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## The Dienone-Phenol Rearrangement

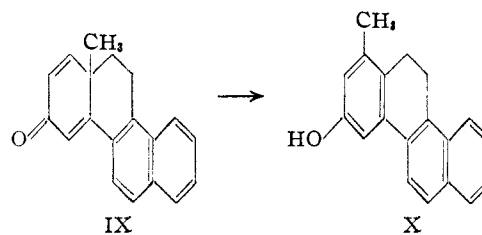
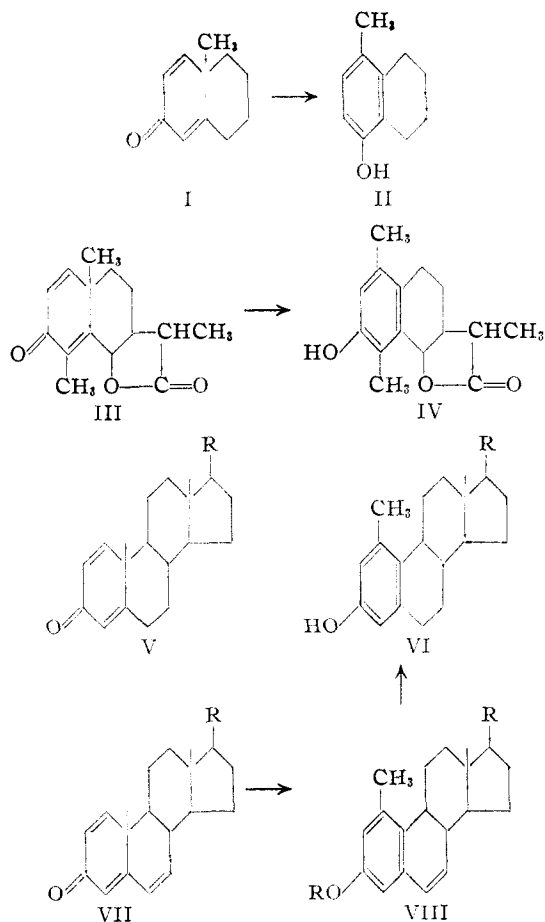
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9-Methyl-3-keto- $\Delta^{1,2;4,10}$ -hexahydronaphthalene (I) can be converted into the corresponding  $\Delta^{1,2;4,10;5,6}$ -tetrahydro derivative (XI) by *N*-bromosuccinimide bromination followed by collidine dehydrobromination. Acid-catalyzed rearrangement of this trienone and catalytic hydrogenation of the product yielded 1-methyl-3-hydroxy-5,6,7,8-tetrahydronaphthalene (XIII). This sequence of reactions not only proves the course of the acid-catalyzed rearrangement of steroidal 1,4,6-trien-3-ones but also demonstrates that the presence of a double bond in conjugation to the 1,4-dien-3-one system causes the dienone-phenol rearrangement to proceed by migration of the angular methyl group rather than the secondary alkyl group.

Recently, Woodward and Singh<sup>1</sup> have shown that the dienone-phenol rearrangement of the naphthalenic dienone I leads to the 1-methyl-4-hydroxyphenol(II) rather than the 3-hydroxy isomer XIII, which would have been expected by analogy to the santonin-desmotroposantonin (III  $\rightarrow$  IV) rearrangement.<sup>2</sup> This in turn has thrown open to question the 1-methyl-3-hydroxy structure

VI assigned to a considerable number of dienone-phenol rearrangement products of steroidal 1,4-dien-3-ones (V).<sup>3</sup>

Subsequently, it was demonstrated<sup>4,5</sup> that steroidal 1,4,6-trien-3-ones (VII)<sup>6</sup> on rearrangement, followed by hydrogenation of the 6-7 double bond (of VIII) yield phenols, different from those obtained on rearrangement<sup>3</sup> of 1,4-dien-3-ones (V), and which are believed to be the authentic 1-methyl-3-hydroxyphenols (VI) of the steroid series on the basis of: (a) formal analogy to the proved rearrangement in the chrysene series (IX  $\rightarrow$  X)<sup>7</sup>; (b) consideration of the reaction mechanism<sup>4,4</sup>; and (c) the physical and biological properties of the new steroidal phenols (alkali-solubility, estrogenic activity). It has now been possible to prove this supposition by studying the reaction in the naphthalene series.



As has already been illustrated in the steroid series,<sup>8</sup> *N*-bromosuccinimide bromination of a 1,4-dien-3-one (V) leads to the corresponding 6-bromo derivative, which can be dehydrobrominated with collidine to yield the corresponding 1,4,6-trien-3-one (VII), characterized by the typical ultraviolet absorption maxima at 222, 256 and 298  $m\mu$ . Application of this method to 9-methyl- $\Delta^{1,2;4,10}$ -hexahydronaphthalene (I)<sup>1</sup> (ultraviolet maximum<sup>1</sup> at 240  $m\mu$ ) afforded in 65% yield 9-methyl-3-keto-

(3) Cf. Inhoffen, *Angew. Chem.*, **59**, 207 (1947), and Djerassi and Scholz, *J. Org. Chem.*, **13**, 697 (1948), for leading references.

(4) Djerassi, Rosenkranz, Romo, Pataki and Kaufmann, *This Journal*, **72**, 4540 (1950).

(5) Romo, Djerassi and Rosenkranz, *J. Org. Chem.*, **15**, 896 (1950).

(6) Djerassi, Rosenkranz, Romo, Kaufmann and Pataki, *This Journal*, **72**, 4534 (1950).

(7) Wilds and Djerassi, *ibid.*, **68**, 1715 (1946).

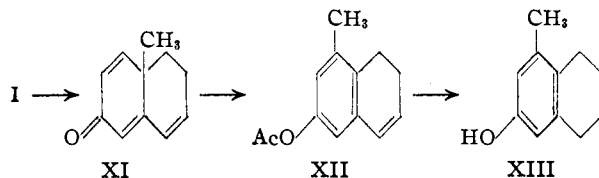
(8) Kaufmann, Pataki, Rosenkranz, Romo and Djerassi, *ibid.*, **72**, 4531 (1950).

(1) Woodward and Singh, *This Journal*, **72**, 494 (1950).

(2) Cf. Huang-Minlou, Lo and Chu, *ibid.*, **65**, 1780 (1943), and references cited therein.

$\Delta^{1,2;4,10;5,6}$ -tetrahydronaphthalene (XI), which exhibited maxima at 220, 252 and 298  $m\mu$  in good agreement with the values obtained in the steroid series.<sup>6</sup> Similarly, the 2,4-dinitrophenylhydrazone of the naphthalenic trienone XI possessed maxima at 314  $m\mu$  ( $\log \epsilon$  4.02) and 410  $m\mu$  ( $\log \epsilon$  4.76) as was to be expected on the basis of earlier work in the steroid series.<sup>9</sup> Warming of the trienone XI with acetic anhydride-*p*-toluenesulfonic acid produced an oily acetate with u. v. maxima at 262 and 320  $m\mu$  in accordance with the expression XII,<sup>10</sup> and catalytic hydrogenation now led to the known 1-methyl-3-hydroxy-5,6,7,8-tetrahydronaphthalene (XIII).<sup>1,11</sup>

It is clear, therefore, that the presence of an additional double bond in conjugation to the 1,4-dien-3-one system (VII, IX, XI) causes the dienone-phenol rearrangement to proceed by migration of the angular methyl group (VIII, X, XII) in contrast to the migration of the secondary alkyl substituent<sup>1</sup> of simple 1,4-dien-3-ones such as I and V. The mechanism of these changes has already been discussed.<sup>1,4,12</sup>



### Experimental<sup>13</sup>

#### 9-Methyl-3-keto- $\Delta^{1,2;4,10;5,6}$ -tetrahydronaphthalene (XI).

—A mixture of 4.3 g. of 9-methyl-3-keto- $\Delta^{1,2;4,10;5,6}$ -hexahydronaphthalene (I),<sup>1</sup> 6.0 g. of *N*-bromosuccinimide, 0.1 g. of benzoyl peroxide and 100 cc. of dry carbon tetrachloride was refluxed with illumination from a G.E. RSP2 Photospot lamp for 30 minutes. After cooling, the succinimide was filtered, the solvent removed quickly under reduced pressure and the residue was refluxed with 25 cc. of  $\gamma$ -collidine for 15 minutes. Dilution with ether and filtration afforded 5.1 g. (95%) of collidine hydrobromide. The

(9) Djerassi and Ryan, *THIS JOURNAL*, **71**, 1000 (1949).

(10) 6-Dehydro steroids of type VIII exhibit similar maxima (ref. 4, 5, 6).

(11) We are greatly indebted to Prof. R. B. Woodward, Harvard University, for supplying us with an authentic sample of this phenol for comparison purposes.

(12) Arnold, Buckley and Richter, *THIS JOURNAL*, **69**, 2322 (1947).

(13) We are grateful to Srta. Amparo Barba for the microanalyses and to Srta. Paquita Revaque for the spectral determinations. Unless noted otherwise, ultraviolet spectra were measured in 95% ethanol solution.

ether filtrate was washed free of collidine with dilute hydrochloric acid, dried and evaporated. Fractional distillation through a short Vigreux column yielded 2.8 g. (65%) of the trienone XI as a pale yellow oil with b.p. 89–90° at 0.02 mm.,  $n_D^{20}$  1.5901, ultraviolet maxima at 220  $m\mu$  ( $\log \epsilon$  4.02), 252  $m\mu$  ( $\log \epsilon$  4.03) and 298  $m\mu$  ( $\log \epsilon$  4.16).

*Anal.* Calcd. for  $C_{11}H_{14}O$ : C, 82.47; H, 7.55. Found: C, 82.28; H, 7.93.

The dinitrophenylhydrazone was prepared in ethanol solution by refluxing for 5 minutes with a few drops of concd. hydrochloric acid; recrystallization from ethyl acetate gave dark vermilion crystals with m.p. 148–150°, ultraviolet maxima (chloroform) at 265  $m\mu$  ( $\log \epsilon$  4.18), 314  $m\mu$  ( $\log \epsilon$  4.02) and 410  $m\mu$  ( $\log \epsilon$  4.76). The ultraviolet maxima of the dinitrophenylhydrazone of Woodward's dienone I<sup>1</sup> were at 302  $m\mu$  ( $\log \epsilon$  3.68) and 400  $m\mu$  ( $\log \epsilon$  4.78) in good agreement with expectation.<sup>9</sup>

*Anal.* Calcd. for  $C_{17}H_{16}O_4N_4$ : C, 59.99; H, 4.74. Found: C, 60.05; H, 5.00.

**1-Methyl-3-hydroxy-5,6,7,8-tetrahydronaphthalene (XIII).**—A solution of 0.5 g. of the above trienone XI and 0.1 g. of *p*-toluenesulfonic acid in 15 cc. of acetic anhydride was heated on the steam-bath for 4 hours. After hydrolyzing the excess anhydride with water, the oily acetate XII was taken up with ether and washed with sodium carbonate, dried and evaporated; yield 0.41 g., ultraviolet maxima at 262  $m\mu$  ( $\log \epsilon$  3.83) and 302  $m\mu$  ( $\log \epsilon$  3.55).<sup>10</sup> The oil was shaken in ethyl acetate solution in an atmosphere of hydrogen with 0.100 g. of palladium-on-charcoal catalyst until the hydrogen uptake ceased (one hour), the catalyst was filtered, the solvent evaporated and the residue refluxed for 8 hours under nitrogen with 5.0 cc. of concd. hydrochloric acid and 60 cc. of ethanol. Dilution with water, extraction with ether, evaporation of the solvent and vacuum sublimation gave 0.14 g. of colorless solid with m.p. 98–101°. Recrystallization from hexane-ether yielded the analytical sample of 1-methyl-3-hydroxytetrahydronaphthalene (XIII) with m.p. 103–104°, depressed on admixture with an authentic specimen of this substance (m.p. 104–105°<sup>1,11</sup>); the ultraviolet absorption spectrum was typical of that of a phenol, with a maximum at 280  $m\mu$  ( $\log \epsilon$  3.32) and a minimum at 250  $m\mu$  ( $\log \epsilon$  2.45).

*Anal.* Calcd. for  $C_{11}H_{14}O$ : C, 81.36; H, 8.71. Found: C, 81.32; H, 8.64.

The *p*-nitrobenzoate was prepared by heating the phenol XIII (both the rearrangement product and the authentic sample<sup>11</sup> gave the same derivative) with twice its weight of *p*-nitrobenzoyl chloride in pyridine for 1 hour and recrystallizing the product from methanol; m.p. 116–118°.

*Anal.* Calcd. for  $C_{18}H_{17}O_4N$ : C, 69.44; H, 5.51. Found: C, 69.76; H, 5.78.

For comparison, 1-methyl-4-hydroxy-5,6,7,8-tetrahydronaphthalene (II)<sup>1</sup> with m.p. 86–87° was converted into its *p*-nitrobenzoate, which showed m.p. 146–148° after recrystallization from chloroform-methanol.

*Anal.* Calcd. for  $C_{18}H_{17}O_4N$ : C, 69.44; H, 5.51. Found: C, 69.63; H, 5.47.

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