carbethoxyporphyrin and 100 mg. of potassium hydroxide were suspended in 25 cc. of ethylene glycol. The mixture was heated in a metal-bath at 200° for five hours, then cooled and diluted with water. The solution was acidified with 0.4 cc. of concentrated hydrochloric acid and the porphyrin removed by filtration, dried, dissolved in hot pyridine and precipitated with three volumes of methanol. On cooling, 55 mg. of impure porphyrin was obtained. This was purified for analysis by repetition of the pyridine, methanol treatment and then by crystallization from a chloroform–methanol mixture.

Anal. Calcd. for $C_{28}H_{22}O_8N_4$: C, 61.99; H, 4.09. Found: C, 62.12; H, 4.25.

1,4,5,8-Tetramethylporphyrin (XIII). (a) **From Tetramethyltetracarbethoxyporphyrin.**—About 5 cc. of anhydrous glycerol was heated in a metal-bath to 290° and 0.1 g. of potassium hydroxide and 100 mg. of tetramethyltetracarbethoxyporphyrin added. The air was displaced by nitrogen and the mixture stirred occasionally. After two hours an additional 0.1 g. of potassium hydroxide and 3–4 cc. of glycerol were added and the mixture heated for another hour. It was then cooled, diluted with 100 cc. of water and filtered. The residue was dissolved in 40 cc. of chloroform and 50 cc. of methanol added. The yield was 38 mg. (67.5%) of crystalline porphyrin.

Anal. Calcd. for $C_{24}H_{22}N_4$: C, 78.66; H, 6.05. Found: C, 78.58; H, 5.98.

(b) **From Tetramethyltetracarboxyporphyrin.**—About 20 mg. of crude tetramethyltetracarboxyporphyrin was heated in glycerol with 0.1 g. of potassium hydroxide for two and a half hours at 290° and then isolated as described above. Less than a milligram of material was obtained.

1,4,5,8-Tetramethyl-2,3,6,7-tetrabromoporphyrin (XIV).—Twenty-five milligrams of tetramethylporphyrin was dissolved in 100 cc. of hot chloroform and to this was added about 100 mg. of bromine in chloroform. A precipitate soon appeared and methanol was added to complete its separation. The porphyrin was collected on a filter paper and crystallized from 75 cc. of hot nitrobenzene. Long, needle-like crystals appeared on cooling. These were collected and washed with chloroform; yield 39 mg. or 84%.

Anal. Calcd. for $C_{24}H_{18}N_4Br_4$: C, 42.26; H, 2.66. Found: C, 42.35; H, 2.80.

Summary

1. A new porphyrin condensation, proceeding at room temperature, has been recorded.

2. This condensation gives relatively good yields of 1,4,5,8-tetramethyl-2,3,6,7-tetracarbethoxyporphyrin, a type of porphyrin not available with earlier synthetic methods.

3. Derivatives of this porphyrin have been prepared.

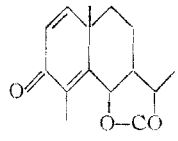
BALTIMORE 18, MD. RECEIVED SEPTEMBER 30, 1949

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

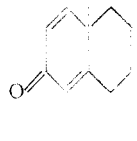
Synthesis and Rearrangement of Cyclohexadienones

BY R. B. WOODWARD* AND TARA SINGH†

Cyclohexadienones were first prepared, and many of their remarkable properties were first observed, in the course of von Auwers' classical studies on the nature of the neutral products formed through the action of chloroform and alkalies on *o*- and *p*-substituted phenols.[1] Subsequently, the establishment of the presence of a cyclohexadienone ring in the natural product santonin (I),[2] and the use of cyclohexadienone



I



II

intermediates in the aromatization of ring A of the sterol nucleus,[3] engendered renewed interest in the chemical properties of cyclohexadienones, and in methods for their synthesis. Cyclohexadienones have been prepared from phenols by von Auwers' methods, from cyclohexanones by bromination and dehydrohalogenation, and by a ring-synthetic method suggested by Paranjpe, and reduced to practice by Wilds and Djerassi[4] (*vide infra*).

In this communication, we describe a new synthetic method which we have used for the synthesis of 10-methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene (II) and demonstrate the nature of the rearrangement which this ketone undergoes under the influence of acidic reagents. The synthetic method is in effect an extension of the well-known method introduced by Robinson for the construction of polycyclic cyclohexenones by condensation of a cyclic ketone with methyl vinyl ketone, or a suitable progenitor of the latter.[5] Thus, we have found that when the sodium derivative of 2-methylcyclohexanone is condensed with methyl ethinyl ketone, the ketone (II) is produced directly, though in low yield. Pure 10-methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene is a liquid, b. p. 123–124° (3 mm.); it was characterized by the preparation of a crystalline red dinitrophenylhydrazone, m. p. 127–129°, and through its infra-

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(1) von Auwers and v. Erggelet, *Ber.*, **32**, 3598 (1899); v. Auwers and Winternitz, *ibid.*, **35**, 465 (1902); v. Auwers and Keil, *ibid.*, **35**, 4207 (1902), and many subsequent papers.

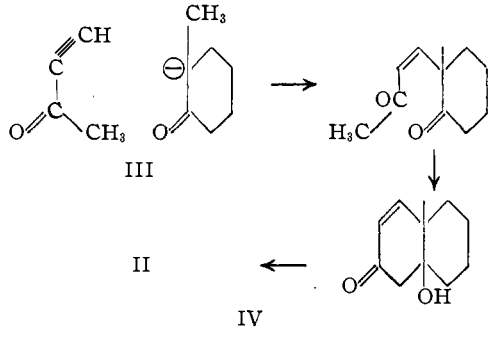
(2) Clemo, Haworth and Walton, *J. Chem. Soc.*, 1110 (1930).

(3) Inhoffen and Huang-Minlon, *Naturwissenschaften*, **26**, 756 (1938); Inhoffen, Zühlsdorff and Huang-Minlon, *Ber.*, **73**, 451 (1940); Inhoffen, *Angew. Chem.*, **53**, 473 (1940); Inhoffen and Zühlsdorff, *Ber.*, **74**, 604, 1911 (1941); Wilds and Djerassi, THIS JOURNAL, **68**, 1712 (1946); Inhoffen, *Angew. Chem.*, **59A**, 207 (1947); Djerassi and Scholz, THIS JOURNAL, **70**, 1911 (1948); Inhoffen and Stoeck, *Ann.*, **563**, 127 (1949); Inhoffen, Stoeck and Lübcke, *ibid.*, **563**, 177 (1949).

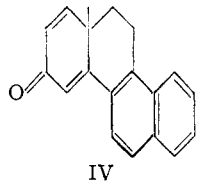
(4) Wilds and Djerassi, THIS JOURNAL, **68**, 1716 (1946).

(5) du Feu, McQuillin and Robinson, *J. Chem. Soc.*, 53 (1937), and many subsequent papers.

red (Fig. 2) and ultraviolet spectra (Fig. 1). The latter (λ_{max} = 240 mμ (log ϵ = 4.1)) is very similar to that of 10-dichloromethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene, prepared from ar-β-tetralol by the action of chloroform and alkali.[6] It seems clear that the synthesis involves a Michael addition of the cyclic ketone anion (III) to the α,β-unsaturated system of the ethinyl ketone, followed by an internal aldol condensation and dehydration; it is not impossible that the order of the steps may be reversed.



The ketone (II) was also prepared, in rather better yield, from 2-methyl-2-formylcyclohexanone by condensation with acetone, following the elegant method used by Wilds and Djerassi for the synthesis of the tetracyclic ketone (IV).[4] The use of this method, without the specific experimental conditions now known to be essential to



its success, for the synthesis of the ketone described in this paper was initially claimed by Paranjpe, *et al.*[7] However, the description of the ketone given by the Indian workers and, in particular, the phenomena which they claim to have observed in connection with the rearrangement of their substance (*vide infra*), make it abundantly clear that they did not in fact have the ketone (II) in hand.

We turn now to the remarkable rearrangement brought about by the action of acidic reagents on (II). It seems firmly established that santonin (I) undergoes acid catalyzed rearrangement to desmotroposantonin (VII) with migration of a methyl group to an adjacent position.[2] The mechanism of this change is clear; the conjugate acid (Va ↔ Vb, *etc.*) from santonin suffers a change of the Wagner–Meerwein type, and the resulting species (VI) loses a proton, with concomitant aromatization. Wilds and Djerassi

(6) Woodward, THIS JOURNAL, **62**, 1208 (1940).

(7) Paranjpe, Phalnikar, Bhide and Nargund, *Rasayanam*, **1**, 233 (1943); *cf. C. A.*, **38**, 4266 (1944).

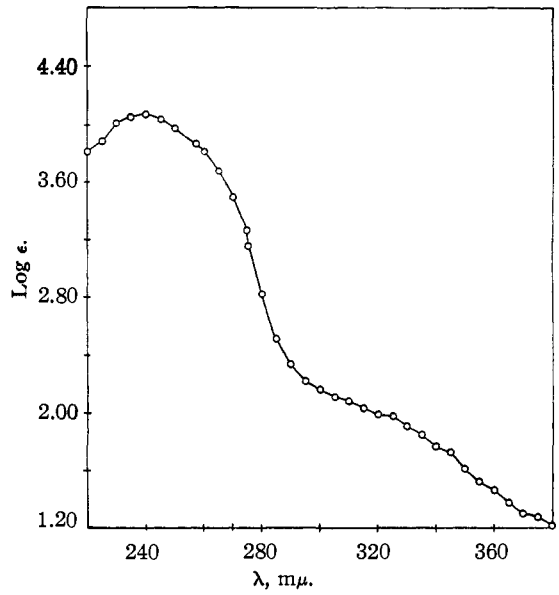
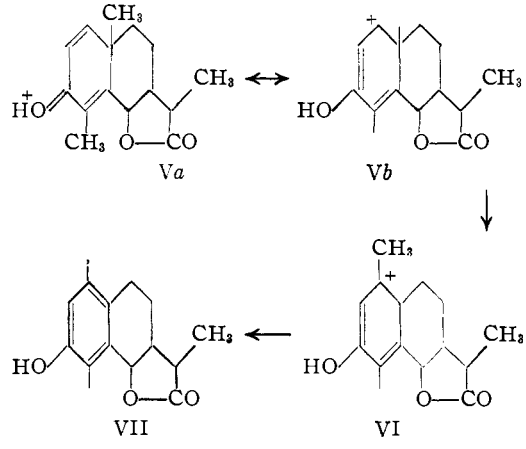
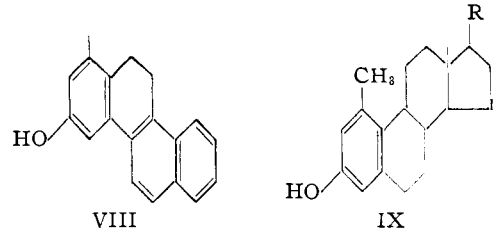


Fig. 1.—Ultraviolet absorption spectrum of 10-methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene in ethanol.

showed that the cyclohexadienone (IV) undergoes a precisely similar rearrangement to the



phenol (VIII), whose structure was rigorously proven by synthesis.[4] These changes have been used in support of the assignment of the structures (IX, R = C_8H_{17} *or* OH) to the phenolic rearrangement products[3] from $\Delta^{1,4}$-cholestadienone-3 (XXXIII, R = C_8H_{17}) and $\Delta^{1,4}$-androstadienol-17-one-3 (XXXIII, R = OH). Arnold has shown recently that a similar change takes



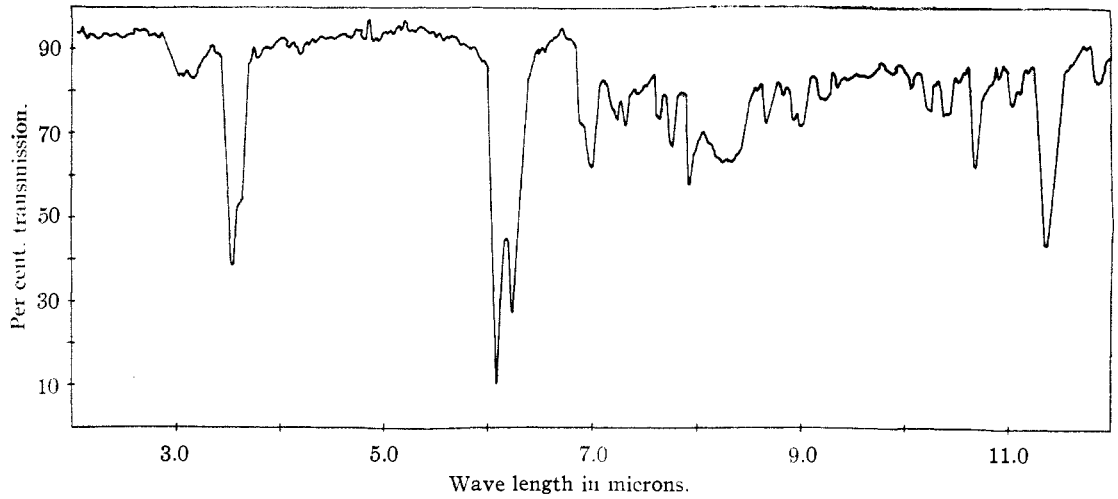
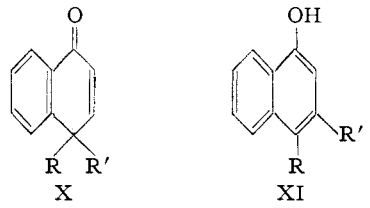
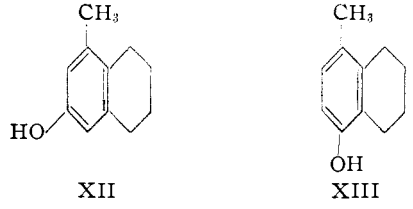


Fig. 2.—Infrared absorption spectrum of 10-methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene in chloroform.

place in the conversion of ketones of the structure (X) to the phenols (XI).[8] In the light of this con-



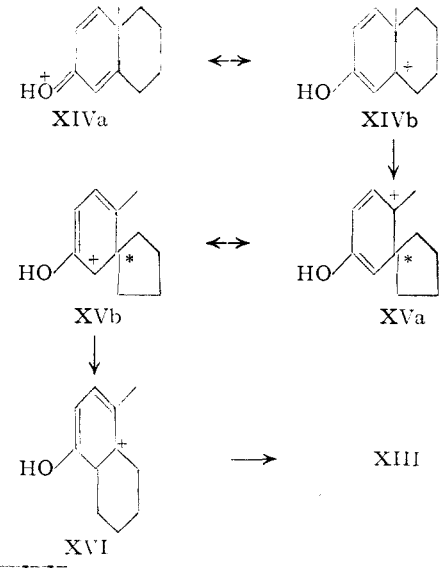
siderable body of evidence, it would be expected that the dienone (II) would rearrange in the presence of acidic reagents to the phenol (XII). In fact, the reaction takes a very different course.



When (II) is treated with acetic anhydride containing a drop of sulfuric acid, it is converted smoothly into a phenol acetate, m. p. 82°, which is hydrolyzable to a phenol, $C_{11}H_{14}O$, m. p. 87.5–88.5°. The phenol (XII) has been synthesized by Prelog,[9a] by Solov'eva and Preobrazhenskii[9b] and in this Laboratory by demethylation of the Clemmensen reduction product of 7-methoxy-5-methyltetralone-1.[10] The substance prepared by these methods at 105° (105°,[9b] 108°[9a]) and is clearly not identical with the phenol from (II).[11]

The rearrangement product was ultimately shown to be 4-methyl-*ar*-1-tetralol (XIII) by direct comparison with a sample of the latter prepared by synthesis (γ-(2-methoxy-5-methylphenyl)-butyric acid[12] → 5-methoxy-8-methyltetralone-1 → 5-methoxy-8-methyl-1,2,3,4-tetrahydronaphthalene → (XIII)).

It is now clear that in the rearrangement of the ketone (II) the methyl group retains its position, and that the ring methylene group (C.5) migrates. The changes may involve one of two processes: (i) the conjugate acid (XIVa ↔ XIVb, etc.)



(8) Arnold and Buckley, THIS JOURNAL, **71**, 1781 (1949); Arnold, Buckley and Richter, *ibid.*, **69**, 2322 (1947).

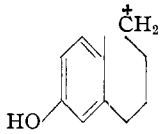
(9) (a) Prelog, Metzler and Jeger, *Helv. Chim. Acta*, **30**, 675 (1947); (b) *J. Gen. Chem. U. S. S. R.*, **15**, 60 (1945) (*cf. C. A.*, **40**, 1820 (1946)).

(10) Ruzicka and Sternback, *Helv. Chim. Acta*, **23**, 360 (1940).

(11) Paranjpe, *et al.* (ref. 7), claim to have prepared the phenol (XII) by the rearrangement of the dienone (II). The phenol was described as melting at 70°, and the claim was made that identity was established by comparison with an authentic sample synthesized from 7-methoxy-5-methyltetralone-1 by the method which we have used. It is now clear that these investigators could not have had the phenol (XII) in hand; further the phenol actually obtained from the rearrangement of (II) does not agree in properties (*vide supra*) with the substance described by Paranjpe. We can only conclude that the Indian group did not succeed in preparing the cyclohexadienone (II); the identity of the substances described by them remains obscure for the present.

(12) Desari and Wali, *Proc. Ind. Acad. Sciences*, (A) **6**, 144 (1937) (*cf. C. A.*, **23**, 509 (1938)).

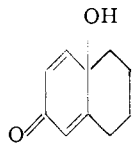
undergoes a normal Wagner–Meerwein rearrangement to (XVa—XVb, etc.); the distribution of positive charge in the latter hybrid cation permits a further Wagner–Meerwein change in which one *or the other* of the two methylene groups attached to the quaternary atom (starred) may move. The resulting species (XVI) then loses a proton to give the observed product (XIII). (ii) Alternately, the migrating group accepts the positive charge from the ring, and the cationic center in the resulting intermediate (XVII) attacks the ring in the position ortho to the hydroxyl group in a normal electrophilic substitution reaction. Differentiation between the possible



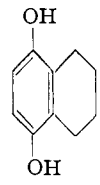
XVII

mechanisms is of considerable importance in connection with the detailed mechanism of Wagner–Meerwein rearrangements in general, and the matter deserves clarification through the study of appropriately substituted dienones; such experiments are now under way in our Laboratory.

It is worthy of note that a number of recorded isomerizations undoubtedly involve migrations similar in type to that established here for the rearrangement of the dienone (II). Most closely analogous is the rearrangement of (XVIII) to the hydroquinone (XIX).[13] The transformation

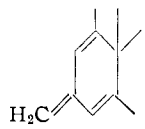


XVIII

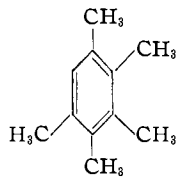


XIX

of the semibenzene (XX) to pentamethylbenzene (XXI)[14] is another case. A more involved but

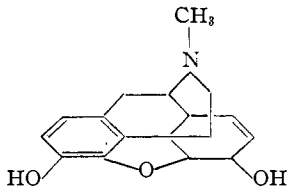


XX

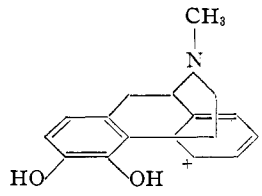


XXI

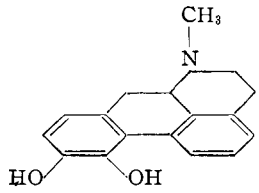
in principal identical case is presented by the transformation of morphine (XXII), undoubtedly through an intermediate such as (XXIII), to apomorphine (XXIV).[15] In this case it is of interest that the migration either of the aromatic



XXII

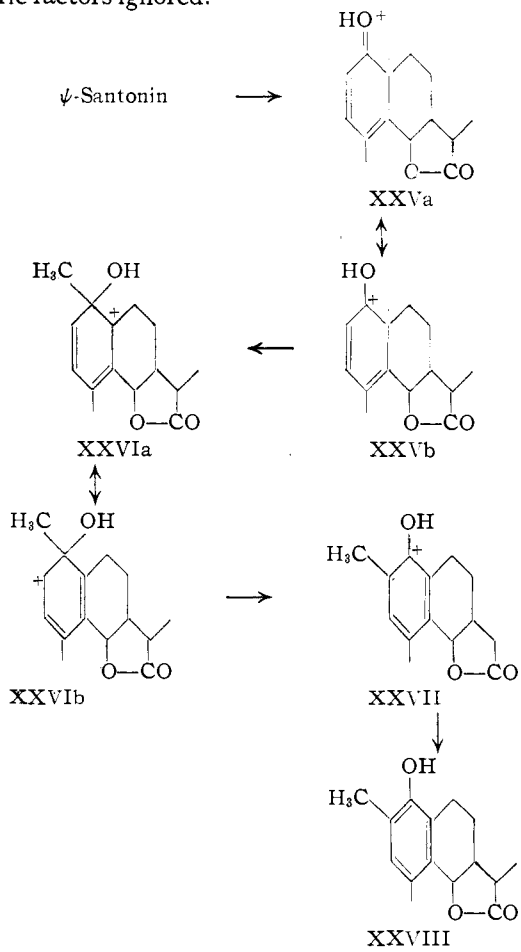


XXIII



XXIV

ring or of the ethanamine chain would lead to the same product. However, steric factors require the ether oxygen atom in (XXII) and in the immediate precursor of (XXIII), to be *trans* to the ethanamine chain; since the migration is very probably concerted with the breaking of the C.5–O bond, it seems likely that it is the *trans*-disposed chain which moves, rather than the aromatic group, whose migration tendency would be larger than that of the saturated chain, were steric factors ignored.



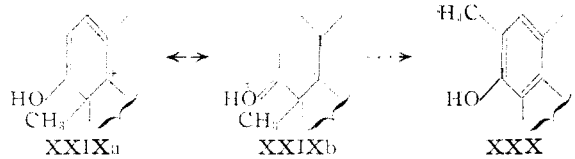
(13) Asahina, *Ber.*, **71**, 1424 (1938).

(14) von Auwers and Ziegler, *Ann.*, **425**, 279 (1921).

(15) *Cf.* Henry, "Plant Alkaloids," Blakiston's Son & Co., Inc., Philadelphia, Pennsylvania, 1949, p. 214, *ff.* for general references, and Small, Faris and Mallonee, *J. Org. Chem.*, **5**, 334 (1940), for a recent discussion of the mechanism of the change.

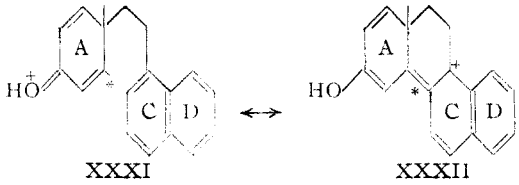
The formation of desmotropo-ψ-santonin (XXVIII) from ψ-santonin[16] may well involve a rearrangement essentially similar in type to those discussed above. Thus, XXVIII may be formed from a progenitor possessing the carbon skeleton typical of santonin (I) and its congeners through the series (XXV)–(XXVIII).

It is of interest to examine the circumstances which bring about the 1,2-migration of a methyl group in some cyclohexadienones, and the 1,3-migration of another group in others. In the case of santonin (I) a change exactly analogous to that observed with (II) is of course impossible, since the position to which the wandering group must become attached (C.1) already bears a substituent. Thus, changes parallelling II—XIII (above) would lead in this case to an intermediate (XXIXa $\leftrightarrow$ XXIXb), and the completion of the reaction would require a further series of changes (XXIX—XXX) analogous to those outlined above (XXV—XXVII) for the case of ψ-santonin. Although qualitatively such a scheme is not implausible, the whole process would



XXIXa XXIXb XXX

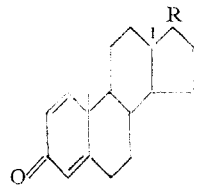
be so complicated a one, probably involving the traversal of a large number of energy barriers, that it is perhaps not surprising that the much simpler 1,2-shift of the methyl group takes precedence in this case.[17] Similar circumstances cannot be adduced to rationalize the well-authenticated shift of a methyl group in the rearrangement of the hydrochrysene ketone (IV) to (VIII). In this case we suggest the following considerations. In the conjugate acid (XXXI) the positive charge will be distributed not only over ring A,



XXXI XXXII

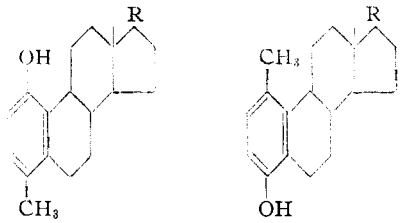
but also through rings C and D (*cf.* XXXII and four other such forms). This circumstance will confer considerable double bond character on the bond (starred) joining rings A and C. Now whatever the detailed mechanism of the reaction, a shift in this case analogous to that involved in the change (II)→(XIII) must necessarily involve rotation about the A–C bond. Since the partial double bond character of that bond will provide a considerable barrier to rotation, the rearrangement which occurs in the simple case is here retarded, and methyl migration supervenes.

Finally, we consider the rearrangement of the steroid dienones (XXXIII, R = C_8H_{17} *or* OH), which has been considered hitherto to involve



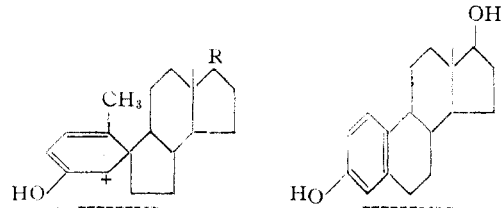
XXXIII

methyl migration.[3] We discern in these cases no special factors which favor the simple 1,2-shift over the type of rearrangement demonstrated in this communication to be characteristic for the simple model dienone (II). We observe that the latter reaction in these cases can lead to phenols of the structures (XXXIV, R = C_8H_{17} *or* OH) or (XXXV, R = C_8H_{17} *or* OH). Of these two possibilities we prefer XXXIV; rearrangement by mechanism (ii) (above) would lead directly



XXXIV XXXV

to that product, and should the reaction proceed by mechanism (i), through an intermediate (XXXVI), it may be expected that the secondary group will migrate more readily in the steps which



XXXVI XXXVII

complete the change than will the primary group. While there is at present no rigorous evidence which demonstrates that these phenols are correctly represented by (XXXIV, R = C_8H_{17} *or* OH) rather than (IX, R = C_8H_{17} *or* OH), there is strong presumptive evidence that such is the case. Thus, these substances possess marked cryptophenolic properties,[3,18] as compared with

(16) Clemo and Cocker, *J. Chem. Soc.*, 30 (1946); Cocker, Cross and Lipman, *Nature*, **163**, 288 (1949).

(17) It will be observed that the series of changes just outlined provides a theoretical path for the conversion of santonin to an aromatic substance having the 2,4-dimethyl-1-naphthol skeleton found in *desmotropo-ψ-santonin*. These circumstances suggest the interesting, though probably remote, possibility that ψ-santonin is much more closely related to santonin than has been suspected, and that a subtle constitutional difference between the two molecules leads to rearrangement by the simple 1,2-shift in the latter case, and by the more complicated path in the former.

(18) Drs. C. R. Scholz and Carl Djerassi have informed us privately that they have confirmed these observations.

estradiol (XXXVII), of which (IX, R = OH) is simply the 1-methyl derivative. Further, the phenol from (XXXIII, R = OH) is completely devoid of estrogenic activity[3,18]; this fact must be considered most remarkable if the methylestradiol structure (IX, R = OH) be accepted, particularly in view of the relative non-specificity in this type of hormonal action. Finally, Inhoffen and Zühlsdorff converted the phenol from (XXXIII, R = C_8H_{17}) into a *mono*-bromo derivative, and in an attempt to demonstrate that a second position ortho to the phenolic hydroxyl group was open, treated the bromo derivative with sodium nitrophenyldiazotate; while coupling did in fact take place, *the bromine atom was displaced in the reaction.* Such behavior is characteristic of bromophenols with no open ortho or para positions,[19] and although a special feature[20] was present in the case studied by the German investigators, the experiment may be considered to provide strong evidence in favor of the structure (XXXIV, R = C_8H_{17}) rather than (IX, R = C_8H_{17}) for the phenol, since a monobromo derivative from (IX) would very probably have given a normal coupling product in which the bromine atom was retained, or (with so powerful a coupling agent) a bis azo compound with loss of bromine. We conclude that the phenols formed by the isomerization of the steroid dienones (XXXIII) very probably possess either structure (XXXIV) or (XXXV), of which the former is the more likely.

Experimental

Methylethinylcarbinol, b. p. 108.5–110° (758 mm.), was prepared in 58% yield by the addition of sodium acetylide to acetaldehyde in liquid ammonia.[21] The alcohol was oxidized to **methyl ethinyl ketone**, b. p. 84–86°, essentially according to the method of Bowden, *et al.*,[22] in 33% yield. **2-Methylcyclohexanone**, b. p. 165–166°, was most smoothly prepared from 2-methylcyclohexanol by an adaptation of the above oxidation procedure.[22]

10-Methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene (II)

A.—By condensation of 2-methylcyclohexanone and methyl ethinyl ketone: A mixture of 30 g. of 2-methylcyclohexanone, 4.8 g. of sodium hydride and 200 cc. of anhydrous ether was stirred with glass beads for forty-eight hours, after which no further hydrogen was evolved. The resulting suspension of the sodium enolate of methylcyclohexanone was cooled in an ice-bath and a solution of 13.6 g. of methyl ethinyl ketone in 50 cc. of anhydrous ether was added gradually. The color of the reaction mixture changed rapidly from yellow to dark red. Stirring was continued for three to four hours at ice-bath temperature and then for six hours at room temperature. The reaction mixture was then decomposed with dilute hydrochloric acid in the cold and extracted repeatedly with ether. The ether extracts were washed with water and dilute sodium bicarbonate solution, and then dried over anhydrous sodium sulfate. The residue after concentration of the ether solution was separated into the following fractions by distillation *in vacuo:* (1) Recovered 2-methylcyclohexanone; (2) b. p. 115–125° (5 mm.) (3.0 g.); (3) b. p. 125–150° (5 mm.) (8.0 g.). Fraction (2) consisted largely of the desired ketone and gave in good yield a scarlet 2,4-dinitrophenylhydrazone, m. p. 127–129°.

Anal. Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.70; H, 5.27; N, 16.37. Found: C, 59.68; H, 5.58; N, 16.44.

The corresponding fractions (2) from a number of experiments were combined and fractionated through a sixty-plate concentric tube column. The fraction boiling at 123–124° (3 mm.) was pure 10-methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene. It was convertible in quantitative yield to the above mentioned 2,4-dinitrophenylhydrazone and absorbed the theoretical volume of hydrogen on catalytic hydrogenation. Its ultraviolet spectrum (Fig. 2) possessed a maximum at 240 mμ (log ε = 4.1). The infrared spectrum of the ketone is shown in Fig. 1. The pure ketone is almost colorless but darkens readily on exposure to air and light.

B. From 2-Methyl-2-formylcyclohexanone.—2.8 g. of 2-formyl-2-methylcyclohexanone,[23] 25 cc. of pure acetone, 1.7 g. of piperidine and 1.2 g. of acetic acid were heated under reflux for seventy-two hours. Most of the acetone was then removed from the orange reaction-mixture at the pump and the residue was taken up in ether; the ether solution was washed with dilute hydrochloric acid, water, bicarbonate solution, again water, dried over anhydrous sodium sulfate and concentrated. The residue was dissolved in 25 cc. of absolute methanol and heated under reflux for six hours, after the addition of 3 cc. of 50% aqueous potassium hydroxide. After removal of the alcohol under reduced pressure the residue was diluted with water and extracted with ether. The dried concentrated ether solution left a slightly orange oil from which the 2,4-dinitrophenylhydrazone of II could be obtained in 62% yield.

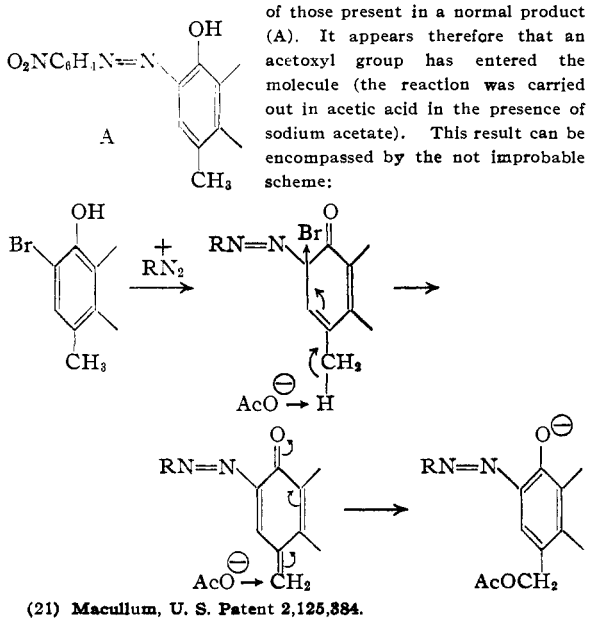
Hydrogenation of the Dienone II.—900 mg. of the pure ketone was dissolved in 30 cc. of absolute ethanol and shaken with hydrogen in the presence of reduced platinum oxide at 23.5° and 760 mm. 276 cc. of hydrogen (theory, 270 cc.) were absorbed in twenty-five minutes. After removal of the catalyst and the alcohol the clear colorless residue was converted into the 2,4-dinitrophenylhydrazone, which crystallized from absolute ethanol in clusters of silky orange needles, m. p. 125.5–127°.

Anal. Calcd. for $C_{17}H_{22}N_4O_4$: C, 58.95; H, 6.36; N, 16.19. Found: C, 58.49; H, 6.31; N, 16.18.

By hydrogenation of 10-methyl-2-keto-$\Delta^{1(9)}$octalone, du Feu, McQuillin and Robinson obtained[24] a methyl-β-

(19) *Cf.* Hewett and Mitchell, *J. Chem. Soc.*, 1167 (1906); Huang-Minlon, Lo and Chen, THIS JOURNAL, **66**, 1954 (1944).

(20) The coupling product contained the atoms $C_2H_2O_2$ in excess of those present in a normal product (A). It appears therefore that an acetoxyl group has entered the molecule (the reaction was carried out in acetic acid in the presence of sodium acetate). This result can be encompassed by the not improbable scheme:



(21) **Macullum, U. S. Patent 2,125,384.**

(22) Bowden, Heilbron, Jones and Weedon, *J. Chem. Soc.*, 39 (1946).

(23) Sen and Mondal, *J. Ind. Chem. Soc.*, **5**, 609 (1928).

(24) du Feu, McQuillin and Robinson, *J. Chem. Soc.*, 53 (1937).

decalone which gave a dinitrophenylhydrazone, m. p. 152–152.5°. It is possible that our dinitrophenylhydrazone is a stereoisomer or a polymorph of that obtained by du Feu, *et al.*, or that our saturated ketone is a stereoisomer of that obtained by the English workers.

Rearrangement of 10-Methyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene.—162 mg. of the ketone was dissolved in 10 cc. of acetic anhydride, and 100 mg. of concentrated sulfuric acid dissolved in 3 cc. of acetic anhydride was added. The reaction was slightly exothermic and the color changed through pink, red, and reddish-green to bluish-green. The reaction mixture was allowed to stand at room temperature for six hours and then shaken with 40 cc. of cold water until all of the acetic anhydride had been hydrolyzed. The acetate of the phenol XIII separated as a crystalline mass which was removed and crystallized from dilute ethanol; 120 mg. of long shining needles, m. p. 82°, was obtained.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.23; H, 7.92.

Sixty mg. of the above acetate dissolved in 6 cc. of absolute ethanol was heated under reflux for six hours with 0.5 cc. of concentrated hydrochloric acid. After removal of the solvent *in vacuo* the residue was taken up, washed with water and dried over anhydrous sodium sulfate. Evaporation of the ether left a thick oil which solidified on cooling and scratching. Crystallization from petroleum ether gave 30 mg. of the pure phenol (XIII) as shining needles, m. p. 87.5–88.5°.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.48; H, 8.64. Found: C, 81.36; H, 8.71.

Synthesis of 4-Methyl-ar-2-tetralol.—To a cooled solution of 4.2 g. of γ-(4-methoxy-2-methylphenyl)-butyric acid[12] in 20 cc. of benzene, 5.5 g. of phosphorus pentachloride was added in small portions with shaking. The mixture was allowed to come to room temperature and let stand for two hours with occasional shaking. To the cooled mixture, 3.8 cc. of stannic chloride in 10 cc. of anhydrous benzene was then added in small portions. After half an hour the reaction mixture, which contained a greenish-yellow precipitate, was poured on to crushed ice. Ether and a small amount of concentrated hydrochloric acid was then added. After shaking until two clear layers were obtained the ether–benzene layer was separated and washed successively with dilute hydrochloric acid, water, dilute sodium hydroxide and again with water. The residue from the dried concentrated extract crystallized overnight. On crystallization from petroleum ether, 2 g. (50%) of 7-methoxy-5-methyltetralone-1, m. p. 56–57°, was obtained. Ruzicka and Sternback,[10] who prepared the ketone by cyclization of the butyric acid with phosphorus pentoxide in benzene, report m. p. 56–57°.

Five grams of mossy zinc, 0.5 g. of mercuric chloride, 0.3 cc. of concentrated hydrochloric acid and 10 cc. of water was stirred together for five minutes. The water was decanted and 2 cc. of water, 4 cc. of concentrated hydrochloric acid, 2 cc. of toluene, 1.0 g. of the above tetralone and a few drops of glacial acetic acid were added consecutively to the amalgamated zinc. The reaction mixture was heated under reflux for forty hours. Fresh additions of 1 cc. of concentrated hydrochloric acid were made at intervals of eight to ten hours. The reaction mixture was then diluted with 25 cc. of water and extracted with ether. The residue from the dried concentrated ether extract was taken up in 10 cc. of glacial acetic acid and 3 cc. of 48% hydrobromic acid. After the reaction mixture had been heated under reflux for six hours, the acetic acid was removed *in vacuo*. The reddish-colored residue was suspended in water, just neutralized with dilute alkali and extracted with ether. The dried concentrated ether extract left an oily residue which solidified on cooling and scratching. On recrystallization from petroleum ether containing a little ether, 4-methyl-ar-2-tetralol, m. p. 104–105°, was obtained.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.36; H, 8.71. Found: C, 81.23; H, 8.60.

Solov'eva and Preobrazhenskii[9] report m. p. 104–105° and Prelog, *et al.*,[9] report m. p. 108°. On admixture with the phenol from the rearrangement of the ketone II, m. m. p. 62–78°.

Synthesis of 4-Methyl-ar-1-tetralol.—In our hands, the condensation of *p*-cresol methyl ether with succinic anhydride according to method of Desai and Wali[12] gave largely β-(2-hydroxy-5-methylbenzoyl)-propionic acid. The demethylation was complete when two and one-half moles of aluminum chloride was used. The acid crystallized from benzene in shining leaflets, m. p. 135–136°, and gave a bluish-violet color with ferric chloride.

Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.46; H, 5.77. Found: C, 63.27; H, 5.88.

The hydroxy-keto acid could not be methylated with methyl sulfate and alkali. Clemmensen reduction according to the procedure used above for the reduction of 7-methoxy-5-methyltetralone-1 proceeded smoothly. From 50 g. of keto acid, 30 g. of once-recrystallized (toluene) butyric acid was obtained. After several recrystallizations from toluene, **γ-(2-hydroxy-5-methylphenyl)-butyric acid** separated as bold cubes, m. p. 88–89°.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.04; H, 7.22. Found: C, 67.90; H, 7.5.

Unlike the corresponding keto acid, the butyric acid could be methylated readily with methyl sulfate and alkali in the usual fashion. The resulting γ-(2-methoxy-5-methylphenyl)-butyric acid, m. p. 65–66°, was also obtained, following Desai and Wali,[12] by Clemmensen reduction of β-(2-methoxy-5-methylbenzoyl)-propionic acid, obtained from *p*-cresol methyl ether and succinic anhydride under the conditions described by Rosenmund and Shapiro.[25]

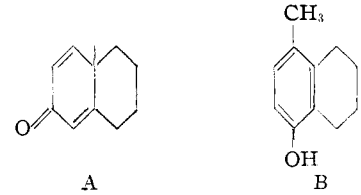
When 5 g. of the acid was cyclized as described above for the isomeric butyric acid, 3 g. of crude oily 5-methoxy-8-methyltetralone was obtained, which gave a red 2,4-dinitrophenylhydrazone, m. p. 215–217°. One gram of the crude tetralone was reduced by the Clemmensen method and demethylated directly with hydrobromic acid exactly as described in the above analogous case. The **4-methyl-ar-1-tetralol** thus obtained crystallized from petroleum ether in stout needles, m. p. 87.5–88.5°. No depression in melting point was observed on admixture of this synthetic phenol with the phenol from the rearrangement of the dienone II.

On short treatment with warm acetic anhydride in the presence of a drop of sulfuric acid the synthetic phenol was converted into an acetate, m. p. 82°, whose melting point was not depressed on admixture with the acetate of the phenol from II.

The infrared spectrum of the synthetic phenol and that of the phenol from II were identical.

Summary

The dienone (A) has been synthesized by two methods, and shown to rearrange to 4-methyl-ar-1-tetralol (B). The mechanism of the change is discussed. It is suggested that a number of known reactions follow a similar course, and that in particular the aromatization of steroid dienones leads to products of structures different from those which have hitherto been accepted.



A B

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(25) Rosenmund and Shapiro, *Arch. Pharm.*, **272**, 313 (1934).