Tetrahedron Letters No. 12, pp 971 - 972, 1974. Pergamon Press. Printed in Great Britain.

ACID CATALYSED CYCLISATION OF 1-(2,5-DIKETO-1-METHYLCYCLOPENTYL)-3-(2,4-DIMETHOXYPHENYL)-5-METHYLHEXA-2,4-DIENE - SYNTHESIS OF A B-NOR STEROID DERIVATIVE

T.R. Kasturi*, E.M. Abraham and R.S. Prasad
Department of Organic Chemistry, Indian Institute of Science,
Bangalore-560012, India

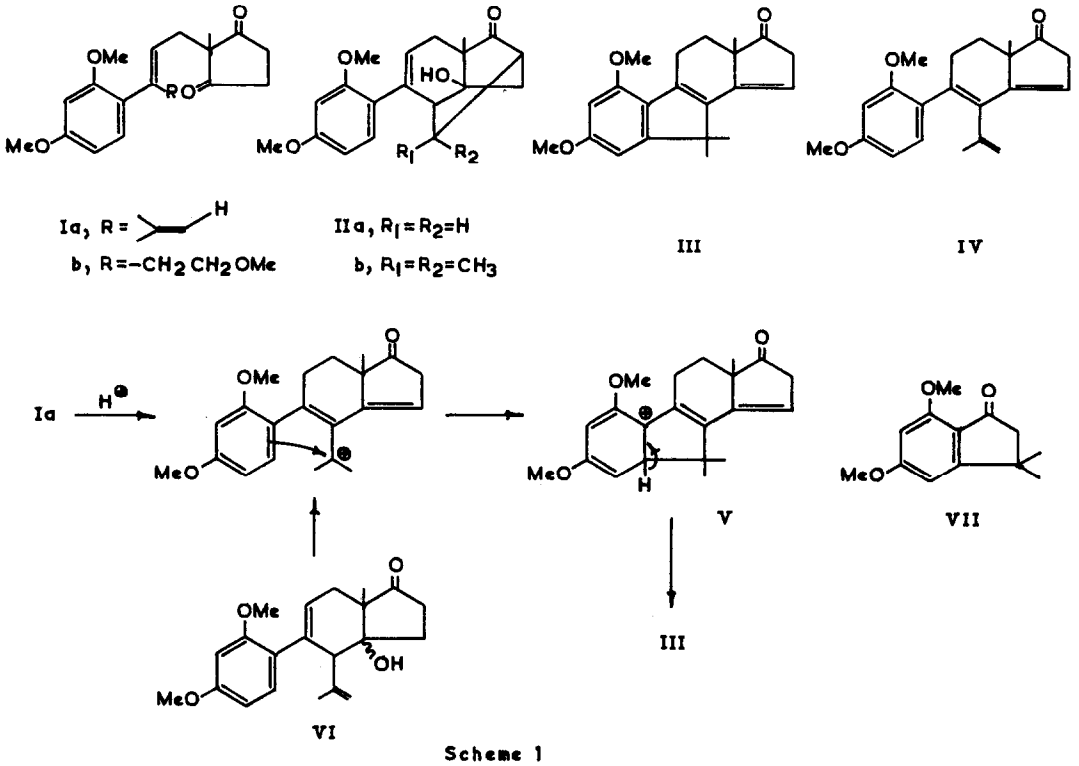
(Received in UK 14 January 1974; accepted for publication 8 February 1974)

We have recently described[1] an unusual cyclisation of a B-seco steroid intermediate (Ib) to a homo-brendane derivative (IIa). We now report the synthesis of a B-nor steroid derivative (III) by a novel acid catalysed cyclisation.

Grignard reaction of 2,4-dimethoxyphenyl- Δ^2-isovalerophenone with vinyl magnesium bromide followed by condesnation with 2-methylcyclopenta-1,3-dione afforded the seco dione (Ia)[2], M^+ 342, NMR ($COCl_3$); 1.18 (s,3H, CH_3), 1.4 (d,J=1.5 Hz,3H, $=\underset{H}{C}-\underline{CH}_3$), 1.78 (d,J=1.5 Hz,3H, $=CH-\underline{CH}_3$), 3.73, 3.78 (s,6H, methoxyls), 5.42 (t,J=7 Hz,1H, $=\underline{CH}-CH_2$), 5.85 (bs,1H, $=\underline{CH}-CH_3$), 6.3-6.6 (m,2H, ar.H) and 6.95 δ (d,J=8 Hz,1H, ar.H). The seco dione (Ia) on treatment with ethanolic hydrochloric acid[3] under reflux did not yield either the expected homo-brendane derivative (IIb) or the B-seco steroid derivative (IV). However, a solution of the seco dione (Ia) in methylene chloride on treatment with conc. sulphuric acid at 0° afforded a solid (75%), m.p. 109° M^+ 324, IR (nujol): 1745 cm^{-1}, UV λ_{max}^{EtOH} (nm): 242 (9250), 296 (14,970), 306 (18,500) and 326 (15,000), NMR (CCl_4): 1.06 (s,3H, CH_3), 1.29, 1.35 (s,6H, gem. dimethyl), 1.4-2.1 (m,2H), 2.6-3.4 (m,4H), 3.79, 3.81 (s,6H, methoxyls), 5.7 (bs,1H), 6.21 (d,J=1.5 Hz, 1H, ar.H) and 6.4 δ (d,J=1.5 Hz, 1H, ar.H). The presence of only two aromatic protons with meta coupling indicated cyclisation involving the aromatic ring. The aforementioned data could be explained on the basis of structure III. Structure III for this compound was confirmed by an unambiguous synthesis starting from 5,7-dimethoxy-3,3-dimethylindan-1-one (VII) following the Torgov's method.

The mechanism of formation of this compound (III) can be visualised as shown in Scheme 1. This mechanism is supported by the fact that the alcohol (VI)[4] on treatment with conc. sulphuric acid yields the same nor-steroid derivative (III). The facile

cyclisation involving the meta position may be contrasted with the behaviour of 3-(2,4-dimethoxyphenyl)-propionic acid and 3-(2,4-dimethyoxyphenyl)-isovaleric acid in similar cyclisations[5,6].



Scheme 1

Further elaboration of III to steroid analogues and a study of their biological properties are in progress.

REFERENCES AND NOTES

1. T.R. Kasturi, R. Ramachandra, K.M. Damodaran and Kalyani Vijayan, Tetrahedron Letters, 5059 (1972).

2. All new compounds reported gave satisfactory elemental analyses.

3. A solid containing both the carbonyls intact has been obtained in this reaction. Structure of this solid is under investigation.

4. The alcohol (VI) was obtained during column chromatography (alumina) of the seco dione (Ia); NMR ($CDCl_3$); 1.19 (s,3H, CH_3), 1.7 (bs,3H, $H_2C=C-\underline{CH_3}$), 1.18-2.6 (m,7H), 3.75 (s,6H, methoxyls), 4.88 (bs,1H, terminal CH_2), 5.0 (bs,1H, terminal CH_2), 5.6-5.75 (m,1H, $=\underline{CH}$), 6.32-5.5 (m,2H, ar.H) and 6.97δ(d,J=9 Hz,1H, ar.H).

5. T.R. Kasturi and E.M. Abraham, Indian J. Chem. (In press).

6. Attempts to cyclise 3-(2,5-dimethoxyphenyl)-propionic acid and 3-(2,4-dimethoxyphenyl)-isovaleric acid to the corresponding indanones did not yield the required products.