

suggests that eburicol may be a key intermediate in the conversion of lanosterol into eburicoic acid.

The isolation of **1c** is the first instance of the occurrence in a microorganism of a compound related to lanosterol which does not have the normal eight- or nine-carbon side chain.

Experimental Section

All melting points are uncorrected. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were determined on a Beckman IR 5. Ultraviolet spectra were run in 95% EtOH on a Beckman DK2. Nmr spectra were run on a Varian A-60 instrument. ORD spectra were obtained on a Cary 60 apparatus. All tlc was performed using silica gel G according to Stahl.

Extraction of *F. officinalis*.—Finely ground specimens of *F. officinalis* (9 kg) were placed in a Lloyd extractor and extracted with petroleum ether (bp 30–60°) for a period of 3 weeks. Solvent was removed each day and the solution was concentrated. The extracted material was combined and stored at 10° until the extraction was completed.

Isolation of Ergosterol.—The petroleum ether was removed and the mixture was dissolved in methanol and allowed to stand for several days. The precipitate which formed was separated into strong and weak acids and neutral compounds by extraction of an ether solution with sodium bicarbonate and sodium hydroxide. The neutral materials were recrystallized from methanol to give 3.5 g of ergosterol, mp 160–162° (lit.¹³ mp 162°). The acetate of ergosterol was prepared by use of acetic anhydride and pyridine to give material: mp 170–172° (lit.¹³ mp 181°); ultraviolet 263, 271, 282, and 294 m μ . The methanol was removed from the mother liquors and the mixture was treated with urea under complexing conditions¹⁴ to remove most of the fatty substances. The isolated fatty materials were not investigated further. The strong and weak acids were removed as before from the material which did not complex with the urea.

The neutral material was saponified in 0.75 N potassium hydroxide in methanol and worked up in the usual fashion,¹⁵ and the respective weak and strong acids were combined with those from above. The unsaponifiable portion was treated with urea as before to give 21 g of material which did not form a complex with urea. The mixture was chromatographed on 900 g of Florisil.⁵

Materials eluted from the column by less polar eluents than benzene were combined and rechromatographed on Florisil.⁵ The only identified component of this mixture was 30 mg of squalene which was established by comparison of the vapor phase chromatography retention time, tlc, and infrared spectrum with those of known squalene.

Eburicol (1b).—The substances eluted by solvent systems from benzene to (5:95) ether in benzene were rechromatographed on Florisil.⁵ Benzene eluted 150 mg of eburicol: mp 159–162° from methanol, $[\alpha]_D +62.5^\circ$ (*c* 0.12, chloroform) (lit.¹⁶ mp 158–159°, $[\alpha]_D +66^\circ$). Eburicyl acetate was prepared by use of acetic anhydride and pyridine to give material: mp 142–143°, $[\alpha]_D +68.5^\circ$ (*c* 0.07, chloroform) (lit.¹⁶ mp 138–139°, $[\alpha]_D +66^\circ$). Eburicyl acetate synthesized from eburicoic acid was found to be identical in all of its characteristics with those of the naturally occurring material.

3 α -Hydroxy-4,4,14 α -trimethyl- Δ^8 -5 α -pregnen-20-one (Compound 1d).—Compound **1c** was eluted from the column with (1:99) ether in benzene. Two recrystallizations from methanol gave 80 mg of compound: mp 230–232°; $[\alpha]_D +109^\circ$ (*c* 0.18, dioxane); infrared bands at 3550 and 1695 cm⁻¹; nmr methyl peaks at τ 9.27, 9.12, 9.02, and 7.92 and in a 1:1:3:1 ratio; ultraviolet λ_{max} 235 m μ (log ϵ 3.08), 243 (3.11), 250 (2.90); ORD $[\alpha]_{625} +90^\circ$, $[\alpha]_{589} +109^\circ$, $[\alpha]_{513} +2370^\circ$, $[\alpha]_{267} -2170^\circ$, $[\alpha]_{260} -1950^\circ$ (*c* 0.18, dioxane); mass spectrum mol wt 358; tlc 1:9 acetone in chloroform.

3 α -Acetoxy-4,4,14 α -trimethyl- Δ^8 -5 α -pregnen-20-one.—To a solution of 1 ml of acetic anhydride was added 15 mg of com-

pound **1c**. The mixture was heated at reflux for 4 hr and worked up as before. One recrystallization from methanol gave acetate, mp 250–252°, $[\alpha]_D +48^\circ$ (*c* 0.05, chloroform), tlc 100% chloroform.

4,4,14 α -Trimethyl- Δ^8 -5 α -pregnen-3,20-dione (Compound 1e).—To 0.36 ml of a solution containing 20 mg of chromium trioxide and 32 mg of sulfuric acid per milliliter of 90% aqueous acetone was added with stirring a solution containing 24 mg of **1c** in 10 ml of reagent grade acetone. The reaction was allowed to proceed for 20 min and excess reagent was destroyed by adding 1 ml of 95% ethanol. Water was added and the diketone was extracted with chloroform. The chloroform extract was dried over sodium sulfate and evaporated to dryness *in vacuo*. Recrystallization from acetone furnished 20 mg of the 3,20-diketone **1e**: mp 207–210°, $[\alpha]_D +138^\circ$ (*c* 0.10, chloroform), and infrared at 1709 cm⁻¹. This compound had the same *R_f* on tlc (100% CHCl₃), superimposable infrared, and no depression of mixture melting point when compared with the diketone prepared from an authentic sample of the β isomer.

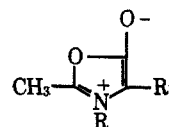
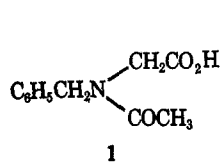
Mesoionic Oxazolones. A New Synthesis and Electrophilic Substitution Reaction

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Attempting to prepare the acid chloride of N-acetyl-N-benzylglycine (**1**) by treatment with oxalyl chloride, we isolated instead a bright yellow, crystalline material of empirical formula C₁₃H₁₀ClNO₄. The product was an acid chloride, but not the expected one. The identity of this material was suggested by the work of Huisgen and co-workers, who prepared a new class of mesoionic oxazolones (*e.g.*, **2**) from substituted glycines by a modified Dakin–West procedure.²



- 2**, R = CH₃; R' = C₆H₅
3, R = CH₂C₆H₅; R' = COCOCl
4, R = CH₂C₆H₃(OCH₃)₂; R' = COCOCl
5, R = CH₂C₆H₅; R' = H

That our product was the 4-chloroglyoxyloyl derivative (**3**) was established by the infrared spectrum (potassium bromide disk) which showed strong bands at 1800 and 1785 cm⁻¹ due to the acid chloride and α -carbon carbonyl groups, respectively, and a strong, broad band at about 1610 cm⁻¹ probably resulting from the ring carbonyl and iminium groups, and by the nmr spectrum (hexadeuterioacetone) which displayed a five-proton band at δ 7.43 due to the phenyl group, a two-proton singlet at 5.71 due to the α -benzyl hydrogens, and a three-proton methyl singlet at 2.75.

(13) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 100.

(14) H. Schlenk and R. T. Holman, *J. Am. Chem. Soc.*, **72**, 5001 (1950).

(15) J. Cason and H. Rapaport, "Laboratory Text in Organic Chemistry," Prentice-Hall Co., Inc., Englewood Cliffs, N. J., 1950, p 83.

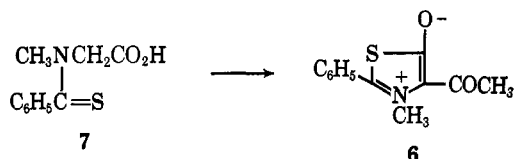
(16) F. W. Lahey and P. H. A. Strasser, *J. Chem. Soc.*, 873 (1951).

(1) National Academy of Sciences–National Research Council Senior Visiting Scientist, 1966–1967.

(2) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Schaefer, *Angew. Chem. Intern. Ed. Engl.*, **3**, 136 (1964).

The 3,4-dimethoxybenzyl derivative (4) was also prepared.

The remarkable facility with which the intermediate oxazolone (5) undergoes electrophilic substitution probably reflects the ready polarizability of the lactone enolate grouping. This reaction is reminiscent of the uncatalyzed formation of 3-indoleglyoxyloyl chloride from oxalyl chloride and indole,³ as well as a similar reaction of thienopyrrole.⁴ Closely analogous to our reaction and that of Huisgen's group is the production of the acetylated mesoionic thiazolone 6 from thiobenzoylsarcosine (7) and acetic anhydride, earlier reported by Lawson and Searle.⁵



From the relative positions of the ring and side-chain carbonyl groups one might anticipate some potential for 3 as a chelating agent, and in fact a solution of 3 in tetrahydrofuran readily extracted the cobalt from indicating Drierite, thereby changing in color from yellow to emerald green.⁶

Experimental Section

Instrumentation.—Nuclear magnetic resonance spectra were obtained using the Varian Model A-60 spectrometer with tetramethylsilane as internal standard. For infrared spectra the Beckman IR-12 was used. The mass spectrometer employed was the Hitachi Perkin-Elmer Model RMU-6D. The Mechrolab vapor pressure osmometer was used for molecular weight determination. Combustion analyses were performed by Mr. Carmine Di Pietro of Natick Labs.

N-Acetyl-N-benzylglycine (1).—N-Benzylglycine sodium salt was prepared by hydrogenation (1 atm) of a solution of 0.10 mole each of glycine, benzaldehyde, and sodium hydroxide in 250 ml of methanol over 0.5 g of prerduced platinum oxide. After the theoretical uptake of hydrogen had been noted, the mixture was filtered and most of the methanol was removed by rotary evaporation. The sodium salt was obtained essentially quantitatively by precipitation with isopropyl alcohol. N-Benzylglycine sodium salt (10 g) was suspended in 20 ml of pyridine, and 10 g of acetic anhydride was added with cooling. The mixture was allowed to stand for 12 hr after becoming homogeneous, then was poured onto ice and dilute hydrochloric acid. Extraction with chloroform provided 10–11 g of acetyl derivative, mp 126–128° (lit.⁷ mp 126.5) after recrystallization from acetone.

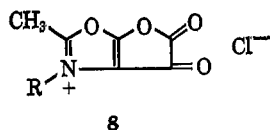
N-Acetyl-N-(3,4-dimethoxybenzyl)glycine.—Glycine was reductively alkylated with 3,4-dimethoxybenzaldehyde and acetylated as described above for 1. Recrystallized from acetone, the product had mp 118–120°.

(3) M. E. Speeter and W. C. Anthony, *J. Am. Chem. Soc.*, **76**, 6208 (1954).

(4) G. W. Michel and H. R. Snyder, *J. Org. Chem.*, **27**, 2689 (1962).

(5) A. Lawson and C. E. Sarle, *J. Chem. Soc.*, **1957**, 1556.

(6) A referee has suggested 8 as a plausible alternative to the oxazolone structure. However, these compounds are more reasonably acid chlorides than enol lactones because (1) an analytically pure sample of 3 reacted instantaneously with water to give hydrochloric acid, (2) the experimental molecular weight corresponds to that of 3 rather than that of 8, which should be only half as great, (3) it is difficult to rationalize chelation in terms of structure 8, and (4) there is no evidence from the work of Huisgen's group to suggest that the lactone carbonyl of 2, *e.g.*, is nucleophilic.



(7) H. Scheibler and P. Baumgarten, *Ber.*, **55**, 1358 (1922).

Anal. Calcd for C₁₃H₁₇NO₅: C, 58.41; H, 6.41; N, 5.24. Found: C, 58.25; H, 6.25; N, 5.24.

Anhydro-3-benzyl-4-chloroglyoxyloyl-5-hydroxy-2-methyl-1,3-oxazolium Hydroxide (3).—To 2.0 g of N-acetyl-N-benzylglycine was added 5 g of oxalyl chloride. The reaction that ensued was vigorous but not noticeably exothermic. After about 1 hr a solid precipitated which was collected by filtration and washed with benzene. The yield was 2.2 g (82%), and the product melted with vigorous decomposition at 123–126° after recrystallization from tetrahydrofuran. This material decomposed in the preheater of the mass spectrometer to give carbon dioxide as the volatile product of greatest mass and abundance.

Anal. Calcd for C₁₃H₁₀ClNO₄: C, 55.82; H, 3.60; N, 5.01; mol wt, 280. Found: C, 56.05; H, 3.66; N, 5.10; mol wt, 285 ± 9, 0.7% in benzene.

Anhydro-3-(3,4-dimethoxybenzyl)-4-chloroglyoxyloyl-5-hydroxy-2-methyl-1,3-oxazolium Hydroxide (4).—From 1.0 g of N-acetyl-N-(3,4-dimethoxybenzyl)glycine and 2–3 g of oxalyl chloride was prepared as above 1.2 g (95%) of a pale yellow solid, mp 112–114° dec, after recrystallization from tetrahydrofuran.

Anal. Calcd for C₁₅H₁₄ClNO₄: C, 53.03; H, 4.15; N, 4.12. Found: C, 53.2; H, 4.08; N, 4.23.

A Study of Hindered Internal Rotation in Some N-Vinyl-Substituted Amides by Nuclear Magnetic Resonance Spectroscopy¹

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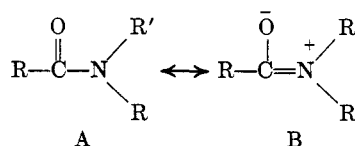
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Pauling³ has suggested that the C–N amide bond should possess considerable double-bond character arising from resonance between the following structures.



The height of the potential energy barrier to free rotation is then dependent upon the amount of this double-bond character. Numerous workers^{4–9} have utilized nmr to study various N,N-disubstituted amides and have determined energy barriers based upon the

(1) Abstracted in part from the M.S. thesis of D. G. Gehring, University of Delaware, 1965.

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(3) L. Pauling, "The Nature of the Chemical Bond," 2nd ed, Cornell University Press, Ithaca, N. Y., 1940, pp 133, 207–208.

(4) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

(5) M. T. Rogers and J. C. Woodbrey, *J. Phys. Chem.*, **66**, 540 (1962).

(6) W. D. Phillips, *J. Chem. Phys.*, **23**, 1363 (1955).

(7) C. Franconi, *Scienza E. Tecnica*, (ns), **4**, 183 (1960).

(8) C. Franconi, R. A. Ogg, Jr., and G. Fraenkel, *Arch. Sci. (Geneva)*, **13**, 543–549 (1960), Spectrum No. 1.

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