[Contribution from the Department of Chemistry, Duke University]

Modes of Cleavage of Ethyl Benzoyl- and Ethyl Mesitoyl-dimethylacetate with Bases[1]

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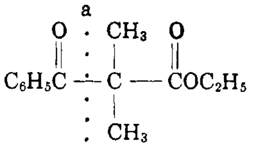
Ethyl benzoyldimethylacetate (I) and ethyl mesitoyldimethylacetate (II) were cleaved by potassium hydroxide and sodium alkoxides. The cleavage of I occurred exclusively at the ketone group whereas that of II involved mainly or exclusively the ester group. The latter cleavage required more drastic conditions than the former, both being the result of relative rates of reaction of the basic anion at the two positions.

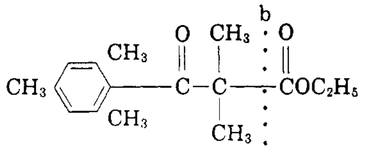
Hope and Perkin[2] observed that, whereas alkylated acetoacetic esters exhibit ketonic cleavage with dilute alkali, alkylated benzoylacetic esters undergo considerable acidic cleavage to form benzoic acid.

It has now been found that ethyl benzoyldimethylacetate (I) and ethyl mesitoyldimethylacetate (II) undergo with basic reagents cleavages at "a" and "b" respectively. The results are summarized in Table I.



$C_6H_5CO-C(CH_3)_2-COOC_2H_5$

I



II

In agreement with the earlier observation,[2] β-keto ester I was cleaved exclusively at "a" to form benzoic acid by 5% as well as 60% refluxing aqueous potassium hydroxide, although only about one-third of the β-keto ester had reacted with the dilute alkali after 12 hours. Likewise β-keto ester I underwent exclusive cleavage at "a" with 20 mole-per cent sodium ethoxide in refluxing ethanol to form ethyl benzoate and ethyl isobutyrate. Similar reverse Claisen type condensations are well known.[3]

As might be expected, β-keto ester II was found to be much less reactive than β-keto ester I. Thus, II was recovered unchanged after long refluxing with 5% potassium hydroxide or ethanolic sodium ethoxide. Even after refluxing with sodium *n*-butoxide in *n*-butanol the only reaction observed was an alcohol-ester exchange. However, II was cleaved on refluxing with 60% potassium hydroxide or with sodium hexoxide in *n*-hexanol, the cleav-

TABLE I

Cleavages of β-Keto Esters by Basic Reagents

β-Keto Ester	Basic Reagent	Solvent	Time, hours	Product of Cleavage at "a"	%	Product of Cleavage at "b"	%	Recovered β-Keto Ester, %
I[a]	5% KOH	H_2O	12	Benzoic acid	30		0	64
I	60% KOH	H_2O	12	Benzoic acid	87		0	0
I	$NaOC_2H_5$[b]	C_2H_5OH	2	Ethyl benzoate	93		0	0.5
				Ethyl isobutyrate	16[c]			
II[d]	5% KOH	H_2O	144		0		0	95
II	60% KOH	H_2O	312	Mesitoic acid	2.5	Isobutyromesitylene	71	18
II	$NaOC_2H_5$[b]	C_2H_5OH	300		0		0	97
II	$NaOC_4H_9$[b]	n-C_4H_9OH	156		0		0	87[e]
II	$NaOC_6H_{13}$[b]	n-$C_6H_{13}OH$	30		0	Isobutyromesitylene	62	26
						Dialkyl carbonates	61[f]	

[a] Ethyl benzoyldimethylacetate. [b] Only 20 mole-percent of reagent used. [c] Much ester probably lost. [d] Ethyl mesitoyldimethylacetate. [e] The *n*-butyl ester of II was obtained. [f] A mixture of ethyl hexyl carbonate (26%) and dihexyl carbonate (35%) was obtained.

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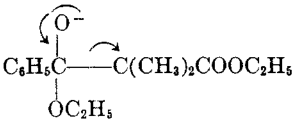
[1] Supported by the National Science Foundation.

[2] E. Hope and W. H. Perkin, *J. Chem. Soc.*, **95**, 2042 (1909).

[3] See C. R. Hauser and B. C. Hudson, *Org. Reactions*, **1**, 269 (1942).

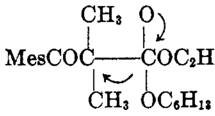
age occurring largely at "b" to form isobutyromesitylene. Thus with the former reagent the ratio of cleavage at "b" to that at "a" was about 28:1, while with the sodium alkoxide cleavage occurred exclusively at "b". In addition to the isobutyromesitylene, ethyl hexyl and dihexyl carbonates were obtained with the sodium alkoxide. The dihexyl carbonate evidently arose from an alcohol-ester exchange either before or after cleavage.

Although the reverse of such cleavages can be brought about to form certain β-keto esters, the present conditions do not permit these condensations. Indeed, sodium ethoxide is probably incapable of effecting the benzoylation of ethyl isobutyrate with ethyl benzoate to form β-keto ester I or the carbethoxylation of isobutyromesitylene to give β-keto ester II. The present results evidently arise from relative rates of reaction of the basic anion at the ketone and ester groups. In β-keto ester I, the ketone group is the more reactive whereas in β-keto ester II, in which the rate of reaction at the ketone group has been greatly diminished by the mesityl group, the ester group is the more reactive. There is probably little difference in the reactivity of the ester groups of the two β-keto esters. The mechanism of cleavage at "a" with ethoxide ion involves intermediate III and that at "b" with hexoxide ion, intermediate IV.



$C_6H_5C(O^-)(OC_2H_5)—C(CH_3)_2COOC_2H_5$

III



$MesCOC(CH_3)_2—C(O)(OC_6H_{13})OC_2H_5$

IV

EXPERIMENTAL[4]

Cleavages of β-keto esters[5] with basic reagents. Table I. A. Procedure with potassium hydroxide. A mixture of 0.1 mole of the β-keto ester and 250 ml. of 5% or 60% aqueous potassium hydroxide was heated on the steam-bath for the time given in Table I. After cooling, the aqueous alkaline mixture was shaken with ether, and the two layers were separated. The ethereal layer was dried over Drierite, the solvent removed, and the residue fractionally distilled to give the neutral products. The aqueous alkaline layer was acidified, and the precipitated carboxylic acid was collected on a funnel.

B. Procedure with sodium alkoxides. A solution of 0.1 mole of the β-keto ester and 0.02 mole of the sodium alkoxide in 150 ml. of the corresponding absolute alcohol was refluxed for the time given in Table I. Approximately 100 ml. of the alcohol then was removed by distillation. The residue was poured on a mixture of crushed ice and 5 ml. of 6 *N* hydrochloric acid and the resulting mixture was extracted with ether. The ethereal solution was washed with water, dried over Drierite, and the solvent was removed. The residue was fractionally distilled to give the cleavage products, and recovered β-keto ester.

C. Identification of products. The products listed in Table I were identified as described below.

Benzoic acid, after one recrystallization from water melted at 121–121.5°; a mixture m.p. with an authentic sample was the same.

Ethyl benzoate boiled at 85–87° at 10 mm., n_D^{25} 1.5029, reported b.p. 94.05° at 14 mm.[6] A sample was saponified to give benzoic acid, m.p. and mixture m.p. 121–121.5°.

Ethyl isobutyrate boiled at 107–110°, n_D^{25} 1.3859, reported b.p. 111°.[7] A sample was saponified to give isobutyric acid; m.p. of *p*-bromophenacyl derivative 77.5–78°, reported m.p. 76.8°.[8]

Mesitoic acid, after one recrystallization from 90–120° ligroin, melted at 151.5–152°; a mixture m.p. with an authentic sample was the same.

Isobutyromesitylene boiled at 123–124° at 10 mm., n_D^{25} 1.5082, reported b.p. 142–143° at 19 mm.[5] A sample of this ketone was converted to its sodio derivative by means of sodium, and the sodio ketone was treated with benzoyl chloride to give the O-benzoyl derivative, m.p. 87–87.5°, reported m.p. 87–88°.[9]

n-Butyl mesitoyldimethylacetate (see note *e*, Table I) boiled at 169° at 5 mm., n_D^{25} 1.5032.

Anal.[10] Calc'd for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.97; H, 9.37.

Dihexyl carbonate (see note *f* Table I) boiled at 139–140° at 10 mm., 275–276° at atmospheric pressure, n_D^{25} 1.4272, reported b.p. 275°, n_D^{25} 1.4262.[11] A sample was saponified to give *n*-hexanol, b.p. 155–157°, reported 157.5°.[12] The *3,5-dinitrobenzoate* melted at 58.5–59°, reported m.p. 58.4°.[13]

Ethyl hexyl carbonate (see note *f* Table I) boiled at 77–78° at 10 mm., n_D^{25} 1.4144. This product was not further identified.

DURHAM, N. C.

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(4) Melting and boiling points are uncorrected.

(5) Ethyl benzoyldimethylacetate (I) and ethyl mesitoyldimethylacetate (II) were prepared by the method of P. L. Bayless and C. R. Hauser, *J. Am. Chem. Soc.*, **76**, 2306 (1954).

(6) C. Rechenberg, *J. prakt. Chem.*, **101**, 112 (1921).

(7) J. Timmermans, *Bull. soc. chim. Belg.*, **31**, 389 (1922).

(8) W. L. Judefind and E. E. Reid, *J. Am. Chem. Soc.*, **42**, 1043 (1920).

(9) R. C. Fuson, C. H. Fisher, G. E. Ullyot, and W. O. Fugate, *J. Org. Chem.*, **4**, 111 (1939).

(10) Analysis by Galbraith Laboratories, Knoxville, Tenn.

(11) S. T. Bowden and E. T. Butler, *J. Chem. Soc.*, 75 (1939).

(12) R. Bilterys and J. Gisseleire, *Bull. soc. chim. Belg.*, **44**, 567 (1935).

(13) G. B. Malone and E. E. Reid, *J. Am. Chem. Soc.*, **51**, 3424 (1929).