

A NOVEL RING ENLARGEMENT

S. Swaminathan, Joseph P. John<sup>1</sup> and S. Ramachandran<sup>2</sup>

Department of Organic Chemistry, University of Madras, Madras-25

(Received 8 June 1962)

THE vinyl alcohol<sup>3</sup> (Ia) when treated with equivalent or catalytic amounts of potassium hydroxide in aqueous methanol solution furnishes, on working up without acidification, an isomeric product (II), m.p. 58.4-59.4° (ether) in 60-65 per cent yield. [Found: C, 75.8, 75.8; H, 8.8, 8.6;  $\lambda_{\max}^{\text{EtOH}}$  247 m $\mu$  ( $\epsilon$ , 13,286). Calc. for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C, 75.7; H, 8.8.] The same product<sup>4</sup> is also obtained by a similar treatment of the epimeric vinyl alcohol<sup>3</sup> (Ib), or the diacetate<sup>5</sup> (III) of Ia. Compound (II) undergoes smooth dehydro-

<sup>1</sup> Research Fellow, University of Madras.

<sup>2</sup> Department of Chemistry, University of Michigan, Ann Arbor, Michigan.

<sup>3</sup> These compounds were obtained by hydrogenation with Pd/CaCO<sub>3</sub> in pyridine solution of the corresponding ethynyl alcohols reported by M.S. Newman, S. Ramachandran, S.K. Sankarappa and S. Swaminathan, *J. Org. Chem.* **26**, 727 (1961). The compounds gave satisfactory analyses and had the following properties:

Ia: m.p. 77-78°;  $\lambda_{\max}^{\text{EtOH}}$  242 m $\mu$  ( $\epsilon$ , 13,000)

$\lambda_{\max}^{\text{CHCl}_3}$  2.8 (OH), 6.0 ( $\begin{array}{c} \text{---C---C---} \\ || \\ \text{C} \end{array}$ ) 6.1 (C=C) and 11.4 (=CH<sub>2</sub>)

Ib: m.p. 124-125°;  $\lambda_{\max}^{\text{EtOH}}$  242 m $\mu$  ( $\epsilon$ , 14,920)

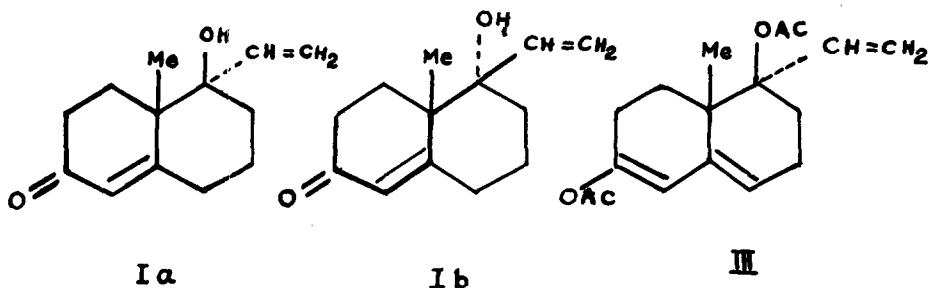
$\lambda_{\max}^{\text{CHCl}_3}$  2.8, 6.0, 6.12 and 11.35.

<sup>4</sup> Identity established by mixed m.p. determination and comparison of I.R. spectra.

<sup>5</sup> This compound was obtained by selective hydrogenation with Pd/CaCO<sub>3</sub> in alcohol solution of the corresponding ethynyl diacetate reported by Newman *et al.* (*loc.cit.*)

$\lambda_{\max}^{\text{EtOH}}$  235 m $\mu$  ( $\epsilon$  = 18,800).  $\lambda_{\max}^{\text{CHCl}_3}$  5.75, 6, 6.1, 8.0-8.4,

10.1 and 10.86.



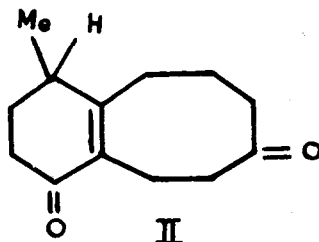
genation (Pd on charcoal) with loss of two hydrogen atoms only to give a phenol (IVa), m.p. 148-149°, [Found: C, 76.5; H, 7.9.  $\lambda_{\max}^{\text{EtOH}}$  221 m $\mu$  ( $\epsilon$ , 7,391) and 288 m $\mu$  ( $\epsilon$ , 2,084). Calc. for  $\text{C}_{13}\text{H}_{16}\text{O}_2$ : C, 76.5; H, 7.8.] also characterized as the methyl ether (IVb), m.p. 62.6-63.6°. [Found: C, 77.0; H, 8.5.  $\lambda_{\max}^{\text{EtOH}}$  219 m $\mu$  ( $\epsilon$ , 8,776) and 286 m $\mu$  ( $\epsilon$ , 2,000). Calc. for  $\text{C}_{14}\text{H}_{18}\text{O}_2$ : C, 77.1; H, 8.3.]

The I.R. spectrum ( $\text{CHCl}_3$ ) for II shows main absorptions at 5.85 $\mu$  (non-conjugated C=O), 6.0 $\mu$  (conjugated C=O) and 6.15 $\mu$  (C=O) respectively and indicates absence of hydroxyl and vinyl groups. The main I.R. absorptions ( $\text{CHCl}_3$ ) for IVa are at 2.72 $\mu$  (free OH), 2.97 $\mu$  (bonded OH), 5.88 $\mu$  (non-conjugated C=O) and 6.28 $\mu$  (aromatic C=C) respectively while those for IVb are at 5.85 $\mu$  (non-conjugated C=O), 7.93 $\mu$  (-OCH<sub>3</sub>) and 6.25 $\mu$  (aromatic C=C) respectively.

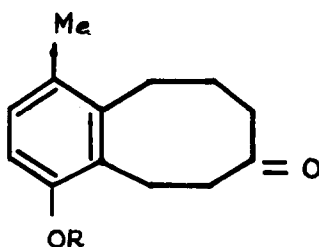
The NMR spectrum<sup>6</sup> of II while confirming the absence of hydroxyl group shows, in contrast to that of Ia, complete absence of any olefinic hydrogen atom and also that the methyl group is present no longer as an angular methyl group but is part of the system  $\text{CH}_3 - \text{CH} \begin{smallmatrix} \text{C} \\ \diagdown \\ \text{X} \end{smallmatrix}$ , where X may be  $\begin{smallmatrix} & \text{C} \\ & \diagdown \\ & \text{C} \end{smallmatrix}$  but not alkyl or hydrogen.

<sup>6</sup> According to Dr. G.V.D. Tiers, the NMR spectrum of II has a doublet methyl peak at 8.79 $\tau$  suggestive of the presence of  $\text{CH}_3 - \text{CH} \begin{smallmatrix} \text{C} \\ \diagdown \\ \text{X} \end{smallmatrix}$  and three broad peaks at 7.46, 7.61 and 7.72 $\tau$  - none of which can be attributed to an acetyl group.

We interpret the evidence summarized on p. 730 as indicating the following structure<sup>7</sup> for compound (II).



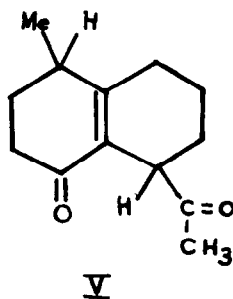
The phenol obtained by dehydrogenation and its methyl ether should then be formulated as below:



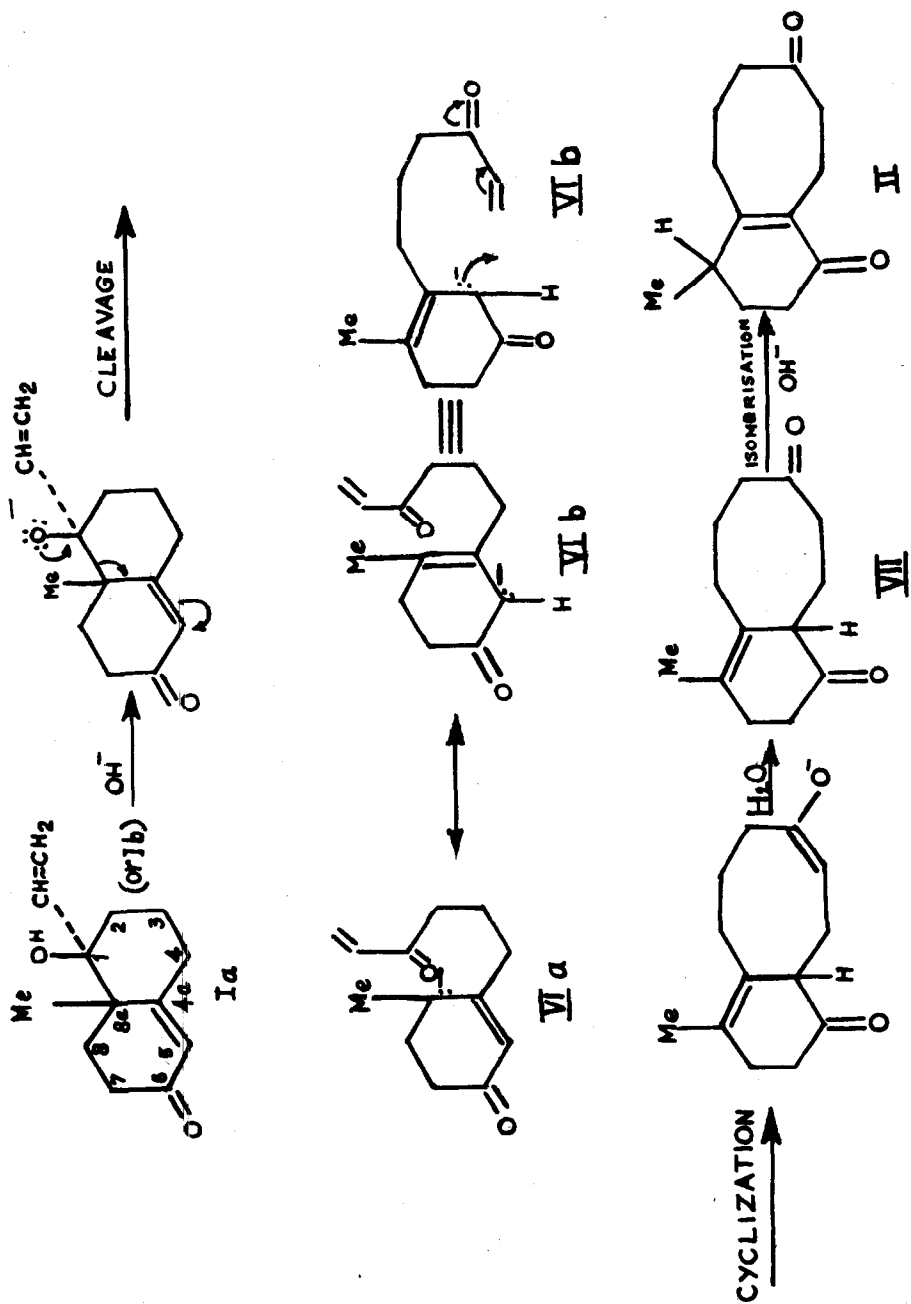
**IV a**,     $R = H$

**IV b**,     $R = CH_3$

<sup>7</sup> An alternate structure for consideration is V.



It has to be ruled out, however, on the following grounds: (1) Compound (II) does not give a positive iodoform test. (2) Compound (II) loses two H atoms and only two on dehydrogenation to give IVa, whereas according to structure (V), six hydrogen atoms may easily be lost leading to a naphthol derivative. (3) The NMR shows no peaks for  $-COCH_3$ .



The formation of II from either Ia or Ib, probably involves initial ring cleavage followed by recyclization to an eight-membered ring as visualized on p. 732.

The ring cleavage<sup>8</sup> involved in the conversion of Ia or Ib to the same mesomeric anion (VIa)  $\longleftrightarrow$  (VIb) is due most likely to overcrowding and consequent strain around the C<sub>1</sub> - C<sub>8a</sub> bond. The cyclohexanone intermediate (VIb) has a negative charge on the carbon atom  $\alpha$  to the ring carbonyl and on the next carbon atom a six-carbon side-chain with a terminal vinyl group conjugated  $\alpha, \beta$  to a second carbonyl group. An intramolecular Michael type addition may be expected to follow naturally, leading to the eight-membered ring intermediate (VII), which on alkaline isomerization gives the more stable conjugated enedione (II). The conversion of III to II must involve saponification to the parent vinyl alcohol (Ia) followed by rearrangement.

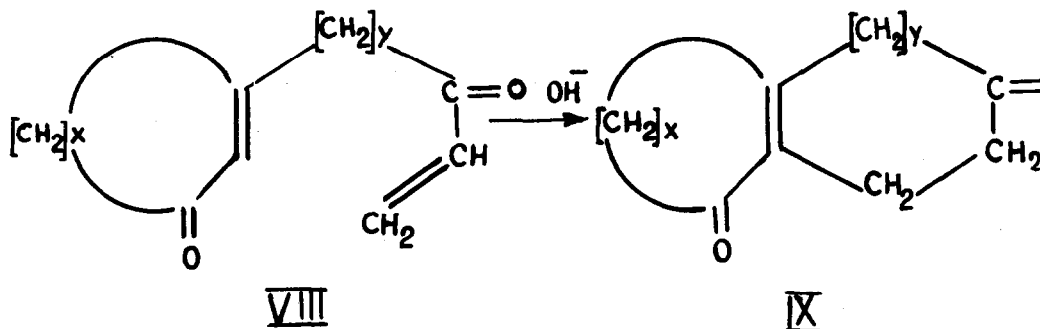
The conversion of Ia or Ib to II involves therefore the incorporation in a single step of two carbon atoms in toto into a six-membered ring to form an eight-membered ring - a type of ring enlargement that does not seem to have been reported so far. The ease with which the energetically unfavourable eight-membered ring is formed can only be ascribed to the susceptibility of the mesomeric anion (VIa)  $\longleftrightarrow$  (VIb) to undergo ready internal cyclization.

It is likely that the cyclization of VIa to II may be only one instance of a rather general method of ring closure in which compounds of the type (VIII) are cyclizable to those of the type (IX) in presence of base.

Work is in progress to study the cyclization of compounds of the type (VIII) prepared or generated in situ by cleavage of vinyl compounds of the

---

<sup>8</sup> Similar ring cleavages during microbiological transformations of steroids have been reported recently by R.M. Dodson and R.D. Muir, J. Amer. Chem. Soc. **83**, 4627, 4631 (1961).



type (Ia) or (Ib) and also by more direct methods. An unequivocal synthesis of II is also under study.

Acknowledgements - Our grateful thanks are due to Dr. G.V.D. Tiers of Minnesota Mining and Manufacturing Company for providing us with the NMR spectra and their interpretation. One of the authors (J.P.J.) wishes to thank the University of Madras for the award of a Fellowship.