

Fig. 5.—Zero-order plot of the decomposition of intermediate III at 30°, $(C_2H_5)_2AlCl$ concn. 5.8 millimolar; $(C_5H_5)_2TiCl_2$ concn.: ●, 5.8 millimolar; ○, 2.9; □, 1.45; △, 0.72.

ethylene, if formed, would undoubtedly have polymerized under our conditions, the amount of gas evolved using a large amount of toluene as a solvent was too great for the reaction to be exclusively one of disproportionation. Apparently the nature of the solvent and the experimental conditions have some effect on the course of the reaction.

Evidence had been presented in previous papers^{2,3} that some tetravalent titanium must be present for soluble catalysts derived from bis-(cyclopentadienyl)-titanium dichloride to show their high activity. In an attempt to identify the active catalytic species, a comparison was made between the concentration of intermediate III and the initial rate of polymerization of ethylene. This was done both during the formation of complex III and during its decomposition (see Experimental section). As can be seen in Fig. 3, there is a reasonably good correlation between intermediate III concentration and initial polymerization rate, although there is considerable scatter in the decomposition curve. It seems reasonable to conclude from these results that the active catalyst in this system is complex III, to which we have assigned the structure $(C_5H_5)_2C_2H_5TiCl \cdot C_2H_5AlCl_2$, or some species in equilibrium with it or readily

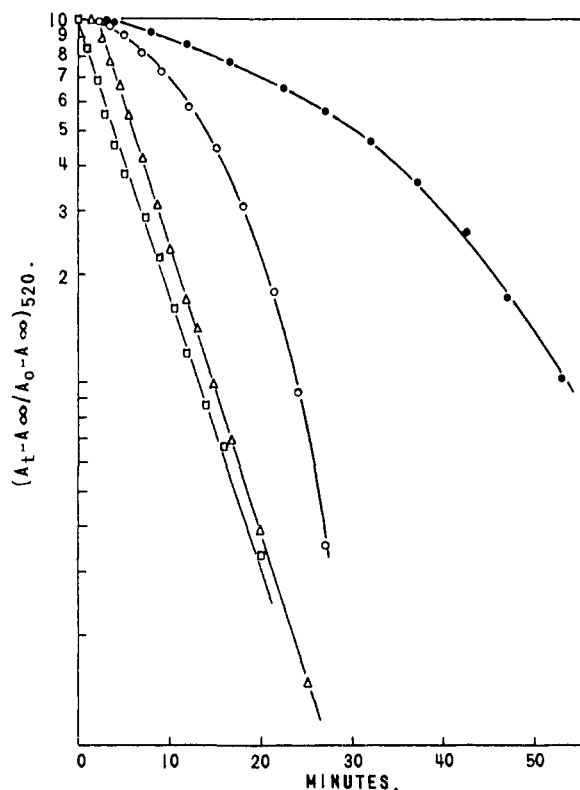


Fig. 6.—First-order plot of the decomposition of intermediate III at 30°, $(C_2H_5)_2AlCl$ concn. 5.8 millimolar; $(C_5H_5)_2TiCl_2$ concn.: ●, 5.8 millimolar; ○, 2.9; □, 1.45; △, 0.72.

derived from it. If our assumption is correct that the mechanism of olefin polymerization is fundamentally the same with heterogeneous catalysts, the active ingredient in Ziegler polymerization is an alkylated transition metal compound complexed with a Lewis acid, such as $(C_2H_5)_2AlCl$, $AlCl_3$, $TiCl_4$, $TiCl_3$ and the like.

Acknowledgments.—We are indebted to Drs. H. M. Spurlin, H. G. Tennent and H. Boardman for many stimulating discussions.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Condensation of Phenylacetic Acid with Certain Ketones to Form α -Phenyl- β -hydroxy Acids by Alkali Amides. Equilibrium Factors¹

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RECEIVED AUGUST 31, 1959

The disodio and dilithio salts of phenylacetic acid, prepared by means of two equivalents of sodium amide or lithium amide in liquid ammonia, were condensed with benzophenone and with cyclohexanone to form the corresponding α -phenyl- β -hydroxy acids. Yields up to 93% were realized for both acids, but a metallic cation effect was observed in the condensations with cyclohexanone in which the yield was better with lithium amide than with sodium amide. The monosodium salts of the β -hydroxy acids were cleaved in aqueous solution to regenerate the corresponding ketone and sodium phenylacetate. Consideration is given to the factors governing the condensation and cleavage.

It has previously been shown that phenylacetic acid can be alkylated³ or added conjugatively to certain

α,β -unsaturated carbonyl compounds⁴ by means of sodium amide in liquid ammonia. Examples of

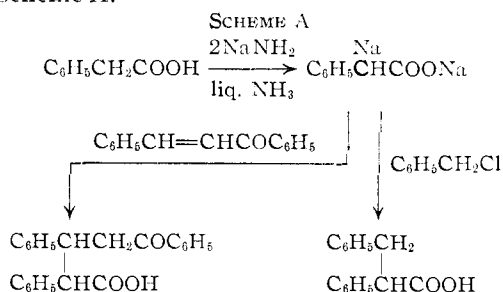
(1) Supported by the Office of Ordnance Research, U. S. Army.

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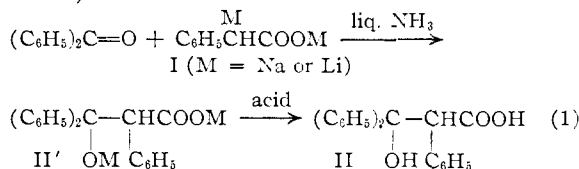
(3) C. R. Hauser and W. J. Chambers, *THIS JOURNAL*, **78**, 4942 (1956).

(4) C. R. Hauser and M. T. Tetenbaum, *J. Org. Chem.*, **23**, 1146 (1958).

these condensations, which involve the intermediate formation of disodio phenylacetate, are illustrated in Scheme A.

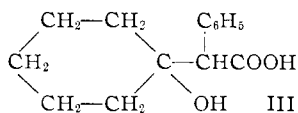


It has now been found that disodio- or dilithio-phenylacetate (I), prepared by means of two molecular equivalents of sodium amide or lithium amide in liquid ammonia, can enter into an aldol type of condensation with certain ketones to form α -phenyl- β -hydroxy acids. Thus, the condensation of the dialkali salt I with benzophenone presumably formed dialkali salt II', which, on acidification under appropriate conditions, gave the α -phenyl- β -hydroxy acid II in yields of 87-93% (equation 1).



These excellent yields of β -hydroxy acid II were obtained when the liquid ammonia was replaced by ether and the resulting ethereal suspension of II' poured into 10% hydrochloric acid. Lower yields of II were obtained when the ethereal suspension was shaken with water and the aqueous layer, which was alkaline, allowed to stand before acidification. Under these conditions, the β -hydroxy acid salt underwent partial or complete cleavage to regenerate benzophenone and sodium phenylacetate. In one experiment in which the alkaline solution from a 0.1-mole run was allowed to stand at room temperature for about an hour before acidification, essentially none of the β -hydroxy acid II was isolated. This cleavage is further considered in the next section.

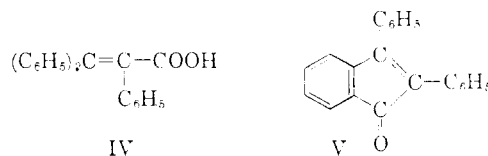
Similarly dilithiophenylacetate (I, M = Li) was condensed with cyclohexanone to produce, on acidification, the α -phenyl- β -hydroxy acid III in yields of 90-93%.



Disodiophenylacetate (I, M = Na) also was condensed with cyclohexanone to form the β -hydroxy acid III, but the yield was only 64% under similar conditions. Apparently disodiophenylacetate effected relatively more ionization of an α -hydrogen of the ketone than dilithiophenylacetate,⁵ thereby leaving relatively less of the reagent and free ketone to condense to form III.

(5) See C. R. Hauser and W. H. Puterbaugh, *THIS JOURNAL*, **75**, 4756 (1953).

The β -hydroxy acids II and III were identified by comparison of their melting points with reported values in the literature and by neutralization equivalents. β -Hydroxy acid II was also dehydrated to give a 76% yield of the α,β -unsaturated acid IV, which was cyclized to produce a 52% yield of the indenone V. These reactions appear to be useful for the syntheses of IV and V.

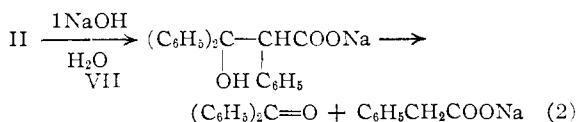


Blicke and Raffelson⁶ have effected the aldol type of condensation of sodio-magnesium-phenylacetate (VI) with benzophenone and cyclohexanone to form the β -hydroxy acids II and III in yields of 35 and 84%, respectively. They prepared the intermediate sodio-magnesium salt VI, which is

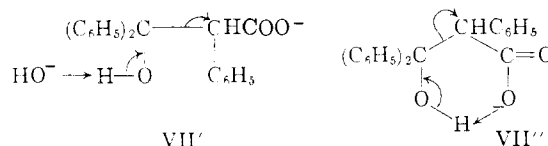


called the Ivanov reagent,⁷ by refluxing sodium phenylacetate with isopropylmagnesium chloride in ether for five hours. We believe that disodio- or dilithiophenylacetate is preferable not only because it can be prepared within a few minutes but also because it has given better yields of the β -hydroxy acids, especially II.

Cleavage of β -Hydroxy Acids. Equilibrium Factors.—Various β -hydroxy acids have previously been cleaved in the presence of excess alkali.⁸⁻¹⁰ We have observed that β -hydroxy acid II or III is cleaved by only an equivalent of aqueous alkali (equation 2).



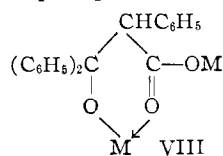
Mechanism VII' has previously been considered to operate with excess alkali.¹⁰ Mechanism VII'' also appears possible with an equivalent of alkali.



Since the cleavage products are more stable thermodynamically than VII, we suggest that one of the factors in the condensation of the disodio- or dilithiophenylacetate (I) with the ketone in liquid ammonia is the formation of the more weakly basic dianion II'.¹¹ Contributing factors might be

- (6) F. F. Blicke and H. Raffelson, *ibid.*, **74**, 1730 (1952).
- (7) D. Ivanov and A. Spassov, *Bull. soc. chim. France*, [4] **49**, 377 (1931).
- (8) K. Michel and K. Spitzauer, *Monatsh.*, **22**, 1109 (1901).
- (9) D. Ivanov and J. Popov, *Bull. soc. chim. France*, [4] **49**, 1547 (1931).
- (10) C. S. Rondstvedt and M. E. Rowley, *THIS JOURNAL*, **78**, 3804 (1956).
- (11) For a similar suggestion in the condensation of sodium diphenylmethide with benzophenone see P. J. Hamrick, Jr., and C. R. Hauser, *ibid.*, **81**, 3146 (1959).

chelation as indicated in VIII, especially when M is lithium, and the precipitation of the product.



Experimental¹²

Disodio- and Dilithiophenylacetate (I).—To a stirred suspension of 0.2 mole of sodium amide¹³ or lithium amide¹⁴ in 250 ml. of liquid ammonia was added 13.6 g. (0.1 mole) of phenylacetic acid in 70 ml. of dry ether to produce green and black solutions, respectively. These solutions were assumed to contain 0.1 mole of the dialkali salts I.

Condensation of I with Benzophenone.—To a stirred solution of I (M = Na) in 250 ml. of liquid ammonia was added 18.2 g. (0.1 mole) of benzophenone dissolved in 50 ml. of ether to produce a white precipitate. After 10 minutes the ammonia was removed on the steam-bath as 300 ml. of ether was added. The resulting ethereal suspension of a white solid was poured into 200 ml. of 10% hydrochloric acid containing about 100 g. of crushed ice. After shaking well, the suspension was filtered and the solid collected on a Büchner funnel. Additional solid was recovered by evaporating the ether layer of the filtrate. The combined solids were washed with water and recrystallized from dioxane to give 26.7 to 29.6 g. (87–93%) yields of α,β -triphenyl- β -hydroxypropionic acid (II), m.p. 205–206°, reported⁶ 206–207°; neut. equiv. calcd. for C₂₁H₁₈O₃ 318.4, found 315.

Similarly an ethereal solution of 0.1 mole of benzophenone was added with stirring to the black solution of 0.1 mole of dilithiophenylacetate (I, M = Li) in liquid ammonia to produce a white precipitate. The reaction mixture was worked up as described above for the disodio reagent I to give the β -hydroxy acid II, m.p. 205–206°, in yields of 90–93% in a series of three runs. Admixture of a sample with the product obtained from the condensation employing the disodio salt I showed no depression of the melting point.

Condensation of I with Cyclohexanone.—To a stirred solution of 0.1 mole of the dilithio salt I in liquid ammonia was added 9.8 g. (0.1 mole) of cyclohexanone in 50 ml. of dry ether to produce a white precipitate. After 15 minutes the ammonia was removed on the steam-bath while 300 ml. of dry ether was being added. The ethereal suspension was poured into 200 ml. of 10% hydrochloric acid solution containing about 100 g. of crushed ice. Sufficient ether was added to dissolve any solid remaining and, after shaking, the two layers were separated. The ethereal layer was dried over Drierite and filtered. Evaporation of the ether gave the crude α -(1-hydroxycyclohexyl)-phenylacetic acid (III)

which was recrystallized from 95% ethanol to give 21–22 g. (90–93%) of III, m.p. 143–144°, reported⁶ m.p. 139–140°; neut. equiv. calcd. for C₁₄H₁₈O₃ 234.3, found 232.

Similarly cyclohexanone (9.8 g., 0.1 mole) in 50 ml. of dry ether was added with stirring to 0.1 mole of the disodio salt I in liquid ammonia to produce a white precipitate. The reaction mixture was handled as was that obtained with the dilithio salt I (M = Li) as described above. The yield of α -(1-hydroxycyclohexyl)-phenylacetic acid (III) was 15 g. (64%), m.p. 143–144°, from ethanol.

Dehydration of II Followed by Cyclization.—To 75 ml. of glacial acetic acid containing a few drops of concentrated sulfuric acid was added 3.18 g. (0.01 mole) of II, and the mixture was refluxed for four hours. There was obtained a crude product which after several crystallizations from acetic acid gave 2.4 g. (76%) of triphenylacrylic acid (V), m.p. 210–212°, reported¹⁵ m.p. 213°. This melting point was not depressed on admixture with an authentic¹⁶ sample.

A solution of 2.0 g. (6.7 mole) of triphenylacrylic acid (V) in 10 ml. of concentrated sulfuric acid and 15 ml. of glacial acetic acid was heated for 6 hours. 2,3-Diphenylindanone (0.98 g., 52%), m.p. 150°, reported¹⁷ m.p. 150–151°, was obtained from the acid solution.

Cleavage of β -Hydroxy Acid II.—To 3.18 g. (0.01 mole) of II was added 10 ml. of 1 N sodium hydroxide solution and the mixture was diluted to about 50 ml. The resulting solution was heated on the steam-bath for 6 hours. After cooling, the solution was extracted with four 25-ml. portions of ether. The combined ethereal extracts were evaporated on the steam-bath, and the residue was taken up in 25 ml. of ethanol. To the alcoholic solution was added excess 2,4-dinitrophenylhydrazine reagent whereupon a precipitate separated. The mixture was stored in the refrigerator overnight before the solid was collected on a weighed sintered glass funnel, washed with distilled water and dried to constant weight in a desiccator. There was obtained 3.6 g. (99%) of benzophenone 2,4-dinitrophenylhydrazone, m.p. 238–239°, reported¹⁸ m.p. 238°.

The aqueous alkaline solution was concentrated to about 20 ml., and acidified with concentrated hydrochloric acid. After standing overnight in the refrigerator the solid phenylacetic acid was collected on a weighed sintered glass funnel and dried in a desiccator to constant weight to give 1.26 g. (93%) of the acid.

Cleavage of β -Hydroxy Acid III.—To 2.34 g. (0.01 mole) of III was added 10 ml. of 1 N sodium hydroxide solution, and the solution was diluted to about 50 ml. After heating on the steam-bath for 6 hours, the solution was cooled and treated as in the cleavage of II described above. There was obtained 2.4 g. (87%) of cyclohexanone 2,4-dinitrophenylhydrazone, m.p. 159–161°, reported¹⁹ m.p. 160°, and 1.2 g. (90%) of phenylacetic acid.

DURHAM, N. C.

(15) I. Heilbron, "Dictionary of Organic Compounds," Vol. II, Oxford University Press, New York, N. Y., 1953, p. 409.

(16) The authentic sample was obtained from the hydrolysis of triphenylacrylonitrile; see F. Bodroux, *Compt. rend.*, **152**, 1594 (1911).

(17) The similar cyclization of the ethyl ester of V has been described by E. Weitz and A. Scheffer, *Ber.*, **54**, 2327 (1921).

(18) Reference 15, Vol. I, p. 256.

(19) See ref. 15, Vol. I, p. 638.

(12) All melting points were taken on a Fisher-Johns melting point block.

(13) See C. R. Hauser, F. W. Swamer and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 122.

(14) See C. R. Hauser and W. H. Puterbaugh, *THIS JOURNAL*, **75**, 1068 (1954).