Compound IV and Acetyl Derivative.—A mixture of 0.4 g. of the product from alkaline formaldehyde treatment of II, 1.0 g. of 10% palladium–charcoal catalyst, and 50 ml. of glacial acetic acid was shaken under hydrogen (40 lb.) at 80° for 1.5 hours. Filtration of the catalyst and evaporation of the solvent gave glassy material which crystallized partly in the presence of methanol. Trituration with this solvent afforded 0.2 g. of colorless crystals, m.p. 227–230°. Recrystallization from methanol-ether gave pure material, m.p. 230–232°.

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.98; H, 5.40.

Acetylation with refluxing acetic anhydride (2 hours), evaporation of excess reagent, and recrystallization from methanol gave colorless crystals, m.p. 175–176.5°. After drying the material at 80°, a hemihydrate was obtained.

Anal. Calcd. for $C_{24}H_{24}O_9 \cdot {}^1/_2H_2O$: C, 61.93; H, 5.41. Found: C, 61.83; H, 5.49.

After further drying at 100°, a weight loss of 1.4% (calcd.: 1.93%) was detected, and anhydrous material was obtained.

Anal. Calcd. for $C_{24}H_{24}O_9$: C, 63.15; H, 5.30. Found, C, 63.44; H, 5.25.

The infrared spectrum (chf.) had an intense peak at 5.65–5.68 μ. The ultraviolet spectrum (ethanol) had λ_{max} 294 mμ (log ϵ 3.58) with an inflection at 235 mμ (log ϵ 4.30) and a valley at 283 mμ (log ϵ 3.56), and was in all respects very similar to the spectrum of compound V.[6]

BETHESDA 14, MD.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

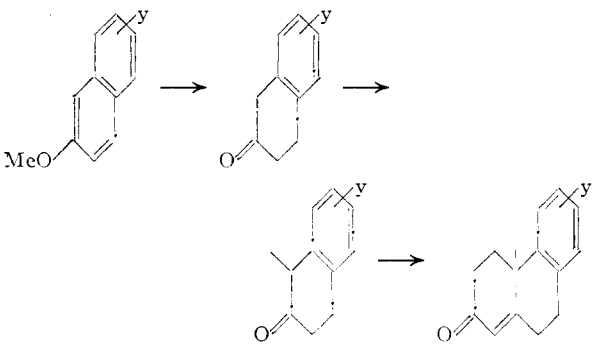
Addition Reactions of 1-Methyl-2-naphthol with Unsaturated Ketones[1]

BY ERNEST WENKERT AND TRAVIS E. STEVENS[2]

RECEIVED NOVEMBER 17, 1955

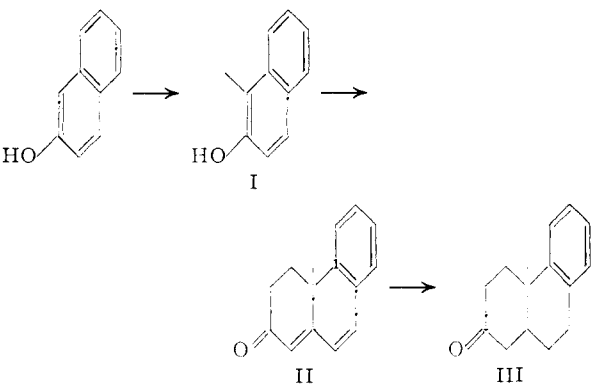
The base- and acid-catalyzed addition reactions of methyl vinyl, methyl β-chlorovinyl and methyl ethynyl ketones with 1-methyl-2-naphthol are described. The structure and stereochemistry of the products are elucidated. A new synthetic route to hydrophenanthrones is presented.

As part of their later total synthesis of the steroid nucleus,[3] Cornforth and Robinson introduced in 1946[4] a simple, attractive method for the conversion of a naphthol derivative into a hydrophenanthrone. Formally this process involved a reduction followed by two alkylations

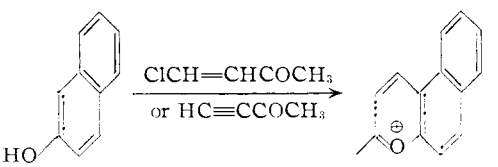


While the introduction of only one alkyl group at a time into the intermediate tetralone had caused some difficulty at first, this obstacle has been overcome by the utilization of a heterogeneous reaction process[5] and perhaps more interestingly by the prior transformation of the tetralone into its ene-amine.[6]

In connection with a contemplated terpene and/or steroid synthesis it was of interest to ascertain whether the above reaction sequence could be reversed, *i.e.*, the alkylations to precede the reduction. For this purpose the introduction of a butanone



side chain into 1-methyl-2-naphthol (I) came under consideration. Various cases of *ortho*-alkylation of phenols *via* their β-addition to α,β-unsaturated ketones are already on record. The acid-catalyzed version of this reaction is the usual synthetic route to benzopyrrylium salts, *e.g.*, by the use of methyl β-chlorovinyl[7] and methyl ethynyl ketones[8]



Base-catalyzed addition reactions, Michael reactions, have been reported also, *e.g.*[9,10]

(1) Part of this work was presented at the Symposium on the Chemistry of Natural Products, Technion, Haifa, Israel, June 28-29, 1955.

(2) National Science Foundation Predoctoral Fellow, 1953-1955.

(3) H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann and R. Robinson, *J. Chem. Soc.*, 361 (1953).

(4) J. W. Cornforth and R. Robinson, *ibid.*, 676 (1946).

(5) C. A. Grob and W. Jundt, *Helv. Chim. Acta*, **31**, 1891 (1948).

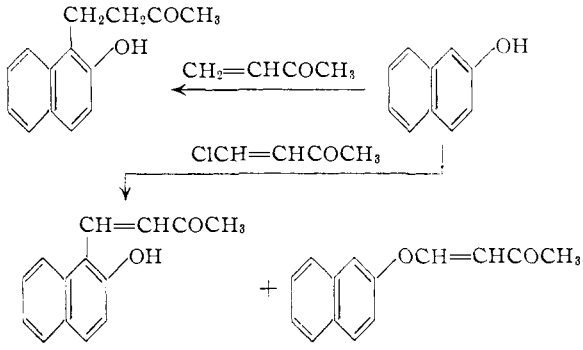
(6) G. Stork, R. Terrell and J. Szmuszkovicz, THIS JOURNAL, **76**, 2029 (1954); and private communicaton from Professor Stork.

(7) A. N. Nesmeyanov, N. Kochetkov and M. Rybinskaya, *Izvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk.*, 479 (1953) [*C. A.*, **48**, 10015 (1954)]; *Doklady Akad. Nauk. S.S.S.R.*, **93**, 71 (1953) [*C. A.*, **49**, 3953 (1955)].

(8) A. W. Johnson and R. Melhuish, *J. Chem. Soc.*, 346 (1947).

(9) S. A. Miller and R. Robinson, *ibid.*, 1535 (1934); F. J. McQuillin and R. Robinson, *ibid.*, 586 (1941).

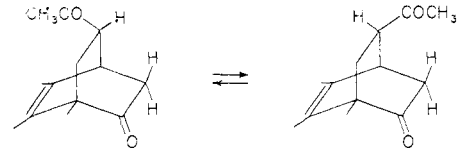
(10) N. K. Kochetkov, M. Rybinskaya and A. N. Nesmeyanov, *Doklady Akad. Nauk. S.S.S.R.*, **79**, 799 (1951) [*C. A.*, **46**, 6102 (1952)].



The Michael reaction of 1-methyl-2-naphthol (I) and methyl vinyl ketone with potassium *t*-butoxide in *t*-butyl alcohol yielded three neutral products. Two of these were $C_{15}H_{16}O_2$ compounds, while the third, obtained in trace amounts, was a $C_{19}H_{22}O_3$ product. The C_{15}-isomers possessed similar physical and chemical properties, none of which agreed with formulation II. Both the 104 and 109° products were white in color, had only low-intensity absorption maxima in the ultraviolet at 264, 272 and 294 mμ, the first two being indicative of an unconjugated tetralin nucleus, and revealed only an unconjugated carbonyl band at 1715 cm.$^{-1}$ but no OH peaks in the infrared. The ready formation of yellow di-2,4-dinitrophenylhydrazones disclosed the presence of two unconjugated ketonic functions in both compounds. The combined experimental facts, added to a mechanistic interpretation of the reaction path (*vide infra*), permitted the assignment of formula VII to the products.

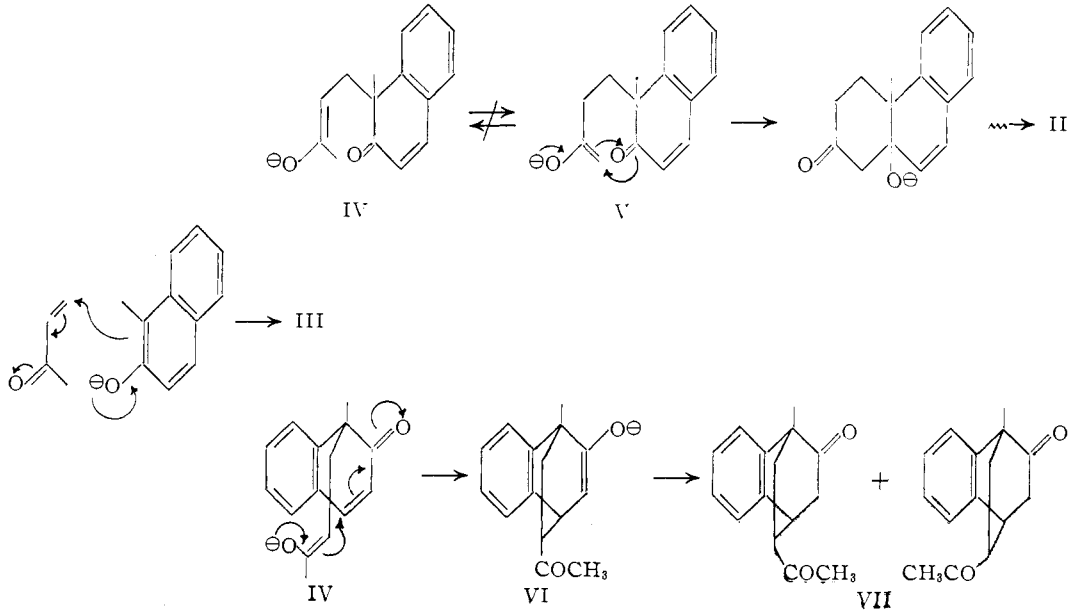
The initial enolate anion IV, obtained by the β-addition of naphthoxide ion to methyl vinyl ketone, would have had to have undergone prototropic exchange with the solvent to yield V, which ionic species is the only one that would have been able to proceed to II. Apparently, however, the enolate ion IV underwent an intramolecular Michael addition, yielding VI, from which the two diketones VII are derived.

The two epimeric ketones were interconvertible in base. Equilibrium mixtures containing 67 and 64% of the 109° compound were obtained by exposure of the ketones to sodium ethoxide solution. These values compared favorably with 0.62, the product ratio in the original *t*-butoxide-induced synthesis of the compounds, and implied that the 109° product was slightly thermodynamically more stable than its isomer. Since the two compounds differ from each other only by the presence in one of them of a single 1,3-diaxial non-bonded interaction—between the acetyl group and an opposing hydrogen atom—the 109° ketone must be the one which does not contain this steric interference and hence be VIIa, while the 104° isomer can be assigned part structure VIIb.

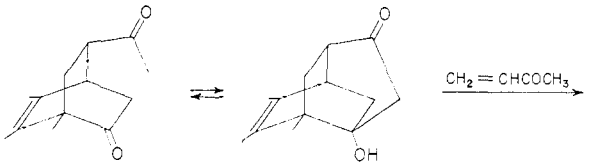


VIIa VIIb

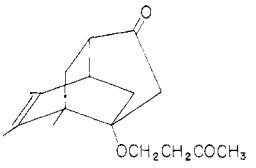
The molecular formula $C_{19}H_{22}O_3$ of the third product of the Michael reaction indicated it to be the product of a reaction involving vinyl ketone and naphthol in a 2:1 molar ratio. Its ultraviolet spectrum revealed low-intensity maxima at 265 and 295 mμ, characteristic again of merely tetralin and saturated keto chromophores. A 1710 cm.$^{-1}$ carbonyl peak in its infrared spectrum, its easy conversion to a di-2,4-dinitrophenylhydrazone and the lack of any carbonyl absorption in the infrared spectrum of the latter pointed to the fact that two oxygen atoms in the C_{19}-product were part of two unconjugated, straight-chain or six-membered cyclic ketonic groups. Lack of OH absorption and the presence of a broad band at 1100 cm.$^{-1}$ in the infrared suggested that the third oxygen atom was part of an ether linkage. Part structure VIII is the most readily derivable formula for the compound compatible with all the experimental facts.



Its formation can be envisaged to involve a β-addition of the internal aldol of VIIb to methyl vinyl ketone.[11]



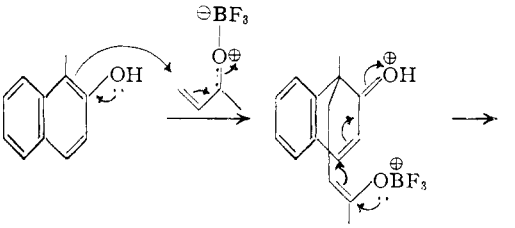
VIIb



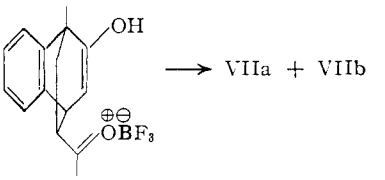
VIII

When the reaction between the unsaturated ketone and 1-methyl-2-naphthol (I) was carried out in the presence of boron trifluoride in ether solution, the isomeric diketones VIIa and b were produced. A product ratio 7:1 in favor of the less stable VIIb indicated, as expected, the absence of any final equilibrium between the two ketones as well as a preferred orientation of the BF_3-complexed acetyl group away from the benzene ring during the process of the internal β-addition, *i.e.*, in IX. This directed addition most likely is the consequence of the both electronically and sterically unfavorable interaction between the aromatic nucleus and the OBF_3 complex.[12]

On the basis of the findings thus far it became clear that, in order to arrive at structure II, or its equivalents, and thereby by-path the internal β-addition, the reaction had to be modified in essentially one of two ways, (a) hydroxylic solvents of greater acidity than *t*-butyl alcohol be used to enhance the possibility of prototropic exchange between the primary intermediate and solvent (*cf.* IV → V); (b) β-halovinyl or ethynyl methyl ketones to be used in place of methyl vinyl ketone to trap intermediates IV, IX or their equivalents, by their undergoing β-elimination of halogen or proton transfer with the solvent, respectively.



IX



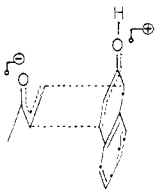
IX

A Michael reaction between 1-methyl-2-naphthol (I) and methyl vinyl ketone in the presence of sodium ethoxide in ethanol solution yielded merely the starting naphthol. When, however, the reaction was attempted in ethanol solution saturated with gaseous hydrogen chloride, a 6% yield of a yellow product along with 89% of recovered naphthol could be realized. The same product could be obtained to the extent of 26%, along with small amounts of the diketones VIIa and b, when the reaction was carried out in a glacial acetic acid medium and *p*-toluenesulfonic acid was used as catalyst. The product was shown to be a $C_{15}H_{14}O$ compound and was identified easily as the desired hydrophenanthrone II by the fact that it formed a purple 2,4-dinitrophenylhydrazone, had ultraviolet absorption maxima at 242 mμ (log ε 4.23) and 354 mμ (log ε 4.17) and showed a carbonyl absorption peak in the infrared at 1655 cm.$^{-1}$.

The reaction of I and methyl β-chlorovinyl ketone in potassium *t*-butoxide–*t*-butyl alcohol led to a $C_{15}H_{14}O_2$ compound. This proved to be the O-alkylation product X, since it was hydrogenatable over palladium–charcoal to a dihydro derivative whose ultraviolet spectrum, maxima at 230 mμ (log ε 4.84), 282 mμ (log ε 3.72), 322 mμ (log ε 3.23) and 335 mμ (log ε 3.23), showed the presence of a naphthoxy group, whose infrared spectrum, carbonyl peak at 1710 cm.$^{-1}$, revealed a saturated ketone, and whose 98% conversion to 1-methyl-2-naphthol in methanolic sodium hydroxide indicated unambiguously that the dihydro compound was the ketone XI. Since the latter was in reality the O-alkylation product of the naphthol I and methyl vinyl ketone, it was of interest to discover whether it could be made to revert to the C-alkylation products. This indeed was accomplished when a *t*-butoxide treatment of XI transformed it into a mixture of the three diketones VIIa, VIIb and VIII. The product ratio 0.63 of

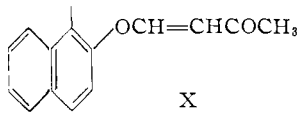
(11) Various references can be cited for the intramolecular aldolization of cyclic 1,5-diketones, *e.g.*, R. Rabe, *Ber.*, **37**, 1672 (1904); V. Prelog and M. Osgan, *Helv. Chim. Acta*, **36**, 1640 (1953); G. Stork and J. Szmuszkovicz, Abstracts of Papers, 125th Meeting Amer. Chem. Soc., Kansas City, March, 1954, p. 36N, of which the last also portrays the alkylation of a tertiary alcohol by methyl vinyl ketone and an internal Michael condensation resulting therefrom.

(12) In the bis-β-additions that occur in both acid- and base-catalyzed reactions, the second (internal) addition undoubtedly is many times faster than the first. As a consequence, it may be permissible to consider the reaction a concerted process with a *formal* transition state such as

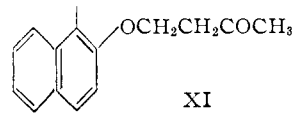


This picture is especially attractive because of the similarity with the Diels–Alder reaction, which has been shown most recently to take place even with phenols serving as "dienes" [K. Takeda and K. Kitahonoki, *J. Pharm. Soc. Japan*, **71**, 860 (1951); **73**, 280 (1953); K. Takeda, S. Nagakura and K. Kitahonoki, *Pharm. Bull. (Japan)*, **1**, 135 (1953); K. Takeda, Abstracts of the 14th International Congress of Pure and Applied Chemistry, Zürich, July 21–27, 1955, p. 270; R. C. Cookson and N. S. Wariyar, *Chemistry and Industry*, 915 (1955)]. While the success of such reaction, on contrast to the failure of the diene synthesis with non-hydroxylic aromatic compounds is in large measure due to a secondary process, the ketonization of the enolic adduct, it is not unreasonable to assume that partial hydrogen transfers during the interaction of phenol and dienophile may aid in lowering the transition state of the Diels–Alder reaction itself. The resulting quasi-ionic intermediates would be *formally* identical to those of the bis-β-additions discussed above.

VIIa to VIIb was in good agreement with previously obtained equilibration data.[13]



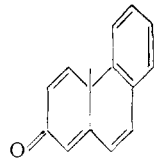
X



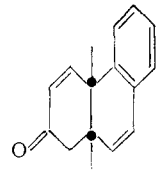
XI

No change in reaction time affected the type or yield of product in the above Michael reaction. Likewise, the use of the anhydrous sodium naphthoxide in acetonitrile or dioxane solution did not alter the reaction products. When methanolic sodium hydroxide was used, the starting naphthol was recovered unchanged. Acid catalysis was not investigated thoroughly, since, had the C-alkylation taken place in this case, the resulting trienone would have been expected to be unstable with respect to a dienone–phenol rearrangement.

When methyl ethynyl ketone was exposed to 1-methyl-2-naphthol (I) in the presence of potassium *t*-butoxide catalyst in *t*-butyl alcohol solution, three products could be obtained along with a 25% recovery of naphthol: 25% of the naphthoxybutenone X, a small amount of yellow oil and 26% of an isomer of X. The oil refused to become completely homogeneous even after repeated chromatographic purification but could be converted into a deep purple 2,4-dinitrophenylhydrazone whose analysis indicated the oil to be a $C_{15}H_{12}O$ compound. The major product, a $C_{15}H_{14}O_2$ compound, revealed ultraviolet absorption maxima at 222 mμ (log ε 4.45) and 264 mμ (log ε 3.88), characteristic of α,β-unsaturated carbonyl and styryl chromophores, respectively, and showed an OH peak at 3340 cm.$^{-1}$ and conjugated carbonyl absorption at 1675 cm.$^{-1}$ in the infrared. On this basis its structure was represented by XIII, a *cis* arrangement tentatively being assigned mainly because of the lower likelihood of a butenone side chain forming a *trans* bridge.[14] Since this ketone produced the same deep purple 2,4-dinitrophenylhydrazone, apparently with concomitant loss of water, as the oily by-product, the latter obviously must have been the trienone XII.

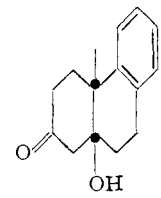


XII

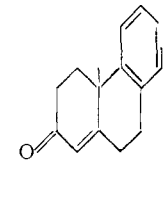


XIII

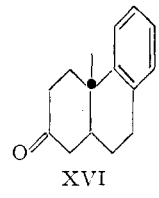
Hydrogenation of the unsaturated ketol XIII yielded its tetrahydro derivative XIV, which on dehydration with *p*-toluenesulfonic acid in benzene gave the unsaturated ketone XV. Reduction of the latter compound by lithium in liquid ammonia led to a crystalline *trans*-hydrophenanthrone (XVI).[15] On the other hand, catalytic hydrogenation of XV, XII or II gave only a 10–15% yield of *trans* compound along with oily (f.p. between 0 and −10°) *cis*-ketone XVII as major product. The two isomeric hydrophenanthrones could be distinguished easily from each other by their different infrared spectra, *p*-nitrophenylhydrazones and semicarbazones.



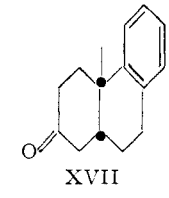
XIV



XV



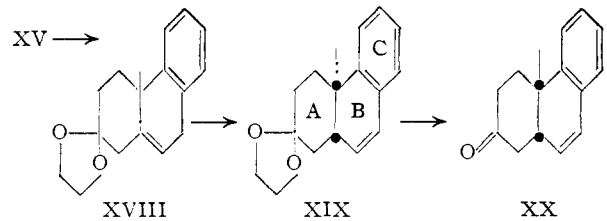
XVI



XVII

Having achieved the initial goal, that of developing a new synthetic route to hydrophenanthrones capable of being elaborated further to terpenic or steroidal nuclei, it became of interest to discover which of the two possible steric arrangements of the hydrophenanthrene skeleton is more thermodynamically stable. There were two reasons for not categorically favoring the *trans* system.[15] Firstly, the difference of stability of even the two unsubstituted 9-methyldecalins amounts to less than one kcal.[16] Secondly, there are two recorded cases of hydrophenanthrones, containing keto functions adjacent to the epimerizable bridgehead hydrogen atom, which yielded mixtures on equilibration,[17,18] wherein, at least in one case,[18] the *cis* form predominated.

The unsaturated ketone XV was converted to its ethylene ketal, whose structure was assumed to be XVIII by analogy with ketals of Δ^4-3-keto-steroids.[19] Whereas the compound was not purified, the lack of carbonyl absorption in its infrared spectrum indicated that the keto group was fully masked. Drastic potassium hydroxide treatment transformed the ketal to its double-bond isomer XIX which, without isolation, was hydrolyzed by dilute acid to a crystalline ketone XX. The latter exhibited saturated carbonyl absorption in the infrared and an ultraviolet absorption maximum at 267 mμ (log ε 3.99), characteristic of the styryl



XVIII XIX XX

(13) The ready conversion of O-alkylated to C-alkylated products may suggest that even in the original Michael addition of methyl vinyl ketone to naphthol a rapid equilibrium with XI precedes the rate-determining C-alkylation.

(14) *Cf.* F. McQuillin, *J. Chem. Soc.*, 528 (1955).

(15) D. H. R. Barton and C. H. Robinson, *ibid.*, 3045 (1954).

(16) R. B. Turner, THIS JOURNAL, **74**, 2118 (1952).

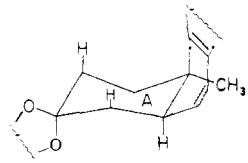
(17) The Wolff–Kishner reduction of the keto acid VIII in W. E. Parham, E. L. Wheeler and R. M. Dodson, *ibid.*, **77**, 1166 (1955).

(18) Footnote 2 in M. V. Mijovic, E. Sundt, E. Kyburz, O. Jeger and V. Prelog, *Helv. Chim. Acta*, **38**, 237 (1955).

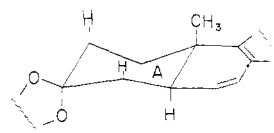
(19) For a most recent case *cf.* S. Bernstein, M. Heller and S. M. Stolar, THIS JOURNAL, **77**, 5327 (1955).

chromophore. Catalytic hydrogenation of this substance yielded cleanly the *cis*-ketone XVII, indicating the *cis* nature also of its precursors XIX and XX.

While the low yield of XX weakens any rigorous argument regarding the configurational stability of the hydrophenanthrene skeleton, the fact that only one compound could be obtained from the equilibration of XVIII and XIX, even though its isomer was searched for meticulously, strongly suggests that the *cis* product in the case on hand is the more stable system. An inspection of molecular models of XIX and its *trans* isomer (*cf.* part structures XXI and XXII, respectively) reveals that the main difference between the two structures lies in the fact that the *cis* compound XXI has merely the planar "face" of the axial benzene ring C opposing the two axial hydrogen atoms, situated 1,3 to it, while in the *trans* compound XXII the consequently bulkier angular methyl group is in non-bonded interaction with these hydrogen atoms.

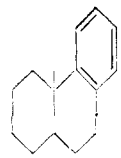


XXI



XXII

It must be added that molecular models of the *cis*- and *trans*-octahydrophenanthrenes (XXIII) show that a similar, albeit less rigorous, conformational argument can be made even in this case in favor of a greater stability of the *cis* system. Hence, any synthesis of hydrophenanthrene derivatives, which has as its ultimate goal the attainment of an A/B *trans* ring fusion and which during or after the formation of such juncture engages an equilibrium step involving the bridgehead hydrogen atom, may lead at best to mixtures, at worst to the *cis* system.



XXIII

Experimental[20]

Reactions of Methyl Vinyl Ketone and 1-Methyl-2-naphthol. With Potassium *t*-Butoxide Catalyst.—1-Methyl-2-naphthol (5.0 g.) and 2.8 ml. of freshly distilled methyl vinyl ketone were added to 60 ml. of *t*-butyl alcohol in which 0.13 g. of potassium had been dissolved. The solution was shaken and allowed to stand at room temperature for 10 hr. After the mixture was poured into 200 ml. of water and neutralized with acetic acid, it was extracted with ether and the extract washed with water, dried over magnesium sulfate and evaporated to an oily residue. The latter was extracted five times with 100-ml. portions of hot petroleum ether and the combined, cooled extracts chromatographed on a Celite–silicic acid column. Elution with petroleum ether–ether (19:1) gave 1.76 g. (35.2%) of 1-methyl-2-naphthol, m.p. 110–111°. The 5:1 eluate yielded a product, m.p. 102–103°, which on recrystallization from petroleum ether gave 0.69 g. (9.6%) of white prisms of 1-methyl-5,6-benzo-8-acetylbicyclo[2,2,2]octan-2-one (VIIb), m.p. 103–104°; spectra: infrared: C=O 1715 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 264 mμ (ε 410), 272 mμ (ε 410), 294 mμ (ε 440); $\lambda_{min.}$ 244 mμ (ε 130).

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.96; H, 7.03.

It gave a yellow di-2,4-dinitrophenylhydrazone which was recrystallized from ethanol–ethyl acetate, m.p. 238–239° dec.

Anal. Calcd. for $C_{27}H_{24}O_8N_8$: C, 55.11; H, 4.11; N, 19.04. Found: C, 54.96; H, 3.84; N, 18.6.

The 3:1 eluate gave the stereoisomeric diketone VIIa, m.p. 104–106°. Recrystallization from petroleum ether produced 1.11 g. (15.4%) of hard white needles, m.p. 108–109°; spectra: infrared: C=O 1715 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 264 mμ (ε 390), 270 mμ (ε 360), 294 mμ (ε 390); $\lambda_{min.}$ 244 mμ (ε 150).

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.89; H, 7.07.

Its yellow di-2,4-dinitrophenylhydrazone was recrystallized from chloroform–ethyl acetate, m.p. 277–278° dec.

Anal. Calcd. for $C_{27}H_{24}O_8N_8$: C, 55.11; H, 4.11; N, 19.04. Found: C, 54.77; H, 3.93; N, 18.8.

The mixed melting point of the isomeric diketones was 80–84°.

The gummy residue, remaining after the extractions with petroleum ether, was decolorized with charcoal and crystallized from ethanol, yielding 0.38 g. (4%) of crystalline substance, m.p. 234–238°. Three recrystallizations from 95% ethanol gave white platelets of 1-methyl-2-(3-keto-1-butoxy)-5,6-benzo-9-ketotricyclo[2,2,2,$2^{2,8}$]decane (VIII), m.p. 244–245°; spectra: infrared: C=O 1710 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 265 mμ (ε 300), 295 mμ (ε 400); $\lambda_{min.}$ 248 mμ (ε 200).

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.56; H, 7.30.

Its yellow di-2,4-dinitrophenylhydrazone was recrystallized from ethanol–ethyl acetate, m.p. 262–264° dec.

Anal. Calcd. for $C_{31}H_{30}O_9N_8$: N, 17.0. Found: N, 16.6.

With Sodium Ethoxide Catalyst.—1-Methyl-2-naphthol (2.00 g., 12.7 mmoles) was added to 40 ml. of absolute ethanol in which 0.29 g. (12.6 mmoles) of sodium had been dissolved. On cooling the solution in ice, 1.2 ml. of freshly distilled methyl vinyl ketone was added and the solution left standing at 5° for 24 hr. It then was diluted by water and extracted with ether, the extract washed with water, dried over magnesium sulfate and evaporated to dryness. The residue was taken up in refluxing petroleum ether which on cooling deposited crystals of 1-methyl-2-naphthol, m.p. 110–111°. Chromatography of the filtrate on Celite–silicic acid yielded nothing other than further starting material.

With Boron Trifluoride Catalyst.—A solution of 4.0 g. of 1-methyl-2-naphthol and 2.3 ml. of freshly distilled methyl vinyl ketone in 35 ml. of anhydrous ether was added dropwise, with cooling, to a solution of 1.9 g. of boron trifluoride in 12 ml. of anhydrous ether. After an 11-hr. period at room temperature the mixture was poured into an ice-water–hydrochloric acid mixture, the solution made alkaline with sodium hydroxide solution, neutralized with acetic acid and extracted with ether. The organic extract was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated to a dark oil. The latter was extracted six times with 80-ml. portions of refluxing petroleum ether and the cooled, combined extracts chromatographed on a Celite–silicic acid column. Elution with petroleum ether–ether (19:1) gave 2.24 g. (56%) of starting naphthol, m.p. 110–111°. From the 7:1 eluate 1.33 g. (23%) of the ketone VIIb, m.p. 102–103°, could be obtained. Since further elution gave only oily material, it was taken up in 9:1 petroleum ether–ether and chromatographed on another Celite–silicic acid column. The 2:1 eluate yielded 60 mg. of ketone VIIa, m.p. 107–108°, after recrystallization from petroleum ether. Rechromatography of the residues on yet another column produced 0.13 g. (3.3% total yield) of additional ketone VIIa, m.p. 107–108°.

With *p*-Toluenesulfonic Acid Catalyst.—1-Methyl-2-naphthol (5.0 g., 31.6 mmoles) and methyl vinyl ketone

(20) The use of the Baird infrared spectrophotometer of the Institute of Atomic Research, Ames, Iowa, is hereby gratefully acknowledged.

(7.0 g., 0.10 mole) were added to a solution of 5.5 g. of *p*-toluenesulfonic acid hydrate in 80 ml. of glacial acetic acid. After shaking vigorously, the solution was allowed to stand at room temperature for 11 hr. The reaction mixture then was poured into 500 ml. of water, partially neutralized with 10% sodium bicarbonate solution and dried over magnesium sulfate, the chloroform was evaporated leaving a dark oil. The latter was extracted with eight 100-ml. portions of hot petroleum ether and the cooled, combined extracts chromatographed on a Celite–silicic acid column. The 19:1 petroleum ether–ether eluate gave 2.36 g. (47.2%) of starting material, m.p. 110–111°. The 9:1 fraction gave a yellow oil which solidified after trituration with petroleum ether, thus yielding 1.21 g. (18.3%) of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (II) as hard yellow clusters melting at 95–97°. Recrystallization from petroleum ether produced pale yellow needles, m.p. 97–98°; spectra: infrared: C=O 1655 cm.$^{-1}$ (s); ultraviolet: λ_{max} 242 mμ (ε 16,800), 354 mμ (ε 14,900).

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.72. Found: C, 85.67; H, 6.58.

Its purple, crystalline 2,4-dinitrophenylhydrazone was recrystallized from ethanol–ethyl acetate, m.p. 213–215° dec.

Anal. Calcd. for $C_{21}H_{18}O_4N_4$: C, 64.61; H, 4.65; N, 14.35. Found: C, 64.30; H, 5.06; N, 14.7.

The 2:1 eluate yielded 0.19 g. of ketone VIIa, m.p. 107–108°. The non-crystalline fractions were recombined in petroleum ether and rechromatographed on Celite–silicic acid. However, the infrared spectra of the various eluates still indicated incomplete separation. As a consequence chromatography on alumina of a petroleum ether–benzene (1:1) solution of the again recombined fractions was attempted. Elution with benzene and benzene–ether (1:1) followed by fractional crystallization from petroleum ether led to an additional 0.48 g. (7.3%) of ketone II, m.p. 95–97°, 0.13 g. of ketone VIIa, m.p. 105–106°, and 20 mg. of ketone VIIb, m.p. 98–100°.

With Hydrochloric Acid Catalyst.—When a reaction between methyl vinyl ketone and 1-methyl-2-naphthol was carried out in absolute ethanol solution saturated with dry hydrogen chloride gas under the same conditions as in the *p*-toluenesulfonic acid run, 89.4% of starting naphthol was recovered and 6.5% of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (II) was produced.

Base-catalyzed Equilibration of Ketones VIIa and VIIb.—Ketone VIIb (0.50 g., 2.2 mmoles) was added to 20 ml. of absolute ethanol, containing 2.2 mmoles of sodium ethoxide and the solution left standing at room temperature for 10 hr. The pale yellow mixture was poured into 100 ml. of water, neutralized with acetic acid and extracted with chloroform. The extract was washed with water, dried over magnesium sulfate and evaporated leaving a colorless oil. Chromatography of a petroleum ether solution of the oil on a Celite–silicic acid column led to 195 mg. of starting ketone (VIIb), m.p. 103–104°, on elution with 4:1 petroleum ether–ether and 290 mg. of its isomer VIIa, m.p. 107–108°, from further fractions.

When 0.50 g. of VIIa was treated in like manner, it was converted to a mixture of 185 mg. of VIIb, m.p. 103–104°, and 290 mg. of starting material, m.p. 107–108°.

Reactions of Methyl β-Chlorovinyl Ketone and 1-Methyl-2-naphthol. In *t*-Butyl Alcohol.—1-Methyl-2-naphthol (5.00 g., 31.6 mmoles) and methyl β-chlorovinyl ketone (3.50 g., 35.0 mmoles) were added to 75 ml. of a cooled *t*-butyl alcohol solution wherein 1.50 g. (38.4 mmoles) of potassium had been dissolved and the red solution left at room temperature for 8 hr. It then was poured into 300 ml. of water, neutralized with acetic acid and extracted with chloroform. The extract was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated under reduced pressure leaving a dark oil. After extraction of the oil by five 80-ml. portions of hot petroleum ether, the combined, cooled extract was chromatographed on a Celite–silicic acid column. Elution with petroleum ether–ether (32:1) gave 2.15 g. (43%) of starting material, m.p. 110–111°. Further elution (19:1) yielded 2.49 g. (34.8%) of 4-(1-methyl-2-naphthoxy)-3-buten-2-one (X), m.p. 68–70°. On rechromatography and similar elution of several of the oily fractions an additional 0.19 g. (3.8%) of starting naphthol and 0.58 g. (8.1%) of the ketone X, m.p. 68–70°, were obtained. Recrystallization of the product from petroleum ether gave long white needles, m.p. 70–71°; spectra: infrared: C=O 1680 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 245 mμ (ε 24,600); $\lambda_{min.}$ 240 mμ (ε 23,900).

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.47; H, 6.26.

In Aqueous Methanol.—1-Methyl-2-naphthol (1.0 g.) and 0.80 ml. of methyl β-chlorovinyl ketone were added to a cooled solution of 1.0 g. of sodium hydroxide in 15 ml. of water and 5 ml. of methanol. After 18 hr. at room temperature the reaction was worked up in the same fashion as the *t*-butoxide run. However, a 96% recovery of only starting naphthol could be made.

In Dioxane.—Sodium 1-methyl-2-naphthoxide was prepared by dissolving a known amount of sodium hydroxide in methanol and adding an equimolar quantity of 1-methyl-2-naphthol to the methanolic solution. The salt, obtained by evaporation of the solvent under reduced pressure, was dried at 80° (1 mm.) for 2 hr.

Methyl β-chlorovinyl ketone (0.85 g., 8.1 mmoles) was added to 25 ml. of purified dioxane containing 1.20 g. (6.67 mmoles) of sodium 1-methyl-2-naphthoxide. After 10 hr. at room temperature the red-colored reaction mixture was poured into 200 ml. of water, neutralized with acetic acid and extracted with chloroform. After being washed with sodium bicarbonate solution and water, the organic extract was dried over magnesium sulfate and concentrated to an oily residue. A petroleum ether solution of the oil was chromatographed on a Celite–silicic acid column. Elution with petroleum ether–ether (19:1) gave 0.17 g. (16%) of starting naphthol, while the 9:1 eluate led to 0.84 g. (56%) of the butenone X, m.p. 68–70°. The 5:1 eluate yielded a small amount of substance, m.p. 205–208° dec., which was not investigated further.

In Acetonitrile.—Methyl β-chlorovinyl ketone (0.85 g., 8.1 mmoles) was added at 40° to a stirred mixture of 1.20 g. (6.67 mmoles) of sodium 1-methyl-2-naphthoxide in 30 ml. of acetonitrile. After warming for one hour, the solution was heated to 70° for ten minutes. After an additional 9 hr. at room temperature the reaction mixture was worked up in the same manner as in the dioxane run; 0.16 g. (15%) of starting naphthol, 0.82 g. (54%) of X, m.p. 68–70°, and a trace of the 205–208° dec. substance (*cf.* dioxane run) were isolated.

4-(1-Methyl-2-naphthoxy)-2-butanone (XI).—A mixture of 500 mg. of 4-(1-methyl-2-naphthoxy)-3-buten-2-one (X) and 150 mg. of 5% palladium-on-charcoal catalyst in 25 ml. of ethyl acetate was hydrogenated at atmospheric pressure and room temperature. Hydrogenation ceased spontaneously after the uptake of one mole of hydrogen at the end of 3 hr. Filtration and evaporation of the solution gave a pale yellow oil which on crystallization from petroleum ether was transformed into white crystals, m.p. 45–47°. Chromatography of a petroleum ether solution of the substance on a Celite–silicic acid column produced 20 mg. of 1-methyl-2-naphthol, m.p. 110–111°, from petroleum ether–ether (19:1) elution and 4-(1-methyl-2-naphthoxy)-2-butanone (XI), m.p. 50–51°, from the 9:1 eluate. Two recrystallizations from petroleum ether yielded an analytical sample, m.p. 51–52°; spectra: infrared: C=O 1710 cm.$^{-1}$ (s); ultraviolet: λ_{max} 230 mμ (ε 69,000), 282 mμ (ε 5200), 322 mμ (ε 1700), 335 mμ (ε 1700).

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.90; H, 7.07.

Base-catalyzed Reactions of XI. A. With Methanolic Hydroxide.—Five hundred milligrams of the naphthoxybutanone XI was added to a mixture of 0.75 g. of sodium hydroxide in 5 ml. of water and 50 ml. of methanol. The solution was refluxed in a nitrogen atmosphere for 2 hr., cooled, poured into 200 ml. of water and the aqueous solution neutralized with acetic acid and extracted with chloroform. The organic extract was washed with sodium bicarbonate solution and water and evaporated to dryness. A benzene solution of the residue yielded 0.34 g. (98%) of 1-methyl-2-naphthol, m.p. 109–110°, after filtration through a short alumina column and usual work-up.

B. With Potassium *t*-Butoxide.—One milliliter of *t*-butyl alcohol in which 8.6 mg. of potassium had been dissolved was added to a solution of 500 mg. of XI in 10 ml. of *t*-butyl alcohol. The pale yellow mixture was left standing at room temperature with occasional shaking for 15 hr., after which time it was poured into 100 ml. of water, neutralized with acetic acid and extracted with chloroform.

After a bicarbonate and water washing and drying over magnesium sulfate, the organic extract was evaporated to an oil which on petroleum ether extraction left a small gummy residue. On crystallization from 95% ethanol, the latter yielded 20 mg. of white crystals, m.p. 236–238°, whose mixed m.p. with VIII (m.p. 244–245°) was 241–242°, and whose infrared spectrum characterized it as VIII. The petroleum ether extract was chromatographed on Celite–silicic acid column and eluted with petroleum ether–ether. The 19:1 eluate gave 160 mg. of 1-methyl-2-naphthol, m.p. 110–111°, the 9:1 eluate gave 85 mg. of diketone of VIIb, m.p. 102–103°, and the 4:1 fraction 135 mg. of diketone VIIa, m.p. 106–107°.

The Reaction of Methyl Ethynyl Ketone and 1-Methyl-2-naphthol.—1-Methyl-2-naphthol (5.00 g., 31.6 mmoles) was added to 60 ml. of *t*-butyl alcohol in which 0.13 g. (3.3 mmoles) of potassium had been dissolved. After cooling the solution to 15°, 2.40 g. (35.4 mmoles) of 3-butyn-2-one was added under a nitrogen atmosphere and the mixture allowed to stand, with occasional shaking, for 24 hr. at room temperature; 250 ml. of water then was added, the aqueous mixture neutralized with acetic acid and extracted with chloroform. The extract was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated, leaving a dark, tarry residue. Extraction of the tar with five 80-ml. portions of petroleum ether left a dark, solid residue. The extracts were chromatographed on Celite–silicic acid and eluted with petroleum ether–ether. The 32:1 eluate contained 1.27 g. (25.4%) of starting naphthol, m.p. 110–111°, the 19:1 fraction had 1.80 g. (25.4%) of ketone X, m.p. 68–70°, the 4:1 eluate gave a yellow oil and the 2:1 fraction produced 1.67 g. of 4a-methyl-10a-hydroxy-4a,10a-dihydro-2(1H)-phenanthrone (XIII), m.p. 131–133°. Recrystallization of this substance from petroleum ether–benzene gave white crystals, m.p. 132–134°; spectra: infrared: OH 3340 cm.$^{-1}$ (w), C=O 1675 cm.$^{-1}$ (s); ultraviolet: λ_{max} 222 mμ (ε 28,000), 264 mμ (ε 7500).

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.99; H, 6.26.

Its deep purple 2,4-dinitrophenylhydrazone was recrystallized from ethanol–ethyl acetate, m.p. 202–203° dec.

Anal. Calcd. for $C_{21}H_{16}O_4N_4$: C, 64.94; H, 4.16; N, 14.43. Found: C, 64.92; H, 4.13; N, 14.7.

When an ethanol solution of the dark residue from the initial petroleum ether extraction was put on a short charcoal–Celite column and eluted with ethanol–ethyl acetate, an additional 0.21 g. (25.6% total yield) of XIII, m.p. 131–133°, was obtained.

A petroleum ether–benzene solution of the yellow oil from the silicic acid chromatogram was chromatographed on alumina. Elution with benzene yielded 300 mg. of a pale yellow oil which even on rechromatography on alumina did not change its physical characteristics. It would crystallize on standing overnight at −10°, but would revert to an oil on warming to 5°. It gave a deep purple 2,4-dinitrophenylhydrazone, m.p. 194–196° dec., mixed m.p. with the derivative (m.p. 202–203° dec.) of XIII 194–196° dec. The oil, thus 4a-methyl-2(4aH)-phenanthrone (XII), may have been contaminated with some other substance in view of the formation of a small amount of orange crystals along with the purple hydrazone.

4a-Methyl-10a-hydroxy-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XIV).—A mixture of 200 mg. of ketone XIII, 50 mg. of 5% palladium-on-charcoal catalyst in 20 ml. of 95% ethanol was hydrogenated at atmospheric pressure and room temperature. The hydrogen absorption was complete at the end of 1 hr. and a two-mole uptake. The solution was filtered and the ethanol evaporated under reduced pressure, leaving a white residue, m.p. 155–157°. Two recrystallizations from petroleum ether–benzene gave white prisms, m.p. 157–158°; spectra: infrared: OH 3380 cm.$^{-1}$ (m); C=O 1705 cm.$^{-1}$ (s); ultraviolet: λ_{max} 265 mμ (ε 400).

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88. Found: C, 77.97; H, 7.71.

It yielded a bright red 2,4-dinitrophenylhydrazone which crystallized as plates from ethanol–ethyl acetate, m.p. 204–205° dec.

Anal. Calcd. for $C_{21}H_{20}O_4N_4$: C, 64.27; H, 5.14; N, 14.28. Found: C, 64.16; H, 5.10; N, 14.4.

4a-Methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XV).—The ketol XIV (200 mg.) was added to 25 ml. of dry benzene containing 100 mg. of *p*-toluenesulfonic acid hydrate and 200 mg. of calcium chloride. The solution was heated at 50° for 30 minutes and then allowed to cool and stand at room temperature with occasional shaking for an additional hour. The mixture was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated to dryness. A petroleum ether–benzene (1:1) solution of the residue was filtered through a short alumina column to give 170 mg. of white crystals, m.p. 88–90°, which on two recrystallizations from petroleum ether turned into white prisms, m.p. 89–90°; spectra: infrared: C=O 1665 cm.$^{-1}$ (s); ultraviolet: λ_{max} 239 mμ (ε 18,000).

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.56; H, 7.42.

Its bright red, plate-like 2,4-dinitrophenylhydrazone, m.p. 203–204°, did not depress the m.p. of the same derivative of ketol XIV.

***trans*-4a-Methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XVI).**—A solution of 200 mg. of ketone XV in 20 ml. of dry ether was added to a solution of 100 mg. of lithium in 100 ml. of liquid ammonia. After thirty minutes 2.0 g. of ammonium chloride was added and the ammonia allowed to evaporate. The residue was taken up in chloroform–water and the aqueous layer washed with chloroform. The combined organic extracts were washed with dilute hydrochloric acid, sodium bicarbonate solution and water and the chloroform removed by evaporation. A benzene–petroleum ether (3:2) solution of the solid residue was chromatographed on alumina. Elution of the column with the same solvent pair gave 140 mg. of *trans*-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XVI), m.p. 104–106°. Recrystallization from petroleum ether yielded plates, m.p. 107–108°; spectra: infrared: C=O 1710 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 265 mμ (ε 400); $\lambda_{min.}$ 240 mμ (ε 200).

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.06; H, 8.46. Found: C, 84.05; H, 8.58.

Its semicarbazone crystallized from aqueous ethanol as white platelets, m.p. 220–221° dec.

Anal. Calcd. for $C_{16}N_{21}ON_3$: C, 70.81; H, 7.80; N, 15.49. Found: C, 70.72; H, 7.76; N, 15.5.

The orange *p*-nitrophenylhydrazone was recrystallized from ethanol, m.p. 178–180° dec.

Anal. Calcd. for $C_{21}H_{23}O_2N_3$: C, 72.18; H, 6.63; N, 12.03. Found: C, 71.97; H, 6.34; N, 11.9.

Catalytic Hydrogenations of Enones II, XII and XV. A. Reduction of II.—A mixture of 800 mg. of ketone II and 200 mg. of 5% palladium-on-charcoal in 40 ml. of 95% ethanol was hydrogenated at 740 mm. and 25°. Hydrogen absorption ceased after 8 hr. and an uptake of two moles of H_2. After removal of the catalyst by filtration and evaporation of the filtrate, a petroleum ether solution of the oily residue was chromatographed on alumina. Elution with petroleum ether–benzene (3:1) gave a clear oil, while continued elution with increasing quantities of benzene gave a solid fraction, which on recrystallization from petroleum ether yielded 90 mg. of crystals, m.p. 104–106°. Admixture of this compound with *trans*-ketone XVI (m.p. 107–108°) gave m.p. 106–107°, and its infrared spectrum proved to be superimposable on that of XVI.

The oil, from the first and major fractions of the chromatogram, was rechromatographed on alumina again yielding an oil, whose infrared spectrum had the same carbonyl band as XVI but was otherwise distinctly different from XVI. This substance, consequently *cis*-4a-methyl-3,4,4a,9,10,10a-hexahydra-2(1H)-phenanthrone (XVII), could not be induced to crystallize at room temperature although it became crystalline at −10°.

Its semicarbazone crystallized from aqueous ethanol as sparkling white platelets, m.p. 195–197° dec., mixed m.p. with the derivative of XVI 199–201° dec. with preliminary darkening.

Anal. Calcd. for $C_{16}H_{21}ON_3$: C, 70.81; H, 7.80; N, 15.49. Found: C, 70.86; H, 7.90; N, 15.4.

Its yellow *p*-nitrophenylhydrazone was recrystallized from aqueous ethanol, m.p. 148–150° dec.

Anal. Calcd. for $C_{21}H_{23}O_2N_3$: C, 72.18; H, 6.63; N, 12.03. Found: C, 71.78; H, 6.73; N, 12.3.

B. Reduction of XII.—A mixture of 260 mg. of trienone XII and 100 mg. of 5% palladium-on-charcoal catalyst in 15 ml. of ethanol was hydrogenated at atmospheric pressure and room temperature. Hydrogen absorption corresponding to three moles was complete in 10 hr. After filtration and evaporation of the solution, a petroleum ether solution of the residue was chromatographed on alumina. Elution with petroleum ether–benzene (3:2) gave 120 mg. of an oil whose infrared spectrum was identical to that of ketone XVII. Its semicarbazone melted at 193–195° and did not depress the melting point of the same derivative of XVII. Further elution of the column yielded oils whose infrared spectra indicated them to be mixtures of XVI and XVII.

C. Reduction of XV.—A mixture of 200 mg. of monoenone XV and 100 mg. of 5% palladium-on-charcoal catalyst in 15 ml. of 95% ethanol was hydrogenated at 740 mm. and 25°. Hydrogen absorption ceased after 1 hr. and an uptake corresponding to the reduction of one double bond. The solution was filtered and evaporated and a petroleum ether solution of the residual oil chromatographed on alumina. Ten fractions were eluted using 2:1 petroleum ether–benzene and 1:1 solvent pair. Their infrared spectra indicated the contents to be mainly XVII mixed with about 10% XVI. A combination of the first two fractions was converted to a semicarbazone, which after two recrystallizations from aqueous ethanol melted at 195–197° dec. No depression was observed in the melting point on admixture with authentic semicarbazone of XVII.

***cis*-4a-Methyl-3,4,4a,10a-tetrahydro-2(1H)-phenanthrone (XX).**—A solution containing 1.50 g. of hydrophenanthrone XV and 3.5 ml. of ethylene glycol in 150 ml. of benzene was distilled until 120 ml. of solution remained. After the addition of 40 mg. of *p*-toluenesulfonic acid hydrate and the attachment of a water separator, the solution was refluxed and stirred for 4 hr. The cooled mixture was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated, leaving a thick oil. Its infrared spectrum indicated the absence of any ketone. As a consequence the oily ketal was used in the next reaction without further purification. Its ultraviolet spectrum exhibited a maximum at 265 mμ (ε 400).

One gram of the ketal was added to 50 ml. of ethylene glycol containing 2.0 g. of potassium hydroxide and the solution heated under a nitrogen atmosphere at 190° for 5 hr. The cooled mixture then was poured into 250 ml. of water, neutralized with acetic acid, filtered and both residue and filtrate extracted with chloroform. The organic extracts were washed with sodium bicarbonate and water, dried over magnesium sulfate and evaporated. The residue was dissolved in 60 ml. of 95% ethanol containing 10 ml. of 10% sulfuric acid and refluxed on a steam-bath for 1 hr. The cooled reaction mixture was poured into 250 ml. of water and extracted with chloroform. The latter was washed with sodium bicarbonate solution and water, dried over magnesium sulfate and evaporated. A benzene–petroleum ether (3:2) solution of the organic residue was chromatographed on alumina and eluted by the same solvent pair. The infrared spectra of the first fractions showed the presence of a considerable amount of unhydrolyzed ketal, as a consequence of which they were recombined and again put into 10 ml. of 10% sulfuric acid and 40 ml. of 95% ethanol and refluxed on a steam-bath for 1 hr. The resulting hydrolysate, combined with the remaining eluates of the chromatogram, was rechromatographed on alumina and reëluted as a petroleum ether–benzene (1:1) solution. A reaction product of 125 mg. of 4a-methyl-3,4,4a,10a-tetrahydro-2(1H)-phenanthrone, m.p. 65–67°, was obtained, which on two recrystallizations from petroleum ether gave white plates, m.p. 68–69°; spectra: infrared: C=O 1710 cm.$^{-1}$ (s); ultraviolet: $\lambda_{max.}$ 267 mμ (ε 9800); $\lambda_{min.}$ 234 mμ (ε 3000).

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.87, 84.36; H, 8.01, 7.61.

Further elution of the column with benzene gave a trace of product whose infrared spectrum was identical with that of starting ketone XV.

Reduction of XX.—A mixture of 55 mg. of ketone XX, 20 mg. of palladium-on-charcoal catalyst in 15 ml. of 95% ethanol was hydrogenated at atmospheric pressure and room temperature. Hydrogen absorption ceased spontaneously at the end of 45 minutes and a one-mole uptake. The solution was filtered and evaporated in a stream of nitrogen. The infrared spectrum of the residue was identical with that of XVII. A benzene solution of the residue was filtered through a short alumina column. The infrared spectrum of the benzene eluate was identical with that of the crude residue. The oil was converted to a semicarbazone, which melted at 191–193° dec. after one recrystallization from ethanol. Its mixed melting point with an authentic semicarbazone of XVII was 192–194° dec. The infrared spectra of the two semicarbazones were identical.

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The 20-Epimer of the C_{22}-Lactone from Tigogenin[1]

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3β,16β-Dihydroxy-20-iso-bisnorallocholanic 22→16-lactone has been prepared. The parent acid lactonized upon acetylation at room temperature. The resulting acetoxy lactone XI opened its lactone ring less readily than the 20-epimer which, however, has the energetically preferred structure. The results are interpreted in terms of steric repulsion of the C-18 and C-21 methyl groups. This concept is useful for assigning configurations at C-20 provided the stability of both isomers can be compared.

Several years ago[2] in a study of the rates of methanolysis of some steroids carrying acetoxy groups in the 16- and 20-positions an anomaly was encountered which seemed explicable on the following assumption: the space adjacent to the angular methyl group at C-13 is too restricted to readily accommodate bulky substituents of C-20 and, therefore, those conformations are preferred which place the hydrogen rather than the methyl group at C-20 next to the methyl at C-13. One would expect to observe the influence of such methyl–methyl interference on chemical behavior most readily if the rotation around the C-17 to C-20 bond is prevented by ring closure, as the two stereoisomers at C-20 might show differential stability. A good case for such a study would result if C-20 and C-16 were joined in a 5-membered ring on the β-side of the molecule since this situation produces in the models of one of the stereoisomers (Ia) a very close approach of the two methyl groups, C-18 and C-21.

Several investigators have applied this concept of

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(2) H. Hirschmann and F. B. Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950).