H), 1.86 (t, 3H, J = 2Hz), 1.96 (s, 5H), 3.89 (d, of d, 1H, J = 14 Hz and 2 Hz), 4.27 (d or d, 1H, J = 14 Hz and 1.5 Hz), 4.93 (br, d, 1H, J = 8 Hz), 5.35 (m, 1H), 5.48 (br d, 1H, J = 8 Hz), 5.82 (m, 1H), 6.23 (br s, 2H), 9.23 (s, 3H), (Found: C, 63.37; H, 6.49; N, 5.68. Calcd for $C_{27}H_{32}N_2O_7$: C, 65.31; H, 6.50; N, 5.64%).

(c) *Phenyl urethane* **5c**. Cyclic **4** (182 mg, 0.604) dissolved in pet-ether (1.0 mL) was added to phenyl isocyanate (72 mg, 0.604 mmol) at room temp. This soln was then concentrated with gentle heat to approximately 0.25 mL, sealed under N_2 and heated at 45° for 10 hr. After cooling to room temp the mixture was then column chromatographed on silica gel using 10% ether/pet-ether as an eluant to afford 160 mg (63%) of **5c** as a colorless foam which failed to crystalize from pet-ether at −78°: IR (CCl_4) 1740 cm^{-1}; NMR ($CDCl_3$) δ1.02 (s, 6H), 1.4–1.8 (m, 4H), 1.70 (s, 3H), 1.85 (t, 3H, J = 2Hz), 1.95 (s, 5H), 3.86 (d of d, 1H, J = 14 Hz and 2 Hz), 4.27 (d of d, 1H, J = 14 Hz and 1.5 Hz), 4.8–5.2 (m, 2H), 5.49 (br d, 1H, J = 8 Hz), 5.75 (m, 1H), 6.20 (br s, 2H), 6.89 (br s, 1H), 7.1–7.6 (m, 5H). (Found: C, 76.65; H, 8.28; N, 3.40. Calcd for $C_{27}H_{15}NO_3$: C, 76.92; H, 8.37; N, 3.32%).

Oxidation of alcohol **4** *to enone* **6**

(±)-(E, E) - 4 - *Methyl* - 2 - 2 [*methyl* - 4 - (2, 6, 6 - *trimethyl* - 1 - *cyclohexen* - 1 - *yl*) - 1, 3 - *butadienyl*] - 2*H* - *pyran* - 3(6*H*) - *one* (**6**). Dry pyridine (1.5 mL) was added to a stirred suspension of anhyd CrO_3 (1.2 g, 12 mmol) in dry CH_2Cl_2 (30 mL). After stirring 3 hr at room temp the red soln was cooled to 0° under N_2 and **4** (365 mg, 1.21 mmol) dissolved in dry CH_2Cl_2 (10 mL) was added. After stirring for 30 min at 0° the mixture was then passed through a short column of Florisil (60–100 mesh). The Florisil column was then washed with CH_2Cl_2 (50 mL) and then ether (50 mL). Concentration *in vacuo* of the combined organic solns followed by column chromatography on silica gel using 5% ether/pet-ether as an eluant gave 113 mg (31%) of **6** as a colorless oil: UV max (95% EtOH) 238 nm (ε 23,000), 267 nm (ε 13,000); IR (CCl_4) 1695 cm^{-1}; NMR (100 MHz-see Fig. 2); mass spectrum (LRMS), m/z (rel intensity), 300 (m^+, 45), 285 (15), 161 (100), 119 (95), 111 (55), 105 (59), 69 (63), 55 (75), 41 (69). (Found: 300.3104 (MS), 4.9 ppm error (by HRMS). Calcd for $C_{20}H_{28}O_2$: 300.2089).

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REFERENCES

[1]P. Karrer and E. Jucker, *Helv. Chim. Acta* **28**, 717 (1945).
[2]P. Karrer and E. Jucker, *Ibid.* **30**, 559 (1947).
[3]A. I. Scott, *Interpretation of Ultraviolet Spectra of Natural Products*, pp. 45–50. Macmillan, New York (1964).
[4]G. V. Troitskii, *Biokhimiya* **13**, 7 (1948); *Chem. Abstr.* **42**, 8169 (1948).
[5]Y. Ogata, Y. Kosugi, and K. Tomizawa, *Tetrahedron* **26**, 5939 (1970).
[6]The term *chemopreventative agent* simply means the utilization of a chemical substance as a prophylactic agent in the prevention of disease. See: M. B. Sporn, N. M. Dunlop, D. L. Newton and J. M. Smith, *Fed. Proc., Am. Soc. Exp. Biol.* **35**, 1332 (1976).
[7]The structures depicted in this paper are racemates; however, only one enantiomer is shown for simplicity.
[8]L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis* pp. 819–820. Wiley, New York (1967).
[9]W. Vetter, G. Englert, N. Rigassi and U. Schwieter, *Carotenoids*, (Edited by O. Isler) pp. 189–266. Birkhäuser Verlag, Basel (1971).
[10]N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry* pp. 42 and 108–110. Holden-Day, San Francisco (1964).
[11]C. C. Hinckley, *J. Am. Chem. Soc.* **91**, 5160 (1969).
[12]D. Swern, *Org. React.* **7**, 378 (1953).
[13]F. B. Jungalwala and H. R. Cama, *Biochem. J.* **95**, 17 (1965).
[14]K. V. John, M. R. L. Lakshmanan, and H. R. Cama, *Ibid.* **103**, 539 (1967).
[15]Epoxidation of retinyl acetate and methyl retinoate with *m*-CPBA in ether–Na_2HPO_4 gives the respective 5, 6-eqoxides in 50% and 66% yield, respectively. S. C. Welch and A. S. C. P. Rao unpublished results.
[16a]P. Chamberlain, M. L. Roberts and G. H. Whitham, *J. Chem. Soc.* B, 1374 (1970); [b]J. L. Pierre, P. Chantemps and P. Arnaud, *Bull. Soc. Chim. Fr.* 1317 (1969); [c]H. Christol, D. Duval, and G. Solladie, *Ibid.* 689 (1968); [d]K. D. Bingham, G. D. Meakins, and J. Wicha, *J. Chem. Soc.* C, 570 (1969); [e]H. B. Henbest, *Proc. Chem. Soc.* 159 (1963); H. B. Henbest and I. McClenaghan, *Chem. Ind.* 462 (1962); [f]M. L. Sassiver and J. English, *J. Am. Chem. Soc.* **82**, 4891 (1960; [g]W. M. Hoehn, *J. Org. Chem.* **23**, 929 (1958); [h]H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.* 1958 (1957); [i]H. B. Henbest and B. Nichols, *Ibid.* 4608 (1957).
[17]Y. Ogata, K. Tomizawa and K. Takagi, *Tetrahedron* **29**, 47 (1973).
[18]K. L. Loening, Nomenclature Director, Chemical Abstracts Service, P. O. Box 3012, Columbus, OH 43210.