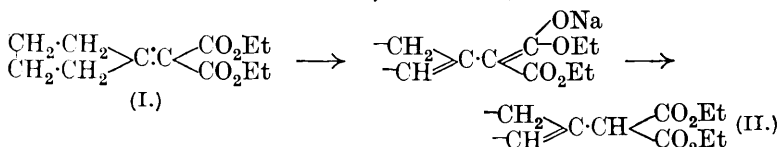


CV.—*The Chemistry of the Three-carbon System. Part XXIV. The Regeneration of Esters from their Sodio-derivatives.*

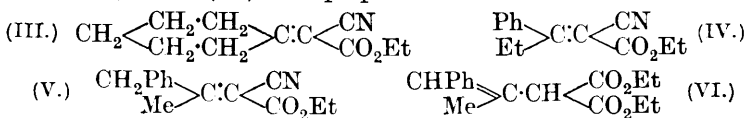
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It has already been suggested that the function of activating groups in enhancing the mobility of a three-carbon system is connected with the capacity of the mobile hydrogen to enter such groups (compare Kon and Speight, J., 1926, 2727). For instance, the rapid interconversion of $\alpha\beta$ - and $\beta\gamma$ -unsaturated ketones in presence of sodium ethoxide is no doubt due to the formation of the sodio-derivatives of the enolic form of the ketone; or, in terms of the ionic hypothesis of tautomerism, the change proceeds through the establishment of an equilibrium between the ions of the two keto-forms and the common enol ion (Ingold, Shoppee, and Thorpe, J., 1926, 2477; Linstead, J., 1929, 2498). There are thus two equilibria—one involving only the keto-enol system of the activating group, the other the three-carbon system as well.

One of the chief differences between keto-enol and three-carbon systems is the greater mobility of the former; it should, therefore, be possible to realise conditions under which only the keto-enol change can proceed to completion, without causing mobility of the adjacent three-carbon system and thus giving rise to a "false equilibrium." This would be expected in systems sufficiently acidic to form stable enols and in the absence of polar catalysts. For instance, if the $\alpha\beta$ -unsaturated ethyl *cyclopentylidenemalonate* (I) were converted into the sodio-derivative, which is necessarily derived from the $\beta\gamma$ -form, and hydrogen could be introduced in place of sodium under conditions precluding complete equilibration, the enol produced should be converted into its own keto-form, which is the hitherto unknown $\beta\gamma$ -isomeride (II).



The ester (I) and ethyl α -cyanocyclohexylideneacetate (III) were chosen for the investigation; in addition, *ethyl α -cyano- β -ethylcinnamate* (IV) and *ethyl α -cyano- and α -carbethoxy- γ -phenyl- β -methylbutenoates* (V) and (VI) were prepared:



Although the results so far obtained are of a preliminary character, they show that it is possible to arrest three-carbon tautomerism to some extent whilst allowing keto-enol equilibrium to be established in the manner suggested. The method adopted consists in forming the sodio-derivative of the ester, preferably in a neutral solvent, and decomposing it by the addition of a weak organic acid such as benzoic acid, at a low temperature; after removal of the sodium benzoate, the ester is isolated by evaporation of the solvent, somewhat on the lines of Knorr's classical work on ethyl acetoacetate.

Negative results were always obtained with the cyano-ester (III), but the ester (I) gave definite indications of a change. The ester obtained from the sodio-derivative not only had a lower boiling point, density, and refractive index, but showed a considerable increase in additive power towards iodine chloride: all these properties are consistent with the $\beta\gamma$ -unsaturated structure. Oxidation with ozone led to a substance having the properties both of an aldehyde and of a β -ketonic ester, as would be expected from such a structure.

Even careful hydrolysis of the new ester gave the original acid and no isomeride has yet been obtained.

Although esterification of the pure acid by way of its silver salt (Kon and Speight, *loc. cit.*) leads to the pure $\alpha\beta$ -ester (I), esterification in presence of a strong mineral acid gives an ester containing a considerable quantity of the $\beta\gamma$ -form, in some cases as much as is present in the ester prepared by regeneration from the sodio-derivative. The esters obtained by different processes differ considerably in properties; that obtained by the direct condensation of *cyclopentanone* with ethyl malonate is mainly the $\alpha\beta$ -ester, whereas acidification of the sodio-derivative in alcoholic solution without special precautions yields an ester containing a considerable proportion of the $\beta\gamma$ -form: this "equilibrium ester" appears to have a fairly constant composition; it is difficult to estimate the proportion of the two isomerides in it by the iodometric method, as the pure $\beta\gamma$ -ester has in all probability not been obtained.

It was hoped to gain a means of comparison by determining the iodine addition of the pure $\beta\gamma$ -ester of the *cyclohexane* series (ethyl *cyclohexenylmalonate*). This ester was prepared by the silver-salt process from the pure acid, which had a very high affinity for iodine (91.4%), in contrast with that of the *cyclopentane* acid (0.35%); but the ester had a low iodine value and therefore was valueless for our purpose.

Cyano-esters with a phenyl group in the β - and especially in the γ -position appeared likely to pass readily into the $\beta\gamma$ -forms (compare Linstead and Williams, J., 1926, 2735; Johnson and Kon,

ibid., p. 2748), and for this reason the esters (IV) and (V) were synthesised: they were found to have the $\alpha\beta$ -unsaturated structure, unlike Linstead and Williams's cyano-ester, but although they yielded $\beta\gamma$ -unsaturated alkylation products, the $\beta\gamma$ -isomerides could not be obtained from them. The condensation product of benzyl methyl ketone and ethyl malonate was abnormal in structure, and the *acid* obtained from it on hydrolysis had lost the elements of water (compare Linstead and Williams, *loc. cit.*); in addition, the double bond was already in the $\beta\gamma$ -position, because the acid yielded benzaldehyde on oxidation: it has not yet been fully investigated.

EXPERIMENTAL.

Ethyl α -Cyanocyclohexylideneacetate (III).—The ester was prepared by the method of Harding, Haworth, and Perkin (J., 1908, 93, 1949) and had the properties recorded by Birch, Kon, and Norris (J., 1923, 123, 1361): the value 53.94 given there for $[R_L]_D$ is a misprint for 53.594.

The $\alpha\beta$ -structure of the ester was confirmed by oxidation: 5 g. of the ester were treated with the required amount of ice-cold neutral 3% aqueous potassium permanganate and the solution was kept for an hour; cyclohexanone, isolated by steam-distillation and extraction with ether, was identified in the form of semicarbazone (m. p. and mixed m. p. 165—166°).

The ester (1/10 g.-mol.) was slowly added to 2.3 g. of "molecular" sodium covered with dry ether. The reaction was vigorous, but it was difficult to induce all the sodium to react. Finally, light petroleum was added and the precipitated sodio-derivative was collected rapidly, suspended in dry ether, and treated with 1/10 mol. of benzoic acid in dry ether. When the yellow colour had disappeared, the ethereal solution was washed with aqueous sodium carbonate and with water, dried over calcium chloride, and evaporated, finally in a vacuum. The properties of the ester obtained, $d_4^{16.8}$ 1.0616, $n_D^{16.8}$ 1.48327, changed but little after distillation (b. p. 160—164°/18 mm.). In another experiment the preparation of the sodio-derivative was carried out in benzene solution, which was preferable to ether, with a similar result. In a third experiment the regeneration was carried out at -20° by means of dry hydrogen chloride or by means of less than the calculated amount of glacial acetic acid (containing a little acetic anhydride to ensure the absence of water) and the washing was omitted. In all cases the ester had the same iodine addition (about 5% in one hour) as that of the pure $\alpha\beta$ -ester, and this did not change on treatment with sodium ethoxide. The change in physical properties was therefore clearly due to a certain amount of reduction of the cyano-ester during the formation

of the sodio-derivative. In order to obviate this, sodium ethoxide, freed from excess of alcohol, was used to form the sodio-derivative, which was then precipitated with a large volume of light petroleum and treated with benzoic acid; no indication of the existence of a β -ester was obtained.

Ethyl cyclopentylidenemalonate (I).—The ester was prepared by the method of Kon and Speight (*loc. cit.*), but it was found convenient to modify the process of isolation as follows. The almost black reaction product of cyclopentanone and ethyl malonate was mixed with 3—4 volumes of light petroleum and well shaken; the acetanilide and the tarry matter formed were precipitated and the very troublesome and wasteful process of washing was thus obviated. The almost clear petroleum solution was filtered, washed with water and alkali, and dried; on evaporation it gave a fair yield of the required ester, d_4^{25} 1.0613, n_D^{25} 1.4696, iodine addition in 1 hour (in chloroform solution by the method of Linstead and May; *J.*, 1927, 2565) 11.1%.

The ester on hydrolysis gave the acid already described by Kon and Speight; the iodine addition of the pure acid in sodium bicarbonate solution was only 0.35% in 1 hour. This was esterified through the silver salt and the ester produced had b. p. 160°/20 mm., d_4^{25} 1.0618, n_D^{25} 1.47301, $[R_L]_D$ 59.75 (compare Kon and Speight, *loc. cit.*), iodine addition in 1 hour 1.5%.

The first experiments on the regeneration of the ester from its sodio-derivative were carried out with "molecular" sodium in benzene in the manner described on p. 777; a definite indication of change was obtained. In later experiments, sodium ethoxide was prepared from specially dehydrated alcohol, the excess of alcohol carefully removed in a vacuum at 100°, and the ester added together with some petroleum (b. p. 40—60°); when the sodio-derivatives had formed, more petroleum was added and the solid allowed to settle. The petroleum solution was decanted, the residue again washed with petroleum (the sodio-derivative can also be filtered off), and benzoic acid in dry ether added to the sodio-derivative with shaking, more petroleum then being added. The gelatinous sodium benzoate was filtered off, and the petroleum solution washed with dilute aqueous sodium carbonate, washed, dried, and evaporated. The ester, obtained in 30—50% yield, varied but little in properties; the best specimen had b. p. 147—148°/19 mm., d_4^{25} 1.0511, n_D^{25} 1.45743, $[R_L]_D$ 58.37 (calc., 58.02), and an iodine addition of 38.4%; it consisted, therefore, mainly of *ethyl* Δ^1 -cyclopentenylmalonate (II) (Found: C, 64.0; H, 8.0. $C_{12}H_{18}O_4$ requires C, 63.7; H, 8.0%). The molecular refraction shows an exaltation of only 0.35 unit (comparable with that found by Kon and Speight

for the α -methyl derivative and for cyclohexenylmalonic ester), due, no doubt, to the conjugation of the two carbethoxy-groups. The ester did not give a colour with ferric chloride.

The petroleum solution decanted from the sodio-derivative was acidified with hydrochloric acid, washed with sodium carbonate solution, and evaporated, yielding a further quantity of ester; this had a lower iodine addition—about 30%—and presumably was the “equilibrium ester.”

A specimen of the $\beta\gamma$ -ester, prepared by direct esterification as described below, was treated with alcoholic sodium ethoxide, and the product isolated without special precautions; it had b. p. 142—150°/20 mm., d_4^{21} 1.0551, n_D^{21} 1.46191, $[R_L]_D$ 58.91, and an iodine addition of 28.0%, and was thus very similar to the preceding ester.

When sodium methoxide was used in place of the ethoxide in the above preparation, the product obtained was *methyl ethyl cyclopentenylmalonate*; after redistillation it boiled at 137—138°/18 mm. and had d_4^{21} 1.09776, n_D^{21} 1.46380, iodine addition about 37% (Found: C, 62.0; H, 7.3. $C_{11}H_{16}O_4$ requires C, 62.2; H, 7.6%).

The $\beta\gamma$ -ester was also produced when the solid $\alpha\beta$ -acid was kept in contact with 1% alcoholic hydrogen chloride (8 vols.) at room temperature; the acid slowly dissolved in the course of 10 days and the ester was then isolated and the considerable unesterified portion again treated with alcoholic hydrogen chloride. The ester had b. p. 146—148°/20 mm., d_4^{22} 1.0546, n_D^{22} 1.45923, $[R_L]_D$ 58.65; the iodine addition was 37.5%, so the ester was evidently mainly the $\beta\gamma$ -form. In another instance, the acid was boiled with a saturated solution of hydrogen chloride in absolute alcohol for a short time; the ester produced was mainly the $\alpha\beta$ -form.

The $\beta\gamma$ -ester, dissolved in ethyl acetate, was treated with ozonised oxygen at 0°, the ozonide was freed from the solvent and decomposed by warm water, and the product isolated by means of ether and distilled. Much decomposition (elimination of alcohol?) took place and a definite fraction was not obtained, the greater part boiling between 140° and 150°/11 mm. This gave an intense blue colour, slowly changing to red, with ferric chloride, and Schiff's test, and was thus an aldehyde and a β -ketonic ester, presumably $CHO \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH(CO_2Et)_2$; the carbon content, however, agrees better with the formula $CHO \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_2 \cdot CO_2Et$ (Found: C, 59.1; H, 7.2. $C_9H_{14}O_4$ requires C, 58.0; H, 7.6%); crystalline derivatives could not be obtained from it.

The $\beta\gamma$ -ester was hydrolysed by means of cold 5% alcoholic sodium hydroxide, and the acid isolated in the usual manner. The

$\alpha\beta$ -acid, m. p. 171° , was isolated in quantity; a more soluble constituent was also present, but it could not be obtained pure. An attempt to prepare the pure $\beta\gamma$ -ester by partial esterification of the crude acid obtained above (compare Eccott and Linstead, J., 1929, 2153) was unsuccessful; the ester produced had a slightly lower iodine addition than the specimen from which it was derived.

Ethyl cycloHexenylmalonate.—The pure acid, m. p. 150° (Kon and Speight), was found to have an iodine addition of 91.4% in 1 hour. It was esterified through the silver salt, giving an ester, b. p. $160^\circ/20$ mm., $d_4^{20.9}$ 1.0504, $n_D^{20.9}$ 1.4646, iodine addition 7.5%. Another specimen of the ester was separated into two portions by distillation, but both had practically identical properties and iodine additions (7.4 and 8.1%). After treatment of the ester with sodium ethoxide without special precautions, the iodine addition rose somewhat (9.6%). The ozonisation of the ester was repeated, Kon and Speight's results being confirmed.

Ethyl α -Cyano- β -ethylcinnamate (IV).—Ethyl cyanoacetate (57 g.) and propiophenone (67 g.) were mixed with 1 c.c. of piperidine and heated on the steam-bath for 3 days. The product was dissolved in ether, washed with dilute hydrochloric acid and with water, dried, and distilled. Most of the initial material was recovered, but some 12 g. of an oil, b. p. 182 — $188^\circ/17$ mm., were collected. The yield of this oil could be increased to about 28 g. by adding anhydrous sodium sulphate to the reaction mixture to facilitate the separation of the water formed in the reaction. Condensation also took place in the presence of sodium ethoxide in alcohol (11.5 g. of sodium in 150 c.c. of alcohol), the mixture being heated until the whole of the solid ethyl sodiocyanoacetate had disappeared (about 2 hours); the yield of high fraction contained in the neutral reaction product was about 20 g. The recovered material could be used again. The fraction of b. p. 182 — $188^\circ/17$ mm. gave on careful redistillation a large fraction, b. p. $185^\circ/15$ mm., consisting of *ethyl α -cyano- β -ethylcinnamate*, $d_4^{19.8}$ 1.0695, $n_D^{19.8}$ 1.53803, $[R_L]_D$ 67.01 (calc., 64.26) (Found: C, 73.2; H, 6.5. $C_{14}H_{15}O_2N$ requires C, 73.4; H, 6.6%). The structure of the ester was confirmed by oxidation with permanganate exactly as described on p. 777; propiophenone was obtained in good yield and identified in the form of its semicarbazone.

All attempts to obtain the $\beta\gamma$ -isomeride from the sodio-derivative were unsuccessful.

The ester was readily ethylated through its sodio-derivative, prepared with the aid of "molecular" sodium in benzene. The new ester, *ethyl α -cyano- β -phenyl- α -ethyl- Δ^{β} -pentenoate*,



had b. p. 182—186°/16 mm., $d_4^{17.2}$ 1.0545, $n_D^{17.2}$ 1.52175, $[R_L]_D$ 74.33 (calc., 73.50) (Found: C, 74.9; H, 7.3. $C_{16}H_{19}O_2N$ requires C, 74.7; H, 7.4%). Like other similar compounds, the ethylated cyano-ester readily lost carbethoxyl in the form of ethyl carbonate on being kept with an equivalent of sodium ethoxide at 35° for 24 hours, giving β -phenyl- α -ethyl- Δ^{α} -pentenonitrile, b. p. 142—146°/14 mm., $d_4^{19.0}$ 0.9856, $n_D^{19.0}$ 1.54052, $[R_L]_D$ 58.97 (calc., 57.98) (Found: C, 83.6; H, 7.7. $C_{13}H_{15}N$ requires C, 84.3; H, 8.2%).

Attempted Condensation of Propiophenone and Ethyl Malonate.—It was not found possible to obtain a condensation product from these substances under any of the conditions tried.

Ethyl α -Cyano- γ -phenyl- β -methyl- Δ^{α} -butenoate (V).—Benzyl methyl ketone (134 g.), ethyl cyanoacetate (113 g.), and piperidine (2.5 c.c.) were kept at room temperature for 3 days with occasional shaking. Water began to separate after about 3 hours. The mixture was worked up as described on p. 780, and the product distilled under reduced pressure; after unchanged materials had passed over, an oil was obtained which on redistillation gave 46 g. of the ester (V): a small quantity was also obtained from the lower fractions, and there was hardly any high-boiling fraction. The ester had b. p. 182—184°/11 mm., $d_4^{19.0}$ 1.0790, $n_D^{19.0}$ 1.53401, $[R_L]_D$ 66.00 (calc., 64.26) (Found: C, 73.5; H, 6.6. $C_{14}H_{15}O_2N$ requires C, 73.4; H, 6.6%). It gave benzyl methyl ketone in good yield (semicarbazone, m. p. 189—190°) on oxidation with neutral permanganate, its structure thus being confirmed.

Attempts to obtain the $\beta\gamma$ -isomeride were unsuccessful. From the sodio-derivative prepared with the aid of sodium ethoxide by the method described on p. 778, the ester was regenerated unchanged, the iodine addition being the same before and after the experiment (3.8% in 1 hour). When "molecular" sodium was used, some change in the physical properties of the ester took place, but this was due to reduction; no rise in iodine addition was observed.

The ester was ethylated as described on p. 780. The product did not boil uniformly, doubtless owing to the presence of a small amount of reduced material, but a considerable fraction, b. p. 190—192°/13 mm., was obtained consisting of ethyl α -cyano- γ -phenyl- β -methyl- α -ethyl- Δ^{β} -butenoate, $d_4^{18.2}$ 1.0452, $n_D^{18.2}$ 1.51986, $[R_L]_D$ 74.76 (calc., 74.50) (Found: C, 74.4; H, 7.4. $C_{16}H_{19}O_2N$ requires C, 74.7; H, 7.4%). When this ester was treated with sodium ethoxide, ethyl carbonate and γ -phenyl- β -methyl- α -ethyl- Δ^{α} -butenonitrile, $CH_2Ph.CMe.CEt.CN$, were produced. The latter on redistillation boiled at 159—161°/16 mm. and had $d_4^{18.4}$ 0.97806, $n_D^{18.4}$ 1.52469, $[R_L]_D$ 57.97 (calc., 57.98) (Found: C, 83.9; H, 8.3. $C_{13}H_{15}N$ requires C, 84.3; H, 8.2%).

Condensation of Benzyl Methyl Ketone with Ethyl Malonate.—The condensation was carried out by the method of Kon and Speight (*loc. cit.*). From 1 g.-mol. of the ketone, about 10 g. of a fraction, b. p. 180—188°/14 mm., presumably consisting of the ester (VI), were obtained. On hydrolysis with alkali, the ester gave an acid, $C_{12}H_{10}O_3$ (Found: C, 71.4; H, 5.1. *M*, by titration, 196.5. $C_{12}H_{10}O_3$ requires C, 71.3; H, 5.0%; *M*, 202. $C_{12}H_{12}O_4$ requires C, 65.5; H, 5.4%). On oxidation with alkaline permanganate the acid yielded benzaldehyde, which was identified by means of its semicarbazone.

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