LXXVIII.—*The Acetoacetic Ester Condensation.*

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IN 1922 the whole question of the mechanism of the acetoacetic ester condensation was reopened by Scheibler and Ziegner (*Ber.*, **55**, 789), who stated that the product of the action of sodium or of sodamide upon ethyl acetate (subsequently referred to as the "final product" in the present paper) is not ethyl sodioacetoacetate but a derivative of orthoacetoacetic acid of the structure (I). The mechanism of the reaction was considered to be as follows:

$$CH_3{\cdot}CO_2Et \xrightarrow{\text{Na or NaNH}_2} CH_2{:}C(ONa){\cdot}OEt \xrightarrow{CH_3{\cdot}CO_2Et} CH_3{\cdot}CO{\cdot}CH_2{\cdot}C(ONa)(OEt)_2 \quad \text{(I.)}$$

and the ortho-ester structure was assigned to the final product essentially as a result of the observation that it is decomposed by water with formation of keten acetal in 16% yield according to the equation

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}C(ONa)(OEt)_2 \longrightarrow CH_3{\cdot}CO_2Na + CH_2{:}C(OEt)_2.$$

Scheibler and Friese (*Annalen*, 1925, **445**, 143) found that the "final product" reacts with benzaldehyde to produce cinnamic ester, whereas ethyl sodioacetoacetate is without action upon benzaldehyde under the same experimental conditions. Since cinnamic ester is produced by the interaction of sodium, ethyl acetate, and benzaldehyde (Claisen's cinnamic ester synthesis), the "final product" was stated to be a kind of molecular complex in which the ester enolate fragment, $CH_2{:}C(ONa){\cdot}OEt$, has a certain independence.

The structure (I) has been criticised by Adickes (*Ber.*, 1926, **59**,

2522) on the ground that such a substance would readily decompose into ethyl sodioacetoacetate and alcohol and moreover that the formation of such an additive compound of sodium ethoxide and acetoacetic ester would be an exception to the regularities which he had established between the structure of esters and their ability to form addition compounds with sodium ethoxide (*Ber.*, 1925, **58**, 1992; 1926, **59**, 2522; 1927, **60**, 272).

The mechanism of the reaction advanced by Scheibler also appears to be incapable of explaining the fact that only esters containing two α-hydrogen atoms undergo the acetoacetic ester condensation smoothly. Scheibler and Friese (*loc. cit.*, p. 149) assert that *iso*butyric ester undergoes slow and incomplete " self condensation " in the presence of sodium ethoxide, as may be recognised by the formation of the keten acetal when the product is decomposed with water, but state that the product " cannot yield a compound analogous to ethyl sodioacetoacetate by further loss of alcohol." This explanation appears to be inadequate, because there seems to be no reason why $CHMe_2{\cdot}CO{\cdot}CMe_2{\cdot}C(ONa)(OEt)_2$ should be incapable of hydrolysis in presence of acids to $CHMe_2{\cdot}CO{\cdot}CMe_2{\cdot}CO_2Et$ in the same way that (I) passes into acetoacetic ester. Moreover, the experiments of Dieckmann (*Ber.*, 1900, **33**, 2670) on the reversibility of the acetoacetic ester condensation are difficult to reconcile with the new mechanism.

We have prepared the " final product " of the acetoacetic ester condensation by the action both of sodium and of sodamide upon highly purified ethyl acetate, and have condensed it with a variety of alkyl and acyl halides. By using sodamide, Scheibler and Ziegner (*loc. cit.*) obtained the " final product " in 94% yield and stated that it is less contaminated with impurities than the product obtained by the action of sodium. The largest yield obtained by us by repeating this preparation under the prescribed condition was approximately 60% and the product contained both sodium acetate and sodium acetamide (40—50%), as was shown by analysis and by an examination of the products formed on condensation with benzyl chloride, etc. Titherley (J., 1902, **81**, 1520) found that much sodium acetate and sodium acetamide are produced by the action of sodamide upon ethyl acetate and Freund and Speyer (*Ber.*, 1902, **35**, 2321) obtained a very small yield of acetoacetic ester (16%, calculated on the ethyl acetate, or 8·4%, calculated on the sodamide) by this method of preparation. The sodium acetate is probably produced by the saponification of ethyl acetate by sodium ethoxide (compare Geuther, *Jahresber.*, 1868, 513) produced in secondary reactions (compare Oppenheim and Precht, *Ber.*, 1877, **9**, 320; Scheibler, Ziegner, and Peffer, *Ber.*, 1922, **55**, 3921).

If the " final product " has the structure (I), it is to be anticipated that its condensation with alkyl halides would result in the formation of an ortho-ester, whereas if it is a molecular compound (II) in which the fragment $CH_2{:}C(OEt){\cdot}ONa$ has a sufficient independence, *C*-substitution should occur and ethyl acetate should be liberated (compare Scheibler, Marhenkel, and Bassanoff, *Ber.*, 1925, **58**, 1198):

$$\text{(II.)}\ \left\{\begin{array}{c} CH_2{:}C(OEt){\cdot}ONa \\ CH_3{\cdot}CO_2Et \end{array}\right\} + RCl \longrightarrow \begin{array}{c} R{\cdot}CH_2{\cdot}CO_2Et \\ + \\ CH_3{\cdot}CO_2Et \end{array}$$

Frankland and Duppa (*Phil. Trans.*, 1866, **156**, 37) condensed the " final product " with various alkyl halides, but unfortunately added water before distillation of the product, so that the mono- and di-alkylacetic esters which they obtained might have been formed by the " acid fission " of the corresponding acetoacetic esters. Seseman (*Ber.*, 1873, **6**, 1086), however, obtained mono- and di-benzylacetic acids by saponification of the substance produced by the condensation of the " final product " with benzyl chloride and assumed that mono- and di-benzylacetic esters were formed in the primary reaction. We find that neither of these esters is present and that the product contains benzyl- and dibenzylacetoacetic esters together with benzyl acetate and that acetobenzylamide * is formed in addition when sodamide is used instead of sodium for the preparation of the " final product." In no case have we detected the formation of either ortho-esters or *C*-substituted acetic esters when the " final product " is condensed with alkyl or acyl halides (butyl iodide and benzoyl chloride in addition to those mentioned in this paper), and the products are substantially those which would be formed from a mixture of ethyl sodioacetoacetate with sodium acetate (and sodium acetamide when sodamide is used in the preparation).

When the dry " final product " is heated, it begins to decompose at about 130° with distillation of a small quantity of ethyl alcohol, ethyl acetate, and a trace of acetone. On the other hand, it reacts with ethyl iodide below 100° to form ethyl ethylacetoacetate. The results obtained point to the conclusion that " the final product " is very easily transformed into ethyl sodioacetoacetate even if this substance is not already present in it. The formation of keten acetal and the ability of the " final product " (unlike ethyl sodioacetoacetate) to condense with benzaldehyde constitute the only

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* The formation of acetobenzylamide (68% yield, calculated on the sodium acetamide present) was unexpected, since Titherley (J., 1901, **79**, 391) states that substituted amides are not formed by the action of alkyl halides on sodium acetamide. We are investigating this reaction further.

evidence available at present in favour of the structure assigned to it by Scheibler. Since keten acetal is produced in so small a yield and the " final product " is never approximately homogeneous, the formation of the acetal may be the result of a secondary reaction. We have not made investigations in this region because Scheibler (*Annalen*, 1925, **445**, 150, footnote) is investigating the keten acetals. We find that ethyl sodioacetoacetate reacts with benzaldehyde with considerable violence, and this reaction will be discussed in a subsequent communication.

EXPERIMENTAL.

The ethyl acetate employed was purified first by Roberts's modification (*J. Soc. Chem. Ind.*, 1924, **43**, 296T) of Wade's method (J., 1905, **87**, 1656) and finally by digestion with phosphorus pentoxide (Perkin, J., 1884, **45**, 491; Inglis and Knight, P., 1907, **23**, 198). It boiled at 76·7—77·2°/760 mm. The ether employed in the preparation of the " final product " was carefully freed from alcohol and moisture, and all the reagents were dried before use. Precautions were taken in all the experiments to prevent the absorption of moisture.

Preparation of the " Final Product " from Sodamide.—The prescriptions of Scheibler and Ziegner (*Ber.*, 1922, **55**, 801) were followed exactly and 65 g. and 73 g. of the dry product were obtained from portions of 150 g. of ethyl acetate. Small portions of the product were extracted with ether (in an atmosphere of dry hydrogen) to remove traces of acetamide, and the residue was freed from ether at 40° in a vacuum [Found: Na, 22·7, 21·5; N, 41·4, 31·4 in the respective preparations. Calc. for $CH_3\cdot CO\cdot CH_2\cdot C(ONa)(OEt)_2$: Na, 11·6%. Calc. for $CH_3\cdot C(ONa){:}CH\cdot CO_2Et$: Na, 15·1%].

Action of Heat upon the " Final Product " obtained by the Action of Sodium.—When the dry " final product " (100 g.) was heated, a liquid began to distil at about 130° and the residue became dark brown. The decomposition appeared to be complete at about 190° and the distillate (20 g.) on fractionation yielded ethyl acetate, alcohol, and a trace of acetone. It did not immediately decolorise dilute alkaline permanganate, so that keten acetal was probably absent (compare Scheibler and Ziegner, *loc. cit.*).

Condensation of Benzyl Chloride with the " Final Product " prepared from Sodium.—The " final product " (67 g.) was heated at 200° with benzyl chloride (150 g.: 77·5 g. in excess of the amount equivalent to the sodium present) until the mixture was no longer alkaline (7·5 hours). Sodium chloride was removed from the dark red liquid and was washed with purified ether, the washings being added to the red liquid. The ether was removed on the water-bath and the residue yielded the following initial fractions when distilled at 15 mm.: (1) 70—90° (60 g.), (2) 90—100° (14 g.), (3) 100—120° (20 g.), (4) 120—127° (12 g., partly solid), (5) 127—190° (29·5 g., mostly solid), (6) 190—197° (13 g.), (7) 197—240° (7 g.), (8) residue (2—3 g., mainly sodium chloride). Systematic refractionation and purification yielded benzyl chloride, benzyl acetate (21 g. Equiv. by saponification, 147·9. Calc., 150), acetamide, acetobenzylamide (m. p. 60—60·5°; identified by conversion into benzylamine hydrochloride, m. p. 248°), and αα-dibenzylacetoacetic ester (0·8 g.; identified by conversion into dibenzylacetic acid, m. p. 89·5—90°). No α-benzylacetoacetic ester was isolated and none of the fractions gave a coloration with ferric chloride solution.

Condensations with the " Final Product " prepared from Sodium.—(1) *With ethyl iodide.* Ethyl iodide (b. p. 71·3—72·3°; 200 g.) was heated on the water-bath with the dry " final product " (181 g.) until the mixture was no longer alkaline (9 hours). The sodium iodide was filtered off and extracted with purified ether, the extract being added to the filtrate. Systematic fractionation of the product yielded ethyl iodide (11 g.), ethyl acetate (19 g.), and ethyl ethylacetoacetate (96 g.). Sodium iodide and a viscous oil remained in the distilling flask, but no diethylacetoacetic ester could be isolated from it by extraction with ether and subsequent distillation.

(2) *With benzyl chloride.* The " final product " (135 g.) was condensed with benzyl chloride (177·5 g.: 40 g. in excess of the amount equivalent to the sodium present) under the conditions previously described and the product was worked up in the same way. The initial fractions obtained at 15 mm. were: (1) 78—85° (45·5 g.), (2) 85—130° (32 g.), (3) 130—175° (64 g.), (4) 175—220° (12 g.), (5) 220—240° (35·5 g.), (6) residue (2—3 g.). Systematic refractionation yielded benzyl chloride, benzyl acetate (b. p. 101—105°/15 mm. Equiv. by saponification, 168. Calc., 150. Identified by saponification to benzyl alcohol and oxidation to benzoic acid), α-benzylacetoacetic ester (b. p. 165·2°/15 mm.), and αα-dibenzylacetoacetic ester (m. p. 56°).

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