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ON THE MECHANISM OF THE DIENONE-PHENOL REARRANGEMENT OF A 2-METHYL-1,4-DIEN-3-ONE

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IT is well known that cross-conjugated cyclohexadienones of the general type I rearrange on treatment with aqueous mineral acids to a mixture of two phenolic products, types III and VI.[1,2] Evidence has been presented that the formation of the tetrahydro-1-naphthol derivatives (type III) involves rearrangement through a spiro intermediate II (path A).[3] The formation of the tetrahydro-2-naphthol products (type VI) can be most easily explained in terms of a simple 1,2-migration of the angular methyl substituent (path C). However, a second, albeit more complex, reaction pathway can be invoked to account for the formation of products of the type VI (path B): initial migration of the methyl group to the alternate angular position, followed by further rearrangement of the resulting cation IV through a spiro intermediate V.

Caspi and Grover[4] have recently demonstrated that in the rearrangement of androsta-1,4-dien-3,17-dione (VII) to 1-methylestrone (VIII)

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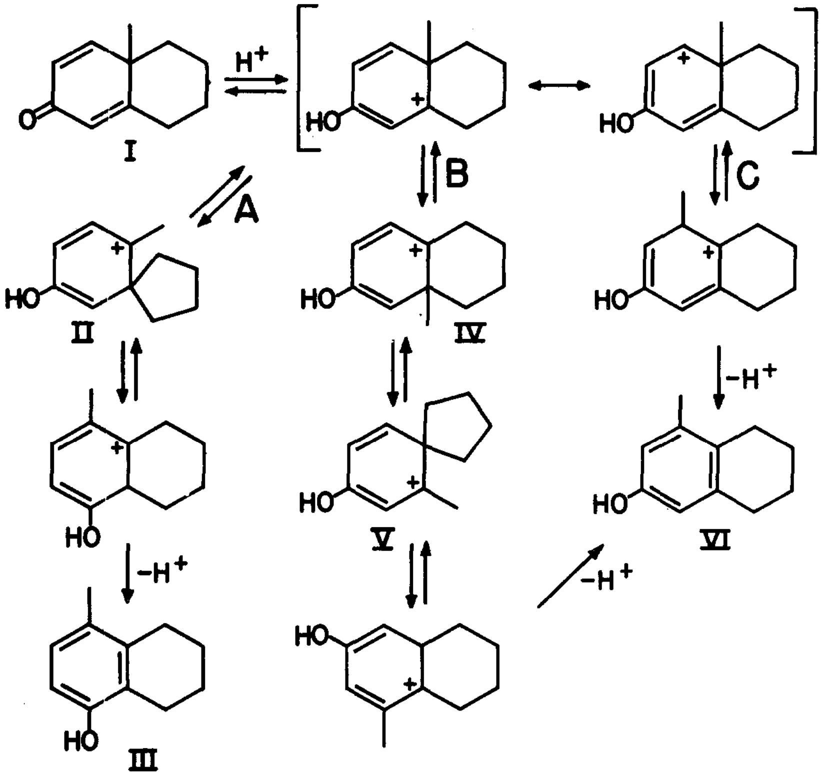
[1] A. S. Dreiding, W. J. Pummer, and A. J. Tomasewski, J. Amer. Chem. Soc., 75, 3159 (1953).

[2] P. J. Kropp, ibid., in press.

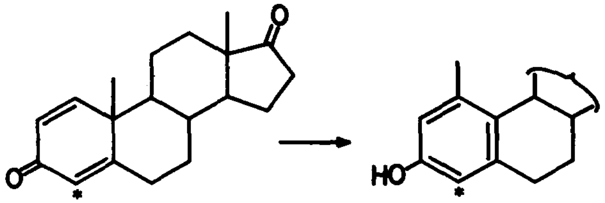
[3] (a) R. B. Woodward in A. Todd, "Perspectives in Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, p. 178; (b) S. M. Bloom, J. Amer. Chem. Soc., 80, 6280 (1958).

[4] E. Caspi and P. K. Grover, Tetrahedron Letters, 591 (1963).



<u>path C and not path B operates</u>. Thus rearrangement of a specimen of the dienone VII which had been labelled at C-4 with C^{14} gave 1-methylestrone (VIII) in which all of the C^{14} had remained at C-4, as predicted by path C. Rearrangement *via* path B, on the other hand, would have resulted in migration of the labelled carbon from C-4 in the starting material to C-2 in the 1-methylestrone product.

Another way to distinguish between the involvement of path B or of path C would be to study the rearrangement of a methyl-substituted dienone



VII VIII

such as the 2-methyldienone IX.[5a] We wish to report that rearrangement of IX in 50% sulfuric acid or in concentrated hydrochloric acid at 100° gives, in addition to the path-A product X,[5] both the phenol XII,[6] as predicted by path C, *and the path-B product XI*.[7] The path-B product XI predominates over the path-C product XII by a factor of 1.4-1.8.

The results are summarized in Table I. The three phenolic products were identified by direct comparison (infrared and n.m.r. spectra and mixed melting point determinations) with authentic samples synthesized independently as previously reported.[5a,6,7c] The phenols XI and XII were obtained as mixtures which could not be resolved by chromatography on silica gel or activity II alumina or by gas chromatography. However, the relative amounts of XI and XII present in the mixtures could be ascertained from integration of the n.m.r. spectra; the aromatic proton

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[5] (a) R. Futaki, *J. Org. Chem.*, **23**, 451 (1958); (b) W. Cocker, C. Lipman, and D. R. A. Whyte, *J. Chem. Soc.*, 1519 (1950); (c) S. Senda and H. Izumi, *Yakugaku Zasshi*, **81**, 964 (1961) [*Chem. Abstr.*, **55**, 27222 (1961)].

[6] W. Cocker, *J. Chem. Soc.*, 36 (1946).

[7] (a) L. F. Fieser and W. C. Lothrop, *J. Amer. Chem. Soc.*, **58**, 2050 (1936); (b) K. Paranjpe, N. L. Phalnikar, B. V. Bhide, and K. S. Nargund, *Rasayanam*, **1**, 233 (1943) [*Chem. Abstr.*, **38**, 4267 (1944)]; (c) M. Yanagita and R. Futaki, *J. Org. Chem.*, **21**, 949 (1956); (d) M. Yanagita, S. Inayama, M. Hirakura, and F. Seki, *ibid.*, **23**, 690 (1958).

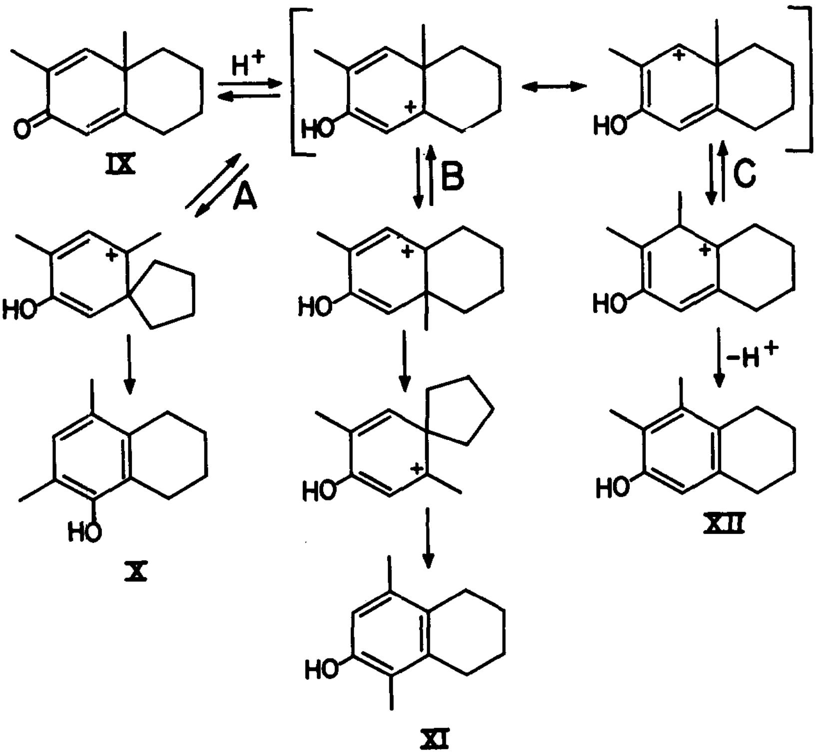


TABLE I

Acid-catalyzed Rearrangement of 3,4aβ-Dimethyl-5,6,7,8-tetrahydro-2(4aH)-naphthalenone (IX)

	Yields (%)		
Conditions	X	XI	XII
50% Sulfuric Acid[1]	35[a]	27[b]	20[b]
Conc. Hydrochloric Acid[1]	30[a]	32[b]	18[b]

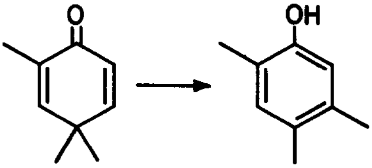
[a] Yield based on material isolated by column chromatography.

[b] Yield based on n.m.r. analysis of mixture of XI and XII isolated by column chromatography.

of XI, at 3.52 τ, is well separated from that of XII (3.62 τ). Pure specimens of XI and XII could be separated from the mixtures by fractional recrystallization from ether-hexane solutions.

Retreatment of the mixture of XI and XII under the reaction conditions failed to change appreciably the relative proportions of the two phenols. Moreover, similar treatment of pure specimens of either XI or XII failed to result in the formation of any of the other isomer. Thus XI and XII appear to be formed directly from the dienone IX by paths B and C, respectively, and not by interconversion of the phenolic products themselves.

These results indicate that the rearrangement of androsta-1,4-dien-3,17-dione (VII) by path C to the exclusion of any detectable amount of rearrangement by path B cannot be generalized to all 1,4-dien-3-ones. The occurrence of rearrangement by path B in the case of the 2-methyl-dienone IX is probably attributable to the unfavorable steric crowding of two adjacent methyl substituents on an aromatic ring; in this case initial migration of the methyl substituent to the alternate angular position is favored over migration to C-1, which is adjacent to the methyl group at C-2. A similar tendency to avoid formation of an ortho-dimethyl-substituted product is exhibited by 2,4,4-trimethylcyclohexa-2,5-dienone (XIII), which is reported[7d] to undergo acid-catalyzed rearrangement to pseudocumenol (XIV) in 70% yield.



XIII XIV

A comparison of the behavior of the dienones VII and IX illustrates once again the exceedingly delicate balance between various alternate pathways in the dienone-phenol rearrangement and the pronounced effects that can be exerted on this balance by subtle structural features.[8] Further studies of structural effects in the dienone-phenol rearrangement are in progress.

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[8] *Cf.* discussion in ref. 2.