

The Chemistry of 2*H*-3,1-Benzoxazine-2,4-(1*H*)dione (Isatoic Anhydride) **5**. Synthesis of the [1]Benzopyrano[3,2-*c*]quinoline Ring System

Gary M. Coppola and Goetz E. Hardtmann

Department of Medicinal Chemistry, Pharmaceutical Division, Sandoz, Inc.,
Route 10, East Hanover, New Jersey 07936

Received February 9, 1979

The reaction of isatoic anhydrides with the anion derived from ethyl *o*-fluorobenzoylacetate to furnish [1]benzopyrano[3,2-*c*]quinolines is described. An analogous reaction with 3-azaisatoic anhydride furnishes **1b**, or with tricyclic anhydride **3**, system **4** is isolated. Spectral data is also discussed.

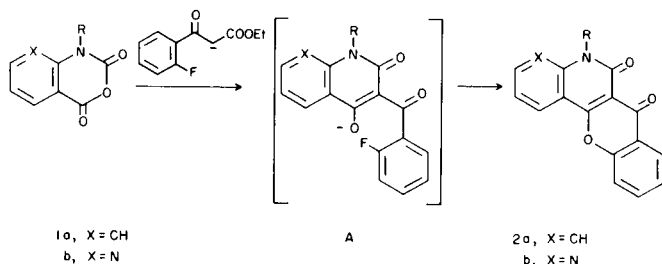
J. Heterocyclic Chem., **16**, 829 (1979).

Sir:

In previous report (1,2) we have shown the versatility of isatoic anhydrides (**3**) as useful intermediates in the synthesis of interesting polycyclic heterocycles.

The ease of displacement of activated aromatic fluorine atoms is well known (4-7) and the possibility of the combination of this type of reaction in conjunction with a ring opening of an isatoic anhydride presented the possibility of a facile entrance into the formation of complex heterocycles.

Carbanions of active methylene compounds have been shown to react readily with isatoic anhydrides (**1a**) to yield 2-oxo- or 4-oxoquinolines (**1**). When the anion of ethyl *o*-fluorobenzoylacetate was allowed to react with **1a**, 5-substituted-6*H*-[1]benzopyrano[3,2-*c*]quinoline-6,7-(5*H*)diones (**2a**), or when X = N, 5-substituted-6*H*-[1]benzopyrano[3,2-*c*]naphthpyridine-6,7-(5*H*)diones (**2b**) were produced in moderate yield. The products were presumably formed by the displacement of the activated fluorine atom by the enolate ion of **A**.

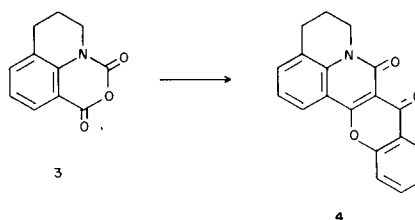


In general, 0.1 mole of sodium hydride (50% in mineral oil, pentane washed) was added in portions to a solution of 0.1 mole of ethyl *o*-fluorobenzoylacetate in 250 ml. of DMA. When the generation of hydrogen ceased, a solution of the anhydride (**1** or **3**) was added. The mixture was heated at 120° for 18 hours. Upon cooling, the product precipitated from the reaction mixture. It was filtered and recrystallized from methylene chloride/ethanol (see Table 1).

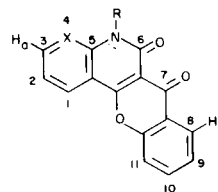
0022-152X/79/040829-02\$02.25

Compound **1b** (R = CH₃) was obtained by the alkylation of 3-azaisatoic anhydride (**8**) with methyl iodide in the presence of sodium hydride at 25°; m.p. = 169-172°, yield = 75%.

Employment of tricyclic anhydride **3** (**9**) under similar conditions resulted in the formation of pentacycle **4**, m.p. = 341° dec., yield = 28%.



The infrared spectra of compounds of type **2** exhibited two carbonyl absorptions. The frequency of absorption of the carbonyl located at position 7 occurred between 1695 and 1680 cm⁻¹, while the absorption of the amide carbonyl at position 6 occurred between 1640 and 1620 cm⁻¹.



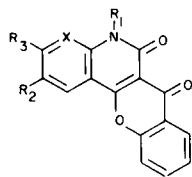
In the nmr spectra (when X = CH) the aromatic protons appeared between δ 8.0 and 7.1. The only signal appearing farther downfield was that of H_b which was observed as a multiplet between δ 8.4 and 8.3. When X = N (eg., **13**), the signal for H_a was also observed and was located at δ 8.6 while H_b was at δ 8.25.

REFERENCES AND NOTES

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Table 1



Compound No.	X	R ₁	R ₂	R ₃	M.p., °C	Yield, %	Molecular Formula	Analysis			
								Calcd.	(Found)		
								C	H	N	Cl
5	CH	CH ₃	H	H	301-303	47	C ₁₇ H ₁₁ NO ₃	73.6 (73.7)	4.0 (4.2)	5.1 (4.9)	
6	CH	CH ₃	Cl	H	295-298	20	C ₁₇ H ₁₀ NO ₃ Cl	65.5 (65.3)	3.2 (3.5)	4.5 (4.6)	11.4 (11.6)
7	CH	CH ₃	CH ₃	H	304-307	48	C ₁₈ H ₁₃ NO ₃	74.2 (73.9)	4.5 (4.8)	4.8 (4.7)	
8	CH	CH ₃	H	COOCH ₃	307-309	25	C ₁₉ H ₁₃ NO ₃	68.1 (67.9)	3.9 (4.3)	4.2 (4.1)	
9	CH	Et	H	H	266-269	40	C ₁₈ H ₁₃ NO ₃	74.2 (74.0)	4.5 (4.7)	4.8 (4.6)	
10	CH	CH ₂ CH=CH ₂	H	H	238-240	43	C ₁₉ H ₁₃ NO ₃	75.2 (75.6)	4.3 (4.5)	4.6 (4.5)	
11	CH	cyclopropylmethyl	H	H	232-235	43	C ₂₀ H ₁₃ NO ₃	75.7 (75.6)	4.8 (5.1)	4.4 (4.3)	
12	CH	phenylmethyl	H	H	290-292	32	C ₂₃ H ₁₅ NO ₃	78.2 (78.2)	4.3 (4.6)	4.0 (4.0)	
13	N	CH ₃	H	H	307-310	25	C ₁₆ H ₁₀ N ₂ O ₃	69.1 (69.3)	3.6 (3.9)	10.1 (10.0)	

cyclic Chem., submitted for publication.

(3) Throughout this paper the names "isatoic anhydride" and "2H-3,1-benzoxazine-2,4(1H)dione" are used interchangeably. Commercial sources still prefer the first name whereas *Chemical Abstracts* subscribes to the latter. We have adopted the *Chemical Abstracts* numbering system for substituted isatoic anhydrides, but we feel that it will be easier to read if we use the expression "N-substituted isatoic anhydride" rather than "N-substituted

2H-3,1-benzoxazine-2,4(1H)dione".

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