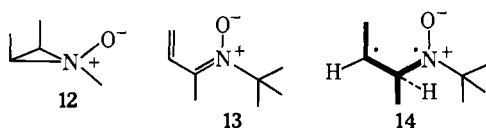


and analysis (glpc) of the olefinic material showed that it was 100% *trans*-2-butene.<sup>13</sup>



In summary, aziridine *N*-oxides behave in the same way as was earlier demonstrated for episulfoxides, showing dual pathways A and B which are stereochemically distinct. The complete stereospecificity of olefin formation for oxide 9 (*R* = *tert*-butyl) does not militate against the earlier radical interpretation of path B, since the lower temperature required for the aziridine *N*-oxide decompositions would favor retention of stereochemistry in the diradical 14, a temperature dependence which was also observed in the episulfoxide case.<sup>1</sup> In general, the rearrangement path A seems to be more facile when the stereochemistry is favorable; however, substitution with large hindering groups brings the rate of the two processes together.

**Acknowledgment.** We wish to thank the U. S. Public Health Service, the National Science Foundation, the Petroleum Research Fund, administered by the American Chemical Society, Eli Lilly and Company, and Hoffman La Roche for support of this research.

(13) Glpc analysis was on a column of 5% silver nitrate saturated tetraethylene glycol, Chromosorb P (10 ft × 1/8 in.) at 0°.

(14) A. P. Sloan Fellow, 1969–1971.

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### The Absolute Configurations at C-20 and C-22 in Ecdysones

Sir:

Although close to 40 ecdysones have been characterized to date,<sup>1</sup> the full stereochemistry of the side chain has only been elucidated for  $\alpha$ -ecdysone (1) (X-ray).<sup>2</sup> However,  $\alpha$ -ecdysone is the only ecdysone which lacks a 20-hydroxyl group, all other ecdysones having hydroxyl groups at both C-20 and C-22. Hence, nmr comparison of proton signals close to these chiral centers is not applicable in deducing the configurations at C-20 and C-22.

However, the natural ecdysones, excepting  $\alpha$ -ecdysone and shidasterone (epimeric at C-20 and/or C-22<sup>3</sup>), have very similar nmr signals originating from the moiety close to C(20)–C(22); thus, the 2,3,22-triacetates all have the following values (data in CDCl<sub>3</sub>): 1.24 (s, Me, 21-H), 0.85 (s, Me, 18-H), 4.8–4.9 ppm (dd, 22-H, *J* = 4 and 8 Hz).<sup>1</sup> This clearly suggests that all natural ecdysones excepting the two quoted above have identical configurations at these two centers.

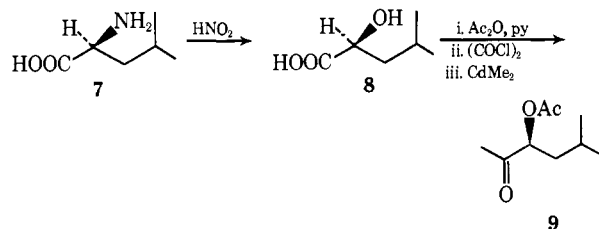
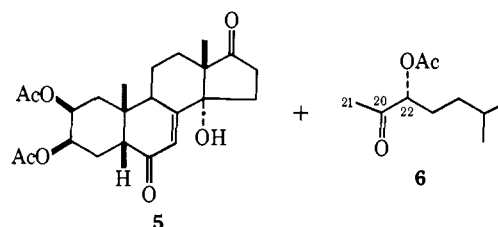
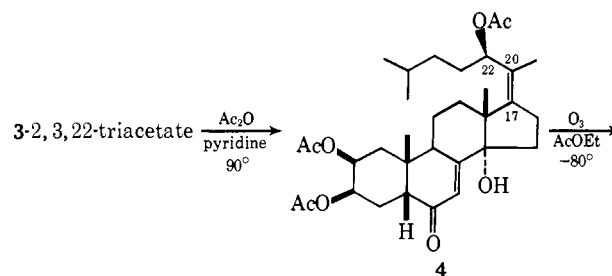
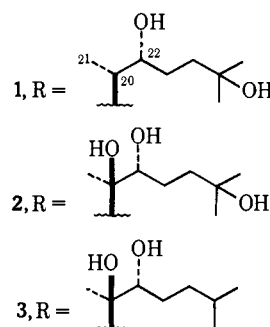
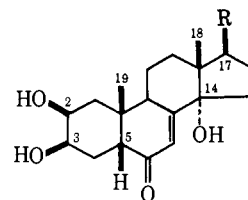
On the other hand, in view of the fact that the biological activity of synthetic ecdysones epimeric at C-20 and/or C-22 is much lower than natural ecdysones,<sup>4</sup>

(1) K. Nakanishi, *Pure Appl. Chem.*, in press.

(2) R. Huber and W. Hoppe, *Chem. Ber.*, **98**, 2403 (1965).

(3) T. Takemoto, Y. Hikino, T. Okuyama, S. Arihara, and H. Hikino, *Tetrahedron Lett.*, 6095 (1968).

(4) See, e.g., I. T. Harrison, J. B. Siddall, and J. H. Fried, *ibid.*, 3457 (1966).



establishment of configurations at these two centers becomes a problem of prime importance.

The rapid *in vivo* conversion of  $\alpha$ -ecdysone to  $\beta$ -ecdysone going through no other detectable intermediate<sup>5-7</sup> suggests that the C-22 configurations are identical in the two ecdysones. Furthermore, the production of both  $\beta$ -ecdysone (2) and ponasterone A (3) upon catalytic hydrogenation of a 20,22,25-trihydroxy-23-yne side chain<sup>8</sup> furnished direct evidence for the identity of the two respective centers in 2 and 3. Beyond this there is no chemical evidence which allows one to deduce the C-20 and C-22 configurations. In the following we provide data which establish the configurations as 20*R*,22*R*. These configurations are iden-

(5) D. S. King and J. B. Siddall, *Nature (London)*, **221**, 955 (1969).

(6) H. Moriyama, K. Nakanishi, D. S. King, T. Okauchi, J. B. Siddall, and W. Hafferl, *Gen. Comp. Endocrinol.*, **15**, 80 (1970).

(7) L. Cherbas and P. Cherbas, *Biol. Bull.*, **138**, 115 (1970).

(8) G. Hüppi and J. B. Siddall, *Tetrahedron Lett.*, 1113 (1968).

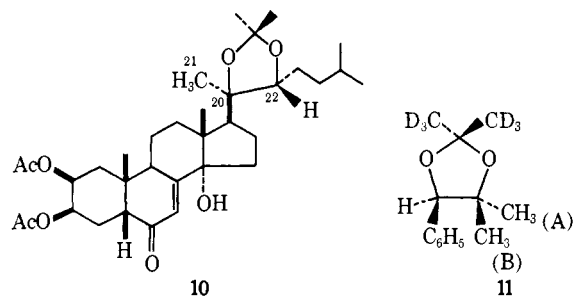
tical with those deduced for the intermediate involved in the cholesterol to pregnenolone conversion.<sup>9</sup>

Treatment of ponasterone A (3) 2,3,22-triacetate under vigorous acetylating conditions (acetic anhydride-pyridine, 90°, 20 hr) gave in 50–70% yield the 17,20-ene 4: powder; nmr (CDCl<sub>3</sub>) 0.85 (s, 19-H), 0.87 (d, 26- and 27-H), 1.03 (s, 18-H), and ca. 5.5 ppm (m, 22-H).<sup>10</sup> The 17,20-ene 4 (100 mg) upon ozonolysis at –80° yielded the methyl ketone 6 (10 mg), oil, together with rubrosterone 2,3-diacetate (5) mp 195–198°, exhibiting the same spectral properties as originally reported.<sup>11</sup> The methyl ketone 6 had the following properties: M<sup>+</sup> at *m/e* 186; ir (CHCl<sub>3</sub>) 1731 cm<sup>-1</sup> (br); nmr (CDCl<sub>3</sub>) 0.86 (d, 6 H, *J* = 6 Hz, *i*-Pr), 1.1–1.5 (m, 5 H, CH<sub>2</sub>CH<sub>2</sub>CH), 2.11 (s, 6 H, OAc and CH<sub>3</sub>), ca. 5.0 ppm (m, 1 H, CHOAc); ORD (EtOH) [ $\phi$ ]<sub>293</sub> –1.09 × 10<sup>3</sup> (trough). The ketol acetate 9 of known configuration was next prepared from L-(–)-leucine (7) by conversion to L-leucic acid (8)<sup>12</sup> ORD (EtOH) [ $\phi$ ]<sub>226</sub> +2.9 × 10<sup>3</sup> (peak). It is well proven that the stereochemistry of the chiral center is retained in this reaction due to neighboring participation of the carboxyl group.<sup>13</sup> The acetate of 8 (300 mg) was then converted to the ketol acetate 9 by the sequence: (1) treatment with sodium bicarbonate to give the sodium salt, (2) reaction with oxalyl chloride, (3) reflux for 3 hr in benzene with dimethylcadmium to yield ketone 9 (30 mg; oil; M<sup>+</sup> at *m/e* 172; ir (CHCl<sub>3</sub>) 1737 cm<sup>-1</sup> (br); nmr (CDCl<sub>3</sub>) 0.95 (d, 6 H, *J* = 6 Hz, *i*-Pr), 1.2–1.8 (m, 3 H, CH<sub>2</sub>CH), 2.15 (s, 6 H, OAc and CH<sub>3</sub>), ca. 5.0 ppm (m, 1 H, CHOAc); ORD (EtOH) [ $\phi$ ]<sub>296</sub> +7.32 × 10<sup>2</sup> (peak)).

As the  $\alpha$ -ketol acetates 6 and 9 differ only by one methylene group, which has no effect on the sign of the Cotton effect, and since the ORD curve of 9 of established *S* absolute configuration is positive, the configuration of 6 having an antipolar ORD curve must be *R*. This applies to all other naturally occurring 20,22-dihydroxyecdysones characterized so far (excepting shidasterone).

As for the configuration of C-20-hydroxylated ecdysones, the *R* configuration was established by nmr experiments. Irradiation of the 20-Me group (1.13 ppm) of ponasterone A 2,3-diacetate 20,22-monoacetone (10),<sup>14</sup> mp 157–159°, resulted in a 13% increase in height of the 22-H (3.63 ppm) resonance without an increment in the integrated area; *i.e.*, disappearance of the small W-type coupling between 21-H and 22-H. This demands a trans relationship between the 20-CH<sub>3</sub> and 22-H in 10 and therefore a 20*R* configuration for ponasterone A. Had the 20-CH<sub>3</sub> and 22-H been in a cis

relationship (20*S*), an NOE would have been observed between the 21 and 22 protons rather than a W-type coupling.



This is corroborated by the behavior of (1*R*)-1-phenyl-2-methylpropane-1,2-diol-*d*<sub>6</sub> acetone (11).<sup>15</sup> Namely, irradiation of the methyl resonance A cis to the 1-methine proton showed an 11% NOE, whereas irradiation of the trans methyl B showed a 16% increase in peak height (W-type coupling) with no increase in integrated area. This situation is the basis of a new simple but rigorous nmr method for determining erythro *vs.* threo configurations of certain glycols and will be described in detail elsewhere.<sup>16</sup>

Thus the 20*R*,22*R* configurations of ponasterone A and other 20-hydroxyecdysones have been unambiguously established.<sup>17,18</sup>

**Acknowledgment.** We thank Mr. I. Miura, Columbia University, for NOE measurements.

(15) This compound was prepared by the reaction of *D*-mandelic acid methyl ester with excess methylmagnesium bromide, followed by short treatment of the resulting diol with acetone-*d*<sub>6</sub> and *p*-toluene-sulfonic acid catalyst.

(16) D. A. Schooley, M. Koreeda, and K. Nakanishi, to be published.

(17) M. K. acknowledges the Naito Foundation for financial support and D. A. S. acknowledges support of Public Health Service Grant No. GM 44,322 for a postdoctoral fellowship. The research was supported by Public Health Service Grant No. CA-11572. This paper comprises Part XXI on Insect Hormones; for Part XX see M. Koreeda, K. Nakanishi, and M. Goto, *J. Amer. Chem. Soc.*, **92**, 7512 (1970).

(18) After submission of this article, we learned that a very recent X-ray study of  $\beta$ -ecdysone (ecdysterone) had arrived at the same stereochemical conclusion: B. Dammeier and W. Hoppe, *Chem. Ber.*, **104**, 1660 (1971).

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(9) N. K. Chaudhuri, R. Nickolson, H. Kimball, and M. Gut, *Steroids*, **15**, 525 (1970); *cf.* N. K. Chaudhuri, R. Nickolson, J. G. Williams, and M. Gut, *J. Org. Chem.*, **34**, 3767 (1969).

(10) Geometry of the 17,20-ene is tentatively depicted as in 4 since hydroboration (rear attack) followed by hydrogen peroxide oxidation (20-hydroxyl) and then manganese dioxide oxidation of the 6-allylic alcohol gave a compound having the same retention time as ponasterone A in high-pressure liquid chromatography and tlc. If the product were indeed ponasterone A, the C-20 configuration of which has now been shown to be 20*R*, the double bond configuration of the 17,20-ene would be as shown in 4. However, the cis-trans isomerism is immaterial for the present deductions.

(11) T. Takemoto, Y. Hikino, H. Hikino, S. Ogawa, and N. Nishimoto, *Tetrahedron Lett.*, 3053 (1968).

(12) H. Scheibler and A. S. Wheeler, *Chem. Ber.*, **44**, 2684 (1911).

(13) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 368.

(14) K. Nakanishi, M. Koreeda, S. Sasaki, M. L. Chang, and H. Y. Hsu, *Chem. Commun.*, 915 (1966).

## Pentachlorocyclopentadienyl Salts and Organomercury Derivatives. Synthesis and Infrared and Nuclear Quadrupole Resonance Spectra

*Sir:*

Although the pentachlorocyclopentadienide anion (C<sub>5</sub>Cl<sub>5</sub><sup>-</sup>) has often been mentioned as an intermediate,<sup>1-4</sup> no solid salts of it have been described, nor has

(1) E. T. McBee and D. K. Smith, *J. Amer. Chem. Soc.*, **77**, 389 (1955).

(2) E. T. McBee, R. A. Halling, and C. J. Morton, unpublished studies; R. A. Halling, Ph.D. Thesis, Purdue University, 1965; *Diss. Abstr.*, **B**, **27** (2), 409 (1966).

(3) L. G. Feoktistov and A. S. Solonar, *J. Gen. Chem. USSR*, **37**, 931 (1967).

(4) V. Mark, *Tetrahedron Lett.*, 295 (1961).