

SYNTHESIS OF *N*-(2-DIALKYLAMINOETHYL)-2-OXO-2*H*-1-BENZO-(THIO)PYRAN-3-CARBOXAMIDINES

Youssef El-Ahmad^{a1}, Jean-Daniel Brion^{*b1}, and Pierre Reynaud^a

^aLaboratoire de Chimie Thérapeutique I, UFR des Sciences Pharmaceutiques, rue JB.Clément, 92296 Châtenay-Malabry Cedex, France

^bLaboratoire de Chimie Thérapeutique, UFR des Sciences Pharmaceutiques, 1, rue G. Veil, 44035 Nantes Cedex, France

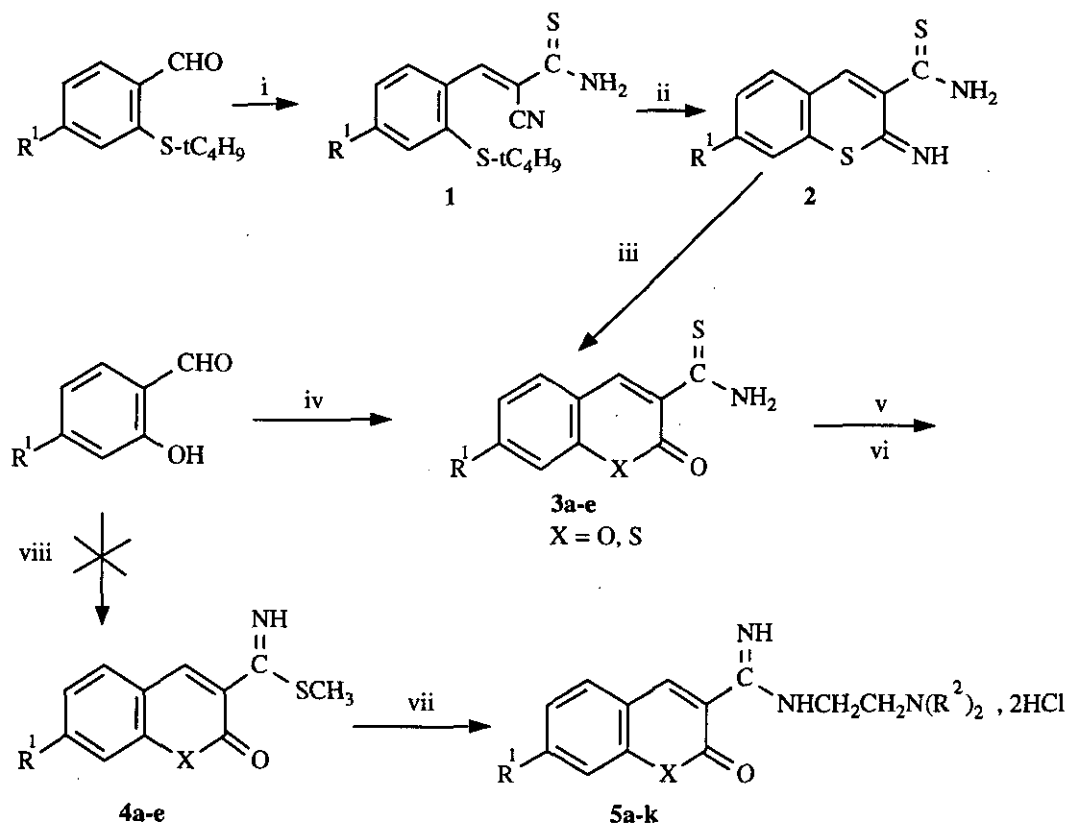
Abstract- An improved method for the preparation of *N*-(2-dialkylaminoalkyl)-substituted 2-oxo-2*H*-benzo(thio)pyran-3-carboxamides from the corresponding methyl (thio)coumarin-3-carboximidothioates is described.

Coumarins and thiocoumarins exhibit various biological activities, for example as anticoagulants, photointercalants or enzyme inhibitors.² Introduction of the *N*-dialkylaminoethylcarboxamide pharmacophore^{3,4} in these heterocycles leads to the products (**5a-k**) which present an interesting "dual potential" from pharmacological viewpoint.

To our best knowledge, only the preparation of 2*H*-1-benzopyran-3-carboxamide and of its 8-methoxy derivative is appeared in the literature.⁵ As neither the amine exchange reaction⁶ of the 2-oxo-2*H*-1-benzo(thio)pyran-3-carboxamides⁵ with *N,N*-dialkylaminoethylamine, nor direct condensation of 2-hydroxybenzaldehyde with ethyl *N*-(2-dialkylaminoethyl)carboxamidinoacetate ($C_2H_5OC(O)CH_2C(NH)NHCH_2CH_2NR_2$) gave the desired products, we used the following method to obtain (**5a-k**).

The 2*H*-1-benzo(thio)pyran-3-carbothioamides (**3a-e**), treated with iodomethane in a DMF/acetone mixture in the case of (**3a-d**) (or in acetone in the case of **3e**), lead to the corresponding imidothioesters hydroiodides (thioimidates) (Scheme 1). The free bases (**4a-e**), obtained after alkaline treatment with triethylamine in dioxane (Table 2), react with *N,N*-dialkylethylenediamine dihydrochlorides in ethanol (or DMSO or DMSO/ethanol) at around 80°C to give the expected amidinium dichlorides (**5a-k**) (yield: 46-75%, see Table 3).

Scheme 1



i = $\text{NCCH}_2\text{C}(\text{S})\text{NH}_2$, $\text{CH}_3\text{COONH}_4$, CH_3COOH ; ii = polyphosphoric acid; iii = 2N HCl

iv = $\text{C}_2\text{H}_5\text{OC}(\text{O})\text{CH}_2\text{C}(\text{S})\text{NH}_2$, piperidine, benzene; v = CH_3I , DMF (or dioxane), acetone

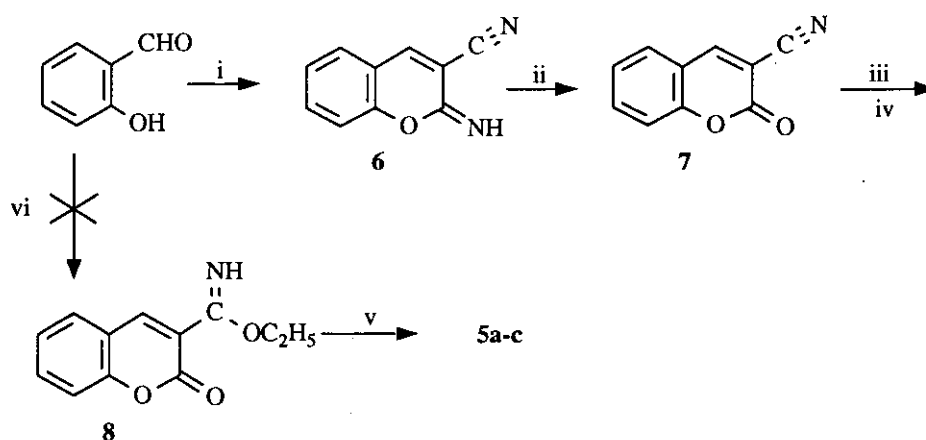
vi = $\text{N}(\text{C}_2\text{H}_5)_3$, dioxane; vii = $\text{H}_2\text{NCH}_2\text{CH}_2\text{N}(\text{R}^2)_2$, 2HCl

viii = $\text{C}_2\text{H}_5\text{OC}(\text{O})\text{CH}_2\text{C}(\text{NH})\text{SCH}_3$, piperidine, benzene

The coumarins (**3a-d**) are easily obtained by direct condensation of 2-hydroxybenzaldehyde with ethyl thiocarbamoylacetate under basic catalytic conditions (yield: 59-92%). In the case of thiocoumarin (**3e**), as there are difficulties to obtain the thiosalicylic aldehyde, the method of Meth-Cohn and Tamowski^{7,8} using 2-*tert*-butylthiobenzaldehyde and cyanothioacetamide is by far preferred. Cyclisation of the thiocinnamamide (**1**) with polyphosphoric acid leads to iminobenzothiopyran (**2**)⁸, which is hydrolysed into **3e** (Scheme 1). For **5a-c** ($\text{X} = \text{O}$), we also verified the reactivity of ethyl 2*H*-1-benzopyran-3-carboximidates (**8**) towards *N,N*-dialkylethylenediamines. Although the yields are of the same order, we advocate the first methodology which presents two main advantages: speed and safety.

Indeed **8** was prepared from the 3-cyanocoumarin (**7**) by Pinner's reaction according to general conditions (Scheme 2),³ after condensation of 2-hydroxybenzaldehyde with malononitrile giving the 2-imino-2H-1-benzopyran-3-carbonitrile (**6**), which was hydrolysed to **7**;⁹ however the compound (**6**) is particularly difficult to handle as highly lacrymatory and sternutatory.

Scheme 2



i = $\text{CH}_2(\text{CN})_2$, piperidine, $\text{C}_2\text{H}_5\text{OH}$; ii = H_3O^+ ; iii = HCl , $\text{C}_2\text{H}_5\text{OH}$, dioxane; iv = $\text{N}(\text{C}_2\text{H}_5)_3$, dioxane; v = $\text{H}_2\text{NCH}_2\text{CH}_2\text{N}(\text{R}^2)_2$, 2HCl , DMF , $\text{C}_2\text{H}_5\text{OH}$; vi = $\text{C}_2\text{H}_5\text{OC}(\text{O})\text{CH}_2\text{C}(\text{NH})\text{OR}$, piperidine, benzene.

Finally, we attempted the preparation of the imino(thio)esters (**4a-e**) or (**8**) directly from 2-hydroxybenzaldehyde and malonic derivative ($\text{C}_2\text{H}_5\text{OC}(\text{O})\text{CH}_2\text{C}(\text{NH})\text{XR}$) was unsuccessful.

EXPERIMENTAL

Mp are measured by Buchi-Tottoli apparatus. Ir spectra are recorded with Perkin-Elmer apparatus in chloroform or in potassium bromide (1%). $^1\text{H-Nmr}$ spectra are recorded with Varian T60 spectrometer in a solution (CDCl_3 , DMSO-d_6 , CD_3OD or D_2O). The shifts are expressed in ppm from TMS (s, d, t, m, m, meaning singlet, doublet, triplet, multiplet and broad multiplet respectively).

3-(2-tert-Butylthiophenyl)-2-cyanothiopropenamide (**1**) ($\text{R}_1 = \text{H}$).

A mixture of 2-tert-butylthiobenzaldehyde⁷ (19.4 g, 0.1 mol), cyanothioacetamide^{10,11} (8.6 g, 0.1 mol), ammonium acetate (1.5 g, 0.02 mol) and acetic acid (5 ml) was heated in dry benzene (80 ml) for 18 h.

The solvent was removed under reduced pressure to afford the crude **1**, which was crystallized from benzene to give orange coloured crystals; yield: 19.6 g (71%), mp 155°C . $^1\text{H-Nmr}$ (CDCl_3): 1.35 (s, 9H, $(\text{CH}_3)_3$),

7.40-7.80 (m, 5H, $H_{6,7,8}$ and NH_2), 8.20 (s, 1H, H_4), 9.6 (s, 1H, H_{eth}). Ir ($CHCl_3$): 3350-3180 (NH), 2210 (CN), 1635 ($C=C$) cm^{-1} . Anal. Calcd for $C_{14}H_{16}N_2S_2$: C, 60.83; H, 5.83; N, 10.13. Found: C, 61.08; H, 6.02; N, 9.98.

2-Imino-2H-1-benzothiopyran-3-carbothioamide (2) ($R_1 = H$)

A mixture of (1) (2.76 g, 10 mmol) and polyphosphoric acid (100 g) was heated with vigorous stirring at 100°C for 2 h. After cooling, the mixture was added to crushed ice and neutralised by 30% NaOH solution while the temperature not exceeding +5°C. The solid was filtered, washed with H_2O and dried. The product was crystallized from ethyl acetate; yield: 1.65 g (75 %), mp 91°C. 1H -Nmr ($DMSO-d_6$): 7.55 (m, 3H, $H_{6,7,8}$), 7.75 (m, 1H, H_5), 8.55 (s, 1H, H_4), 10.30 (m, 2H, NH_2), 11.0 (s, 1H, NH). Ir (KBr): 3200 (NH), 1650 ($C=N$), 1600 (NH_2) cm^{-1} . Anal. Calcd for $C_{10}H_8N_2S_2$: C, 54.52; H, 3.66; N, 12.72. Found: C, 54.34; H, 3.61; N, 12.93.

2-Oxo-2H-1-benzothiopyran-3-carbothioamide (3a-d) ($X=O$)

General procedure :

In a flask fitted with Dean-Stark apparatus, 2-hydroxybenzaldehyde (18.3 g, 0.15 mol) and ethyl thiocarbamoylacetate¹¹ (22.10 g, 0.15 mol) were dissolved in benzene (20 ml) with few drops of piperidine and heated to reflux until the quantity of H_2O (2.7 ml) was convenient (30 min). After cooling, the solid was filtered and washed several times with ether.

Yield, ir and 1H -nmr are listed in Table 1.

2-Oxo-2H-1-benzothiopyran-3-carbothioamide (3e) ($X=S$, $R_1 = H$)

2-Iminothiocoumarin (2) (2.20 g, 10 mmol) was heated under reflux for 2 h in 2N HCl solution (20 ml). After cooling, the mixture is neutralised by a stoichiometric quantity of 2N NaOH (20ml). The thiocoumarin (3e) was collected by filtration and crystallized from ethyl acetate; yield: 1.86 g (84%), mp 175°C. 1H -Nmr ($CDCl_3$): 7.40-7.65 (m, 3H, $H_{6,7,8}$), 7.90 (m, 1H, H_5), 9.25 (s, 1H, H_4), 9.85 (m, 2H, NH_2). Ir (KBr): 3310 (NH), 1690 ($C=O$), 1600 (NH_2) cm^{-1} . Anal. Calcd for $C_{10}H_7NOS_2$: C, 54.27; H, 3.19; N, 6.33. Found: C, 54.56; H, 3.39; N, 6.58.

Methyl 2-oxo-2H-1-benzothiopyran-3-carboximidothioate (4a-d) ($X=O$)

General procedure:

(3a-c) ($R_1 = H$, OCH_3 , $OCH_2C_6H_5$) (0.1 mol) was dissolved in DMF (250 ml) (or in dioxane (250 ml) for (3d) ($R = OCH_2COOC_2H_5$) (0.1 mol)). To the solution cooled to 0°C (filtered if necessary, dry acetone (150 ml) followed by iodomethane (20 ml, 0.32 mol) was added. The mixture was maintained at rest for 24 h away from light. The hydroiodide were collected by filtration and washed with ether. Hydroiodide salt (0.1 mol) was suspended in dioxane (500 ml) and triethylamine (14.5 ml, 0.1 mol) was added to the suspension. The mixture became colourless soon. After stirring for 1 h at room temperature, the solvents were removed under reduced pressure. The residue was extracted with $CHCl_3$ (50 ml) and the extract was washed with ice-water, dried (Na_2SO_4) and the solvent was removed *in vacuo*. The imidothioester was used without any purification and was rapidly engaged in the following reaction. Yield and spectra data: see Table 2.

Methyl 2-oxo-2H-1-benzothiopyran-3-carboximidothioate (4e) ($X=S$)

To a solution of 3e (22.10 g, 0.1 mol) dissolved in dry acetone (60 ml), iodomethane (20 ml, 0.32 mol) was

Table 1 : Physicochemical and spectral data of Compounds (3a-e)

Compound	X	R ¹	Yield (%)	mp (°C)	Molecular ^a Formula	Microanalyses (%)			¹ H-nmr (DMSO-d ₆) δ (ppm)
						C calcd found	H calcd found	N calcd found	
3a	O	H	86	227 C ₂ H ₅ OH	C ₁₀ H ₇ NO ₂ S	58.52 58.43	3.44 3.51	6.82 6.70	7.25-8.00 (m, 4H, H ₅₋₈); 8.90 (s, 1H, H ₄); 9.75 (s, 1H, NH); 10.20 (s, 1H, NH).
3b	O	OCH ₃	74	238 C ₂ H ₅ OH/ ether	C ₁₁ H ₉ NO ₃ S	56.15 55.93	3.86 3.92	5.95 6.07	3.90 (s, 3H); 7.05 (dd, J = 9 Hz, J = 2 Hz, 1H, H ₆); 7.10 (d, J = 2 Hz, 1H, H ₈); 8.00 (d, J = 9 Hz, 1H, H ₅); 9.00 (s, 1H, H ₄); 9.80 (s, 1H, NH); 10.30 (s, 1H, NH).
3c	O	OCH ₂ C ₆ H ₅	59	201 C ₂ H ₅ OH/ ether	C ₁₇ H ₁₃ NO ₃ S	65.58 65.73	4.21 4.04	4.50 4.58	5.25 (s, 2H); 6.95-7.20 (m, 2H, H _{6,8}); 7.20-7.50 (m, 5H, C ₆ H ₅); 7.85 (d, 1H, J = 9 Hz, H ₅); 9.00 (s, 1H, H ₄); 9.75 (s, 1H, NH); 10.00 (s, 1H, NH).
3d	O	OCH ₂ COOC ₂ H ₅	92	214 C ₂ H ₅ OH/ ether	C ₁₄ H ₁₃ NO ₅ S	54.72 54.57	4.26 4.15	4.56 4.69	1.20 (t, J = 7 Hz, 3H); 4.20 (q, J = 7 Hz, 2H); 5.00 (s, 2H) 6.90-7.10 (m, 2H, H _{6,8}); 7.85 (d, J = 9 Hz, 1H, H ₅); 9.00 (s, 1H, H ₄); 9.70 (s, 1H, NH); 10.00 (s, 1H, NH).
3e	S	H	84	175 C ₂ H ₅ OH	C ₁₀ H ₇ NO ₂ S	54.28 54.56	3.19 3.39	6.33 6.58	7.40-7.65 (m, 3H, H _{6,7,8}); 7.90 (m, 1H, H ₅); 9.25 (s, 1H, H ₄); 9.85 (m, 2H, NH ₂).

^aIr (KBr): 3300-3160 (NH); 1680 (C=O) cm⁻¹

Table 2 : Physicochemical and spectral data of Compounds (4a-e)

Compound	X	R ¹	Yield (%)	Molecular ^a Formula	Microanalyses (%) ^b			¹ H-nmr (DMSO-d ₆) δ (ppm)	ir(KBr) (cm ⁻¹)
					C calcd found	H calcd found	N calcd found		
4a	O	H	45	C ₁₁ H ₉ NO ₂ S	38.06 38.21	2.90 2.75	4.03 4.12	2.50 (s, 3H); 7.15-7.85 (m, 4H, H ₅₋₈); 8.30 (s, 1H, H ₄); 9.90 (s, 1H, NH).	3250, 1725, 1610, 1600
4b	O	OCH ₃	49	C ₁₁ H ₉ NO ₃ S	38.21 38.05	3.21 3.32	3.71 3.82	2.50 (s, 3H); 3.90 (s, 3H); 6.80 (d, J = 2 Hz, 1H, H ₈); 6.85 (dd, J = 9 Hz, J = 2 Hz, 1H, H ₆); 7.50 (d, J = 9 Hz, 1H, H ₅); 8.20 (s, 1H, H ₄); 9.85 (s, 1H, NH).	3250, 1710, 1610, 1600
4c	O	OCH ₂ C ₆ H ₅	71	C ₁₈ H ₁₅ NO ₃ S	47.69 47.52	3.56 3.74	3.09 3.25	2.45 (s, 3H); 5.15 (s, 2H); 6.80-7.00 (m, 2H, H _{6,8}); 7.35-7.45 (m, 5H, C ₆ H ₅); 7.45 (d, 1H, J = 9 Hz, H ₅); 8.15 (s, 1H, H ₄); 10.50 (s, 1H, NH).	3250, 1710, 1610, 1600
4d	O	OCH ₂ COOC ₂ H ₅	38	C ₁₅ H ₁₅ NO ₅ S	43.18 43.05	3.87 3.75	3.36 3.52	1.30 (t, J = 7 Hz, 3H); 2.45 (s, 3H); 4.20 (q, J = 7 Hz, 2H); 4.60 (s, 2H); 6.60 (d, 1H, J = 2 Hz, H ₈); 6.75 (dd, 1H, J = 9 Hz, J = 2 Hz, H ₆); 7.35 (d, J = 9 Hz, 1H, H ₅); 8.00 (s, 1H, H ₄); 10.10 (s, 1H, NH).	3250, 1745, 1690, 1610, 1600
4e	S	H	78	C ₁₀ H ₇ NOS ₂	36.37 36.25	2.77 2.93	3.86 3.72	2.55 (s, 3H); 7.30-7.90 (m, 4H, H ₅₋₈); 8.25 (s, 1H, H ₄); 9.90 (s, 1H, NH).	3280, 1660, 1635, 1600

a : Use without any crystallization

b : Analysed as hydroiodide

Table 3 : Physicochemical data of Compounds (5a-k)

Compound	X	R ¹	N(R ²) ₂	Reaction Solvent	Conditions Time(h)/ Temp(°C)	Yield (%)	mp (°C)	Molecular Formula	Microanalyses (%)		
									C calcd found	H calcd found	N calcd found
5a	O	H	N(CH ₃) ₂	DMF/C ₂ H ₅ OH (3/1)	4/80	46	243 C ₂ H ₅ OH	C ₁₄ H ₁₉ N ₃ O ₂ Cl ₂	50.60 50.39	5.72 5.85	12.65 12.48
5b	O	H	N(C ₂ H ₅) ₂	DMSO	6/80	70	250 C ₂ H ₅ OH	C ₁₆ H ₂₃ N ₃ O ₂ Cl ₂ , H ₂ O	50.80 50.84	6.66 6.70	11.11 11.13
5c	O	H	Morpholine	DMSO	6/80	59	249 C ₂ H ₅ OH	C ₁₆ H ₂₁ N ₃ O ₃ Cl ₂	51.33 51.54	5.61 5.85	11.23 10.99
5d	O	OCH ₃	N(CH ₃) ₂	DMF/C ₂ H ₅ OH (2/1)	4/80	52	239 C ₂ H ₅ OH/ ether	C ₁₅ H ₂₁ N ₃ O ₃ Cl ₂	49.72 49.14	5.25 5.79	11.60 11.14
5e	O	OCH ₃	N(C ₂ H ₅) ₂	C ₂ H ₅ OH	4/78	75	186 C ₂ H ₅ OH/ ether	C ₁₇ H ₂₅ N ₃ O ₃ Cl ₂ , 0.50 H ₂ O	51.72 51.66	6.51 6.30	10.64 10.56
5f	O	OCH ₃	Morpholine	C ₂ H ₅ OH	5/78	70	252 C ₂ H ₅ OH/ ether	C ₁₇ H ₂₃ N ₃ O ₄ Cl ₂ , 0.50 H ₂ O	49.40 49.39	5.85 5.77	10.17 10.16
5g	O	OCH ₂ C ₆ H ₅	N(CH ₃) ₂	DMF/C ₂ H ₅ OH (1/1)	3/80	36	224 C ₂ H ₅ OH	C ₂₁ H ₂₅ N ₃ O ₃ Cl ₂	57.53 57.29	5.70 5.86	9.59 9.40
5h	O	OCH ₂ COOC ₂ H ₅	N(CH ₃) ₂	DMSO	6/95	62	216 C ₂ H ₅ OH	C ₁₈ H ₂₅ N ₃ O ₅ Cl ₂	49.77 49.55	5.76 5.90	9.68 9.51
5i	S	H	N(CH ₃) ₂	C ₂ H ₅ OH	2/78	75	234 C ₂ H ₅ OH	C ₁₄ H ₁₉ N ₃ OCl ₂ S	48.23 48.25	5.50 5.45	12.06 11.95
5j	S	H	N(C ₂ H ₅) ₂	C ₂ H ₅ OH	2/78	62	240 C ₂ H ₅ OH	C ₁₆ H ₂₃ N ₃ OCl ₂ S	51.06 51.01	6.16 6.28	11.16 11.13
5k	S	H	Morpholine	C ₂ H ₅ OH	2/78	67	260 C ₂ H ₅ OH/ ether	C ₁₆ H ₂₁ N ₃ O ₂ Cl ₂ S	49.23 49.19	5.42 5.24	10.76 10.59

Table 4 : Spectroscopic data of Compounds (5a-k)

Compound	Solvent	^1H -nmr δ (ppm)	ir(KBr) (cm^{-1})
5a	CD_3OD^a	3.05 (s, 6H); 3.60 (t, $J = 7$ Hz, 2H); 4.00 (t, $J = 7$ Hz, 2H); 7.35-7.60 (m, 2H, $\text{H}_{6,8}$); 7.65-7.90 (m, 2H, $\text{H}_{5,7}$); 8.90 (s, 1H, H_4).	3480, 3380, 2650, 1710, 1670, 1630, 1600
5b	CD_3OD^a	1.40 (t, $J = 7$ Hz, 6H); 3.40 (q, $J = 7$ Hz, 4H); 3.60 (t, $J = 7$ Hz, 2H); 4.05 (t, $J = 7$ Hz, 2H); 7.30-7.55 (m, 2H, $\text{H}_{6,8}$); 7.65-7.90 (m, 2H, $\text{H}_{5,7}$); 8.85 (s, 1H, H_4).	3480, 3380, 2600, 1710, 1670, 1630, 1605
5c	D_2O^a	3.45-3.80 (m, 6H); 3.90-4.15 (m, 6H); 7.40-7.70 (m, 2H, $\text{H}_{6,8}$); 7.75-7.80 (m, 2H, $\text{H}_{5,7}$); 8.75 (s, 1H, H_4).	3480, 3380, 2650, 1705, 1670, 1630, 1600
5d	CD_3OD^a	3.05 (s, 6H); 3.60 (t, $J = 7$ Hz, 2H); 3.95 (s, 3H); 4.00 (t, $J = 7$ Hz, 2H); 7.00 (d, $J = 2$ Hz, 1H, H_8); 7.05 (dd, $J = 9$ Hz, $J = 2$ Hz, 1H, H_6); 7.75 (d, $J = 9$ Hz, 1H, H_5); 8.90 (s, 1H, H_4).	3500, 3380, 2500, 1710, 1670, 1630, 1595
5e	CD_3OD^a	1.25 (t, $J = 7$ Hz, 6H); 3.30 (m, 6H); 3.80 (s, 3H); 4.45 (t, $J = 7$ Hz, 2H); 6.90 (d, $J = 2$ Hz, 1H, H_8); 7.05 (dd, $J = 9$ Hz, $J = 2$ Hz, 1H, H_6); 7.75 (d, $J = 9$ Hz, 1H, H_5); 8.70 (s, 1H, H_4).	3480, 3380, 2650, 1710, 1675, 1620, 1600
5f	D_2O^a	3.45-3.75 (m, 6H); 3.85-4.25 (m, 6H); 3.90 (s, 3H); 6.95 (d, $J = 2$ Hz, 1H, H_8); 7.15 (dd, $J = 9$ Hz, $J = 2$ Hz, 1H, H_6); 7.70 (d, $J = 9$ Hz, 1H, H_5); 9.00 (s, 1H, H_4).	3480, 3380, 2650, 1705, 1670, 1630, 1600
5g	CD_3OD^a	3.05 (s, 6H); 3.60 (t, $J = 7$ Hz, 2H); 4.00 (t, $J = 7$ Hz, 2H); 5.25 (s, 2H); 7.10 (dd, $J = 9$ Hz, $J = 2$ Hz, 1H, H_6); 7.25-7.50 (m, 6H, Har, H_8); 7.75 (d, $J = 9$ Hz, 1H, H_5); 8.85 (s, 1H, H_4).	3480, 3375, 2550, 1710, 1670, 1630, 1600
5h	DMSO-d_6	1.05 (t, $J = 7$ Hz, 3H); 2.90 (s, 6H); 3.55 (m, 2H); 3.90-4.15 (m, 2H); 4.20 (q, $J = 7$ Hz, 2H); 5.05 (s, 2H); 7.00 (d, $J = 2$ Hz, 1H, H_8); 7.15 (m, 1H, H_6); 7.80; (d, $J = 9$ Hz, 1H, H_5); 9.00 (s, 1H, H_4); 9.70 and 11.50 (m, 4H, NH).	3500, 3380, 2650, 1710, 1675, 1630, 1600
5i	DMSO-d_6	2.85 (s, 6H); 3.45 (t, $J = 7$ Hz, 2H); 4.00 (t, $J = 7$ Hz, 2H); 7.50-8.10 (m, 4H, $\text{H}_{5,8}$); 8.95 (s, 1H, H_4); 9.95 and 11.00 (m, 4H, NH).	3400, 2500, 1680, 1640
5j	DMSO-d_6	1.35 (t, $J = 7$ Hz, 6H); 3.30 (m, 6H); 4.10 (t, $J = 7$ Hz, 2H); 7.55-8.10 (m, 4H, $\text{H}_{5,8}$); 8.85 (s, 1H, H_4); 10.00 and 11.25 (m, 4H, NH).	3400, 2600, 1680, 1645
5k	DMSO-d_6	3.50 (m, 6H); 4.00 (m, 6H); 7.55-8.20 (m, 4H, $\text{H}_{5,8}$); 8.90 (s, 1H, H_4); 10.05 and 11.70 (m, 4H, NH).	3400, 2600, 1675, 1630

^aN-H protons exchanged with solvent deuterium

added. After standing for 24 h away from light, the hydroiodide was collected by filtration and washed with ether. The base is obtained in a similar way described above. Yield and spectral data are shown in Table 2.

N-(2-Dialkylaminoethyl)-2-oxo-2H-1-benzo(thio)pyran-3-carboxamidinium dichlorides (5a-k)

General procedure:

The imidothioester (**4a-e**) (0.1 mol) and *N,N*-dialkylethylenediamine dihydrochloride (0.1 mol) were dissolved in the solvent (300 ml) (see Table 3). The mixture was heated according to the operative conditions described in Table 3. Methanethiol was released whereas the amidinium salt sometimes crystallized from the mixture during heating. The solvent was removed under reduced pressure and the residue was washed with chloroform, and then ether.

Operative conditions, yield, mp and spectral data are shown in Tables 3 and 4.

Ethyl 2-oxo-2H-1-benzopyran-3-carboxamidate (8)

2H-1-Benzopyran-3-carbonitrile (**7**) (prepared from (**6**) according the literature⁹) (5 g, 29.2 mmol) was dissolved in dioxane (100 ml) and cooled to about 0°C. To the solution, ethanol (25 ml) was added slowly until just the beginning of precipitation. At 0-5°C, hydrogen chloride gas is bubbled through the solution until saturation. After keeping cool the mixture (near 0°C for 2 weeks), the crystals (**8**) were collected by filtration (1.9 g) and addition of ether led to second crop of hydrochloride. The product was recrystallized from ethanol; yield: 4.86 g (90%), mp >200°C (decomposition); ¹H-nmr (DMSO-d₆): 1.35 (3H, t, J=7 Hz, OCH₂CH₃), 3.50 (2H, q, J=7 Hz, OCH₂CH₃), 7.20-8.05 (4H, m, H_{arom}), 8.75 (1H, s, H₄), 10.00 (2H, m, N⁺H₂); ir (KBr): 3420-3250 (N⁺H), 1640 (C=N) cm⁻¹. *Anal.* Calcd for C₁₂H₁₂NO₂Cl: C, 56.80; H, 4.73; N, 5.52. Found: C, 56.61; H, 4.82; N, 5.67.

The imidoester hydrochloride (2.53 g, 10 mmol) was suspended in dioxane (30 ml) and triethylamine (1.01 g, 10 mmol) was added and then the mixture was stirred for 1 h. Triethylammonium hydrochloride was removed by filtration and the solution was concentrated. After taking up the residue in ether and filtering, the distillation of solvent under *vacuo* afforded (**8**). The product is crystallized from ethanol; yield: 1.75g (87%), mp 66°C; ¹H-nmr (CDCl₃): 1.45 (3H, t, J= 7 Hz, OCH₂CH₃), 4.35 (2H, q, J=7 Hz, OCH₂CH₃), 7.20-7.70 (4H, m, H_{arom}), 8.40 (1H, s, H₄), 9.65 (1H, s, NH); ir (KBr): 3200 (NH), 1710 (C=O), 1630 (C=N) cm⁻¹.

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1. Present address: Y. E. L., Laboratoires Meram, 24, rue Amelot, F75011 Paris; J. D. B., Institut de Recherches Servier, 11, rue des Moulineaux, F92150 Suresnes.
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