demonstrates that vinyl decay, presumably to form end links,[5] must be taken into account.

Let A represent CH_2 groups per gram in the amorphous regions, D the dose in e.v.g.$^{-1}$, $G[X]$ and $G[Vl]$ the number of cross links and vinylene groups produced per 100 e.v. absorbed, [Vi] the vinyl concentration in moles g.$^{-1}$, N Avogadro's number, k_1 the first order vinyl decay constant, and α, β and γ the number of methylene groups added to the amorphous regions per cross link, vinylene group and end link formed by the 140° irradiation, respectively. Then

$$\frac{dA}{dD} = \frac{\alpha G[X]}{100} + \frac{\beta G[Vl]}{100} + \gamma N k_1 [Vi] \qquad (1)$$

Below doses of 8×10^{20} e.v.g.$^{-1}$, $G[X]$ and $G[Vl]$ are constant. Letting M represent the first two terms on the right-hand side of (1), replacing [Vi] by $[Vi]_0 \exp(-k_1 D)$, integrating, setting A/A_0 equal to ϕ_A and rearranging, Eq. (2) results

$$\frac{\phi_A - 1}{D} = \frac{M}{A_0} + \frac{\gamma N [Vi]_0}{A_0} \frac{[1 - e^{-k_1 D}]}{D} \qquad (2)$$

The upper curve of Fig. 1 is a linear plot of $(\phi_A - 1)/D$ *versus* $[1 - \exp.(-k_1 D)]/D$. Equation 2 is seen to be accurately verified for γ and $(\alpha + \beta)$ equal to 79 and 131, respectively. Four long branches extend into the polyethylene from a cross link and three from an end link. Dividing 131 by 4 and 79 by 3, the numbers 33 and 26, respectively, are obtained. These numbers represent the number of methylene groups per chain immobilized by a branch point with respect to the ability to crystallize. Inasmuch as 33 includes the contribution of vinylene groups (which is not expected to be as large as the contribution of a cross link) the agreement is satisfactory. Evidently long branches and gel structure are far more important in inhibiting crystallization than previously imagined[6] for short branches.

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(7) On leave from A. E. R. E., Harwell, England.

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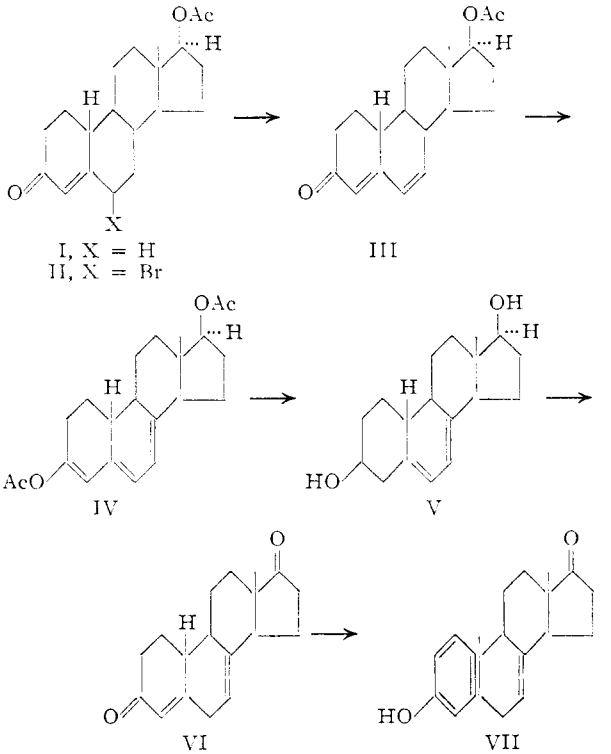
STEROIDS. XCVI.[1] THE SYNTHESIS OF EQUILIN

Sir:

Equilin (VII)[2] is the only known naturally occurring, physiologically active steroid hormone which until now has resisted all attempts at partial or total synthesis. This powerful estrogen is currently only available from mare's urine and it was clearly desirable to develop a synthesis of the hormone in order to permit more extensive clinical work as well as to prepare certain derivatives for biological investigation. The unusual feature of equilin (VII) is the non-conjugated double bond in ring B which is responsible for its ready isomerization with acid[3] or its aromatization to equilenin with palladium in the presence of hydrogen.[4] Consequently conditions had to be developed which did not affect this center of unsaturation and we should now like to record a successful synthesis of equilin.

Dehydrobromination of crude 6-bromo-19-nortestosterone acetate (II) derived from 19-nortestosterone acetate (I)[5] afforded 6-dehydro-19-nortestosterone acetate (III) (m.p. 113–114°, $[\alpha]_D$ −38°,[6] λ_{max}^{EtOH} 282–284 mμ, log ε 4.29; *Anal.* found for $C_{20}H_{26}O_3$: C, 76.62; H, 8.63). This key intermediate was transformed by the procedure employed by Velluz and co-workers[7] in the 19-norcholesterol series into the enol diacetate IV (m.p. 163–165° (dec.), $[\alpha]_D$ −29°, λ_{max}^{EtOH} 300, 312 and 328 mμ, log ε 4.32, 4.41 and 4.27, λ_{max}^{KBr} 5.71, 5.77, 6.05 (w), 6.13 (w) and 8.03 μ)[8] and reduced with sodium borohydride to $\Delta^{5,7}$-19-norandrostadiene-3β,17β-diol (V) (m.p. 192–195°, $[\alpha]_D$ +256°, λ_{max}^{EtOH} 272, 282–284 and 296 mμ, log ε 4.05, 4.06 and 3.80; *Anal.* found for $C_{18}H_{26}O_2$: C, 78.39; H, 9.82). Oppenauer oxidation of V provided 19-nor-$\Delta^{4,7}$-androstadiene-3,17-dione (VI) (m.p. 148–



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(6) All rotations were measured in chloroform solution. We are indebted to Dr. L. Throop and staff for the rotation and spectral measurements.

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(8) This substance decomposed rapidly at room temperature and no analytical sample was secured.

149°, $[\alpha]_D$ +127°, λ_{max}^{EtOH} 238 mμ, log ε 4.16; *Anal.* found for $C_{18}H_{22}O_2$: C, 79.65; H, 8.38) which upon microbiological dehydrogenation[9] with *Corynebacterium simplex*[10] led in over 60% yield to equilin (VII), m.p. 237–240°, undepressed upon admixture with the natural hormone, $[\alpha]_D$ +295°, λ_{max}^{EtOH} 282 mμ, log ε 3.36. The infrared spectra of synthetic and natural equilin were completely superimposable.

Since the starting material, 19-nortestosterone acetate (I), is prepared[5] from estrone which has been synthesized totally,[11] the above reaction sequence also constitutes a formal total synthesis of equilin (VII).

(9) The feasibility of converting a 19-nor-Δ⁴-3-ketosteroid into the corresponding phenol with *C. simplex* already has been demonstrated with 19-norprogesterone (A. Bowers, C. Casas Campillo and C. Djerassi, *Tetrahedron*, **2**, 165 (1958)), and with 19-nortestosterone (S. Kushinsky, *J. Biol. Chem.*, **230**, 31 (1958)).

(10) We are grateful to Dr. Carlos Casas Campillo and staff for the microbiological incubation.

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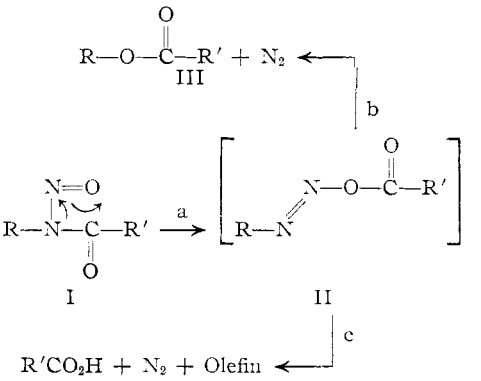
INTRAMOLECULAR REACTIONS OF SECONDARY CARBINAMINE NITROSOAMIDES

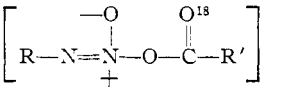
Sir:

Studies of the nitrosoamide reaction have shown[1] that the reaction proceeds in most cases with partial retention of configuration, and that there is an intramolecular path (b) for the formation of the ester. We now report[2] an oxygen-18 tracer study of reaction b pertinent to the mechanism of the reaction and to the problem of "intramolecular inversion."[3] The nitroso derivatives of N-cyclohexyl and N-1-phenylethylnaphthamides-O-18 were rearranged in various solvents; appropriate controls were run. The esters obtained were cleaved and the O-18 analyses were run in the standard way.[4]

The results (Table I, C/E) show that although "mixing" of the label occurred in reaction b, more than one half of the label remained in the carbonyl group in each case. Simiarly, the reaction of 2-naphthoyl chloride O-18 with the silver salt of N-nitrocyclohexylamine yielded (*via* IV) nitrous oxide



containing 0.0 atom % excess O-18 and cyclohexyl naphthoate with 62% of the O-18 in the carbonyl group. Further information was obtained when



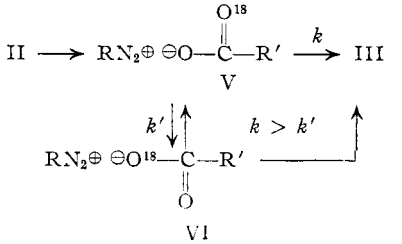
optically pure (−)N-(1-phenylethyl)-N-nitroso-2-naphthamide-carbonyl-O-18 was rearranged. The partially racemized ester was cleaved, the 1-phenylethanol obtained was treated with phenyl isocyanate, and the N-phenylcarbamate was fractionally crystallized. Samples of the DL form and the optically pure levorotatory form (corresponding to retention) were thus obtained. Analyses showed that both contained the same amount of O–18 (Runs 3 and 4); the enantiomers are formed with the same distribution of O–18!

TABLE I

Run	R	Solvent and addend	Retn. of config., %	Atom % excess O-18 RNHCOR′	RO₂CR′	R′CH₂OH	+ ROH	C/E[a]	(−)ROH	(±)ROH
1	Cyclohexyl	CH_3CO_2H		1.233	0.611	0.798	0.431	65/35		
2	(−) 1-Phenylethyl	Dioxane + CH_2N_2[b]	74	1.232	.622	.656	.545	55/45		
3	(−) 1-Phenylethyl	Dioxane + $2HCO_2H$	80	1.232	.607	.696	.514	58/42	0.536	0.537
4	(−) 1-Phenylethyl	CH_3CO_2H	81	1.232	.592	.843	.372	69/31	0.381	0.380

[a] % in C=O/% in ether position. [b] Equilibrated methyl naphthoate was obtained.

A mechanism involving partial mixing of the oxygen atoms prior to the step in which the final configurations are determined accounts satisfactorily for the results; the loss of nitrogen from V or VI could reasonably lead to bond formation on both



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