# Further studies on the Stobbé condensation with 2-methyl cyclohexanone

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Received April 22, 1968

2-Methyl cyclohexanone is condensed with dimethyl succinate in the presence of potassium tertiary butoxide giving a solid mixture of isomers of the corresponding alkylidene and alkenyl half-esters. On alkaline hydrolysis this gives β-carboxy-β-(2-methyl cyclohex-1-enyl)propionic acid. The keto-ester obtained by cyclization of the half-ester yielded the corresponding unsaturated ketone after acid hydrolysis and decarboxylation. Reduction of the keto-ester affords the corresponding α,β-unsaturated ester. Both the unsaturated ketone and ester are easily hydrogenated in the presence of platinum oxide to the corresponding saturated ketone and ester.

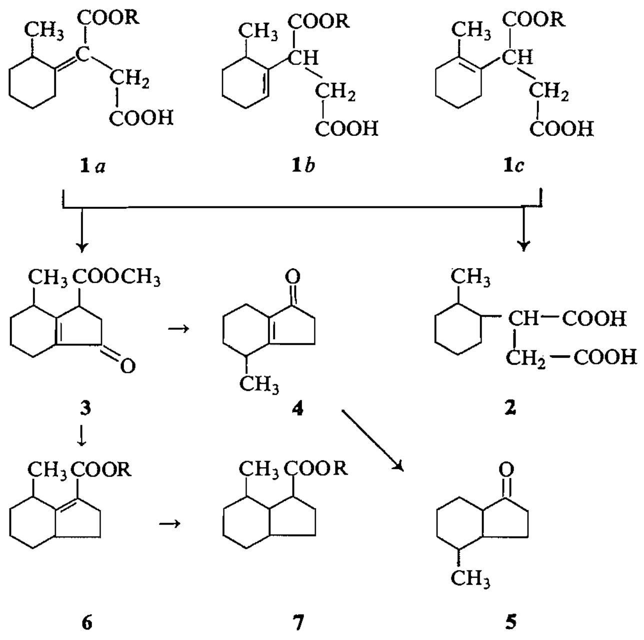
Canadian Journal of Chemistry, 47, 1483 (1969)

Cook and Phillip (1), and Chatterjee and Bhattacharyya (2) reported the Stobbé condensation of 2-methyl cyclohexanone with diethyl and dimethyl succinate respectively in the presence of potassium *t*-butoxide. They obtained the half-ester, β-carbethoxy-β-(2-methyl cyclohex-1-enyl)propionic acid (**1***c*; R = $C_2H_5$) as a solid, and β-carbmethoxy-β-(2-methyl cyclohex-1-enyl)propionic acid (**1***c*; R = $CH_3$) as an oil.

In the present investigation the above reaction was repeated for further study and for the preparation of a methyl perhydroindane nucleus which can be regarded as an intermediate for the synthesis of steroid-like compounds.

2-Methyl cyclohexanone was condensed with dimethyl succinate in the presence of potassium *t*-butoxide (3) to yield the corresponding half-ester as an oil. The yield was found to be greatly increased (from 71% (2) to 90%) by increasing the molality of potassium *t*-butoxide. This oil solidified and was found to be a mixture of isomers (**1***a*, **1***b*, and **1***c*; R = $CH_3$). The ultraviolet (u.v.) absorption spectrum showed one strong band at 225 mμ (ε 10 000), characteristic of α,β-unsaturated esters (see ref. 4, p. 32). This indicated the presence of the half-ester (**1***a*; R = $CH_3$) as one isomer of the mixture. It seems that this isomer is present in a small amount as indicated by the low value of the molecular extinction coefficient. Moreover, no 2-methyl cyclohexanone could be isolated from a mild oxidation of the half-ester mixture using alkaline permanganate at room temperature, but instead a neutral carbonyl compound was obtained which gave a 2,4-dinitrophenyl hydrazone. This substance is still under investigation. Repeating the oxidation at 0° failed to give any neutral carbonyl substance. The infrared (i.r.) spectrum of the half-ester showed bands at 2800–2500 (w), 1750 (s), 935 (v), and 810 (s) $cm^{-1}$, characteristic of the stretching frequencies of hydroxyl and carbonyl groups of saturated acids and esters, the hydroxyl deformation (out of plane) of acids, and the CH (out of plane) deformation vibrations of trisubstituted alkenes respectively (5). These vibrations strongly suggest the presence of the isomer (**1***b*; R = $CH_3$). Finally the nuclear magnetic resonance (n.m.r.) spectrum showed signals at 1.6 and 5.1 p.p.m. (δ), characteristic of a methyl group attached to an unconjugated double bond and a vinyl proton respectively (see ref. 4, p. 175). This indicated the presence of the two isomers (**1***b* and **1***c*; R = $CH_3$).

The half-ester mixture on alkaline hydrolysis gave one homogeneous crystalline dibasic acid, m.p. 157°, which probably has the structure of one of the three possible isomers (**1***a*, **1***b*, and **1***c*; R = H). This acid showed no u.v. absorption in the characteristic region of the α,β-unsaturated acids (220–260 mμ), thus excluding structure (**1***a*; R = H). Its i.r. spectrum showed bands at 2800–2500 (w), 1740 (s), and 930 (v) $cm^{-1}$, characteristic of the stretching frequencies of hydroxyl and carbonyl groups of saturated acids and the hydroxyl deformation (out of plane) of acids respectively (5). The disappearance of the strong band at 810 $cm^{-1}$ characteristic of γ CH of trisubstituted alkenes (shown by the half-ester) excluded structure (**1***b*; R = H) and confirmed structure (**1***c*; R = H) for this unsaturated dibasic acid. The presence of the olefinic linkage was chemically proved by



catalytic hydrogenation giving the known 2-methyl cyclohexyl succinic acid (**2**), m.p. 163–164° (lit. 2, m.p. 155–156°).

The crude half-ester was converted into its acid chloride (6) which was then cyclized (7). The neutral oily product thus obtained was found to be the keto-ester (**3**). It gave a 2,4-dinitrophenyl hydrazone and a semicarbazone.

Acid hydrolysis and decarboxylation of the keto-ester was effected by refluxing with a mixture of glacial acetic acid, constant boiling hydrobromic acid, and water to give the corresponding unsaturated ketone (**4**) in a good yield. It gave a 2,4-dinitrophenyl hydrazone in addition to the known semicarbazone (1).

The u.v. spectra of the keto-ester and the unsaturated ketone in ethanol had maxima at 237 mμ (ε 6162) and 236 mμ (ε 11 000) respectively. These values confirm the presence of α,β-unsaturated ketone grouping (see ref. 4, p. 139).

The unsaturated ketone (**4**) was then hydrogenated at a platinum oxide catalyst, absorbing one mole of hydrogen to give 4-methyl-*cis*-perhydro-indan-1-one (**5**) as a colorless oil. The n.m.r. spectrum showed mainly signals at 0.9 and 1.05 p.p.m. (δ), characteristic of a methyl group attached to a secondary carbon atom. This oil gave a 2,4-dinitrophenyl hydrazone and the known semicarbazone (1).

Clemmensen's reduction of the keto-ester (**3**) afforded mainly a neutral oil, which is probably the α,β-unsaturated ester (**6**; R = $CH_3$) since its observed absorption band $\lambda_{max}$(ethanol) 230 mμ (ε 6021) agrees with those reported for α,β-unsaturated esters in alcoholic solution (8, and ref. 4, p. 143). Alkaline hydrolysis of the unsaturated ester gave the corresponding α,β-unsaturated acid (**6**; R = H) as a colorless oil.

The unsaturated ester was then hydrogenated in the presence of platinum oxide to yield the corresponding saturated ester (**7**; R = $CH_3$) as a colorless oil. The n.m.r. spectrum showed mainly signals at 0.9, 1.05, and 3.6 p.p.m. (δ) corresponding to a methyl group attached to a secondary carbon atom and to a methyl ester group. Alkaline hydrolysis of this oil gave 7-methyl perhydroindan-1-carboxylic acid (**7**; R = H) as a colorless solid.

## Experimental

Infrared spectra were recorded on a Beckmann IR4 double beam spectrometer using a sodium chloride cell. The ultraviolet absorption spectra were determined with a Unicam 700 spectrophotometer.

### *Strobbé Condensation*

A solution of 2-methyl cyclohexanone (22.4 g, 0.2 mole) and dimethyl succinate (44 g, 0.3 mole) in *t*-butanol (40 ml) was added with stirring to a hot solution of potassium *t*-butoxide (from potassium metal, 11.7 g, 0.3 mole, in dry *t*-butanol 200 ml). The experiment was continued as usual (3) and the resulting viscous oil (about 41 g, 90%) solidified on keeping and cooling as glittering colorless crystals (a mixture of isomers **1**; R = $CH_3$), m.p. 126–129° (from aqueous methanol).

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.71; H, 7.96. Found: C, 63.92; H, 7.73.

### *Oxidation of the Half-ester*

The half-ester (1 g) was dissolved in a 20% sodium carbonate solution (10 ml). Aqueous potassium permanganate solution (10%) was added dropwise with stirring till the color of permanganate became permanent. The solution was kept at room temperature for 2 h then extracted with ether. The ethereal layer afforded a brown oil. This gave a 2,4-dinitrophenyl hydrazone as glittering yellow crystals, m.p. 161–162° (from ethanol).

Anal. Found: C, 43.39; H, 3.72; N, 24.57.

### β-*Carboxy*-β-*(2-methyl cyclohex-1-enyl)propionic Acid (1c; R = H)*

The half-ester (2 g) was refluxed in 10% sodium hydroxide solution (20 ml) for 3 h. On acidification this precipitated the unsaturated dibasic acid (**1***c*; R = H), 1.7 g, m.p. 157° (from benzene).

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.26; H, 7.54. Found: C, 62.07; H, 7.78.

### *2-Methyl Cyclohexyl Succinic Acid (2)*

The unsaturated dibasic acid (1 g), dissolved in glacial acetic acid (15 ml), was shaken with hydrogen in the presence of platinum oxide (0.1 g) until uptake of hydrogen (one mole) was complete ($3\frac{1}{2}$ h). This afforded the known saturated diacid (**2**), m.p. 163–164° (from water) (lit. 2, m.p. 155–156° from ether – petroleum ether).

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 61.90; H, 8.29.

### *Cyclization of the Half-ester*

The half-ester (5 g) in dry benzene (50 ml) was treated with pyridine (2.3 ml) and redistilled thionyl chloride (2 ml) at 0° for $\frac{1}{2}$ h. The benzene solution of the acid chloride was decanted from the solid cake, which was then pulverized and washed by decantation with dry benzene. The acid chloride solution and washings were treated with stannic chloride (2 ml) for 15 h at 0°; the benzene solution was then poured on ice and concentrated hydrochloric acid (15 ml) and shaken. This was worked up as usual (7) giving 3-carbmethoxy-4-methyl-4,5,6,7-tetrahydroindan-1-one (**3**) as a pale-yellow liquid, b.p. 110° at 0.6 mm.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 69.98; H, 7.65.

Recrystallization from ethanol yielded a semicarbazone as pale-yellow crystals, m.p. 227–228° (decomp.).

Anal. Calcd. for $C_{13}H_{19}O_3N_3$: C, 58.86; H, 7.17; N, 15.84. Found: C, 58.70; H, 7.12; N, 15.73.

Its 2,4-dinitrophenyl hydrazone melted at 201–202° (decomp., from ethanol).

Anal. Calcd. for $C_{18}H_{20}O_6N_4$: C, 55.67; H, 5.15; N, 15.6. Found: C, 55.45; H, 5.12; N, 15.33.

### *4-Methyl-4,5,6,7-tetrahydroindan-1-one (4)*

The keto-ester (3.4 g) was refluxed with glacial acetic acid (45 ml), constant-boiling hydrobromic acid (26 ml), and water (13 ml) for 1 h. The mixture was poured carefully on crystalline sodium carbonate (125 g) in sufficient water to form a slurry. The product was extracted with ether and dried ($Na_2SO_4$). This yielded 4-methyl-4,5,6,7-tetrahydroindan-1-one as a pale-yellow liquid (2 g), b.p. 84° at 0.4 mm.

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.72; H, 9.12.

It gave a semicarbazone, m.p. 240° (decomp.) from ethanol (1).

Anal. Calcd. for $C_{11}H_{17}ON_3$: C, 63.74; H, 8.27; N, 20.27. Found: C, 63.46; H, 8.25; N, 19.27.

Its 2,4-dinitrophenyl hydrazone melted at 208° (from acetic acid).

Anal. Calcd. for $C_{16}H_{18}O_4N_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.07; H, 5.56; H, 16.96.

### *4-Methyl-cis-perhydroindan-1-one (5)*

A solution of the unsaturated ketone (1.2 g) in glacial acetic acid (10 ml) was shaken with hydrogen in the presence of Adams platinum oxide (0.15 g) until the absorption of hydrogen was ceased. After filtration, the acetic acid was neutralized with sodium carbonate solution. This yielded the saturated ketone as a colorless liquid (0.8 g), b.p. 65–67° at 0.5 mm.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.95; H, 10.59. Found: C, 78.70; H, 10.42.

It gave a semicarbazone as colorless crystals, m.p. 210–212° (decomp.) from ethanol (1).

Anal. Calcd. for $C_{11}H_{19}ON_3$: C, 63.20; H, 9.10; N, 20.10. Found: C, 63.41; H, 8.92; N, 19.88.

Its 2,4-dinitrophenyl hydrazone recrystallized as orange crystals from methanol, and melted at 205–206°.

Anal. Calcd. for $C_{16}H_{20}O_4N_4$: C, 57.83; H, 6.02; N, 17.39. Found: C, 57.97; H, 5.93; N, 17.18.

### *7-Methyl-$^1\Delta^{(8)}$-hexahydroindan-1-carboxylic Acid (6; R = H) and its Methyl Ester (6; R = $CH_3$)*

To amalgamated zinc wool (20 g) in water (20 ml) and concentrated hydrochloric acid (40 ml) was added the keto-ester (5 g) in toluene (35 ml). The mixture was refluxed for 30 h with addition of concentrated hydrochloric acid (10 ml) every 6 h. The toluene layer was separated and the aqueous layer extracted with ether. The combined toluene and ether extracts, after washing with sodium bicarbonate solution, water, and drying ($Na_2SO_4$), afforded mainly the unsaturated ester (**6**; R = $CH_3$) as a pale-yellow oil (3.1 g), b.p. 85° at 0.04 mm.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.23; H, 9.28. Found: C, 74.43; H, 9.54.

A mixture of this oil (1 g) and 5% sodium hydroxide solution (20 ml) was refluxed for 3 h. The alkaline solution, after washing with ether, was cooled in ice and acidified to give the unsaturated acid (**6**, R = H) as a colorless oil, b.p. 92° at 0.05 mm.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.33; H, 8.90. Found: C, 72.97; H, 9.35.

### *7-Methyl Perhydroindan-1-carboxylic Acid (7; R = H) and its Methyl Ester (7; R = $CH_3$)*

A solution of the unsaturated ester (**7**; R = $CH_3$) (2 g) in absolute ethanol (30 ml) was shaken with hydrogen in the presence of Adams platinum oxide (0.2 g), until the absorption of hydrogen ceased. Filtration and removal of the solvent afforded the saturated ester (**7**; R = $CH_3$) as a colorless oil, b.p. 142° at 0.05 mm (1.8 g).

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.47; H, 10.20. Found: C, 73.22; H, 10.09.

The saturated ester (1 g) was refluxed for 6 h with 10% sodium hydroxide solution (10 ml) and ethanol (10 ml). Removal of the alcohol, washing the aqueous residue with ether, then acidification gave the saturated acid (7; R = H) as a colorless oil (0.8 g), b.p. 88–90° at 0.03 mm, which solidified on keeping, m.p. 157–158° (from benzene).

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.52; H, 9.89. Found: C, 72.22; H, 9.91.

## Acknowledgment

The authors thank Dr. Leigh C. Anderson, Professor of Organic Chemistry, University of Michigan, for measuring the nuclear magnetic resonance spectra.

1. J. W. Cook and R. Phillip. J. Chem. Soc. 162 (1948).
2. R. C. Chatterjee and B. K. Bhattacharyya. J. Indian Chem. Soc. **34**, 515 (1957).
3. W. S. Johnson, W. Petersen, and W. P. Schneider. J. Am. Chem. Soc. **64**, 74 (1947).
4. J. C. P. Schwarz. Physical methods in organic chemistry. Oliver and Boyd, Ltd., London. 1965.
5. L. J. Bellamy. The infrared spectra of complex molecules. Methuen & Co. Ltd., London. 1958. pp. 140, 152, 31.
6. J. W. Cook and C. A. Lawrence. J. Chem. Soc. 1637 (1935).
7. M. Elliott. J. Chem. Soc. 2231 (1956).
8. H. E. Ungnade and I. Ortega. J. Am. Chem. Soc. **73**, 1565 (1951).