

being relatively insensitive to steric and electronic effects in the aldehyde moiety.

#### EXPERIMENTAL<sup>11</sup>

*p*-Dimethylaminophenylcarbinols (III). The new amino carbinols listed in Table I were prepared from the appropriate alkyl- or arylmagnesium bromide and *p*-dimethylaminobenzaldehyde, except for the cyclohexyl derivative, which was prepared from cyclohexylmagnesium chloride. The halides (except *m*-bromocumene) and the aldehyde were commercial products. The Grignard reagents were prepared by reaction of the halides, in 2–3 volumes of ether, with a slight excess of magnesium. *p*-Dimethylaminobenzaldehyde was added as a solution in benzene, and the reaction was stirred at room temperature for 2–10 hr. Hydrolysis was accomplished in aqueous ammonium chloride, the ether layer was dried over calcium sulfate, and the residue was recrystallized from benzene–petroleum ether (b.p. 30–60°) [except in the case of 1-(4-dimethylaminophenyl)-4-methyl-1-pentanol, which was crystallized from petroleum ether alone].

*p*-Dimethylaminobenzhydrol, m.p. 69–70° (reported<sup>12</sup> 69–70°) was prepared by the reduction of the ketone with sodium borohydride. *p*-Dimethylaminophenyl-1-naphthylcarbinol, m.p. 98–99° (reported<sup>13</sup> m.p. 97–98°) was prepared as described previously.<sup>13</sup>

*Preparation of the aldehydes.* Sulfanilic acid (60 g., 0.31 mole) was dissolved in a solution of 18.4 g. of sodium carbonate in 200 ml. of water, and diazotized at 0–5° by the addition of 64 ml. of concd. hydrochloric acid and a solution of 24.4 g. of sodium nitrite in 75 ml. of water in portions. When diazotization was complete and a slight excess of nitrous acid was present, the solution was buffered by the addition of 70 g. of sodium acetate in 200 ml. of water (pH ca. 6). A solution of 0.20 mole of the amino carbinol in 500

(11) Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting and boiling points were not corrected for stem exposure.

(12) K. Albrecht, *Ber.*, **21**, 3292 (1888).

(13) F. Sachs and L. Sachs, *Ber.*, **38**, 511 (1905).

ml. of acetone was then added, followed by an additional 250 ml. of acetone. The mixture, which became red in a few minutes, was allowed to stir under a nitrogen atmosphere at 0–5° for 30 min. and then for an additional 30 min. after the removal of the ice bath. The mixture was diluted with water and extracted with ether. After removal of solvent from the dried solution, the aldehyde was distilled under an atmosphere of nitrogen.

*Methyl m-bromobenzoate*, b.p. 69–70°/0.2 mm. (reported<sup>14</sup> b.p. 122.5°/15 mm.), was prepared in 84% yield from commercial *m*-bromobenzoic acid by the method of Clinton and Laskowski.<sup>15</sup>

*m*-Bromophenyldimethylcarbinol. A solution of 150 g. (0.70 mole) of methyl *m*-bromobenzoate in 300 ml. of ether was added to 2.25 moles of methylmagnesium bromide in 1.5 l. of ether and the mixture was stirred overnight. Hydrolysis with aqueous ammonium chloride was followed by isolation in the usual manner. The product, 130 g. (85%), distilled at 79–80°/0.24 mm.

*Anal.* Calcd. for C<sub>9</sub>H<sub>11</sub>BrO: C, 50.25; H, 5.16. Found: C, 50.10; H, 5.03.

*m*-Bromocumene.<sup>16</sup> *m*-Bromophenyldimethylcarbinol (130 g., 0.60 mole) was hydrogenolyzed in three batches, each utilizing 3 g. of 5% palladium-on-charcoal catalyst in 200 ml. of glacial acetic acid and 1 ml. of 70% perchloric acid, under 40 lb. initial hydrogen pressure, at room temperature. Approximately 1 hr. was required for each reaction. After removal of the catalyst the combined acetic acid solutions were combined and about 75% of the acetic acid was removed under reduced pressure. The residue was diluted with water and steam distilled. Fractional distillation yielded 96 g. (80%) of colorless liquid, b.p. 208–210° (reported<sup>17</sup> b.p. 208–210°).

ANN ARBOR, MICH.

(14) A. M. Kellas, *Z. Physik. Chem.*, **24**, 245 (1897).

(15) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **70**, 3135 (1948).

(16) The synthesis of this compound was adapted from an unpublished procedure of Professor R. E. Ireland.

(17) E. C. Sterling and M. T. Bogert, *J. Org. Chem.*, **4**, 20 (1939).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

## Condensation of Alkyl Acetates with Benzophenone by Lithium Amide to Form $\beta$ -Hydroxy Esters. Relative Ease of Self-condensation of Esters<sup>1</sup>

WILLIAM R. DUNNAVANT AND CHARLES R. HAUSER

Received February 8, 1960

The success of the aldol type of condensation of ethyl or isopropyl acetate with benzophenone by lithium amide in liquid ammonia to form the corresponding  $\beta$ -hydroxy ester was found to be dependent on minimizing the self-condensation of the alkyl acetate before adding the ketone to the reaction mixture. This was accomplished either by adding the ketone very soon after the ester or by employing excess reagent over the one equivalent required to form the intermediate lithio ester. This was not necessary with *t*-butyl acetate. When two equivalents of lithium amide were used, the monolithio derivative of the  $\beta$ -hydroxy ester first formed in the condensation was converted to the dilithio derivative of the  $\beta$ -hydroxy ester. This was demonstrated by adding benzyl chloride to the reaction mixture to form the  $\alpha$ -benzyl derivative of the  $\beta$ -hydroxy ester. Consideration is given to the bearing of these results on the earlier general procedure for synthesizing  $\beta$ -hydroxy esters and to the relative ease of self-condensations of the alkyl acetates.

Recently<sup>2</sup> ethyl acetate was condensed with various ketones or aldehydes by means of two molecular equivalents of lithium amide in liquid

ammonia to form the corresponding  $\beta$ -hydroxy esters. For example, this ester was condensed with benzophenone to give  $\beta$ -hydroxy ester I in

(1) Supported by the Office of Ordnance Research, U. S. Army.

(2) W. R. Dunnivant and C. R. Hauser, *J. Org. Chem.*, **25**, 503 (1960).



zation procedure was employed to minimize possible cleavages of the  $\beta$ -hydroxy esters, although it has been shown not to be required in the preparation of  $\beta$ -hydroxy ester I (see note 5 in ref. 2).

TABLE I

YIELDS OF  $\beta$ -HYDROXY ESTERS FROM ALKYL ACETATES AND BENZOPHENONE BY LITHIUM AMIDE UNDER VARIOUS CONDITIONS

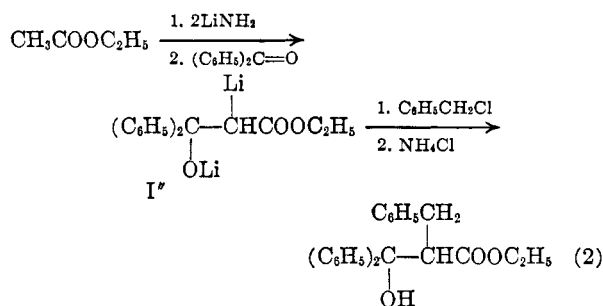
Exp. No.	Alkyl Acetate	Equiv. LiNH <sub>2</sub>	Ioniz. Time, Min. <sup>a</sup>	$\beta$ -Hydroxy Ester	Yield, %
1	Ethyl	1	15-20	I	0 <sup>b</sup>
2	Ethyl	1	0 <sup>c</sup>	I	69, 22 <sup>d</sup>
3	Ethyl	1.1	0.5	I	67
4	Ethyl	1.25	0.5	I	78
5	Ethyl	2	3	I	82
6	Ethyl	2	15-20	I	80-84 <sup>e</sup>
7	Ethyl	3	20	I	60
8	Ethyl	4	20	I	58
9	Isopropyl	1	15-20	II	3 <sup>f</sup>
10	Isopropyl	1	0 <sup>g</sup>	II	82
11	Isopropyl	2	15-20	II	80 <sup>e</sup>
12	<i>t</i> -Butyl	1	15-20	III	71 <sup>e</sup>
13	<i>t</i> -Butyl	1.25	3	III	71
14	<i>t</i> -Butyl	2	15-20	III	87 <sup>b</sup>
15	<i>t</i> -Butyl	2.1	15-20	III	76

<sup>a</sup> The time allowed after adding the ester to the reagent before adding the ketone. <sup>b</sup> A 24% yield of acetoacetic ester was obtained; 89% of the ketone was recovered. <sup>c</sup> Although the ketone was added immediately after the ester, a few seconds probably elapsed. <sup>d</sup> In this experiment the ethyl acetate-lithium amide mixture turned black before all of the ketone was added. <sup>e</sup> Reported previously in ref. 2. <sup>f</sup> A 50%-yield of isopropyl acetoacetate was obtained, and 55% of the ketone was recovered.

It can be seen from Table I that the yields of I were more consistent with an excess of the reagent than with just one equivalent. Thus, even though the ketone was not added until thirty seconds after the ester, 1.1 and 1.25 equivalents of the reagent produced the  $\beta$ -hydroxy ester in yields of 67% and 78% respectively (experiments 3 and 4). The latter yield is about as high as that (80-84%) obtained with two equivalents of the reagent when the ketone was added three or twenty minutes after the ester (experiments 5 and 6).

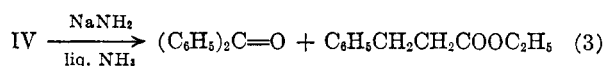
The fact that two equivalents of lithium amide but not one produced  $\beta$ -hydroxy ester I when the ketone was added twenty minutes after the ester indicated that the extra equivalent of the reagent retarded the self-condensation of the ethyl acetate. This was confirmed by treating ethyl acetate alone with two equivalents of the reagent for twenty minutes, after which no acetoacetic ester could be isolated. However, the selfcondensation of ethyl acetate was not stopped indefinitely by an extra equivalent of lithium amide, a 31% yield of acetoacetic ester being obtained with two equivalents of the reagent after two hours. A 40% yield of the  $\beta$ -keto ester was realized with one equivalent of the reagent after only one hour.<sup>4</sup>

Besides retarding the selfcondensation of ethyl acetate, the extra equivalent of lithium amide was found to convert the monolithio  $\beta$ -hydroxy ester I' that is presumably first formed in the condensation of lithio ethyl acetate with benzophenone (see Scheme A) to the dilithio  $\beta$ -hydroxy ester I". This was established by treating the reaction mixture with an equivalent of benzyl chloride, which produced the  $\alpha$ -benzyl derivative IV in 61% yield (Equation 2).



IV was also obtained in 61% yield by treating  $\beta$ -hydroxy ester I with two equivalents of lithium amide followed by one equivalent of benzyl chloride.

That the benzylation product was the  $\alpha$ -benzyl derivative and not the possible benzyl ether of  $\beta$ -hydroxy ester I<sup>5</sup> was supported by its infrared spectrum, which gave strong absorption at 2.8  $\mu$  indicating that the hydroxyl group had been retained. The structure of the benzylation product was established as IV by cleavage with sodium amide in liquid ammonia to form benzophenone and ethyl hydrocinnamate which was saponified and isolated as hydrocinnamic acid (Equation 3).<sup>6</sup>



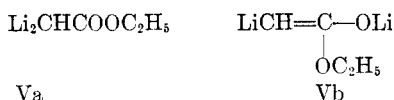
Incidentally, the type of alkylation of the dilithio  $\beta$ -hydroxy ester illustrated in Equation 2 may furnish a useful method for synthesizing not only IV which appears not to have been prepared previously, but also various other  $\alpha$ -alkyl derivatives.

The condensation with two equivalents of lithium amide might appear to involve the intermediate formation of dilithio ethyl acetate, Va or Vb, which might add to the carbonyl group of benzophenone to form directly dilithio  $\beta$ -hydroxy ester

(4) The yields of acetoacetic ester reported here may not represent the maximum amount of the  $\beta$ -keto ester formed, as only 54% of the  $\beta$ -keto ester was recovered in a blank experiment with two equivalents of the reagent for one hour.

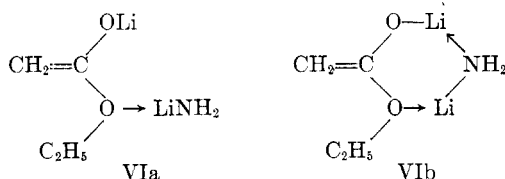
(5) Another preferential benzylation of a carbanion over an oxide anion has been observed with the dianion  $(\text{C}_6\text{H}_5)_2\text{C}=\text{O}^-$ ; P. J. Hamrick and C. R. Hauser, *J. Am. Chem. Soc.*, **81**, 493 (1959).

(6) Reactions with sodium amide will be further considered in a later paper by C. R. Hauser and W. R. Dunnavant.



I". However, lithium amide seems unlikely to be a sufficiently strong base to effect the secondary ionization that would be required to produce dilithio ethyl acetate. Indirect evidence against the formation of an appreciable amount of such a dilithio derivative is the previous observation<sup>7</sup> that treatment of ethyl acetate with two equivalents of lithium amide in liquid ammonia followed by two equivalents of benzyl chloride produced the monobenzyl derivative, ethyl 3-phenylpropionate (30%), but apparently none of the dibenzyl derivative of ethyl acetate. On repeating this experiment, we obtained, besides the monobenzylated ester, some stilbene (17%) which has previously been produced by the action of lithium amide in liquid ammonia on benzyl chloride.<sup>8</sup> The formation of this dimeric olefin may indicate the presence of some essentially free lithium amide, although other bases in the reaction mixture might have effected the reaction.

The reactive intermediate in the condensation of ethyl acetate with benzophenone by two equivalents of lithium amide seems more likely to be essentially monolithio ethyl acetate, possibly coordinated with the extra equivalent of the reagent as in VIa or VIb or in a dimer or trimer.

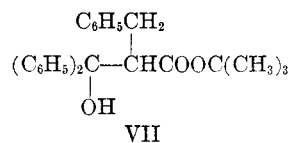


Some sort of coordination is indicated by the fact that an extra equivalent of lithium amide retards the selfcondensation of ethyl acetate (see above) whereas sodium amide, which should coordinate to a smaller degree, fails to exhibit such a retarding effect under similar conditions.<sup>6</sup> The retarding of the selfcondensation of ethyl acetate is presumably the result of more complete ionization of its  $\alpha$ -hydrogen leaving relatively less unchanged ester to enter into condensation with the lithio ester as required by theory.<sup>9</sup> Apparently the two equivalents of lithium amide coordinate with the carbonyl as well as the alkoxide oxygen of ethyl acetate to make the ester an effectively stronger acid. This may lead to the formation of the coordinated monolithio derivative VIa or VIb, or perhaps to an anion of VIb resulting from the

ionization of a hydrogen on nitrogen. The more complete ionization of the  $\alpha$ -hydrogen of ethyl acetate cannot be ascribed solely to a mass action effect by amide ion, as this base is effectively weaker in lithium amide than in sodium amide towards diphenylmethane, which has no point for coordination of a metallic cation. Thus, whereas sodium amide in liquid ammonia converts this hydrocarbon to its anion which can be alkylated,<sup>10</sup> lithium amide produces an insufficient concentration of the carbanion for successful alkylation under similar conditions.<sup>11</sup>

Regardless of the structure of the intermediate lithio ethyl acetate, benzophenone must react preferentially with it rather than with excess lithium amide, as  $\beta$ -hydroxy ester I was obtained in approximately 60% yield when three equivalents or even four equivalents of the reagent were employed (see experiments 7 and 8, Table I). This result cannot be accounted for on the basis that benzophenone first adds reversibly an equivalent of lithium amide to form  $(\text{C}_6\text{H}_5)_2\text{C}(\text{OLi})\text{NH}_2$  and that the lithio ethyl acetate then condenses with the ketone present in equilibrium, as the addition of the amide is effectively irreversible in liquid ammonia. Thus, on first adding benzophenone to two equivalents of lithium amide followed by ethyl acetate, none of  $\beta$ -hydroxy ester I was obtained and the ketone was largely recovered on acidification.

In Table I, although the yields of  $\beta$ -hydroxy ester II from isopropyl acetate were about the same with one or two equivalents of the reagent under the appropriate conditions (experiments 10 and 11), those of  $\beta$ -hydroxy ester III from *t*-butyl acetate appeared to be slightly higher with two or 2.1 equivalents of the reagent (experiments 14 and 15) than with one or 1.25 equivalents (experiments 12 and 13). This might indicate that the maximum yield with *t*-butyl acetate requires the conversion of the product to its dilithio derivative. Some of this derivative was evidently produced on treating  $\beta$ -hydroxy ester III with two equivalents of the reagent, as subsequent addition of benzyl chloride gave VII (10%). The yield could probably be improved by longer reaction time (see Experimental).



On the basis of the present results certain modifications may be made in the earlier procedure<sup>2</sup> for the synthesis of  $\beta$ -hydroxy esters from ethyl acetate and various ketones or aldehydes. The time interval after adding the ester to the reagent before adding the ketone may now be shortened, if de-

(7) C. R. Hauser and W. J. Chambers, *J. Org. Chem.*, **21**, 1524 (1956).

(8) C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *J. Am. Chem. Soc.*, **78**, 1653 (1956).

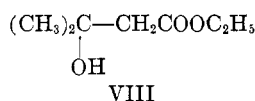
(9) See C. R. Hauser and B. E. Hudson, *Org. Reactions*, Vol. I, 276 (1942).

(10) C. R. Hauser and P. J. Hamrick, Jr., *J. Am. Chem. Soc.*, **79**, 3142 (1957).

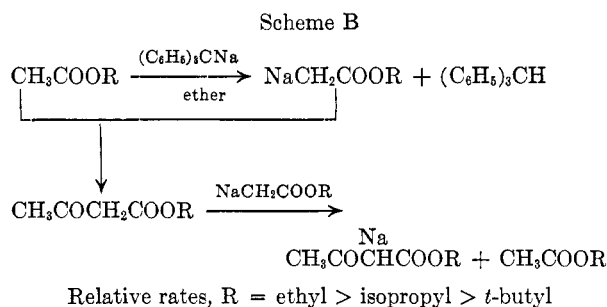
(11) Unpublished results of P. J. Hamrick and C. R. Hauser.

sired, from fifteen to twenty minutes to three minutes or less (see Table I). If this time interval is so shortened, the full extra equivalent of lithium amide is not required even in the condensation of ethyl acetate with benzophenone. However, this is not necessarily true for the condensations of this ester with other ketones, with certain of which the further driving force furnished by the conversion of the product to its dilithio derivative may be required for maximum yield.

While the general procedure employing two equivalents of the reagent has previously been shown<sup>2</sup> to produce good to excellent yields in the condensations of ethyl acetate with certain ketones having  $\alpha$ -hydrogen, it has now been found not to be satisfactory with acetone, with which much tarry material was produced. However, a 44% yield of the corresponding  $\beta$ -hydroxy ester VIII was obtained with 1.25 equivalents of the reagent under special conditions (see Experimental).



*Relative rates of self-condensations of alkyl acetates.* It has previously been observed in this laboratory<sup>12</sup> that ethyl acetate is selfcondensed by sodium triphenylmethide in ether somewhat faster than isopropyl acetate, and that these two esters are selfcondensed much more rapidly than *t*-butyl acetate (Scheme B).



Similar to the observation made above in connection with Scheme A, a small amount of unchanged alkyl acetate present in the equilibrium of the first step is sufficient for the production of good yields of the selfcondensation product, as the alkyl acetate is regenerated continually in the last step. That the equilibrium of the first step, acid-base reaction is far on the side of the ester anion is strikingly illustrated by the almost immediate discharge of the characteristic red color of the sodium triphenylmethide reagent by a molecular equivalent of the alkyl acetate.

In line with these relative rates of selfcondensations of alkyl acetates, treatment of ethyl and isopropyl acetates with equivalents of lithium

amide in liquid ammonia for twenty minutes produced considerable ethyl and isopropyl acetoacetates, whereas similar treatment of *t*-butyl acetate gave no significant amount of its self-condensation product. Addition of benzophenone to the reaction mixtures after this time gave  $\beta$ -hydroxy esters I, II, and III in increasing yields of 0%, 3% and 71%, respectively (see Table I). However, the yield of the ethyl acetoacetate isolated was only about half of that of isopropyl acetoacetate (see notes b and f, Table I). This apparent discrepancy appears to have been due to some destruction of the former  $\beta$ -keto ester<sup>4</sup> or possibly to some attack of the lithium amide at the carbonyl group of ethyl acetate to form acetamide although an attempt to isolate this product was unsuccessful.

### EXPERIMENTAL<sup>13</sup>

*Condensations of alkyl acetates with benzophenone by lithium amide* (Table I). The preparation of the lithium amide in liquid ammonia and the apparatus used were described previously.<sup>2</sup> After the blue color of the lithium metal had been discharged in the main body of the reaction mixture, the reaction flask was shaken manually to effect the conversion of particles of the metal on the walls above the liquid ammonia to lithium amide, which was obtained as a thick, white suspension.

In Table I are summarized the results obtained from the condensations of ethyl, isopropyl, and *t*-butyl acetates with benzophenone to form  $\beta$ -hydroxy esters I, II and III respectively. The  $\beta$ -keto esters resulting from selfcondensations of ethyl and isopropyl acetates are noted in this table. Some typical experiments are described in detail below.

*A. Experiments with ethyl acetate.* In Experiment 1, a solution of 35.2 g. (0.4 mole) of ethyl acetate in an equal volume of dry ether was added to a stirred suspension of 0.4 mole of lithium amide in 440 ml. of commercial, anhydrous liquid ammonia. The reaction flask was then shaken manually to effect contact of the ester with small amounts of lithium amide on the walls of the flask above the main body of the reaction mixture. After stirring for 20 min., 72.8 g. (0.4 mole) of benzophenone in sufficient ether to effect solution (140 ml.) was added. The reaction mixture was stirred for 1 hr. and was then inversely neutralized by pouring it with stirring into a solution of ammonium chloride in liquid ammonia. The ammonia was evaporated on the steam bath as 300 ml. of ether was added. The resulting ethereal suspension was shaken with 200 ml. of cold water and the aqueous layer was extracted with several 100-ml. portions of ether. The combined ethereal solution was dried over magnesium sulfate and then evaporated. The residue was dissolved in boiling petroleum ether (b.p. 60–90°) and the solution treated with charcoal and filtered. The solution was stirred with cooling in an ice bath to precipitate 65 g. (89%) of crystalline benzophenone, m.p. 46–47°. The solvent of the filtrate was removed, and the residue was distilled to yield 7.3 g. (24%) of ethyl acetoacetate, b.p. 73–74° at 14 mm; reported<sup>14</sup> b.p. 74° at 14 mm. The product gave an infrared spectrum identical with that of the authentic  $\beta$ -keto ester, and a positive enol test with ethanolic ferric chloride.

(13) The melting points were taken on a Fisher-Johns melting point apparatus. Infrared spectra were produced with a Perkin-Elmer Infracord using mineral oil mulls. The elemental analysis were by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

(14) Heilbron, *Dictionary of Organic Compounds*, Vol. II, Oxford University Press, New York, N. Y., 1953, p. 486.

(12) Ph.D. thesis, B. Abramovitch, Duke University (1942) p. 33.

In Experiment 2, a solution of 17.6 g. (0.2 mole) of ethyl acetate in an equal volume of ether was added through the addition funnel as rapidly as possible to a stirred suspension of 0.2 mole of lithium amide in 400 ml. of anhydrous liquid ammonia. As frothing occurred, a reaction vessel having a volume twice that of the amide suspension was used. As the last of the ester passed through the stopcock, a solution of 36.4 g. (0.2 mole) of benzophenone in 70 ml. of ether was poured immediately into the addition funnel and allowed to run into the reaction flask as rapidly as possible, the addition funnel being rinsed with a little ether. The mixture was stirred for 1 hr. and was then inversely neutralized with ammonium chloride. The ammonia was replaced by ether. After adding water and thoroughly extracting the aqueous layer with ether, the combined ethereal solution was dried and solvent evaporated. The residue was crystallized from petroleum ether (b.p. 60–90°) to give 37.2 g. (69%) of ethyl  $\beta$ -hydroxy- $\beta$ , $\beta$ -diphenylpropionate (I), m.p. 86–87°; reported<sup>15</sup> m.p. 87°. The filtrate was reduced in volume and cooled with stirring in an ice bath to give 5.3 g. (14%) of crystalline benzophenone, m.p. 46–47°, after two crystallizations from petroleum ether (b.p. 60–90°).

Ethanol is a good crystallizing solvent for  $\beta$ -hydroxy ester I, but isolation of benzophenone is made difficult by its high solubility in this solvent.

*B. Experiments with isopropyl acetate.* In Experiment 9, a solution of 25 g. (0.24 mole) of isopropyl acetate in an equal volume of ether was added to a stirred suspension of 0.24 mole of lithium amide in 400 ml. of anhydrous liquid ammonia. After 15 min., a solution of 43.5 g. (0.24 mole) of benzophenone in 80 ml. of ether was added. After stirring for 1 hr., the reaction mixture was inversely neutralized with ammonium chloride. The ammonia was replaced by ether and water was added. After several ether extractions of the aqueous layer, the combined ethereal solution was dried over magnesium sulfate and then evaporated. The residue was crystallized from 95% ethanol to yield 2.2 g. (3%) of isopropyl  $\beta$ -hydroxy- $\beta$ , $\beta$ -diphenylpropionate (II), as colorless, rod-shaped crystals, m.p. 101–102°.

*Anal.* Calcd. for  $C_{19}H_{22}O_3$ : C, 76.02; H, 7.09. Found: C, 75.93; H, 7.03.

Reducing the volume of the filtrate and cooling gave 37.5 g. (86%) of benzophenone, m.p. 46–47°, after recrystallization from petroleum ether (b.p. 60–90°). The filtrate, following removal of the ketone, was distilled to yield 8.8 g. (50%) of isopropyl acetoacetate, b.p. 78–80° at 10 mm., reported b.p. 79–80° at 11 mm.<sup>16</sup> The  $\beta$ -keto ester gave a positive enol test with ethanolic ferric chloride and reacted with aqueous cupric acetate to give a green crystalline salt, m.p. 177–178°, after two crystallizations from aqueous methanol; reported<sup>17</sup> m.p. 179–180°.<sup>17</sup>

In Experiment 10, a solution of 25 g. (0.24 mole) of isopropyl acetate in an equal volume of ether was added to a stirred suspension of 0.24 mole of lithium amide in 400 ml. of liquid ammonia, followed immediately by 44 g. (0.24 mole) of benzophenone in 100 ml. of ether (see Exp. 2 with ethyl acetate). The resulting gray suspension was stirred for 1 hr. and was inversely neutralized with ammonium chloride. The ammonia was replaced by ether and water was added. After several extractions of the aqueous layer with ether, the combined ethereal solution was dried and evaporated. The residue was crystallized from petroleum ether (b.p. 60–90°) to give 56 g. (82%) of ester II as large colorless, rod-shaped crystals, m.p. 101–102°.

*C. Experiments with *t*-butyl acetate.* In Experiment 12, a solution of 20 g. (0.17 mole) of *t*-butyl acetate in an equal volume of ether was added to a stirred suspension of 0.17 mole of lithium amide in 400 ml. of liquid ammonia. After

stirring for 15 min., 31 g. (0.17 mole) of benzophenone in 60 ml. of ether was added. The resulting mixture was stirred for 1 hr. and was inversely neutralized with ammonium chloride. The ammonia was evaporated to dryness and the solid residue was treated with water and filtered. The dried solid was recrystallized from 95% ethanol to give 36.6 g. (71%) of  $\beta$ -hydroxy ester III, m.p. 93–94°; reported<sup>18</sup> m.p. 92–93°.

*Benzoylation of dilithio derivative I\* to form IV. A. From ethyl acetate and benzophenone.* To a stirred suspension of 0.4 mole of lithium amide in 400 ml. of anhydrous liquid ammonia was added 17.6 g. (0.2 mole) of ethyl acetate in an equal volume of ether. After stirring for 15 min., 36.4 g. (0.2 mole) of benzophenone in 50 ml. of ether was added to form a dark blue, then dark gray suspension. The mixture was stirred for another 15 min., and 25 g. (0.2 mole) of benzyl chloride in 25 ml. of ether was added. An insoluble gray mass formed in the ammonia. Stirring was continued for 1 hr. and the reaction mixture was then inversely neutralized with ammonium chloride. The ammonia was evaporated and the solid residue was stirred with cold water. The resulting mixture was filtered. The solid cake was crystallized from ethanol to yield 42.2 g. (61%) of ethyl  $\alpha$ -benzyl- $\beta$ -hydroxy- $\beta$ , $\beta$ -diphenylpropionate (IV), m.p. 109–109.5° after two crystallizations from ethanol. The infrared spectrum showed ester carbonyl absorption at 5.8  $\mu$  and hydroxyl absorption at 2.8  $\mu$ .

*Anal.* Calcd. for  $C_{24}H_{24}O_3$ : C, 79.97; H, 6.71. Found: C, 79.99; H, 6.70. C, 80.06; H, 6.85.

*B. From  $\beta$ -hydroxy ester I.* To 0.07 mole of lithium amide in 400 ml. of anhydrous liquid ammonia was added 10 g. (0.037 mole) of  $\beta$ -hydroxy ester I in 25 ml. of ether. After stirring for 30 min., 4.66 g. (0.037 mole) of benzyl chloride in 10 ml. of ether was added and the mixture was stirred for 1 hr., followed by neutralization with ammonium chloride. The ammonia was evaporated and the residue was treated with water. The resulting mixture was filtered and the solid cake was crystallized from ethanol to yield 8.8 g. (61%) of  $\beta$ -hydroxy ester IV, m.p. 109–110°. Reducing the volume of the filtrate gave 2.8 g. (28%) recovery of  $\beta$ -hydroxy ester I, m.p. 86–87°. The samples of IV prepared by the two methods gave identical infrared spectra and no mixed melting point depression.

*Cleavage of  $\beta$ -hydroxy ester IV.* To a stirred suspension of 0.017 mole of sodium amide in 200 ml. of anhydrous liquid ammonia was added 5.0 g. (0.014 mole) of  $\beta$ -hydroxy ester IV in ether solution. The resulting solution was stirred for 4 hr. and then was neutralized with ammonium chloride. The ammonia was replaced by ether and water was added. After thoroughly extracting the aqueous layer by ether, the combined ethereal solution was dried over magnesium sulfate and evaporated. The residue was treated with petroleum ether (b.p. 60–90°) and stirred in an ice bath to yield 2.1 g. (84%) of crystalline benzophenone, m.p. 47–48°. The sample gave no mixed melting point depression with, and an infrared spectrum identical with that of an authentic sample of benzophenone.

The petroleum ether filtrate was concentrated and the residue was refluxed with aqueous sodium hydroxide for 4 hr. The cooled alkaline solution was extracted with ether and was then acidified to produce a cloudy solution. The acidified solution was extracted with ether and the ether was evaporated to yield a residual oil. The oil upon crystallization from petroleum ether (b.p. 60–90°) gave 1.62 g. (78%) of crystalline hydrocinnamic acid, m.p. 47–48°; lit.<sup>19</sup> m.p. 48.5°. The admixture melting point with an authentic sample was 47–48°. The infrared spectrum was identical in every respect with that of the authentic sample.

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*Benzoylation of  $\beta$ -hydroxy ester III to give VII.* To a stirred suspension of 0.1 mole of lithium amide in 300 ml. of anhydrous liquid ammonia was added 15 g. (0.5 mole) of  $\beta$ -hydroxy ester III in 25 ml. of anhydrous ether. After stirring the resulting suspension for 20 min., 6.33 g. (0.5 mole) of benzyl chloride in 15 ml. of ether was added slowly. A gray precipitate formed immediately. The mixture was stirred for 1 hr. and was then inversely neutralized with ammonium chloride. The ammonia was evaporated and replaced by ether. Water was added and the aqueous layer was thoroughly extracted by ether. The combined ether solution was dried over magnesium sulfate and evaporated to a colorless oily residue having the odor of benzyl chloride. Treatment of the residue with 95% ethanol permitted crystallization of 3 g. (10%) of *t*-butyl  $\alpha$ -benzyl- $\beta$ -hydroxy- $\beta$ , $\beta$ -diphenylpropionate (VII) in the form of needle-like crystals, m.p. 104–105°. The infrared spectrum showed carbonyl absorption at 5.8  $\mu$ , and hydroxyl absorption at 2.75  $\mu$ .

*Anal.* Calcd. for  $C_{26}H_{28}O_3$ : C, 80.37; H, 7.26. Found: C, 80.29; H, 7.19.

The filtrate from above was reduced in volume and cooled to yield 8.6 g. (57%) of recovered starting ester III, m.p. 92–93° after a second crystallization from ethanol.

*Treatment of ethyl acetate with excess lithium amide followed by benzyl chloride.* To a stirred suspension of 1.0 mole of lithium amide in 600 ml. of liquid ammonia was added 44 g. (0.5 mole) of ethyl acetate in an equal volume of ether. The resulting gray suspension was stirred for 2 min. and 126.6 g. (1.0 mole) of benzyl chloride in 80 ml. of ether was added. After stirring for 1 hr. the ammonia was replaced by ether and the resulting mixture neutralized with cold, dilute hydrochloric acid. There was obtained 33 g. (26%) of recovered benzyl chloride b.p. 66–68° at 20 mm., and 18.2 g. (22%) of ethyl hydrocinnamate, b.p. 245–248° at 758 mm.; reported<sup>20</sup> b.p. 247° at 760 mm. The temperature of the distillate then rose rapidly to about 300°, at which temperature stilbene began to clog the column and appara-

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tus. There was obtained 15.2 g. (17%) of crude stilbene, m.p. 119–120°. After recrystallization from ethanol (Norit), the product melted at 122–123°; reported<sup>21</sup> m.p. 124°.

*Treatment of benzophenone with lithium amide followed by ethyl acetate.* To a stirred suspension of 0.4 mole of lithium amide in 400 ml. of liquid ammonia was added 36.4 g. (0.2 mole) of benzophenone in 100 ml. of anhydrous ether. The gray suspension was stirred for 20 min., and 17.6 g. (0.2 mole) of ethyl acetate in an equal amount of ether was added. The resulting dark black solution was stirred for 1 hr. and was then neutralized with ammonium chloride. There was obtained 30.2 g. (84%) of recovered benzophenone, m.p. 47–48°, none of  $\beta$ -hydroxy ester I being isolated.

*Condensation of lithioethyl acetate with acetone.* To a stirred suspension of 0.62 mole of lithium amide in 400 ml. of anhydrous liquid ammonia was added 44 g. (0.5 mole) of ethyl acetate in an equal volume of ether. The resulting gray suspension was stirred for 2 min., and 21 g. (0.5 mole) of acetone (dried over magnesium sulfate) in a little anhydrous ether was added. The resulting black solution was stirred for 1 hr. and was then inversely neutralized with ammonium chloride. The ammonia was replaced by 300 ml. of ether, and 150 ml. of cold water was added. After thorough extraction of the aqueous layer with ether, the combined ethereal solution was dried and evaporated. The residue was distilled to give 16 g. (25%) of ethyl  $\beta$ -hydroxy- $\beta$ -methylbutyrate (VIII), b.p. 175–176° at 738 mm.; reported<sup>22</sup> b.p. about 180°.

*Anal.* Calcd. for  $C_7H_{14}O_3$ : C, 57.51; H, 9.65. Found: C, 57.41; H, 9.65.

When the reaction was repeated allowing the condensation to proceed for 1 hr. instead of 10 min., a 25% yield of hydroxy ester VIII was obtained.

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[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, UNION CARBIDE CHEMICALS Co.]

## The Oxidation of Unsaturated Acetals and Acylals with Peracetic Acid

DONALD L. HEYWOOD AND BENJAMIN PHILLIPS

Received March 18, 1960

A series of unsaturated dioxolanes, acetals, and acylals based on  $\alpha,\beta$ -unsaturated aldehydes were prepared and oxidized with peracetic acid. The major products in most cases were the anticipated epoxides, but when noncyclic acetals were used, or when the reaction was catalyzed by sulfuric acid, the predominant products of oxidation were the corresponding unsaturated esters. The novel peracid oxidation of acetals to esters was found applicable to saturated acetals also.

The literature concerning epoxides of  $\alpha,\beta$ -unsaturated aldehydes and their acetals and acylals is very sparse. The simplest member of the series, 2,3-epoxypropionaldehyde, has been referred to often in connection with the autoxidation of fats but was synthesized and satisfactorily characterized only recently.<sup>1</sup> Kögl prepared 2,3-epoxybutyraldehyde by lead tetraacetate cleavage of 2,3-6,7-diepoxyoctane-4,5-diol,<sup>2</sup> and the epoxides

of 2-ethyl-2-hexenal and crotonaldehyde were prepared by sodium hypochlorite oxidation of the unsaturated aldehydes.<sup>3</sup> The diethyl and ethylene glycol acetals of 2,3-epoxypropionaldehyde were prepared by dehydrochlorination of the chlorohydrins,<sup>4</sup> and three other acetals (the diethyl and ethylene glycol acetals of 2,3-epoxypropionaldehyde and the ethylene glycol acetal of 2,3-epoxy-3-phenylpropionaldehyde) were prepared by perbenzoic acid

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