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THE STRUCTURES OF α AND ß-PIPITZOLS*

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Pipitzol has been described as a thermal decomposition product of Perezone (III) (1, 2). This reaction was repeated and the reaction product was identical to the one isolated from Perezia cuernavacana. Although Pipitzol appeared to be a homogeneous product, an examination of its NMR spectrum*** suggested that it was a mixture of two closely related components. Eventually, two $C_{15}H_{20}O_3$ sesquiterpene stereoisomers, α-Pipitzol (Ia) and ß-Pipitzol (IIa), with very similar chemical and spectral properties were obtained. α-Pipitzol (Ia) showed m.p. 146-147°, $[\alpha]_D$ +192°, ß-Pipitzol exhibited m.p. 131-132°, $[\alpha]_D$ -172°. Comparison of the NMR spectrum of Perezone (III) with those of the pipitzols, indicate that the side chain and the enedione double bonds of Perezone are involved in the --

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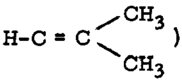
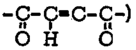
***The NMR spectra were measured in a Varian A-60 spectrometer, in $CDCl_3$ solution, with tetramethylsilane as internal reference. All chemical shifts are reported in ppm as δ values (cps/60).

formation of the Pipitzols, since the two vinyl protons of Perezone, a broad signal at 5.03 (1H,  $H-C=C(CH_3)_2$) and a splitted signal at 6.47 (1H,  $-C(=O)-C(H)=C-C(=O)-$) are not present in the NMR spectra of both Pipitzols. Furthermore, two singlets at 1.51 and 1.62, corresponding to the vinyl methyl groups of the Perezone side chain, appear as two singlets at 1.04 and 1.07 in α-Pipitzol, and a singlet at 1.07 in β-Pipitzol. These products have a vinylic methyl group whose signal has the same chemical shift showed by the methyl substituent of the quinoid nucleus of Perezone at 2.06, whereas the secondary methyl group of Perezone is responsible for a doublet ($J=7$ cps) centered at 1.19, which shows a small displacement in α-Pipitzol to 1.37 and in β-Pipitzol to 1.30. A broad signal at 7.19 of the enolic hydroxyl proton of Perezone is shifted to higher field in α-Pipitzol (6.3) and in β-Pipitzol (6.4). These signals disappear on equilibration with deuterium oxide. The allylic proton of the secondary carbon atom, alpha to the quinonoid ring of Perezone, gave a complex signal centered at 3.03. A sharp signal at 2.83 in α-Pipitzol and at 2.77 in β-Pipitzol is attributed to an allylic proton which does not interact with other protons in the vicinity.

The chemical properties of the Pipitzols combined with the examination of the IR spectra permitted to elucidate the nature of the chromophores. Both stereoisomers are weak acids soluble in strong alkalies and insoluble in sodium carbonate. They gave positive ferric chloride tests (green colour). α-Pipitzol (Ia) yielded and acetate (Ib), m.p. 103-105°, $[\alpha]_D$ +98° and β-Pipitzol acetate (IIb), showed m.p. 105-106°, $[\alpha]_D$ -88°.

Both Pipitzols have an IR band at 1760 cm^{-1} ascribed to a five membered ketone and bands at 3450, 1670 and 1635 cm^{-1} corresponding to a six membered, enolized α-diketone. Under drastic conditions, both Pipitzols yielded mono-oximes (Ic) and (IIc). The cyclopentanone is involved in the formation of the oxime, since the IR band at 1760 cm^{-1} disappears. The IR bands at 3420, 1668 and 1638 cm^{-1} still present are those of the enolized α-diketone. The λ max at 278 mμ, (log ε, 3.87) of both oximes, which in the oxime diacetates (Id) and (IId) are shifted to 248 mμ (log ε, 3.87), confirm the presence of the enolized α-diketone chromophore.

The relative position of the chromophores were elucidated on reduction of the methanolic solution of both Pipitzols with Lithium in liquid Ammonia, which afforded the corresponding Triols (IV) and (V). Periodic acid oxidation of these Triols followed by chromium trioxide treatment, yielded two isomeric γ-lactones (VI) (VII) with empirical formulas $C_{15}H_{22}O_4$*. Both lactones showed IR bands at 3450, (inflection at 2600), 1725 (carboxyl group), and at 1765 cm^{-1} (five membered lactone).

Alkaline hydrogen peroxide oxidation of both Pipitzols eliminated the enolized α-diketone chromophore with loss of four carbon atoms, yielding liquid cyclopentanones ($C_{11}H_{18}O$) (VIII) $[\alpha]_D$ +186° and (IX) $[\alpha]_D$ -289°, characterized as their semicarbazones. The IR spectra of these products had a band at 1740 cm^{-1} corresponding to a five membered ketone. Their NMR spectra showed the presence of three methyl substituents. Three protons can be exchanged in equilibration with MeOD-MeONa. Mass spec-

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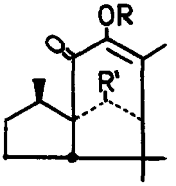
*Satisfactory elemental analyses were obtained for all compounds described trum of the ketone (VIII) gave a M.W. of 166 and the fragmentation pattern is in accord with the structure VIII.

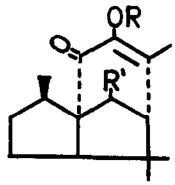
The stereochemistry of α-Pipitzol and β-Pipitzol can be elucidated after consideration of the following facts. The absolute configuration of the secondary methyl group in both Pipitzols is identical to that of the same substituent of Perezone (III) which has been established (3) (methyl β), since this asymmetric center is not involved in the formation of the Pipitzols. The ORD curves of the Pipitzols are of enantiomeric type. α-Pipitzol shows a strong positive Cotton effect ($[\alpha]_{340}$ + 11,200°), whereas the curve of β-Pipitzol exhibits a negative one ($[\alpha]_{332.5}$ -10,200°).

The same features are displayed by the cyclopentanones (VIII) and (IX). The ORD curve of the ketone (VIII) obtained from α-Pipitzol, showed a positive Cotton effect ($[\alpha]_{332.5}$ +6,545°), while that of the ketone (IX) prepared from β-Pipitzol had a negative Cotton effect ($[\alpha]_{317.5}$ -8,820°). Therefore the asymmetric centers at the ring junctions in both Pipitzols and the cyclopentanones are of enantiomeric type.

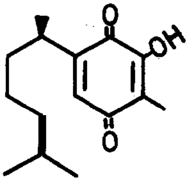
Construction of models and mechanistic considerations permitted only two cis stereochemical structures for the Pipitzols. Because α-Pipitzol and its degradation product VIII show the same positive Cotton effect as the steroid (X) (4), the stereochemical structure of α-Pipitzol is that of Ia, with the asymmetric centers oriented as in Cedrene (5). Likewise, because both β-Pipitzol and its degradation product IX exhibit the same negative Cotton effect as steroid (XI) (4), the stereochemical structure of β-Pipitzol can be represented by IIa.



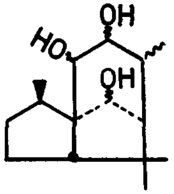
I a, R = H; R'=O
b, R = Ac; R'=O
c, R = H; R'=N-OH
d, R = Ac; R'=N-OAc



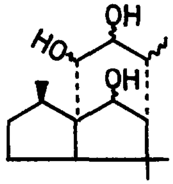
II a, R = H; R'=O
b, R = Ac; R'=O
c, R = H; R'=N-OH
d, R = Ac; R'=N-OAc



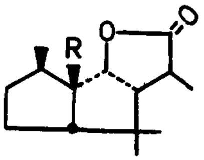
III



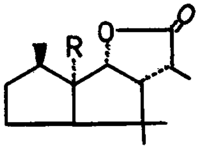
IV



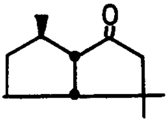
V



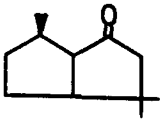
VI R=CO_2H



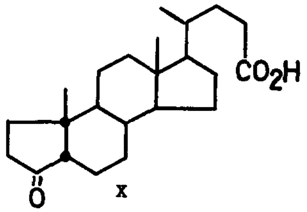
VII R=CO_2H



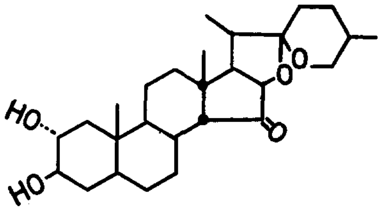
VIII



IX

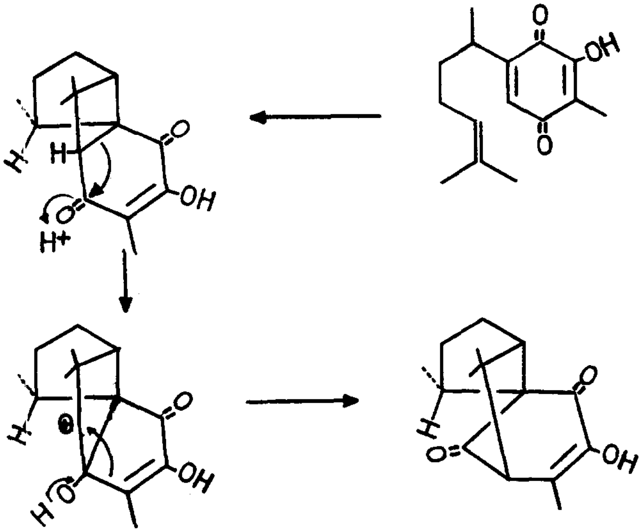


X



XI

A purely speculative mechanism, based on the assumption that Kögl's structure of Perezone (III) is correct (2), is outlined below



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R E F E R E N C E S

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