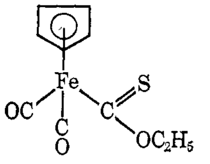
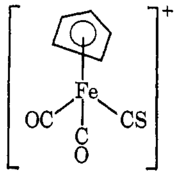
by a method which appears to be applicable to the preparation of other thiocarbonyl complexes.

It has been shown[2] that $Mn(CO)_5^-$ reacts with ethyl chloroformate, $ClC(O)OC_2H_5$, to give $Mn(CO)_5C(O)OC_2H_5$ which on treatment with HCl yields the cation, $Mn(CO)_6^+$. The complex, $C_5H_5Fe(CO)_2C(O)OCH_3$, prepared by a different method, also is converted to the cation, $C_5H_5Fe(CO)_3^+$, on reaction with HCl.[3] We have used similar reactions in the preparation of $[C_5H_5Fe(CO)_2(CS)]^+$. Thus treatment of $NaFe(CO)_2C_5H_5$ (readily accessible from $[C_5H_5Fe(CO)_2]_2$ and excess 1% sodium amalgam[4]) with ethyl chlorothioformate, $ClC(S)OC_2H_5$, gives $C_5H_5Fe(CO)_2C(S)OC_2H_5$ (I) that was obtained as an impure orange-brown product. Its infrared spectrum in pentane solution shows two carbonyl stretching frequencies at 2031 (s) and 1989 cm^{-1} (s) and a C–S stretching absorption at 1250 cm^{-1}. The reaction of a benzene solution of I with gaseous HCl produces a brown oil. Dissolution of the oil in acetone followed by treatment with an acetone solution of NH_4PF_6, filtration, and precipitation with ether gives the pale yellow, air-stable $[C_5H_5Fe(CO)_2(CS)]PF_6$ (II) in approximately 10% yield. It may be recrystallized from acetone–ether.

Anal. Calcd for $[C_5H_5Fe(CO)_2(CS)]PF_6$: C, 26.25; H, 1.38; S, 8.76. Found: C, 26.42; H, 1.53; S, 9.27.



I



II

The infrared spectrum of II taken in a hexachlorobutadiene mull exhibits a strong C–S stretching absorption at 1348 cm^{-1}. This compares with[1] 1299 cm^{-1} for *trans*-$RhCl(CS)[P(C_6H_5)_3]_2$ and 1362 cm^{-1} for $RhCl_3(CS)[P(C_6H_5)_3]_2$. The C–O stretching frequencies of II occur at 2093 (s) and 2064 cm^{-1} (s). Table I compares these values with those of other complexes of the type $[C_5H_5Fe(CO)_2L]^+$. If it is assumed that C–O stretching frequencies indicate the π-bonding ability of L (and there is considerable doubt about the validity of this assumption),[5–7] the data in Table I indicate that the CS group is one of the best π-bonding ligands.

Table I. C–O Stretching Frequencies of $[C_5H_5Fe(CO)_2L]^+$

Complex	ν_{C-O}	Ref
$[C_5H_5Fe(CO)_2(CS)]PF_6$	2093, 2064[a]	
$[C_5H_5Fe(CO)_2(C_2H_4)]PF_6$	2083, 2049	*c*
$[C_5H_5Fe(CO)_2(P(C_6H_5)_3)]Cl$	2066, 2030[a]	*d*
$[C_5H_5Fe(CO)_2(CH_3CN)]PF_6$	2080, 2035[b]	*e*
$[C_5H_5Fe(CO)_2(py)]PF_6$	2070, 2025[b]	*e*

[a] Hexachlorobutadiene mull. [b] CH_2Cl_2 solution. [c] E. O. Fischer and K. Fichtel, *Chem. Ber.*, **94**, 1200 (1961). [d] A. Davison, M. L. H. Green, and G. Wilkinson, *J. Chem. Soc.*, 3172 (1961). [e] P. M. Treichel, R. L. Shubkin, K. W. Barnett, and D. Reichard, *Inorg. Chem.*, **5**, 1177 (1966).

The preparation of other thiocarbonyl complexes of the transition metals is in progress, and the results of these investigations will be reported at a later date.

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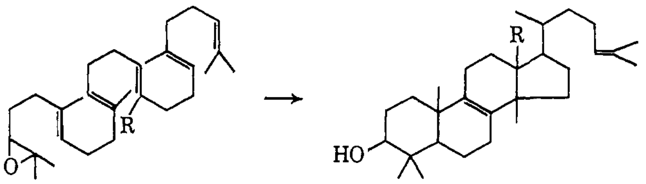
Enzymic Cyclization of 15-Norsqualene 2,3-Oxide

Sir:

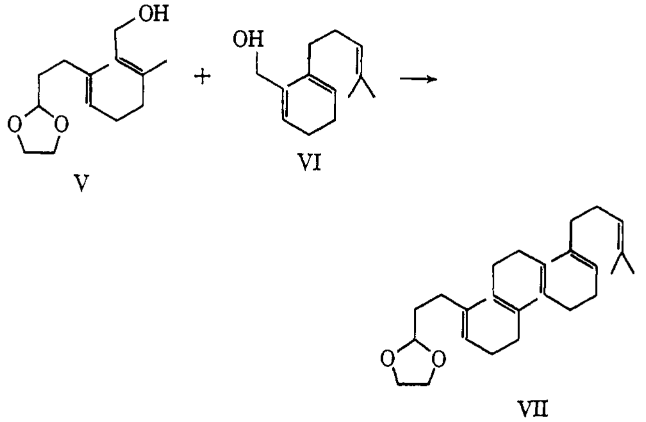
In mechanistic studies of lanosterol (II) biosynthesis we have selectively modified the normal precursor, squalene 2,3-oxide (I), in the central and terminal zones in order to gauge the effect on cyclization and thereby become informed as to the initiation,[1] sequential,[2] and side-chain[3] aspects of the normal annulation. In experiments designed to increase understanding of the factors controlling the later stages of lanosterol formation, especially the methyl–hydrogen migrations, we now find that 15-norsqualene 2,3-oxide (III) is enzymically transformed without incorporation of a proton from the medium to a lanosterol analog of the gross structure IV.



I, R = CH_3
III, R = H

II, R = CH_3
IV, R = H

Synthesis of the radiolabeled substrate III was achieved by employing in the critical stage cross-coupling of the *trans,trans*-acetal dienol V[5] and *trans,trans*-3-norfarnesol



V

VI

VII

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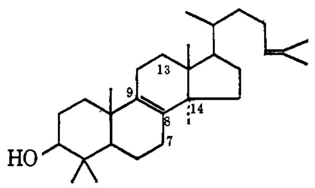
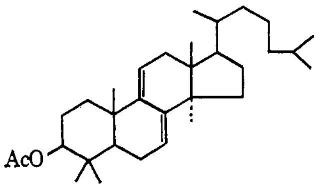
(VI)[6] to pentaene VII, carried out by treatment with $TiCl_3$ and MeLi.[5] After purification as the thiourea adduct and introduction of tritium by exchange with T_2O on the free aldehyde corresponding to V, conversion to the epoxide III was effected by means previously described.[5] The oily, all-*trans* epoxide III exhibited spectral properties, including nmr (60 Mc in $CDCl_3$; TMS internal standard: *trans*-HC=CH, τ 4.58; four >C=CH–, 4.88; >CHO–, 7.30; $10CH_2$, 8.00; 5>C=C(CH_3), 8.31 and 8.40; $(CH_3)_2C$–O–, 8.71 and 8.75) entirely in accord with the assigned structure.

Using methods previously summarized,[2] we incubated 2.46 mg of radiolabeled epoxide III with 120 ml of a clarified microsomal squalene oxide–lanosterol cyclase preparation equivalent to 80 g of rat liver and obtained, after tlc of the nonsaponifiable fraction, 0.680 mg (27% yield based on *dl*-III) of a crystalline compound (A) with the same tlc mobility as that of lanosterol (VIII) (R_f 0.46 in 25% EtOAc–hexane). Both A and its catalytic reduction product (AH_2) were convertible to monoacetate (A-Ac and AH_2-Ac) and trimethylsilyl ethers (A-TMSE and AH_2-TMSE), mass spectra of which indicated the composition $C_{29}H_{48}O$ and $C_{29}H_{50}O$ and AH_2, respectively. More vigorous reduction[8] afforded AH_4-Ac.

A time-averaged 100-MHz nmr spectrum of A in $CDCl_3$–TMS solution (Varian HA-100 instrument) exhibited the following resonances: one vinyl proton (triplet, τ 4.88), one hydroxyl (broad peak, τ 6.52), one proton under oxygen (triplet, τ 6.78), two olefinic methyls (τ 8.31 and 8.40), saturated methyls (τ 9.00, one CH_3; τ 9.03, one CH_3; τ 9.20, two CH_3). Lanosterol (VIII) displayed an essentially identical spectrum except that saturated methyl resonances appeared at τ 8.99 (C_{19}), 9.01 (4α), 9.11 (14α), 9.18 (4β), and 9.30 (C_{18}). Lanosteryl acetate and A-Ac were also found to be very similar with respect to nmr behavior, except in the methyl region (lanosteryl acetate: C_{19}, τ 8.99; $C_{4\alpha,4\beta,14\alpha}$, 9.11; C_{18}, 9.30; and A-acetate: 9.00, one CH_3; 9.11, two CH_3; 9.19, one CH_3).



VIII

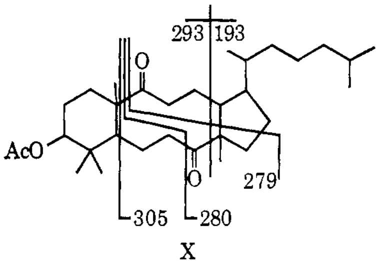


IX

When AH_2-Ac was treated under conditions (HCl-$CHCl_3$ for 48 hr) which equilibrate Δ^8- and Δ^7-dihydrolanosteryl acetate (LH_2-Ac), there was formed in good yield one new isomer (BH_2-Ac) with a longer glpc retention time than that of AH_2-Ac. In contrast to the mass spectrum of AH_2-TMSE,[9] that of its isomer BH_2-TMSE exhibited an intense even-mass peak at *m/e* 274 which can be attributed to a retro-Diels–Alder cleavage of ring B with charge retention by the diene fragment. This structurally highly specific behavior is reconcilable only with a Δ^7 position of the isomerized double bond. An analogous prominent peak is observed at *m/e* 288 in the mass spectrum of the Δ^7 isomer of LH_2-TMSE. The mass spectrum of AH_4-Ac exhibited peaks indicating loss of side chain and C_{15-17} of ring D, with and without associated loss of acetic acid, at *m/e* 243 and 303, respectively.

In order to probe chemically for the position of the nuclear double bond in A, AH_2-Ac was treated for 24 hr with *m*-chloroperbenzoic acid in CH_2Cl_2 over solid Na_2HPO_4 buffer.[10] When the epoxide product (R_f 0.47 in 15% ETOAc–hexane) was exposed for 2 hr to a trace of $HClO_4$ in C_6H_6–HOAc (1:1), a new product (C) formed (R_f 0.63, 15% ETOAc–hexane) which exhibited λ_{max}^{EtOH} 235, 243, and 252 mμ (ϵ ratio 1.00:1.12:0.75, respectively). These data compare favorably with those of dihydroagnosteryl acetate (IX) (R_f 0.63 in 15% EtOAc–hexane) (λ_{max}^{EtOH} 237, 244, and 253 mμ (ϵ ratio 1.00:1.22:0.84, respectively)) and suggest the presence of a Δ^8 double bond in tetracycle A.

Direct structural confirmation of the Δ^8 double bond and C_{13} hydrogen features in isomer AH_2 was derived mainly from the high-resolution mass spectrum of a derivative in which the original double bond position had been marked by suitable functionalization, *viz.*, a seco-diketone acetate ($C_{31}H_{52}O_4$; observed mass 488.3842, calculated mass 488.3865) obtained by treatment of AH_2-Ac with RuO_4. The high-resolution mass spectral fragmentation pattern was compatible with the expected structure X and corresponded well with the spectral data of the homologous seco product XI resulting from LH_2-Ac upon treatment with the same reagent.[11] Major fragmentation processes which furnish evidence for the position of the carbonyl functions are denoted in X as over-all cleavages, not including associated hydrogen-transfer reactions. Thus, for instance, the fragment *m/e* 305 represents the rather characteristic behavior of a cyclic ketone and limits, together with the highly saturated $C_{14}H_{25}$ fragment at *m/e* 193, the possible positions of the carbonyl groups to the original rings B and C.



X

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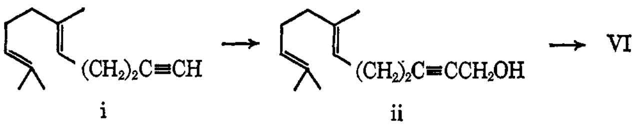
[6] The synthesis of trienol VI involved conversion of the known dienyne i[7] with methyllithium and formaldehyde to the acetylenic alcohol ii, which was reduced by means of lithium aluminum hydride at 65° in THF.



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[9] Notably absent in the mass spectrum of AH_2-TMSE was a peak due to loss of the side chain which would be expected for a tetracyclic structure with a $\Delta^{13(14)}$ double bond. Such loss from a $\Delta^{13(14)}$ case was observed by F. Cohen, R. A. Mallory, and I. Scheer, *Chem. Commun.*, 1019 (1967).

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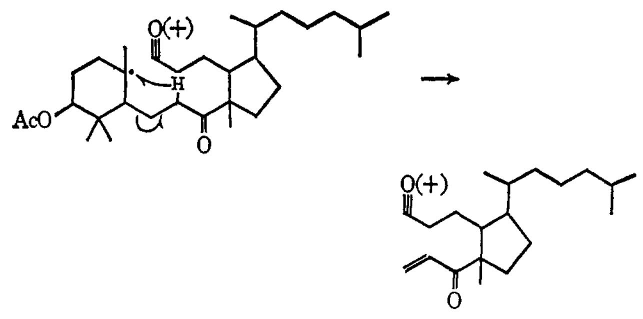
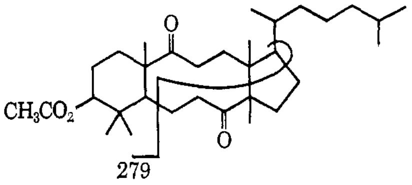
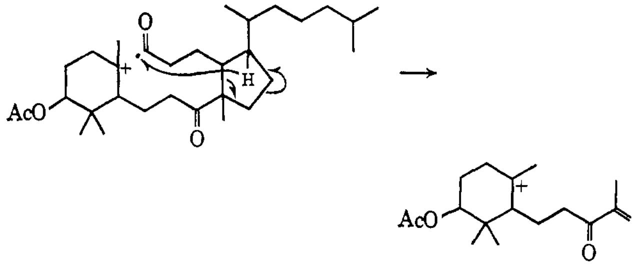


m/e 305 ($C_{20}H_{33}O_2$)

Corresponding fragments occur at m/e 319 and 207 in the spectrum of the higher homolog, XI. Another prominent fragment of the composition $C_{18}H_{32}O_2$ at m/e 280 (m/e 294 in seco-diketolanosterol-Ac) confines the possible carbonyl locations to a sufficiently small area of the B–C ring moiety to permit exclusion of alternative positions based on possible chemical structures of the olefinic precursor. Finally, an abundant fragment recorded at m/e 279 ($C_{17}H_{27}O_3$) obviously comprises such a portion of the molecule as to include C_{14} and C_{15}, since it appears unshifted at the same mass in the spectrum of the lanosterol derivative XI. An alternative formation of this fragment ion would have to include C_{17} in the latter case and thus require the highly unlikely rupture of two bonds attached to the same carbon atom (XI). Genesis of this important ion may be initiated by cleavage α to the carbonyl group with reverse charge distribution, followed by radical-induced fragmentation of the 15,16 and 13,14 bonds.



XI



m/e 279

From the abundant fragment at m/e 279 and associated high-resolution data it is also apparent that C_{14} bears the methyl group which migrated during biosynthesis of IV.

That the cyclization of III is mechanistically analogous to that of the normal substrate I follows from the nonincorporation of ^3H into IV on cyclization of unlabeled III in a medium containing ^3H_2O (0.235 Ci ml).

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

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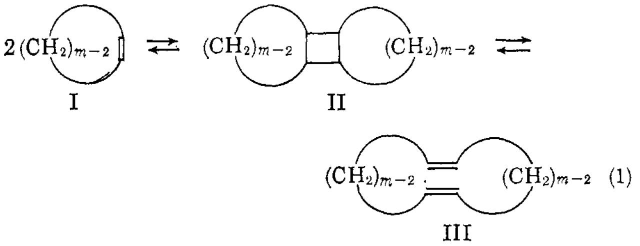
The Synthesis of Carbon Macrocycles to C_{120}

Sir:

We have obtained large unbranched carbocyclic systems by the direct combination of increasing numbers of cyclooctene molecules. The available evidence indicates the formation of rings up to C_{120}, over twice the size of the largest carbocycles previously identified.[1] Such formation of larger from smaller rings is an exception to the usual procedure for the synthesis of macrocycles by cyclization of a linear system. Another exception is the recent report of Story, *et al.*, who found that di- or trimeric cyclic peroxides of cyclic ketones eliminate CO_2 to form carbocycles up to C_{22}.[2]

The procedure we have been investigating may be formally described by eq 1. The intermediate cyclobutane (II) could revert to the C_m cyclic olefin I or form the C_{2m} cyclic diene III. Repetition of (1) with two molecules of III or one of I and one of III could lead to higher cyclic polyolefins. Our initial attempts to carry out transformation 1 photochemically were put aside with the report of the remarkable olefin metathesis reaction observed with linear olefins. Using a WCl_6–$EtAlCl_2$–EtOH catalyst, Calderon, *et al.*, converted 2-pentene into a mixture with 2-butene and 3-hexene,[3] a conversion which may be viewed as going through a transient cyclobutane intermediate. Since a cyclic olefin undergoing a similar transformation



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