

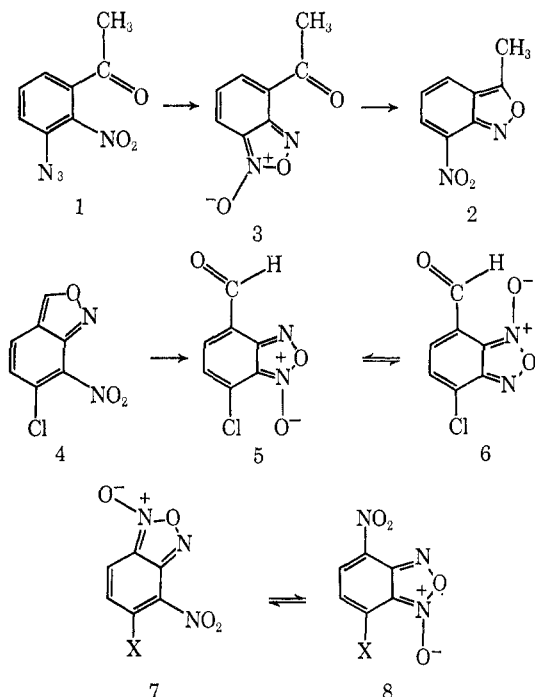
Heterocyclic Rearrangements. XII.¹
The Formation of a Formylbenzofurazan
Oxide from a Nitroanthranil

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A few years ago a new anthranil synthesis was reported, in the decomposition of the nitroazidoacetophenone (1) to form 3-methyl-7-nitroanthranil (2), via the presumed intermediate acetylbenzofurazan oxide (3).²



We now find that nitration of 6-chloroanthranil leads to its 7-nitro derivative 4, which rearranges on heating to 7-chloro-4-formylbenzofurazan oxide (5). The nmr spectrum of 4 (in acetone) shows, as expected, an AB system (τ_A 1.80, τ_B 2.63, $J_{AB} = 9.5$ Hz) and a singlet ($\tau -0.02$). Compound 5, on the other hand, gives at room temperature a very broad, indistinct spectrum, owing to the tautomerism of the furazan oxide ring, which places the formyl and ring protons in rapidly changing environments. On cooling to 0°, 5 shows two distinct AB spectra (τ_A 1.77, τ_B 2.31, $J_{AB} = 8.0$ Hz; $\tau_{A'}$ 2.01, $\tau_{B'}$ 2.12, $J_{A'B'} = 7.0$ Hz) and two singlets from the aldehyde groups ($\tau -0.30$; $\tau' -0.50$), while at 80° one AB and a singlet are observed. The ratio of tautomers (5:6) was ca. 3:4 at 0°, the assignment of spectra to isomers (primed symbols refer to

structure 6) being made on the basis of the chemical shifts of the formyl protons (that in 6 is expected to be deshielded owing to the proximity of the N-oxide group) and of the aromatic protons.³

The rearrangement of nitrobenzofurazan oxides (7 \rightleftharpoons 8) has been described, and the apparent completeness of the conversion of 7 (X = Cl) into 8 (X = Cl) was suggested to be due to steric inhibition of resonance of the nitro group with the ring in 7.^{4,5} The present work establishes the first example of a benzofurazan oxide being formed by a rearrangement of this type from a system other than another benzofurazan oxide; probably steric inhibition again provides the energy to drive the rearrangement in the unexpected direction.

Experimental Section

Melting points are uncorrected. Nmr spectra of acetone solutions were measured on a Perkin-Elmer R10 60-MHz instrument with a variable-temperature probe.

6-Chloro-7-nitroanthranil (4).—6-Chloroanthranil⁶ (1.0 g, 0.065 mol), mp 64° (lit.⁶ mp 65°), was carefully dissolved in 10 cc of cold (0°), concentrated sulfuric acid. To the stirred solution at -5° was added dropwise a solution of potassium nitrate (0.9 g, 0.1 mol) in 20 cc of H₂SO₄. The mixture was stirred at 0° for 1/2 hr, then at 50° for a further 0.5 hr. The red solution was poured onto ice and extracted with methylene chloride. The organic layer was washed with water, dilute Na₂CO₃ solution, and again with water and then dried (Na₂SO₄). Removal of the solvent left a dark orange solid which was carefully crystallized from ethanol as orange plates (0.5 g, 40%): mp 96–97°; ir (Nujol) 1642 (anthranil), 1530, and 1350 cm⁻¹ (NO₂).

Anal. Calcd for C₇H₅ClN₂O₂: C, 42.3; H, 1.5. Found: C, 42.0; H, 1.5.

7-Chloro-4-formylbenzofurazan Oxide (5 \rightleftharpoons 6).—6-Chloro-7-nitroanthranil (0.9 g) was heated 30 min under reflux in 20 ml of glacial acetic acid. The solution was cooled, and an equal volume of water was added. The precipitated solid was crystallized from aqueous ethanol as yellow prisms (0.7 g, 77%): mp 103–104°; ir (Nujol) 1692 (C=O), 1618, 1580, 1545, and 1490 cm⁻¹ (benzofurazan oxide).⁷

Anal. Found: C, 42.5; H, 1.2.

Registry No.—4, 22950-43-2; 5, 22950-44-3.

(3) R. K. Harris, A. R. Katritzky, S. Øksne, A. S. Bailey, and W. G. Paterson, *J. Chem. Soc.*, 197 (1963).

(4) A. J. Boulton and A. R. Katritzky, *Rev. Chim.* (Acad. R. P. Roumaine), **7**, 691 (1962).

(5) P. B. Ghosh, *J. Chem. Soc., B*, 334 (1968).

(6) Altaf-ur-Rahman and A. J. Boulton, *Tetrahedron Suppl.*, **7**, 49 (1966).

(7) J. H. Boyer, D. I. McCane, W. J. McCarville, and A. T. Tweedie, *J. Amer. Chem. Soc.*, **75**, 5290 (1953).

Reaction of Substituted 2-Carboethoxyacetyl-
aminopyridines and Similar Compounds with
Triethyl Orthoformate and Zinc Chloride

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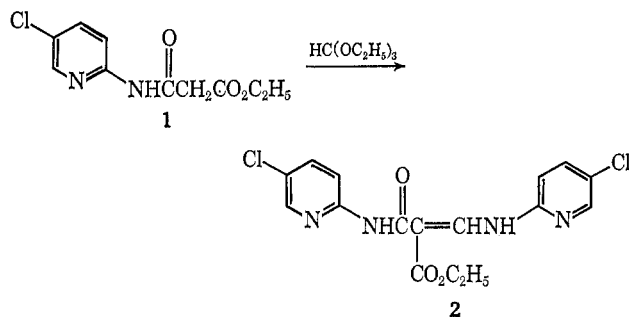
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In an attempt to prepare the ethoxymethylene derivative of 2-(carboethoxyacetyl-amino)-5-chloropyr-

(1) Part XI: A. J. Boulton, I. J. Fletcher, and A. R. Katritzky, *Chem. Commun.*, 62 (1968).

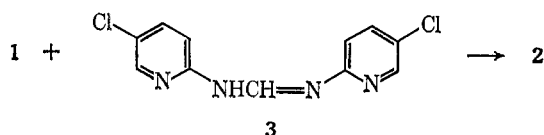
(2) A. J. Boulton, P. B. Ghosh, and A. R. Katritzky, *J. Chem. Soc., B*, 1011 (1968).

idine (1) by reaction of 1 with triethyl orthoformate, acetic anhydride, and zinc chloride, the expected product was not obtained. Instead, when the reaction mixture was cooled, a crystalline product formed which was assigned structure 2 on the basis of elemental analysis, spectral data, and a molecular weight determination.

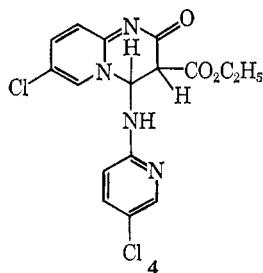


The yield of 2 was 24%, and it could be raised to 41% by conducting the reaction in ethanol instead of acetic anhydride. This result is unusual, since we have found that carbethoxyacetylanilines normally give good yields of ethoxymethylene derivatives.

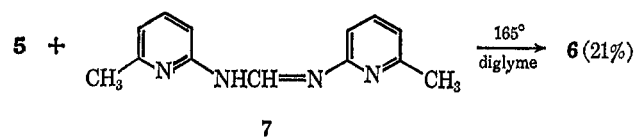
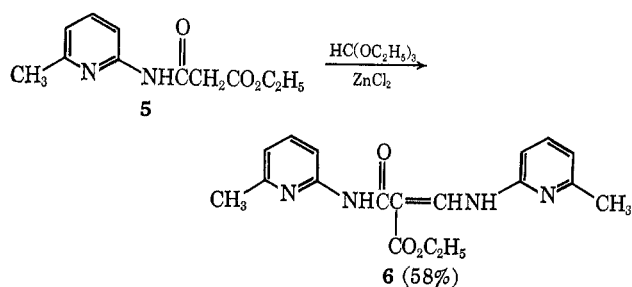
It is known that formamidines derived from aromatic amines react with acidic methylene groups to form compounds such as 2,¹ and this method was used to synthesize 2 independently. The formamidine 3 was prepared by heating 2-amino-5-chloropyridine with triethyl orthoformate, and reaction of 3 with 1 in boiling diglyme gave 2 in 24% yield.



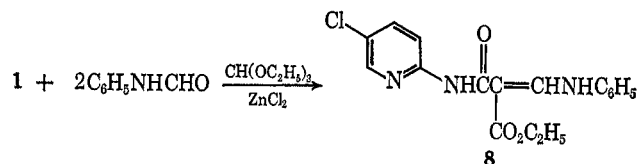
To examine the possibility that 2 possessed a cyclic structure such as 4, the 6-methyl derivative 6, in which



cyclization is very unlikely, was made in the two ways indicated below; the spectral properties of 2 and 6 are very similar and indicate the same structural type.

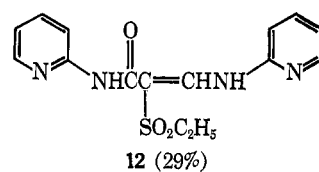
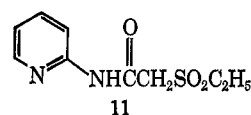
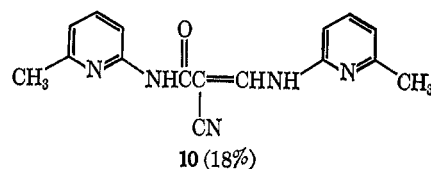
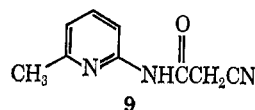


To ascertain whether a simple anilide can replace the second mole of 1 in the production of compounds of type 2, the reaction was run in the presence of a 2 molar excess of formamidine. The product 8 was



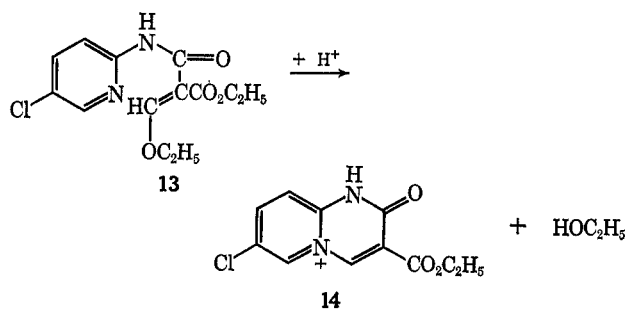
obtained in higher yield (58%) than 2 in the original reaction. No traces of 2 were found. In none of these reactions could a simple ethoxymethylene derivative be isolated.

The reaction of triethyl orthoformate and zinc chloride with the cyanoacetyl derivative 9 and the ethylsulfonylacetyl derivative 11 gave the analogous products 10 and 12 in the yields indicated.



Mechanism.—The first step of the reaction is probably the same as in normal preparations of ethoxymethylene derivatives of active methylene compounds.

The favorable steric arrangement of the pyridine nitrogen in 13 could make the ethoxy group labile,



(1) F. B. Dains, *Ber. Deut. Chem. Ges.*, **35**, 2496 (1902).

TABLE I
CARBETHOXYACETYL, CYANOACETYL, AND SULFONYLACETYL DERIVATIVES OF 2-AMINOPYRIDINES,
2-PYRIDYLFORMAMIDINES

Compound	Empirical formula	Yield, %	Mp, °C	Calcd, %			Found, %		
				C	H	N	C	H	N
1	C ₁₀ H ₁₁ ClN ₂ O ₃ ^a	38	108.5-110	49.48	4.57	11.55	49.22	4.80	11.73
5	C ₁₁ H ₁₄ N ₂ O ₃ ^a	41	87-89	59.46	6.35	12.61	59.28	6.10	12.64
9	C ₉ H ₉ N ₂ O ^a	16	97.5-99.5	61.70	5.18	23.99	61.71	5.00	24.24
11	C ₉ H ₁₂ N ₂ O ₃ S	30	110-112	47.35	5.30	12.27	47.51	5.37	12.27
3	C ₁₁ H ₈ Cl ₂ N ₄	57	197.5-199.5	49.46	3.00	20.98	49.27	3.12	20.89
7	C ₁₃ H ₁₄ N ₄	54	110.5-112.5	69.00	6.24	24.76	68.77	6.19	24.78

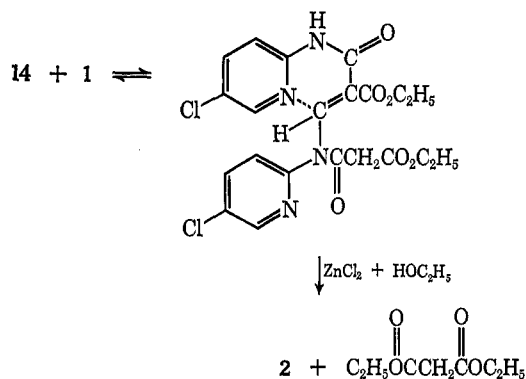
^a Preparation was according to E. A. Ingalls and F. D. Popp, *J. Heterocycl. Chem.*, **4**, 523 (1967), and literature quoted therein.

TABLE II
2-CARBETHOXY-3-2-PYRIDYLAMINOACRYL(2-PYRIDYL)AMIDES AND ANALOGS

Compound	Empirical formula	Yield, %	Mp, °C	Calcd, %								Found, %					Nmr aldimino proton, ppm	
				C	H	N	O	Cl	S	mol wt	C	H	N	O	Cl	S		mol wt
2	C ₁₃ H ₁₄ O ₂ N ₄ O ₃	41	195-197	50.41	3.70	14.70	12.59	18.60		381	50.54	3.72	14.71	12.59	18.60		385 ± 2 ^a	9.38
6	C ₁₈ H ₂₀ N ₄ O ₃	58	150-152	63.52	5.92	16.46					63.40	5.93	16.68					8.97
10	C ₁₆ H ₁₅ N ₅ O	18	182-186	65.51	5.16	23.88					65.47	5.13	24.03					8.57
12	C ₁₃ H ₁₃ N ₄ O ₃ S	29	183-184	54.20	4.85	16.86			9.65		54.39	4.75	16.67			9.42		
8	C ₁₇ H ₁₆ ClN ₃ O ₃	58	170-172	59.05	4.67	12.15					59.00	4.74	12.04					8.35

^aEbullioscopic determination in benzene.

facilitating its departure as an anion leading to **14** as the reactive intermediate. This intermediate should be more reactive than an ethoxymethylene derivative and should be capable of reacting with the amide nitrogen of another molecule of starting material **1**.



Zinc chloride catalyzed removal of the malonyl group would then yield **2**.

Another possibility is partial solvolysis of **1** under the reaction conditions and reaction of free 2-amino-5-chloropyridine with either **13** or **14** to yield **2**. However, some **2** is formed even in the presence of an excess of acetic anhydride, which makes it likely that at least part of the reaction goes *via* attack on **14** by an amide nitrogen.

Experimental Section

All melting points are uncorrected. The microanalyses (see Tables I and II) were carried out by Mr. C. W. Nash and his associates.

Spectral Data.—The ir spectra of **2**, **6**, **8**, **10**, and **12** are quite

straightforward. The ester band is shifted to longer wavelengths compared with those of the starting materials and occurs at 5.95 μ ; the amide I bands and >C=N- bands occur at 6.05 and 6.15 μ .

In the nmr spectra only the hydrogen on the aldimino group is interesting. It is extremely deshielded, almost as much as an aldehydic proton. This proton is easy to spot since it is coupled to the proton on the neighboring nitrogen ($J = 12$ to 14 Hz). Its location ranges from 8.35 to 9.38 ppm (see Table II).

2-Carbethoxy-3-(5-chloro-2-pyridylamino)acryl(5-chloro-2-pyridyl)amide (2) (Table II, the Other Compounds Listed in Table II Were Made in the Same Way).—A solution of 27.4 g (0.1 mol) of **1** and 1.0 g of ZnCl₂ in 70 ml of triethyl orthoformate and 100 ml of absolute ethanol was refluxed for 15 hr. The mixture was then cooled and the product was filtered off. After recrystallizing from Methyl Cellosolve a yield of 15.5 g was obtained.

1,3-Bis(5-chloro-2-pyridyl)formamidine (3) (Table I, the Same Method Was Used for **7**).—A solution of 38.5 g (0.3 mol) of 2-amino-5-chloropyridine and 22 g (0.15 mol) of triethyl orthoformate in 150 ml of diglyme was refluxed for 2 hr. After that, the mixture was cooled and diluted with 100 ml of ethanol. The precipitated product was recrystallized from ethanol. The yield was 23 g.

2-Ethylsulfonylacetylaminopyridine (Table I).—A mixture of 90 g (0.43 mol) of C₂H₅SO₂CH₂CO₂C₄H_{9-n} (made by peracetic acid oxidation of the corresponding sulfide) and 41 g (0.43 mol) of 2-aminopyridine was heated with stirring to 180° for 2 hr when 40 ml of liquid had distilled off. The mixture was then cooled and diluted with 100 ml of 2-propanol. The product crystallized and was recrystallized from 2-propanol. The yield was 30 g.

Registry No.—**2**, 23595-75-5; **3**, 23595-76-8; **6**, 23595-77-9; **7**, 23646-50-6; **8**, 23595-78-0; **10**, 23646-51-7; **11**, 23595-79-1; **12**, 23595-80-4; triethyl orthoformate, 122-51-0; zinc chloride, 7646-85-7.

Acknowledgment.—We would like to gratefully acknowledge the encouragement of this work by Dr. Charles L. Levesque.