1029. *Isatogens. Part I. Base-catalysed Condensation Products of Methyl and Ethyl* o-*Nitrobenzoylacetate and* o-*Nitrobenzoylacetone.*

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When suspended in aqueous sodium hydrogen carbonate at room temperature, methyl and ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone initially underwent self-condensations finally yielding 2-(1-*o*-nitrophenylvinyl)isatogens. 3,5-Di-*o*-nitrophenyl-5-oxopent-2-enoates and 1,3-di-*o*-nitrophenylhex-3-ene-1,5-dione are further products of the reactions of the esters and the ketone, respectively. Piperidine-catalysed condensation of the *o*-nitrobenzoylacetates with esters of isatogenic or *o*-nitrophenylpropiolic acid also gave the pentenoates, and both they and the diketone were converted into the corresponding isatogens on treatment with pyridine.

In the separation of methyl *o*-nitrobenzoylacetate from its precursor, methyl *o*-nitrobenzoylacetoacetate, by the action of carbon dioxide on the potassium derivative of the crude product [1] it was noticed that the mixture became purple when kept for several hours. To investigate this a suspension of methyl *o*-nitrobenzoylacetate in sodium hydrogen carbonate solution was stirred at room temperature for several days. The same colour change was observed and a purple solid slowly separated. Acidification of the purple filtrate gave orange crystals. The same purple and orange compounds were obtained with concentrations of bicarbonate up to 10·0%; they were obtained also when aqueous solutions of the potassium or the ammonium derivative of methyl *o*-nitrobenzoylacetate were stirred, but not from this ester under the influence of sodium hydroxide or carbonate. No deep colours were produced when methyl *o*-nitrobenzoylacetoacetate, diethyl *o*-nitrobenzoylmalonate, methyl α-*o*-nitrobenzoylpropionate, or ω-cyano-2-nitroacetophenone was stirred with sodium hydrogen carbonate solution; but ethyl *o*-nitrobenzoylacetate and *o*-nitrobenzoylacetone both gave purple and orange compounds similar to those derived from the methyl ester.

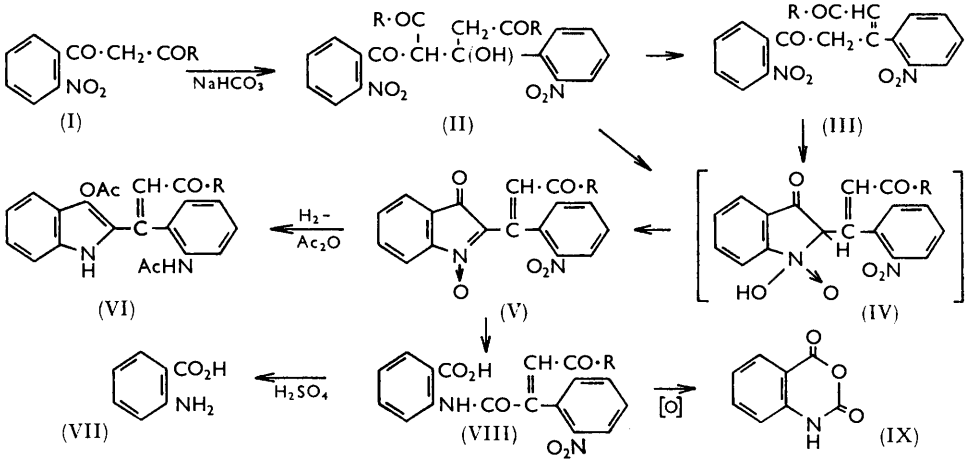
The purple compounds were only sparingly soluble in organic solvents and insoluble in dilute acids; they were soluble in concentrated sulphuric acid and reprecipitated on dilution with water. They were initially insoluble in dilute alkali, but in contact with it all three purple compounds gave the same sequence of colour changes through blue to green, and finally yielded yellow solutions, acidification of which no longer precipitated the purple compounds.

The orange compound from the methyl ester was also isolated as its red piperidinium adduct on reaction of methyl *o*-nitrobenzoylacetate in boiling alcohol, in the presence of piperidine, with methyl or ethyl isatogenate or with methyl or ethyl *o*-nitrophenylpropiolate. None of these reagents gave the red adduct when refluxed with piperidine alone, nor was any such adduct obtained in reactions between methyl *o*-nitrobenzoylacetate and *o*-nitrophenylacetylene or between *o*-nitroacetophenone and methyl isatogenate. The orange compound from the ethyl ester was similarly obtained as its piperidinium adduct by reaction of ethyl *o*-nitrobenzoylacetate with methyl or ethyl isatogenate or with methyl or ethyl *o*-nitrophenylpropiolate. The piperidinium adducts were converted by acid into the orange compounds. The orange compounds were soluble in dilute alkali, giving purple solutions from which they were recovered unchanged on acidification. No purple compounds were isolated on prolonged stirring of the orange compounds with sodium hydrogen carbonate or on treatment with acetic anhydride or sulphuric acid, but this conversion did occur in all three cases when the orange compounds were refluxed in pyridine.

Analyses of the orange compounds indicated in each case the combination of two molecules of the starting material with loss of one methoxycarbonyl, ethoxycarbonyl, or

[1] Coutts, Hooper, and Wibberley, *J.*, 1961, 5058.

acetyl group, and one molecule of water. Analyses of the purple compounds in each case indicated structures containing one molecule of water less than the orange compounds. The expected initial product from the action of aqueous sodium hydrogen carbonate on methyl *o*-nitrobenzoylacetate is the keto-alcohol (II; R = OMe). Hydrolysis of one of the methoxycarbonyl groups followed by decarboxylation and loss of one molecule of water could lead to several structures for the orange compound. We have concluded that the orange compound has structure (III; R = OMe) and that the purple compound has structure (V; R = OMe). The corresponding orange and purple compounds from ethyl *o*-nitrobenzoylacetate have structures (III; R = OEt) and (V; R = OEt), respectively, and those from *o*-nitrobenzoylacetone have structures (III; R = Me) and (V; R = Me).



The infrared spectra of the purple compounds were complex but showed bands in the 1529—1500, 1347—1346, and 863—862 cm.$^{-1}$ regions which could be assigned to the nitro-group or perhaps to the *N*-oxide (cf. Katritzky on spectra of substituted pyridine *N*-oxides [2]), and two bands in the 1724—1684 cm.$^{-1}$ region (carbonyl groups). A band in the 1087—1075 cm.$^{-1}$ region which was also present in methyl isatogenate but absent in the starting materials and orange compounds, and the absence of absorption in the 3600—3000 cm.$^{-1}$ region (OH and NH absent) support the isatogen structure (V). That the purple compounds in fact had this structure was shown by their oxidation, reduction, and hydrolysis. Methyl isatogenate is known [3] to be hydrolysed by alkali to isatin which may be oxidised to, amongst other compounds, isatoic anhydride.[4] We have shown that oxidation of methyl isatogenate with alkaline potassium permanganate yields isatoic anhydride (IX) and that this is also produced, together with *o*-nitrobenzoic acid, by similar oxidation of all three purple compounds. Reduction of 2-pyridylisatogen with zinc and acetic acid in the presence of acetic anhydride yields 3-acetoxy-2-pyridylindole.[5] Analogously the purple compound from *o*-nitrobenzoylacetone yields the indole (VI; R = Me). Heller and Boessneck [6] have shown that methanol and methyl isatogenate in the presence of hydrogen chloride yield an addition product, which loses methanol to re-form the isatogen and is converted by cold sodium hydroxide into *N*-oxalylanthranilic acid. Treatment of an alcoholic suspension of the purple compound (V; R = OMe) with cold sodium hydroxide gave the sequence of colour changes referred to previously, and acidification of the resulting yellow solution liberated a carboxylic acid. If the purple

[2] Katritzky, *Quart. Rev.*, 1959, **13**, 353.
[3] Rodd, " Chemistry of Carbon Compounds," Elsevier, Vol. IV A, p. 90.
[4] Kolbe, *J. prakt. Chem.*, 1884, **30**, 84.
[5] Ruggli and Cuenin, *Helv. Chim. Acta*, 1944, **27**, 649.
[6] Heller and Boessneck, *Ber.*, 1922, **55**, 474.

compound has the isatogen structure (V; R = OMe), then hydrolysis under these conditions, by analogy with the above, could yield the acid (VIII; R = OMe). This structure was supported by the analysis and equivalent weight, and by conversion into anthranilic acid. This material is presumably an intermediate in the permanganate oxidation to isatoic anhydride. A similar acid (VIII; R = Me) was derived by the hydrolysis of 2-(α-acetonylidene-2-nitrobenzyl)isatogen.

The ultraviolet absorption spectra of the orange compounds resembled that of *o*-nitrocinnamic acid, and their infrared spectra showed bands in the 1525—1515, 1355—1345, and 856—855 cm.$^{-1}$ regions (nitro-groups), a band at 1704 cm.$^{-1}$ (carbonyl), and one at 761 cm.$^{-1}$ (*ortho*-disubstituted benzene), but none in the 1087—1075 cm.$^{-1}$ region which had appeared in the purple compounds and methyl isatogenate. The orange colour of this type of compound is to be expected, as is the purple colour of the anion with its increased conjugation. Permanganate oxidation of all three orange compounds yielded *o*-nitrobenzoic acid as the sole isolated product.

Isatogens [7] have been obtained from pyridine or quinoline solutions of several *o*-nitrophenylacetylenes, *o*-nitrostyrenes, and halogenated derivatives thereof by heat or by treatment of their chloroform or benzene solutions with sunlight or nitrosobenzene. The first recorded isatogen, ethyl isatogenate, was isolated by Baeyer [8] by the action of concentrated sulphuric acid on ethyl *o*-nitrophenylpropiolate. There are no references to the preparation of isatogens under conditions such as we have employed, but the formation of indigo by the action of acetone on *o*-nitrobenzaldehyde in the presence of sodium hydroxide [9] or by the action of glucose and sodium hydroxide on *o*-nitrobenzoylacetic acid [10] are both reactions which might well proceed through the intermediate di-isatogen. We suggest that the formation of the isatogen (V) proceeds by attack of the carbanion derived from the ketol (II) on the nitro-group in an analogous manner to the normal carbanion attack on a carbonyl group in an aldol condensation. Reactions in which isatogens are formed are favoured by light; [11] similarly in our experiments a 50% lower yield was obtained in an experiment conducted under identical conditions but in the dark. In the orange compound (III) carbanion formation takes place less readily owing to the absence of the activating COR group, and sodium hydrogen carbonate no longer converts it into the isatogen. The conversion of the orange compounds into the purple compounds, however, did occur with pyridine as catalyst, the conditions being those used in the preparation of isatogens from monohalogenostyrenes.[7] Muth *et al.*[12] have suggested a similar mechanism of carbanion formation from an activated methylene group followed by an aldol-type attack at a nitro-group in their preparation of phenanthridine *N*-oxides from 2-cyanomethyl- or 2-ethoxycarbonylmethyl-2′-nitrobiphenyls. Compounds bearing close structural resemblance to this aldol-type addition compound (IV) are the alcohol adducts of methyl or ethyl isatogenate.[6]

The mechanism for the formation of the orange compounds (III) from the ketols (II) is obvious, but that of their preparation from the piperidine-catalysed reactions of the *o*-nitrobenzoylacetates is at present obscure. The latter reaction, however, does establish which ester group has been removed in the preparation.

The isatogen (V; R = OMe) yielded a mono-oxime, a mononitro-derivative, and an acetone adduct. The analogue (V; R = OEt) gave a similar acetone adduct; the ketone analogue (V; R = Me) gave an isomer on treatment with acetic and hydrochloric acid. The structures of these products have not yet been elucidated but infrared evidence suggests that the isatogen ring remains intact in the oxime and nitro-derivatives.

[7] Sumpter and Miller, " Heterocyclic Compounds with Indole and Carbazole Systems," Interscience Publ. Ltd., London, 1954, p. 154; Smith, *Chem. Rev.*, 1938, **23**, 248.
[8] Baeyer, *Ber.*, 1881, **14**, 1741.
[9] Baeyer and Drewson, *Ber.*, 1882, **15**, 2856.
[10] Overmeyer, *J. Amer. Chem. Soc.*, 1926, **48**, 456.
[11] Splitter and Calvin, *J. Org. Chem.*, 1955, **20**, 1086.
[12] Muth, Ellers, and Folmer, *J. Amer. Chem. Soc.*, 1957, **79**, 6500.

Experimental

Infrared spectra (KBr disc) were determined by Mr. G. S. Hall, Grubb-Parsons Ltd., Newcastle upon Tyne. Equivalent weights were determined, except where otherwise stated, by potentiometric back-titrations.

2-(α-*Methoxycarbonylmethylene*-2-*nitrobenzyl*)*isatogen* (V; R = OMe).—A suspension of methyl *o*-nitrobenzoylacetate (2·0 g.) in 5·0% aqueous sodium hydrogen carbonate (20·0 ml.) was stirred at room temperature for 4 days. Within several hours the solution became purple; after one day the purple *product* (V; R = OMe) had separated and after 3 days no unchanged ester was visible. The solid (0·15 g.) was collected; it recrystallised from aqueous acetone as purple prisms, m. p. 242—243° (decomp.) (Found: C, 61·7; H, 3·4; N, 8·0; OMe, 8·75. $C_{18}H_{12}N_2O_6$ requires C, 61·4; H, 3·4; N, 8·0; OMe, 8·8%), $\nu_{max.}$ 1724s and 1710(sh)m (C=O), 1529s (NO_2), 1346s (NO_2), 1075s (this band was only present in spectra of isatogen derivatives but no assignment could be made), 862w (C–NO_2), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or NO_2 [13]). Methyl isatogenate has $\nu_{max.}$ 1730s and 1703s (C=O), 1504s, 1075m, 860w (C–N), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene).

Stirring aqueous solutions of the potassium or ammonium derivative of methyl *o*-nitrobenzoylacetate gave the same isatogen, m. p. 242—243° (decomp.), in 10—15% yields.

A repetition of the first preparation in a blackened flask gave the same isatogen (0·07 g.), m. p. 242—243° (decomp.).

The compound (V; R = OMe) was insoluble in dilute acid or alkali, and sparingly soluble in acetone and acetic acid, but insoluble in most other organic solvents. It was recovered unchanged after dissolution in concentrated sulphuric acid and reprecipitation with water. A suspension in aqueous acetone or ethanol, on treatment with sodium hydroxide at room temperature, rapidly underwent colour changes from purple to deep blue, to green, and finally to yellow.

Methyl 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OMe).—The purple filtrate remaining after removal of the isatogen in the first of the preceding experiments was acidified with hydrochloric acid, and the liberated oil was extracted in ether, recovered (1·5 g.), and dissolved in ethanol (4·5 ml.). During 2 days at room temperature the solution deposited pale orange prisms (0·11 g.) of the *ester* (III; R = OMe), m. p. 162—164° (decomp.), m. p. 165—166° (decomp.) (from acetic acid) (Found: C, 58·5; H, 3·5; N, 7·4; OMe, 8·4. $C_{18}H_{14}N_2O_7$ requires C, 58·4; H, 3·8; N, 7·6; OMe, 8·4%), $\lambda_{max.}$ 235 (log ε 4·42), 273 mμ (log ε 4·41) [cf. *o*-nitrocinnamic acid, $\lambda_{max.}$ 228 (log ε 4·0), 310 mμ (log ε 4·25)], $\nu_{max.}$ 1704s (C=O), 1525s (NO_2), 1355s (NO_2), 855vw (C–NO_2), and 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or NO_2). Acidification of the filtrates remaining after removal of the isatogen from the reactions of the potassium and ammonium derivatives of methyl *o*-nitrobenzoylacetate gave, after crystallisation, the same orange compound, m. p. 165—166° (decomp.). It was insoluble in dilute acid but soluble in most organic solvents; in dilute alkali it gave a deep purple solution and was recovered unchanged on acidification. Boiling the alkaline solutions removed the colour, after which acidification no longer precipitated the orange compound.

2-(α-*Ethoxycarbonylmethylene*-2-*nitrobenzyl*)*isatogen* (V; R = OEt).—In the manner described above for the methyl ester, ethyl *o*-nitrobenzoylacetate (2·0 g.) with 2·0% sodium hydrogen carbonate solution yielded after 11 days the *isatogen* (V; R = OEt) (0·47 g.), crystallising from aqueous acetone in deep reddish-purple prisms, m. p. 197—198° (decomp.) (Found: C, 62·7; H, 4·2; N, 7·7; OEt, 13·0. $C_{19}H_{14}N_2O_6$ requires C, 62·3; H, 3·8; N, 7·7; OEt, 12·3%). This had solubilities similar to those of the methyl analogue and gave the same sequence of colour changes on treatment of its suspension in aqueous acetone with sodium hydroxide.

Ethyl 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OEt).—Acidification with acetic acid of the purple filtrate left after removal of the preceding isatogen gave an orange oil from which the *pentenoate* (0·16 g.) was isolated by crystallisation from aqueous acetic acid. Recrystallisation yielded orange prisms, m. p. 136—137° (decomp.) (Found: C, 59·1; H, 3·65; N, 7·6; OEt, 11·7%; equiv., 382. $C_{19}H_{16}N_2O_7$ requires C, 59·4; H, 4·2; N, 7·3; OEt, 11·7%; equiv., 384).

2-(α-*Acetonylidene*-2-*nitrobenzyl*)*isatogen* (V; R = Me).—As described for methyl *o*-nitrobenzoylacetate, *o*-nitrobenzoylacetone (4·0 g.) with 5·0% aqueous sodium hydrogen carbonate

[13] Cross, " Introduction to Practical Infra-Red Spectroscopy," Butterworths, London, 1960, p. 70.

(40 ml.) yielded after 5 days the *isatogen* (V; R = Me) (1·81 g.), crystallising from aqueous acetone in deep violet prisms, m. p. 242—243° (decomp.) (Found: C, 63·8; H, 3·5; N, 8·0; OMe, 0. $C_{18}H_{12}N_2O_5$ requires C, 64·3; H, 3·6; N, 8·3%), $\nu_{max.}$ 1699m and 1684m (C=O), 1520s (NO_2), 1347s (NO_2), 1087s, 863w (C–NO_2), 752m cm.$^{-1}$ (*ortho*-disubstituted benzene or NO_2). The mixed m. p. with the isatogen (V; R = OMe) was depressed by only one degree, and the product showed similar solubilities and sequence of colour changes. This isatogen gave a positive iodoform reaction.

1,3-*Di*-o-*nitrophenylhex*-3-*ene*-1,5-*dione* (III; R = Me).—Acidification of the purple filtrate after removal of the preceding isatogen yielded, after washing with ether, a *diketone* (III; R = Me) (0·53 g.) which crystallised from acetic acid in orange prisms, m. p. 185—186° (decomp.) (Found: C, 61·1; H, 3·5; N, 7·9; OMe, 0·5%; equiv., 351. $C_{18}H_{14}N_2O_6$ requires C, 61·0; H, 3·95; N, 7·9%; equiv., 354), $\lambda_{max.}$ 239 (log ε 4·35), 280 mμ (log ε 4·35), $\nu_{max.}$ 1704s (C=O), 1515s (NO_2), 1345s (NO_2), 856vw (C–NO_2), 761m cm.$^{-1}$ (*ortho*-disubstituted benzene or NO_2).

Reactions of the Isatogen (V; R = OMe).—(a) *Oxidation.* The isatogen (0·25 g.) in 5·0% sodium hydroxide (20 ml.) was refluxed with potassium permanganate (3 × 0·5 g.) for 15 min. Methanol was added to reduce the last traces of permanganate, the mixture filtered, and the residual manganese dioxide washed with boiling water. The combined filtrate and washings were acidified with hydrochloric acid, and the resulting suspension extracted with ether. Evaporation of the extract gave the crude product which was extracted with boiling water. The aqueous extract, on cooling, gave *o*-nitrobenzoic acid (0·012 g.), m. p. and mixed m. p. 146—147°. The residue, insoluble in boiling water, crystallised from acetic acid, yielding isatoic anhydride (IX) (0·008 g.), m. p. 233—234° alone and undepressed on admixture with a sample of the product isolated in a similar manner on permanganate oxidation of methyl isatogenate.

(b) *Hydrolysis.* A suspension of the isatogen (0·3 g.) in ethanol (10·0 ml.) was stirred with 20% aqueous sodium hydroxide (2·0 ml.) for 15 min. at room temperature. The resulting clear yellow solution was acidified with hydrochloric acid, and the precipitated solid extracted in ether (2 × 20 ml.). Concentration of the extract gave 2-(β-*methoxycarbonyl*-α-o-*nitrophenylacrylamido*)*benzoic acid* (0·17 g.) which crystallised from ethanol in pale yellow prisms, m. p. 213—214° (decomp.) [Found: C, 58·6; H, 3·8; N, 7·7%; equiv. (titration in neutral acetone), 368. $C_{18}H_{14}N_2O_7$ requires C, 58·4; H, 3·8; N, 7·6%; equiv., 370].

This acid (0·05 g.) was refluxed with 30% sulphuric acid (1·0 ml.) for 90 min. The oil then present was removed by extraction with ether and the aqueous layer adjusted to pH 5·0 with sodium hydroxide and then acetic acid. The resulting suspension was extracted with ether, and the extract evaporated to dryness. The residue (0·01 g.), on crystallisation from water, had m. p. 140—142° alone or mixed with anthranilic acid. It yielded the characteristic red colour (given by anthranilic acid) on fusion with calcium chloride and dissolution in ethanol.

(c) *Oxime.* The isatogen (V; R = OMe) with hydroxylamine hydrochloride and pyridine in ethanol yielded the oxime, crystallising from ethanol in bright yellow needles, m. p. 159—160° (decomp.) (Found: C, 58·5; H, 3·4; N, 11·4. Calc. for $C_{18}H_{13}N_3O_6$: C, 58·85; H, 3·5; N, 11·4%).

(d) *Nitration.* The isatogen (0·08 g.) was heated in concentrated nitric acid (5·0 ml.) at 70—80° for 10 min. (colour change from deep red to orange). Cooling and dilution with water precipitated a *mononitro-derivative* (0·05 g.), orange prisms (from benzene), m. p. 221—223° (decomp.) (Found: C, 55·0; H, 3·2; N, 10·8. $C_{18}H_{11}N_3O_8$ requires C, 54·4; H, 2·8; N, 10·6%), $\nu_{max.}$ 1724m (C=O), 1520s (NO_2), 1345s and 1327(sh)s (NO_2), 1093s, 855vw (NO_2), 746w cm.$^{-1}$ (*ortho*-disubstituted benzene or NO_2).

(e) *Acetone adduct.* A suspension of the isatogen (0·1 g.) in acetone (3·0 ml.) and water (3·0 ml.) was stirred with 20% sodium hydroxide solution (0·4 ml.) for 15 min. at room temperature. The final clear yellow solution was acidified with acetic acid, depositing pale yellow prisms of the *adduct* (0·09 g.), m. p. 171—172° (from acetic acid) (Found: C, 61·3; H, 4·3; N, 6·4; OMe, 7·0. $C_{21}H_{18}N_2O_7$ requires C, 61·4; H, 4·4; N, 6·8; OMe, 7·6%).

Additional Syntheses of Methyl 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate.*—(*a*) Methyl *o*-nitrobenzoylacetate (0·25 g.), methyl *o*-nitrophenylpropiolate (0·2 g.), piperidine (0·1 ml.), and ethanol (4·0 ml.) were refluxed for 1 hr. The bright red *piperidinium adduct* (0·18 g.), m. p. 176—177° (decomp.), which separated was collected (Found: C, 60·5; H, 5·1. $C_{23}H_{25}N_3O_7$ requires C, 60·7; H, 5·5%). Boiling dilute hydrochloric acid converted it quantitatively into the methyl ester (III; R = OMe), m. p. and mixed m. p. 165—166° (decomp.).

Piperidinium hydrochloride, m. p. and mixed m. p. 236—237°, was isolated from the filtrate. The same piperidinium adduct was isolated in similar reactions between methyl *o*-nitrobenzoylacetate and (*b*) ethyl *o*-nitrophenylpropiolate, (*c*) methyl isatogenate, or (*d*) ethyl isatogenate. In all cases treatment with dilute acid or crystallisation from acetic acid gave the free ester.

Oxidation of Methyl 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate*.—The ester (0·25 g.) in sodium hydroxide solution with potassium permanganate gave, as the sole isolated product, *o*-nitrobenzoic acid (0·08 g.), m. p. and mixed m. p. 146—147°.

Conversion of the Pentenoate (III; R = OMe) *into the Isatogen* (V; R = OMe).—The ester (0·1 g.) was heated in pyridine (1·0 ml.) on the water bath for 1 hr., then poured into water (20 ml.), and the precipitated compound (0·03 g.) was collected (centrifuge). Crystallisation from acetic acid gave purple prisms, m. p. and mixed m. p. 242—243°.

Acetone Adduct of 2-(α-*Ethoxycarbonylmethylene*-2-*nitrobenzyl*)*isatogen*.—Treatment of the isatogen (V; R = OEt) (0·085 g.) with acetone and sodium hydroxide as above gave the acetone *adduct* (0·07 g.) crystallising from acetic acid in orange prisms, m. p. 166—167° alone and 150—153° on admixture with the previous acetone adduct (Found: N, 6·5. $C_{22}H_{20}N_2O_7$ requires N, 6·6%).

Additional Syntheses of Ethyl 3,5-*Di*-o-*nitrophenyl*-5-*oxopent*-2-*enoate* (III; R = OEt).—By reactions similar to those employed for the methyl ester, ethyl *o*-nitrobenzoylacetate was caused to react with methyl and ethyl *o*-nitrophenylpropiolate and with methyl and ethyl isatogenate. From all four reactions a red piperidinium adduct was isolated and converted, by treatment with acid, into the ester (V; R = OEt), m. p. and mixed m. p. 136—137°.

Conversion of the Ester (III; R = OEt) *into the Isatogen* (V; R = OEt).—The ester (0·1 g.) was refluxed in pyridine for 1 hr. and then diluted, to yield the isatogen (0·039 g.), m. p. (from acetic acid) and mixed m. p. 197—198° (decomp.).

Reactions of 2-(α-*Acetonylidene*-2-*nitrobenzyl*)*isatogen*.—(a) *Oxidation*. The isatogen (0·25 g.) with alkaline potassium permanganate gave *o*-nitrobenzoic acid (0·016 g.), m. p. and mixed m. p. 145—146°, and isatoic anhydride (0·019 g.), m. p. and mixed m. p. 233—234°.

(b) *Reduction*. The isatogen (0·5 g.), acetic acid (20 ml.), acetic anhydride (15 ml.) and zinc dust (3·0 g.) were refluxed for 90 min. The resulting solution was treated with ethanol (20 ml.) and evaporated to dryness, and the residue extracted with benzene. The extract was evaporated to give the 3-*acetoxy*-2-(2-*acetamido*-α-*acetonylidenebenzyl*)*indole* (VI; R = Me) (0·26 g.) which crystallised from benzene in fawn prisms, m. p. 289—291° (decomp.) (Found: C, 70·45; H, 5·2; N, 7·6. $C_{22}H_{20}N_2O_4$ requires C, 70·2; H, 5·3; N, 7·45%).

(c) *Hydrolysis*. The isatogen (0·1 g.) was hydrolysed with cold sodium hydroxide solution as above. o-(2-o-*Nitrophenyl*-4-*oxopent*-2-*enamido*)*benzoic acid* (VIII; R = Me) (0·05 g.) crystallised from ethanol in pale yellow prisms, m. p. 239—240° (decomp.) (Found: C, 60·9; H, 4·2; N, 7·3. $C_{18}H_{14}N_2O_6$ requires C, 61·0; H, 3·95; N, 7·9%).

Isomerisation of the Isatogen (V; R = Me).—The isatogen (0·1 g.), acetic acid (5·0 ml.), and hydrochloric acid (5·0 ml.) were refluxed for 2·5 hr. The resulting clear red solution was filtered and diluted with water (15 ml.). A trace of unchanged isatogen was removed and the filtrate set aside. The pale pink solid *isomer* which separated was purified by precipitation from its solution in sodium carbonate with dilute acid. Crystallisation from acetic acid gave pale cream needles, m. p. 255—256° (decomp.) (Found: C, 63·6; H, 3·9; N, 8·35. $C_{18}H_{12}N_2O_5$ requires C, 64·3; H, 3·6; N, 8·3%).

Oxidation of the Diketone (III; R = Me).—The diketone (0·25 g.), on oxidation with alkaline permanganate, gave, as the sole isolated product, *o*-nitrobenzoic acid (0·08 g.), m. p. and mixed m. p. 145—146°.

Conversion of the Diketone (III; R = Me) *into the Isatogen* (V; R = Me).—The diketone (0·2 g.) was refluxed in pyridine for 1 hr. and diluted with water, to yield the isatogen (0·065 g.), m. p. (from acetic acid) and mixed m. p. 242—243°.

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