Some 2-(Dialkylamino) Substituted Chromenylium Salts

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The reaction of 2-(dialkylamino)-7-methoxychromones with malononitrile in the presence of acetic anhydride afforded [2-(dialkylamino)-7-methoxy-4*H*-chromen-4-ylidene]malononitriles. When these compounds were refluxed with concentrated hydrochloric (or hydroiodic) acid, 2-(dialkylamino)-7-methoxy(or hydroxy)-4-methylchromenylium salts were obtained. The use of concentrated sulfuric acid or polyphosphoric acid in the hydrolysis was also investigated. The preparation of ethyl [2-(dialkylamino)-7-methoxy-4*H*-chromen-4-ylidene]cyanoacetates and their behavior when treated with acids are also described, as well as the synthesis of some 3-(dialkylamino)-1-methylnaphtho[2,1-*b*]pyrylium salts.

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Pyrylium or chromenylium salts have been widely investigated since they include, for instance, naturally occurring anthocyanines, pyryl cyanine dyes and products useful as photographic developing agents (1-3). Some aspects of the chemical behavior and properties of such 4-methyl substituted compounds have been recently reviewed (4).

Two main routes can be followed in achieving the synthesis of 4-methyl substituted chromenylium salts: suitable starting products can condense in acidic medium, *e.g.*, *o*-hydroxyacetophenone and compounds containing the $CO\text{-}CH_2$ functionality, as well as chromones react with Grignard reagent to give chromenols, which in turn are converted by acids into chromenylium salts (1).

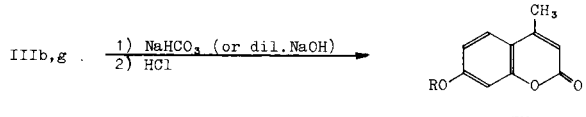
In our continuing investigation of the chemistry and pharmacological properties of pyran derivatives, we have synthesized a number of chromones and benzochromones bearing a dialkylamino substituent adjacent to the heteroatom (5-9). In the present paper we describe a facile method to obtain the 4-methyl substituted chromenylium or benzochromenylium salts corresponding to those compounds.

2-(Dialkylamino)-7-methoxychromones which were chosen for the ease of their preparation and high yields in comparison with other 2-(dialkylamino)chromones (7,9), were condensed with malononitrile in the presence of acetic anhydride to give compounds II. Hydrolysis in refluxing hydrochloric or hydroiodic acid of these products gave rise to the chromenylium salts III in good yield, likely through the complete decarboxylation of the resulting carboxylic acids.

In the literature it has been reported that 2,6-dimethyl-4-pyrone reacts with malononitrile to give the corresponding 4*H*-4-ylidene derivative; treatment of this product with hydrochloric acid led to the partially hydrolized nitrile-amide compound through the transformation of only one cyano group (10). However, when the 3-phenyl-1*H*-naphtho[2,1-*b*]pyran-1-ylidene derivative of the Meldrum's acid was treated with trifluoroacetic acid in the synthesis of a polycyclic vinylogue of 4-pyrone, a small amount of the 1-methyl-3-phenylnaphtho[2,1-*b*]pyrylium salt was formed as a by-product *via* total decarboxylation (11). Thus there is evidence that with dialkylamino substituted derivatives II the presence of an electron releasing nitrogen in the proper position plays a favorable role in the hydrolysis and decarboxylation with the ultimate formation of chromenylium salts, as suggested in the Scheme 1. The structures attributed to the proposed intermediates IIA, IIB and IIC are in accordance with those assigned to the compounds IXa, X and V, respectively (see subsequent discussion).

When compounds IIa-c were refluxed with concentrated hydrochloric acid the recovery of the final chlorides was generally difficult due to their high aqueous solubility. However, the addition of perchloric acid to the chloride solution results in the formation of perchlorates IIIa-c which separate out easily upon cooling. On the other hand when 57% hydroiodic acid was used the insoluble iodides IIIf-h were recovered without any difficulty.

Analyses and spectral properties of II and III, as well as of all other compounds in this paper described, were in accordance with their proposed structures. In this connection, particularly significant in the nmr spectrum of IIa-c was the downfield shift of the H-5 signal as well in the spectrum of IIIb, given as an example, the presence of a singlet at τ 7.34, attributable to the 4-methyl group, and the shift of the H-3 signal into the multiplet of the aromatic protons. Further structural support was obtained by treating IIIb,g with hot saturated aqueous sodium bicarbonate or cold dilute aqueous sodium hydroxide to afford the coumarins IVa,b.

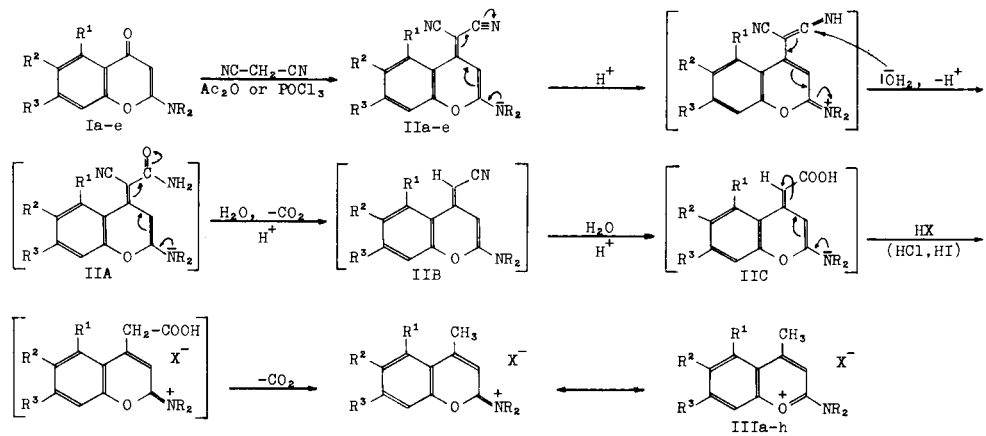


IV

IVa; R = CH_3
IVb; R = H

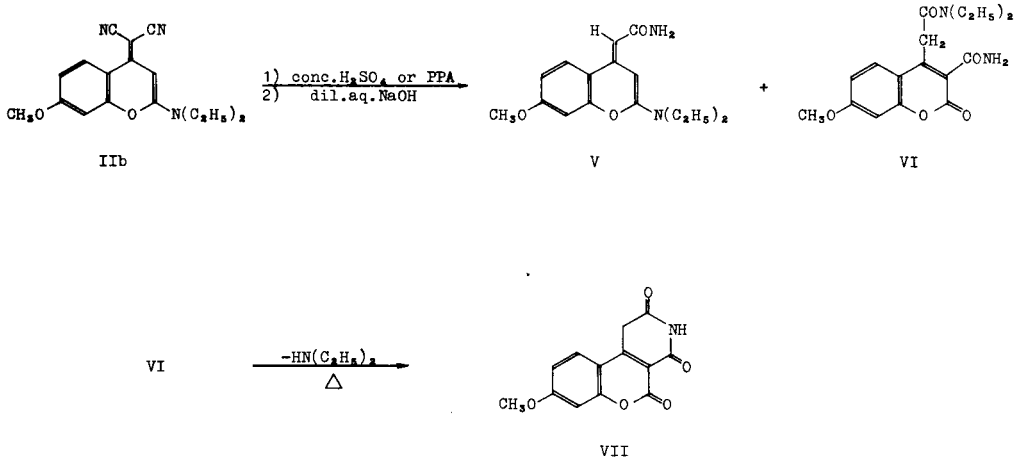
0022-152X/81/05/0863-06$02.25

Scheme 1



					recovered as:
Ia, IIa, IIIa	$R^1=R^2=$ H	$R^3=$ OCH_3	$NR_2=$ $N(CH_3)_2$		$X^-=$ ClO_4^-
Ib, IIb, IIIb	$R^1=R^2=$ H	$R^3=$ OCH_3	$NR_2=$ $N(C_2H_5)_2$		$X^-=$ ClO_4^-
Ic, IIc, IIIc	$R^1=R^2=$ H	$R^3=$ OCH_3	$NR_2=$ N⬡		$X^-=$ ClO_4^-
Id, IId, IIId	$R^1,R^2=$ benzo	$R^3=$ H	$NR_2=$ $N(CH_3)_2$		$X^-=$ I^-
Ie, IIe, IIIe	$R^1,R^2=$ benzo	$R^3=$ H	$NR_2=$ $N(C_2H_5)_2$		$X^-=$ I^-
IIIf	$R^1=R^2=$ H	$R^3=$ OH	$NR_2=$ $N(CH_3)_2$		$X^-=$ I^-
IIIg	$R^1=R^2=$ H	$R^3=$ OH	$NR_2=$ $N(C_2H_5)_2$		$X^-=$ I^-
IIIh	$R^1=R^2=$ H	$R^3=$ OH	$NR_2=$ N⬡		$X^-=$ I^-

Scheme 2



It is interesting to note that during the treatment of IIb with concentrated sulfuric acid or polyphosphoric acid, a mixture of the amides V and VI was normally obtained. The optimum conditions for obtaining the two compounds separately are reported in the Experimental. The formation of the rearrangement product VI must be attributed to the pyran ring opening (12) followed by recyclization. On heating compound VI above its melting point, the tricyclic derivative VII was obtained by loss of diethylamine, as shown in the Scheme 2.

Due to the above reported results and the easy route to chromenylium salts, we were prompted to investigate the behavior in the hydrolysis of other suitable 2-(dialkylamino)-4*H*-chromen-4-ylidene derivatives. Usually chromones do not react well with ethyl cyanoacetate to yield the corresponding 4*H*-chromen-4-ylidene derivatives, but transformation of the chromones into the 4,4-dichloro derivatives or other literature methods make this reaction possible (13,11). In this extent we found that 4*H*-chromene-4-thione VIIIa, which was prepared from Ib through the action of phosphorus pentasulfide, results in good yields of the corresponding chromenylidene derivative IXa.

When this product was subsequently submitted to hydrolysis with refluxing 18% hydrochloric acid, a mixture of the chromenylium salt, which was recovered as the perchlorate IIIb, and the (4*H*-chromen-4-ylidene)acetonitrile X was obtained. On the other hand, treatment with 57% hydroiodic acid gave rise only to the chromenylium iodide IIIg in a reasonable yield, while the use of polyphosphoric acid led to the formation of a mixture of the amide V and the nitrile X, as reported in the Scheme 3.

The *cis* position of carbamoyl, ethoxycarbonyl and cyano groups to H-3 in the compounds V, IXa and X, respectively, is supported by the nmr data and is consistent with the literature references on this topic (13,11). In fact the nmr signal of H-3, which is at τ 4.26 in the dinitrile IIb, appears at τ 4.55 in X, τ 2.25 in IXa and τ 2.92 in V owing to the difference in the anisotropy of those functionalities (14). Also the position of the H-5 signal of these compounds is particularly significant in this connection (see Experimental).

When 1*H*-naphtho[2,1-*b*]pyran-1-ones Id,e (15,5) were condensed with malononitrile, in the presence of phosphorus oxychloride, and when 1*H*-naphtho[2,1-*b*]pyran-1-thione VIIIb (16) was condensed with ethyl cyanoacetate in the presence of acetic anhydride, 1*H*-1-ylidene derivatives IId,e and IXb were obtained, respectively. Hydrolysis of such products with refluxing 57% hydroiodic acid afforded the benzochromenylium salts IIId,e in good yield (Schemes 1 and 3). Concerning the nmr spectra of the above compounds it is interesting to observe that the downfield shift of the H-10 signal is far smaller in the 1*H*-1-ylidene derivatives IId,e and IXb, than in the starting compounds Id,e and VIIIb (15,5,16).

The aqueous or alcoholic solutions of both chromenylium and benzochromenylium salts III produced a deep yellow-green or blue fluorescence under uv light.

EXPERIMENTAL

Melting points were taken on a Fisher-Johns (Electrothermal when above 300°) apparatus and are uncorrected. Ir (in potassium bromide pellets), mass and nmr spectra were obtained with a Perkin-Elmer 257, a Varian MAT-111 (70 eV) and a Perkin-Elmer R 12 (tetramethylsilane as internal reference) spectrometer, respectively. Analyses were performed by Laboratorio di Microanalisi, Istituto di Scienze Farmaceutiche dell'Università di Genova.

[2-(Dialkylamino)-7-methoxy-4*H*-chromen-4-ylidene]malononitriles (IIa-c).

A mixture of 4 mmoles of compound Ia-c (7), 0.78 g. (12 mmoles) of malononitrile and 20 ml. of freshly distilled acetic anhydride was heated at 115° for 2 hours, cooled and poured onto crushed ice. After stirring for a few minutes, the yellow or orange solid which separated out was collected, washed with water and recrystallized from ethanol.

By these conditions the following compounds were obtained.

2-(Dimethylamino) Derivative IIa.

This compound had m.p. 248-249°, yield 53.3%; ir: 2190 and 2170 cm^{-1} (C≡N); nmr (deuteriochloroform): τ 6.79 (s, 6H, N-CH_3), 6.08 (s, 3H, OCH_3), 4.32 (s, 1H, H-3), 3.28-3.05 (m, 2H, H-6, 8), 1.30 (d, 1H, H-5).

Anal. Calcd. for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.53; H, 5.00; N, 15.79.

2-(Diethylamino) Derivative IIb.

This compound had m.p. 208-209°, yield 59.5%; ir: 2200 and 2180 cm^{-1} (C≡N); nmr (deuteriochloroform): τ 8.67 (t, 6H, ethyl CH_3), 6.44 (q, 4H, CH_2), 6.07 (s, 3H, OCH_3), 4.26 (s, 1H, H-3), 3.31-3.03 (m, 2H, H-6,8), 1.32 (d, 1H, H-5); ms: m/e 295 (M^+).

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.13; H, 5.80; N, 14.23. Found: C, 69.12; H, 5.74; N, 14.27.

2-Piperidino Derivative IIc.

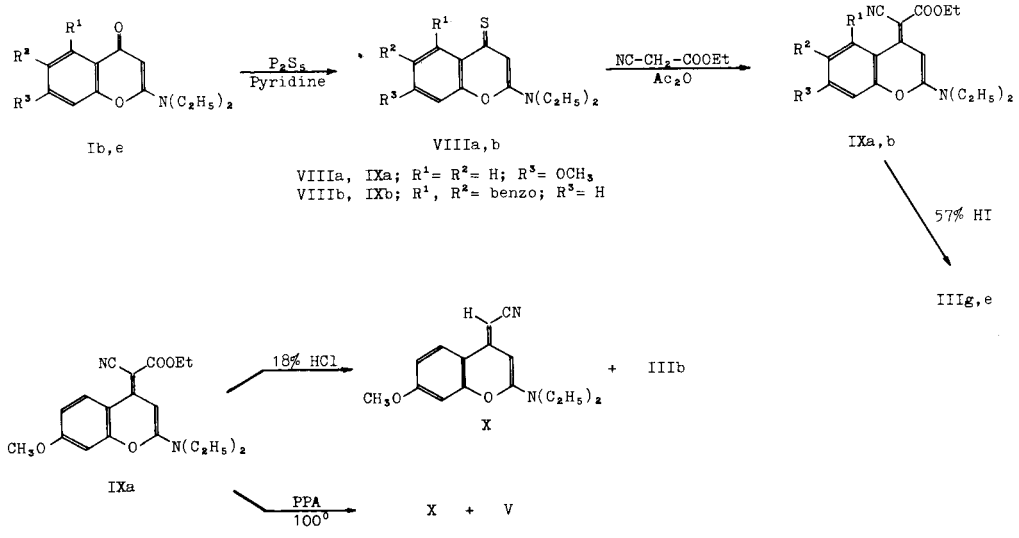
This compound had m.p. 233-234°, yield 67.5%; ir: 2195 and 2175 cm^{-1} (C≡N); nmr (deuteriochloroform): τ 8.25 (mc, 6H, β and γ-CH_2), 6.38 (mc, 4H, α-CH_2), 6.08 (s, 3H, OCH_3), 4.22 (s, 1H, H-3), 3.32-3.05 (m, 2H, H-6,8), 1.37 (d, 1H, H-5).

Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.57; N, 13.67. Found: C, 70.54; H, 5.62; N, 13.57.

[3-(Dialkylamino)-1*H*-naphtho[2,1-*b*]pyran-1-ylidene]malononitriles (IId,e).

The mixture of 1.0 g. of 3-(dialkylamino)-1*H*-naphtho[2,1-*b*]pyran-1-one (Id,e) (15,5), 0.5 g. of malononitrile and 5 ml. of phoshorus oxychloride

Scheme 3



was heated at 95° for 1.5 hours. After removal under vacuum of excess phosphorus oxychloride, a saturated aqueous solution of sodium carbonate was added by stirring and the dark solid obtained was recovered by filtration, washed with water and worked up as described below.

3-(Dimethylamino) Derivative IId.

The dried crude product was filtered through a silica gel column using ethyl acetate as eluant; the red solid which was recovered was recrystallized from ethyl acetate or ethanol, 0.82 g. (68.3%), m.p. 266-267°; ir: 2195 and 2180 cm^{-1} (C≡N); nmr (deuteriotrifluoroacetic acid): τ 6.42 (s, 6H, CH_3), 2.64-1.60 (m, 7H, H-2, 5, 6, 7, 8, 9, 10).

Anal. Calcd. for $C_{18}H_{13}N_3O$: C, 75.24; H, 4.56; N, 14.62. Found: C, 75.50; H, 4.66; N, 14.58.

3-(Diethylamino) Derivative IIe.

The crude material was recrystallized from ethyl acetate with the addition of charcoal; the yellow product obtained weighed 0.80 g. (67.9%) and melted at 204-205°; ir: 2200 and 2180 cm^{-1} (C≡N); nmr (deuteriochloroform): τ 8.69 (t, 6H, CH_3), 6.46 (q, 4H, CH_2), 3.88 (s, 1H, H-2), 2.80-1.95 (m, 5H, H-5, 6, 7, 8, 9), 1.63 (mc, 1H, H-10); ms: m/e 315 (M^+).

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.33. Found: C, 76.26; H, 5.50; N, 13.25.

2-(Dialkylamino)-7-methoxy-4-methylchromenylium Perchlorates (IIIa-c).

The solution of 1.0 g. of each compound IIa-c in 25 ml. of concentrated hydrochloric acid was heated at reflux for 1 hour. After cooling, 20 ml. of 70% perchloric acid was added and the pale pink solid that separated out was collected by filtration and washed with a little water.

By this procedure the following compounds were prepared.

2-(Dimethylamino) Derivative IIIa.

This compound had m.p. 299-300° dec., after recrystallization from aqueous ethanol, yield 84.0%; ir: 1654, 1605 (broad) cm^{-1}; nmr (DMSO-d_6): τ 7.34 (s, 3H, 4-CH_3), 6.52 (near s, 6H, N-CH_3), 6.01 (s, 3H, OCH_3), 2.87-2.46 (m, 3H, H-3, 6, 8), 2.00 (d, 1H, H-5).

Anal. Calcd. for $C_{13}H_{16}ClNO_6$: C, 49.14; H, 5.07; Cl, 11.16; N, 4.41. Found: C, 49.04; H, 5.02; Cl, 11.20; N, 4.43.

2-(Diethylamino) Derivative IIIb.

This compound had m.p. 295-296° dec., after recrystallization from ethanol, yield 86.5%; ir: 1640, 1595 (broad) cm^{-1}; nmr (DMSO-d_6): τ 8.96-8.46 (m, 6H, ethyl CH_3), 7.34 (s, 3H, 4-CH_3), 6.43-5.76 (m, 4H, CH_2), 6.02 (s, 3H, OCH_3), 2.91-2.46 (m, 3H, H-3, 6, 8), 2.03 (d, 1H, H-5).

Anal. Calcd. for $C_{15}H_{20}ClNO_6$: C, 52.10; H, 5.83; Cl, 10.25; N, 4.05. Found: C, 52.12; H, 5.85; Cl, 10.28; N, 4.06.

2-Piperidino Derivative IIIc.

This compound had m.p. 280-281° dec., after recrystallization from ethanol, yield 95.5%; ir: 1648, 1607, 1592 cm^{-1}; nmr (DMSO-d_6): τ 8.50-8.04 (m, 6H, β and γ-CH_2), 7.36 (s, 3H, 4-CH_3), 6.30-5.77 (m, 4H, α-CH_2), 6.01 (s, 3H, OCH_3), 2.96-2.43 (m, 3H, H-3, 6, 8), 2.05 (d, 1H, H-5).

Anal. Calcd. for $C_{16}H_{20}ClNO_6$: C, 53.71; H, 5.63; Cl, 9.91; N, 3.91. Found: C, 53.84; H, 5.66; Cl, 9.97; N, 3.87.

2-(Dialkylamino)-7-hydroxy-4-methylchromenylium Iodides (IIIf-h).

The solution of 1.0 g. of each compound IIa-c in 25 ml. of 57% hydroiodic acid was heated at reflux for 1 hour and the white solid that separated out on cooling was recovered by filtration and washed with a little water.

In this way the following compounds were prepared.

2-(Dimethylamino) Derivative IIIf.

This compound started to precipitate from the boiling solution, m.p. 258-259° dec., after recrystallization from ethanol, yield 96.8%; ir: 3400 (broad) (OH), 1653, 1596 (broad) cm^{-1}; nmr (DMSO-d_6): τ 7.36 (s, 3H, 4-CH_3), 6.53 (s, 6H, N-CH_3), 3.03-2.73 (m, 3H, H-3, 6, 8), 2.08 (d, 1H, H-5).

Anal. Calcd. for $C_{12}H_{14}INO_2$: C, 43.52; H, 4.26; I, 38.32; N, 4.23. Found: C, 43.31; H, 4.34; I, 38.37; N, 4.21.

2-(Diethylamino) Derivative IIIg.

This compound had m.p. 205-206° dec., after recrystallization from absolute ethanol plus ethyl ether, yield 94.6%; ir: 3180 (broad) (OH), 1642, 1590 (broad) cm^{-1}; nmr (DMSO-d_6): τ 8.89-8.49 (m, 6H, ethyl CH_3), 7.34 (s, 3H, 4-CH_3), 6.38-5.87 (m, 4H, CH_2), 3.09-2.68 (m, 3H, H-3, 6, 8), 2.12 (d, 1H, H-5).

Anal. Calcd. for $C_{14}H_{18}INO_2$: C, 46.80; H, 5.05; I, 35.33; N, 3.89. Found: C, 46.60; H, 5.15; I, 35.21; N, 3.80.

2-Piperidino Derivative IIIh.

This compound had m.p. 269-270° dec., after recrystallization from ethanol, yield 98.3%; ir: 3170 (broad) (OH), 1643, 1594 (broad) cm^{-1}; nmr (DMSO-d_6): τ 8.52-8.02 (m, 6H, β and γ-CH_2), 7.37 (s, 3H, CH_3), 6.28-5.78 (m, 4H, α-CH_2), 3.10-2.55 (m, 3H, H-3, 6, 8), 2.11 (d, 1H, H-5).

Anal. Calcd. for $C_{15}H_{18}INO_2$: C, 48.53; H, 4.89; I, 34.19; N, 3.77. Found: C, 48.59; H, 4.97; I, 33.99; N, 3.68.

3-(Dialkylamino)-1-methylnaphtho[2,1-*b*]pyrylium Iodides (IIId,e).

The reaction was carried out in the same manner as described for the former compounds IIIf-h using 1.0 g. of IId or IIe, recrystallizing then from a suitable solvent the yellow-orange solid that separated.

3-(Dimethylamino) Derivative IIId.

This compound was recrystallized from ethanol, m.p. 286-287° dec.; yield 66.9%; ir: 1650, 1548 cm^{-1}; nmr (DMSO-d_6): τ 6.81 (s, 3H, 1-CH_3), 6.46 (s, 6H, N-CH_3), 2.58-1.06 (m, 7H, H-2, 5, 6, 7, 8, 9, 10).

Anal. Calcd. for $C_{16}H_{16}INO$: C, 52.61; H, 4.42; I, 34.75; N, 3.84. Found: C, 52.58; H, 4.35; I, 34.86; N, 3.85.

3-(Diethylamino) Derivative IIIe.

This compound was recrystallized from 1-propanol, m.p. 262-263° dec.; yield 75.4%; ir: 1633, 1547 cm^{-1}; nmr (DMSO-d_6): τ 8.87-8.43 (m, 6H, ethyl CH_3), 6.83 (s, 3H, 1-CH_3), 6.38-5.83 (m, 4H, CH_2), 2.56-1.12 (m, 7H, H-2, 5, 6, 7, 8, 9, 10).

Anal. Calcd. for $C_{18}H_{20}INO$: C, 54.97; H, 5.13; I, 32.27; N, 3.56. Found: C, 54.90; H, 5.11; I, 32.34; N, 3.48.

[2-(Diethylamino)-7-methoxy-4*H*-chromen-4-ylidene]acetamide (V).

A 1.0 g. quantity of IIb was dissolved in 5 ml. of concentrated sulfuric acid and heated at 60° for 10 minutes. The resulting solution was poured onto crushed ice and the mixture was then made basic by the addition of 2*N* aqueous sodium hydroxide. After extraction with chloroform and elimination of the solvent under reduced pressure, the yellowish solid residue ultimately obtained was crystallized from ethyl acetate; there was obtained 0.52 g. (53.3%) of compound V which melted at 203-204° dec.; ir: 3370 and 3165 (NH_2), 1620 (C=O) cm^{-1}; nmr (DMSO-d_6): τ 8.83 (t, 6H, ethyl CH_3), 6.60 (q, 4H, CH_2), 6.13 (s, 3H, OCH_3), 4.44 (s, 1H, α-H), 3.63 (broad s, 2H, NH_2), 3.26-3.00 (m, 2H, H-6, 8), 2.92 (s, 1H, H-3), 2.34 (d, 1H, H-5); ms: m/e 288 (M^+).

Anal. Calcd. for $C_{16}H_{20}N_2O_3$: C, 66.64; H, 6.99; N, 9.72. Found: C, 66.66; H, 6.92; N, 9.65.

N,N-Diethyl [3-carbamoyl-7-methoxy-2-oxo-2*H*-chromen-4-yl]acetamide (VI).

The mixture of 1.0 g. of IIb and 10 g. of polyphosphoric acid was heated with stirring at 100° for 4 hours. After cooling 50 ml. of water was added and the solution was made basic with excess 2*N* aqueous sodium hydroxide. After extraction with chloroform and removal of the solvent under reduced pressure, the yellow solid residue was crystallized from ethanol; there was obtained 0.30 g. (26.7%) of VI which melted at 198-199°; ir: 3440 and 3305 (NH_2), 1695 (α-pyrone C=O), 1675 and 1620 (amide C=O) cm^{-1}; nmr (DMSO-d_6): τ 9.15-8.57 (m, 6H, ethyl CH_3), 6.90-6.36 (m, 4H, N-CH_2), 6.08 (s, 3H, OCH_3), 5.91 (s, 2H, CH_2), 3.10-2.84 (m, 2H, H-6, 8), 2.48-2.12 (m, 3H, H-5 and NH_2); ms: m/e 332 (M^+).

Anal. Calcd. for $C_{17}H_{20}N_2O_5$: C, 61.43; H, 6.07; N, 8.43. Found: C, 61.40; H, 6.02; N, 8.40.

8-Methoxy-2*H*-[1]benzopyrano[3,4-*c*]pyridine-2,4,5-(1*H*,3*H*)trione (VII).

A 0.5 g. sample of the compound VI was heated at 200° for 5 minutes. After cooling, the material was crystallized from glacial acetic acid yielding a white solid (VII, 0.30 g., 76.9%) which melted at 349-350°; ir: broad band 3100-2400, 1670 (broad), 1610 cm^{-1}; ms: m/e 259 (M^+).

Anal. Calcd. for $C_{13}H_9NO_5$: C, 60.23; H, 3.50; N, 5.40. Found: C, 60.31; H, 3.58; N, 5.37.

2-(Diethylamino)-7-methoxy-4*H*-chromene-4-thione (VIIIa).

The mixture of 2.0 g. of the compound Ib, 2.0 g. of phosphorus pentasulfide and 15 ml. of pyridine was heated at reflux for 1 hour and then poured onto crushed ice. The yellow solid that separated out on stirring was recovered, washed with water and crystallized from ethanol. There was obtained 1.3 g. (61.0%) of VIIIa which melted at 147-148°; ir: 1620, 1590, 1560 cm^{-1}; nmr (deuteriochloroform): τ 8.68 (t, 6H, ethyl CH_3), 6.45 (q, 4H, CH_2), 6.09 (s, 3H, OCH_3), 3.29-2.93 (m, 3H, H-3, 6, 8), 1.36 (d, 1H, H-5).

Anal. Calcd. for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.50; N, 5.32; S, 12.17. Found: C, 63.67; H, 6.40; N, 5.41; S, 12.21.

Ethyl [2-(Diethylamino)-7-methoxy-4*H*-chromen-4-ylidene]cyanoacetate (IXa).

A mixture of 1.0 g. (3.8 mmoles) of the compound VIIIa, 1.29 g. (11.4 mmoles) of ethyl cyanoacetate and 20 ml. of freshly distilled acetic anhydride was heated at 115° for 2 hours and then poured onto crushed ice. After stirring, the yellow solid which separated out was collected and washed with water. There was obtained 1.1 g. of nearly pure IXa (yield 84.6%) which melted at 182-183° after crystallization from ethanol; ir: 2180 (C≡N), 1672 (C=O) cm^{-1}; nmr (deuteriochloroform): τ 8.85-8.47 (m, 9H, ethyl CH_3), 6.42 (q, 4H, N-CH_2), 6.10 (s, 3H, OCH_3), 5.72 (q, 2H, OCH_2), 3.26-2.91 (m, 2H, H-6, 8), 2.25 (s, 1H, H-3), 0.82 (d, 1H, H-5); ms: m/e 342 (M^+).

Anal. Calcd. for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 66.48; H, 6.43; N, 8.08.

Hydrolysis of the Compound IXa.

a) With Hydrochloric Acid.

A 1.0 g. sample of the compound IXa was dissolved in 30 ml. of 18% hydrochloric acid and refluxed for 2 hours. After the addition of 20 ml. of water, the mixture was cooled and the white precipitate was collected and dissolved in the minimum of water. Addition of 70% perchloric acid gave rise to 0.35 g. of IIIb, as confirmed by melting point and ir spectrum.

The hydrochloric filtrate was treated with a saturated aqueous solution of sodium bicarbonate and the orange crystalline product which separated out was recovered by filtration and washed with water.

There was obtained 0.3 g. (37.3%) of [2-(diethylamino)-7-methoxy-4*H*-chromen-4-ylidene]acetonitrile (X) which melted at 132-133° after crystallization from ethyl acetate; ir: 2165 cm^{-1} (C≡N); nmr (deuteriochloroform): τ 8.75 (t, 6H, ethyl CH_3), 6.58 (q, 4H, CH_2), 6.14 (s, 3H, OCH_3), 5.50 (s, 1H, α-H), 4.55 (s, 1H, H-3), 3.41-3.10 (m, 2H, H-6, 8), 2.51 (d, 1H, H-5).

Anal. Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.23; H, 6.73; N, 10.31.

b) With Hydroiodic Acid.

A solution of 1.0 g. of IXa in 25 ml. of 57% hydroiodic acid was refluxed for 1 hour. On cooling the solid that separated out was collected, washed with a little water and crystallized from ethanol. There was obtained 0.65 g. (62.0%) of IIIg as confirmed by melting point and ir spectrum.

c) With Polyphoshoric Acid.

The mixture of 1.0 g. of IXa and 10 g. of polyphosphoric acid was heated at 100° for 4 hours. After cooling, 50 ml. of water and then solid sodium bicarbonate were added. Precipitation of X (0.1 g.) (melting point and ir) occurred while the solution was still acid. After removal of the product by filtration, the filtrate was made definitely basic with 2N aqueous sodium hydroxide. There was recovered V (melting point and ir) which weighed 0.35 g. (39.4%) after crystallization from ethyl acetate.

Ethyl [3-(Diethylamino)-1*H*-naphtho[2,1-*b*]pyran-1-ylidene]cyanoacetate (IXb).

A mixture of 1.0 g. (3.5 mmoles) of VIIIb (16), 0.85 g. (7.5 mmoles) of ethyl cyanoacetate and 20 ml. of freshly distilled acetic anhydride was heated at 90° for 2 hours and then poured onto crushed ice. The yellowish solid which separated out was collected, washed with water and crystallized from 1-propanol. There was obtained 0.3 g. (23.5%) of IXb which melted at 156-157°; ir: 2185 (C≡N), 1680 (C=O) cm^{-1}; nmr (deuteriochloroform): τ 8.95-8.36 (m, 9H, CH_3), 6.41 (q, 4H, N-CH_2), 5.75 (q, 2H, OCH_2), 2.87-1.86 (m, 6H, H-2, 5, 6, 7, 8, 9), 1.44 (mc, 1H, H-10).

Anal. Calcd. for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73. Found: C, 72.82; H, 6.21; N, 7.80.

Hydrolysis of the Compound IXb.

A solution of 1.0 g. of IXb in 25 ml. of 57% hydroiodic acid was refluxed for 1 hour. On cooling an orange solid separated out which was collected, washed with a little water and crystallized from 1-propanol. There was obtained 0.70 g. (64.8%) of IIIe, as confirmed by melting point and ir spectrum.

7-Methoxy-4-methylcoumarin (IVa) from IIIb.

The mixture of 0.5 g. of IIIb and 20 ml. of saturated aqueous solution of sodium bicarbonate was heated at 95° for 2 hours. After cooling, concentrated hydrochloric acid was added and the solid which separated out was collected, washed with water and crystallized from ethyl acetate. There was obtained IVa which weighed 0.20 g. (72.7%) and melted at 157-158° [lit. (17) m.p. 159°]. No depression of the melting point was observed when the product was mixed with an authentic sample (17).

7-Hydroxy-4-methylcoumarin (IVb) from IIIg.

The mixture of 0.5 g. of IIIg and 20 ml. of saturated aqueous solution of sodium bicarbonate was heated at 95° for 2 hours. After cooling and addition of concentrated hydrochloric acid the solid that separated out was recovered and crystallized from ethanol. There was obtained 0.19 g. (74.2%) of IVb which melted at 185-186° [lit. (18) m.p. 185°]. No depression of the melting point was observed when this compound was mixed with a sample of the commercial product.

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REFERENCES AND NOTES

(1) "Rodd's Chemistry of Carbon Compounds", Vol. IV, Part E; Elsevier Scientific Publishing Company, Amsterdam, 1977, pp. 68-96.

(2) F. M. Dean, "Naturally Occurring Oxygen Ring Compounds", Butterworths, London, 1963, pp. 388-426.

(3) J. A. Van Allan, G. A. Reynolds and C. C. Petropoulos, *J. Heterocyclic Chem.*, **15**, 365 (1978); G. A. Reynolds and J. A. Van Allan, *ibid.*, **15**, 1225 (1978); K. Maruyama, T. Kuboto, K. Kojima and M. Harada, Japanese Patent 74 16,503, Apr. 23, 1974; *Chem. Abstr.*, **82**, 78776v (1975).

(4) V. V. Mezheritskii, A. L. Wasserman and G. N. Dorofeenko, *Heterocycles*, **12**, 51 (1979).

(5) A. Ermili and G. Roma, *Gazz. Chim. Ital.*, **101**, 269 (1971).

(6) A. Ermili, G. Roma, M. Mazzei, A. Balbi, A. Cuttica and N. Passerini, *Il. Farmaco, Ed. Sci.*, **29**, 225 (1974).

(7) A. Ermili, M. Mazzei, G. Roma and C. Cacciatore, *ibid.*, **32**, 375 (1977).

(8) G. Roma, E. Vigevani, M. Mazzei, A. Ermili, A. Ambrosini and N. Passerini, *ibid.*, **33**, 822 (1978).

(9) A. Ermili, A. Balbi, M. Di Braccio and G. Roma, *ibid.*, **32**, 713

(1977).

(10) M. Ohta and H. Kato, *Bull. Chem. Soc. Japan*, **32**, 707 (1959).

(11) J. A. Van Allan and G. A. Reynolds, *J. Heterocyclic Chem.*, **9**, 669 (1972).

(12) G. Roma, A. Ermili and A. Balbi, *ibid.*, **12**, 1103 (1975).

(13) V. A. Zagorevskii, I. D. Tsvetkova, E. K. Orlova and S. L. Portnova, *Khim. Geterosikl. Soedin.*, 422 (1969).

(14) I. Belsky, *Tetrahedron*, **28**, 1001 (1972).

(15) A. Ermili, G. Roma and A. Balbi, *Gazz. Chim. Ital.*, **101**, 651 (1971).

(16) A. Balbi, G. Roma, M. Di Braccio and A. Ermili, *Il. Farmaco. Ed. Sci.*, **33**, 807 (1978).

(17) H. v. Pechmann and C. Duisberg, *Ber.*, **16**, 2119 (1883).

(18) A. Russell and J. R. Frye, *Org. Synth.*, **21**, 22 (1941).