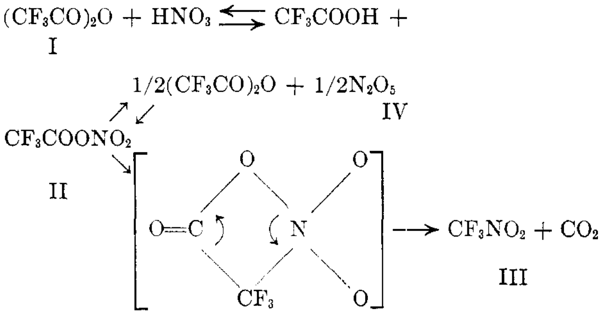

chlorides to nitramines[2] by treatment with silver nitrate. Probably the reason for the low yield of III is the reversible conversion to nitrogen pentoxide (IV). The formation of IV from I and nitric acid has been demonstrated previously[3]; IV would certainly decompose very rapidly at 100°, thus preventing the formation of III.

The reactions of perfluorobutyric anhydride and of perfluorosuccinic anhydride with nitric acid were tried, but in neither case was any nitro compound found in appreciable amount. Probably in these cases IV is formed and decomposes too rapidly to allow formation of nitro compounds. Neither of these anhydrides is completely miscible with nitric acid as is I, and this would doubtlessly affect the reversibility of the reaction in which IV is formed.

EXPERIMENTAL

Reaction of trifluoroacetic anhydride with nitric acid. A mixture of 21.0 g. (0.10 mole) of trifluoroacetic anhydride and 6.3 g. (4.20 cc., 0.10 mole) of 100% nitric acid was placed in a hydrogenation bomb liner and inserted in a stainless steel bomb. The heater was turned on, and in less than an hour the reaction mixture was up to 100°. The mixture was maintained at this temperature for about an additional 5.5 hr., and then was gradually allowed to cool to ambient temperature and allowed to remain overnight. The gas was bled into a standard nitrometer tube (240 cc.) and then into a liquid nitrogen trap. Fourteen fillings of the nitrometer tube (total 3360 cc.) were required to bleed all the gas from the bomb. The gases were passed through a molecular sieve vapor phase chromatography column which irreversibly removed carbon dioxide, nitrogen dioxide, and water. A pure sample of fluoropicrin was thus obtained and eluted from the column. Three 5-cc. aliquots of the original gas sample yielded sufficiently pure fluoropicrin to give a good infrared spectrum. The amount of helium (which had been used as carrier gas in the vapor phase chromatograph) and air in the gas sample were determined by mass spectrometry. The weight of the gas sample was measured by weighing the gas sample tube before and after evacuation. From these data it was calculated that 0.815 g. (7.09%) of pure fluoropicrin was obtained in the reaction.

The fluoropicrin was characterized by means of its infrared and mass spectra. The infrared spectrum showed the reported[4] asymmetrical stretch vibration peaks at 6.13 μ and 6.18 μ and the symmetrical stretch vibration peak at 7.78 μ. The entire infrared spectrum was similar to the reported[5] spectrum of 1-chloro-1,1,2,2-tetrafluoro-2-nitroethane. The mass spectrum showed the expected cracking pattern for a compound with the structure trifluoronitromethane.

Chemistry Division
U. S. Naval Ordnance Test Station
China Lake, Calif.

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[2] W. P. Norris, *J. Am. Chem. Soc.*, **81**, 3346 (1959).

[3] J. H. Robson, *J. Am. Chem. Soc.*, **77**, 107 (1955).

[4] R. N. Haszeldine and J. Jander, *J. Chem. Soc.*, 4172 (1953).

[5] R. N. Haszeldine, *J. Chem. Soc.*, 2525 (1953).

Pyrolysis of 9(11)-Dehydroergosterol Peroxide Acetate

Werner Bergmann[1] and Martin B. Meyers[2]

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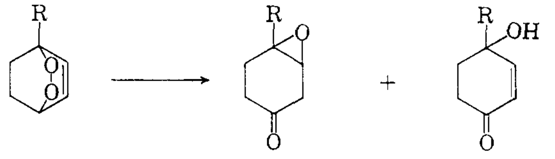
The thermal or base-catalyzed treatment of epidioxide rings attached to secondary-secondary or secondary-tertiary carbon atoms ordinarily gives rise to disproportionation into either or both a β,γ-epoxy ketone and/or a keto-allylic alcohol[3]:



Where the epidioxide ring is attached to two tertiary carbon atoms, as in ergosterol peroxide (I), there must be a rearrangement for disproportionation to take place. This is observed when I is refluxed in a hydrocarbon solvent at around 200°. Two major products are formed, ergost-22-ene-5,6α-epoxy-7-one-3β-ol (II) and ergosta-8,22-diene-5,6α-epoxy-3β,7α-diol (III), where the oxygen function has migrated from C_8 to C_7.[4] The assignment of the nuclear double bond to the Δ^8 position was made by oxidation of the 3-monoacetate of III to 3β-acetoxyergosta-8,22-diene-5,6α-epoxy-7-one (IV), which when treated with potassium iodide in glacial acetic acid gave the known 3β-acetoxyergosta-5,8,22-triene-7-one (V). It was thought that further support for the correctness of this assignment could be made by pyrolysis of 9(11)dehydroergosterol peroxide acetate (VI), which by proceeding in analogous manner to ergosterol peroxide (I) would produce the β,γ-epoxy ketone VII and VIII: Basic isomerization of VII should then lead to IV.

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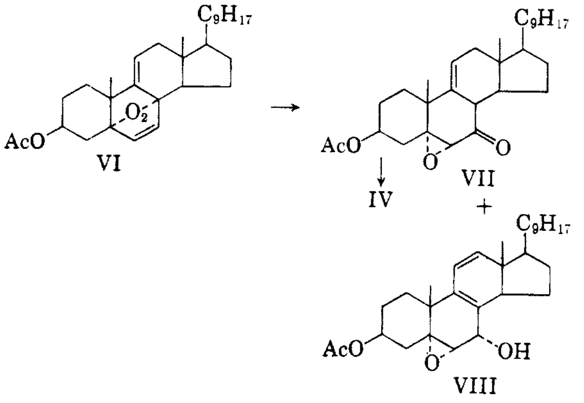
[1] Deceased.

[2] Central Research Laboratories, General Mills, Inc., 2010 East Hennepin Avenue, Minneapolis 13, Minnesota.

[3] (a) W. Bergmann and R. J. Conca, *J. Org. Chem.*, **18**, 1104 (1953); (b) E. J. Agnello, R. Pinson, Jr., and G. D. Laubach, *J. Am. Chem. Soc.*, **78**, 4756 (1956); (c) R. B. Woodward and R. H. Eastman, *J. Am. Chem. Soc.*, **72**, 339 (1950); (d) T. G. Halsall, W. J. Rodewald, and D. Willis, *Proc. Chem. Soc.*, **1958**, 231.

[4] W. Bergmann and M. B. Meyers, *Chem. & Ind. (London)*, **1958**, 655; *Ann.*, **620**, 46 (1959).



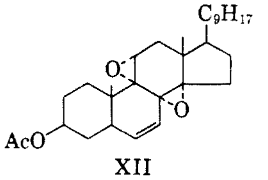
Under conditions sufficient to isomerize I, *i.e.*, one hour refluxing in decane-dodecane mixtures (b.p. 195–200°), VI was recovered unchanged, and prolonged reflux of VI in dodecane (b.p. 214°) in the presence of atmospheric oxygen gave only dark unpurifiable oils. The desired pyrolysis was successfully accomplished by refluxing VI in dodecane under nitrogen for periods of sixty to ninety minutes. Work up of the reaction mixture quickly demonstrated that VI behaves in a highly complex manner on thermal breakdown. On cooling there was deposited a crystalline solid (15–17% yield) (IX). If after filtering IX the mother liquors were allowed to stand three to four weeks, an oil was slowly deposited which amounted to 20–40% by weight of the starting VI. This oil exhibited hydroxyl absorption and a broad band at 5.78 μ in the infrared. Attempts to purify the oil by crystallization or chromatography were unsuccessful. The hydroxyl absorption in this mixture is possibly caused by tertiary hydroxyl groups, as the oil was unchanged after treatment with chromic acid–pyridine complex.

When, after having deposited all insoluble matter, the mother liquors were chromatographed on alumina, elution with 19:1 hexane-benzene yielded about 24% (by weight of starting material) of the deoxygenated 9(11)dehydroergosterol acetate (X). The only previously reported cases of thermal reversal of epidioxide formation have been in the polynuclear aromatic series where, for example, rubrene peroxide loses 80% of its oxygen on heating under vacuum.[5] No detectable amounts of ergosterol are produced on pyrolysis of I; therefore the formation of X must be taken as an indication of the great reluctance of VI to rearrange.

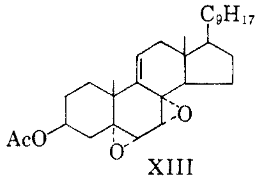
If *Florisil* were substituted for alumina as the absorbent for chromatography of the mother liquors, after the 9(11)dehydroergosterol acetate (X) had been removed, elution with 49:1 hexane-acetone produced a ketone (1.6% yield) which was assigned structure VII (3β-acetoxyergosta-9(11),-22-diene-5,6α-epoxy-7-one as it exhibited $\lambda_{\max}^{\text{KBr}}$ 5.86 μ (α,β-epoxy ketone) and 12.52 μ (epoxide).[6]

Elution of VII from unneutralized alumina brought about isomerization of the β,γ-double bond and yielded a compound which was shown to be identical with IV and thus unambiguously establishing the location of the nuclear double bond in III at Δ^8. Continued elution of the Florisil column gave rise to very small amounts of other compounds with ketonic functions.

The compound IX, isolated by cooling of the pyrolysis mixture, showed in the infrared neither hydroxyl or carbonyl absorption other than the original acetate carbonyl but did possess two sharp bands of medium intensity at 5.94 and 6.06 μ, which were also found in the reduction products of IX. These bands were probably not caused by a conjugated dienoid system, as IX exhibited no noticeable absorption in the ultraviolet above 220 mμ. When IX was allowed to react with chromic acid–pyridine complex, starting material was recovered unchanged. Saponification of IX with methanolic potassium hydroxide gave the free alcohol XI which like IX had two bands of medium intensity at 5.89 and 6.02 μ in the infrared. Elemental analyses of IX and XI showed IX to be isomeric with the starting VI and this was supported by a micro-Rast molecular weight determination on IX. Acid treatment of IX gave rise to an unpurifiable hydroxy ketone. The acid sensitivity of IX combined with its stability towards basic reagents is strikingly similar to the properties which Agnello, Pinson, and Laubach[7] reported for 3β-acetoxyergosta-6,22-diene-8,14α:9,11α-diepoxide (XII). When XII was treated with hydrochloric acid in acetone, an amorphous product was obtained, $\lambda_{\max}$ 256 mμ. It therefore seems plausible that IX may have the diepoxide structure XIII:



XII



XIII

Although an intermediate diepoxide is not found on rearrangement of ergosterol peroxide (I) or its acetate, compounds with such structures have been observed in several other rearrangements of epidioxides.[8] The slowly precipitated oil obtained from the pyrolysis may arise from the thermal breakdown of IX, as the diepoxide pseudoascaridole

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(5) W. Bergmann and M. J. McLean, *Chem. Revs.*, **28**, 367 (1941).

(6) *Cf.*, F. Sallmann and C. Tamm, *Helv. Chim. Acta*, **39**, 1340 (1956); R. H. Bible, Jr., C. Placek, and R. D. Muir, *J. Org. Chem.*, **22**, 607 (1957).

(7) E. J. Agnello, R. Pinson, Jr., and G. D. Laubach, *J. Am. Chem. Soc.*, **78**, 4756 (1956).

(8) (a) O. Matic and D. Sutton, *J. Chem. Soc.*, 349 (**1953**); (b) O. A. Runquist, Ph.D. dissertation, University of Minnesota (1956); (c) C. Dufraisse and J. J. Basselier, *Compt. rend.*, **248**, 700 (1959); (d) G. O. Schenk, *Angew. Chem.*, **64**, 12 (1952); (e) H. Hock and M. Siebert, *Ber.*, **87**, 554 (1954).

gives rise to at least eight different products when held at high temperatures for extended periods.[9]

The presence of at least one epoxide group in IX was shown by its reduction to a diol (XIV) with lithium aluminum hydride; acetylation of XIV by acetic anhydride in pyridine indicated that the reduced epoxide was attached at one end to a tertiary carbon atom as only one of the hydroxyl groups in XIV (presumably the one at 3β) was esterified.

EXPERIMENTAL[10]

Pyrolysis of 9(11)dehydroergosterol peroxide acetate (VI). A. Under a stream of nitrogen, 20 g. of 9(11)dehydroergosterol peroxide acetate[11] was refluxed in 125 ml. of *n*-dodecane for 75 min., then allowed to stand in the refrigerator overnight. Filtration afforded 3.25 g. of *IX*, m.p. 187–195°. A portion of this material (630 mg.) was placed on 15 g. of alumina and eluted with 19:1 benzene-hexane. After recrystallization from methanol, the analytical sample of IX was obtained as plates, m.p. 192–195°; $[\alpha]_D$ +243° (*c* 1.41).

Anal. Calcd. for $C_{30}H_{44}O_4$: C, 76.88; H, 9.46; mol. wt., 468. Found: C, 76.70; H, 9.61; mol. wt., 473 (micro-Rast in camphor).

Saponification of IX was effected by refluxing a solution of 100 mg. of the steroid acetate in a mixture of 0.3 g. of potassium hydroxide, 0.5 cc. of water, and 20 cc. of methanol for 90 min. Water was added to incipient precipitation and cooling gave 72 mg. of a solid (XI), which was recrystallized from aqueous methanol, m.p. 172–175°; $[\alpha]_D$ +274° (*c* 1.04).

Anal. Calcd. for $C_{28}H_{42}O_3$: C, 78.82; H, 9.92. Found: C, 78.75; H, 10.14.

B. In a similar manner 1.0 g. of VI was refluxed 1 hr. in *n*-dodecane under nitrogen. After standing overnight, the solid IX (162 mg., 16%) was removed and the filtrate placed on 30 g. of alumina. Elution with 19:1 hexane-benzene yielded 228 mg. (24%) of 9(11)dehydroergosterol acetate (X), which after recrystallization from methanol melted at 148.5–151°; λ_{max} 310 (ϵ 10,000), 324 (ϵ 11,600), and 339 mμ (ϵ 7300); lit.[12]: m.p. 147.5–149.5°; λ_{max} 311 (ϵ 10,500), 324 (ϵ 12,100) and 341 mμ (ϵ 7500). Further elution of the column produced mixtures.

3β-Acetoxyergosta-9(11),22-diene-5,6α-epoxy-7-one (VII). The final filtrate from part A in the pyrolysis of VI was placed on 300 g. of Florisil and all the 9(11) dehydroergosterol acetate (X) present was removed by elution with 99:1 hexane-acetone. Elution with 49:1 hexane-acetone then gave 325 mg. (1.6%) of VII, m.p. 146.5–149°, which was obtained as small needles after recrystallization twice from methanol, m.p. 149.5–150.5°; $[\alpha]_D$ +29.6° (*c* 1.149).

Anal. Calcd. for $C_{30}H_{44}O_4$: C, 76.88; H, 9.46. Found: C, 76.22; H, 9.65.

3β-Acetoxyergosta-8,22-diene-5,6α-epoxy-7-one (IV). A benzene solution of 50 mg. of VII was placed on 5 g. of unneutralized alumina. After 2 hr. the steroid was eluted with ether and recrystallized from methanol to give material, m.p. 196.5–205°, whose infrared spectrum was identical with that of 3β-acetoxyergosta-8,22-diene-5,6α-epoxy-7-one (IV); lit.[4]: m.p. 209–210°.

Reduction of IX. To a slurry of 1.2 g. of lithium aluminum hydride in 50 cc. of ether there was added 500 mg. of IX. After standing 4 hr. at room temperature, a saturated aqueous solution of ammonium chloride was carefully added. The ethereal layer was separated and the aqueous portion extracted with chloroform. The organic material was combined, dried, and evaporated giving 395 mg. of XIV which on recrystallization from acetone melted at 206–210° dec.; $[\alpha]_D$ +211° (*c* 1.04). Satisfactory elemental analyzes for XIV were not obtained.

One hundred milligrams of XIV was treated overnight with acetic anhydride in pyridine. Workup in the usual manner gave 63 mg. of a solid which was recrystallized from methanol-chloroform and obtained as platelets, m.p. 245.5–248.5°; $[\alpha]_D$ +210° (*c* 1.12); λ_{max}^{KBr} 2.93, 5.75, 5.89, 6.02 μ.

Anal. Calcd. for $C_{30}H_{44}O_4$: C, 76.88; H, 9.46. Found: C, 76.71; H, 9.20.

Reaction of IX *with acid.* To a solution of 100 mg. of IX in 20 cc. of dioxane, there was added a solution of 100 mg. of *p*-toluenesulfonic acid in 2 cc. of water and 3 cc. of dioxane. After standing 18 hr. at room temperature, the reaction mixture was poured into water and extracted with chloroform. The extracts were washed, dried, and evaporated to yield 85 mg. of an oil, which was obtained as an amorphous solid from hexane, m.p. 161–163°; λ_{max}^{KBr} 2.93, 5.74, 5.79 (shoulder), 5.93 μ.

STERLING CHEMISTRY LABORATORY
YALE UNIVERSITY
NEW HAVEN, CONN.

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[9] E. Rick, Ph.D. dissertation, Yale University (1959).

[10] All melting points are corrected. Rotations were measured in chloroform at 25° in a 1 decimeter tube using a photoelectric polarimeter. Infrared spectra were determined in potassium bromide windows. The ultraviolet spectra were determined in absolute alcohol.

[11] A. Windaus and O. Linsert, *Ann.*, **465**, 157 (1928).

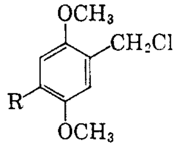
[12] R. Antonucci, S. Bernstein, D. Giancola, and K. J. Sax, *J. Org. Chem.*, **16**, 1159 (1951).

The Synthesis of 2-Chloromethyl-5-alkylhydroquinone Dimethyl Ethers by a Controlled Chloromethylation

GREGORY J. LESTINA AND HOMER W. J. CRESSMAN

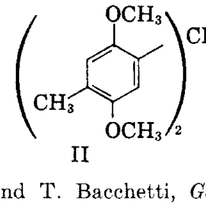
Received February 24, 1960

During the course of our work some hydroquinone dimethyl ethers of Types Ia and Ib were needed.



Ia. R = CH_3
Ib. R = C_8H_{17}

Neither compound had been reported in the literature and a convenient preparation of this class of compounds was not apparent. In fact, an attempt to prepare Ia by the chloromethylation of 2,5-dimethoxytoluene[1] had yielded only 5,5'-methylenebis(toluhydroquinone dimethyl ether) (II).



II

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[1] G. Jacini and T. Bacchetti, *Gazz. chim. ital.*, **80**, 760 (1950).