Hydroxymethylene Ketones. III. The Preparation of Methoxymethylene Ketones[1]

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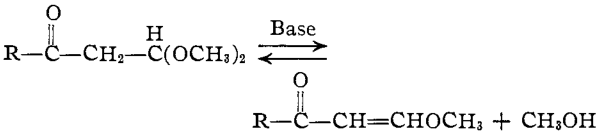
The preparation of ethoxymethyleneacetone by the alkylation of sodium hydroxymethyleneacetone in ethanol with ethyl bromide has been described.[3] In the present work, alkylation of crude sodium hydroxymethyleneacetone with ethyl iodide in ethanol gave a poor yield of an inseparable mixture of ethoxymethyleneacetone and acetoacetaldehyde diethylacetal. Though the difference in the present results and those previously reported probaby lies in the markedly different experimental procedures used, the refractive index of ethoxymethyleneacetone reported by Kaushal[3a] and the conclusions drawn therefrom are apparently in error.

Alkylation of sodium hydroxymethyleneacetone with ethyl iodide in acetone gave a fair yield of crude ethoxymethyleneacetone which could not be obtained in a satisfactory state of purity by fractional distillation. A similar alkylation with methyl iodide gave even poorer yields, no analytically pure products, and apparently carbon as well as oxygen alkylation, so that direct alkylation of sodium hydroxymethylene acetone as a route to alkoxymethyleneacetone was not pursued further.

A consideration of the probable mechanism of formation of β-ketoacetals from chloroviny1 ketones and alcohols in the presence of bases, and of the cleavage of β-ketoacetals by aqueous alkali led us to believe that the reaction



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2-\overset{\displaystyle H}{C}(OCH_3)_2 \xrightleftharpoons{\text{Base}} R-\overset{\overset{\displaystyle O}{\|}}{C}-CH=CHOCH_3 + CH_3OH$$

is reversible. Distillation of several β-ketoacetals from catalytic amounts of sodium methoxide has shown this to be the case, elimination of methanol occurring readily with the formation of methoxymethylene ketones in good yields. A similar reaction has been described recently by Franke and co-workers[4] in which methanol was eliminated from acetoacetaldehyde dimethylacetal by passing it in the vapor phase over a basic catalyst.

No effort has been made to determine optimum conditions for the elimination reaction; however, it was found advantageous to add methanol to the mixture of β-ketoacetal and sodium methoxide. This effect is probably due to the increased solubility of the sodium methoxide. While in most cases the elimination was accomplished at reasonably low temperatures under vacuum, acetoacetaldehyde dimethylacetal and the dimethylacetal of hydroxymethylene diisobutyl ketone invariably gave incomplete conversions under these conditions; the use of higher temperatures at atmospheric pressure was necessary with these two compounds. The products obtained are shown in Table I.

During the preparation of hydroxymethylenepinacolone by the Claisen condensation of methyl formate with pinacolone in the presence of sodium methoxide the evolution of carbon monoxide was observed. Though the fact that formate esters are decomposed to carbon monoxide and alcohol by sodium alkoxide has long been known, the evolution of carbon monoxide in the reactions of methyl formate with such ketones as acetone, methyl ethyl ketone and methyl isobutyl ketone is much less apparent. It was found that in the reaction of 0.5 mole of sodium methoxide, 0.5 mole of pinacolone and 0.75 mole of methyl formate that roughly 1400 cc. of carbon monoxide was produced. It may therefore be advantageous to use an excess of the formate ester in condensations such as this.

The properties of the dimethylacetals derived from hydroxymethylenepinacolone and hydroxymethylenediisobutyl ketone are shown in Table II.

TABLE I

METHOXYMETHYLENE KETONES PREPARED FROM β-KETOACETALS

Compound	Yield, %	Procedure	B.p.		$n^{25}D$	Carbon, %[a]		Hydrogen, %[a]	
			°C.	Mm.		Calcd.	Found	Calcd.	Found
$CH_3—CO—CH=CHOCH_3$[b]	72.6	B	52–53	4–5	1.4653	...	...	...	...
$CH_3CH_2COC(CH_3)=CHOCH_3$	76.4	A	70	4–45	1.4752	65.59	65.48	9.44	9.39
$(CH_3)_2CH—CO—CH=CH—OCH_3$	61.5	A	61–62	3.5	1.4538	65.59	65.28	9.44	9.23
$(CH_3)_3C—CO—CH=CH—OCH_3$	74.1	A	61	3	1.4536	67.57	67.43	9.92	9.83
$(CH_3)_2CH—CH_2—CO—\underset{\underset{\displaystyle CH(CH_3)_2}{\mid}}{C}=CH—OCH_3$	84.8	B	78–79	1	1.4633	71.69	71.31	10.94	10.95

[a] Microanalyses by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England. [b] Franke, *et al.* (ref. 4), report $n^{20}D$ 1.4699, p. 172° at atm. pressure. Alkaline hydrolysis (ref. 5) gave equivalent weights of 100.8 and 101.1; theor., 100.11.

TABLE II

β-Ketoacetal	Yield, %	B.p.		$n^{25}D$	Carbon, %[a]		Hydrogen, %[a]	
		°C.	Mm.		Calcd.	Found	Calcd.	Found
$(CH_3)_3C—CO—CH_2—CH(OCH_3)_2$	54.6	67–70	4	1.4202	62.03	62.20	10.41	10.36
$(CH_3)_2CH—CH_2—CO—\underset{\underset{\displaystyle CH(CH_3)_2}{\mid}}{CH}—CH(OCH_3)_2$	56.8	71–71.5	1	1.4308	66.63	66.91	11.18	11.13

[a] Microanalyses by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England.

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(1) For the previous paper in this series see E. E. Royals and K. C. Brannock, THIS JOURNAL, **76**, 1180 (1954).

(2) National Science Foundation Fellow, 1953–1954.

(3) (a) R. Kaushal, *J. Indian Chem. Soc.*, **20**, 53 (1943); (b) L. Panizzi and M. Sbrillo-Siena, *Gazz. chim. ital.*, **73**, 335 (1943).

(4) W. Franke, R. Kraft, D. Tietjen and H. Weber, *Chem. Ber.*, **86**, 793 (1953).

Experimental

The β-ketodimethylacetals were prepared as described previously.[5]

Alkylation of Sodium Hydroxymethyleneacetone in Ethanol.—The sodium salt was prepared in the usual manner from 23 g. (1 g. atom) of sodium, 58 g. (1 mole) of acetone and 78 g. (1.05 moles) of ethyl formate in 1 l. of absolute ether. Most of the ether was removed under water-pump vacuum, and 181 g. (1.16 moles) of ethyl iodide in 750 ml. of absolute ethanol was added. The mixture was stirred at 50–55° for 10 hours after which time it was neutral to phenolphthalein. The mixture was concentrated by distillation until precipitated sodium iodide caused bumping, cooled, diluted with twice its volume of ether and the precipitated salts removed by filtration. This procedure was repeated twice more, and finally distillation from a claisen flask gave 28.5 g. of product, b.p. 68–72° at 5–6 mm., $n^{25}\text{D}$ 1.4236. The material was at first insoluble in water but dissolved on shaking, gave a positive fuchsin test, and on standing in water gave crystals of triacetylbenzene. Distillation through an efficient column gave no good fraction. A middle cut, b.p. 59.5–60° at 5 mm., $n^{25}\text{D}$ 1.4194, gave on alkaline hydrolysis an equivalent weight of 153.4 (theoretical for acetoacetaldehyde diethylacetal is 160 and for ethoxymethyleneacetone is 114). Reported for the diethylacetal; b.p. 76–77° at 10 mm., $n^{20}\text{D}$ 1.4226[6a]; b.p. 82–87° at 12 mm., $n^{20.5}\text{D}$ 1.4189.[6b]

Alkylation of Sodium Hydroxymethyleneacetone in Acetone.—This sodium salt prepared from 11.5 g. of sodium, 55.5 g. of ethyl formate and 34.8 g. of acetone in 250 ml. of ether, was freed of ether under water-pump vacuum. It was then stirred at 50° with 93.6 g. of ethyl iodide and 400 ml. of acetone for 24 hours at which time the mixture was neutral to phenolphthalein. When worked up as described above there was obtained 19.8 g. of crude product, b.p. 55–70° at *ca.* 5 mm., $n^{25}\text{D}$ 1.4602. Distillation through an efficient column gave 13.3 g. of impure ethoxymethylene acetone, b.p. 68–71° at 7–7.5 mm., $n^{25}\text{D}$ 1.4618 (Kaushal, ref. 3a, reports $n^{33}\text{D}$ 1.6075).

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 64.28; H, 9.46. This impure product gave triacetylbenzene on standing in water, a purple color with ferric chloride, and a positive fuchsin test.

Using similar amounts of reactants and similar conditions but substituting methyl iodide for ethyl iodide there was obtained 12.2 g. of crude product, b.p. 60–95° at 25 mm., $n^{25}\text{D}$ 1.4526. This product darkened rapidly on standing. On attempted fractional distillation crystals of what is presumably the carbon-alkylation product (the solid isomer of hydroxymethylenemethyl ethyl ketone) formed in the condenser while most of the material resinified.

Elimination of Methanol from β-Ketodimethylacetals. Procedure A.—The β-ketodimethylacetal was dissolved in an equal volume of methanol and 1–2% by weight of solid sodium methoxide was added to the solution. Methanol was then removed by distillation at *ca.* 150 mm. until the pot temperature reached 60–75°, and the pressure was then reduced slowly maintaining the same temperature range. After loss of methanol had stopped the product was distilled *in vacuo*. The analytical samples were obtained by distillation through an efficient column, and in all cases the crude product was found to be quite pure.

Procedure B.—The β-ketodimethylacetal was heated slowly in a claisen flask with *ca.* 1% by weight of sodium methoxide to a temperature of 140–170°, while methanol was removed by distillation at atmospheric pressure. The pressure was then lowered while the remaining methanol was removed, and finally the crude product was distilled *in vacuo*. The analytical samples were obtained as in procedure A.

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

[6] (a) A. N. Nesmeyanov, N. K. Kochetkov and M. I. Rybinskaya, *Izvest. Nauk. Akad. S.S.S.R., Otdel Khim. Nauk*, 395 (1951) [*C. A.*, **46**, 3007 (1952)]; (b) Henry J. Richmond, U. S. Patent 2,570,713 (1951).

The Cyclization of α-Substituted Benzylsuccinic Anhydrides

By R. S. Urban[1] and E. M. Beavers

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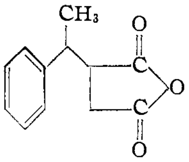
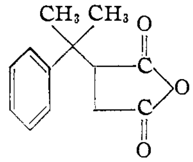
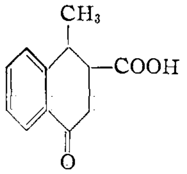
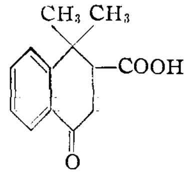
The formation of cyclic ketones by the intramolecular acylation of benzylsuccinic acids (and anhydrides) can, hypothetically, lead to the generation of both five- and six-membered rings, depending upon which carboxyl group condenses at the aromatic nucleus. It has been reported that benzylsuccinic acid,[2a] α-phenylbenzylsuccinic acid[2b] and fluorenylsuccinic anhydride[3] form six-membered rings exclusively.

In the course of another investigation in this Laboratory, α-methylbenzylsuccinic anhydride[4] and α,α-dimethylbenzylsuccinic anhydride[4] (II) were prepared. Since these compounds have never been subjected to cyclization, and since there seemed to be a possibility that steric effects of the *gem*-dimethyl group in the one compound might favor the formation of a planar five-membered ring, we investigated the cyclization of I and II.


I


II


III


IV

When α-methylbenzylsuccinic anhydride (I) was treated with concentrated sulfuric acid, two cyclic isomers were isolated.[5] These were shown to be *cis* and *trans* isomers of 4-methyl-3-carboxy-1-tetralone (III) by Clemmensen reduction,[6] followed by dehydrogenation to the same 1-methyl-2-carboxynaphthalene.

α,α-Dimethylbenzylsuccinic anhydride (II),

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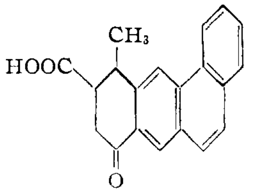
[1] Deceased.

[2] (a) J. von Braun, *Ber.*, **61B**, 441 (1928); E. C. Horning and G. N. Walker, This Journal, **74**, 5147 (1952); A. J. Attwood, A. Stevenson and J. F. Thorpe, *J. Chem. Soc.*, 1755 (1923). (b) C. L. Hewett, *ibid.*, 596 (1936); R. D. Haworth and G. Sheldrick, *ibid.*, 636 (1935).

[3] E. Bergmann and M. Orchin, This Journal, **71**, 1917 (1949).

[4] E. M. Beavers, Brit. Patent 668,574 (Mar. 19, 1952); W. G. Bickford, *et al.*, *J. Am. Oil Chem. Soc.*, **25**, 251 (1948).

[5] J. W. Cook and A. M. Robinson (*J. Chem. Soc.*, 505 (1938)) report the cyclization of a phenanthrene analog to yield the two isomers.



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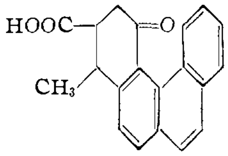

[6] One isomer was identical to the known 1-methyl-2-carboxytetralin.