Acknowledgment. We would like to thank Dr. S. Barcza for helpful discussions and also his staff for providing the spectral and analytical data. We are indebted to Dr. Renate Coombs and her staff for recording the mass spectra.

Registry No.—**1a,** 26859-66-5; **1b,** 61139-60-4; **1c,** 41581-41-3; **1d,** 61139-61-5; **1e,** 28006-50-0; **1f,** 36033-98-4; **1g,** 36033-95-1; **1h,** 36037-78-2; **1i,** 36033-91-7; **2d,** 61139-62-6; **2e,** 61139-55-7; **2f,** 61139-56-8; **2g,** 61139-57-9; **2h,** 61139-58-0; **2i,** 61139-59-1; **3e,** 36033-89-3; **3f,** 36033-99-5; **3g,** 36033-96-2; **3h,** 36037-79-3; **3i,** 36033-92-8; **4e,** 28006-52-2; **4f,** 36033-97-3; **4g,** 36033-94-0; **4h,** 36037-71-1; **4i,** 36033-90-6; **5,** 61139-63-7; **6,** 61139-64-8; **7a,** 61139-65-9; **7b,** 61139-66-0; **8a,** 61139-53-5; **8b,** 61139-54-6; **9,** 61139-67-1; 2-(4-chlorobenzoyl)benzoic acid ethyl ester, 51476-10-9; methyl α-bromo-*o*-toluate, 2417-73-4.

Supplementary Material Available. Additional experimental and spectral and analytical information (Tables II–IV) (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) M. K. Eberle and W. J. Houlihan, *Tetrahedron Lett.*, 3167 (1970).
(2) W. J. Houlihan and M. K. Eberle, U.S. Patent 3 642 814 (1972).
(3) G. Egerer and H. Meyer, *Monatsh. Chem.*, **34,** 69 (1913).
(4) M. K. Eberle, W. J. Houlihan, and P. Schirm, *J. Org. Chem.*, **38,** 3872 (1973).
(5) (a) H. J. Sare and E. F. M. Stephenson, *J. Chem. Soc.*, 1149 (1969); (b) H. D. Bartfeld, W. Flitsch and K. Gurke, *Chem. Ber.*, **107,** 189 (1974).
(6) R. Stolle, *Chem. Ber.*, **63,** 1032 (1932).
(7) S. M. Kupchan and H. C. Wormser, *J. Org. Chem.*, **30,** 3792 (1965).
(8) (a) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Vol. 24, Academic Press, New York, N.Y., 1972; (b) L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley New York, N.Y., 1972, No. 435; (c) W. Adcock and B. D. Gupta, *J. Org. Chem.*, **41,** 1498 (1976).
(9) (a) A. H. Lewin, J. Lipowitz, and T. Cohen, *Tetrahedron Lett.*, 1241 (1965); (b) P. L. Southwick, J. A. Fitzgerald, and G. E. Milliman, *ibid.*, 1247 (1965).
(10) G. C. Brumlik, R. L. Baumgarten, and A. I. Kosak, *Nature (London)*, **201,** 388 (1964).
(11) R. H. Bible, "Interpretation of NMR Spectra", Plenum Press, New York, N.Y., 1965.
(12) We have prepared this known compound[7] more conveniently from *o*-toluic acid methyl ester by direct bromination.

Furazans and Furazan Oxides. 7.[1] Interconversions of Anthranils, Benzofurazan Oxides, and Indazoles

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7-Nitroanthranil (1, R = R′ = H) and 4-formylbenzofurazan oxide (2, R = R′ = H) equilibrate on heating. The latter condenses with primary amines and the resulting imines rearrange to 7-nitroindazoles (8). The corresponding 6-methoxy and 6-chloro derivatives of 1 behave similarly. Neither 5- nor 6-nitroanthranil forms an indazole on heating with aniline or other primary amines.

An example of a general heterocyclic rearrangement which was first described some years ago[2] is the interconversion of 7-nitroanthranils with 4-acylbenzofurazan oxides (1 ⇌ 2). In the earliest case to be investigated[2,3] (1, R = Me; R′ = H) the reaction was found to proceed in the direction 2 → 1, to provide 1 exclusively. Later,[4] an example was discovered (1 ⇌ 2, R = H; R′ = Cl) in which at normal temperatures the furazan oxide isomer 2 was thermodynamically the more stable compound, and it was suggested that steric inhibition of resonance of the nitro group with the ring system of 1 led to its destabilization, with consequent preference for structure 2. We now find that, in the simplest example of this system (1 ⇌ 2, R = R′ = H) the equilibrium balance is finely poised, with only a moderate preference (K = [1]/[2] = ca. 2) for 1.

7-Nitroanthranil (1, R = R′ = H) was prepared as follows. 3-Nitrosalicylaldehyde (3) was warmed with tosyl chloride in dry pyridine. Initially, a small amount of the tosylate 4 separated: this redissolved, and the pyridinium salt[5a] 5 crystallized out. The salt 5 was dissolved in aqueous sodium azide solution, giving the azide 6, which was decomposed in hot toluene.

Condensation of the acyl group of 2 with a primary amine, followed by rearrangement, leads to the formation of 2-substituted indazoles (7 → 8).[2,3] Consistent with this, we find that reflux of the nitroanthranil (1, R = R′ = H) with aniline produces 7-nitro-2-phenylindazole (8, R′ = H; R″ = Ph), through condensation of the intermediate 4-formylbenzofurazan oxide (2, R = R′ = H) with the aniline. An attempt to extend this reaction to the preparation of 2-methyl-7-nitroindazole (8, R′ = H; R″ = Me), by heating 1 (R = R′ = H) with methylamine in ethanol, led to the formation of ethyl 3-nitroanthranilate (9), and the corresponding methylamide (10). It appears that the alkylamine is sufficiently strong a base to

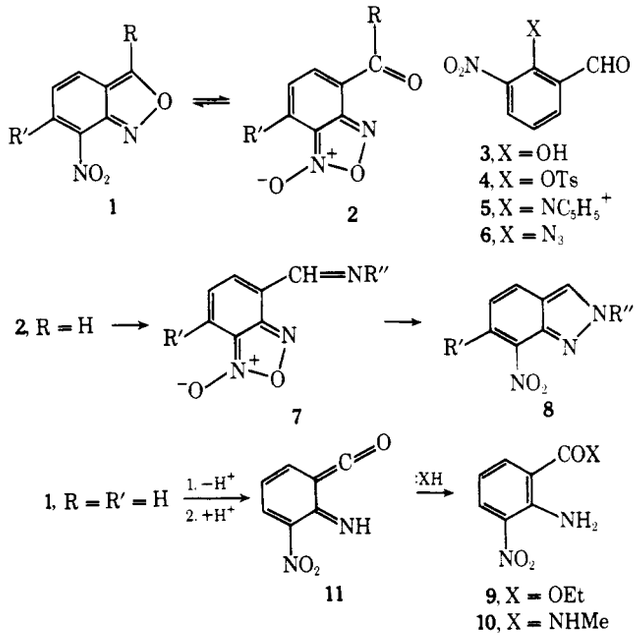


Table I. Indazoles 8 from Benzofurazan Oxides 2 and Amines

Compd	Indazoles 8 R′	R″	Mp, °C	Recrystn solvent	Yield, %	Mol formula	Calcd, % C	H	N	Found, % C	H	N
8a	H	Ph	168–169	C_6H_{14}/EtOAc	74	$C_{13}H_9N_3O_2$	65.3	3.8	17.6	65.2	3.8	17.4
8b	H	Me	145–146	EtOH/H_2O	36	(lit.[22] mp 146–147 °C)						
8c	H	Et	73–74	EtOH/H_2O	45	$C_9H_9N_3O_2$	56.5	4.7	22.0	56.0	4.9	21.3
8d	H	*t*-Bu	Oil		66	$C_{11}H_{13}N_3O_2$	60.3	6.0		59.9	6.1	
8e	H	CH_2Ph	122–123	EtOH/H_2O	37	$C_{14}H_{11}N_3O_2$	66.4	4.4	16.6	65.6	4.5	16.6
8f	Cl	Ph	145–146	EtOAc	71	$C_{13}H_8ClN_3O_2$	57.1	2.9	15.4	57.2	2.9	15.3
8g	Cl	Me	160–161	C_6H_{14}/EtOAc	28	$C_8H_6ClN_3O_2$	45.5	2.8	19.9	45.4	2.8	19.8
8h	OMe	Ph	183.5	C_6H_{14}/EtOAc	62	$C_{14}H_{11}N_3O_3$	62.4	4.1	15.6	62.3	4.0	15.6
8i	OMe	Me	153	EtOH	56	$C_9H_9N_3O_3$	52.2	4.4	20.3	52.3	4.3	20.4

Table II. NMR Spectra of the Nitroindazoles 8 in $CDCl_3$

Compd[a]	Chemical shifts, δ[b] H(3)	H(4)	H(5)	H(6)	$J_{4,5}$[c]	$J_{5,6}$[c]	Other spectral constants[b,c]
8a	8.63	8.09	7.20	8.34	8.2	7.5	Ph: 8.0 (m, 2 H), 7.5 (m, 3 H)
8b	8.22	8.05	7.15	8.32	8.3	7.3	Me: 4.35 (s)
8c	8.25	8.08	7.20	8.36	8.0	7.5	$J_{4,6}$ = 1 Hz. Et: 2.70 (t, 3 H), 4.64 (q, 2 H)
8d	8.30	8.05	7.14	8.27	8.0	7.3	$J_{4,6}$ = 1 Hz. *t*-Bu: 1.80 (s)
8e	8.01	7.98	7.17	8.34	8.2	7.5	CH_2: 5.72 (s), Ph: 7.36 (s)
8f	8.52	7.82	7.12	(Cl)	9.0		Ph: 7.8 (m, 2 H), 7.4 (m, 3 H)
8g	7.90	7.75	6.95	(Cl)	8.5		Me: 4.05 (s)
8h	9.24	8.19	7.29	(OMe)	9.0		OMe: 4.04 (s), Ph: 8.1 (m, 2 H), 7.3 (m, 3 H)
8i	7.96	7.77	6.97	(OMe)	9.0		OMe: 4.20 (s), NMe: 4.00 (s)

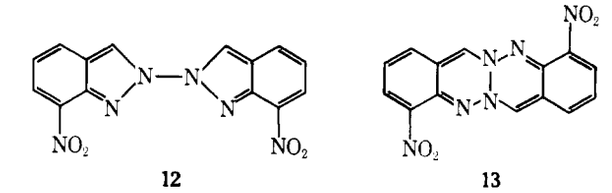
[a] See Table I. [b] δ in parts per million from Me_4Si. [c] *J* in hertz.

cause deprotonation from C(3) of the anthranil **1**; the ketene intermediate (**11**) reacts rapidly with any available nucleophile. Aniline, being less basic under the reaction conditions, does not decompose the anthranil, which therefore has time to rearrange and the formyl group to condense as indicated.

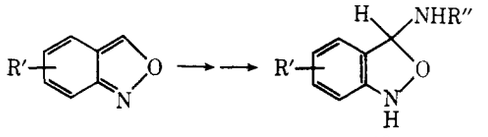
The above argument suggested that a successful reaction with methylamine might ensue if the intermediate 4-formylbenzofurazan oxide were used instead of the anthranil. This compound (**2**, R = R′ = H) was separated by PLC from the mixture produced by thermal equilibration of **1**, after enrichment of the content of the thermodynamically less stable **2**, taking advantage of the fact that the nitroanthranil is considerably less soluble in cold toluene than is the formylbenzofurazan oxide (see Experimental Section). The furazan oxide did indeed condense with a variety of amines (see Table I), to form the corresponding 2-substituted 7-nitroindazoles, but the reaction was not a clean one: with the alkylamines (R″ = Me, Et, $PhCH_2$) a purplish color was usually formed immediately on mixing the reactants, probably because of Meisenheimer complex formation, and the indazoles were contaminated with tarry by-products, which were, however, easily separated by thick layer chromatography. With hydrazine the diindazolyl **12** was formed, the mass spectrum of which showed cleavage of the molecule, with H transfer, to the 7-nitroindazole molecular ion. This provides evidence against the alternative formulation **13**, while the IR spectra contraindicated the unrearranged azine structure.

The substituted nitroanthranils (**1**, R = H; R′ = Cl and OMe) form equilibria with the corresponding furazan oxides **2**, which favor **2** to a greater extent than in the case where R = R′ = H. After a preliminary thermal equilibration of the nitroanthranils, indazoles were formed in satisfactory yields from both aliphatic and aromatic amines in these cases (see Table I).

A reasonable alternative mechanism for the indazole (**8**) formation involves attack of the aniline directly at the anthranil 3 position, followed by ring opening, and recyclization of the phenylhydroxylamine derivative **14**. There is literature precedent to support such a pathway. Thus, anthranil and hydroxylamine have long been known to react to form 2-hydroxylaminobenzaldoxime,[6] and, more recently, Taylor and Bartulin[7] have shown that carbanions condense with anthranil by nucleophilic attack at C(3), followed by ring opening and recyclization, to form a variety of quinoline derivatives. Such a mechanism does not require the presence of the 7-nitro group, and indeed Joshi and Gambhir[8a,b] have reported a number of reactions in which 6-nitroanthranils condense with aromatic amines, to give the corresponding indazoles. We believe, however, that in the present examples the rear-



12 **13**



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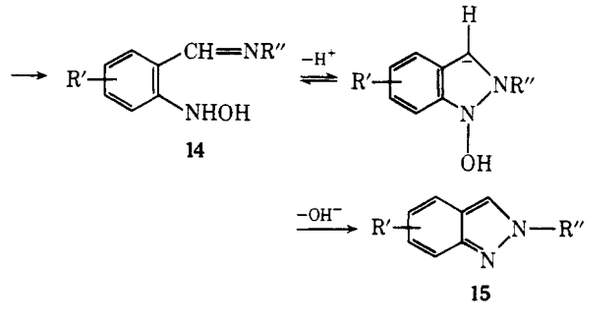

14 **15**

rangement to the 4-formylbenzofurazan oxide *is* a necessary step in the reaction, and furthermore we have been unable to reproduce the results[8a] with 6-nitroanthranil. Indeed, it is clear that, with respect to the reaction with aniline, the report of Joshi and Gambhir must be erroneous: they quote for the product (6-nitro-2-phenylindazole, **15**; R′ = 6-NO_2; R″ = Ph) a melting point of 325 °C. This compound had already been reported[9] in 1940 as melting at 149 °C. We repeated the preparation of Chardonnens and Heinrich,[9] and were able to confirm the identity of their product by NMR and mass spectrometry. We could not isolate from the reaction of 6-nitroanthranil with aniline a product corresponding to that described by Joshi and Gambhir,[8a,c] and so can make no constructive suggestions concerning its structure. We were also unable to prepare the 6,6′-dinitro-2,2′-diindazolyl which they report as arising from 6-nitroanthranil with hydrazine acetate. 5-Nitroanthranil and aniline also gave no indazole: after prolonged heating, with considerable decomposition, only starting nitroanthranil was isolated.

Our results also have a bearing on the mechanism of base-induced decomposition of 3-unsubstituted anthranils, which we represented above as proceeding by initial proton abstraction from C(3) (**1** → **11**).[10] Taylor and Bartulin,[7] on the basis of their work on the reaction of carbon nucleophiles with anthranil, have suggested that addition of the base (as a nucleophile) is the first step, *in general,* and that deprotonation from C(3) of the adduct (cf. **16**) follows, leading to cleavage of the O–N bond and formation of anthranilic acid derivatives (cf. **9**, **10**). This view has recently received support in an authoritative review,[11] which, however, cited in its favor the 6-nitroanthranil results[8a,b] which we now have shown to be, at least in part, incorrect. If nucleophilic addition preceded ring cleavage in the reaction of 7-nitroanthranil (**1**, R = R′ = H) with ethanolic methylamine, the major product (if an indazole is not formed) would be expected to be the amide **10**, not the ester **9**. We consider therefore that the mechanism of Taylor and Bartulin,[7] while essentially correct so far as it concerns their own results, should not be extended to cover the other cases of anthranil conversions into anthranilic acid derivatives.

Experimental Section

Spectrometric instrumentation was as described in earlier parts of this series.[1,12] Silica gel (SiO_2) for preparative layer chromatography (PLC) was Merck Kieselgel 60 PF_{254}. Light petroleum refers to the fraction bp 60–80 °C. Melting points are uncorrected.

1-(2-Formyl-6-nitrophenyl)pyridinium Chloride (5). 3-Nitrosalicylaldehyde[13] (5 g) and tosyl chloride (5.8 g) were separately dissolved in dry pyridine[14] (20 and 40 ml, respectively). The solutions were mixed and a mildly exothermic reaction led to the formation of plates of the tosylate **4**. The mixture was heated to 90 °C for 2 h, when the plates dissolved and yellow prisms of the pyridinium salt **5** separated. These were filtered off, after standing at 0 °C for 12 h, and washed with a little ether: yield 5.4 g (68%), mp 204–205 °C; IR (Nujol) 1690, 1530, 1340 cm^{-1}. Anal. Calcd for $C_{12}H_9ClN_2O_3$: C, 54.5; H, 3.4; N, 10.6; Cl, 13.4. Found: C, 54.3; H, 3.7; N, 10.4; Cl, 12.6.

2-Azido-3-nitrobenzaldehyde (6). Aqueous sodium azide (3 g in 10 ml) was added to the pyridinium chloride **5** (5.3 g) in water (20 ml). After 5 h at 20 °C the precipitated azide **6** was removed by filtration and washed with a little water. A further crop was formed on longer standing of the mother liquors and washings. The azide formed yellow needles, mp 60–61 °C (3.2 g, 82%), from aqueous ethanol: IR (KBr) 2140, 1690, 1525, 1340 cm^{-1}.

Anal. Calcd for $C_7H_4N_4O_3$: C, 43.8; H, 2.1; N, 29.2. Found: C, 44.3; H, 2.1; N, 28.2.

7-Nitroanthranil (1, R = R′ = H) and 4-Formylbenzofurazan Oxide (2, R = R′ = H). The azide **6** (3 g) was heated to reflux in toluene (50 ml) for 5 h. After cooling, some (ca. 0.5 g) impure 7-nitroanthranil separated. The toluene was removed, after filtration, and the residue was taken up in acetone and separated by PLC (SiO_2: two passes toluene/EtOH, 15:1). Two major bands developed, the faster running, after extraction with cold ethanol, affording the furazan oxide (**2**, R = R′ = H) (1.1 g, 42%), and the slower the anthranil (0.7 g, 28%), mp 144–145 °C (lit.[15] mp 144–145 °C). In addition, two fast-moving bands were resolved; one proved to be the unchanged azide **6** (ca. 10 mg), and the other was an isomeric azide (ca. 5 mg), which presumably arose from an impurity in the starting material (**3**).

For the conversion of the anthranil into the furazan oxide, the following procedure was adopted. The anthranil (**1**, R = R′ = H) (ca. 1 g) was heated in refluxing toluene (ca. 10 ml) for 3–4 h, in a recrystallization tube with a side arm containing a glass frit. On cooling, finally in ice, the 7-nitroanthranil, being much less soluble in toluene, largely crystallized out. The solution was expelled through the frit, further toluene was added to the tube, and the process of heating and cooling was repeated until no nitroanthranil crystals separated on cooling. The collected solutions were evaporated to dryness in vacuo, and the residue was separated by PLC as described above.

4-Formylbenzofurazan oxide formed yellow plates, mp 102 °C dec, from acetone: IR (KBr) 1680 (C=O), 1610, 1580, 1550 cm^{-1} (furoxan).

Anal. Calcd for $C_7H_4N_2O_3$: C, 51.2; H, 2.5; N, 17.1. Found: C, 51.7; H, 2.2; N, 16.8.

Thermal equilibration of **1** with **2** (R = R′ = H) at 100 °C in $CDCl_3$ (sealed tube) was established after several hours. The anthranil **1** predominated (ca. 62%); all the furazan oxide bands were exchange broadened (1-oxide ⇌ 3-oxide; cf. ref 4), and so appeared much weaker in the NMR spectrum than those of the anthranil.

6-Chloro-7-nitroanthranil and 7-chloro-4-formylbenzofurazan oxide (**1** and **2**, R = H; R′ = Cl) were prepared as described earlier,[4] but with the following procedural modifications. 4-Chloro-2-nitrotoluene (62 g) was converted into the corresponding benzal diacetate using CrO_3 (100 g) dissolved in acetic anhydride (cf. ref 16), rather than with the solid trioxide.[15] After quenching (ice/water) the crude diacetate (ca. 50 g) was washed with water until the washings were colorless. It was then stirred with 2% aqueous sodium carbonate (300 ml) and filtered. The dried solid was extracted with refluxing light petroleum (bp 60–80 °C) (300 ml), to remove unchanged chloronitrotoluene, and then recrystallized from toluene–light petroleum (1:3), giving the diacetate as prisms (38 g, 37%): mp 121–122 °C (lit.[15] mp 110–111 °C); IR (Nujol) 1760 (C=O), 1530, 1350 cm^{-1} (NO_2).

Anal. Calcd for $C_{11}H_{10}ClNO_6$: C, 45.9; H, 3.5; N, 4.9. Found: C, 46.0; H, 3.6; N, 4.9.

The diacetate was hydrolyzed (HCl/H_2O/EtOH) to the aldehyde,[15] which was reduced to 6-chloroanthranil using stannous chloride.[17] 4-Chloro-2-nitrobenzaldehyde (3.3 g, finely powdered) was added to a stirred solution of stannous chloride dihydrate (12 g) in hydrochloric acid (10 N, 45 ml) at such a rate that the exothermic reaction kept the temperature in the range 27–30 °C. After addition, stirring was continued for 2 h, maintaining the same temperature with a water bath. Water (500 ml) was added, and the mixture was extracted with methylene chloride (3 × 50 ml). The organic extracts were washed with water and 2% aqueous sodium bicarbonate, and were then dried (Na_2SO_4). Removal of solvent left a buff solid which crystallized from light petroleum as white plates (1.9 g, 72%), mp 66–67 °C (lit.[15] mp 61.5–62 °C). The anthranil slowly discolors in the presence of light and air.

The chloroanthranil could also be prepared more conveniently in a one-pot process from the benzal diacetate. The diacetate (10 g) was refluxed for 45 min, with stirring, in hydrochloric acid (10 N, 100 ml), water (20 ml), and ethanol (20 ml). The mixture was then cooled to 25 °C, and, with vigorous stirring, stannous chloride (24 g) in hydrochloric acid (10 N, 50 ml) and water (40 ml) was added slowly, to keep the temperatre at 27–30 °C. Further stirring and workup followed the procedure described above, giving 6-chloroanthranil (3.4 g, 61%). Sometimes a little of the aldehyde impurity was detected (TLC: SiO_2, toluene–ethanol, 15:1) in the product prepared in this way.

Nitration of the anthranil, and rearrangement of the product to the chloroformylbenzofurazan oxide (**2**, R = H; R′ = Cl) was as earlier described.[4] The nitroanthranil was very base sensitive, and a single rapid washing of its methylene chloride extract with ice-cold 1% aqueous sodium bicarbonate was needed to remove nitric acid traces without decomposing the product.

4-Formyl-7-methoxybenzofurazan Oxide (2, R = H; R′ = OMe). 2-Nitroanisaldehyde was prepared by the method of Woodward et al.,[18] and also from *p*-toluidine, by nitration in concentrated sulfuric acid, diazotization, and conversion into 4-hydroxy-2-nitrotoluene, then methylation (Me_2SO_4/NaOH), bromination (NBS), and conversion of the 4-methoxy-2-nitrobenzyl bromide into the aldehyde by Kröhnke's method.[19] The aldehyde was reduced ($SnCl_2/HCl$)[17] to form 6-methoxyanthranil, an oil (40–60% yields), which (0.5 g) was nitrated as described above for the 6-chloro compound. The product (0.45 g, 70%) formed yellow plates, mp 127–129 °C, from ethanol or

light petroleum. The IR spectrum indicated that the solid phase was, at least predominantly, in the formylfuroxan form **2**: ν_{max} (Nujol) 1685 s (C=O), 1618 vs, 1580 vs, 1530 vs, 1500 s, 1460 s, 1435 cm^{-1} s. NMR ($CDCl_3$, −20 °C): two $ABMX_3$ systems, relative intensities 2:1, with δ_A 7.93, δ_B 6.53, δ_M 10.11, δ_X 4.08 ppm, J_{AB} = 8.0 Hz, and $\delta_{A'}$ 8.00, $\delta_{B'}$ 6.70, $\delta_{M'}$ 10.46, $\delta_{X'}$ 4.12, $J_{A'B'}$ = 8.0 Hz. These sets of signals coalesced over the range 35–50 °C, to give a single $ABMX_3$ pattern (at 60 °C), with $\delta_{A''}$ 7.87, $\delta_{B''}$ 6.54, $\delta_{M''}$ 10.32, $\delta_{X''}$ 4.12 ppm, $J_{A''B''}$ = 8.0 Hz. These data are compatible with the existence in solution of a remarkably rapid (above 50 °C) equilibrium between the nitroanthranil (**1**, R = H; R′ = OMe) and *one* of the (1-oxide ⇌ 3-oxide) tautomers of the formylbenzofurazan oxide **2**, the other tautomer being present in undetectably small proportion, but we consider that the more probable explanation is that the NMR spectrum below 35 °C shows the *two* formylbenzofurazan oxide tautomers in a rather slow equilibrium,[20] with the nitroanthranil being an undetected intermediate in their formation, thermodynamically less stable than either furoxan form. The fact that the coupling constants J_{AB} and $J_{A'B'}$ are the same is more in harmony with the latter explanation.

Anal. Calcd for $C_8H_6N_2O_4$: C, 49.5; H, 3.1; N, 14.4. Found: C, 49.3; H, 3.1; N, 14.2.

7-Nitro-2-phenylindazole (8, R′ = H; R″ = Ph). Method A. 7-Nitroanthranil (**1**, R = R′ = H) (0.05 g) was heated under reflux for 20 h in dry tetrahydrofuran (6 ml) with aniline (0.08 g). The solvent was removed by distillation and the residue was recrystallized from hexane/ethyl acetate to give the indazole (0.045 g, 62%), mp 168–169 °C. For analytical and NMR spectral details see Tables I and II. MS M^+ *m/e* 239 (base peak).

Method B. 4-Formylbenzofurazan oxide (**2**, R = R′ = H) (0.06 g) and aniline (0.034 g) were stirred at 25 °C for 4 h in ethanol (25 ml) containing three drops of acetic acid. The yellow precipitate of the indazole (0.065 g, 74%) which formed was filtered off and recrystallized from ethanol.

Reaction of 7-Nitroanthranil with Methylamine. 7-Nitroanthranil (0.5 g) was heated to reflux for 30 min with 30% ethanolic methylamine (10 ml). Removal of solvent under reduced pressure, followed by PLC (SiO_2, hexane/ethyl acetate, 7:3) of the residue gave ethyl 3-nitroanthranilate (**9**, 0.2 g, 32%): mp 108 °C (lit.[21] mp 109 °C); IR (Nujol) 3450, 3350 (NH_2), 1690 (C=O), 1525, 1380 cm^{-1} (NO_2). A minor component was identified as the corresponding *N*-methylamide (**10**): mp 157 °C: IR (Nujol) 3480, 3400, 3370 (NH, NH_2), 1655 (C=O), 1580, 1340 cm^{-1} (NO_2). Anal. Calcd for $C_8H_9N_3O_3$: C, 49.2; H, 4.6; N, 21.5. Found: C, 49.4; H, 4.6; N, 21.4.

Various modifications of the conditions of the above reaction were tried, using buffered methylamine, and using ethanol and acetic acid mixtures as solvent, but in no case was any indazole isolated.

2-Methyl-7-nitroindazole (8, R′ = H; R″ = Me). 4-Formylbenzofurazan oxide (0.08 g) in ethanol (30 ml) and acetic acid (3 drops) was treated with methylamine in ethanol (30%, 0.06 ml). The color immediately changed from light yellow to purplish brown. After stirring for 4 h at 20 °C the now dark brown solution was diluted with water (60 ml) and extracted with dichloromethane (3 × 10 ml). The extracts were dried (Na_2SO_4), passed through a short silica gel column, and then concentrated to small volume and applied to SiO_2 PLC plates. Elution with toluene/ethanol (15:1) gave as the major mobile band the 2-methyl-7-nitroindazole, which was extracted with ethanol. For physical, analytical, and mass spectral data, see Tables I and II.

2-Ethyl-, 2-*tert*-butyl-, and 2-benzyl-7-nitroindazole (8, R′ = H; R″ = Et, *t*-Bu, CH_2Ph), and 2-methyl-6-chloro- and -6-methoxy-7-nitroindazole (8, R′ = Cl and OMe; R″ = Me) were prepared by methods similar to that described for the 2-methyl-7-nitroindazole, from the corresponding amine and the benzofurazan oxide **2**. The 2-phenyl compounds (**8**, R′ = Cl and OMe; R″ = Ph) were prepared from the benzofurazan oxides with aniline in refluxing tetrahydrofuran, the products being isolated by removal of solvent and recrystallization. Physical, analytical, and NMR spectral data are listed in Tables I and II. In addition, all the nitroindazoles showed the expected bands in their IR spectra due to the nitro groups, and a medium intensity peak at 1635–1630 cm^{-1}, from the indazole ring. Mass spectra were obtained for compounds **8a–f** (see Table I); in all but the *tert*-butyl case (**8d**), in which M^+ (219) was 53% of the base peak at *m/e* 163, the parent ion was the base peak.

7,7′-Dinitro-2,2′-diindazolyl (12). 4-Formylbenzofurazan oxide (0.05 g) in ethanol (20 ml) was stirred for 9 h at 20 °C with hydrazinium chloride (0.016 g) and sodium acetate (0.05 g). A yellow solid which separated was washed with water and recrystallized from aqueous ethanol, to afford the dinitrodiindazolyl **12** as a microcrystalline mass (0.015 g, 30%): mp 323 °C dec; MS *m/e* 324 (M^+, 100), 62 (52), 192 (47), 90 (30), 88 (23), 163 (21), 204 (20); IR (KBr) 1635 m, 1515 s (NO_2), 1445 m, 1380 m, 1360 m, 1335 s, 1310 cm^{-1} s (NO_2).

Reaction of 6-Nitroanthranil with Aniline. Repetition of the directions of Joshi and Gambhir,[8a] and also modifying the conditions by using both shorter and longer periods of reflux, led to a complex mixture of products, with, in some cases, recovery of a little starting nitroanthranil. Trituration with hot acetic acid left much material undissolved. The acetic acid soluble fraction again proved to be a mixture of components, from which no crystalline fraction was isolated. No 6-nitro-2-phenylindazole was found (TLC) to be present in the solution. We were likewise unsuccessful in our attempts to isolate a characterizable product from the reaction with hydrazine acetate.[8a]

6-Nitro-2-phenylindazole (15, R′ = 6-NO_2; R″ = Ph). 2-Amino-4-nitrotoluene was converted by the method of Chardonnens and Heinrich[9] into the indazole: mp 150 °C (lit.[9] mp 149 °C); NMR δ 8.82 (d, $J_{3,7}$ = 1 Hz, H-3), 8.57 (br s, H-7), 8.3–7.9 (m, H-5 and *o*-phenyl), 7.7–7.4 (m, H-4 and *m*-, *p*-phenyl); MS *m/e* 239 (M^+, 100), 192 (58), 193 (47), 77 (45), 166 (43), 181 (37), 209 (30).

Reaction of 5-Nitroanthranil with Aniline. 5-Nitroanthranil[15] was heated under reflux with aniline, both alone and in tetrahydrofuran. After a few hours the solutions became dark in color. Removal of solvent left a tarry residue which yielded only recovered nitroanthranil on extraction with light petroleum.

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Registry No.—**1** (R = R′ = H), 4104-37-4; **1** (R = H; R′ = Cl), 22950-43-2; **1** (R = H; R′ = OMe), 61062-97-3; **2** (R = R′ = H), 61062-98-4; **2** (R = R′ = H) 3-oxide derivative, 61062-99-5; **2** (R = H; R′ = Cl), 30080-04-7; **2** (R = H; R′ = Cl) 3-oxide derivative, 61063-00-1; **2** (R = H; R′ = OMe), 61063-01-2; **2** (R = H; R′ = OMe) 3-oxide derivative, 61063-02-3; **3**, 5274-70-4; **4**, 61063-03-4; **5**, 61063-04-5; **6**, 61063-05-6; **8a**, 61063-06-7; **8b**, 13436-58-3; **8c**, 41926-13-0; **8d**, 61063-07-8; **8e**, 61063-08-9; **8f**, 61076-93-5; **8g**, 4199-39-7; **8h**, 61063-09-0; **8i**, 61063-10-3; **9**, 61063-11-4; **10**, 61063-12-5; **12**, 61063-13-6; **15** (R′ = 6-NO_2; R″ = Ph), 61063-14-7; aniline, 62-53-3; methylamine, 74-89-5; ethylamine, 75-04-7; *tert*-butylamine, 75-64-9; benzylamine, 100-46-9; tosyl chloride, 98-59-9; pyridine, 110-86-1; 4-chloro-2-nitrotoluene, 89-59-8; 4-chloro-2-nitrobenzaldiacetate, 1530-56-9; 4-chloro-2-nitrobenzaldehyde, 5551-11-1; 6-chloroanthranil, 14313-60-1; *p*-toluidine, 106-49-0; 4-hydroxy-2-nitrotoluene, 2042-14-0; 4-methoxy-2-nitrobenzyl bromide, 57559-52-1; 4-methoxy-2-nitrobenzaldehyde, 22996-21-0; 6-methoxyanthranil, 61063-15-8; hydrazinium chloride, 14011-37-1.

References and Notes

(1) Part 6: R. Nutiu and A. J. Boulton, *J. Chem. Soc., Perkin Trans. 1*, 1327 (1976).
(2) A. J. Boulton, P. B. Ghosh, and A. R. Katritzky, *Angew. Chem., Int. Ed. Engl.*, **3**, 693 (1964).
(3) A. J. Boulton, P. B. Ghosh, and A. R. Katritzky, *J. Chem. Soc. B*, 1011 (1966).
(4) A. J. Boulton and R. C. Brown, *J. Org. Chem.*, **35**, 1662 (1970).
(5) (a) D. Allan and J. D. Loudon, *J. Chem. Soc.*, 821 (1949). (b) A similar method for the replacement of an activated phenolic substituent was used[5c] in a thyroxine synthesis. (c) J. R. Chalmers, G. T. Dickson, J. Elks, and B. A. Hems, *J. Chem. Soc.*, 3424 (1949).
(6) O. Buhlmann and A. Einhorn, *Ber.*, **34**, 3788 (1901); E. Bamberger and E. Demuth, *ibid.*, **34**, 4015 (1901).
(7) E. C. Taylor and J. Bartulin, *Tetrahedron Lett.*, 2337 (1967).
(8) (a) S. S. Joshi and I. R. Gambhir, *J. Org. Chem.*, **26**, 3714 (1961). (b) I. R. Gambhir and S. S. Joshi, *J. Indian Chem. Soc.*, **41**, 43 (1964). (c) In an earlier reinvestigation[8d] of the reaction between aniline and 6-nitroanthranil, a small amount of a product, mp 320 °C, *was* obtained. Such a high melting point is indicative of strong (e.g., hydrogen bonding) intermolecular associations in the crystal. Analogous compounds prepared from 4-halo-6-nitroanthranils[8b] also melted in the range 300–350 °C, and we consider that their assignment to indazole structures is likewise erroneous. (d) D. P. Clifford, Ph.D. Thesis, University of East Anglia, 1967.
(9) L. Chardonnens and P. Heinrich, *Helv. Chim. Acta*, **23**, 1399 (1940).
(10) G. Del Re, *Tetrahedron*, **10**, 81 (1960); K.-H. Wünsch and A. J. Boulton, *Adv. Heterocycl. Chem.*, **8**, 321 (1967).
(11) H. C. van der Plas, "Ring Transformations of Heterocycles", Vol. I, Academic Press, New York, N.Y., 1973, p 297.
(12) A. J. Boulton and D. Middleton, *J. Org. Chem.*, **39**, 2956 (1974).
(13) Aldrich Chemical Co.
(14) A. I. Vogel, "A Textbook of Practical Organic Chemistry", 3d ed., Longmans, London, 1956, p 175. The presence of water results in lower yields.
(15) Altaf-ur-Rahman and A. J. Boulton, *Tetrahedron, Suppl. 7*, 49 (1966).

(16) T. Nishimura, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 713.
(17) J. Bartulin, Ph.D. Thesis, University of Princeton, 1968. We thank E. C. Taylor for bringing this work to our attention. Careful temperature control was needed, even when using stannous chloride, to avoid the twin hazards of underreduction (leaving unchanged nitroaldehyde) and overreduction (forming amino aldehyde), both leading to awkward separations and reduced yields.
(18) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958).
(19) Cf. A. Kalir, *Org. Synth.*, **46**, 81 (1966).
(20) (a) "Coalescence temperatures" in the NMR spectra of benzofurazan oxides are usually in the region 0–20 °C ($\Delta G^{\ddagger}$ ca. 14 kcal mol^{-1}),[20b] although 4,7 disubstitution (with halogen atoms) has been reported[20c] to raise the energy barrier by ca. 1.4 kcal mol^{-1}. (b) A. J. Boulton, A. R. Katritzky, M. J. Sewell, and B. Wallis, *J. Chem. Soc. B*, 914 (1967). (c) F. B. Mallory, S. L. Manatt, and C. S. Wood, *J. Am. Chem. Soc.*, **87**, 5433 (1965).
(21) E. Zacharias, *J. Prakt. Chem.*, **43**, 435 (1891).
(22) J. Elguero, A. Fruchier, and R. Jacquier, *Bull. Soc. Chim. Fr.*, 2075 (1966).

Photochemical Solvent Addition to 2(5*H*)-Furanone. Hydrocarbon Solvents

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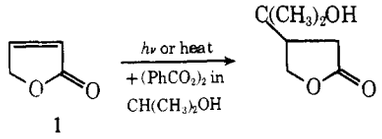
The α,β-unsaturated lactone 2(5*H*)-furanone was shown to add hydrocarbon solvent across its carbon–carbon double bond in three different ways characterized by different β/α addition product ratios. Direct irradiation with ultraviolet light or benzene sensitization afforded a $\beta/\alpha = 1$ while "chemical sensitization" using acetophenone or benzophenone gave a $\beta/\alpha \gg 1$. A benzoyl peroxide initiated reaction gave $\beta/\alpha = 2$.

Photochemical solvent additions to cyclic α,β-unsaturated carbonyl compounds have been reported by many workers.[1-8] In general, alcoholic and ether solvents have been found to add to the β position almost exclusively. In the case of 2-cyclopentenone evidence has been presented both in favor of[1] and against[2] a radical chain process. Ketone sensitizers have been discussed as energy[1-4] and hydrogen transfer[5a,9] agents.

The α,β-unsaturated lactone, 2(5*H*)-furanone (1), has been shown to add isopropyl alcohol in a similar (β) fashion under both photochemical and free radical chain (benzoyl peroxide initiated) conditions[5b] (see eq 1). Only in the cases of 2-cyclopentenone[1,2] and 1[5b] has evidence been gathered concerning the mechanism of the solvent addition. We wish to report our results with this lactone in which we have evidence of at least three different patterns of solvent addition.

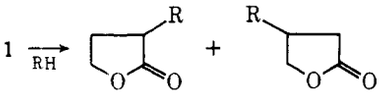


(1)

1

Results

The lactone 1 was allowed to react with cyclohexane or toluene solvent under the following conditions: (a) direct irradiation of dilute (7 mM) deoxygenated solutions at room temperature; (b) irradiation of dilute deoxygenated solutions containing benzoyl peroxide at room temperature; (c) irradiation of dilute deoxygenated solutions containing various sensitizers at room temperature; and (d) heating of dilute deoxygenated solutions containing benzoyl peroxide at the boiling point of the solution. The products derived from 1 in cyclohexane were 3- and 4-cyclohexyldihydro-2(3*H*)-furanone (**2** and **3**, respectively) in 90 ± 10% combined yield. In toluene the products were 3- and 4-benzyldihydro-2(3*H*)-furanone (**4** and **5**) (see eq 2). The structures of these photoproducts were confirmed by comparison with samples independently prepared by previously reported methods.[10] In each case the isomeric photoproducts were separated by gas chromatography (VPC) and the relative amounts of the isomers determined. The results are summarized in Table I. The product ratio in each case provides a "fingerprint" of the mechanism(s) involved in that reaction.



(2)

R = cyclohexyl **2** **3**
R = benzyl **4** **5**

A careful examination of the ultraviolet absorption spectra of 1, acetophenone plus 1, and acetophenone alone in cyclohexane showed no new bands and the presence of 1 did not modify or quench phosphorescence emission from acetophenone. No phosphorescence emission from 1 could be detected. The disappearance of 1 was not quenched by 0.10 M 1,3-cyclohexadiene in a direct irradiation but **2** and **3** were not among the products formed in this reaction.

A series of Pyrex-filtered irradiations of 1 in cyclohexane containing various concentrations of acetophenone and an experiment using a moderate concentration of benzophenone were done. The results are shown in Table II.

Discussion

The ratios of the solvent adducts (β/α) for the various addition reactions fall into three categories. We believe that these categories indicate at least three different pathways for the formation of these photoproducts.

The exclusive formation of the β adduct **3** in the acetophenone and the predominant formation of **3** in the benzophenone sensitized reactions is similar to the sensitized addition of solvent to 2-cyclopentenone reported by several workers.[1,2,6] A mechanism similar to that proposed by Wagner[5a] would involve hydrogen abstraction by the n,π^* triplet

Scheme I