alanine methyl ester dihydrobromide (XI) [$\lambda_{max}^{CH_3OH}$ 234 mμ (ε 3640). *Anal.* Calcd. for $C_{26}H_{31}N_5O_6Br_2$: C, 46.7; H, 4.68; N, 10.01; Br, 23.9. Found: C, 45.73; H, 4.99; N, 10.40; Br, 22.59] or cbz-glycylhistidylphenylalanine (XII) [77.5% yield, m.p. 200° dec., $[\alpha]_D^{30}$ + 15.4° (methanol). *Anal.* Calcd. for $C_{25}H_{27}N_5O_6$: C, 60.8; H, 5.52; N, 14.2. Found: C, 60.51; H, 5.65; N, 14.11], respectively. The *N*(Im)-cbz group may be removed also with catalytic hydrogenation.

From these results it has been demonstrated that *N*(Im)-cbz-histidine derivatives, which can be prepared by the simple and convenient procedure, are of potential utility as intermediates in the synthesis of histidine peptides.

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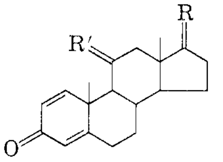
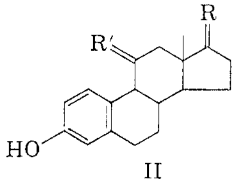
An Aromatization Reaction of A Cross-Conjugated Dienone System with Zinc

Sir:

We wish to report a new A-ring aromatization reaction of the dienone system with zinc under mild conditions. When refluxed with zinc in pyridine[1] or ethylene glycol, androstan-1,4,9(11)-triene-3,17-dione (Ia) undergoes A-ring aromatization with elimination of the angular methyl group to form Δ^9-estrone (IIa)[2] in excellent yield (75%). In a similar manner the treatment of 17α,21-dihydroxypregnan-1,4,9(11)-triene-3,20-dione acetate (Ib; 21-acetate) or its BMD derivative (Ic) in pyridine yielded, respectively, A-ring aromatic corticoids,[3] IIb 21-acetate, (yield: 35%), m.p. 210–212°, $[\alpha]_D^{20}$ +174° (dioxane), $\lambda_{max}^{CH_3OH}$ 263, 298 mμ (ε 18,000, 3,100), λ_{max}^{Nujol} 814 cm.$^{-1}$, (*Anal.* Calcd. for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08. Found: C, 71.48; H, 6.98); IIb, m.p. 248–250°; $[\alpha]_D^{20}$ +176° (dioxane); IIb, 3,21-diacetate, m.p. 188–190°, $[\alpha]_D^{20}$ +136° (chloroform), or IIc (yield: 72%), m.p. 247–248°, $[\alpha]_D^{20}$ +31° (dioxane), which was converted to IIb by acetic acid hydrolysis. 3-Keto-1,4,6-triene (Id) gave Δ^6-estrone (IId)[4] (yield, 10–15%) in the same reaction.

In the case of 3-keto-1,4-dienes or their C-11 substituted derivatives different rearrangement products were obtained. Treatment of Ie with zinc in pyridine provided a mixture of *p*-cresol type rearrangement product (IIIe)[5] (yield, 80%) and estrone (IIe) (yield, 4%). The 11β-hydroxy compound (If) yielded IIIf, m.p. 223–224°, $[\alpha]_D^{15}$ +249° (chloroform), $\lambda_{max}^{CH_3OH}$ 282–286 mμ (ε 2,340), methyl ether, m.p. 213–214°, $[\alpha]_D^{15}$ +303° (chloroform), which was confirmed by conversion to the IIIe methyl ether by dehydration and hydrogenation. However, the 11-keto compound (Ig) suffered rupture of C_9-C_{10} bond with concomitant A-ring aromatization to give the 9//10 seco compound (IV), m.p. 212–214°. It was identical in all respects with an authentic specimen of IV obtained from Ig by pyrolysis.[6]


I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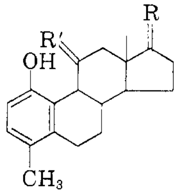
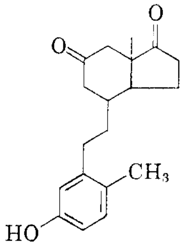
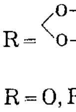

III


IV

a. R = O, R′ = H, $\Delta^{9(11)}$
b. R = α-OH, —CO—CH₂OH, R′ = H, $\Delta^{9(11)}$
c. R =  R′ = H, $\Delta^{9(11)}$
d. R = O, R′ = —H, —H, Δ^6
e. R = O, R′ = —H, —H
f. R = O, R′ = β-OH, —H
g. R = R′ = O

Santonin was converted to desmethyldesmotroposantonin (V) (yield, 40%), m.p. 223–227°, $[\alpha]_D^{20}$ +115° (chloroform), $\lambda_{max}^{CH_3OH}$ 286.5 mμ (ε 2,820), λ_{max}^{Nujol} 811 cm.$^{-1}$, NMR[7] τ, 7.60 ppm. (one benzenoid methyl) (*Anal.* Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.10; H, 6.93), acetate, m.p. 144–146° (*Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.08; H, 6.50.), by the same reaction in pyridine. The structure of V was confirmed by the palladium-charcoal dehydrogenation which led to 1-methyl-7-ethyl-

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(1) Pyridine containing *ca.* 10 mole equivalents of water was used.

(2) B. J. Magerlein and J. A. Hogg, *J. Am. Chem. Soc.*, **80**, 2220 (1958).

(3) B. J. Magerlein and J. A. Hogg, *J. Am. Chem. Soc.*, **80**, 2226 (1958).

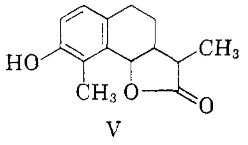
(4) St. Kaufman, J. Pataki, G. Rosenkranz, J. Romo, and C. D. Djerassi, *J. Am. Chem. Soc.*, **72**, 4531, 4534 (1950).

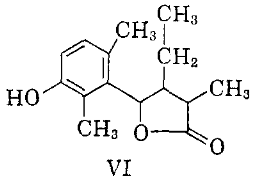
(5) A. S. Dreiding and A. Voltman, *J. Am. Chem. Soc.*, **76**, 537 (1954).

(6) B. J. Magerlein and J. A. Hogg, *Tetrahedron*, **2**, 80 (1958).

(7) τ values were calculated assuming τ chloroform (solvent) = 2.75 ppm.

2-naphthol,[8] m.p. 93–94°. The reation in ethylene glycol gave the 9//10 seco compound (VI) as a solvated crystal, m.p. 100–108°, λ_{max}^{Nujol} 815 cm.$^{-1}$ NMR[7] τ, 7.69, 7.75 ppm. (two benzenoid methyl), 9.13 ppm. triplet (methyl of ethyl group). The substance after the crystal solvent is removed is an oil, $[\alpha]_D^{20}$ −25° (chloroform), $\lambda_{max}^{CH_3OH}$ 288 mμ (ϵ 3,000), (*Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.26; H, 8.12), acetate, m.p. 145–150° (*Anal.* Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.58; H, 7.61).


V


VI

Methane generated from all the reactions involving the loss of the angular methyl group, was detected by gas chromatography. As only starting material was recovered from the reaction in anhydrous pyridine, ethylene glycol or water in pyridine may be a hydrogen donor in the reaction. The treatment of the above dienone (Ie) or trienone (Ia or Id) in acetic acid with zinc[9] does not give an aromatic A-ring steroid, but a substance assumed to be a bis compound showing polyene absorption. The detailed presentation of these reactions will be published in a forthcoming report.

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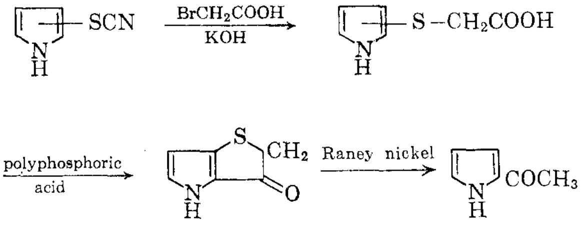
(8) T. Kariyone, T. Fukui, and T. Omoto, *Yakugakuzassi* (Tokyo), **78**, 710 (1958).

(9) The reaction of a B-ring dienone to an aromatic compound and that of santonin to the bis compound with zinc in acetic acid has been reported. D. H. R. Barton and B. R. Thomas, *J. Chem. Soc.*, 1842 (1953). K. Tsuda, E. Ohki, and J. Suzuki, *Chem. and Pharm. Bull.* **9**, 131 (1961). J. Simonsen, *The Terpenes*, Vol. III, p. 273, Cambridge Univ. Press (1952).

On the Thiocyanation of Pyrrole

Sir:

Matteson and Snyder[1] have recently claimed that thiocyanation of pyrrole with methanolic thiocyanogen at −70° or with cupric thiocyanate at 0° yields 3-thiocyanopyrrole (I) (m.p. 41.5–43°). This is rather unexpected since most reagents attack pyrroles at an unsubstituted α-position in preference to an unsubstituted β-position. They proved the structure of the thiocyanopyrrole by converting it to the (pyrrolylthio)acetic acid (II) which was ring closed to 2*H*,3*H*-thieno[3,2-*b*]pyrrole-3-one (III) and desulfurized to authentic 2-acetylpyrrole (IV)



In connection with our work on the NMR spectra of heteroaromatic compounds,[2–5] we have studied the NMR spectrum of thiocyanopyrrole and some of its derivatives. The three bands in the aromatic region of thiocyanopyrrole display the shifts[6] τ_A = 3.10, τ_B = 3.47, τ_C = 3.85 p.p.m. and the coupling constants J_{AB} = 1.5, J_{AC} = 2.9, and J_{BC} = 3.6 c/s, which prove that the compound formed is the 2- isomer. This conclusion is based on comparison of the above NMR parameters with those observed in other pyrroles[5] and in 2- and 3-thiocyanothiophenes.[2] Furthermore, the NMR spectrum of the methylthiopyrrole obtained through the reaction of the thiocyanopyrrole with alkali and methyl iodide[1] is in agreement only with that expected for the 2- isomer (τ_A = 3.28, τ_B = 3.77, τ_C = 3.90 p.p.m., J_{AB} = 1.5, J_{AC} = 2.8, and J_{BC} = 3.4 c/s). The same methylthiopyrrole (b.p. 87–90°/17 mm., n_D^{20} 1.5730. *Anal.* Calcd. for C_5H_7NS: C, 53.06; H, 6.23; N, 12.38; S, 28.33: Found: C, 53.17; H, 6.42; N, 12.35; S, 28.25) is obtained by treating pyrrolemagnesium iodide with dimethyl disulfide and also by treating pyrrole with methylsulfenyl chloride. These results provide independent evidence that the methylthiopyrrole is the 2-isomer, as it is known that these types of reactions lead to α-substitution.[7,8]

The NMR spectrum of the aldehyde obtained through Vilsmeier formylation of the methylthiopyrrole shows that the compound formed is 2-

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(2) S. Gronowitz, and R. A. Hoffman, *Arkiv Kemi*, **16**, 539 (1960).

(3) R. A. Hoffman and S. Gronowitz, *Arkiv Kemi*, **16**, 563 (1960).

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(5) S. Gronowitz, A-B. Hörnfeldt, B. Gestblom, and R. A. Hoffman, *Arkiv Kemi*, *in press*.

(6) The NMR spectra were obtained with a Varian Associates Model V-4300b spectrometer operating at 40 Mc/s. The chemical shifts [τ-values, *cf.* G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)] were obtained from dioxane solutions to which were added traces of piperidine in order to eliminate the complicating effects of the couplings with the *N*-hydrogens.

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(8) A. H. Corwin in R. C. Elderfield, ed., *Heterocyclic Compounds*, Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1950, Chapter VI.