2,2-Disubstituted-1,2-dihydro-3*H*-indol-3-ones by Base- and Thermal-induced Cyclisations of *o*-Azidophenyl s-Alkyl Ketones and *o*-Azidobenzoyl Esters

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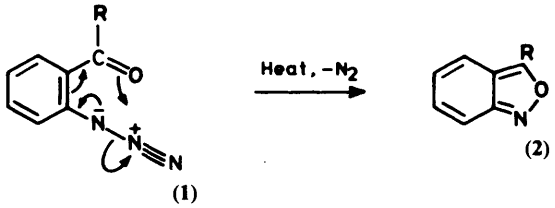
o-Azidophenyl s-alkyl ketones in ethanolic potassium hydroxide at room temperature undergo loss of nitrogen and cyclisation to 2,2-dialkyl-1,2-dihydro-3*H*-indol-3-ones in high yield. Kinetic data ($E_{act.}$ 62.4 and 71.6 kJ mol^{-1}, respectively) obtained for the *o*-azidophenylisopropyl and *o*-azidophenylcyclohexyl ketones support an assisted nitrogen loss from the azide *via* the enolate ion, rather than a nitrene reaction. 1,2-Dihydro-3*H*-indol-3-ones, along with in some cases 2,1-benzisoxazoles, have also been obtained by the thermolysis and spray vacuum pyrolysis of other *o*-azidophenyl alkyl ketones, diethyl *o*-azidobenzoyl malonate, and ethyl *o*-azidobenzoyl(phenyl)acetate.

In preliminary publications the base-induced intramolecular cyclisations of *o*-azidoanilides[1] and *o*-azidophenyl s-alkyl ketones[2] to 2-aryl-1,2-dihydro-3*H*-indazol-3-ones and 2,2-dialkyl-1,2-dihydro-3*H*-indol-3-ones (2,2-dialkylindoxyls), respectively, have been described. These represent the first examples of base-induced, rather than the more usual thermal-induced,[3] decomposition and cyclisation of *o*-substituted aryl azides, and constitute useful synthetic routes to these ring-systems. We now report experimental details for 2,2-dialkyl-1,2-dihydro-3*H*-indol-3-one formation, together with some kinetic data and further examples of azide cyclisations to yield more highly functionalised indolinones.

Thermal decomposition of an *o*-azidoaryl ketone (**1**) is an established route[4] to the 2,1-benzisoxazole (anthranil) (**2**) ring-system, and occurs by a concerted pericyclic mechanism,[5] as illustrated in Scheme 1, rather than *via* a nitrene intermediate.†



a; R = Me
b; R = $CHMe_2$
c; R = CH(Me)Ph
d; R = CH(Me)Et
e; R = cyclopentyl
f; R = cyclohexyl
g; R = $CH(Ph)CO_2Et$

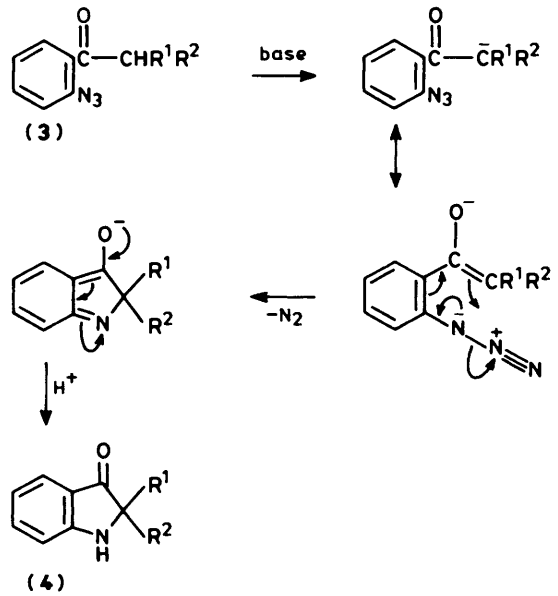
Scheme 1.

However, we have found[2] that in basic solution, the *o*-azidophenyl s-alkyl ketones (**3a-e**) undergo an alternative cyclisation to yield the 2,2-dialkyl-1,2-dihydro-3*H*-indol-3-ones (**4a—e**). In no case was any 2,1-benzisoxazole, or other product, isolated.

The efficiency (generally yields >85%) of this process together with the mild (25 °C) reaction conditions employed, indicated a much lower energy pathway for this cyclisation than for 2,1-benzisoxazole production, for which activation energies of the order 110 kJ mol^{-1} have been obtained.[5] We were prompted, therefore, to carry out rate-studies on the base-induced decompositions of some *o*-azidophenyl s-alkyl ketones in order to determine $E_{act.}$ for indolinone formation.

† An alternative, but less favoured,[5] mechanism involving an intramolecular 1,3-dipolar cycloaddition of the azide to the carbonyl group followed by loss of nitrogen has also been proposed.[6]

Studies on the cyclisation of the *o*-azidophenyl s-butyl ketone (**3c**) to 2-ethyl-2-methyl-1,2-dihydro-3*H*-indol-3-one (**4c**) revealed that the reaction could be effected by a variety of bases (NaH–DMF, NaH–THF, NaOMe, and NaOH). However, ethanolic potassium hydroxide proved to be the most effective reagent and brought about complete (>90%) reaction within 3—4 h at room temperature. Reactions rates for the

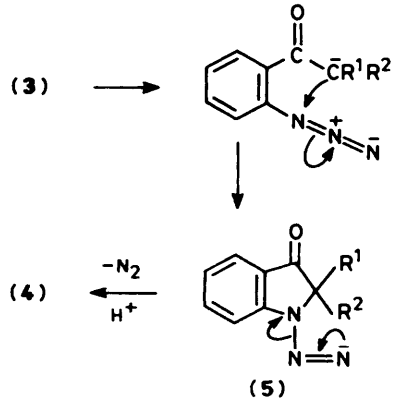


a; $R^1 = R^2$ = Me
b; R^1 = Me, R^2 = Ph
c; R^1 = Me, R^2 = Et
d; $R^1 = R^2 = -(CH_2)_4-$
e; $R^1 = R^2 = -(CH_2)_5-$
f; $R^1 = R^2 = CO_2Et$
g; $R^1 = CO_2Et$, R^2 = Ph
h; $R^1 = R^2$ = H

Scheme 2.

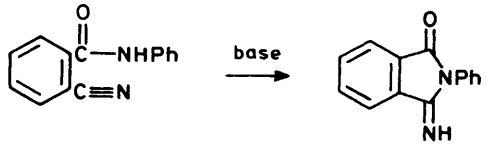
cyclohexyl-(**3e**) and the isopropyl-(**3a**) ketones were obtained spectrophotometrically (u.v.) by monitoring the appearance of the strong indoxyl end-absorption at 395 nm. Kinetic measurements were taken in the temperature range 15—45 °C, higher temperatures being avoided so as to minimise any competing thermal induced cyclisations to 2,1-benzisoxazoles. A first-order rate was noted and plots of $\log_{10} k$ *vs.* $1/T$ yielded for the cyclohexyl- and isopropyl-ketones activation energies ($E_{act.}$) of 71.6 ± 7 kJ mol^{-1} and 62.4 ± 6 kJ mol^{-1}, respectively.

These values are significantly lower than those recorded for other assisted aryl azide decompositions,[5] and may indicate an anchimerically assisted loss of nitrogen (Scheme 3) from the



Scheme 3.

azido ketone anion rather than as suggested earlier[2] a 6π-pericyclic process (Scheme 2) involving the enolate π-system. In fact, activation energies of the same order of magnitude (*i.e.* 50—70 kJ mol^{-1}) to those obtained for indolinone formation have been recorded for similar base-catalysed intramolecular cyclisations; *e.g.*, the cyclisation of *o*-cyanobenzanilide to 3-imino-2-phenylisoindolinone (Scheme 4).[7] Interestingly, structure (**5**) is equivalent to one of the several possible transition states considered by Hall and his co-workers[8] for assisted azide decompositions.



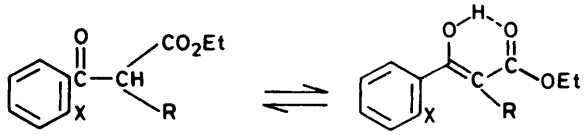
Scheme 4. $E_{act.}$ (DMSO as solvent) = 54 kJ mol^{-1}; $E_{act.}$ (DMF as solvent) = 67 kJ mol^{-1}

The possibility that indolinones were being produced by a base-catalysed rearrangement of an initially formed 2,1-benzisoxazole* rather than directly from the azido ketone was discounted when it was found that 2,1-benzisoxazoles could be recovered after treatement for several h with ethanolic potassium hydroxide. Investigation (t.l.c.) of the reaction mixture failed to detect any of the bright yellow spiro-indoxyls.

As expected, thermal decomposition of the azido ketones (**3a**, **e**) in boiling xylene at 140—145 °C gave the 3-alkyl-2,1-benzisoxazoles (**2a**, **f**). However, for the other azido ketones, (**3b**, **c**, and **d**) 2,1-benzisoxazole formation was accompanied by small amounts (3—5%) of the amino ketone.

In an attempt to extend these decomposition reactions to the preparation of 2,2-disubstituted 1,2-dihydro-3*H*-indol-3-ones, capable of further modification to novel tricyclic systems, the *o*-azidobenzoyl derivatives of diethyl malonate and ethyl phenylacetate have been prepared and their cyclisation reactions studied.

Neither of these esters underwent cyclisation in basic solution. They were recovered unchanged from cold ethanolic potassium hydroxide, whereas on heating in basic solution uncharacterised decomposition products resulted. However, diethyl *o*-azidobenzoylmalonate (**6a**), on thermolysis in boiling xylene and



(**6**)
a; R = CO_2Et, X = N_3
b; R = Ph, X = N_3
c; R = CO_2Et, X = NO_2

(**7**)
a; R = CO_2Et, X = N_3
b; R = Ph, X = N_3

in contrast to the *o*-azidoaryl ketones (**1**) and (**3**), gave not the expected 2,1-benzisoxazole, but 2,2-diethoxycarbonyl-1,2-dihydro-3*H*-indol-3-one (**4f**) generally in excellent yield (80%).† In a similar manner ethyl *o*-azidobenzoyl(phenyl)acetate (**6b**) on thermolysis in boiling *o*-dichlorobenzene, furnished the indol-3-one (**4g**), albeit in lesser yield (50%).

Inspection of the ^{1}H n.m.r. spectra of the azido esters (**6a**) and (**6b**) suggested an explanation for these unexpected results. In keeping with other benzoylmalonates and related acyl esters,[10] the esters exist as unstable tautomeric mixtures in which initially,‡ the intramolecularly hydrogen bonded enol forms (**7a**) and (**7b**) are substantial components (45 and 33%, respectively). Hence, the azide on thermolysis has available an alternative mode of cyclisation *via* a 6π-pericyclic reaction with the π-bond of the enol form. Preliminary kinetic data[11] for the thermolysis of the azido diester (**6a**) indicate an activation energy of 100—120 kJ mol^{-1}, a value of the same order as that noted for 2,1-benzisoxazole formation. This preference for cyclisation to a 1,2-dihydroindol-3-one rather than to a 2,1-benzisoxazole may reflect the difference in the former case of producing a fully benzenoid heterocyclic system, rather than, as in the latter instance, an *ortho*-quinonoid system.

The yield of indolinone diester (**4f**) from the thermolysis of the *o*-azidobenzoyl malonate (**6a**) decreased sharply (17%) on subjecting the azide to spray vacuum pyrolysis (s.v.p.)[12] at 300 °C. The phenyl acetate derivative (**6b**) on s.v.p. under similar conditions gave a mixture of the 2,1-benzisoxazole (**2g**) (65%) and the 2-ethoxycarbonyl-2-phenylindolinone (**4g**) (30%).

Although the formation of 1,2-dihydro-3*H*-indol-3-ones by thermolysis of *o*-azidoaryl alkyl ketones has not been reported previously, the rearrangement of 3-methyl-2,1-benzisoxazole (**2a**) to 1,2-dihydro-3*H*-indol-3-one (**4h**) is known.[13] We have confirmed this report and have found that indigotin is produced, albeit in low yield (*ca.* 15%), when 3-methyl-2,1-benzisoxazole, or its precursor *o*-azidoacetophenone, is subjected to s.v.p. at 320 °C.

Pyrolysis of *o*-azidophenyl isopropyl ketone (**3a**) at 300 °C gave 3-isopropyl-2,1-benzisoxazole (**2b**) as the sole product. The benzisoxazole was surprisingly stable, and on s.v.p. at 420 °C gave only 2,2-dimethyl-1,2-dihydro-3*H*-indol-3-one (**4a**) in low yield (19%).

Attempts to prepare 2,2-disubstituted 1,2-dihydro-3*H*-indol-3-ones by deoxygenative cyclisation[14] of *o*-nitrophenyl alkyl ketones with triethyl phosphite was successful only with the diethyl malonate derivative (**6c**). The indolone diester (**4f**) was obtained, but in poor yield (19%).

* 2,1-Benzisoxazoles are stable towards base, although 3-methyl-2,1-benzisoxazole (**2a**) ring-opens to 2-aminoacetophenone on prolonged heating with aqueous sodium hydroxide.[9]

† Latterly, we have found the yields of (**4f**) obtained from thermolysis of the diester (**6a**) in boiling xylene to be unpredictable. Occasionally, only small amounts (< 20%) are produced along with much tar. So far we are unable to explain this puzzling feature.

‡ The % enol content of (**6a**) decreases (< 10%) on allowing the diester to stand.

Table 1. *o*-Azidophenyl s-alkyl ketones (3)

Compd.	Yield %	$\nu_{max.}$ (liquid film)/cm^{-1} $\nu(N_3)$	$\nu(C{=}O)$	^{1}H N.m.r. $\delta(CDCl_3)$ p.p.m.
(3a)	73	2 120	1 680	7.3 (4 H, m, ArH), 3.5 (1 H, q, C*H*Me$_2$), and 1.2 (6 H, d, CH*Me*$_2$)
(3b)	79	2 125	1 680	7.2 (9 H, m, ArH), 3.8 (1 H, q, CH), and 1.6 (3 H, d, Me)
(3c)	73	2 120	1 685	7.4 (4 H, m, ArH), 3.3 (1 H, q, CH), 8.5 (2 H, m, CH_2), 9.0 (3 H, d, CH*Me*), and 9.1 (3 H, t, CH_2*Me*)
(3d)	65	2 120	1 680	7.6 (4 H, m, ArH), 3.8 (1 H, m, CH), and 1.8 (8 H, m, 4 × CH_2)
(3e)	72	2 120	1 685	7.4 (4 H, m, ArH), 3.3 (1 H, m, CH), and 1.5 (10 H, m, 5 × CH_2)

Table 2. 2,2-Disubstituted 1,2-dihydro-3*H*-indol-3-ones (4).[a]

Compd.	Yield (%)	M.p. (°C)	Lit. m.p. (° C)	$\lambda_{max.}$/nm (log ε)[b] (EtOH)
(4a)	89	89	89[18]	395 (3.61)[c]
(4b)	67	113	113[19]	402 (3.66)
(4d)	87	79	79[20]	396 (3.63)
(4e)	96	135	136[21]	392 (3.58)

[a] All display in i.r. $\nu_{max.}$(Nujol), 3 140 ± 5 (NH), and 1 675 ± 5 cm^{-1} (C=O). [b] End absorption. [c] δ_C (26 MHz; $CDCl_3$); 205.08 (s, C=O), 159.55 (s, C-7a), 137.0 (d, C-6), 124.79 (d, C-4), 119.28 (s, C-3a), 118.5 (d, C-5), 112.3 (d, C-7), 63.73 (s, C-2), and 24.22 (q, 2 × Me).[22]

The absence of the usual triplet nitrene mediated products, *e.g.* amines and azo compounds,[3] in the thermolyses leading to 2,2-disubstituted indolin-3-ones, suggests that as with the base-catalysed cyclisations (Scheme 2), heterocycle formation is *via* a concerted assisted loss of nitrogen from the azide rather than *via* a nitrene-controlled pathway. In contrast, the isomerisations of 3-alkyl-2,1-benzisoxazoles to 1,2-dihydro-3*H*-indol-3-ones presumably involve O–N bond cleavage of the isoxazole ring, (a well known reaction under photolytic conditions[4]), and cyclisation of the singlet (or triplet) *o*-nitrenoaryl ketone so formed at the proximate alkyl side chain.

As mentioned in the preliminary communication, all attempts so far to extend the base-induced azide decomposition to other azidoaryl ketones, *e.g.* *o*-azidoacetophenone, have led only to complex mixtures of mainly tarry products. It is likely that under the basic reaction conditions any 2-mono-substituted indoxyls formed would be lost in subsequent base-catalysed condensations. These aspects of the reaction are still under investigation.

Experimental

I.r. spectra were recorded as Nujol mulls or liquid films on a Perkin-Elmer 297 or 257 grating i.r. spectrophotometer. ^{1}H and ^{13}C N.m.r. spectra were measured, unless otherwise stated, for $CDCl_3$ solutions ($SiMe_4$ as internal standard) on Perkin-Elmer R32 90 MHz and Varian Associates CFT 20 spectrometers, respectively. Mass spectra were obtained on an A.E.I. MS12 mass spectrometer, and u.v. spectra as ethanol solutions on a Unicam SP 800A spectrophotometer.

All m.p.s are uncorrected and distillation of liquid samples was performed using a Kugelrohr apparatus. T.l.c. was on 'Camlab' Polygram alumina or silica n/u.v.$_{254}$ plates, column chromatography was carried out on Camag alkaline alumina (pH 9.3—9.7), 100—250 mesh, and medium pressure chromatography was on Merck silica gel 60H (7736). Elemental analyses were performed by Butterworth Laboratories, Teddington, Middlesex.

Table 3. 3-Alkyl-2,1-benzisoxazoles (2) by thermolysis of *o*-azidoaryl s-alkyl ketones

Compd.	Yield (%)	M.p. (°C) (b.p. °C/mmHg)	Found (%) (Required) C	H	N	Molecular formula
(2b)	94	(78 0.2)	74.6 (74.5)	6.7 (6.8)	8.8 (8.7)	$C_{10}H_{11}NO$
(2d)	93	(88 0.2)[a]				
(2e)	87	(116/0.2)				
(2f)	98	58 (120/0.2)	77.7 (77.6)	7.4 (7.5)	7.0 (7.0)	$C_{13}H_{15}NO$

[a] Satisfactory analyses could not be obtained due to contamination by small amounts of *o*-aminophenyl alkyl ketones.

Table 4. Kinetic data for the base induced cyclisations of *o*-azidophenylcyclohexyl-(3e) and isopropyl-ketones (3a) to 1,2-dihydro-3*H*-indol-3-ones (4e) and (4a) respectively

Azide	10^4k/s^{-1}	Temp. (K)	T/K × 10^3
(3e)	2.15	290.6	3.44
	3.42	296.0	3.38
	3.57	298.1	3.35
	5.88	304.6	3.28
	8.96	307.6	3.25
	27.83	317.1	3.15
(3a)	1.96	288.4	3.47
	2.93	290.2	3.45
	2.96	293.3	3.41
	3.61	295.5	3.39
	4.61	298.0	3.36
	5.70	300.4	3.33
	7.07	303.0	3.30
	11.29	308.0	3.25
	15.71	313.0	3.20
	20.32	317.9	3.15

o-Azidoacetophenone (1; R = Me), m.p. 20 °C [lit.,[15] 22.5 °C; $\nu_{max.}$ (liquid film) 2 140 (N_3) and 1 680 cm^{-1} (C=O)] was prepared from *o*-nitroacetophenone[16] by reduction (Pd–C; H_2) followed by diazotisation and azidation as in the following procedure.

Preparation of o-Azidophenyl s-Alkyl Ketones (3a—e). *General Procedure.*—A solution of the *o*-aminophenyl alkyl ketone, prepared[17] by the action of an excess of Grignard reagent on *o*-aminobenzonitrile in dilute hydrochloric acid (1:1), was diazotised at 0 °C in the normal manner using aqueous sodium nitrite. The cold diazonium chloride solution was filtered rapidly, and then added slowly (5—10 min) to a cold stirred solution of sodium azide (1 equiv.) and sodium acetate (10 equiv.) in water. [CAUTION—HN_3 is highly toxic. All operations involving NaN_3 should be carried out in an efficient fumehood.] The reaction mixture was extracted with diethyl ether, the extracts dried ($MgSO_4$), and the solvent removed at room temperature (rotary evaporator under reduced pressure). [CAUTION—most azides decompose violently when heated and should not be distilled or otherwise heated.]

The resulting liquid azides were purified by column chromato-

graphy on alumina, with light petroleum (b.p. 40—60 °C)–diethyl ether (4:1) as eluant. The light and heat sensitive azides were characterised spectroscopically. Details are given in Table 1.

Base-induced Decomposition of o-*Azidophenyl s-Alkyl Ketones: General Method.—Preparation of* 2-*ethyl*-2-*methyl*-1,2-*dihydro*-3H-*indol*-3-*one* (**4c**). To a solution of potassium hydroxide (1 g) in ethanol (20 ml) was added *o*-azidophenyl s-butyl ketone (**3c**) (1 g) and the mixture was stirred at room temperature for 2—3 h. The excess of solvent was then removed under reduced pressure, and water (30 ml) was added to the yellow semi-solid residue. The resulting mixture was extracted with diethyl ether (2 × 30 ml), and the combined extracts were dried ($MgSO_4$) and evaporated to yield a yellow solid which was purified by column chromatography [Al_2O_3; light petroleum (b.p. 40—60 °C)–diethyl ether (4:1) as eluant] to give 2-*ethyl*-2-*methyl*-1,2-*dihydro*-3H-*indol*-3-*one* (**4c**) as a yellow solid (0.75 g, 87%), m.p. 64 °C (b.p. 120 °C/0.5 mmHg) (Found: C, 75.6; H, 7.5; N, 8.0. $C_{11}H_{13}NO$ requires C, 75.4; H, 7.4; N, 8.0%); $\lambda_{max.}$(EtOH) 397 nm (log ε 3.64); $\nu_{max.}$(Nujol) 3 140 (NH) and 1 675 cm^{-1} (C=O).

The other 1,2-dihydro-3*H*-indol-3-ones (**4a**, **b**, **d**, and **e**) were obtained similarly; details are given in Table 2.

The 1,2-dihydro-3*H*-indol-3-one (**4c**) was also obtained (yields in brackets) by treating the azidophenyl alkyl ketone (**3c**) with NaH–DMF at 80 °C for 3 h (14%); with NaH in boiling THF (25%); with NaOMe–MeOH under reflux for 2 h (56%); and with NaOH in ethanol at room temperature (47%).

3-*Alkyl*-2,1-*benzisoxazoles* (**2**): *General Method.*—A solution of the *o*-azidoaryl alkyl ketone (0.5 g) in dry xylene was heated under reflux until all the azide (as shown by i.r. and/or t.l.c.) had disappeared (*ca.* 2 h). The solution was cooled and the excess of solvent removed (rotary evaporator) to yield the 3-alkyl-2,1-benzisoxazole, in some cases, in admixture with the *o*-aminophenyl alkyl ketone. Details are given in Table 3.

Kinetic Measurements on o-*Azidophenyl Isopropyl Ketone* (**3a**) *and* o-*Azidophenyl Cyclohexyl Ketone* (**3e**).—The kinetic measurements were carried out on a Unicam SP800 spectrophotometer using 1 cm matched quartz cells that were calibrated for the solvent system (EtOH) before each measurement. The azide and ethanolic potassium hydroxide solutions were 5.82×10^{-4}M and 1.87M, respectively; the same concentrations of reactants were maintained throughout. Temperature variations were less than ±0.4 °C at the temperatures employed. The azide and ethanolic KOH were brought to reaction temperature, prior to mixing, by immersion in a thermostatted bath for 30 min—1 h. At time zero, the azide was added to the base at which point time measurement was begun. U.v. scanning times were 45 s and the reactions were followed to 90% completion.

For a first-order reaction, expressed in terms of the concentration of 1,2-dihydro-3*H*-indol-3-one, [P], and assuming 100% conversion

$$\ln \frac{[P]_\infty}{[P]_\infty - [P]_t} = kt \qquad (1)$$

The weak dependence of absorbance, *A*, on temperature can be neglected for the small range (17.5—44.5 °C) of temperatures used and, therefore, equation (1) can be expressed in terms of absorbance, *A*, as

$$\ln \frac{A_\infty - A_o}{A_\infty - A_t} = kt \qquad (2)$$

For a first-order reaction a plot of $\log_{10}(A_\infty - A_t)$ *vs.* time (*t*) should be linear with slope = $-k/_{2.303}$. *A* was measured at $t = 0$, and thereafter at regular 2—5 min intervals. A_∞ at 395 nm = 2.07.

Rate constants at 6 different temperatures were calculated (Table 4). A plot of $\log_{10} k$ *vs.* T(K × 10^3) (at least squares method) gave a straight line with a slope of value -3.74×10^3 K which yielded (R = 8.314 J K^{-1} mol^{-1}) $E_{act.}$ = 71.6 ± 7 kJ mol^{-1}. A similar kinetic run on the *o*-azidophenyl isopropyl ketone at ten temperatures in the range 15.3—44.8 °C (288.4—317.9 K) (Table 4) gave $E_{act.}$ = 62.4 ± 6 kJ mol^{-1}.

Preparation of α-(o-*Azidobenzoyl*) *Esters.*—*Diethyl* o-*azidobenzoylmalonate* (**6a**) (87%) was prepared by treating diethyl ethoxymagnesiomalonate[16] with *o*-azidobenzoyl chloride.[23] The azide was purified by column chromatography [SiO_2; light petroleum (b.p. 40—60 °C)–diethyl ether as eluant] and was isolated as a pale yellow oil; $\nu_{max.}$(liquid film), 1 750, 1 720, 1 680 (C=O), and 2 130 cm^{-1} (N_3); δ_H (90 MHz; $CDCl_3$) 7.15 and 7.95 (4 H, m, ArH), 5.5 (s, keto CH), 13.5 (s, enol OH), 3.80—4.45 (4 H, overlapping quartets, 2 × CH_2), and 0.83—1.40 (6 H, overlapping triplets, 2 × Me); keto–enol ratio (55:45); *m/z* 305 (M^+). Similarly prepared and purified was *diethyl* o-*nitrobenzoylmalonate* (**6c**) (93%), m.p. 54 °C (Found: C, 54.6; H, 4.9; N, 4.7. $C_{14}H_{15}NO_7$ requires C, 54.4; H, 4.9; N, 4.5%); $\nu_{max.}$ (liquid film) 1 730, 1 710, 1 660 (C=O), 1 520, and 1 340 cm^{-1} (NO_2); δ_H (90 MHz; $CDCl_3$), 7.37 and 8.24 (4 H, m, ArH), 4.97 (s, keto CH), 14.0 (s, enol OH), 3.78—4.02 (2 H, q, CH_2), 4.20—4.50 (2 H, q, CH_2), 0.8—0.95 (3 H, t, Me), and 1.23—1.40 (3 H, t, Me); *keto–enol* ratio (18:82); *m/z* 309 (M^+). Ethyl *o*-azidobenzoyl(phenyl)acetate (**6b**) (75%) was obtained by treating ethyl phenylacetate at −78 °C successively with lithium *N*-isopropylcyclohexylamide and *o*-azidobenzoyl chloride.[24]

The azide was isolated as a yellow oil and purified as for the azidoester (**6a**): $\nu_{max.}$ 1 730, 1 700 (C=O), and 2 120 cm^{-1} (N_3); δ_H (90 MHz; $CDCl_3$) 7.0–7.6 (9 H, m, ArH), 3.6 (s, keto CH), 15.85 (s, enol OH), 4.1–4.4 (2 H, q, CH_2) and 1.1–1.4 (3 H, t, Me); keto–enol ratio (66:33); *m/z* 309 (M^+).

2,2-*Diethoxycarbonyl*-1,2-*dihydro*-3H-*indol*-3-*one* (**4f**).—To boiling xylene contained in a 100 ml round-bottomed flask fitted with a condenser and dropping funnel was added dropwise over 10 min a solution of diethyl *o*-azidobenzoylmalonate (**6a**) (1 g) in xylene (20 ml). After 1 h the reaction was complete (as shown by the absence of azide on t.l.c.) and the excess of solvent was removed (rotary evaporator) to give the product as a yellow semi-solid residue which was purified by column chromatography [Al_2O_3; light petroleum (b.p. 40—60 °C) as eluant], and then by distillation (Kugelrohr) to give 2,2-diethoxycarbonyl-1,2-dihydro-3*H*-indol-3-one (**4f**) (80%) as yellow crystals, m.p. 81 °C (b.p. 112 °C/1 mmHg) (Found: C, 60.9; H, 5.6; N, 5.2. $C_{14}H_{15}NO_5$ requires C, 60.6; H, 5.4; N, 5.05%); $\nu_{max.}$(Nujol) 3 350 (NH), 1 720, and 1 700 cm^{-1} (C=O): δ_H ($CDCl_3$; 90 MHz) 6.7—6.8 (4 H, m, ArH), 5.75 (1 H, s, NH), 4.2—4.4 (4 H, q, 2 × CH_2), and 1.20—1.35 (6 H, t, 2 × Me); δ_C ($CDCl_3$; 26 MHz) 188.69 (s, C-3), 164.1 (s, 2 × CO_2R), 160.99 (s, C-7a), 137.44 (d, C-6), 124.86 (d, C-4), 120.34 (s, C-3a), 119.12 (d, C-5), 113.26 (d, C-7), 75.39 (C-2; under $CDCl_3$ signal), 62.67 (t, 2 × OCH_2), and 13.41 (q, 2 × $-CH_2Me$); *m/z* 277 (M^+).

Decompositions were also carried out in boiling bromobenzene (0.5 h; 60% yield), boiling *o*-dichlorobenzene (0.25 h; 79% yield), and boiling chlorobenzene (1.5 h; 62% yield). The azido diester remained unchanged in boiling toluene (6 h).

2-*Ethoxycarbonyl*-2-*phenyl*-1,2-*dihydro*-3H-*indol*-3-*one* (**4g**).—Ethyl *o*-azidobenzoyl(phenyl)acetate (**6b**) (1 g) was heated in boiling *o*-dichlorobenzene for 30 min, after which time the azide had disappeared (t.l.c.). Work-up and purification as in the previous experiment gave 2-*ethoxycarbonyl*-2-*phenyl*-1,2-

dihydro-3H-*indol*-3-*one* (**4g**) (48%) as a viscous red oil which became semi-solid only after a long period of time; m.p. 90 °C (light petroleum b.p. 60—80 °C) (Found: C, 72.2; H, 5.35; N, 5.0. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.3; N, 5.0%); $\nu_{max.}$ (liquid film) 3 350 (NH) 1 740, and 1 700 cm^{-1} (C=O); δ_H ($CDCl_3$; 90 MHz), 7.1—7.6 (9 H, m, ArH), 5.8 (1 H, s, NH), 4.2—4.5 (2 H, t, CH_2), and 1.1—1.4 (3 H, t, Me); *m/z* 281 (M^+).

Thermolysis of the azide in boiling xylene gave the indolinone in 45% yield.

Spray Vacuum Pyrolysis of o-*Azidoaryl Ketones and* 2,1-*Benzisoxazoles: General Method.*—The liquid azide or 2,1-benzisoxazole (2—3 g) was subjected to s.v.p. at 300—450 °C in the apparatus described previously.[12] The pyrolysis tube was loosely packed with glass wool, and the reactant was introduced into the system in a fine stream of dry nitrogen over a period of 2—3 h. The pyrolysate was collected on a liquid nitrogen cooled cold finger, which after being allowed to come to room temperature, was washed with solvent (generally CH_2Cl_2). Separation and purification of the products was achieved either by fractional crystallisation, or more usually, by medium-pressure column chromatography on silica.

(*a*) *S.V.P. of* o-*azidoacetophenone* (**1**; R = Me) The azide (3 g) was pyrolysed at 300 °C over 2 h to give an impure pale yellow pyrolysate [1,2-dihydro-3*H*-indol-3-one (**4h**)?] which when set aside in air rapidly became blue and on separation from starting material gave indigotin (0.5 g), identical with an authentic sample.[25]

(*b*) *S.V.P. of* 3-*methyl*-2,1-*benzisoxazole* (**2a**). The methyl benzisoxazole (2.7 g), prepared by thermolysis of *o*-azidoacetophenone in boiling xylene, on pyrolysis under the conditions given in (*a*), gave indigotin (0.66 g, 15%) and much tar.

(*c*) *S.V.P. of* o-*azidophenyl isopropyl ketone* (**3a**). The azide (4 g) was pyrolysed at 350 °C for 3 h to give 3-isopropyl-2,1-benzisoxazole (**2b**) (3.2 g, 94.5%).

(*d*) *S.V.P. of* 3-*isopropyl*-2,1-*benzisoxazole* (**2b**). The 2,1-benzisoxazole (2.5 g) was pyrolysed at 450 °C over 2 h to give a yellow pyrolysate which on purification by column chromatography [Al_2O_3; light petroleum (b.p. 60—80 °C)–ethyl acetate (9:1; v/v)] yielded 3-isopropyl-2,1-benzisoxazole (1.9 g), and on further elution, with ethyl acetate, 2,2-dimethyl-1,2-dihydro-3*H*-indol-3-one (**4a**) (0.47 g, 19%).

(*e*) *S.V.P. of diethyl* o-*azidobenzoylmalonate* (**6a**). The azido diester (3.5 g) was pyrolysed at 300 °C over 3 h to give after separation by column chromatography [SiO_2; light petroleum (b.p. 40—60 °C)–ethyl acetate (7:3; v/v)] as eluant, 2,2-diethoxycarbonyl-1,2-dihydro-3*H*-indol-3-one (**4f**) (0.14 g, 17%). Further elution with methanol gave only uncharacterised tarry material.

(*f*) *S.V.P. of ethyl* o-*azidobenzoyl*(*phenyl*)*acetate* (**6b**). The azido ester (1.8 g) was pyrolysed at 350 °C over 1 h: purification of the pyrolysate by medium pressure chromatography [(SiO_2), with light petroleum (b.p. 60—80 °C)–CH_2Cl_2 (3:2) as eluant] gave 3-[α-(ethoxycarbonyl)benzyl]-2,1-benzisoxazole (**2 g**) (0.1 g, 6%), m.p. 127 °C (light petroleum b.p. 60—80 °C) (Found: C, 72.4; H, 5.35; N, 5.0. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.3; N, 5.0%); $\nu_{max.}$(Nujol) 1 720 cm^{-1} (C=O); δ_H ($CDCl_3$, 90 MHz) 10.4 (br, enol–OH), 8.0—8.35 and 6.95—7.75 (9 H, m, ArH), 5.15 (s, CH), 4.0—4.35 (2 H, q, CH_2), and 0.9—1.25 (3 H, t, Me). Further elution yielded indoxyl (4 g), m.p. 90 °C (0.45 g, 30%).

Reduction of Diethyl o-*Nitrobenzoylmalonate* (**6c**) *with Triethyl Phosphite.*—A solution of diethyl *o*-nitrobenzoylmalonate (1 g) and triethyl phosphite (8 ml) in dry xylene (45 ml) was heated under reflux for 12 h. The excess of reagent and solvent were removed under reduced pressure and the semi-solid residue chromatographed (Al_2O_3). Elution with light petroleum (b.p. 40—60 °C) gave 2,2-diethoxycarbonyl-1,2-dihydro-3*H*-indol-3-one (**4f**) (19%) as pale yellow crystals, m.p. 81 °C.

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