6-Azasteroidal Analogues from α-Hydroxymethylene Ketones

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Received December 14, 1973

Sir:

In connection with our studies on heterocyclic ring systems from α-hydroxymethylene ketones (1) we wish now to report the synthesis of some 6-azasteroidal analogues, in order to study their biological properties.

Treatment of the 2-acetyl-3-cyclohexane-1,3-dione (2) with *m*-anisidine in refluxing ethanolic solution afforded, in 95% yield, the 2-α-(*m*-methoxyanilino)ethylidenecyclohexane-1,3-dione (I), m.p. 132°, exhibiting ir bands at 1640, 1605 and 1565 cm^{-1} and nmr (deuteriochloroform) NH signal at δ (ppm) ~ 15, thus supporting the keto-amine structure (3).

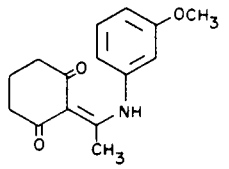
Compound I was cyclodehydrated with PPA at 100°, giving only II, m.p. 147°, in 70% yield. Nmr signals (deuteriochloroform) of the aromatic protons gave a pattern which can be approximatively interpreted as an ABX system; δ_A 7.24 *d* (H-4), δ_B 7.07 *dd* (H-2), δ_X 7.75 *d* (H-1); J_{AB} = 2.5 Hz, J_{AX} < 1 Hz and J_{BX} = 9 Hz.

The values of the reported coupling constants exclude the alternative structure resulting from the cyclization *ortho* to the methoxy group.

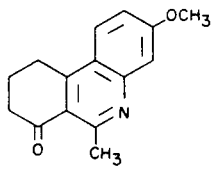
The phenanthridone derivative II upon treatment with ethyl formate and sodium methoxide in benzene solution afforded 3-methoxy-6-methyl-7-oxo-8-hydroxymethylene-7,8,9,10-tetrahydrophenanthridine (III), m.p. 173°, nmr (deuteriochloroform) δ 7.76 *bs* (=C*H*-OH). The hydroxymethylene ketone III so obtained was the intermediate for 6-azasteroidal analogues; in fact by reaction of III with hydrazine hydrate was obtained the 4-methyl-7-methoxy-10,11-dihydro-2*H*-pyrazolo[3,4-*i*]phenanthridine (IV), m.p. 234°, in 75% yield; nmr (DMSO-d_6): δ 7.52 *t* (J = 0.7 Hz) (=CH-N) and 12.70 *bs* (NH). Moreover, the reaction of the intermediate III with hydroxylamine hydrochloride in ethanol with sodium acetate at room temperature, gave the 3α-hydroxy-4-methyl-7-methoxy-10,11-dihydro-Δ^1-isoxazolino[5,4-*i*]phenanthridine (V), m.p. 229°, in 80% yield; its structure was confirmed by nmr spectrum (DMSO-d_6): δ (ppm) ~ 3.60 *m* (C-11*a* H), 7.58 *d* (J = 5.5 Hz) (-CH=N-) and 10.70 *s* (OH); these data are in agreement with those reported for similar structures (4,5). In addition, the isoxazoline derivative V was also readily dehydrated with trifluoroacetic acid to give 4-methyl-7-methoxy-10,11-dihydroisoxazolo[5,4-*i*]-phenanthridine (VI), m.p. 178°, nmr (deuteriochloroform) δ 8.30 *s* and (DMSO-d_6) δ 8.55 *s* (-CH=N).

The details will be discussed in the forthcoming full paper.

Satisfactory spectral data and elemental analyses were obtained for all the compounds described.



I



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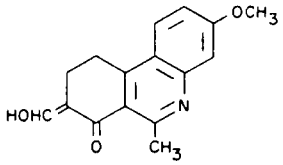

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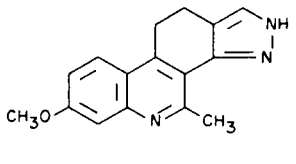

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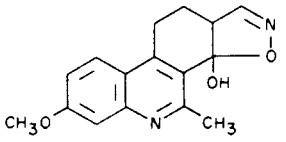
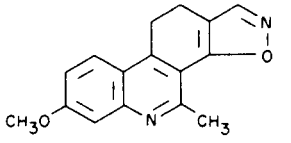


V



VI

Acknowledgment.

This work was supported by the Consiglio Nazionale delle Ricerche, Rome, Italy.

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