form, and dried *in vacuo* to give the crude product. Recrystallization of the crude product from ethanol (100 ml) gave the essentially pure material in three crops: yield, 1.53 g (71%). Spectral data indicated the product was 98% pure. Thin layer chromatography using chloroform–methanol (9:1) as the eluent showed a trace impurity which was removed by recrystallization from ethanol.

Acknowledgment.—The authors are indebted to Dr. W. J. Barrett and members of the Analytical and Physical Chemistry Division of Southern Research Institute who performed most of the microanalytical and spectral determinations reported.

Opening of Ring B of Lanosterol by Beckmann Fission of a γ-Keto Oxime Tosylate

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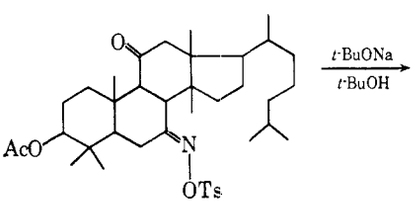
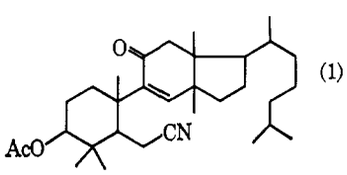
Application of a second-order Beckmann rearrangement to a γ-keto oxime, such as that derived from a 7,11-dione derivative of a steroid nucleus, provides a potentially convenient way of opening ring B. In particular, treatment of 3-acetoxylanostane-7,11-dione 7-oxime tosylate with sodium *t*-butoxide in *t*-butyl alcohol (I) has been found to lead to the anticipated reaction with generation of the nitrile (II) (eq 1). The

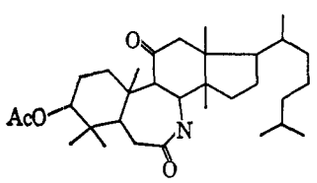


I



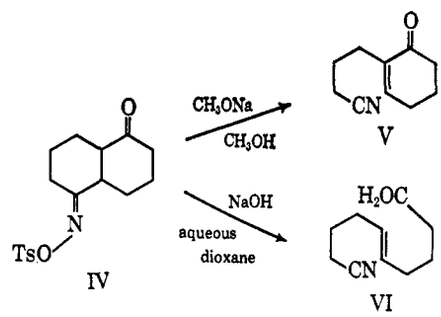
II (1)

parent oxime of (I) on treatment with phosphorus pentachloride gives the expected lactam (III).[2,3]



III

A similar ring-opening fragmentation reaction was observed by Grob[4] in the conversion of the γ-keto oxime (IV) to the unsaturated ketonitrile (V) by treatment with sodium methoxide; treatment with 1 *N* sodium hydroxide in aqueous dioxane led to an unsaturated nitrile acid, presumed to be VI (eq 2).



(2)

The γ-keto oxime tosylate, I, was prepared by refluxing the 7,11-dione in hydroxylamine hydrochloride with pyridine in alcohol, the 11-keto function being much less reactive than the carbonyl group at C-7 by virtue of steric hinderance from the angular methyl groups at C-10 and C-13. Treatment of the resulting oxime with sodium hydride in ether followed by toluenesulfonyl chloride yielded the oxime tosylate (I).

The infrared spectrum in chloroform of the product obtained from (I) by treatment with sodium *t*-butoxide in *t*-butyl alcohol showed bands at ν_{max} 2245 cm^{-1} for the nitrile, 1725 for the ester, 1658 for the unsaturated ketone, and 1601 for the carbon–carbon double bond. The ultraviolet spectrum had λ_{max} 246 mμ (log ε 3.83). These spectral observations thus confirm the structure of the product as II.

Experimental Section

3-Acetoxylanostane-7,11-dione.—The procedure of Ruzicka[5] was used without modification, 3-acetoxylanostene being oxidized with chromic acid to 3-acetoxylanost-8-ene-7,11-dione in 58% yield and the double bond being reduced with zinc dust in glacial acetic acid to give the product in 81% yield, mp 221–223° (lit.[6] mp 222–224°).

3-Acetoxylanostane-7,11-dione 7-Oxime.—The procedure was essentially that of Falco, *et al.*[3] 3-Acetoxylanostane-7,11-dione (488 mg, 1.0 mmole) was dissolved in absolute ethanol (30 ml) and hydroxylamine hydrochloride (1.0 g, 15 mmoles) and pyridine (12 ml) were added. The resulting solution was refluxed for 6 hr, neutralized with dilute sulfuric acid, and extracted with benzene. Chromatographic separation on alumina and crystallization from ethanol gave 383 mg of white needles of the monoxime, mp 211–213° (lit.[3] mp 213–214°).

3-Acetoxylanostane-7,11-dione 7-Oxime Tosylate.—A solution of 3-acetoxylanostane-7,11-dione 7-oxime (100 mg, 0.2 mmole) in 10 ml of dry ether was stirred and cooled in ice while 15 mg (0.30 mmole) of a 50% suspension of sodium hydride in mineral oil was added. The solution was then refluxed under nitrogen with vigorous stirring for 24 hr. A solution of *p*-toluenesulfonyl chloride (36 mg, 0.19 mmole) in 10 ml of dry ether was added dropwise. The ether suspension was stirred for 3 hr at room temperature and the ether solution drawn up through a piece of cotton into a capillary pipette. Great care was taken to exclude air and moisture. The resulting clear solution was evaporated under reduced pressure in rotary evaporator. The white needles thus obtained were dissolved in a small amount of carbon tetrachloride and ligroin was added. In this way 52 mg (70%) of white needles of the tosylate were obtained, mp 243–246°.

Anal. Calcd for $C_{39}H_{59}O_6SN$: C, 70.00; H, 8.83; S, 4.79; N, 2.09. Found: C, 69.77; H, 8.91; S, 4.84; N, 1.83.

Nitrile II.—To a solution of 3-acetoxylanostane-7,11-dione 7-oxime tosylate (35 mg, 0.052 mmole) in 10 ml of *t*-butyl alcohol was added dropwise 5 ml of a sodium *t*-butoxide suspension made

(1) Contribution No. 3551.
(2) C. S. Barnes, D. H. R. Barton, J. S. Fawcett, and B. R. Thomas, *J. Chem. Soc.*, 2339 (1952).
(3) M. Falco, W. Voser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **35**, 2430 (1952).
(4) W. Eisele, C. Grob, and E. Renk, *Tetrahedron Letters*, 75 (1963).
(5) L. Ruzicka, E. Rey, and A. C. Muhr, *Helv. Chim. Acta*, **27**, 472 (1944).
(6) C. Dorée, J. F. McGhie, and F. Kurzer, *J. Chem. Soc.*, 988 (1948).

from 50 mg of sodium. The suspension was refluxed for 1 hr. Water was added dropwise with stirring and the suspension was neutralized with dilute hydrochloric acid. Extraction with ether gave an oil which was chromatographed on alumina. The pale yellow oil obtained in intermediate fractions was crystallized from ligroin (30–60°) to give a white substance. Further recrystallization from ligroin yielded 7 mg (29% yield) of white crystals, mp 246–246.5°. Spectral data gave $\nu_{max}^{CHCl_3}$ 2245, 1725, 1658, and 1602 cm^{-1}; λ_{max}^{EtOH} 246 mμ (log ε 3.83).

Anal. Calcd for $C_{32}H_{51}O_3N$: C, 77.21; H, 10.33; N, 2.82. Found: C, 77.46; H, 10.51; N, 3.04.

A Stereoselective Synthesis of α- and β-Agarofuran

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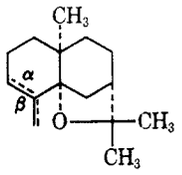
Bhattacharyya and coworkers[3] isolated α- and β-agarofuran from agarwood oil and, on the basis of chemical degradation and spectroscopic evidence, assigned the structures depicted by I to these compounds.[4]



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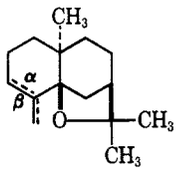
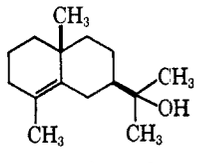
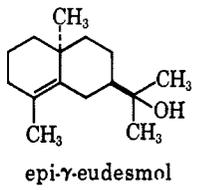


II

Barrett and Büchi[5] deduced that the isopropoxy bridge of the agarofurans was more likely β-oriented as shown in II and supported their conclusion by synthesizing α-agarofuran. During the past year we have been working on potential synthetic routes to the agarofurans. Our initial plans along these lines called for the use of γ-eudesmol[6] as the starting material, but many of our early studies were conducted with the more accessible isomer, 10-epi-γ-eudesmol. The recent structure revision of the agarofurans[5] prompted us to continue our early work in the epi series where certain promising intermediates had been prepared. Consequently, we can now report a stereoselective synthesis of α- and β-agarofuran which fully supports the structures proposed by Barrett and Büchi.



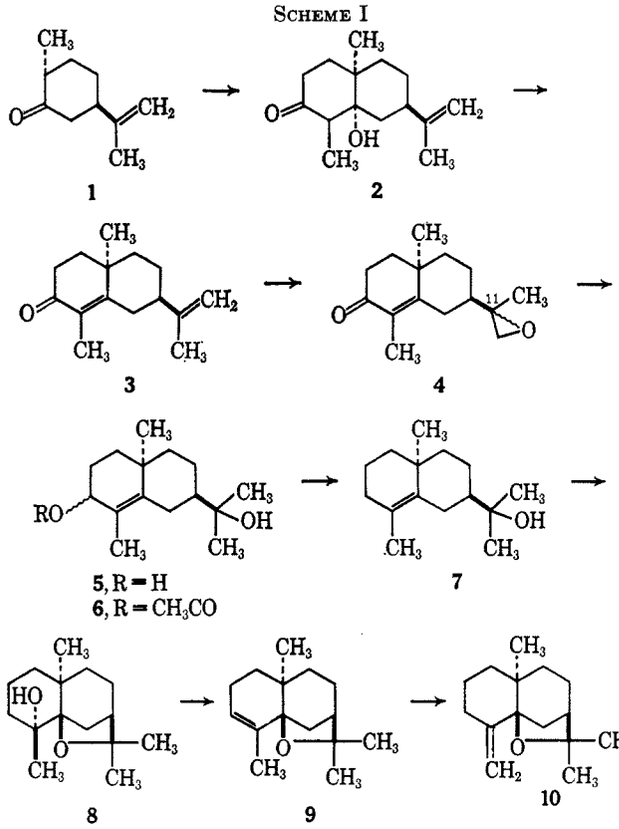
γ-eudesmol



epi-γ-eudesmol

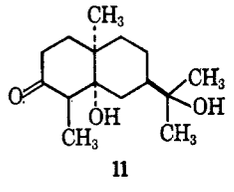
(−)-10-Epi-α-cyperone (**3**)[7] was prepared *via* condensation of (+)-dihydrocarvone (**1**) with ethyl vinyl ketone and dehydration of the resulting crystalline ketol **2**[8] with aqueous base (Scheme I). Conversion to

SCHEME I

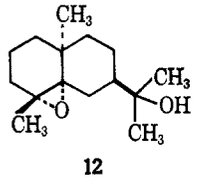


the oxirane derivative **4** (undoubtedly a mixture of diastereoisomers at C-11) was effected using 1 equiv of *m*-chloroperoxybenzoic acid.[9] Reduction of **4** with lithium aluminum hydride afforded the diol **5** which was directly acetylated and reduced with lithium in ammonia[10] to give 10-epi-γ-eudesmol (**7**) in nearly 70% over-all yield based on the ketol **2**.

An alternative route to diol **5** involving oxymercuration[11] of epi-α-cyperone (**3**) was examined and abandoned when difficulty was encountered in reducing the organomercury intermediate. Perhaps for the same reason, the crystalline keto diol **11** could be prepared in only 40% yield from ketol **2** using the oxymercuration procedure.



11



12

Epoxidation of 10-epi-γ-eudesmol (**7**) with *m*-chloroperoxybenzoic acid did not afford the expected oxirane **12**, but gave instead the naturally occurring[4] tetrahydrofuran derivative, 4-hydroxydihydroagarofuran

(1) Fellow of the Alfred P. Sloan Foundation, 1966–1968.

(2) National Institutes of Health Predoctoral Fellow, 1965–1967.

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(5) H. C. Barrett and G. Büchi, *J. Am. Chem. Soc.*, **89**, 5665 (1967). We are grateful to Professor Büchi for disclosing his results to us prior to publication.

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(8) *Cf.* J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).

(9) *Cf.* A. R. Pinder and R. A. Williams, *J. Chem. Soc.*, 2773 (1963).

(10) *Cf.* A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *ibid.*, 1969 (1957).

(11) H. C. Brown and P. Geoghegan, Jr., *J. Am. Chem. Soc.*, **89**, 1522 (1967).