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# XVI.—o-*Nitrobenzoylacetic Acid.*

By Edward Rushton Needham and William Henry Perkin, jun.

In the year 1881 (*Ber.*, **14**, 1742), Baeyer showed that, when ethyl *o*-nitrophenylpropiolate is treated with sulphuric acid and the product poured into water, ethyl isatogenate is formed, and in explaining this remarkable process, he assumed that intramolecular change took place according to the scheme

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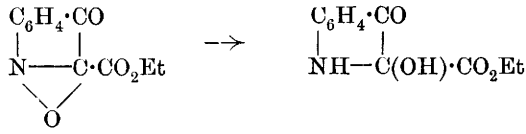
At a later date (*Ber.*, 1882, **15**, 780) the same author, having discovered the reduction of ethyl isatogenate to ethyl indoxanthinate, explained this reaction by modifying the formula of the former ester and represented its relationship to the latter thus:

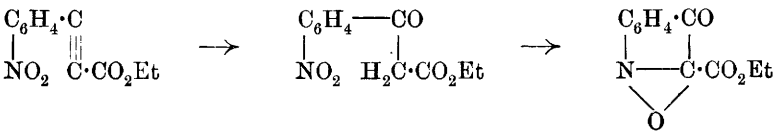


Ethyl isatogenate. Ethyl indoxanthinate.

Subsequently he published a preliminary notice on benzoylacetic acid (*Ber.*, 1882, **15**, 2705) showing that its ethyl ester is produced when ethyl phenylpropiolate is dissolved in sulphuric acid and the product poured on to ice.

As far as we know, no explanation of the remarkable intramolecular change from ethyl *o*-nitrophenylpropiolate to ethyl isatogenate has ever been published, but the following series of changes has always appeared to one of us to be a possible explanation.

Just as ethyl phenylpropiolate when acted on by sulphuric acid takes up the elements of water yielding ethyl benzoylacetate, so in the case of ethyl *o*-nitrophenylpropiolate the first product of the reaction is probably ethyl *o*-nitrobenzoylacetate, which is then converted into ethyl isatogenate by an internal condensation brought about by the excess of sulphuric acid present:



During the course of a long series of researches on ethyl benzoylacetate, carried out some years ago, many attempts were made to prepare ethyl *o*-nitrobenzoylacetate, not only with the object of testing the above view of the mechanism of the formation of ethyl isatogenate, but also on account of the close relationship which exists between ethyl *o*-nitrobenzoylacetate and many members of the indigo group. The attempts were, however, all unsuccessful at the time.

In 1896 (*Annalen*, **291**, 67) Claisen described a very convenient method for preparing ethyl benzoylacetate, which consists in acting on two molecules of ethyl sodioacetoacetate with benzoyl chloride and then decomposing the sodium compound of ethyl benzoylacetoacetate thus produced by boiling with ammonia and ammonium chloride:

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$$2CH_3\cdot CO\cdot CHNa\cdot CO_2Et + C_6H_5\cdot COCl = \begin{matrix} C_6H_5\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!CNa\cdot CO_2Et + CH_3\cdot CO\cdot CH_2\cdot CO_2Et + NaCl$$

$$\begin{matrix} C_6H_5\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!CNa\cdot CO_2Et + H_2O = C_6H_5\cdot CO\cdot CH_2\cdot CO_2Et + CH_3\cdot CO_2Na.$$

This process gives an excellent yield, and is not only much simpler than the preparation from ethyl phenylpropiolate and sulphuric acid, but is also to be preferred to the earlier method of Claisen and Lowman (*Ber.*, 1887, **20**, 653) which consists in acting on a mixture of ethyl benzoate and ethyl acetate with sodium.

After experimenting with Claisen's process with very satisfactory results, we endeavoured to prepare ethyl *o*-nitrobenzoylacetate by a similar series of reactions, and were ultimately successful. When the ethyl sodioacetoacetate is treated with *o*-nitrobenzoyl chloride under the conditions described in the experimental part of this paper, the sodium compound of ethyl *o*-nitrobenzoylacetoacetate,

$$\begin{matrix} NO_2\cdot C_6H_4\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!CNa\cdot CO_2Et,$$

is produced, and, when this is decomposed with hydrochloric acid, a red oil is obtained, which consists of nearly pure ethyl *o*-nitrobenzoylacetoacetate,

$$\begin{matrix} NO_2\cdot C_6H_4\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!CH\cdot CO_2Et.$$

This substance is not new, but has already been prepared by Gevekoht (*Annalen*, 1883, **221**, 323), who proved its constitution by showing that, when boiled with dilute sulphuric acid, it yields *o*-nitroacetophenone, $NO_2\cdot C_6H_4\cdot CO\cdot CH_3$. When the sodium compound of ethyl *o*-nitrobenzoylacetoacetate is digested with ammonia and ammonium chloride, it is decomposed with the elimination of the acetyl group, and a red oil is produced which is crude *ethyl o-nitrobenzoylacetate*,

$$NO_2\cdot C_6H_4\cdot CO\cdot CH_2\cdot CO_2Et.$$

This is readily purified by conversion into the green, crystalline, copper compound, $NO_2\cdot C_6H_4\cdot CO\cdot CHCu\cdot CO_2Et$, and is thus obtained as a pale reddish-brown oil, which in its properties closely resembles ethyl benzoylacetate.

Experiments were next made on the action of concentrated sulphuric acid on ethyl *o*-nitrobenzoylacetate in the expectation that ethyl isatogenate would result, but we found, to our surprise, that the sulphuric acid had simply acted as a hydrolysing agent, and that the product of the action was *o-nitrobenzoylacetic acid*,

$$NO_2\cdot C_6H_4\cdot CO\cdot CH_2\cdot CO_2H.$$

Even when the ester was heated with sulphuric acid at 90°, large

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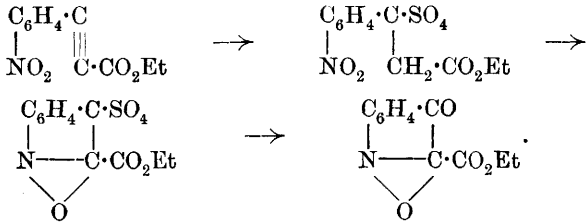
quantities of *o*-nitrobenzoylacetic acid were formed, showing clearly that under these conditions there is no tendency for internal condensation to take place between the nitro-group and the methylene radicle.

The experiments described in this paper clearly prove that ethyl *o*-nitrobenzoylacetate is not an intermediate step in the conversion of ethyl *o*-nitrophenylpropiolate into ethyl isatogenate, and the problem of the mechanism of this remarkable reaction therefore remains unsolved.

In this conversion of ethyl *o*-nitrophenylpropiolate into ethyl isatogenate, it is possible that an additive compound with sulphuric acid may first be formed, this substance then undergoing internal condensation to yield a product, which, when decomposed with water, gives rise to ethyl isatogenate:



*Preparation of Ethyl* o-*Nitrobenzoylacetoacetate*,

$$NO_2\cdot C_6H_4\cdot CO\cdot \underset{\displaystyle CH_3\cdot CO}{\overset{\displaystyle |}{C}}H\cdot CO_2Et$$

In preparing considerable quantities of this ester, we used a process based on the conditions recommended by Claisen (*Annalen*, 1896, **291**, 67) for the preparation of ethyl benzoylacetate, and which differs in many respects from that described by Gevekoht (*Annalen*, 1883, **221**, 323). *o*-Nitrobenzoic acid (100 grams) contained in a fractionating flask is gradually mixed with phosphorus pentachloride (135 grams), and as soon as the reaction, which commences in the cold, has slackened, the whole is heated on the water-bath until the crystals of the acid have entirely dissolved. The flask is then connected with the vacuum apparatus, and the phosphorus oxychloride distilled off at the lowest possible temperature. Sodium (31 grams) is now dissolved in 400 grams of absolute alcohol, and the solution made up to 500 c.c. by the addition of more alcohol. Pure ethyl acetoacetate (90 grams) is mixed with 250 c.c. of the sodium ethoxide solution, the whole cooled to 0°, and 56 grams of the *o*-nitrobenzoyl chloride added in small quantities at a time and with frequent shaking, care being taken that the temperature does not rise above 5°. After half an hour, 125 c.c. of the sodium ethoxide solution are added, and, after

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thoroughly mixing, 28 grams of the acid chloride run in under the same conditions as before, then the whole is again left for half an hour and treated with the rest of the sodium ethoxide and *o*-nitrobenzoyl chloride. After remaining overnight at the ordinary temperature, the thick, yellow precipitate, which consists of the sodium compound of ethyl *o*-nitrobenzoylacetoacetate mixed with sodium chloride, is collected at the pump, and washed first with alcohol, and then with ether. It is then added to excess of dilute hydrochloric acid, cooled by the addition of powdered ice, and the whole shaken thoroughly with ether. The ethereal solution is washed with dilute aqueous sodium hydrogen carbonate, dried over calcium chloride, and evaporated, when a brownish-red oil is obtained which consists of nearly pure *ethyl* o-*nitrobenzoylacetoacetate*.

0·1696 gave 8·0 c.c. of nitrogen at 20° and 750 mm. N = 5·3.
$C_{13}H_{13}O_6N$ requires N = 5·0 per cent.

Ethyl *o*-nitrobenzoylacetoacetate is a reddish-brown oil which gives a reddish-violet coloration when its solution in alcohol is mixed with ferric chloride. It dissolves in dilute aqueous caustic potash, and on adding a concentrated solution of this reagent a crystalline potassium compound, $C_{13}H_{12}O_6NK$, separates (compare Gevekoht, *loc. cit.*).

*Ethyl* o-*Nitrobenzoylacetate*, $NO_2 \cdot C_6H_4 \cdot CO \cdot CH_2 \cdot CO_2Et$.

In the preparation of ethyl *o*-nitrobenzoylacetate from ethyl *o*-nitrobenzoylacetoacetate, a method similar to that employed by Claisen (*loc. cit.*) in analogous cases, was adopted.

The crude sodium compound of ethyl *o*-nitrobenzoylacetoacetate, in quantities of 100 grams, was mixed with a solution of ammonium chloride (25 grams) in water (500 c.c.); 10 c.c. of concentrated aqueous ammonia, diluted with 90 c.c. of water, were then added, and the mass vigorously stirred with a turbine. As soon as the sodium compound had completely dissolved, the whole was mixed with powdered ice, acidified with hydrochloric acid, and at once extracted with ether. After washing with water, drying over anhydrous sodium sulphate and evaporating, crude ethyl *o*-nitrobenzoylacetate remains as a brown oil, the yield being about 50 grams. This ester was purified in the following way. A solution of the blue cuprammonium compound, prepared by adding ammonia in slight excess to copper sulphate, was placed in a strong bottle, mixed with the crude ethyl *o*-nitrobenzoylacetate dissolved in ten times its volume of ether, and vigorously shaken on the machine for 6 hours; the deep green copper compound, which had separated, was collected and washed, first with water and then with ether After drying in a vacuum desiccator, the copper compound was

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rapidly dissolved in excess of boiling toluene, from which it separates usually as a green powder, but if the crystallisation takes place very slowly and from dilute solutions, the substance is sometimes obtained in the form of definite violet crystals. When heated, this compound explodes with the formation of a thick, brown smoke, a behaviour which rendered its analysis very difficult. Ultimately the substance was first decomposed by gently warming with concentrated sulphuric acid, and, after driving off the excess of sulphuric acid, the residue was heated over the blowpipe, but, even in this way, a slight loss was unavoidable.

0·3050 gave 0·0406 CuO. Cu = 10·7.
0·4172 ,, 0·0568 CuO. Cu = 11·0.
$NO_2 \cdot C_6H_4 \cdot CO \cdot CHCu_{\frac{1}{2}} \cdot CO_2Et$ requires Cu = 11·8 per cent.

In order to obtain pure ethyl *o*-nitrobenzoylacetate, the copper compound was ground to a fine paste with water, mixed with powdered ice, and decomposed by shaking with dilute hydrochloric acid and ether. The ethereal solution was washed thoroughly with water and dilute aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulphate, evaporated, and the residual light brown oil left in a vacuum desiccator over sulphuric acid for two days.

0·1481 gave 0·3034 $CO_2$ and 0·0641 $H_2O$. C = 55·8; H = 4·8.
0·2459 ,, 12·2 c.c. of nitrogen at 17° and 754 mm. N = 5·9.
$C_{11}H_{11}O_5N$ requires C = 55·7; H = 4·6; N = 5·9 per cent.

*Ethyl* o-*nitrobenzoylacetate* has, so far, not been obtained in a crystalline condition; when cooled to −10°, it solidifies to a transparent resin which does not crystallise on rubbing. The alcoholic solution gives, with ferric chloride, an intense orange-red coloration which has a much yellower tint than that shown by either ethyl *p*- or *m*-nitrobenzoylacetate. It dissolves readily and completely in dilute caustic potash solution, forming an intense yellow solution, and is reprecipitated on the addition of acids, but if the yellow solution is mixed with concentrated aqueous caustic potash, a deep yellow, viscid oil separates, which when stirred vigorously, solidifies to a yellow cake of crystals, consisting of the *potassium* derivative of *ethyl* o-*nitrobenzoylacetate*, $NO_2 \cdot C_6H_4 \cdot CO \cdot CHK \cdot CO_2Et$. This product was drained on porous porcelain, rubbed up with a little water, and again transferred to porous porcelain, and after repeating this process, it was dried at 100° and analysed with the following result:

0·1450 gave 0·0466 $K_2SO_4$. K = 14·4.
$C_{11}H_{10}O_5NK$ requires K = 14·2 per cent.

This potassium compound dissolves readily in water and when

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acidified and extracted with ether, pure ethyl *o*-nitrobenzoylacetate is obtained as an almost colourless oil. When ethyl *o*-nitrobenzoylacetate is dissolved in dilute aqueous caustic soda and a strong solution of caustic soda added, the sodium compound is precipitated, but it is much more soluble than the potassium compound, and was not further investigated. Attempts were made to prepare the pure sodium compound by adding ether to the solution of the ester in the calculated quantity of sodium ethoxide, but no separation took place. If the same experiment is carried out with either ethyl *p*- or *m*-nitrobenzoylacetate, the sodium compound separates at once as a deep yellow, crystalline precipitate.

o-*Nitrobenzoylacetic acid*, $NO_2 \cdot C_6H_4 \cdot CO \cdot CH_2 \cdot CO_2H$.

When ethyl *o*-nitrobenzoylacetate dissolves in concentrated sulphuric acid heat is generated, and the dark brown solution, when left for two or three days and then diluted with powdered ice, yields a brown solid which becomes almost colourless when drained on porous porcelain. The solid residue, which consists of almost pure *o*-nitrobenzoylacetic acid, may be crystallised from water if the operation is rapidly carried out, but otherwise there is a great loss owing to decomposition into *o*-nitroacetophenone and carbon dioxide. The colourless needles thus obtained were dried over sulphuric acid and analysed with the following results:

0·1756 gave 0·3351 $CO_2$ and 0·0575 $H_2O$. C = 52·0; H = 3·4.
0·2274 ,, 13·2 c.c. of nitrogen at 16° and 760 mm. N = 6·7.
$C_9H_7O_5N$ requires C = 51·7. H = 3·3; N = 6·7 per cent.

o-*Nitrobenzoylacetic acid* melts at about 117—120° with vigorous decomposition, evidently yielding carbon dioxide and *o*-nitroacetophenone. It is readily soluble in alcohol and almost insoluble in cold, light petroleum; it dissolves moderately readily in warm benzene, and crystallises on cooling in colourless needles. The alcoholic solution of the pure acid gives a deep red coloration with ferric chloride. The composition of the acid was further controlled by titration, when it was found that 0·177 gram required for neutralisation 0·0335 gram of caustic soda, whereas this amount of a monobasic acid, $C_9H_7O_5N$, should neutralise 0·0339 gram of the alkali.

In order to study the decomposition products of *o*-nitrobenzoylacetic acid, 3 grams of the pure acid were boiled with water, when a brisk effervescence took place, due to the evolution of carbon dioxide, and a heavy oil separated. This was extracted with ether, the ethereal solution washed with dilute aqueous sodium carbonate, dried over calcium chloride and evaporated, when an oil remained which was identified as *o*-nitroacetophenone.

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0·1601 gave 11·9 c.c. of nitrogen at 15° and 745 mm. N = 8·4.

$C_8H_7O_3N$ requires N = 8·5 per cent.

Five grams of pure ethyl *o*-nitrobenzoylacetate were dissolved in 20 c.c. of concentrated sulphuric acid and heated in a water-bath at 90° for 10 minutes. On cooling and diluting with ice, a solid soon separated which consisted of nearly pure *o*-nitrobenzoylacetic acid, and was finally purified in the manner already described.

0·2251 gave 13·1 c.c. of nitrogen at 15° and 750 mm. N = 6·8.

$C_9H_7O_5N$ requires N = 6·7 per cent.

This experiment shows that the ethyl ester when heated with concentrated sulphuric acid is simply hydrolysed without undergoing any internal condensation.

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