used for the D-*gluco* analog[9,11] was used. 2-Amino-2-deoxy-α-D-galactose hydrochloride[13] (I, 1.00 g.) was placed in a 25-ml. Erlenmeyer flask equipped with a Teflon-covered stirring bar and a drying tube, acetyl bromide (2.5 g., 5 mole equiv.) was added, and the vigorously stirred mixture was heated slowly during 30 min. to 55° (oil bath temperature). This temperature was maintained for 1 hr., during which time the mixture became red and slowly solidified. At this point the flask was cooled and was connected to a water pump aspirator through a series of four 8-in. U-tubes containing soda lime. After all the acid vapors were absorbed (about 3 hr.), the residue was extracted with dry methylene chloride, the undissolved residue removed by filtration, and the filtrate decolorized with activated carbon. Dry ether was added to the solution to the point of incipient crystallization, and the mixture was refrigerated overnight to give II as pink plates, yield 900 mg. or 76% (range 65–90%) based on the amount of I which had undergone reaction, m.p. 144–148° dec., $[\alpha]^{23}D$ +160 ± 2° (*c* 0.7, chloroform); specific optical rotatory dispersion curve (*c* 0.34, 26°) +100 (700), +157 (600), +231 (500), +403 (400), +574° (350 mμ); λ_{max}^{KBr} 5.74 vs (OAc), 6.11 w, 6.70 m (NH_3^+), 7.34 m (CH_3C), 11.80 w (equatorial H at C-1), 13.45 μ w (C–Br?); X-ray powder diffraction data[12]: 12.96 vs (2), 8.76 w, 8.04 w, 6.03 vs (1,1), 5.31 w, 4.33 vs (1,1), 4.15 m, 4.04 s, 3.93 s, 3.58 w, 3.02 vs (3), 2.87 s. Recrystallization from methylene chloride and ether gave a less colored product, but the melting point and specific rotation did not change significantly.

Anal. Calcd. for $C_{12}H_{19}Br_2NO_7$: C, 32.09; H, 4.26; Br, 35.56; N, 3.12. Found: C, 32.01; H, 4.44; Br, 35.37; N, 3.12.

The methylene chloride-insoluble material was dissolved in aqueous ethanol (decolorizing carbon), and recovered by evaporation; yield, 400 mg. This material was treated with acetyl bromide as already described, and a further quantity of II was isolated, in similar yield.

When higher reaction temperatures were employed, the amount of methylene chloride-insoluble material remaining diminished, and was negligible when the reaction temperature was raised to 70°. However, under these more vigorous conditions, the product was deep red in color, and required several recrystallizations for acceptable purity. Reaction at room temperature for extended periods gave very little product. Efficient stirring was essential for success of the reaction.

The bromo sugar II underwent no decomposition when stored in a desiccator for 6 weeks. The infrared spectrum of II was very similar to that exhibited by the D-*gluco* analog.

A crude product, m.p. 161°, considered to contain II, has been prepared by another route,[14] but no analytical or other physical data were given.

Methyl 3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-β-D-galactopyranoside (III).—A solution of the bromo sugar II (500 mg.) in dry methanol (5 ml.) was shaken overnight with an excess of dry silver carbonate and finely ground Drierite.[15] The mixture was filtered through Celite,[16] and the filtrate evaporated to a colorless sirup which failed to crystallize. The product gave a positive ninhydrin reaction, migrated as a single zone (R_f = 0.75) on thin layer chromatograms with 8:1:1 benzene–methanol–pyridine as developer, and did not reduce Fehling solution.

Conversion of the product to the hydrobromide salt with an equivalent of hydrogen bromide in methanol, followed by evaporation, gave a hygroscopic sirup, λ_{max}^{KBr} 2.97 s (NH), 5.73 vs (OAc), 6.12 w, 6.63 μ w (NH_3^+). The product was not obtained crystalline.

Methyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (IV).—The sirupy hydrobromide product from the preceding preparation was dissolved in a cold mixture of dry pyridine (5 ml.) and acetic anhydride (2.5 ml.), and left for 3 hr. at room temperature. The mixture was poured into water, and the product was extracted with chloroform. The extract was washed with water, and the final traces of pyridine were removed by shaking the extract with aqueous cadmium chloride solution. The cadmium chloride–pyridine complex was filtered, and the dried extract evaporated to a crystalline residue. Recrystallization from methanol gave IV as large prisms; yield 200 mg. (55% calculated on II), m.p. 212–216°. A further recrystallization gave analytically pure product; m.p. 215–217°, $[\alpha]^{23}D$ −15 ± 1° (*c* 1.5, chloroform); λ_{max}^{KBr} 3.03 m (NH), 5.70 s (OAc), 6.03 s, 6.40 m (NHAc), 7.28 m (CH_3C), 11.13 μ w (axial H at C-1); X-ray powder diffraction data[12]: 13.27 s, 7.97 vs (1,1), 7.38 vs (3), 6.92 m, 6.15 vs (2), 5.5 w, 4.93 s, 4.57 m, 4.37 m, 4.15 m, 3.95 vs (1,1), 3.75 s.

Anal. Calcd. for $C_{15}H_{23}NO_8$: C, 49.84; H, 6.42; N, 3.87. Found: C, 50.09; H, 6.44; N, 3.91.

The following constants have been recorded[7] for this compound, prepared by a different procedure: m.p. 216–217°, $[\alpha]^{23}D$ −17 ± 1° (*c* 1.84, chloroform).

(13) A product of Pfanstiehl Laboratories, Waukegan, Ill. The authors thank Dr. D. G. Doherty, of Oak Ridge National Laboratory, Oak Ridge, Tenn., for a gift of this material.

(14) K. Onodera and T. Komano, *J. Org. Chem.*, **26**, 3932 (1961).

(15) Anhydrous calcium sulfate, a product of W. A. Hammond Drierite Co., Xenia, Ohio.

(16) Celite, a siliceous filter-aid, product of the Johns-Manville Co., N. Y.

The Chromous Chloride Reduction of Ergosterol Epidioxide[1]

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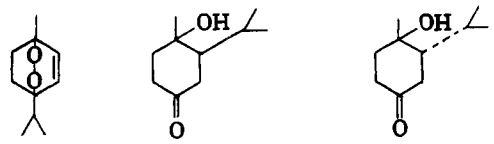
The reduction of ascaridole (I) with ferrous ion is reported to yield,[2] besides ascaridole glycol, a mixture of two stereoisomeric hydroxy ketones II and III.



I II III

Formation of the isomeric ketones is thought to arise by one electron transfer from ferrous ion to the oxide bridge, generating a tertiary alkoxy radical. The alkoxy radical fragments to an α,β-unsaturated cyclohexenone and an isopropyl radical, followed by isopropyl radical attack on the β-carbon of the cyclohexenone. Further electron and proton acquisitions yield the observed products II and III.

To establish whether one-electron reduction by a metal ion on ergosteryl acetate epidioxide (IV) would follow a similar reaction course and generate a steroidal *t*-alkoxy radical, the reduction of IV was studied.

Treatment of epidioxide IV with chromous chloride[3] in ethanolic hydrochloric acid resulted in rapid reduction. Chromatography of the materials formed yielded ergosteryl acetate (V), a dimeric substance, $C_{60}H_{90}O_4$ (VI), and the hydroxy acetate (VII), all formed in equal yields of about 30%.

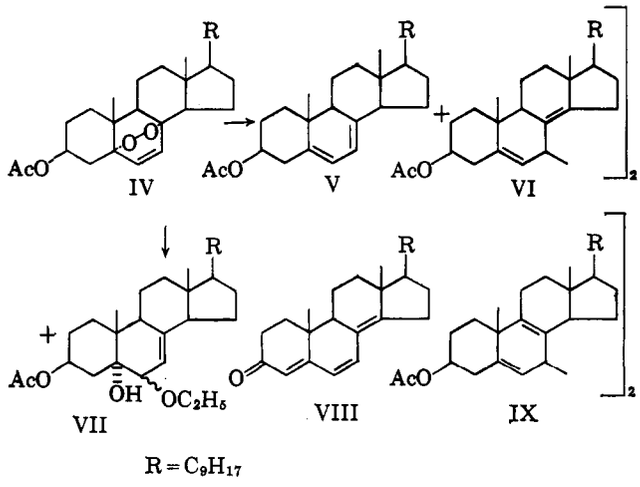
The structures are assigned as follows. The dimer VI showed no selective ultraviolet absorption. Saponification of the dimer diacetate yielded a diol which differed from the well known bisergostatrienol (IX),[4] the product of photodimerization of ergosterol. The n.m.r. spectrum of the dimer VI indicated vinyl proton absorp-

(1) This work was supported by Public Health Service Research Grant AM-05183 from the National Institute of Arthritis and Metabolic Diseases.

(2) D. Brown, B. T. Davis, T. G. Halsall, and A. R. Hands, *J. Chem. Soc.*, 4492 (1962).

(3) J. Kochi, *J. Am. Chem. Soc.*, **84**, 1193 (1961), has reported that the chromous ion reduction of tertiary alkyl hydroperoxides affords products of *t*-alkoxy radical fragmentation and the corresponding tertiary alcohols.

(4) A. Windaus and P. Borgeaud, *Ann.*, **460**, 235 (1928).



$R = C_9H_{17}$

tion at 4.77 τ, broad C-3 proton absorption characteristic of protons adjacent to an acetoxyl function at 5.3 τ, and a broad band at 6.83 τ. These protons appear in a relative intensity ratio of 3:1:1.[5]

Oxidation of the dimeric diol with chromium trioxide in pyridine or under the Oppenauer conditions resulted in fission of the dimer to the monomeric ergostatetraenone (VIII).[6]

Based on these data, we assign the structure VI to the dimer, a Δ^{14} double bond isomer of bisergostatrienol.

The hydroxy acetate VII exhibited in the infrared a pair of bands for an acetate carbonyl at 5.80 and 5.85 μ which Henbest has shown to be characteristic of 5α-hydroxy 3β-acetates.[7] The presence of the ethoxyl group in VII was revealed by the characteristic n.m.r. bands with a methylene quartet at 6.43 τ. The vinyl proton region of the n.m.r. was also in accord with the Δ^7 unsaturation (4.85 τ), with a relative intensity of 3 (C_7–C_{22}–C_{23}).

Oxidation of the hydroxy acetate VII with chromic acid yielded the corresponding C-6 ketone, which has been prepared previously by dichromate oxidation of ergosteryl acetate.[8]

Formation of the reduction products V, VI, and VII can be explained by assuming the initial formation of an intermediate 5α,8α-diol by reduction of the epidioxide.[9]

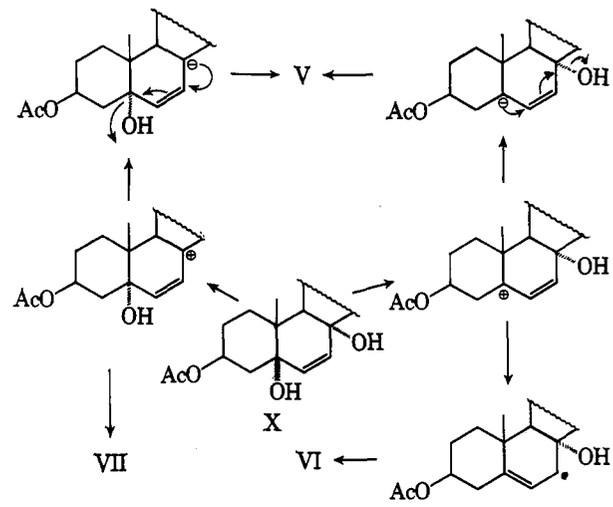
To verify this assumption, the reduction of the 5α,8α-diol X with chromous chloride was next studied. The diol was prepared in an independent manner by zinc and alkali treatment of ergosterol epidioxide.[10]

The results of the reduction of the diol were identical with those of the epidioxide and afforded the same three reduction products, all in yields of approximately 30%.

The mode of formation of the reduction products can now be accounted for by postulating the initial acid-catalyzed formation of either of the allylic carbonium ions at C-5 or C-8 from the diol.[11] Reaction of the allylic carbonium ion at C-7 with the ethanol medium accounts for the formation of the ethoxy derivative VII.[12]

Electron acquisition by the C-5 carbonium ion from chromous ion leads to an allylic radical, which couples and forms the dimer through C-7.[13] Further dehydration of the remaining C-8 α-ols toward the proton at C-14 affords the observed dimeric compound VI.

The origin of the ergosterol acetate from the chromous chloride reduction of its 5,8-epidioxide can be visualized as arising from either the C-5 or C-8 carbonium ion by a two-electron acquisition from the reducing agent. This intermediate anion expels either the C-5 or C-8 hydroxyl group to form the homoannular diene ergosterol.



Experimental[14]

Reduction of Ergosteryl Acetate Epidioxide with Chromous Chloride.—An acidic, ethanol solution (1200 ml.) of chromium trichloride (312 g. of chromic chloride, 1280 ml. of ethanol, and 275 ml. of concentrated hydrochloric acid) was percolated through granular (20-mesh) zinc; the blue chromous solution generated in this manner was passed directly into a stirring solution of 10.2 g. of ergosteryl acetate epidioxide in 675 ml. of tetrahydrofuran and 675 ml. of ethanol under a carbon dioxide atmosphere. A precipitate formed before the addition of chromous reagent had been completed. The blue-green mixture was stirred at room temperature under a carbon dioxide atmosphere for 4 hr. It was then poured into 2 l. of water, filtered, and washed with water. The solid was dried, dissolved in a minimum of benzene, and chromatographed on 300 g. of Florisil. The first two benzene fractions (250 ml. each) eluted 2.61 g. of ergosteryl acetate.

(5) For comparative purposes the n.m.r. spectrum of bisergostatrienol acetate (IX) showed vinyl proton absorption (C-6, C-22, C-23) at 4.83 τ, the C-3 protons at 5.3 τ, and the C-7 protons at 7.0 τ in the ratio of 3:1:1.

(6) D. H. R. Barton and T. Brunn, *J. Chem. Soc.*, 2728 (1951). The mechanism of fragmentation of the dimer to the monomeric ketone is unknown. The thermal fission of bisergostatrienol to neoergosterol is a related process. It is of interest to note that oxidation of bisergostatrienol under Oppenauer conditions also yielded a small but detectable amount of the same ergostatetraenone.

(7) H. B. Henbest, G. D. Meakins, and T. I. Wrigley, *ibid.*, 2633 (1958).

(8) M. Fieser, A. Quilico, A. Nickon, W. E. Rosen, E. J. Tarlton, and L. F. Fieser, *J. Am. Chem. Soc.*, **75**, 4066 (1953).

(9) In ref. 2, Kochi has demonstrated that the chromous ion reduction of *t*-alkyl hydroperoxides affords a large proportion of *t*-alcohol formed by bimolecular reduction of the intermediate *t*-alkoxy radical.

(10) A. Windaus and O. Linsert, *Ann.*, **465**, 148 (1928).

(11) R. B. Clayton, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 2015 (1953), have shown that 5α,8α-diols dehydrate readily under mild acidic conditions to Δ^7 unsaturated compounds.

(12) In addition to the ethoxy derivative VII, a smaller quantity of product arising from reaction of the ion with water to yield the corresponding C-6 alcohol was isolated. This is described in the Experimental section.

(13) The coupling of carbonium ions to dimers in the presence of chromous chloride has been observed by J. B. Conant, L. F. Small, and B. S. Taylor, *J. Am. Chem. Soc.*, **47**, 1959 (1925), and more recently by C. E. Castro, *ibid.*, **83**, 3262 (1961). The stereochemistry of the dimer at C-7–C-7′ is not known.

(14) Melting points were taken on a Fisher-Johns melting point apparatus. A Perkin-Elmer Infracord was used to obtain the infrared spectra. Ultraviolet absorption data were obtained from a Beckman Model DB spectrophotometer. Rotations were determined in chloroform at 1% concentrations unless otherwise stated.

The next benzene fractions (1500 ml. total) contained 1.89 g. of solid that crystallized from methylene chloride–ethanol, m.p. 204–208°, $[\alpha]^{25}D$ −95°, λ^{Nujol} 5.75 and 5.80 μ (OCCH$_3$), for VI.

Anal. Calcd. for $C_{60}H_{90}O_4$: C, 82.32; H, 10.36; mol. wt., 875.5. Found: C, 82.56; H, 10.12; mol. wt., 876.

Elution was continued with 10% ether in benzene (1000 ml.) and 2.36 g. of 3β-acetoxy-6-ethoxy-7(8),22-ergostadien-5α-ol was obtained. After crystallization from methylene chloride–ethanol, the sample VII melted at 167–168°. Further crystallization gave an analytical sample, m.p. 174–175°, $[\alpha]^{26}D$ −95°, λ^{Nujol} 2.91 (–OH), 5.80 and 5.89 μ (–OC–CH$_3$).

Anal. Calcd. for $C_{32}H_{52}O_4$: C, 76.75; H, 10.47. Found: C, 76.90; H, 10.20.

When 750 mg. of the chromatographic fraction of VI was crystallized from ether, 90 mg. of colorless crystalline material (m.p., 225–260°) was obtained. Further crystallization gave an analytical sample, m.p. 259–263°, $[\alpha]^{26}D$ −49° (0.75%).

The analyses was calculated as 3β-acetoxy-7(8),22-ergostadiene-5α-6β-diol.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.94; H, 10.19.

Acetylation of 35 mg. of this C-6 alcohol with acetic anhydride in pyridine yielded 25 mg. of the 3,6-diacetate which, after trituration with methanol, melted at 165–166°, $[\alpha]^{24}D$ −129°; lit.[8] m.p. 171°, $[\alpha]D$ −146°.

Oxidation of 3β-Acetoxy-6-ethoxy-7(8),22-ergostadien-5α-ol.—A solution of 200 mg. of the steroid in 40 ml. of acetone was treated dropwise, at room temperature, with Jones chromium trioxide solution until a slight excess was present. The mixture was filtered through Celite, and the volume of the filtrate was reduced to approximately one-half under reduced pressure; it was then poured into ice–water (200 ml.). The precipitate was filtered and washed with water. After crystallization from methylene chloride–ethanol, the 3β-acetoxy-7(8),22-ergostadien-5α-ol-6-one melted at 253–259°, λ_{max}^{ether} 240 mμ (12,000). Another recrystallization raised the melting point to 261–263°, $[\alpha]^{25}D$ −1° [lit.[8] m.p. 269°, $[\alpha]D$ ±0, $\lambda_{max}^{ethanol}$ 248 (12,900)].

Hydrolysis of the Dimer VI.—The dimer VI with aqueous potassium hydroxide in methanol dioxane (1:1) yielded a diol, after crystallization from acetone, m.p. 191–193°, λ^{Nujol} 2.9 μ (OH), $[\alpha]^{26}D$ −258° (pyridine); reported[3] for bisergostatrienol, m.p. 202–203°, $[\alpha]^{16}D$ −209 (pyridine). A mixture melting point determination showed m.p. 181–190°.

Oxidation of the Dimer VI. A.—A solution of 200 mg. of the diol prepared from VI in 20 ml. of pyridine was added to a mixture of anhydrous chromium trioxide (300 mg.) and 10 ml. of pyridine. The mixture was allowed to stand at room temperature for 18 hr. It was poured into ice–water, and sodium bisulfite was added to decompose excess chromium trioxide. Hydrochloric acid was added until the solution was slightly acidic and the precipitate was filtered and washed with water. The yellow solid (132 mg.) was dissolved in a minimum amount of benzene and chromatographed on 6 g. of acid-washed alumina (Merck). Benzene (65 ml.) eluted 56 mg. of 4,6,8(14),22-ergostatetraen-3-one, m.p. 108–113°, $\lambda_{max}^{ethanol}$ 350 mμ (24,500), $[\alpha]^{25}D$ +526°; lit.[7] m.p. 114–115°, $[\alpha]^{35}D$ +590, $\lambda_{max}^{ethanol}$ 348 mμ (26,500).

B.—To 200 mg. of VI in 10 ml. of benzene and 10 ml. of acetone was added 1.8 g. of aluminum *t*-butoxide. After refluxing the mixture for 6 hr. under a nitrogen atmosphere, 10 ml. of a 1:1 mixture of acetone–benzene was added. After 13 hr. of refluxing, an additional 1.0 g. of aluminum *t*-butoxide and 10 ml. of acetone–benzene (1:1) was added. After refluxing for 23 more hr., the solution was cooled and 25 ml. of benzene was added. The mixture was poured into a cold dilute solution of sulfuric acid and Rochelles salt. The benzene layer was separated, and a benzene extract (50 ml.) of the aqueous layer was added. The benzene was washed with two 100-ml. portions of water and with saturated salt solution (50 ml.). It was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure to leave a yellow oil weighing approximately 500 mg. The oil was dissolved in a minimum amount of benzene and filtered through a column of Florisil (4 g.). A benzene wash (25 ml.) yielded 420 mg. of a yellow-brown oil. This oil was then redissolved in benzene and chromatographed on 12 g. of Florisil. Benzene (160 ml.) eluted 332 mg. of a multicomponent oil. Methylene chloride (150 ml.) eluted 70 mg. of 4,6,8(14),22-ergostatetraen-3-one of an estimated 80% purity by its ultraviolet spectrum. The infrared spectrum and thin layer chromatography showed this material to be identical with that prepared *via* the chromium oxide–pyridine oxidation.

Reduction of 3β-Acetoxy-6,22-ergostadiene-5α,8α-diol (X) with Chromous Chloride.—The triol corresponding to X was obtained by the method of Windaus and Linsert[10] and acetylated with pyridine and acetic anhydride to yield X. A solution of 1.51 g. of X in 150 ml. of tetrahydrofuran and 150 ml. of ethanol was treated with 180 ml. of chromous chloride reagent in a manner identical with that employed for the reduction of the epidioxide IV. A colorless solid (1.37 g.) obtained by this procedure was chromatographed on 45 g. of Florisil. The first two benzene fractions (50 ml. each) eluted 451 mg. of ergosteryl acetate. The next three benzene fractions totalling 220 ml. eluted 354 mg. of the dimer diacetate VI. Elution with ether (100 ml.) afforded 515 mg. of the hydroxy acetate VII. The physical and spectral characteristics of the products obtained from this reduction were identical in all respects with the compounds obtained from the reduction of ergosteryl acetate epidioxide.

The Reactions of Nortricyclyl and Dehydronorbornyl Chloride with Sodium

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An interest in whether α-elimination would occur in the reaction of nortricyclyl chloride with sodium, since β-elimination is prevented by Bredt's rule, prompted the investigation reported here.

Nortricyclyl chloride (I) reacts with sodium in decane at 85–90° to produce a 19–20% yield of C_7 hydrocarbons, isolated directly from the reaction mixture by vacuum distillation. Vapor phase chromatographic and infrared analysis of this volatile hydrocarbon mixture demonstrated that there were four components present: nortricyclene (II), 71%; norbornene (III), 10%; and two additional C_7H_{10} hydrocarbons, 5.9%, 13.1%. The ultraviolet and infrared spectra indicated that the structures of these two hydrocarbons must be reasonably limited to 3-vinylcyclopentene (IV) and 4-vinylcyclopentene (V). The 13.1% component showed only end absorption in the ultraviolet (ϵ_{210} 250), while the infrared spectrum indicated a vinyl double bond (ν_{max} 905, 992, 1638 cm.$^{-1}$)[2] and a cyclopentene double bond (ν_{max} 1610 cm.$^{-1}$).[3] The spectra of the 5.9% component were very similar (end absorption, ϵ_{210} 1774; ν_{max} 910, 990, 1608, and 1635 cm.$^{-1}$). The n.m.r. spectrum of this minor component exhibits complex multiplet absorption centered at 4.38 (3.0 H), 5.04 (1.8 H), and 6.70 τ (0.9 H) and a complex absorption region, 7.50–8.50 τ (4.0 H), while the major (13.1%) component shows complex multiplet absorption centered at 4.16 and 4.39 (3.1 H), 5.08 (2.0 H), and a complex absorption region 6.93–8.10 τ (4.9 H). In both cases the internal olefinic absorption near 4.38

(1) National Defense Act Fellow, 1959–1962.

(2) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, Chap. 3.

(3) R. N. Jones and C. Sandorfy, "Technique of Organic Chemistry, Volume IX. Chemical Applications of Spectroscopy," W. West, Ed., Interscience Publishers, Inc., New York, N. Y., 1956, p. 371.