

TRACER STUDIES ON THE MECHANISM OF THE DIENONE-PHENOL REARRANGEMENT  
WITH MINERAL ACIDS

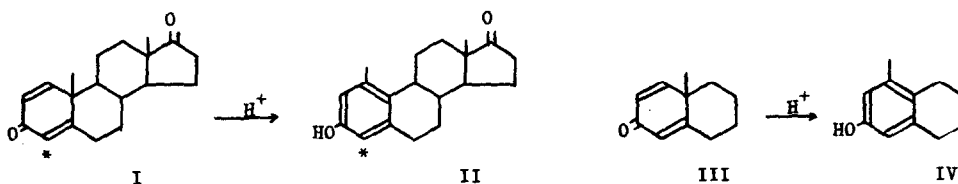
REIJI FUTAKI

Hoshi College of Pharmacy

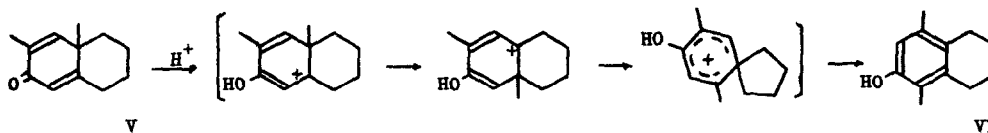
2, Ebara, Shinagawa-ku, Tokyo, Japan

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The dienone-phenol rearrangement of 1,4-androstadiene-3,17-dione(I) and 10-methyl-1,4-hexadiene-3-one(III) on treatment with aqueous mineral acids to yield mostly 1-methylestrone(II) and 1-methyl-3-tetralol(IV) respectively, was first reported by Dreiding<sup>1)</sup>. Later Capsi<sup>2)</sup> proved the rearrangement of (I) to (II) was caused by a simple 1,2-shift of the angular methyl group, finding the position of <sup>14</sup>C in (I) was not changed in (II).



However, Kropp<sup>3)</sup> proposed another pathway involving initial migration of the angular methyl group to the alternate angular position, followed by further rearrangement through a spiro intermediate, obtaining 1,4-dimethyl-3-tetralol(VI) as a major product of the rearrangement of 2,10-dimethyl-1,4-hexadiene-3-one(V) under the same conditions.



The author now wishes to report the results of tracer studies of 10-methyl-1,4-hexadiene-3-one [<sup>9-14</sup>C] (III) to (IV) under the same conditions.

**Rearrangement** The labeled dienone<sup>4)</sup>(III)(500mg) was treated with 50%  $H_2SO_4$  at  $100^\circ$  for 30 min under stirring at the specified conditions by Dreiding<sup>1)</sup> to give the tetralol(IV)(200mg), white crystals, m.p.101-103 $^\circ$ .

**Degradation** The above tetralol(IV)(800mg, including the inactive pure one 600mg, m.p.104-105 $^\circ$ , by independent synthesis, lit.<sup>1)</sup>104-105 $^\circ$ ) was mixed with  $K_2CO_3$ (200mg), added with xylene (30ml), and treated with 2 mols equivalent dimethyl sulphate under reflux for 4 hrs, followed by steam distillation under caustic alkaline conditions to give the methyl ether(VII)(650mg), colourless liquid, b.p.108-110 $^\circ$ /2.5mm.

Chromic acid oxydation of the above ether(VIII)(1,000mg, including the inactive one, 300mg) in glacial acetic acid under stirring and ice cooling gave the 9-ketone(VIII)(650mg), b.p.135-138 $^\circ$ /2.5mm, yellow crystalline mass, m.p.67-69 $^\circ$ , the pure specimen for counting, colourless plates(from ethanol), m.p.70-71 $^\circ$ (lit.<sup>5)</sup>70.5 $^\circ$ ).

The mixture of the above ketone(VIII)(600mg, hereafter no dilution with the inactive one), KOH(2g), ethanol(10ml) and  $NH_2OH \cdot HCl$ (600mg) was refluxed for 2 hrs. After pouring into water, extraction with ether and evaporation gave the oxime(IX)(500mg), faintly purple coloured plates, m.p.151-153 $^\circ$ , analytically pure sample, white long plates(from dil. ethanol), m.p.153-154 $^\circ$ .

The oxime gave the Beckmann rearranged lactam(X) when it was heated with polyphosphoric acid at 130 $^\circ$  for 10 min, followed by pouring into water. Tan plates, m.p.149-151 $^\circ$ , yield almost quantitative. Analytically pure sample, colourless plates, m.p.151-152 $^\circ$ (from water). showed marked depression of m.p. mixed with (IX).

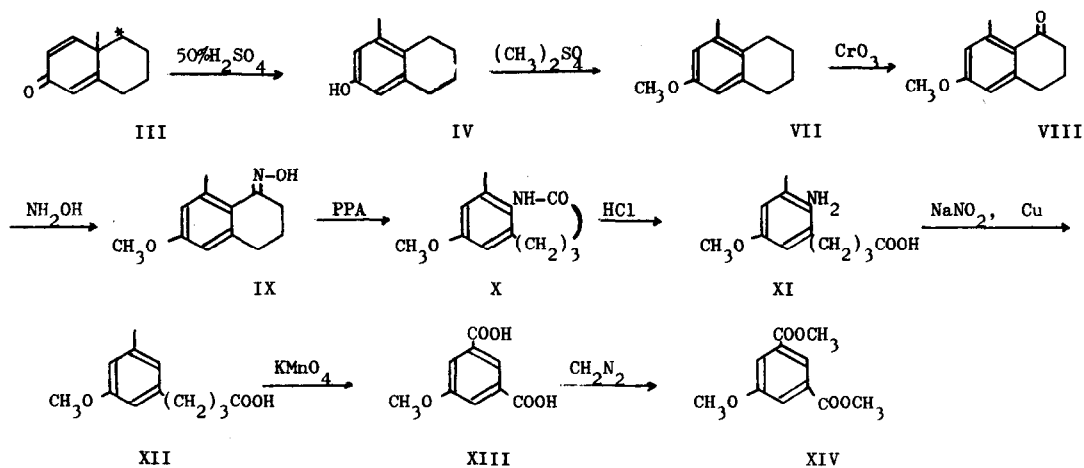
The lactam(X) was cleaved to the amino acid(XI) by boiling with conc.HCl for 30 min. The aqueous solution of the evaporated mass precipitated white needles of (XI)(250mg), m.p.67-71 $^\circ$ , when it was added by aqueous NaOAc. Analytically pure sample, white needles(from benzene), m.p.97-98 $^\circ$ .

The amino acid(XI) was deaminated to give (XII) by diazotation at 15 $^\circ$  with  $NaNO_2$  in 10%  $H_2SO_4$ , followed by pouring into boiling ethanol suspended with Cu powder. The fraction soluble in aqueous  $NaHCO_3$  was distilled to give white crystalline mass(150mg), b.p.163-165 $^\circ$ /2.5mm. Specimen for analysis and counting, colourless plates(from ether-petr. ether), m.p.44-46 $^\circ$ .

The acid(XII) dissolved in 5% KOH was dropped by small excess of  $KMnO_4$  solution under stirring in a boiling water-bath. The dicarboxylic acid(XIII), ether extractible, was finally precipitated from its aqueous  $NaHCO_3$  solution by acidifying with dil.HCl as white needles, m.p.230-260 $^\circ$ (sublim.) (lit.<sup>6)</sup>263 $^\circ$ )

The dicarboxylic acid(XIII) was treated with diazomethan ether solution to give colourless

plates of the dimethyl ester (XIV), m.p.108-109° (from ethanol), which was identified with the authentic specimen prepared starting with sym-xyleneol.

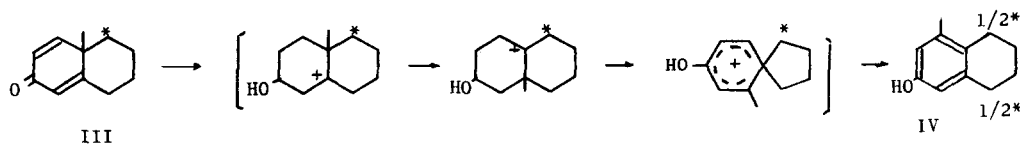


Radioactivity measurement The samples were mounted on stainless-steel dishes ( $\phi$  2.5cm), with thickness of ca.0.9mg/cm<sup>2</sup>, and counted by a low background 2K-gasflow-counter (background 1.91  $\pm$  0.18 cpm), for 10 min getting about 10,000 counts for (VII) and (XII), and 4,000 counts for (XIV).

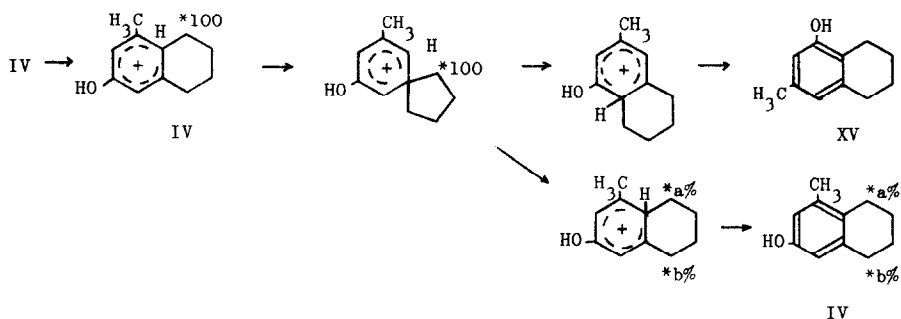
VII	430 cpm/ $\mu$ mol
XII	427 cpm/ $\mu$ mol
XIV	193 cpm/ $\mu$ mol

Results and Discussion Comparison between (VIII) and (XII) shows the measurement has fair accuracy. The ratio of (XIV) to (VIII) tells us that the rearrangement passes mostly through a pathway participated by a spiro intermediate as follows. The difference between the expected and observed values in XIV (430/2 - 193) may indicate minor concurring of the simple 1,2-shift pathway.

On the other hand, if the simple 1,2-shift is entire, no activity in XIV should be observed, because all of <sup>14</sup>C locating only on carboxylic carbon of (XII) would be lost in (XIV).



Recently Dreiding <sup>7)</sup> reported a new phenol-phenol rearrangement of 1-methyl-3-tetralol(IV) to 3-methyl-1-tetralol(XV) with 80% yield when the former was treated with 70% HClO<sub>4</sub> at 80° for 2 hrs, and proposed the mechanisms as follows.



Though it is well confirmed by gas-chromatography that the conditions exploited by the author <sup>1)</sup> does not cause this thermodynamically controlled rearrangement to give (XV), still there seems to be the possibility that the spiro intermediate as above, if it is involved partly in the conditions, may give rise to the labelled position isomer(IV'). This possibility cannot be excluded a priori to explain the distribution of <sup>14</sup>C in (VIII). This problem is left to further studies.

Acknowledgement The author wishes to express his thanks to Misses K.Daimon, J.Ishijima and T.Hayashi of this school for their technical assistance.

#### References

All m.p. were taken on a Kofler block and uncorrected. Elemental analysis of (IX),(X),(XI) and (XII) gave satisfactory results.

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The labelled dienone was prepared after the previous method.

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