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The Relationship of Bisanthranil to its Structural Isomer and Related Compounds

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A spectroscopic, mass spectroscopic, and chemical examination of bisanthranil, m. p. 185°, and of its structural isomer, m. p. 302°, has confirmed the lactone structure of the former and the amide structure of the latter. The spectra were compared with those of 2-phenylindazol-3-one, 2-(2-carboxyphenyl)indazol-3-one, 2-phenyl-3,1-benzoxazin-4-one, isatoic anhydride, and dianthranilide.

TREATMENT of 2,2′-dicarboxyhydrazobenzene with acetic anhydride leads to the formation of a compound $C_{14}H_8N_2O_2$, m. p. 185°, designated "bisanthranil" by Heller.[1] He considered two structures, (I) and (II), for this compound and opted in favour of (I). Under the influence of heat, bisanthranil is converted into an isomeric compound, m. p. 302°, which was considered to possess structure (IIIb).[1,2] The latter compound had previously been reported by Freundler,[3-7] who obtained it through alkaline reduction of 2-nitrobenzyl alcohol, by Carré[8-12] through heating 2′-carboxy-2-formylazobenzene or by treating 2,2′-dicarboxyhydrazobenzene with phosphorus pentachloride, and by Bamberger[2,13,14] through photo-irradiation of 2,2′-diformylazoxybenzene or by treating the latter with boiling acetic acid. More recently the compound with m. p. 302° was obtained as a reaction product of azobenzene and carbon monoxide under pressure.[15,16]

On the basis of the i.r. absorption spectra of the compound with m. p. 185°, which exhibits a strong lactone or ester carbonyl band, and of the compound with m. p. 302°, which exhibits a strong amide carbonyl absorption, Mosby[17] ascribed structure (III) to the former and structure (II) to the latter compound. These may be designated respectively as indazolo[2,3-*a*]-[3,1]benzoxazin-5-one and indazolo[2,1-*a*]indazole-6,12-dione.

We have carried out further spectroscopic, chemical, and mass spectroscopic examination of the compounds in question as well as of the related model compounds: 2-phenylindazol-3-one (IV; R = H), 2-(2-carboxyphenyl)indazol-3-one (IV; R = CO_2H), 2-phenyl-3,1-benzoxazin-4-one (V), isatoic anhydride (VI), and dianthranilide (VII). As reported below the results generally support the structures proposed by Mosby.

The i.r. measurements of absorption in the 6μ region are shown in Table 1. The strong similarities between the spectrum of the compound with m. p. 185° and that of 2-phenyl-3,1-benzoxazin-4-one (V) clearly support the lactone structure (III) for the former which we will therefore refer to as indazole benzolactone.

A study of model compounds showed that those containing the grouping O=C–O–C=X exhibit an i.r. band at about 1805 cm.$^{-1}$ (Table 1). However, this band is not present in the spectrum of the indazole benzolactone and therefore suggests the structures (IIIb) or (IIIc) rather than the quinonoid structure (IIIa). On the other hand, the observed bands at 1645 and 1740 cm.$^{-1}$ may possibly arise from an *o*-quinone grouping[18] so a clearcut decision between the possible ground structures (IIIa), (IIIb), or (IIIc) cannot be made from

TABLE 1

Infrared absorption bands*

Structure	I.r. bands (cm.$^{-1}$)	Structure	I.r. bands (cm.$^{-1}$)
(III; a, b, or c)	1780 (9·7)	(V)	1809 (2·6)
	1740 (6·7)		1780 (9·8)
	1645 (10·0)		1750 (8·0)
	1620 (9·5)		1720 (5·0)
	1600 (7·3)		1620 (9·0)
			1605 (8·7)
			1580 (8·2)
(VI)	1805 (6·0)	Phthalic anhydride	1855 (7·6)
	1780 (9·6)		1805infl. (6·8)
	1735 (9·6)		1790 (7·6)
	1690sh (8·2)		1760 (9·0)
	1660sh (7·0)		1600 (5·4)
	1610 (8·9)		
	1605 (8·5)		
(II)	1740 (8·7)	(IV; R = H)	1670infl. (9·3)
	1720sh (9·6)		1650 (9·7)
	1690 (10·0)		1620infl. (9·2)
	1670sh (9·6)		1600 (9·0)
	1625 (10·0)		
	1598 (9·2)		
(IV; R = COOH)	1720 (9·8)	(VIIa)	1690sh (9·8)
	1650infl. (7·5)		1680 (10·0)
	1630 (9·6)		1655 (9·9)
	1605 (9·9)		1620 (9·5)
	1570 (9·8)		1595 (9·0)

* Relative intensities of absorption bands with respect to the strongest band in the 6μ region are shown in brackets.

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[1] G. Heller, *Ber.*, 1916, **49**, 523.
[2] E. Bamberger, *Ber.*, 1911, **44**, 1966.
[3] P. Freundler, *Compt. rend.*, 1903, **136**, 370.
[4] P. Freundler, *Compt. rend.*, 1904, **138**, 289.
[5] P. Freundler, *Bull. Soc. chim. France*, 1904, [3], **31**, 449.
[6] P. Freundler, *Bull. Soc. chim. France*, 1904, [3] **31**, 876.
[7] P. Freundler, *Compt. rend.*, 1904, **138**, 1425.
[8] P. Carré, *Compt. rend.*, 1905, **140**, 663.
[9] P. Carré, *Ann. Chim. Phys.*, 1905, [8] **6**, 408.
[10] P. Carré, *Bull. Soc. chim. France*, 1905, [3] **33**, 1161.
[11] P. Carré, *Compt. rend.*, 1906, **143**, 54.
[12] P. Carré, *Bull. Soc. chim. France*, 1906, [3] **35**, 1275.
[13] E. Bamberger, *Ber.*, 1907, **39**, 4252.
[14] E. Bamberger and J. Lublin, *Ber.*, 1909, **42**, 1676.
[15] W. W. Pritchard, U.S.P. 2,769,003/1956.
[16] Shigeki Horie, *J. Chem. Soc. Japan*, 1959, **80**, 1038.
[17] W. L. Mosby, *Chem. and Ind.*, 1957, 17.
[18] W. Otting and G. Staiger, *Chem. Ber.*, 1955, **88**, 828.

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the i.r. spectrum. The spectrum of the compound with m. p. 302° shows a strong band near 1700 cm.$^{-1}$ with subsidiary bands at 1740, 1720, and 1670 cm.$^{-1}$ indicative of a fused γ-lactam structure with ring strain [19] as shown in (II). Reduction in ring strain as in 2-phenylindazol-3-one and 2-(2-carboxyphenyl)indazol-3-one causes a shift of the absorption bands to longer wavelengths. The compound with m. p. 302° may therefore be referred to as benzoylene indazolone, *i.e.*, (II). Its complete i.r. spectrum differs markedly from that of the indazolebenzolactone thus confirming that the compounds are structural isomers and not stereoisomers. The differences noted in the u.v. spectra also point to the presence of different chromophoric systems.

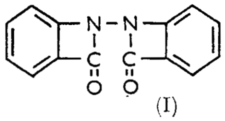
Structure (I) may be eliminated from further consideration since it was found that treatment of 2-(2-carboxyphenyl)indazol-3-one with boiling acetic anhydride for a few minutes yielded approximately equal quantities of benzoylene indazolone and indazole benzolactone. The indazole structure is unlikely to change under these conditions. Likewise the possibility of a rearrangement involving nitrogen–nitrogen group migration during interconversion of the two compounds (III) and (II) to give a compound of structure (VIII) can be excluded since alkaline hydrolysis of both compounds furnished the same carboxyphenylindazolone.

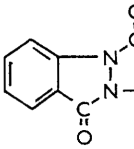
The thermal stability of indazole benzolactone (III) and of the benzoylene indazolone (II) was examined. Heating (III) in a sealed tube at 280° for 24 hours converted it into (II) with some tar formation. Compound (II) under the same conditions remained unchanged in m. p. and i.r. spectrum, although it did exhibit thermochromic change, being deep yellow at 280°, and reverting to the colourless form on cooling. The mechanism of the change was not investigated, but it might arise through broadening of the near visible absorption band (3540 Å) owing to thermal redistribution of molecules among other energy states.[20]

A different mechanism probably applies to the thermochromism which was observed when dianthranilide (VIIa) was heated. At 360°, a yellow sublimate was obtained which when separately heated, softened around 160° and progressively changed into the colourless dianthranilide (m. p. 320°) again. The i.r. spectrum of the yellow sublimate possessed increased absorption at 1740 cm.$^{-1}$ and a new band near 3440 cm.$^{-1}$. The changes observed might arise through nitrogen–oxygen migration of H with generation of phenhomazine or quinonoid structures such as (VIIb) or (VIIc).

The chemical stability of the compounds (III) and (II) was also examined. Treatment of (III) with boiling acetic anhydride progressively converted it into (II), the conversion being substantially complete after 24 hours. The benzoylene indazolone (II) was unaffected by similar treatment.

Further confirmation of the lactone nature of (III) was obtained by comparing the relative rates of alkaline hydrolysis of (II) and (III) using the hydrolytic stability of a blank and of 2-(2-carboxyphenyl)indazolone as upper and lower base lines, respectively. As can be seen from the Experimental section, the hydrolysis of the indazole benzolactone is rapid compared to that of benzoylene indazolone and is close to completion after 40 minutes under the conditions used.


(I)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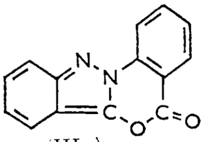
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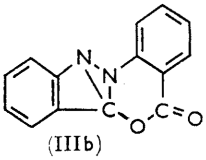
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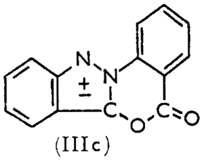
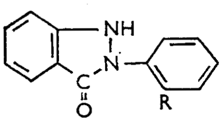
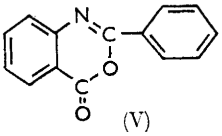
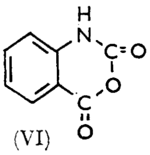

(IIIc)



(IV)


(V)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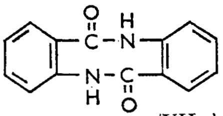
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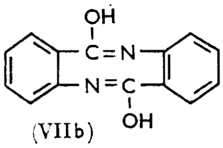
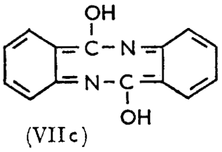
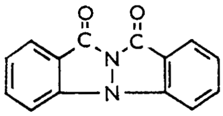

(VIIb)


(VIIc)


(VIII)

We now sought to confirm further the structures of (II) and (III) by comparing their mass spectra with those of the model compounds 2-phenylindazol-3-one (IV; R = H), 2-(2-carboxyphenyl)indazol-3-one (IV; R = CO_2H), and 2-phenyl-3,1-benzoxazin-4-one (V). Indeed the latter compounds gave spectra which could be rationalised on the basis of the fragmentation modes shown in Table 2.

The mass spectra of the compounds (IV) with R = H and R = CO_2H were similar after the latter had lost its carboxy-group as CO and H_2O. The ions $m/e = 154$ and 153 were shown by mass measurement to correspond to the fragments $C_{11}H_8N$ and $C_{11}H_7N$. These fragments must arise after elimination of a nitrogen conjoined with a ring CH, as HCN, with probable bond formation at the point of elision. Similar bond formation has been noted on elimination of CO from anthraquinone subjected to electron impact.[21] The presence

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[19] P. E. Gagnon, J. L. Boivin, R. MacDonald, and L. Yaffe, *Canad. J. Chem.*, 1954, **32**, 823.

[20] W. T. Grubb and G. B. Kistiakowsky, *J. Amer. Chem. Soc.*, 1950, **72**, 419.

[21] J. H. Beynon, G. R. Lester, and A. E. Williams, *J. Phys. Chem.*, 1959, **63**, 1861.

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in the spectrum of (IV; R = H) of a metastable ion at $m/e = 51{\cdot}7$ indicates a direct fission of $210^+ \longrightarrow 104^+ + 106$ whilst in (IV; R = CO_2H) $m/e = 41{\cdot}7$ indicates the fission $254^+ \longrightarrow 103^+ + 151$. The compound (V) behaved quite differently to (IV; R = H or CO_2H). Both CO and CO_2 were eliminated and in each case a metastable ion was observed. Other fragmentation modes involved removal of the pendant phenyl group and fission of the carbon–nitrogen bond. All three compounds gave strong doubly charged parent ions.

TABLE 2

Main fragments in mass spectra

m/e	I (%) [a]	Formula [b]	Fragmentation path	Neutral fragment
			Compound (IV; R = H)	
210	100	$C_{13}H_{10}N_2O$	Molecular ion	—
181	35	$C_{12}H_9N_2$	$210^+ \xrightarrow{*} 181^+ + 29$	CHO
154	4	$C_{11}H_8N$	$181^+ \xrightarrow{*} 154^+ + 27$	HCN
104	19	C_7H_4O	$210^+ \xrightarrow{*} 104^+ + 106$	$C_6H_6N_2$
			Compound (IV; R = CO_2H)	
254	12	$C_{14}H_{10}N_2O_3$	Molecular ion	—
236	100	$C_{14}H_8N_2O_2$	$254^+ \xrightarrow{*} 236^+ + 18$	H_2O
208	19	$C_{13}H_8N_2O$	$236^+ \xrightarrow{*} 208^+ + 28$	CO
181	2	$C_{12}H_7NO$	$208^+ \longrightarrow 181^+ + 27$	HCN
180	4	$C_{12}H_8N_2$	$208^+ \xrightarrow{*} 180^+ + 28$	CO
179	8	$C_{12}H_7N_2$	$208^+ \xrightarrow{*} 179^+ + 29$	CHO
153	2	$C_{11}H_8N$	$180^+ \longrightarrow 153^+ + 27$	HCN
			Compound (V)	
223	100	$C_{14}H_9NO_2$	Molecular ion	—
195	4	$C_{13}H_9NO$	$223^+ \xrightarrow{*} 195^+ + 28$	CO
179	48	$C_{13}H_9N$	$223^+ \xrightarrow[\text{(broad)}]{*} 179^+ + 44$	CO_2
167	2	$C_{12}H_9N$	$195^+ \longrightarrow 167^+ + 28$	CO
146	18	$C_8H_4NO_2$	$223^+ \xrightarrow{*} 146^+ + 77$	C_6H_5
105	66	C_7H_5O	$195^+ \xrightarrow{*} 105^+ + 90$	C_6H_4N
90	13	C_6H_4N	$179^+ \longrightarrow 90^+ + 89$	C_7H_5
77	60	C_6H_5	$105^+ \longrightarrow 77^+ + 28$	CO
			Compound (II)	
236	100	$C_{14}H_8N_2O_2$	Molecular ion	—
208	22	$C_{13}H_8N_2O$	$236^+ \xrightarrow{*} 208^+ + 28$	CO
180	5	$C_{12}H_8N_2$	$208^+ \xrightarrow{*} 180^+ + 28$	CO
179	12	$C_{12}H_7N_2$	$208^+ \xrightarrow{*} 179^+ + 29$	CHO
153	3	$C_{11}H_7N$	$180^+ \xrightarrow{*} 153^+ + 27$	HCN
126	1	$C_{10}H_6$ †	$153^+ \xrightarrow{*} 126^+ + 27$	HCN
104	3	C_7H_4O	$208^+ \longrightarrow 104^+ + 104$	$C_6H_4N_2$
93	2	C_6H_5O †	$208^+ \xrightarrow{*} 93^+ + 115$	C_6H_5N + HCN
90	6	C_6H_4N	$179^+ \longrightarrow 90^+ + 89$	C_6H_3N
63	6	C_5H_3	$90^+ \xrightarrow{*} 63^+ + 27$	HCN

* Denotes a metastable ion was observed. † Not mass measured.

[a] I = % intensity of base peak. [b] Formula derived from accurate mass measurement.

The mass spectrum of benzoylene indazolone (II) also showed a strong doubly charged parent ion. The spectrum revealed that the primary fragmentation route is the successive elimination of 2 molecules of CO with formation of a strong metastable ion in each case (see Table 2). A metastable ion near $m/e = 130$ indicated fission of $180^+ \longrightarrow 153^+ + 27$ which corresponds to elimination of HCN as in the case of (IV; R = H and CO_2H). In a second fragmentation path the preferred ion lay at $m/e = 179$ ($C_{12}H_7N_2$).

The mass spectrum of benzoylene indazolone was also examined for any evidence that the structure might be (I), which would probably give fragments at masses $P/2$ and $(P - CO)/2$. These masses were indeed found but the presence of weak ions at $m/e = 118{\cdot}5$ and $90{\cdot}5$ showed them to be entirely due to doubly charged ions.

Unexpectedly, the mass spectrum of the indazole benzolactone (III) was identical with that of benzoylene indazolone. From the known instability of the oxygen–carbon linkage of the lactone it must be concluded that under electron impact immediate rearrangement to benzoylene indazolone occurs. Rearrangement of lactones under these conditions has been reported for other systems.[22, 23]

All the data given above therefore fully confirm the lactone structure of bisanthranil, *i.e.*, indazole benzolactone (III), and the amide structure for the benzoylene indazolone (II).

EXPERIMENTAL

Ultraviolet absorption spectra of compounds in methylene dichloride solution (except where stated) were measured on the Optica CF 4 double-beam recording spectrophotometer. Molecular weights of compounds were determined from their mass spectra, measured on an A.E.I. MS 9, using the direct insertion probe technique. Infrared absorption spectra of solids (1 mg.) dispersed in KBr discs were measured on a Perkin-Elmer Infracord.

Indazolo[2,3-a][3,1]*benzoxazine*-5-*one*.—This was prepared by refluxing 2,2′-dicarboxyhydrazobenzene in acetic anhydride for 20 min.[1] The lactone was repeatedly crystallised from toluene, taken up in dry benzene, filtered through a thin layer of alumina (pH 4·5), and finally recrystallised from benzene as soft pale yellow needles, m. p. 185°. The i.r. absorption spectrum showed no band at 1700 cm.$^{-1}$ (absence of amide) (Found: C, 71·3; H, 3·3; N, 11·8%; *M*, 236·059. Calc. for $C_{14}H_8N_2O_2$: C, 71·2; H, 3·4; N, 11·8%; *M*, 236·059); $\lambda_{\text{max.}}$ 294 and 304sh mμ (log ε 4·21 and 4·09). Extinction coefficients, ε, at 420, 500, 600, and 650 mμ (toluene solution) were 13·6, 1·4, 0·9, and 0·7, respectively.

Indazolo[2,1-a]*indazole*-6-12-*dione*.—This compound was best prepared by prolonged (10—24 hr.) treatment of 2,2′-hydrazobenzoic acid with boiling acetic anhydride,

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[22] L. Friedman and F. A. Long, *J. Amer. Chem. Soc.*, 1953, **75**, 2832.

[23] F. W. McLafferty, *Analyt. Chem.*, 1959, **31**, 82.

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from which the indazolone crystallised on cooling in ice. Recrystallisation from benzene or toluene gave the indazolone as prisms, m. p. 302° (Found: C, 71·2; H, 3·3; N, 12·0%; *M*, 236·059. Calc. for $C_{14}H_8N_2O_2$: C, 71·2; H, 3·4; N, 11·9%; *M*, 236·059); $\lambda_{max.}$ 242, 262, 270, and 354 mμ (log ε 4·66, 4·06, 4·09, and 4·20, respectively). Extinction coefficients, ε ,at 400, 420, and 480 mμ (methylene dichloride) were 9·3 ,0·6, and 0·4, respectively.

Indazolo[2,1-*a*]indazole-6,12-dione was recovered unchanged (m. p. and i.r. spectrum) after heating for 24 hr. at 280°. At this temp. it had a deep yellow colour, but again became colourless on cooling.

2-(2-*Carboxyphenyl*(*indazol*-3-*one*.—This was prepared by hydrolysing the lactone, m. p. 185°, with aqueous sodium hydroxide (10%) for 1 hr. on a steam-bath. After filtration to remove a little insoluble material and cooling to 0° the free acid was liberated by addition of ice-cold hydrochloric acid and was recrystallised from aqueous ethanol (under nitrogen) as white needles. On heating, the compound was smoothly converted into indazolo[2,1-*a*]-indazole-6,12-dione, so therefore had the same m. p. 302°. It differed from the dione in its rapid solubility in aqueous alkali (Found: C, 66·1; H, 4·1; N, 11·2. Calc. for $C_{14}H_{10}N_2O_3$: C, 66·1; H, 4·0; N, 11·0%).

Alkaline hydrolysis (4 hr. at 90°) of benzoylene indazolone produced the same compound, confirmed by direct comparison of i.r. spectra.

2-*Phenylindazol*-3-*one*.—This was prepared [24] by treating 2-phenylhydrazine benzoic acid with phosphoryl chloride in pyridine, and had m. p. 216° (from ethanol) (Found: C, 74·2; H, 4·8; N, 13·6. Calc. for $C_{13}H_{10}N_2O$: C, 74·3; H, 4·8; N, 13·3%).

2-*Phenyl*-3,1-*benzoxazin*-4-*one*.—This was prepared [25] by refluxing benzoylanthranilic acid with acetic anhydride, and had m. p. 121° (from benzene) (Found: C, 75·2; H, 4·0; N, 6·3. Calc. for $C_{14}H_9NO_2$: C, 75·3; H, 4·0; N, 6·3%).

Isatoic Anhydride and Phthalic Anhydride.—These were commercial samples purified by crystallisation (dioxan) and sublimation, respectively.

Dianthranilide.—This was prepared from methyl anthranilate by the literature method [26] and was recrystallised from ethanol, m. p. 339—340° (Found: C, 70·4; H, 4·2; N, 11·7%; *M*, 238·075. Calc. for $C_{14}H_{10}N_2O_2$: C, 70·6; H, 4·2; N, 11·8%; *M*, 238·075).

Cyclisation of 2-(2-*Carboxyphenyl*(*indazol*-3-*one*.—The acid was either suspended in acetic anhydride for 10 days at room temp. or refluxed with acetic anhydride for 5 min. and immediately cooled. Either method gave almost equal quantities of the lactone, m. p. 185°, and of the benzoylene indazolone, m. p. 302°, confirmed by mixed m. p. and i.r. spectra.

Comparative Rates of Hydrolysis.—The alkaline hydrolysis rates of 2-(2-carboxyphenyl)indazol-3-one (IV; R = CO_2H), its lactone m. p. 186° (III), and of indazolo[2,1-*a*]indazole-6,12-dione (II) were compared as follows. Each compound (50 mg.) was dissolved in 'AnalaR' dioxan (20 ml.), freshly distilled from sodium, and deoxygenated distilled water (10 ml.) in an enclosed cell and the soln. maintained at 41° ± 1°. Immersed in the soln. were the bulbs of a thermometer and a glass electrode, and a potassium chloride–Agar bridge linking the soln. with saturated potassium chloride soln. containing a saturated calomel reference electrode. A Pye pH-meter was used to determine the pH of the solution. 0·1N-Sodium hydroxide (2·20 ml.) was added from a burette, and as soon as the solutions were mixed the pH was noted (maximum value), and thereafter at regular intervals. The results, together with a blank run are in Table 3. Duplicate experiments were in good agreement.

TABLE 3

pH values showing comparative hydrolysis rates

Time (min.)	Blank	(IV; R = CO_2H)	(III) (M. p. 185°)	(II) (M. p. 302°)
0	13·25	10·15	11·10	13·11
5	13·25	10·11	10·64	12·35
10	13·25	10·06	10·55	11·95
20	13·21	9·95	10·50	11·56
40	13·08	9·88	10·38	11·28

Conversion Experiments.—The lactone (III) (200 mg.) was refluxed with 'AnalaR' acetic anhydride (10 ml.) for a given period. The solution was cooled for 1 hr. in an ice-bath, and the separated solid filtered off, washed with petroleum, dried, and weighed. M. p., mixed m. p., and i.r. spectrum showed this was benzoylene indazolone (II). The filtrate was evaporated under reduced pressure with addition of benzene. The recovered solid was weighed and shown to be unchanged lactone (m. p. and i.r. spectrum). The results are in Table 4.

TABLE 4

Time of reflux	Lactone (III) (m. p. 185°)	Benzoylene indazolone (II) (m. p. 302°)
1 hr.	56%	44%
6 hr.	15	85
24 hr.	<2·5	97·5

Treatment of the benzoylene indazolone (II) with boiling acetic anhydride for 6 or for 24 hr. led to no rearrangement; only starting material was recovered.

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