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THE SYNTHESIS OF 3,3,4-TRIMETHYLCYCLOPENTANONE. II

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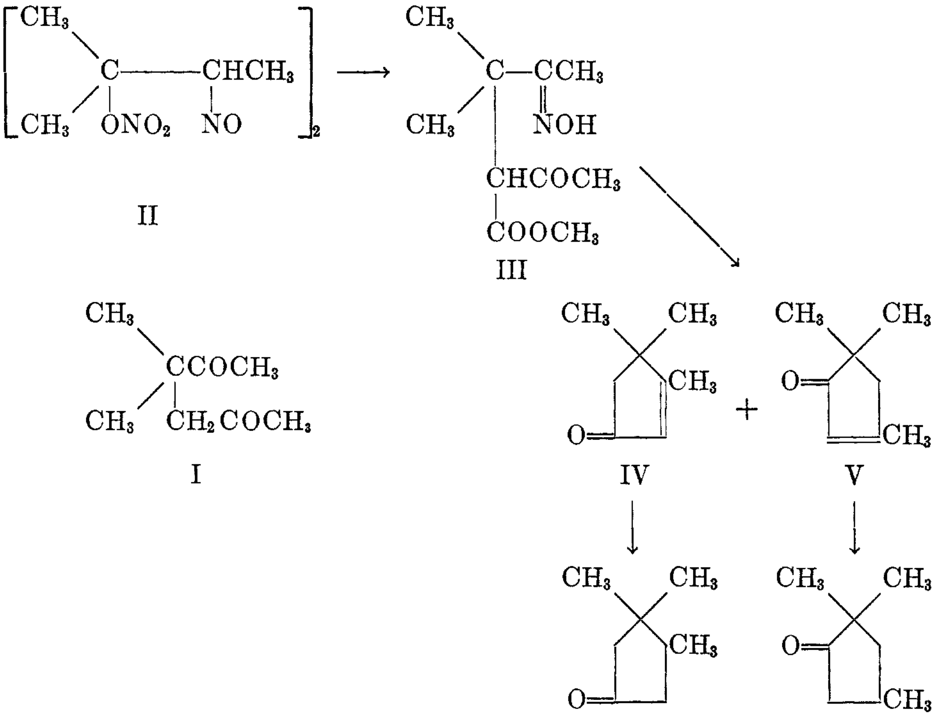
The preceding paper (1) reports the synthesis of the above-named ketone by two closely related paths; several possible alternative methods of synthesis are also listed. To these may be added the following: 3,3-dimethylhexandione-2,5 (I) on cyclization (2) should yield a mixture of (IV) and (V) from which the desired ketone (VI) could be obtained. (I) might conceivably be made by methylation of acetonylacetone or by the action of chloroacetone on sodium methyl isopropyl ketone.



II

III

I

IV

V

VI

VII

The literature (3, 4) discloses that the equivalent of these reactions has already been carried out by Wallach. His synthesis started from "bis-trimethylethylene nitrosate" (II) which was condensed with sodium methyl acetoacetate to give the compound (III). Treatment of this latter with 50% potassium hydroxide yielded an unsaturated ketone fraction which, on the basis of analogy (5), would be expected to be a mixture of (IV) and (V). Actually Wallach (3) characterized but one trimethylcyclopentenone, which he regarded as (V);

reduction (4) of his crude ketone product gave a mixture of saturated isomers. While pointing out that these isomers[1] might correspond to (VI) and (VII), Wallach left open the question of assigning definite structures.

The repetition of these experiments led to the isolation from (III) of two isomeric unsaturated ketones, which were separated by careful fractionation; reduction afforded the corresponding saturated ketones. The structure of the higher-boiling saturated isomer is established by virtue of its identity with ketone (VI) obtained (1) from 3,4,4-trimethylcyclohexanone. The structures of the parent unsaturated ketone (IV) and of the related pair (V) and (VII) follow indirectly and find further substantiation in the properties of these substances (see Table I). A comparison of the Table with that in the paper next preceding (5) brings out not uninteresting resemblances between the 5-ring ketones (IV), (V), (VI), and (VII) and their correspondingly numbered 6-ring analogs.

TABLE I

	IV[a]	V	VI[b]	VII[c]
Boiling point	b.p.$_{20}$ 87.5–88.0°	b.p.$_{20}$ 76.5–77.0°	b.p.$_{742}$ 173–175°	b.p.$_{742}$ 157–158°
Semicarbazone	m.p. 199.5–200.0° forms rapidly	m.p. 205.0–205.5° forms slowly	m.p. 213.5–214.0°	m.p. 171.0–171.3°
Derivative with hydroxyl amine	oil presumably an oxime	oxime m.p. 108.0–108.2°	m.p. 99.8–100.0°	m.p. 79.7–80.0°
Derivatives with *p*-nitrobenzaldehyde			di-*p*-nitrobenzal derivatives m.p. 204.7–205.1° m.p. 202.0–202.5°	mono-*p*-nitrobenzal derivative m.p. 99.3–99.5°
Reaction with bisulfite	none	none	reacts slowly	none

[a] Wallach (3) reported as a derivative of this compound the semicarbazone, m.p. 199–200°.

[b] Wallach (4) reported for this compound: b.p. 167–171°, semicarbazone, m.p. 214°, oxime, m.p. 110°.

[c] Wallach (4) reported for this compound: b.p. 162–168°, semicarbazone, m.p. 178°, oxime, m.p. 78°.

The author wishes to thank Dr. E. R. Buchman for suggesting this problem and for helpful advice in connection with the work.

EXPERIMENTAL PART

Preparation of unsaturated ketone mixture.[2] "Bis-trimethylethylene nitrosate" (II) was prepared as indicated in the literature (7) by passing oxides of nitrogen into a solution of 60 cc. of trimethylethylene in 150 cc. of glacial acetic acid which was kept cooled to the

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[1] Chemisches Zentralblatt (6) refers to these as 2,2,4-trimethylcyclopentanone "Nr. 1" and "Nr. 2". It is thus understandable how any but the most thorough literature survey would have failed to disclose their bearing upon the naphthene ketone problem (1).

[2] No appreciable amount of 3-methylcyclopenten-2-one was obtained from the action of aqueous alkali on acetonylacetone; much tar was formed.

point where solid acetic acid separated. The nitrogen dioxide was generated by the action of nitric acid on copper turnings (superior to the action of concentrated nitric acid on arsenic trioxide); the passage of gas was stopped as soon as the solution turned green, and the crystals which had separated were filtered off and washed with acetic acid and with water. The resulting white crystalline material[3] was air dried (44% yield); further small amounts of crude (II) were precipitated from the mother liquors by addition of water.

The nitrosate prepared in this manner proved suitable for conversion into (III); Wallach (3) had claimed that a specially purified (II) was necessary. Nine and six-tenths grams of sodium was dissolved in 160 cc. of methanol, 52 g. of methyl acetoacetate added, and the solution cooled. Sixty-four grams of (II) was then added and the mixture heated cautiously to initiate the reaction which proceeded exothermally; cooling of the reaction flask with running tap water was necessary to prevent loss of solvent through the condenser. The reaction was complete in five minutes, at the end of which the solvent was removed *in vacuo* and the residue refluxed for four hours from a copper retort with 450 g. of potassium hydroxide and 450 cc. of water, and then steam distilled. In a parallel experiment, after the reaction was complete, the solution was filtered from the sodium nitrate which had separated, the filtrate evaporated and (III) isolated from the residue by recrystallization from alcohol-acetone; m.p. 148.5–149.0° (analysis), turns reddish on exposure to light.

The steam distillates from three of the above sized runs were combined, saturated with ammonium sulfate, extracted several times with isopropyl ether, the ether extracts dried over sodium sulfate and fractionated.[4] The main fraction, b.p. 75–90° at 20 mm., consisted for the most part of (IV) and (V) and amounted to 73 g., 49% yield from (II).

3,4,4-Trimethylcyclopenten-2-one (IV) was obtained in an 11% yield from (II) on refractionation of the unsaturated ketone mixture through a precision column, b.p. 87.5–88.0° at 20 mm., d_4^{30} 0.925, n^{30}_D 1.4720. Analysis and behavior on reduction disclosed the presence of a small amount of nitrogen-containing impurity; the constants given are therefore only approximately correct for pure (IV).

Anal. Calc'd for $C_8H_{12}O$: C, 77.37; H, 9.74.
Found: C, 76.64; H, 9.97.

(IV) did not react with aqueous sodium bisulfite solution. The oxime was obtained as an oil; the semicarbazone formed readily, m.p. 199.5–200.0° from ethanol.

Anal. Calc'd for $C_9H_{15}N_3O$: C, 59.64; H, 8.34; N, 23.19.
Found: C, 59.84; H, 8.31; N, 23.60.

3,5,5-Trimethylcyclopenten-2-one (V) was obtained as above in 12% yield from (II), b.p. 76.5–77.0° at 20 mm., d_4^{30} 0.906, n^{30}_D 1.4608.

Anal. Calc'd for $C_8H_{12}O$: C, 77.37; H, 9.74.
Found: C, 76.35; H, 9.87.

(V) also did not form a bisulfite addition compound. The product obtained with hydroxylamine was found difficult to purify by recrystallization; it was sublimed at 2 mm. and the crystalline sublimate recrystallized from isopropyl ether, needles, m.p. 108.0–108.2°.

Anal. Calc'd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06.
Found: C, 69.23; H, 9.41; N, 10.28.

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[3] Attention may be directed to the fact that (II) cannot be stored. An explosion occurred when a sample, which had stood in a stoppered bottle for 2½ weeks without noticeable alteration, suddenly decomposed completely.

[4] From the forerun was isolated about one-half gram of acetone oxime (analysis, mixed m.p.) b.p. *ca.* 61° at 20 mm., m.p. 61.0–61.2° from petroleum ether. With an equivalent amount of picric acid this substance gave a picrate, quite soluble in the usual solvents, m.p. 82.0–82.2° from isopropyl ether-alcohol (analysis). The addition compound lost its acetone oxime on drying *in vacuo* at room temperature.

The analysis discloses that the derivative is an oxime; higher molecular weight amorphous material also sublimed, so that the formation of hydroxylaminooxime cannot be excluded. By comparison with its isomer, the semicarbazone formed at an extremely slow rate; for its preparation the components were allowed to stand in aqueous solution at room temperature for two weeks, m.p. 205.0–205.5° from ethanol-water.

Anal. Calc'd for $C_9H_{15}N_3O$: C, 59.64; H, 8.34; N, 23.19.
Found: C, 59.96; H, 8.31; N, 23.53.

3,3,4-Trimethylcyclopentanone (*VI*) was prepared by catalytic reduction (5) of (IV), b.p. 169–171° (173–175° corr.) at 742 mm., d_4^{26} 0.892, n^{26}_D 1.4380 (analysis). The crude reduction product contained a small amount of volatile base, possibly ammonia, arising from the nitrogen-containing impurity in (IV). (VI) reacted slowly with saturated aqueous bisulfite solution [means of separation from (VII)]. The derivatives, including the di-*p*-nitrobenzal derivatives, were identical with those described (1) previously (mixed m.p.'s). The m.p. of the oxime (100.8–101.0° corr.) was unchanged after repeated recrystallization (Wallach reported 110°).

2,2,4-Trimethylcyclopentanone (*VII*) was formed by catalytic reduction of (V), b.p. 153–154° at 742 mm., d_4^{26} 0.871, n^{26}_D 1.4279.

Anal. Calc'd for $C_8H_{14}O$: C, 76.14; H, 11.18.
Found: C, 75.15; H, 11.26.

(VII) did not form a bisulfite addition compound. It reacted with semicarbazide somewhat less readily than its isomer; semicarbazone m.p. 171.0–171.3° from alcohol.

Anal. Calc'd for $C_9H_{17}N_3O$: N, 22.93. Found: N, 22.90.

The oxime was crystallized from alcohol and sublimed at 3 mm. for analysis, m.p. 79.7–80.0°; *in vacuo* it is noticeably volatile even at room temperature.

Anal. Calc'd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92.
Found: C, 68.02; H, 10.59; N, 10.11.

A pale yellow mono-*p*-nitrobenzal derivative was obtained in the usual manner, m.p. 99.3–99.5° from methanol.

Anal. Calc'd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40.
Found: C, 69.95; H, 6.93; N, 5.94.

SUMMARY

A convenient method for the synthesis of 3,3,4-trimethylcyclopentanone has been described.

3,4,4-Trimethylcyclopenten-2-one, 3,5,5-trimethylcyclopenten-2-one and 2,2,4-trimethylcyclopentanone have been characterized.

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REFERENCES

(1) Buchman and Sargent, *J. Org. Chem.*, **7**, 148 (1942).
(2) Compare Robinson, *J. Chem. Soc.*, **1938**, 1390; see also Goldberg and Müller, *Helv. Chim. Acta*, **21**, 1699 (1938).
(3) Wallach, *Ann.*, **408**, 202 (1915).
(4) Wallach, *Ann.*, **437**, 193 (1924).
(5) Buchman and Sargent, *J. Org. Chem.*, **7**, 140 (1942).
(6) *Chem. Zentr.*, Formula index 1922–1924, page 223.
(7) Wallach, *Ann.*, **241**, 288, (1887).