could be obtained by careful recrystallization from acetone–petroleum ether.

Anal. Calcd. for $C_{19}H_{26}O_6$: C, 65.12; H, 7.48. Found: C, 65.10; H, 7.66.

Resolution of the Hemisuccinate II and Recovery of (–)-I.—A dry mixture of 430 g. of the hemisuccinate II and 490 g. of anhydrous brucine alkaloid was dissolved in 9.5 l. of boiling acetone, and the solution was allowed to cool. Crystals began to deposit, and after 4 hours the supernatant liquor was decanted, evaporated to $^1/_2$ volume, and placed in the refrigerator overnight to effect the precipitation of a second crop. The combined weight of the two crops was 415 g. (90%, $[\alpha]^{25}D$ $-94 \pm 2°$ (c 1, methanol)). Recrystallization from ethanol gave 392 g. (85%) of the brucine salt of (–)-I hemisuccinate, m.p. 145–152°, $[\alpha]^{25}D$ $-102 \pm 2°$ (c 1, methanol). Further recrystallization did not affect the rotation. The brucine salt (392 g.) was added to 1000 ml. of 1.5 M potassium carbonate solution, and the liberated brucine was extracted with chloroform. The aqueous solution was heated at 100° for 2.5 hours, cooled to 0°, and the crystals which formed were collected on a filter (106 g.). The filtrate was then extracted continuously for 2 days with chloroform. Evaporation of the chloroform extract left 20 g. of crystalline residue. The combined crystals were recrystallized from methanol, yielding 116 g. (70%) of (–)-I, m.p. 225°, $[\alpha]^{25}D$ $-225 \pm 2°$ (c 1, chloroform). Further recrystallization did not affect either the melting point or the rotation.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.18; H, 8.74.

The remainder of the compounds appearing in Tables I and II were prepared from (–)-I by previously published procedures.[3]

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RAHWAY, N. J.

Hydroxymethylene Ketones. II. Orientation in the Condensation of Methyl Ethyl and Methyl *n*-Propyl Ketones with Methyl Formate

BY E. EARL ROYALS AND KENT C. BRANNOCK[1]

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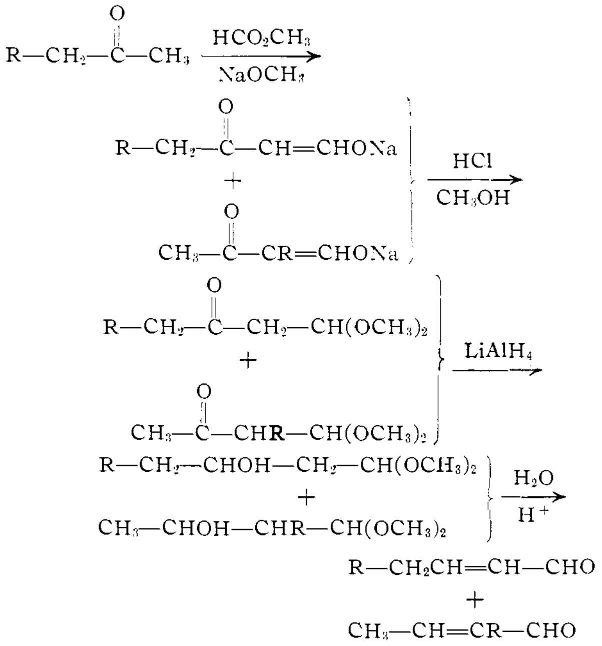
The work of Benary[2] indicated that the condensation of methyl ethyl ketone with ethyl formate occurs at both the methyl and methylene units of the ketone. At the same time Benary detected only one isomer from the condensation of methyl *n*-propyl ketone with ethyl formate. Tracy and Elderfield,[3] and Joshi, Kaushal and Deshapande[4] detected only the methylene condensation product in the methyl ethyl ketone–ethyl formate reaction; however, in both cases multistep reaction sequences were used in which a minor isomer could easily be lost. While it is true that the predominant isomer from the methyl ethyl ketone–formic ester reaction is the methylene condensation product, and that from methyl *n*-propyl ketone is the methyl condensation product, the present work shows that appreciable amounts of the other isomers are formed under the usual reaction conditions.

In the first paper of this series[5] the preparation of β-ketodimethyl acetals from hydroxymethylene ketones was described. Based on distillation data of their β-ketoacetals it was concluded that both hydroxymethylenemethyl ethyl ketone and hydroxymethylene-*n*-propylmethyl ketone consisted of mixtures of isomers arising from condensation of the ketones with methyl formate at their methyl and methylene groups. This conclusion has now been confirmed chemically by the reaction sequence



$$\mathrm{R{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH_3} \xrightarrow[\mathrm{NaOCH_3}]{\mathrm{HCO_2CH_3}} \left.\begin{array}{c}\mathrm{R{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH{=}CHONa}\\ +\\ \mathrm{CH_3{-}\overset{\overset{O}{\|}}{C}{-}CR{=}CHONa}\end{array}\right\} \xrightarrow[\mathrm{CH_3OH}]{\mathrm{HCl}}$$

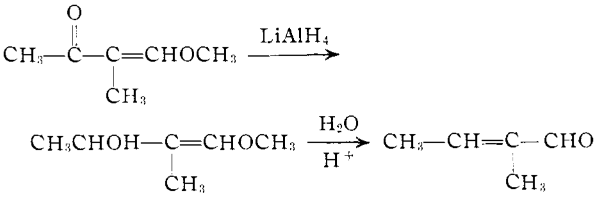
$$\left.\begin{array}{c}\mathrm{R{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}CH(OCH_3)_2}\\ +\\ \mathrm{CH_3{-}\overset{\overset{O}{\|}}{C}{-}CH\mathbf{R}{-}CH(OCH_3)_2}\end{array}\right\} \xrightarrow{\mathrm{LiAlH_4}}$$

$$\left.\begin{array}{c}\mathrm{R{-}CH_2{-}CHOH{-}CH_2{-}CH(OCH_3)_2}\\ +\\ \mathrm{CH_3{-}CHOH{-}CHR{-}CH(OCH_3)_2}\end{array}\right\} \xrightarrow[\mathrm{H^+}]{\mathrm{H_2O}} \begin{array}{c}\mathrm{R{-}CH_2CH{=}CH{-}CHO}\\ +\\ \mathrm{CH_3{-}CH{=}CR{-}CHO}\end{array}$$

The yields of α,β-unsaturated aldehydes obtained from this reaction sequence are excellent, and the procedure is being investigated in this Laboratory as a synthetic method of wide applicability for this type of compound.

Although a quantitative separation of the α,β-unsaturated aldehydes in each case was impossible, we estimate that under our experimental conditions condensation of methyl ethyl ketone with methyl formate occurred to the extent of *ca.* 20–26% at the methyl group and *ca.* 74–80% at the methylene group while with methyl *n*-propyl ketone condensation was *ca.* 25–33% methylene and 67–75% methyl.

By a similar procedure the methoxymethylene-ethyl methyl ketone obtained previously[5] was shown to be derived from the methylene condensation product of methyl ethyl ketone and methyl formate.[6]



$$\mathrm{CH_3{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{CH_3}{|}}{C}{=}CHOCH_3} \xrightarrow{\mathrm{LiAlH_4}}$$

$$\mathrm{CH_3CHOH{-}\underset{\underset{CH_3}{|}}{C}{=}CHOCH_3} \xrightarrow[\mathrm{H^+}]{\mathrm{H_2O}} \mathrm{CH_3{-}CH{=}\underset{\underset{CH_3}{|}}{C}{-}CHO}$$

Experimental

The boiling points reported are uncorrected. Melting points (unless otherwise specified) were determined on a calibrated Fisher–Johns melting point apparatus.

β-Ketoacetal from Methyl Ethyl Ketone.—The crude β-ketodimethylacetal from methyl ethyl ketone,[5] 73 g. (0.5

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[1] National Science Foundation Fellow, 1953–1954.

[2] Erich Benary, *Ber.*, **59**, 2198 (1926).

[3] A. H. Tracy and R. C. Elderfield, *J. Org. Chem.*, **6**, 63 (1941).

[4] S. N. Joshi, R. Kaushal and S. S. Deshapande, *J. Indian Chem. Soc.*, **18**, 479 (1941).

[5] E. E. Royals and K. C. Brannock, THIS JOURNAL, **75**, 2050 (1953).

[6] P. Seifert and H. Schinz, *Helv. Chim. Acta*, **34**, 728 (1951), have reported a similar sequence in the cyclic series which gave excellent yields of the α,β-unsaturated aldehydes.

mole calculated as β-ketoacetal) in 100 ml. of ether was added over a 65-min. period to 9.5 g. (0.25 mole) of lithium aluminum hydride in 400 ml. of ether. Stirring was continued for 1 hr. and the excess lithium aluminum hydride was destroyed by the cautious addition of 35 ml. of methyl formate followed by 50 ml. of water. The mixture was filtered, and the solids were washed with ether. The ether was removed by distillation and the residual oil was refluxed with 150 ml. of 2% (by volume) sulfuric acid containing a few crystals of hydroquinone under a 2-ft. Fenske column until no more methanol was obtained (3 hours). The residue was extracted with four 50-ml. portions of ether and dried over sodium sulfate. After removal of the ether by distillation, the 40.5 g. of residue was distilled using a Todd column, 90 cm. (5 mm.), with a monel spiral packing to give 31.9 g. of α,β-unsaturated aldehydes and 6.9 g. of residue. The major fractions were 19.5 g., b.p. 116–119°, n^{25}_{D} 1.4426 and 5.6 g., b.p. 121.5–123°, $n^{25}\mathrm{D}$ 1.4391. The 116–119° fraction was identified as tiglic aldehyde by conversion to the 2,4-dinitrophenylhydrazone, carmine crystals from chloroform, m.p. 220–220.5° (reported m.p. 220°[7]) and the *p*-nitrophenylhydrazone, from heptane–ethanol, m.p. 185–186° (reported m.p. 181°[8]).

The 121.5–123° fraction (this b.p. is probably lower than the true b.p. since it was depressed by the presence of a small amount of water liberated from the still-pot material during the latter stages of the distillation) was identified as 2-pentenal by conversion to the 2,4-dinitrophenylhydrazone, orange needles from alcohol–chloroform, m.p. 159–159.5° (reported m.p. 160°[9]), and the semicarbazone from dilute alcohol m.p. 179.5–180° (reported m.p. 179°,[10a] 180°[10b]).

Although complete separation of the two aldehydes was impossible, we estimate the amounts present to be *ca.* 23.5 g. of tiglic aldehyde and *ca.* 8.4 g. of 2-pentenal. Based on the amount of distilled aldehydes this corresponds to 26% methyl and 74% methylene condensation of methyl ethyl ketone with methyl formate; 8.4 g. of 2-pentenal corresponds to *ca.* 20% of the theoretical amount of α,β-unsaturated aldehyde to be obtained from the starting material.

Methoxymethylene ethyl Methyl Ketone.—The methoxymethylene ketone described previously[5] was shown to be derived from the methylene condensation product of methyl ethyl ketone and methyl formate.

The methoxymethylene ketone, 2 g., in 10 ml. of ether was added over a 10-min. period to 0.5 g. of lithium aluminum hydride in 25 ml. of ether. After 20 min. 5 ml. of methyl formate was added cautiously followed by 5 ml. of water. The ether layer was decanted, the ether was removed by distillation, and the residue was refluxed for 1 hr. with 20 ml. of 3% (by volume) sulfuric acid. The mixture was extracted with three 10-ml. portions of ether, the ether was removed by distillation and the residue taken up in ethanol to a total volume of 10 ml.

Using aliquots of this solution the 2,4-dinitrophenylhydrazone and *p*-nitrophenylhydrazone of tiglic aldehyde were obtained which were identical with those described above. The semicarbazone of tiglic aldehyde melted over a considerable range depending on the rate and duration of heating; *e.g.*, in a sealed capillary heated in a bath from room temp., m.p. 207° uncor.; introduced into the bath preheated to 200°, m.p. 219° uncor.; reported m.p. 200–208°,[11] 219°,[8] 225°[12] and 225.6°.[7]

β-Ketoacetal from Methyl *n*-Propyl Ketone.—The β-ketoacetal prepared as described[5] from redistilled commercial sample of reagent grade methyl *n*-propyl ketone was carried through the reaction sequence leading to 2-ethylcrotonaldehyde and 2-hexenal. Satisfactory derivatives of 2-ethylcrotonaldehyde could not be obtained, apparently due to the presence of 2-methylpentenal which arose from diethyl ketone in the commercial product. Therefore, pure methyl *n*-propyl ketone was prepared by the following simplification of a described procedure.[13] Sodium, 34.5 g. (1.5 g. atom), was dissolved in 750 ml. of absolute ethanol (freshly distilled from sodium ethoxide) and 195 g. (1.5 moles) of ethyl acetoacetate was added. Over a 20-min. period 250 g. (1.6 mole) of ethyl iodide was added and the mixture was stirred and heated under reflux for 14 hr. after which time the reaction mixture was neutral to litmus. The homogeneous solution was concentrated by distillation until sodium iodide began crystallizing, 150 ml. of water was added and the remaining ethanol removed as its water azeotrope. The organic phase was separated and stirred for 5 hr. at room temperature with 76 g. of sodium hydroxide in 1,500 ml. of water. A mixture of 77 ml. of concd. sulfuric acid and 100 ml. of water was then added slowly to the solution, the mixture was heated to boiling, cooled and extracted with two 150-ml. portions of ether. The ether layer was dried over calcium chloride to remove most of the alcohol, and distilled using a 2-ft. Fenske column to give 16 g. of the ethanol–methyl *n*-propyl ketone azeotrope, b.p. 77°, 73 g. (57%) of methyl *n*-propyl ketone, b.p. 100–101°, $n^{20}\mathrm{D}$ 1.3888 and 24 g. of residue.

From the ketone, the β-ketodimethylacetal was prepared as described[5] in 67.5% yield (calculated as pure β-ketoacetal; the actual yield is slightly greater due to the presence of a small amount of methoxymethylene ketone).

The crude β-ketodimethylacetal, 54 g. (0.337 mole as β-ketoacetal) in 100 ml. of ether was added over a 45-min. period to 7.2 g. (0.19 mole) of lithium aluminum hydride in 300 ml. of ether. Stirring was continued for 15 min. and 25 ml. of ethyl formate was added cautiously followed by 30 ml. of water. The mixture was filtered and the ether was removed by distillation. The residue was refluxed with 150 ml. of 2% (by volume) of sulfuric acid containing a few crystals of hydroquinone on a 2-ft. Fenske column for 5 hr. while methanol was removed at the head. The residue was extracted with three 50-ml. portions of ether and dried over sodium sulfate. After removal of the ether by distillation, the residue was distilled using the previously described Todd solution to give 25.4 g. of α,β-unsaturated aldehydes and 5.5 g. of residue. The major fractions were 6.6 g., b.p. 129–135°, $n^{25}\mathrm{D}$ 1.4433 and 15.7 g., b.p. 141–146°, $n^{25}\mathrm{D}$ 1.4432. The 129–135° fraction was identified as 2-ethylcrotonaldehyde by conversion to the 2,4-dinitrophenylhydrazone, orange needles from ethanol–chloroform, m.p. 168–169° (identical with the derivative from authentic 2-ethylcrotonaldehyde which had $n^{25}\mathrm{D}$ 1.4440[14]) and the semicarbazone, plates from dilute alcohol, m.p. 211–212° (identical with the derivative obtained from the authentic sample: reported m.p. 194°,[15] 194–195°[16] and 210°[17]). The 141–146° fraction (again, this b.p. was probably depressed by the liberation of a small amount of water from the material in the still-pot) was identified as 2-hexenal by conversion to the 2,4-dinitrophenylhydrazone, orange crystals from alcohol–chloroform, m.p. 146–146.5° (identical with the derivative from authentic 2-hexenal which had $n^{25}\mathrm{D}$ 1.4439[14]; reported m.p. 144°[9,18] and the semicarbazone, from dilute alcohol, m.p. 175–176° (identical with that from the authentic sample: reported m.p.'s 179°,[10a] 175–176°[10b] and 173°[19]).

Although complete separation of the aldehydes was impossible, we estimate the mixture to consist of *ca.* 8.4 g. of 2-ethylcrotonaldehyde and *ca.* 17 g. of 2-hexenal. This corresponds to *ca.* 33% methylene and *ca.* 67% methyl condensation of methyl *n*-propyl ketone with methyl formate: 8.4 g. of 2-ethylcrotonaldehyde would correspond to *ca.* 25% of the theoretical amount of α,β-unsaturated aldehydes to be obtained from the starting β-ketoacetal.

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[14] We are indebted to the Carbide and Carbon Chemicals Corporation for a generous sample of 2-ethylcrotonaldehyde and to Dr. R. I. Hoaglin of that company for a generous sample of 2-hexenal.

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