[Contribution from the Pharmaceutical Research Institute, Medical School, Keio-Gijuku University]

Santonin and Related Compounds. X. Preparation and Bromination-Dehydrobromination of *cis*- and *trans*-4,9-Dimethyl-3-decalones[1]

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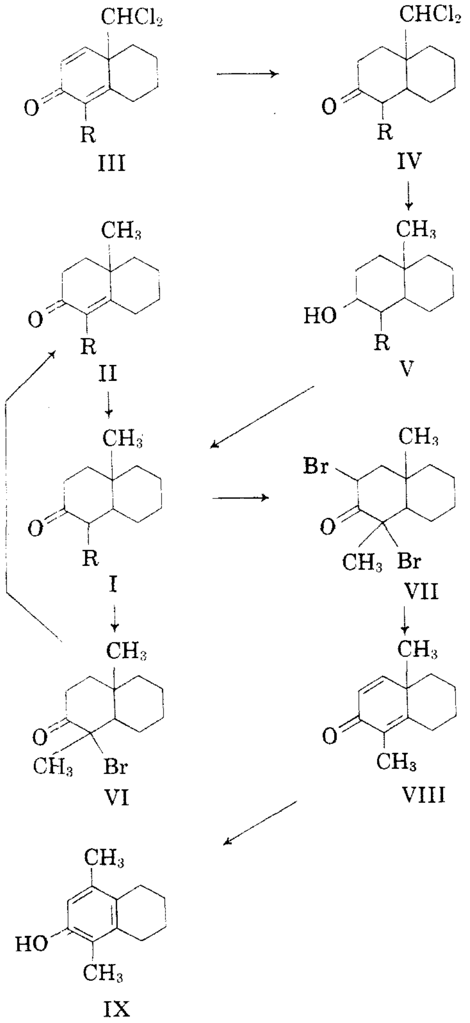
trans-4,9-Dimethyl-3-decalone (IbA), earlier supposed to be *cis*, was prepared from the dichloromethyl-dienone (IIIb) by a tedious procedure. Later, this *trans*-ketone, together with the *cis*-isomer (IbB), became readily accessible, since we developed a new convenient method for separating the isomeric mixture of these ketones (Ib) obtained by hydrogenation of the monoenone (IIb). The configurations at the ring juncture of both ketones were established by unequivocal syntheses. The monobromo derivative (VI) of each pure ketone always gave the monoenone (IIb) on treatment with a variety of bases. Dehydrobromination of the dibromo derivative (VII) of each ketone resulted in the formation of the cross-conjugated dienone (VIIIb), which, in turn, was rearranged to a phenol (IX) with acid.

It was previously shown[2,3] that *trans*-9-methyl-3-decalone (Ia) with bromine afforded the 2-bromo- and 2,4-dibromo-compounds, which were dehydrobrominated to yield the products of different types depending on the bases used. It appeared of interest to extend the bromination-dehydrobromination reaction to 2,9-dimethyl-3-decalone (Ib) for a study of the effect of the methyl group at the 4-position on these reactions.



Series (a): R=H. Series (b): R=CH$_3$

Recently, Gunstone and Heggie[4] reported that on bromination with N-bromosuccinimide and subsequent dehydrobromination, the ketone (Ib) gave a variable mixture which probably consisted of the Δ^1-, Δ^4-, and more unsaturated compounds. Furthermore these authors reported that dibromination-dehydrobromination of the ketone (Ib) also resulted in a complicated mixture containing mono-, di-, and tri-enones. Their starting ketone (Ib), prepared by catalytic hydrogenation of 3-keto-4,9-dimethyl-Δ^4-octahydronaphthalene (IIb), was assigned a *cis* configuration by these authors from the mode of its formation, but in all probability the other possible isomers were not completely separated. On repetition of their reaction, it was found that the dihydro product from IIb formed a mixture of 2,4-dinitrophenylhydrazones, from which by persistent fractional recrystallization the reported derivative, m.p. 186°, of one isomer (IbA) was separated at most in 30% yield. Incidentally, the derivative, m.p. 160°, of another possible isomer (IbB) was isolated from the mother liquor of the above derivative, but not consistently and in a minute amount. Though the hydrazone readily regenerated the parent ketone in pure form with pyruvic acid, it is evident that this tedious procedure is not suitable even for the preparation of the predominant ketone (IbA) in a fair amount. Consequently, the method reported for preparing the pure *trans*-9-methyl-3-decalone (Ia) from the dichloromethyl-dienone (IIa) through IVa and Va was applied to the present case.

3-Keto-4-methyl-9-dichloromethyl-$\Delta^{1,4}$-hexahydronaphthalene (IIIb), which was comparatively inaccessible as reported,[5] was readily hydrogenated

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[1] This work was supported in part by grant in aid for Scientific Research from the Ministry of Education of Japan.

[2] Yanagita and Tahara, *J. Org. Chem.*, **18**, 792 (1953).

[3] Yanagita and Yamakawa, *J. Org. Chem.*, **21**, 500 (1956).

[4] Gunstone and Heggie, *J. Chem. Soc.*, 1437 (1952).

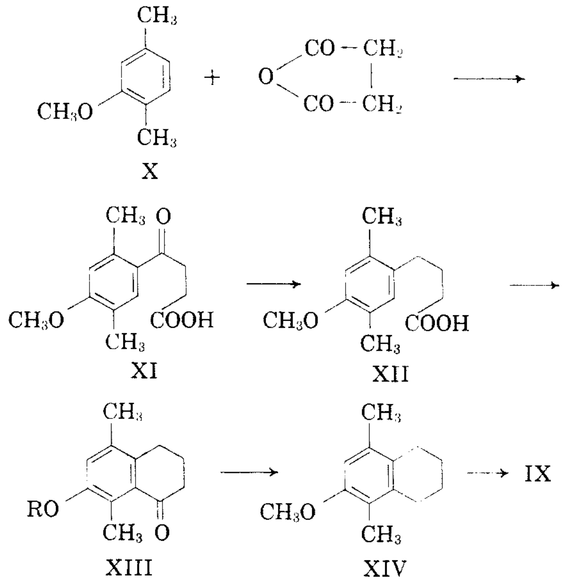
[5] Harukawa and Ishikawa, *J. Pharm. Soc. Japan*, **70**, 48 (1950).

over palladium-charcoal under ordinary conditions. The tetrahydro product, obtained almost quantitatively, was a possible isomeric mixture of the ketones (IVb), from which only one pure isomer was isolated in a 60% yield. After removal of this solid, there remained an oil which gave only the 2,4-dinitrophenylhydrazone of the same isomer. Reduction of the solid isomer with sodium and wet ether gave rise to an oily alcohol (Vb), which was presumed to be stereochemically not homogeneous, but formed only one *p*-nitrobenzoate in a good yield. On analogy with Va,[2,13] it may be assumed that the predominant alcohol possesses the hydroxyl group in an equatorial position. This mixture was oxidized with chromic acid to give a ketone, which formed the 2,4-dinitrophenylhydrazone, m.p. 186°, identical with that of the ketone (IbA) obtained from the monoenone (IIb). This troublesome method, employed at the early stage of this work, was abandoned since a new efficient procedure was developed for separating the isomeric mixture of the ketone (Ib), which will be described below.

A monobromo compound (VIA), prepared from the pure ketone (IbA) with 1.1 equivalents of bromine, was treated with a variety of bases. The product was always the monoenone (IIb), which, depending on the bases used, formed the 2,4-dinitrophenylhydrazone in three modifications; two red crystals, m.p. 160–162° and m.p. 198–200°, and a yellow one, m.p. 210–211°. The red form of the higher melting point, which is identical with the known derivative of IIb,[3] is dimorphic with the other red one as shown by the facile conversion of the latter to the former with hot acetic acid. The yellow form, showing the melting point depression on admixture with the stable red form, was converted into the latter on treatment with 50% methanolic sulfuric acid. It appears that these two derivatives are geometrical isomers about the $C = N$ bond. From these results, it may be assumed that the monobromination in IbA took place at the 4-position.

A 2,4-dibromo derivative (VII), prepared from the pure ketone (IbA) by treatment with 2.1 equivalents of bromine, was reacted with γ-collidine, quinoline, or sodium acetate and afforded in about 20–30% yield a dienone, characterized as 2,4-dinitrophenylhydrazone. On purification of this derivative by chromatography, a trace amount of the derivative of the monoenone (IIb) was occasionally isolated. By comparison of the ultraviolet spectra of the 2,4-dinitrophenylhydrazones, the dienone was shown to be identical with 3-keto-4,9-dimethyl-$\Delta^{1,4}$-hexahydronaphthalene (VIII), the synthesis of which was recently published.[4,6] An attempt to rearrange the dienone (VIII) to the phenol with acid was previously reported to be unsuccessful.[4] This rearrangement was now carried out to a phenol (IX) with acetic anhydride and concentrated sulfuric acid under the usual conditions. This afforded strong support for the structure (VIII) of the dienone. Though the 2,4-dinitrophenylhydrazone of our dienone had a constant melting point 12° lower than that reported for the derivative of VIII,[4,6] this discrepancy of the melting point may possibly be due to dimorphism.

The structure (IX) of the above phenol was confirmed by independent synthesis. *o*-Xylenol methyl ether (X) was succinoylated using aluminum chloride and the resulting keto acid (XI) was reduced to the acid (XII) by the Clemmensen procedure. Cyclization of the acid with concentrated sulfuric acid gave, along with a phenol (XIII, R = OH), the ketone (XIII, R = OCH_3), which was reduced to XIV. Demethylation of XIV with hydrobromic acid led to the desired phenol (IX), identical with the rearranged product of the dienone (VIII).



After several attempts to find an effective method for separating the hydrogenation mixture of the ketones obtained from the monoenone (IIb), it was found that diethyl oxalate reacted preferentially with one isomer in the mixture to form a glyoxalate. Thus, on treatment with 1.2 equivalents of diethyl oxalate in the presence of sodium ethoxide at room temperature, this mixture (Ib) afforded in a 70% yield an alkali-soluble glyoxalate (XV), together with 22% recovery of the ketone. The glyoxalate fraction was warmed with aqueous sodium hydroxide to give the parent ketone, which, though still not sterically homogeneous, was converted to the 2,4-dinitrophenylhydrazone of IbA in a better yield and in a more pure state than the original mixture (Ib). The recovered ketone quantitatively formed the 2,4-dinitrophenylhydrazone, m.p. 160°, of the other isomer (IbB), which derivative, as described above, is isolated only with great difficulty from the hydrazone mixture of Ib.

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(6) Hills and McQuillin, *J. Chem. Soc.*, 4060 (1953).

It seemed desirable to examine further the unexpected stereoselectivity of diethyl oxalate toward the isomeric decalone derivatives with different configurations at the ring juncture. It would be expected that when diethyl oxalate is employed in an adequately small amount on the condensation reaction, the glyoxalate would give the ketone (IbA) of higher purity and the recovered fraction would represent the difficultly separable ketonic mixture. This proved to be the case. The recovered fraction, forming an unseparable mixture of the 2,4-dinitrophenylhydrazones, was again subjected to reaction with the same equivalent of diethyl oxalate to give IbA from the glyoxalate fraction and IbB from the neutral recovered fraction.

These isomeric ketones were differentiated by infrared spectrum and refractive index, precluding the possibility that the difference of the melting points of their hydrazones may be ascribed to the geometrical isomerism about the C = N bond or dimorphism. To compare more precisely the reactivity of these ketones toward diethyl oxalate, each pure substance was allowed to react with this reagent under the conditions employed for the mixture (Ib). Both condensation reactions apparently proceeded similarly to give the glyoxalate fraction in comparable yield (66%) with that of the corresponding fraction from the mixture (Ib). This result gave no reliable answer to the problem about the relative rate of the reactions of these ketones with diethyl oxalate.

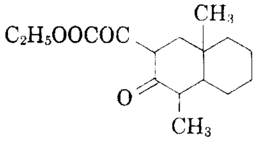
The pure ketone (IbB) was subjected to bromination-dehydrobromination in the same way as with IbA. A monobromo compound (VIB) was treated with γ-collidine or sodium acetate to give, in 35% or 55% yield respectively, the monoenone (IIb), which formed only the red form, m.p. 198–200°, of the 2,4-dinitrophenylhydrazone. This indicated that IbB was probably brominated at the 4-position, as was IbA. A 2,4-dibromo derivative (VIIB) of the ketone (IbB), on collidine treatment, gave rise to the dienone (VIII) in a comparable yield with that from VIIA. Since this product formed the 2,4-dinitrophenylhydrazone in a relatively pure form, attempt was not made to detect the monoenone (IIb) from the reaction mixture.

The present observations that both ketones (IbA and IbB) of steric purity yielded only one product (IIb) on bromination-dehydrobromination reactions are in a marked contrast to the foregoing results of the mixture (Ib) reported by Gunstone and Heggie,[4] which was also repeated in the present work. The formation of the complicated mixture of the unsaturated ketones from Ib by these reactions may be explained by the deduction that, like diethyl oxalate, bromine reacts preferentially with one isomer (presumably IbA) in this mixture forming products brominated in varying degrees, which, in turn, may be dehydrobrominated to a mixture of unsaturated ketones.

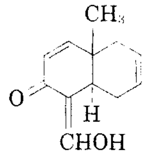
It is generally accepted that in *trans*-3-decalone, with or without the angular methyl group, the Δ^2-enol is sterically more favored than the Δ^3-enol, and bromination preferentially takes place at the 2-position.[7] The fact that the two ketones (IbA and IbB) are brominated at the 4- rather than the 2-position, may indicate that electronic effect predominates over the steric interaction in these reactions.

Now we turn our attention to the stereochemistry of the two ketones (IbA and IbB). Since both isomers are quite stable to acid and bases, the methyl group at the 4-position in both possibly assumes an equatorial conformation. Consequently, these isomers must differ in the configuration at the ring juncture. As shown in the present work, the one isomer (IbA), earlier supposed to be *cis*,[4] was derived from the dichloromethyl ketone (IVb) which was prepared from the dienone (IIIb) by catalytic hydrogenation. It was established[2,3] that the analogous dienone (IIIa) with a dichloromethyl group at the angular position yielded predominantly a *trans*-product (IVa) on similar hydrogenation. Apparently it favored a *trans*-assignment at the ring juncture in IbA. This assignment finds further support in the fact that the monoenone (IIb) gave rise to IbA on reduction with lithium and liquid ammonia, which is known to afford a thermodynamically more stable isomer.[8] It became desirable to determine the configuration of these ketones by unambiguous methods.

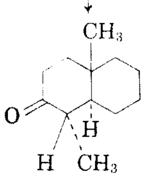
The 4-hydroxymethylene ketone (XVI), prepared from an authentic sample of *trans*-3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene[9] as reported previously,[10] was readily catalytically hydrogenated, with absorption of 4 equivalents of hydrogen, to the ketone (XVII), which was identified with IbA as the 2,4-dinitrophenylhydrazone.



XV



XVI



XVII

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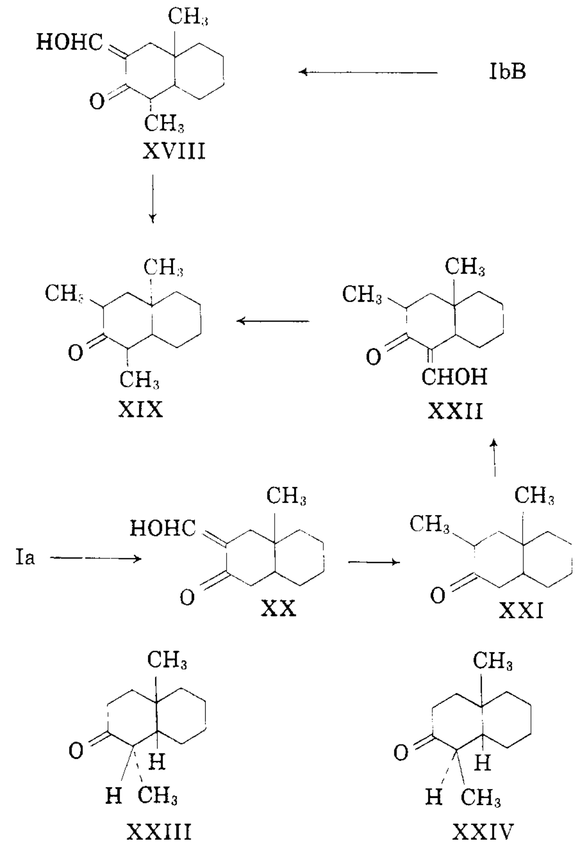
(7) For example see Corey and Sneen, *J. Am. Chem. Soc.*, **77**, 2505 (1955).

(8) Barton and Robinson, *J. Chem. Soc.*, 3045 (1954).

(9) The authors are deeply indebted to the Organic Chemicals Division of the Monsanto Chemical Company for generous gifts of this material.

(10) Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952).

On the other hand, the assignment of the *cis*-structure to the other isomer (IbB), though it became self-evident, was proved by the following reaction sequence: Formylation of IbB followed by hydrogenation of the resulting hydroxymethylene ketone (XVIII) yielded 2,4,9-trimethyl-3-decalone (XIX), which was also derived from *cis*-9-methyl-3-decalone (Ia) by the double formylation-hydrogenation through the *cis*-2,9-dimethyl-3-decalone (XXI). The location of the methyl group at the 2-position in XXI was evidenced by the non-identity of this compound with IbB.



In view of the flexibility of *cis*-decalin ring, a decision between XXIII and XXIV as representing the correct stereoformula for IbB cannot be made on the basis of the present data. However, from the postulation of the configuration for the *cis*-decalin derivative developed by Dauben, *et al.*,[11] it may be assumed that the structure XXIII in which the two methyl substituents have a *trans* relationship is preferred.

It is known[12,13] that on catalytic hydrogenation, the Δ^4-3-octalone with an angular methyl group yields a *cis*-decalone while replacement of the angular methyl group by a larger grouping (carbethoxyl or dichloromethyl) favors a *trans* product. The present observation of the predominant formation of the *trans*-decalone (IbA) by the hydrogenation of the monoenone (IIb) adds an analogous example of an unusual steric course on catalytic hydrogenation of the Δ^4-3-decalone system. This steric aspect of IIb may be accounted for by an increase in catalyst hindrance due to the two methyl groups, as suggested for the above instance by Dauben, *et al.*[12]

In conclusion, a remark should be made on the configurations of three stereoisomers of the tetrahydrosantonin, produced by catalytic hydrogenation of α-santonin where the two methyl groups are located at the 4- and 9-positions as in IIb. It was reported in the previous paper of this series[14] that α- and γ-tetrahydrosantonin possess, respectively, the *cis*- and *trans*-configurations at the juncture of the six-membered rings. However, the properties reported for the α-tetrahydro compound, the predominant formation from α-santonin by catalytic hydrogenation and the greater reactivity toward bromine in respect to the γ-isomer, are analogous with the above cited behavior of the *trans*-ketone (IbA) rather than that of the *cis*-ketone (IbB).

EXPERIMENTAL[15]

1-Methyl-ar-2-tetralol.[16] This substance was made from 2-naphthol-1-aldehyde by application of the method reported for the preparation of methyl 1-methyl-ar-2-tetralol ether.[17] A suspension of 100 g. of powdered 2-naphthol-1-aldehyde,[18] m.p. 78–79°, in 500 cc. of ethanol was shaken under hydrogen (50 atmospheres) at 50–60° in the presence of Raney nickel (10 g.). When about two molar equivalents of hydrogen were absorbed in 2 hours and slow gas absorption was noted, the hydrogenation was stopped. The pressure of hydrogen was raised to 100 atmospheres, and the hydrogenation was again started at 100–110°. After about 5 hours, an additional two molar equivalents of hydrogen were absorbed. The catalyst was filtered off and the filtrate was evaporated, leaving brown crystals which were dissolved in benzene and shaken with 10% sodium hydroxide. Acidification of the alkaline solution precipitated 57 g. (57%) of white needles, m.p. 106–107°. Two recrystallizations from petroleum ether-benzene raised the m.p. to 113°. Reported, m.p. 113–114.5°[17] and m.p. 113°.[19]

The benzene solution, shaken with sodium hydroxide, was washed with water, dried, and evaporated. An oily

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(11) Dauben, Tweit, and Mannerskantz, *J. Am. Chem. Soc.*, **76**, 4420 (1954).

(12) Dauben, Tweit, and MacLean, *J. Am. Chem. Soc.*, **77**, 48 (1955).

(13) Yanagita, Yamakawa, Tahara, and Ogura, *J. Org. Chem.*, 20 1767 (1955).

(14) Yanagita and Tahara, *J. Org. Chem.*, **20**, 959 (1955).

(15) All melting points were determined on the Kofler block. Intrared absorption spectra (a Perkin-Elmer model 21 double beam spectrophotometer was used) were determined by Mr. Shindo, the Takamine Research Laboratory, Sankyo Co., Ltd., Tokyo, to whom the authors are greatly indebted. Microanalyses were by Miss Shibuya, and the ultraviolet measurements by Miss Suzuki, both of this School.

(16) After this work was completed, Hall [*J. Am. Chem. Soc.*, **77**, 6376 (1955)] reported the improved method for preparing this material.

(17) Martin and Robinson, *J. Chem. Soc.*, 491 (1943).

(18) Fosse, *Bull. soc. chim.*, [3] **25**, 371 (1901).

(19) Adkins and Hoger, *J. Am. Chem. Soc.*, **71**, 2965 (1949).

residue was distilled to give 15 g. (15%) of a colorless oil, b.p. 130–136° at 10 mm., probably consisting mostly of 1-methyl-2-decalol for which the b.p. 125° at 12 mm. was reported.[19]

3-Keto-4-methyl-9-dichloromethyl-Δ^{1,4}-hexahydronaphthalene (IIIb). This substance was prepared from 1-methyl-ar-2-tetralol with chloroform and aqueous sodium hydroxide by the procedure reported previously.[5] The product (13%), m.p. 153–154°, was recrystallized from methanol to long plates, m.p. 156°. Reported, m.p. 156°[5] and m.p. 154°.[20]

4-Methyl-9-dichloromethyl-3-decalone (IVb). The above dichloromethyl-dienone (IIIb, 15 g.) was catalytically hydrogenated over palladium-charcoal in the manner previously described for IIIa.[2] After filtering from the catalyst, the reaction mixture was evaporated under reduced pressure leaving a colorless viscous oil (15 g.) which mostly solidified on standing in a refrigerator for a few days. The solid (9.0 g., 60%), m.p. 62–63°, separated from the oil by suction, was recrystallized from a small amount of methanol to white plates, m.p. 66°; $\lambda_{\max}^{\text{EtOH}}$ 248 mμ (log ε 3.30).

Anal. Calc'd for $C_{12}H_{18}Cl_2O$: C, 58.06; H, 7.25. Found: C, 57.86; H, 7.29.

It formed quantitatively a 2,4-dinitrophenylhydrazone, m.p. 186–187°, which was recrystallized from ethanol to red plates, m.p. 193–193.5°.

Anal. Calc'd for $C_{18}H_{22}Cl_2N_4O_4$: C, 50.34; H, 5.36. Found: C, 50.22; H, 4.87.

This ketone was recovered unchanged after being heated at 160–170° for 30 minutes, or standing in concentrated sulfuric acid overnight. It showed that the methyl group at the 4-position in IVb assumes an equatorial position.

The above, oil, removed from the crystals (IVb), gave, in 54% yield, the same 2,4-dinitrophenylhydrazone, m.p. 156–158°, of IVb. Recrystallization from methanol raised the m.p. to 193° (mixture m.p.). Attempt to isolate the derivative of other possible isomers from the mother liquor of the recrystallizations of IVb failed.

4,9-Dimethyl-3-decalol (Vb). This compound was prepared from the above ketone (IVb, 4.0 g.) by reduction with sodium and wet ether according to the method reported for Va.[2] The oily product (2.8 g.) was distilled giving 2.56 g. (88%) of a colorless oil, b.p. 105–106° at 5 mm. It formed in 94% yield a *p-nitrobenzoate*, m.p. 65–80°, which was recrystallized from ethanol to leaflets, m.p. 107–108°.

Anal. Calc'd for $C_{19}H_{25}NO_4$: N, 4.23. Found: N, 4.19.

trans-4,9-Dimethyl-3-decalone (IbA). To a solution of 0.66 g. of potassium dichromate and 0.6 cc. of concentrated sulfuric acid in 70 cc. of water was added 1.0 g. of the above alcohol (Vb). The mixture was rapidly stirred for 3 hours at room temperature, and then at 55° for an additional hour. The reaction solution was steam-distilled, and the distillate was shaken with ether. Drying and evaporation of the ether solution gave 0.91 g. of a pale yellow oil, which was purified through a 2,4-dinitrophenylhydrazone. A solution of 0.91 g. of the oil in 2 cc. of methanol was added to a slight excess of 2,4-dinitrophenylhydrazine in methanolic sulfuric acid solution, and was allowed to stand at room temperature for 2 hours. The hydrazone (1.26 g., 70%), m.p. 160°, was recrystallized from methanol to yellow needles, m.p. 186°. It showed no depression of the m.p. on admixture with the derivative of IbA prepared from the monoenone (IIb) described in the following paragraph.

The crude hydrazone (1.26 g.) was added to 10 cc. of freshly distilled pyruvic acid and 60 cc. of 50% acetic acid, and was heated for 3 hours on a boiling water-bath. The reaction mixture was made alkaline with sodium carbonate and was steam-distilled. The distillate was shaken with ether and the ether layer was dried and evaporated leaving 0.60 g. of a red oil, which was fractionated to 0.5 g. (83%) of a colorless oil (IbA), b.p. 98–99° at 3 mm. It formed quantitatively the above hydrazone, m.p. 186° (after crystallization from ethanol).

On standing in 50% ethanolic sulfuric acid overnight or refluxing in 2% methanolic sodium hydroxide for 30 minutes, this ketone was recovered unchanged (identified as its 2,4-dinitrophenylhydrazone).

3-Keto-4,9-dimethyl-Δ^{4}-octahydronaphthalene (IIb). This substance was prepared from 2-methylcyclohexan-1-one and N-diethylaminopentan-3-one methiodide according to the method first reported by Gunstone and Heggie.[4] The product (54%) showed b.p. 132–134° at 7 mm.; $\lambda_{\max}^{\text{EtOH}}$ 247.5 mμ (log ε 4.17). Reported,[4] b.p. 99–100° at 1 mm.; $\lambda_{\max}^{\text{EtOH}}$ 248 mμ (log ε 4.14). It formed a 2,4-dinitrophenylhydrazone, m.p. 198–200° (after recrystallization from ethanol). Reported, m.p. 198–199°.[4]

Hydrogenation of 3-keto-4,9-dimethyl-Δ^{4}-octahydronaphthalene (IIb). The above monoenone (IIb, 14.1 g.) was hydrogenated over palladium-charcoal (prepared from 30 cc. of 1% palladium chloride solution and 2 g. of charcoal) essentially by the procedure described briefly by Gunstone and Heggie.[4] About one molar-equivalent (1803 cc.) of hydrogen was absorbed within 25–30 minutes. The product (Ib), b.p. 108–110° at 6 mm., amounted to 13.77 g. (98%), is stable to permanganate in acetone solution, contrary to the observation reported by these authors.[4]

It formed quantitatively a mixture of 2,4-dinitrophenylhydrazones, m.p. 160–167°, which (0.86 g.) was fractionally recrystallized from ethanol giving 0.23 g. (26%) of the hydrazone of the *trans*-ketone (IbA), as yellow needles, m.p. 186–187°. Reported, m.p. 186°.[4]

Incidently the mother liquors of recrystallization of the above derivative on standing precipitated the derivative of the other isomeric ketone (IbB), as yellow-brown scales, m.p. 158–159°. Recrystallization from ethanol raised the m.p. to 160°.

Anal. Calc'd for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71; N, 15.55. Found: C, 60.22; H, 6.95; N, 15.43.

By this procedure, the latter derivative, m.p. 160°, was not obtained consistently and the yield was very low. An attempt was made to separate the hydrazone mixture by chromatography on alumina, but this trial failed.

Separation of a mixture of the isomeric ketones (IbA and IbB). To a stirred solution of sodium ethoxide, prepared from 0.50 g. of sodium and 10 cc. of absolute ethanol, was added dropwise, with ice-cooling, 3.95 g. of the above hydrogenation product from the monoenone (IIb) in 15 minutes, and then 3.8 g. (1.2 equivalents) of diethyl oxalate was added in 10 minutes. After the stirring was continued for additional 2 hours, the ice-bath was taken away, and the mixture was allowed to stand overnight at room temperature. The brown reaction was diluted with ice-water, immediately acidified with dilute acid, and extracted 3 times with ether. The ether solution was shaken with aqueous sodium bicarbonate and then with 5% sodium hydroxide solution. Acidification of the yellow alkaline solution gave an oil which was taken up in ether. Evaporation of the dried ether solution left 4.27 g. (70%) of a glyoxalate fraction (XV), as a tan liquid, giving a red-violet color with alcoholic ferric chloride. The brown bicarbonate solution similarly afforded a dark viscous oil (0.28 g.), giving the same color with alcoholic ferric chloride.

The above alkali-soluble oil was dissolved in 80 cc. of 5% aqueous sodium hydroxide and heated on a boiling water-bath for 2.5 hours. Soon a pale yellow oil separated forming an upper layer, which was taken up in ether, and the ether solution was washed with dilute alkali and then with water, and dried. Evaporation of the ether solution gave 2.1 g. of a light yellow oil, which consisted mainly of the *trans*-ketone (IbA). Similar treatment of the bicarbonate-soluble fraction afforded 0.10 g. of a neutral oil (IbA). The combined neutral oil was fractionated to 1.93 g. of a colorless oil, b.p. 110–113° at 6 mm. It formed quantitatively a 2,4-dinitrophenylhydrazone, m.p. 168–172°, which was recrystallized from ethanol to yellow needles,

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(20) Ukita, Nojima, and Nagasawa, *J. Pharm. Soc. Japan*, 72, 1327 (1952).

m.p. 186–187° (mixture m.p.) (37% from the starting ketone mixture).

The pure *trans*-ketone, regenerated from the hydrazone as described above, showed n_D^{25} 1.4915, λ_{max}^{liquid} 3.4 (s), 3.7 (w), 5.8 (s), 6.6 (w), 6.9 (s), 7.3 (m), 7.4 (m), 7.5 (m), 7.6 (w), 7.8 (w), 7.9 (w), 8.1 (w), 8.2 (w), 8.6 (m), 8.7 (m), 8.8 (m), 8.9 (w), 9.1 (w), 9.5 (w), 9.6 (w), 9.9 (w), 10.3 (w), 10.7 (w), 11.0 (w), 11.2 (w) μ.

It formed in 77% yield a *semicarbazone*, m.p. 168–174°, which was recrystallized from ethanol to prisms, m.p. 183°; λ_{max}^{EtOH} 227 mμ (log ϵ 1.14).

Anal. Calc'd for $C_{13}H_{23}N_3O$: N, 17.71. Found: N, 17.53.

The original ether solution, separated from the glyoxalate fraction, was dried and evaporated leaving 0.85 g. of a pale yellow oil, which was distilled to give 0.74 g. of the *cis*-ketone (IbB), as a colorless oil, b.p. 95–100° at 3 mm.; n_D^{25} 1.4911. It formed quantitatively the 2,4-dinitrophenylhydrazone, m.p. 148–155°, which on two recrystallizations from ethanol gave tan leaflets, m.p. and mixture m.p. 160°. The pure IbB, regenerated from the hydrazone, showed λ_{max}^{liquid} 3.4 (s), 3.7 (w), 5.8 (s), 6.5 (w), 6.9 (s), 7.2 (m), 7.4 (m), 7.7 (w), 7.8 (w), 7.9 (w), 8.0 (w), 8.1 (w), 8.2 (w), 8.5 (m), 8.7 (m), 8.8 (w), 8.9 (m), 9.1 (w), 9.4 (m), 9.9 (m), 10.0 (w), 10.3 (m), 10.6 (w), 10.7 (w), 11.2 (w) μ.

The *semicarbazone*, prepared in 77% yield, was recrystallized from ethanol to rods, m.p. 208–210°; λ_{max}^{EtOH} 228 mμ (log ϵ 1.14).

Anal. Calc'd for $C_{13}H_{23}N_3O$: N, 17.71. Found: N, 17.43.

Gunstone and Heggie[4] reported the semicarbazone, m.p. 189–190°, from the hydrogenation mixture (Ib) of the monoenone (IIb).

In another experiment, the ketone mixture (Ib) was allowed to react with 0.6 equivalent of diethyl oxalate under similar conditions. Condensation of 2.0 g. of the ketone mixture with 0.9 g. of diethyl oxalate in the presence of 0.15 g. of sodium in 0.6 cc. of absolute ethanol gave 0.80 g. of the bicarbonate-soluble and 1.18 g. of the alkali-soluble fractions and 1.14 g. of the neutral recovered ketone. The combined glyoxalate fractions, showing a positive ferric chloride test, were decomposed with alkali to give 0.62 g. of a neutral oil which on distillation gave 0.60 g. (30%) of a colorless oil, b.p. 105–107° at 6 mm., consisting chiefly of the *trans*-ketone (IbA). It formed quantitatively the 2,4-dinitrophenylhydrazone, m.p. 178–182°, which after two crystallizations from ethanol showed the m.p. 186° (mixture m.p.). The neutral recovered fraction was distilled to give 1.0 g. of a colorless oil, b.p. 105–107° at 6 mm., forming quantitatively a 2,4-dinitrophenylhydrazone, m.p. 130–142°. Repeated recrystallization from ethanol failed to yield crystals of constant m.p., showing that the oil was still not homogeneous. This oil was again reacted with 0.45 g. of diethyl oxalate and 0.073 g. of sodium in 1.4 cc. of absolute ethanol under the above conditions. The glyoxalate fraction (0.66 g.) with alkali afforded 0.33 g. of an oil, which was fractionated to 0.30 g. (15%) of the relatively pure IbA, b.p. 107° at 6 mm. It formed quantitatively the 2,4-dinitrophenylhydrazone, m.p. 160–167°, which after two crystallizations from ethanol had the m.p. 186° (mixture m.p.). The total yield of IbA was 45% from the starting mixture. The neutral fraction (0.48 g.) was distilled to give 0.43 g. (21%) of the *cis*-ketone (IbB) as a colorless oil, b.p. 105–107° at 6 mm. It formed quantitatively the 2,4-dinitrophenylhydrazone, m.p. 160° (mixture m.p.) (after recrystallization from ethanol).

Individual reactions of the cis- and trans-ketones (IbA and IbB) *with diethyl oxalate.* Each pure ketone was allowed to react with 1.2 equivalents of diethyl oxalate under the conditions described above for the mixture of the ketones (Ib). The *trans*-ketone (IbA, 1.0 g.), purified through the 2,4-dinitrophenylhydrazone, gave, with 0.25 g. (25%) of the recovered ketone, 1.03 g. of a glyoxalate fraction, which with alkali gave back the parent ketone (0.54 g., 54%). The pure *cis*-ketone (IbB, 1.0 g.) afforded, with recovery of 0.28 g. (28%) of the ketone, 1.02 g. of a glyoxalate fraction, regenerating 0.39 g. (39%) of the ketone with alkali. In both cases, the recovered ketone, after distillation, was identified as the 2,4-dinitrophenylhydrazone.

trans-4-Hydroxymethylene-3-keto-9-methyl-$\Delta^{1,6}$*-hexahydronaphthalene* (XVI). This was prepared from 3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene[9] and ethyl formate according to the procedure reported by Woodward, *et al.*[10] The product was a light brown oil (60%), giving a red-violet color with alcoholic ferric chloride. This was used without purification for the next step.

trans-4,9-Dimethyl-3-decalone (IbA). A solution of 0.18 g. of the above hydroxymethylene ketone (XVI) in 3 cc. of methanol was shaken under hydrogen in the presence of palladium-charcoal, prepared from 0.5 cc. of a 1% palladium chloride solution and 0.2 g. of charcoal, until the gas absorption was complete. About 4 molar-equivalents (94 cc.) of hydrogen were absorbed in 2 hours. After filtration of the catalyst and distillation of the methanol at reduced pressure, the residual oil, showing a negative ferric chloride test, was distilled to give 0.13 g. of the *trans*-ketone (IbA), as a colorless oil, b.p. 106–108° at 7 mm. It formed almost quantitatively the 2,4-dinitrophenylhydrazone, m.p. 175–180°. Recrystallization from ethanol raised the m.p. to 186–187°, undepressed on admixture with the sample described above.

Anal. Calc'd for $C_{18}H_{24}N_4O_4$: N, 15.55. Found: N, 15.05.

Hydrogenation of the monoenone (IIb) *with lithium and liquid ammonia.*[21] The monoenone (IIb, 1.0 g.) was reduced with 0.3 g.[22] of lithium in 50 cc. of liquid ammonia by the procedure reported earlier for 3-keto-9-methyl-Δ^4-octahydronaphthalene (IIa).[13] Evaporation of ammonia left an oily residue, which was steam-distilled. The distillate was shaken with ether and evaporation of the ether gave a pale yellow oil (0.5 g.), quantitatively forming the 2,4-dinitrophenylhydrazone, m.p. 186° (after two recrystallizations from ethanol). It showed no depression of the m.p. on admixture with the same derivative of the *trans*-ketone (IbA) described above. From the residue of the steam-distillation, the starting monoenone (IIb) was isolated in a small amount as the 2,4-dinitrophenylhydrazone, m.p. 198–200° (after chromatography on alumina and recrystallization from ethanol).

cis-2,9-Dimethyl-3-decalone (XXI). *cis*-9-Methyl-3-decalone (Ia, 1.0 g.), m.p. 45–47°, prepared from the monoenone (IIa) by catalytic hydrogenation as reported previously,[10] was reacted with 2.2 cc. of ethyl formate in the presence of dried sodium ethoxide (from 0.3 g. of sodium) by the procedure reported for the above hydroxymethylene ketone (XVI).[10] The product (XX) was obtained as a light brown oil (1.05 g., 90%), giving a violet color with ferric chloride in alcohol.

The above crude oil (XX, 1.0 g.) was hydrogenated with palladium-charcoal as described above for IbA from XVI. About two molar-equivalents of hydrogen were absorbed in 1 hour. The oily product, showing a negative ferric chloride test, was distilled to give a pale yellow oil (XXI, 0.85 g., 91%), b.p. 105–108° at 6 mm. It formed in 90% yield a 2,4-dinitrophenylhydrazone, m.p. 146–152°, which was recrystallized from ethanol to yellow-brown needles, m.p. 164–165°. On admixture with the derivative of *cis*-4,9-dimethyl-3-decalone (IbB), the m.p. was depressed to 140–145°.

Anal. Calc'd for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71; N, 15.55. Found: C, 60.26; H, 6.87; N, 15.29.

cis-2,4,9-Trimethyl-3-decalone (XIX). (*a*). *From cis-2,9-dimethyl-3-decalone* (XXI). The above 2,9-dimethyl-3-decalone (XXI, 0.60 g.) was again formylated and then was hydrogenated as described for XXI in the preceding paragraph. The hydroxymethylene ketone (XXII) was

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(21) This experiment was carried out by Mr. Ogura in our laboratory.

(22) Correction; reference 13, page 1770, line 25, read "0.3 g. of lithium" instead of "3 g. of lithium."

obtained as a red syrup (0.42 g., 63%), giving a violet color with alcoholic ferric chloride. Hydrogenation of the crude XXII (0.38 g.) and two distillations of the product yielded a colorless oil (0.23 g., 66%), b.p. 105–106° at 5 mm., giving a negative ferric chloride test. It formed quantitatively a *2,4-dinitrophenylhydrazone*, m.p. 145–150°, after standing with the above hydrazone reagent for 4 days. Recrystallization from ethanol gave long yellow plates, m.p. 173–174°.

Anal. Calc'd for $C_{19}H_{26}N_4O_4$: C, 60.94; H, 7.00; N, 14.96. Found: C, 61.22; H, 6.70; N, 14.87.

(*b*). *From cis-4,9-dimethyl-3-decalone* (IbB). The *cis*-ketone (IbB, 0.50 g.), b.p. 105–107° at 6 mm., purified through the 2,4-dinitrophenylhydrazone, was subjected to formylation and subsequent hydrogenation as described above for XXI. The hydroxymethylene ketone (XVIII), a light-red liquid, weighed 0.51 g. (88%), giving a violet color with alcoholic ferric chloride. Hydrogenation of the crude XVIII proceeded smoothly giving the trimethyl ketone (XIX), a colorless liquid (87%), 101–102° at 3 mm. On standing with the hydrazine reagent for 2 days, this oil formed in 62% yield the 2,4-dinitrophenylhydrazone, m.p. 140–151°, which was recrystallized from ethanol to yellow long plates, m.p. 173–174°, undepressed on admixture with the derivative of XIX described in (*a*).

Monobromination of trans-4,9-dimethyl-3-decalone (IbA). To a stirred solution of 0.1 g. of the *trans*-ketone (IbA) in 1 cc. of glacial acetic acid was added, dropwise, a solution of 0.1 g. of bromine in 1 cc. of the same solvent at room temperature. Bromine was absorbed rapidly and the reaction was complete in a few minutes. The reaction mixture was poured into much water and extracted with ether. The ether solution was washed with aqueous sodium bicarbonate and then with water, and dried. Evaporation of the ether gave 0.14 g. (93%) of the crude monobromide (VIA).

Monobromination of the *trans*-ketone also readily took place in chloroform solution. To a stirred solution of 0.30 g. of the ketone (IbA) in 3 cc. of chloroform was added, dropwise, a solution of 0.3 g. of bromine in 3 cc. of the same solvent, with ice-cooling. Washing with water, drying, and evaporation of the chloroform solution gave 0.45 g. (quantitatively) of the monobromo compound (VIA), as a pale yellow oil.

In the early stage of this experiment, it was observed that IbA was brominated rather slowly in acetic acid containing a little water even in the presence of hydrobromic acid, and it required about 2 hours on a 0.10-g. scale.

The monobromo compound was used without purification for the next step.

Dehydrobromination of trans-4-bromo-4,9-dimethyl-3-decalone (VIA). (*a*). *With quinoline.* The above monobromo compound (VIA), prepared from IbA (0.10 g.), was heated with 0.5 cc. of quinoline at 150–160° for 10 minutes. The dark red reaction mixture was poured into iced dilute hydrochloric acid and extracted with ether. The ether solution was washed with 5% sodium hydroxide and then with water, and dried. Evaporation of the ether gave a red oil (0.09 g.), which was fractionated to 0.05 g. (50%) of a pale yellow oil, b.p. 145–150° at 5 mm. (bath temperature). This oil formed almost quantitatively a mixture of 2,4-dinitrophenylhydrazones, m.p. 160–172°. Recrystallization from ethanol separated this mixture into two crops. The more readily precipitated crystals consisted of red plates, m.p. 178–186°, which showed no sharp m.p. even after further recrystallization from ethanol. This hydrazone was heated to reflux in a small amount of glacial acetic acid for 2 hours, and after cooling, the solution was seeded with the derivative of the monoenone (IIb) described above. There was obtained the hydrazone of IIb, showing the constant m.p. 198–200° (mixture m.p.).

The other crop, obtained from the mother liquor of crystallizations of the above hydrazone, consisted mainly of yellow needles, which after repeated recrystallization from ethyl acetate had the m.p. 210–211°; $\lambda_{max}^{CHCl_3}$ 377 mμ (log ε 4.14) and inflection 296 mμ (log ε 4.06). It showed an obvious depression of the m.p. (about 140°) on admixture with the above red form of the m.p. 198–200°.

Anal. Calc'd for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19; N, 15.63. Found. C, 58.38; H, 5.95; N, 14.48.[23]

The yellow crystals (0.02 g.) were dissolved in 40 cc. of warm 50% methanolic sulfuric acid and the solution was allowed to stand at room temperature overnight. The reaction mixture was poured into much water, and the red-brown solid (0.01 g.), m.p. 180–185°, was filtered and was chromatographed on alumina (1.0 g.). Elution with carbon tetrachloride gave red crystals, m.p. 197–199°, which after one recrystallization from ethanol had the m.p. 198–200°, undepressed on admixture with the above red hydrazone of IIb.

The monobromo ketone (VIA), prepared from IbA with bromine and acetic acid containing a little water, was similarly reacted with quinoline to give a pale yellow oil, b.p. 145–150° at 5 mm. (bath temperature). It formed a 2,4-dinitrophenylhydrazone, m.p. 155–158°, which was repeatedly recrystallized from ethanol to red plates, m.p. 160–162°.

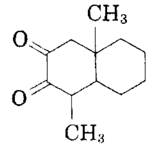
Anal. Calc'd for $C_{18}H_{22}N_4O_4$. N, 15.63. Found. N, 15.44.

On refluxing in glacial acetic acid and subsequent seeding as described above, this substance was converted to the stable red form, m.p. 198–200° (mixture m.p.).

(*b*). *With γ-collidine.* The monobromo ketone (VIA), prepared from IbA (0.15 g.), was gently refluxed for 15 minutes with 1 cc. of purified γ-collidine (b.p. 169–170°), yielding 0.15 g. (83%) of collidine hydrobromide. After processing in the usual manner,[2] a brown oily product (0.10 g.) was fractionated to 0.05 g. (33%) of the monoenone (IIb), a pale yellow oil, b.p. 140–145° at 5 mm. (bath temperature). It formed, in 81% yield, the red 2,4-dinitrophenylhydrazone, m.p. 160–175°, which had the m.p. 198–200° after treatment with hot acetic acid and seeding as described above. The yellow hydrazone was not detected in this reaction mixture.

(*c*). *With sodium acetate.* The monobromo ketone (VIA), prepared from IbA (0.30 g.), was heated with 0.4 g. of anhydrous sodium acetate in 2.5 cc. of glacial acetic acid on a boiling water-bath for 3 hours. The red reaction mixture was poured into much water and extracted with ether. The ether solution was washed successively with 10% sodium carbonate, 5% sodium hydroxide, and water. Evaporation of the dried ether extract gave an oil, which was distilled to give IIb (0.18 g., 60%), as a pale yellow oil, b.p. 110–115° at 4 mm. It formed in 80% yield the 2,4-dinitrophenylhydrazone, m.p. 170–175°, from which, by the procedure described in the section (*a*), the red form, m.p. 198–200°, was chiefly obtained, along with a small amount of the yellow form, m.p. 210–211° (both mixture m.p.).

The above alkaline washing was acidified and extracted with ether. Evaporation of the dried extract gave a trace amount of a brown oil, showing a dark violet color with alcoholic ferric chloride. Presumably it indicated that the reaction of VIA with the acetate ion afforded, though in a trace amount, the α-diketone (XXV), under a possible rearrangement and subsequent air-oxidation.



XXV

(*d*). *With 2,4-dinitrophenylhydrazine.* To a solution of the monobromo ketone (VIA), prepared from IbA (0.10 g.), in 1 cc. of methanol was added a solution of 0.15 g. of 2,4-

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(23) Repeated analysis of this substance yielded low carbon and nitrogen values. This compound burns with difficulty to a tar even with an open flame.

dinitrophenylhydrazine and 0.3 cc. of concentrated sulfuric acid in 2.25 cc. of methanol. After standing for 2 hours at room temperature, the reaction mixture was poured into water and the hydrazone (0.12 g., 60%) of IIb was filtered, washed with methanol, and dried, m.p. 170–181°. On crystallization from ethyl acetate gave 0.07 g. of the yellow form, m.p. 205°, which after further recrystallization from the same solvent had the m.p. 210–211° (mixture m.p.).

The mother liquor of the first recrystallization of the yellow crystals gave 0.05 g. of a solid, which was chromatographed on 1.5 g. of alumina and eluted with carbon tetrachloride. The more readily eluted fractions gave the stable red form (0.01 g.), m.p. 198–200° (mixture m.p.) (after recrystallization from ethanol and treatment with acetic acid followed by seeding as described above). The less readily eluted fractions afforded additional 0.01 g. of the yellow crystals.

Dibromination-dehydrobromination of trans-4,9-dimethyl-3-decalone (IbA). *Formation of 3-keto-4,9-dimethyl-*$\Delta^{1,4}$*-hexahydronaphthalene* (VIII). The *trans*-ketone (IbA) was treated with 2.1 equivalents of bromine in chloroform solution as described for the monobromo ketone (VIA). The yield of the product was quantitative, and this was used without purification for the following step.

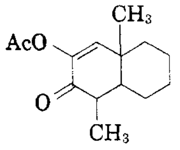
(*a*). *With γ-collidine.* The dibromo ketone (VIIA), prepared from 0.50 g. of IbA, was gently refluxed for 50 minutes with 4 cc. of γ-collidine, yielding 0.94 g. (78% as 2 equivalents) of collidine hydrobromide. After working up in the usual manner, a dirty red oil (0.46 g.) was fractionated to 0.14 g. (28%) of a pale yellow oil, b.p. 145–150° at 6 mm. (bath temperature). After two vacuum distillations, an oil, showing $\lambda_{\max}^{\text{EtOH}}$ 238 mμ (log ε 4.29) and inflection 300 mμ (log ε 3.82), formed almost quantitatively the deep red 2,4-dinitrophenylhydrazone, m.p. 195–210°. Chromatography on alumina (0.5 g.) and elution with carbon tetrachloride gave dark red scales, m.p. 220–224°. Recrystallization from *n*-butanol raised the m.p. to 226–227°; $\lambda_{\max}^{\text{EtOH}}$ 260 mμ (log ε 4.16), 315 mμ (log ε 3.80), and 409 mμ (log ε 4.47), identical with the ultraviolet spectrum previously reported for the cross-conjugated dienone (VIII).[4] When this sample was mixed with the same derivative of 3-keto-4,9-dimethyl-$\Delta^{4,5}$-hexahydronaphthalene, m.p. 215°,[4] the m.p. was depressed to 194–200°.

Anal. Calc'd for $C_{18}H_{20}N_4O_4$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.95; H, 5.23; N, 15.56.

The 2,4-dinitrophenylhydrazone of the dienone (VIII) has been reported to have the m.p. 238–239°,[4,6] but an attempt to raise the above m.p. of our sample was unsuccessful.

(*b*). *With quinoline.* The dibromo ketone (VIIA), prepared from 0.30 g. of IbA, was heated for 15 minutes with 2 cc. of quinoline at 160–170°, and worked up as described for the monobromo compound (VIA). A brown oil so obtained was distilled to give 0.11 g. (36%) of a yellow oil, b.p. 118–123° at 7 mm. It formed in 82% yield a 2,4-dinitrophenylhydrazone, m.p. 170–185°. This derivative (0.18 g.) was dissolved in warm 50% methanolic sulfuric acid, and after standing overnight at room temperature, the mixture was poured into much water. The precipitated solid was recrystallized from ethanol to give 0.05 g. of deep red scales, m.p. 203–210°, which was chromatographed on alumina (2.5 g.) and eluted with carbon tetrachloride. The more readily eluted fractions gave a trace amount of the red hydrazone, m.p. 198–200° (mixture m.p.) (after recrystallization from ethanol), of the monoenone (IIb). The less readily eluted fractions afforded the dienone (VIII) hydrazone, m.p. 214–217°, which after recrystallization from ethanol had the m.p. 222–224° (mixture m.p.).

(*c*). *With sodium acetate.* The dibromo ketone (VIIA), prepared from 0.50 g. of IbA, was treated with 1.5 g. of anhydrous sodium acetate in 5 cc. of glacial acetic acid as described above for the monobromo ketone (VIA). There was obtained a red-brown syrup (0.53 g.) as the neutral product, along with the alkali-soluble fraction (0.03 g.), which gave a dirty violet color with alcoholic ferric chloride, presumably due to the α-diketone (XXV). From the formation of the α-diketone fraction in a relative amount in the acetolysis, it may be assumed that the neutral fraction contains the acetoxy-enone (XXVI), the precursor of the α-diketone (XXV). To remove XXVI, the neutral fraction was refluxed for 30 minutes with 3 cc. of 1% methanolic potassium hydroxide. The reaction mixture was diluted with water, acidified, and extracted with ether. The ether extract gave 0.31 g. of a neutral oil and 0.05 g. of an alkali-soluble fraction, as a red-brown viscous oil (possibly XXV), giving a dirty violet color with alcoholic ferric chloride. This oil was resistant to crystallization and was not further investigated. The neutral oil was distilled to give 0.13 g. (26%) of a yellow oil, b.p. 145–150° at 5 mm. (bath temperature). It formed almost quantitatively a 2,4-dinitrophenylhydrazone, m.p. 185–189°, which was treated with methanolic sulfuric acid and then chromatographed as described above for the quinoline reaction (*b*). The hydrazone, m.p. 198–200° (mixture m.p.), of the monoenone (IIb) was isolated, but the derivative of the dienone (VIII) was not obtained in a highly pure state, showing the m.p. 210–211° (mixture m.p. 215–220°).



XXVI

Monobromination-dehydrobromination of cis-4,9-dimethyl-3-decalone (IbB). Employing the conditions described above for the *trans*-ketone (IbA), the *cis*-ketone (IbB) was brominated with bromine and then was treated with bases. Collidine treatment of the crude monobromo ketone (VIB), prepared almost quantitatively from 0.20 g. of IbB, gave a red oil (0.13 g.), which was twice distilled to yield 0.05 g. of a colorless oil, b.p. 140–145° at 5 mm. (bath temperature): $\lambda_{\max}^{\text{EtOH}}$ 241 mμ (log ε 4.19). It formed almost quantitatively a 2,4-dinitrophenylhydrazone, m.p. 135–150°, which after treatment with hot acetic acid followed by seeding as described above, had the m.p. 199–200°, undepressed on admixture with the stable red hydrazone of the monoenone (IIb).

On reaction with anhydrous sodium acetate, the monobromo ketone (IbB) gave a dark red oil, yielding on two distillations a pale yellow oil (30%), b.p. 140–145° at 6 mm. (bath temperature). It formed in 75% yield a 2,4-dinitrophenylhydrazone, m.p. 160–173°, which gave the red hydrazone, m.p. 198–200°, of IIb as described above. In this reaction a trace amount of an alkali-soluble fraction, giving a dirty violet color with alcoholic ferric chloride, was obtained, as in the case of the *trans*-isomer (VIA).

Dibromination-dehydrobromination of cis-4,9-dimethyl-3-decalone (IbB). Dibromination of the *cis*-ketone (IbB, 0.50 g.) followed by treatment with γ-collidine was carried out exactly as described for the *trans*-ketone (IbA). It gave 1.10 g. (85% as 2 equivalents) of collidine hydrobromide. A dark red oil (0.36 g.) was twice distilled to yield 0.065 g. (13%) of the dienone (VIII), as a colorless oil, b.p. 145–150° at 6 mm. (bath temperature). It formed in 75% yield a 2,4-dinitrophenylhydrazone, m.p. 190–203°, which gave a pure sample, m.p. 226–227° (mixture m.p.), only by recrystallization from ethanol, unlike in the case of the *trans*-isomer (IbA).

Dienone-phenol rearrangement of 3-keto-4,9-dimethyl-$\Delta^{1,4}$*-hexahydronaphthalene* (VIII). A solution of the above dienone fraction (VIII, 0.05 g.) in 3.3 cc. of acetic anhydride was added to a mixture of 0.18 cc. of concentrated sulfuric acid and 1 cc. of acetic anhydride. Immediately, a slightly exothermic reaction took place. After standing for two days at room temperature, the pale yellow mixture was diluted with 10 cc. of water to decompose the acetic anhydride, and was extracted with ether. The ether solution was washed with aqueous sodium bicarbonate and then with water, and dried. Evaporation of the ether gave a yellow syrup (0.05 g.), which was heated with 6 cc. of ethanol containing 0.5 cc. of concentrated hydrochloric acid on a water-bath. The reaction mixture was evaporated under reduced pressure, and the oily residue was diluted with water, and taken up in ether. The ether solution was repeatedly shaken with 20% sodium hydroxide, and the alkaline extracts, combined, were acidified and extracted with ether. Evaporation of the dried ether solution gave 0.02 g. of pale yellow crystals, m.p. 70–83°. Two recrystallizations from benzene-petroleum ether afforded white needles, m.p. 101–103°. It showed no depression of the m.p. on admixture with the sample (IX) prepared as described in the following paragraphs.

In some runs, the phenol (IX) was obtained as crystals only after seeding from the alkali-soluble fraction.

β-(2,5-Dimethyl-4-methoxybenzoyl)propionic acid (XI). To a rapidly stirred solution of 4.1 g. of succinic anhydride and 5.27 g. of *p*-xylenol methyl ether (X), prepared from *p*-xylenol,[24] 13 g. of aluminum chloride was added in small portions at 30–40°. After the addition was complete, the red mixture was stirred at 40–45° for additional 2 hours. The deep red reaction was worked up as usual to give 8.5 g. (93%) of acidic material, m.p. 131–132°. An analytical sample was obtained by recrystallization from dilute ethanol as colorless needles, m.p. 132°.

Anal. Calc'd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 66.16; H, 6.96.

γ-(2,5-Dimethyl-4-methoxyphenyl)butyric acid (XII). The above keto-acid (XI, 8.3 g.) in 20 cc. of toluene was heated to reflux for 6 hours with 24 g. of zinc amalgam, 15 cc. of water, and 35 cc. of concentrated hydrochloric acid. Five cc. each of concentrated hydrochloric acid was added to the refluxed reaction 6 times during a period of 6 hours. After cooling, ether was added to the reaction mixture to dissolve the precipitated crystals, and the organic layer was separated. The aqueous solution was diluted with about the same volume of water and was shaken with ether. The combined organic solutions were mixed with 30 cc. of 10% sodium hydroxide and the organic solvent was removed by steam-distillation. To the residual alkaline solution was added 3 cc. of dimethyl sulfate and the mixture was heated for 2 hours on a boiling water-bath. After cooling, the reaction solution was acidified to give 7.1 g. (91%) of crystals (XII), m.p. 98°. An analytical sample was obtained by recrystallization from dilute ethanol as colorless slender plates, m.p. 103°.

Anal. Calc'd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.99; H, 8.04.

1-Keto-5,8-dimethyl-7-methoxy-1,2,3,4-tetrahydronaphthalene (XIII). The above acid (XII, 6.0 g.), powdered, was added in small portions to 30 cc. of concentrated sulfuric acid, and soon a yellowish-brown clear solution was obtained. After being warmed at 70° for 10 minutes, the solution was chilled with ice-water and poured into much water. The separated brown solid was taken up in ether and the ether solution was washed three times with dilute sodium hydroxide, then with water, and dried. Evaporation of the ether gave 4.82 g. (88%) of yellow crystals,, m.p. 62°. An analytical sample was obtained by recrystallization from benzene-petroleum ether as colorless prisms, m.p. 63°.

Anal. Calc'd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.35; H, 7.93.

The above alkaline washing was acidified and extracted with ether. Drying and evaporation of the ether extract gave 0.40 g. (7%) of 1-keto-5,8-dimethyl-7-hydroxy-1,2,3,4-tetrahydronaphthalene (XIII, R = OH), m.p. 155–165°. An analytical sample was obtained by recrystallization from dilute ethanol as white scales, m.p. 174–175°.

Anal. Calc'd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.75; H, 7.41.

This phenol was also obtained in 86% yield from the methoxy ketone (XIII, R = OCH_3) by refluxing with hydrobromic acid in acetic acid as described below for IX.

5,8-Dimethyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (*methyl 1,4-dimethyl-ar-2-tetralol ether*) (XIV). The above methoxy ketone (XIII, R = OCH_3) (4.82 g.) was reduced by the Clemmensen method as described above for XII. The product was distilled to give 3.6 g. (80%) of a colorless oil, b.p. 130° at 4 mm., which immediately solidified, m.p. 37–38°. An analytical sample was obtained by recrystallization from ethanol as white needles, m.p. 39°.

Anal. Calc'd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.23; H, 9.75.

1,4-Dimethyl-ar-2-tetralol (IX). A solution of the above methyl ether (XIV, 2.0 g.) in 9 cc. of glacial acetic acid was heated to reflux for 3 hours with 20 cc. of 48% hydrobromic acid. After cooling, the deep brown mixture was poured into much water, and the separated crystals were collected, and dissolved in 10% sodium hydroxide (about 15 cc.). The alkaline solution, after treatment with charcoal, was acidified. The precipitated solid (1.43 g., 77%), m.p. 103–104°, was recrystallized from benzene-petroleum ether to white needles, m.p. 104–104.5°.

Anal. Calc'd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.67; H, 9.46.

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