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

ANALOGS OF SANTONIN. III. DEHYDROBROMINATION OF 2-BROMO- AND 2,6-DIBROMO-2,4,4-TRIMETHYLCYCLOHEXAN-1-ONE[1,2]

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In the first paper of this series (1), it was reported that the products obtained on dehydrobromination of the 2,6-dibromo-4,4-dimethylcyclohexan-1-one (VIa) were substances of different types depending on the reagents used. With sodium acetate and acetic acid, VIa gave the α-diketone (VIIa) and its monoacetate, while with quinoline the dienone (XIa) was obtained in a poor yield, along with the predominant bromoënone (Xa).

For the purpose of comparison, we investigated the bromination and subsequent dehydrobromination of 2,4,4-trimethylcyclohexan-1-one (Vb), where the methyl group at the 2-position corresponds to that at the 4-position in tetrahydrosantonin.

The starting material (Vb), which is previously recorded (2), was prepared from 4-dichloromethyl-2,4-dimethylcyclohexa-2,5-dien-1-one (Ib) (3) by application of the method of von Auwers and Lange for Ia (4). Catalytic hydrogenation of Ib resulted in a mixture of the two possible stereoisomers of the dichloromethyl ketone, the predominant one (III) in a crystalline form and the other as an oil (II) which on standing for about a month was completely converted into the solid one. From this, it may be concluded that in II the methyl group at the 2-position is in *trans*-form to the dichloromethyl group, while in III both groups are in the *cis*-position. The dichloroketone was smoothly reduced with sodium and ether to the alcohol (IV) in a good yield and one form of the two possible isomers was almost exclusively obtained to which a possible *trans*-configuration is assigned on the basis of the mode of its formation. This alcohol (IV) was readily oxidized to the ketone (Vb). However, this troublesome method was abandoned since we developed an improved procedure for preparing Vb which will be described below.

2,6-Dibromo-2,4,4-trimethylcyclohexan-1-one (VIb), obtained from Vb with two moles of bromine, was reacted with sodium acetate and glacial acetic acid to give the known α-diketone (VIIb) and a crystalline bromoënone (Xb) in 7% and 25% yields, respectively. The α-diketone, like (VIIa), showed a pronounced ferric chloride color, and of the two possible enol forms (VIIIb and IXb), the latter is preferred because of its ultraviolet spectrum (λ_{max}^{EtOH} 274.5 mμ, ϵ 19620) (5). The formulation for the bromoënone as Xb is based on analogy

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[2] We wish to thank Mr. E. Oki, Pharmaceutical Institute, Kyushu University, for aid in the early stages of these experiments.

with that of Xa, and both compounds possess the same peak at 241 mμ in the ultraviolet spectrum (Fig. 1).

The fact that on ozonolysis of the bromoënone acetic acid was not detected by paper chromatography, excluded the possibility of the structure X'b for the bromoënone. On reduction with zinc dust and alcohol, the bromoënone (Xb) gave in a 53% yield the known monoënone (XIIIb) while Xa was recovered unchanged. Xb was hydrolyzed on prolonged heating with diluted sulfuric acid to give the α-diketone (VIIb) in an 88% yield.

Treatment of the dibromide (VIb) with quinoline and γ-collidine at about 100° gave predominantly the bromoënone (Xb) in 33 and 47% yields, respectively. In addition, a very small amount of a dienone (XIb) was isolated as the 2,4-dinitrophenylhydrazone. When the reaction was conducted at 170°, the anticipated 2,4,4-trimethylcyclohexa-2,5-dien-1-one (XIb), along with a trace of Xb, was obtained as a chief product in a more satisfactory yield (about 30%)

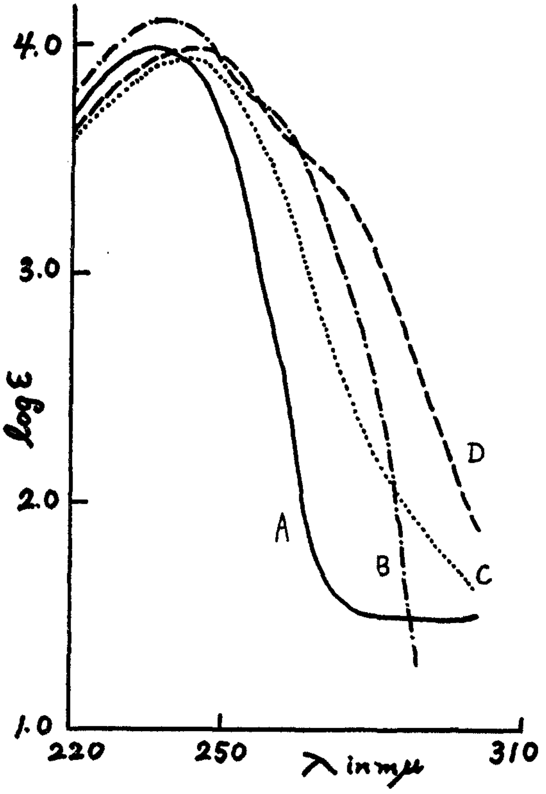
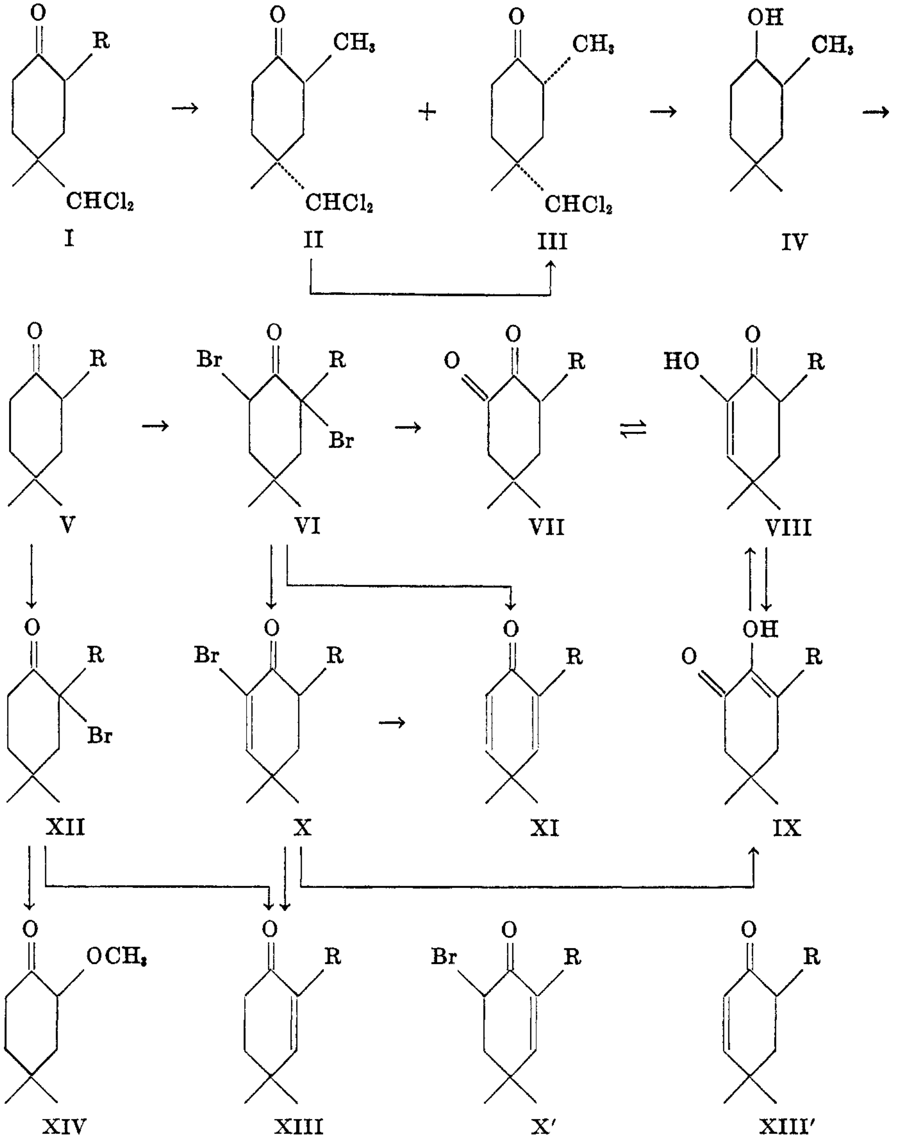


Fig. 1. Ultraviolet Absorption Spectra

A. 2,4,4-Trimethylcyclohex-2-en-1-one (XIIIb)
B. 2,4,4-Trimethylcyclohexa-2,5-dien-1-one (XIb)
C. 6-Bromo-2,4,4-trimethylcyclohex-5-en-1-one (Xb)
D. 2-Bromo-4,4-dimethylcyclohex-2-en-1-one (Xa)

than that of XIa from VIa. It is notable that VIb, on heating alone, was converted to Xb and the monoënone (XIIIb) in 25% and 10% yield respectively.



Series (a): R = H, Series (b): R = CH_3

The dienone was readily hydrogenated to the parent ketone (Vb). Structure (XIb) was assigned on the basis of analogy with XIa and supported by the ultraviolet spectrum (Fig. 1). However, its dienone-phenol rearrangement to pseudocumenol by means of sulfuric acid and acetic anhydride was effected with much more difficulty than in the case of XIa.

This result seems to be comparable with the unsuccessful attempt by Gunstone and Heggie (7) in the similar rearrangement of 2,5,6,7,8,10-hexahydro-2-keto-1,10-dimethylnaphthalene. Santonin was found to undergo rearrangement under the same conditions to the acetate of α-desmotroposantonin in a moderate yield. These difficulties encountered in the rearrangement appear to be connected with the presence of the α-methyl group in the unsaturated system.

It is surprising that the bromoënone (Xb) on treatment with γ-collidine and quinoline at 170° was dehydrobrominated to the dienone (XIb) in 25% and 35% yields, respectively. From this result, it is self-evident that the conversion of the dibromide (VIb) to the dienone involves, at least in part, the intermediate formation of Xb.

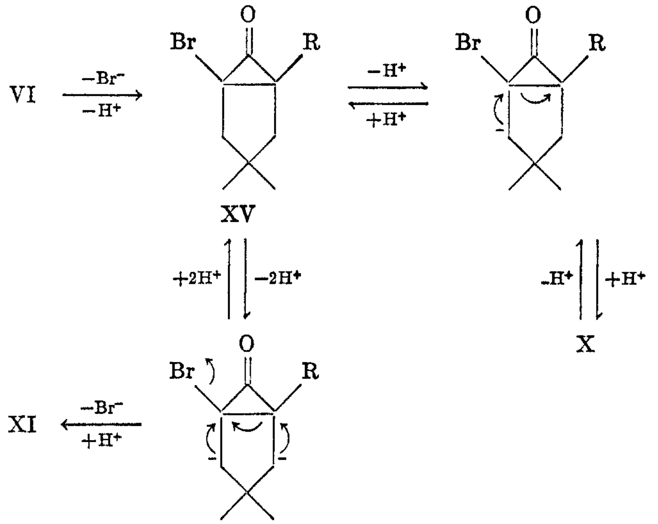
When brominated with one mole of bromine or N-bromosuccinimide, the ketone Vb gave, in 55% or 64% yield, a monobromide (XIIb), which, unlike the dibromide, is stable enough to be distilled. The monobromide was readily dehydrobrominated with sodium acetate, γ-collidine, and 2,4-dinitrophenylhydrazine to the known monoënone (XIIIb) in satisfactory yields.

It has previously been reported (8) that a monobromo derivative, prepared from 2-methylcyclohexan-1-one with bromine, reacted with pyridine and 2,4-dinitrophenylhydrazine to give different unsaturated products, Δ^4- and Δ^2-ketone, respectively. This observation is not in accord with the present results, and would make it necessary to consider the alternative structure (XIII'b) for the monoënone, for which the formation of this substance from Xb seems favorable. On repetition of the reaction, however, it was found that, contrary to the previous report (8), monobromo-2-methylcyclohexan-1-one when treated with bases including pyridine invariably yielded Δ^2- ketone. From this, the small possibility of the formulation as XIII'b for the monoënone was completely excluded, and it can therefore be concluded that in the debromination of Xb to XIIIb the unexpected facile migration of double bond takes place simultaneously.

Following the procedure of Franke and Bueren (9) which was published while this work was in progress, vinyl ethyl ketone was readily condensed with isobutyraldehyde in the presence of sodium methoxide to give, in a 56% yield, the monoënone (XIIIb), which was quantitatively hydrogenated to the ketone (Vb), as reported (2b). This constitutes a very useful method for preparing Vb.

Contrary to XIIb, XIIa on reaction with Brady's reagent under the usual conditions gave no unsaturated compound, but only a 2,4-dinitrophenylhydrazone of ketol methyl ether (XIV), which is stable to refluxing with acetic acid.

As a mechanism of the formation of the bromoënone (Xa) from the dibromide (VIa), it was previously suggested (1) that it involves the intermediate formation of X'a with subsequent migration of the double bond. However this postulation is quite unlikely, since the result (8) cited there as an instance for the double bond migration during dehydrobromination was denied in the present work as described above. Also it seems an unreasonable assumption that the process pass through 2,2-dibromoketone resulting from bromine migration in allylic rearrangement of enol form of VIa. Following the explanation developed for the Faworskii reaction by Loftfield (10), instead, an ionic mechanism for the reactions of VI with bases, which involves the intermediate formation of the cyclopropane ring (XV), is suggested.



It may be assumed that on dehydrobromination the hypothetical intermediate (XV) is in a prototropic equilibrium with X. The latter is greatly favored at lower temperature, while at higher temperature this equilibrium may be broken down by the conversion of XV into XI.

EXPERIMENTAL[3]

4-Dichloromethyl-2,4-dimethylcyclohexa-2,5-dien-1-one (I). This was prepared from *assym-m*-xylenol[4] essentially according to the procedure of von Auwers, *et al.* (3). The yield was 26% in a pure state, m.p. 54–56°. Reported, m.p. 56° (3). The *semicarbazone* had m.p. 190–193°. Reported, m.p. 182–186° (3).

4-Dichloromethyl-2,4-dimethylcyclohexan-1-one (II *and* III). The above dienone was hydrogenated in methanol with palladium-charcoal and absorption of 2 moles of hydrogen proceeded quite rapidly. After removal of the catalyst, the mixture was concentrated under reduced pressure, and the oil so obtained was distilled giving a colorless liquid (97%), b.p. 118–119° at 6 mm., which slowly solidified on standing in a refrigerater. The solid, which was separated from the oil by suction, was recrystallized from petroleum ether giving white prisms, m.p. 50–51.5°.

Anal. Calc'd for $C_9H_{14}Cl_2O$: C, 51.65; H, 6.74.
Found: C, 51.33; H, 6.30.

The semicarbazone, prepared quantitatively, had m.p. 158–160° (after two recrystallizations from alcohol).

Anal. Calc'd for $C_{10}H_{18}Cl_2N_3O$: C, 45.11; H, 6.39; N, 15.78.
Found: C, 45.05; H, 6.24; N, 15.43.

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[3] All temperatures are not corrected. Microanalyses were by Miss C. Shibuya; ultraviolet measurements by Miss M. Suzuki.

[4] We wish to thank Prof. E. Ochiai, Pharmaceutical Institute, Tokyo University, for the gift of this material.

The 2,4-dinitrophenylhydrazone, prepared quantitatively, orange-yellow needles, had m.p. 161–163°, (after one recrystallization from alcohol).

Anal. Calc'd for $C_{15}H_{18}Cl_2N_4O_4$: C, 46.27; H, 4.63.

Found: C, 46.29; H, 4.86.

The oily residue gave the same 2,4-dinitrophenylhydrazone, and, on standing for a month, was completely converted to the solid isomer.

cis-2,4,4-Trimethylcyclohexan-1-ol (IV). This was prepared from an isomeric mixture of II and III by a slight modification of the published procedures (4). To a mixture of 30 g. of the ketone and 20 g. of sodium wire was added dropwise, with slow stirring, 250 cc. of water under ice-cooling. Caution must be taken to keep a slow and uniform evolution of hydrogen gas, and the addition took about 50 hours. The ether solution, separated from the water layer, was washed and concentrated. The oil so obtained was distilled giving 18.5 g. (91%) of aromatic colorless liquid, b.p. 71–75° at 8 mm. Reported, b.p. 192° (2a).

The *p-nitrobenzoate* was prepared almost quantitatively as colorless needles of m.p. 61–63° (after one recrystallization from alcohol).

Anal. Calc'd for $C_{16}H_{21}NO_4$: C, 66.78; H, 7.24; N, 4.81.

Found: C, 66.98; H, 7.21; N, 4.70.

2,4,4-Trimethylcyclohexan-1-one (Vb). This was prepared in 80–90% yield from the above alcohol by oxidation with sodium dichromate and dilute sulfuric acid in the usual manner. It was a colorless liquid, b.p. 87–89° at 30 mm. with a camphor-like odor. Reported, b.p. 191° (2a).

The semicarbazone, colorless needles, m.p. 165–166°, (after recrystallization from alcohol). Reported, m.p. 164–165° (2a), 163–164° (2c).

Anal. Calc'd for $C_{10}H_{19}N_3O$: N, 21.32. Found; N, 21.39.

The 2,4-dinitrophenylhydrazone was prepared quantitatively as orange yellow crystals, m.p. 148–149°, (after recrystallization from alcohol). Reported, m.p. 150–151° (2c).

Anal. Calc'd for $C_{15}H_{20}N_4O_4$: N, 17.49. Found: N, 17.11.

2,6-Dibromo-2,4,4-trimethylcyclohexan-1-one (VIb). The above ketone (2.0 g.) was brominated with 5.0 g. of bromine in the manner described for VIa (1) except that the reaction was started in the presence of hydrobromic acid. The product was 4.3 g. (quantitative) of pale yellow oil. This material was used for the next step without further purification, because it is unstable even at room temperature.

Reaction of dibromide (VIb) *with sodium acetate.* A mixture of 4.3 g. of VIb, 9.0 g. of anhydrous sodium acetate, and 25 cc. of glacial acetic acid was heated on a boiling water-bath for 3 hours. The reaction mixture was worked up in the manner described for VIa.

(*a*). *Neutral product.* The alkali-insoluble fraction was a brown viscous oil (2.6 g.), which soon solidified. After removing most of the oil by suction, 0.6 g. of crystals, m.p. 70–76°, 6-bromo-2,4,4-trimethylcyclohex-5-en-1-one (Xb), was obtained. The oil (1.44 g.) was distilled to give a fraction, b.p. 86–92° at 7 mm., from which an additional 0.16 g. (total, 26%) of Xb was isolated. Recrystallization from petroleum ether gave white needles, m.p. 75–77°, $\lambda_{\max}^{\text{EtOH}}$ 241 mμ.

Anal. Calc'd for $C_9H_{13}BrO$: C, 49.77; H, 6.03.

Found: C, 50.19; H, 5.75.

It formed in a 83% yield a *2,4-dinitrophenylhydrazone* as orange-red prisms, m.p. 159–161°. Recrystallization from alcohol frequently caused the decomposition into the parent substance.

On hydrogenation with palladium-charcoal in methanol, Xb absorbed rapidly two moles of hydrogen to yield the initial ketone (Vb), identified as the *semicarbazone*, m.p. 165° (mixture m.p.).

Ozonized oxygen was introduced into a solution of 0.25 g. of Xb in 20 cc. of chloroform, under cooling with methanol and Dry Ice, and the ozonide soon began to separate out as a solid. After 1.5 hours, the reaction mixture was worked up as reported (13). From the steam-distillate, acetic acid was not detected by the usual paper chromatography (hydrazide-silver reaction).

(*b*). *Acidic product.* The alkali-soluble fraction was a pale yellow oil (0.16 g.), which soon solidified. One recrystallization from petroleum ether gave 50 mg. (7.3%) of 4,4,6-trimethylcyclohexa-1,2-dione (VIIb), m.p. 75–85°, which on further recrystallization from the same solvent had m.p. 91°. It showed no depression of m.p. when mixed with the sample described in the next paragraph.

α-Diketone (VIIb) *from bromoënone* (Xb). A mixture of 0.4 g. of Xb and 20 cc. of 10% sulfuric acid was heated on a boiling water-bath, and soon the sublimation of white needles began. During the reaction the crystals were occasionally collected, and after 33 hours, there was obtained 0.25 g. (88%) of VIIb. Recrystallization from petroleum ether gave white elongated prisms, m.p. 90–92°. Reported, m.p. 90° (6). It was sublimable at about 58° at 3 mm., and gave a deep violet color with ferric chloride.

Anal. Calc'd for $C_9H_{14}O_2$: C, 70.08; H, 9.16.
Found: C, 70.28; H, 8.98.

The *glyoxime* was obtained in a 40% yield as slightly pink prisms, m.p. 171–173.5° (after two recrystallizations from dilute alcohol). Reported, m.p. 177–178° (6).

Reduction of bromoënone (Xb) *to monoënone* (XIII b). A solution of 0.35 g. of Xb in 20 cc. of absolute alcohol was refluxed with 3.5 g. of acid-washed zinc dust for 6 hours. On cooling, the mixture was filtered free from zinc and concentrated under a reduced pressure. The residual liquid was mixed with water and taken up with ether. Washing, drying, and concentration of the ether extract gave a faintly colored liquid (0.22 g.), which was fractionated to yield 0.115 g. (52.5%) of a colorless liquid, the monoënone (XIIIb), b.p. 73–75° at 13 mm. or b.p. 52–53° at 4 mm. $\lambda_{\max}^{\mathrm{EtOH}}$ 235 mμ.

It formed quantitatively a *2,4-dinitrophenylhydrazone,* m.p. 163–164°. Recrystallization from alcohol gave shiny, scarlet platelets, m.p. and mixture m.p. 164–165°.

Anal. Calc'd for $C_{15}H_{18}N_4O_4$: C, 56.40; H, 5.66.
Found: C, 56.72; H, 5.15.

Xa, m.p. 85–86°, $\lambda_{\max}^{\mathrm{EtOH}}$ 241 mμ, was treated with zinc dust in the same manner, but was recovered unchanged.

Reaction of the dibromide (VIb) *with γ-collidine and quinoline at a lower temperature.* To 10 cc. of purified γ-collidine (b.p. 169–170°) was added 4.3 g. of VIb, and there a slightly exothermic reaction took place, separating the collidine-hydrobromide. The mixture was heated on a boiling water-bath for 30 minutes. On cooling, the dark brown mixture was diluted with ether, and the hydrobromide (4.38 g., 76% for 2 moles) was filtered off. The ether solution was washed with dilute acid, then with dilute alkali, dried, and concentrated. There was obtained an oily product (1.95 g.), which soon solidified. After removing most of the oil by suction, there was obtained 0.91 g. of white needles, m.p. 74–76.3°, the bromoënone (Xb), which on recrystallization from petroleum ether showed m.p. and mixture m.p. 75–78°.

The oil, separated from the solid, was fractionally distilled, and two fractions of b.p. 95–110° at 18 mm. (0.25 g.) and b.p. 160–200° (bath temperature) at 18 mm. (0.16 g.) were obtained. The first fraction was further fractionated into two fractions of b.p. 75–80° at 14 mm. (0.1 g.) and b.p. 90–117° at 14 mm. (0.1 g.). The lower-boiling fraction, a pale yellow liquid (5.3%), gave in a 68% yield a *2,4-dinitrophenylhydrazone,* m.p. 157–173°, of the dienone (XIb), which on recrystallization from alcohol gave m.p. and mixture m.p. 175–177°.

The higher-boiling fractions, which solidified, gave an additional 65 mg. of Xb (total 32.3%).

VIb was treated with the purified quinoline under the same conditions. The reaction mixture was poured into cold dilute hydrochloric acid and soon the separated oil solidified. After being worked up as above, there was obtained a 47.4% yield of Xb, along with the dienone fraction (3.7%) b.p. 85–100° at 15 mm. The latter formed in a 76% yield the 2,4-dinitrophenylhydrazone of XIb.

Decomposition of the dibromide (VIb) *on heating alone.* Compound VIb (0.7 g.) was heated on a boiling water-bath, and soon the material became dark colored with violent evolution of hydrogen bromide gas. After 3 hours, a very viscous oil so obtained was chilled and dissolved in ether. The ether solution was passed through alumina, and the ether eluate was concentrated, leaving 0.29 g. of a brown oil, which solidified. After removing most of the oil by suction, there was obtained 85 mg. (18%) of the bromoënone (Xb), m.p. 69–74°, which on recrystallization gave m.p. and mixture m.p. 74–77°.

The separated oil was fractionated into two fractions of b.p. 120–130° and b.p. 130–150° at 5 mm. (both bath temperatures). The lower-boiling fraction (30 mg., 10%), gave the 2,4-dinitrophenylhydrazone of the monoënone (XIIIb), m.p. and mixture m.p. 164–165° (after recrystallization from benzene-alcohol). The higher-boiling fraction yielded an additional 30 mg. of Xb (total 25%).

Reaction of dibromide (VIb) *with γ-collidine and quinoline at higher temperature. 2,4,4-Trimethylcyclohexa-2,5-dien-1-one* (XIb). A mixture of 4.3 g. of VIb and 10 cc. of purified γ-collidine was placed in the pre-heated oil-bath at 120°, and the bath temperature was raised to 170° within 10 minutes. After this temperature was kept for 30 minutes, the reaction mixture was worked up as described in the preceding paragraph. The neutral fraction, a dark red oil, was fractionated into two fractions of b.p. 80–83° at 10 mm. (0.6 g.) and b.p. 110–115° at 7 mm. (0.11 g.). The lower-boiling fraction was redistilled to give 0.5 g. of a pale yellow liquid (XIb) with camphorlike odor, $\lambda_{\max}^{\mathrm{EtOH}}$ 237 mμ. It formed quantitatively a *2,4-dinitrophenylhydrazone*, m.p. 174–178°, which was twice recrystallized from alcohol to give hair-like, orange-red needles, m.p. 179–181°.

Anal. Calc'd for $C_{15}H_{16}N_4O_4$: C, 56.95; H, 5.12; N, 17.91.
Found: C, 57.08, 57.28; H, 4.90, 5.22; N, 17.89, 18.10.

The higher-boiling fraction, a pale yellow oil which solidified on standing, was recrystallized from petroleum ether giving a trace (5 mg.) of bromoënone (Xb), m.p. and mixture m.p. 71–75°.

The alkali solution, separated from the ether layer, gave a trace (5 mg.) of the α-diketone, m.p. 75–85° (mixture m.p. of 82–89° with the sample, m.p. 90–92°).

With industrial collidine fraction, the yield of the dienone was considerably decreased.

When purified quinoline was used in place of γ-collidine, the dienone, b.p. 88–90° at 15 mm. was obtained in a 33.5% yield but the α-diketone was not isolated.

Hydrogenation of the dienone in methanol with palladium-charcoal gave the initial ketone (Vb), identified as the semicarbazone, m.p. and mixture m.p. 165–166°.

Pseudocumenol from dienone (XIb). To a mixture of 0.4 g. of XIb and 5 cc. of the freshly distilled acetic anhydride was added a mixture of 0.45 g. of concentrated sulfuric acid and 1 cc. of acetic anhydride, and the whole was allowed to stand at room temperature for 40 hours. The faintly brown mixture was poured into 50 cc. of water, and warmed on a water-bath. On cooling, the almost clear solution was repeatedly shaken with ether. The ether solution was washed with sodium dicarbonate, dried, and evaporated, leaving a pale yellow oil (0.39 g.) which did not form a 2,4-dinitrophenylhydrazone. This oil was hydrolyzed by refluxing in 16 cc. of alcohol with 12 cc. of 35% hydrochloric acid for 10 hours. The reaction mixture was poured into water, and most of the alcohol was removed under a reduced pressure. The brown oil which separated was taken up into ether and the ether extract was shaken with dilute alkali, dried, and evaporated, leaving an oil (0.125 g.). The alkali solution was acidified, shaken with ether, and the ether solution was dried and evaporated. There was obtained a pale yellow oil, which crystallized on seeding with pseudocumenol prepared from 2,5-dimethyl-*p*-hydroxybenzaldehyde (1) by the Clemmensen reduction. Two recrystallizations from petroleum ether gave 85 mg. (23%) of fine white needles, m.p. 43–57°. On further repeated sublimation a small amount of pure crystals, m.p. 66–69°, alone and on admixture with the sample, m.p. 72°, were obtained.

Santonin was subjected to the dienone-phenol rearrangement under the same conditions to give the acetate of α-desmotroposantonin, m.p. 153–155°, in a 54% yield.

Dienone (XIb) *from bromoënone* (Xb). Compound Xb (0.25 g.) was treated with 1 cc. of purified γ-collidine as described for XIb from the dibromide (VIb). The collidine hydrobromide was isolated in a 97% yield. The neutral product, a pale yellow liquid (95 mg.) was fractionated to give 40 mg. (25%) of a colorless, aromatic liquid (XIb), b.p. 95–110° (bath-temperature) at 7 mm. It formed in a quantitative yield the *2,4-dinitrophenylhydrazone,* m.p. 177–179°, which on two recrystallizations from alcohol had m.p. 178–181° (alone and in admixture).

Use of the purified quinoline in place of collidine gave a 35% yield of XIb.

2-Bromo-2,4,4-trimethylcyclohexan-1-one (XIIb). (*a*). Compound Vb (2.0 g.) was brominated with 2.3 g. of bromine in the manner described for the dibromide (VIb). The brown oil thereby obtained was fractionated, giving 1.68 g. (55%) of an almost colorless oil, b.p. 63–67° at 5 mm. or 57–61° at 3 mm. The higher-boiling fraction gave a small amount of Xb, which was presumably derived from the contaminated dibromide (VIb).

(*b*). Compound Vb (1.0 g.) was refluxed in carbon tetrachloride (20 cc.) with N-bromosuccinimide (1.3 g.) and benzoyl peroxide (0.1 g.). The reaction was completed within 10 minutes and 0.71 g. (86%) of succinimide was isolated. The product was fractionated giving 1.01 g. (64.5%) of pale yellow oil, b.p. 65–71° at 7 mm. The higher-boiling fraction gave a small quantity of Xb.

2,4,4-Trimethylcyclohex-2-en-1-one (XIIIb). (*a*). *From the monobromide* (XIIb). XIIb (1.0 g.) was heated with 1.7 cc. of purified γ-collidine on a boiling water-bath for 30 minutes. The reaction mixture was worked up as described above. Fractionation of the oily product (0.64 g.) gave 0.44 g. (70%) of an aromatic, colorless liquid, b.p. 67–68° at 10 mm. It formed quantitatively a *2,4-dinitrophenylhydrazone,* m.p. 140–152°, which on three recrystallizations from alcohol afforded red platelets, m.p. 163°. It showed no depression of m.p. when mixed with a sample prepared by the condensation (*b*).

When the reaction was conducted at 170°, XIIIb, b.p. 81–82° at 20 mm. was obtained in a 77% yield.

The same procedure with sodium acetate as described for VIb was followed in this preparation, and XIIIb, b.p. 65–66° at 8 mm. was obtained in a 68% yield.

To XIIb (33 mg.) was added the Brady's reagent containing 30 mg. of 2,4-dinitrophenylhydrazine, and the mixture was allowed to stand at room temperature overnight. There was obtained the same 2,4-dinitrophenylhydrazone, m.p. 164°. Attempts to isolate the 2,4-dinitrophenylhydrazone of XIIb itself by reducing the reaction time (11) failed.

(*b*). *By condensation.* The published procedures for XIIIa (9) were applied in this preparation. To potassium methoxide (prepared from 0.4 g. of potassium and 2.0 cc. of absolute methanol) was added a mixture of 10.8 g. of vinyl ethyl ketone (12) and 9.3 g. of isobutyraldehyde in small portions with stirring, the temperature being kept below 50° by occasional cooling with ice-water. The addition was completed in 20 minutes, and the mixture was acidified with a few drops of acetic acid, poured into water, and extracted with ether. Drying and concentration of the ether extract gave an oil, which was fractionated giving 10.0 g. (56.5%) of an aromatic colorless liquid, b.p. 56.5–57.5° at 4.5 mm. $\lambda_{\max}^{\text{EtOH}}$ 235 mμ. Reported, b.p. 195–196° (2a, b). It formed quantitatively a *2,4-dinitrophenylhydrazone,* m.p. 160–164°, which on one recrystallization from alcohol gave red platelets, m.p. 164–165°.

Anal. Calc'd for $C_{15}H_{18}N_4O_4$: N, 21.46. Found: N, 21.31.

The semicarbazone was prepared quantitatively as white crystals, m.p. 156–158°. Reported, m.p. 158–159° (2a).

Anal. Calc'd for $C_{10}H_{18}N_3O$: N, 21.64. Found; N, 21.88.

The material, as reported (2b), was readily hydrogenated to the ketone (Vb).

2-Methylcyclohex-2-en-1-one. 2-Methylcyclohexan-1-one was monobrominated and subsequently dehydrobrominated with pyridine, exactly according to the procedure previously reported (8). The monobromo ketone was obtained in 27% yield: pale yellow liquid, b.p. 65–69° at 10 mm. The monoënone was obtained in a 19% yield as a pale yellow liquid, b.p. 110–115° at 125 mm. $\lambda_{\max}^{\text{EtOH}}$ 235 mμ (log ε 3.56).

This formed almost quantitatively the *2,4-dinitrophenylhydrazone,* m.p. 201–203°. It showed no depression of m.p. when mixed with a sample of m.p. 204–206°, prepared from the same bromide by the Mattox-Kendall procedure. Reported, m.p. 207.5–208.5° (8, 13).

Anal. Calc'd for $C_{13}H_{14}N_4O_4$: C, 53.77; H, 4.86; N, 19.30.

Found: C, 53.77; H, 4.66; N, 19.47.

The monoënone was further identified as the *semicarbazone*, m.p. 205–208° (mixture m.p.) Reported, m.p. 207–210° (13), 205° (8).

SUMMARY

1. Dehydrobromination of 2,6-dibromo-2,4,4-trimethylcyclohexan-1-one (VIb) gave the α-diketone (VIIb), bromoënone (Xb), dienone (XIb), and monoënone (XIIIb), depending on the reagents employed and the reaction conditions.

2. The monobromoketone (XIIb) on dehydrobromination produced invariably the monoënone (XIIIb).

3. A mechanism for the dehydrobromination of the dibromide (VIb) is proposed.

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REFERENCES

(1) YANAGITA, TAHARA, AND OKI, *J. Pharm. Soc. Japan*, **71**, 1060 (1951).
(2) (a) WALLACH AND SCHEUNERT, *Ann.*, **324**, 107 (1902). (b) VON AUWERS, *Ann.*, **420**, 111 (1920). (c) BRENNER AND SCHINZ, *Helv. Chim. Acta*, **35**, 1625 (1952).
(3) VON AUWERS AND KIEL, *Ber.*, **35**, 4207 (1903); VON AUWERS AND KÖCHRITZ, *Ann.*, **352**, 289 (1907); VON AUWERS AND ZIEGLER, *Ann.*, **425**, 246 (1921).
(4) VON AUWERS AND LANGE, *Ann.*, **401**, 303 (1913).
(5) FIESER AND FIESER, *Natural Products Related to Phenanthrene*, 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 269.
(6) WALLACH, *Ann.*, **437**, 148 (1924).
(7) GUNSTONE AND HEGGIE, *J. Chem. Soc.*, 1437 (1953).
(8) RINNÈ, DEUTSCH, BOWMAN, AND JOFFE, *J. Am. Chem. Soc.*, **72**, 5759 (1950).
(9) FRANK AND BUEREN, German Patent 833,648, March 10, 1952; *Chem. Abstr.*, **47**, 2205 (1953).
(10) LOFTFIELD, *Ann. Repts on Progr. Chem.* (*Chem. Soc. London*), **48**, 124 (1951).
(11) RAMIREZ AND KIRBY, *J. Am. Chem. Soc.*, **74**, 4331 (1952).
(12) WOODWARD, SONDHEIMER, TAUB, HEUSLER, AND MCLAMORE, *J. Am. Chem. Soc.*, **74**, 4139 (1952).
(13) WARNHOFF AND JOHNSON, *J. Am. Chem. Soc.*, **75**, 494 (1953).