Condensed Benzopyrans II (1). Some Derivatives of 3*H*-Pyrano[3,2-*f*]quinoline

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Received August 8, 1977

The reaction of 6-aminocoumarin with some ethoxymethylene compounds and dimethyl acetylenedicarboxylate led to condensation products which on thermal cyclizations afford new derivatives of 3*H*-pyrano[3,2-*f*]quinoline (IIa-IIc).

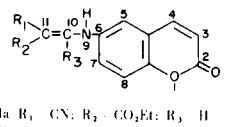
J. Heterocyclic Chem., **15**, 159 (1978)

Previously 6-aminocoumarin has been used in a Skraup's synthesis to give the parent ring system 3*H*-pyrano[3,2-*f*]-quinoline (2). It has also been condensed with β-ketonic esters and the condensation products cyclized to give 8-, or 8,9-disubstituted 3*H*-pyrano[3,2-*f*]quinolines (3).

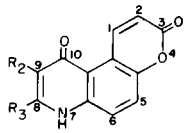
The condensation of 6-aminocoumarin with ethoxymethylene derivatives of various active methylene compounds in a Gould-Jacobs reaction (4) could lead to other derivatives of 3*H*-pyrano[3,2-*f*]quinoline. Another useful reagent dimethyl acetylenedicarboxylate (5) could also be made to react with 6-aminocoumarin and the condensation product could be cyclized likewise. However, diethyl ethoxymethylenemalonate is the only ethoxymethylene compound that has been used in this type of synthesis giving ethyl 7,10-dihydro-10-oxo-3*H*-pyrano[3,2-*f*]quinoline-9-carboxylate which on hydrolysis and *N*-ethylation gave an acid containing antibacterial and antihelmintic properties (6).

We would now like to report the condensation of 6-aminocoumarin with other ethoxymethylene compounds and with dimethyl acetylenedicarboxylate and the subsequent cyclizations of the condensation products obtained in these reactions. The products Ia-Id were formed during the condensation of 6-aminocoumarin with the appropriate reagents and when Ia, Ib, and Id were heated under reflux in Dowtherm, the cyclized products IIa-IIc were obtained in good yields (see experimental). The condensation product Ic, however, could neither be cyclized under these thermal conditions nor with phosphoryl chloride.

The infrared absorption spectra of the cyclized products (Table III) indicate that these compounds exist mainly in the pyridone tautomeric form as represented by the structural formulae IIa-IIc.



Ia R_1: CN; R_2: CO_2Et; R_3: H
Ib R_1: COMe; R_2: CO_2Et; R_3: H
Ic R_1: R_2: COMe; R_3: H
Id R_1: H; R_2: R_3: CO_2Me



IIa R_2: CN; R_3: H
IIb R_2: COMe; R_3: H
IIc R_2: H; R_3: CO_2Me

EXPERIMENTAL

The pmr spectra were taken on a 60 MHz Hitachi Perkin-Elmer model R-20B using tetramethylsilane as an internal reference. Infrared absorption spectra were measured on a Perkin-Elmer model 180, samples were examined as potassium bromide pellets.

The elemental analyses were carried out on a Perkin-Elmer model 240. Melting points were observed on a Fisher-Johns apparatus and are uncorrected.

The following starting materials were obtained according to the literature methods: 6-aminocoumarin, m.p. 162-163° (7); ethyl ethoxymethylenecyanoacetate (EMCA), b.p. 115-120°/6 mm (8); ethyl ethoxymethyleneacetoacetate (EMAE), b.p. 126-132°/4 mm (9); and ethoxymethyleneacetylacetone (EMAA), b.p. 106-110°/2 mm (10).

Condensations of 6-Aminocoumarin with Ethoxymethylene Compounds.

To a stirring solution of 0.1 mole of 6-aminocoumarin in 200 ml. of ethanol, there was added 0.1 mole of the ethoxymethylene compounds (EMCA, EMAE, and EMAA). The reaction mixture was heated under reflux for 1 hour, allowed to cool down to the room temperature and then filtered. The filtered product was purified by crystallization from ethanol. The compounds Ia, m.p. 210-212°; Ib, m.p. 135-136°; and Ic, m.p. 234-235° were thus obtained in yields of 86; 77; and 83%, respectively (Tables I and II).

With Dimethyl Acetylenedicarboxylate.

A mixture of 0.01 mole of dimethyl acetylenedicarboxylate and 0.01 mole of 6-aminocoumarin in 10 ml. of anhydrous methanol was heated under reflux for a period of 6 hours. After it had cooled down to the room temperature, the reaction mixture was filtered and Id was crystallized from methanol, m.p. 124-125°, yield 94% (Tables I and II).

Table I

Elemental Analyses (a)

Compound No.	Formula	C (%)	H (%)	N (%)
Ia	$C_{15}H_{12}N_2O_4$	63.46 (63.38)	4.31 (4.26)	9.78 (9.86)
Ib	$C_{16}H_{15}NO_5$	64.07 (63.78)	4.92 (5.02)	4.57 (4.65)
Ic	$C_{15}H_{13}NO_4$	66.06 (66.41)	4.73 (4.83)	4.88 (5.16)
Id	$C_{15}H_{13}NO_6$	59.11 (59.41)	4.21 (4.32)	4.25 (4.62)
IIa	$C_{13}H_6N_2O_3$	65.87 (65.55)	2.62 (2.54)	11.76 (11.76)
IIb	$C_{14}H_9NO_4$	66.07 (65.88)	3.83 (3.55)	5.56 (5.48)
IIc	$C_{14}H_9NO_5$	61.58 (62.00)	3.35 (3.34)	5.17 (5.16)

(a) Figures in parentheses represent calculated values.

Table II

Spectroscopic Properties of (Coumarin-6-yl)aminomethylene Compounds (Ia-Id)

Compound No.	Pmr δ (J in Hz) H-3 ($J_{3,4}$)	H-4 ($J_{3,4}$)	H-5; H-7; H-8	H-9 ($J_{9,10}$)	H-10 ($J_{9,10}$)	Other signals	Solvent	Infrared (cm^{-1})
Ia	6.45, d (10)	7.95, d (10)	7.40, m	10.65, d (13)	8.30, d (13)	1.24 (m, CH_3), 4.20 (m, CH_2)	DMSO-d_6	3500-3200 (NH); 2220 (C≡N); 1680 (ester C=O); 1720 (pyrone C=O)
Ib	6.45, d (10)	7.97, d (10)	7.51, m	12.61, d (14)	8.36, d (14)	1.31 (t, CH_3) 4.21 (q, CH_2) (ester C_2H_5); 3.55 (acetyl CH_3)	DMSO-d_6	3500-3200 (NH); 1715 (ester C=O); 1715 (pyrone C=O); 1605 (acetyl C=O)
Ic	6.52, d (10)	7.99, d (10)	7.55, m	12.55, d (13)	8.38, d (13)	2.41 (s, CH_3) (a)		3500-3200 (NH); 1720 (pyrone C=O); 1630, 1610 (acetyl C=O)
Id	6.40, d (10)	7.62, d (10)	7.10, m	9.62, s		5.48 (s, H-11); 3.70 (s, CH_3); 3.75 (s, CH_3)	Deuterio-chloroform	3500-3200 (NH); 1740, 1670 (ester C=O) 1725 (pyrone C=O)

(a) 2.39 (s, CH_3) and 2.55 (s, CH_3) in deuteriochloroform.

Table III

Infrared Absorptions (cm^{-1}) of 3*H*-Pyrano[3,2-*f*]quinolines (IIa-IIc)

Compound No.	NH (a)	Pyrone C=O	Pyridone C=O	Other absorptions
IIa	3450	1730	1635	2245 (C≡N).
IIb	3450	1725	1630	1640 (acetyl C=O)
IIc	3310	1730	1630	1710 (ester C=O)

(a) All broad bands.

Cyclizations.

Compounds Ia, Ib, and Id (0.003 mole) were heated under reflux in 15 ml. of Dowtherm for a period of 20 minutes, 1 hour and 15 minutes, and 40 minutes, respectively. After the reaction mixture had cooled down to the room temperature, petroleum ether (b.p. 40-60°) was added and the precipitate filtered off, washed with petroleum ether (b.p. 40-60°) until it was free of Dowtherm and then crystallized to give the products IIa, m.p. > 300° (water-*N*,*N*-dimethylformamide); IIb, m.p. > 300° (water-*N*,*N*-dimethylformamide); and IIc, m.p. > 300° (methanol) in yields of 86; 88; and 87%, respectively (Tables I and III).

Acknowledgments.

We would like to thank Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for the award of a scholarship to André Luis Gemal.

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