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Synthesis of Biscoumarins and Biscoumarinyl Ketones†

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SUMMARY

The synthesis of 3,3′ and 3,4′-biscoumarins is described. 3-(ω-Carbethoxyacetyl)coumarins were synthesised and converted to 3,3′-biscoumarinyl ketones and 3,4′-biscoumarins. The absorption characteristics and dyeing properties of the compounds are reported.

1. INTRODUCTION

The importance of the coumarin heterocycle as a fluorophore is well known. We have described in earlier papers[1,2] the synthesis of fluorescent coumarins with heterocyclic substituents at the 3-position.

We were intrigued by the possibility of linking two coumarin moieties to see whether there could be a marked enhancement in the emission characteristics. Rather surprisingly, there is very little information of such biscoumarin derivatives. Two useful intermediates for such a synthesis are coumarin-3-acetic acid derivatives (**2a, b**) and coumarin-4-acetic acids (**4a–f**). We described the synthesis of the first type of intermediate in our earlier paper.[1] The preparation of coumarin-4-acetic acids from reactive phenols and acetonedicarboxylic acid have been described.[3,4]

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2. RESULTS AND DISCUSSION

Reaction of the coumarin-3-acetic acid derivatives (**2a, b**) with 4-diethylaminosalicylaldehyde (**1a**) gave rise to the corresponding 3,3′-biscoumarins (**3a, b**) as evidenced by elemental analysis, UV spectra (bathochromic shift due to increased conjugation), enhancement of fluorescence and mass spectrum (**3a**).

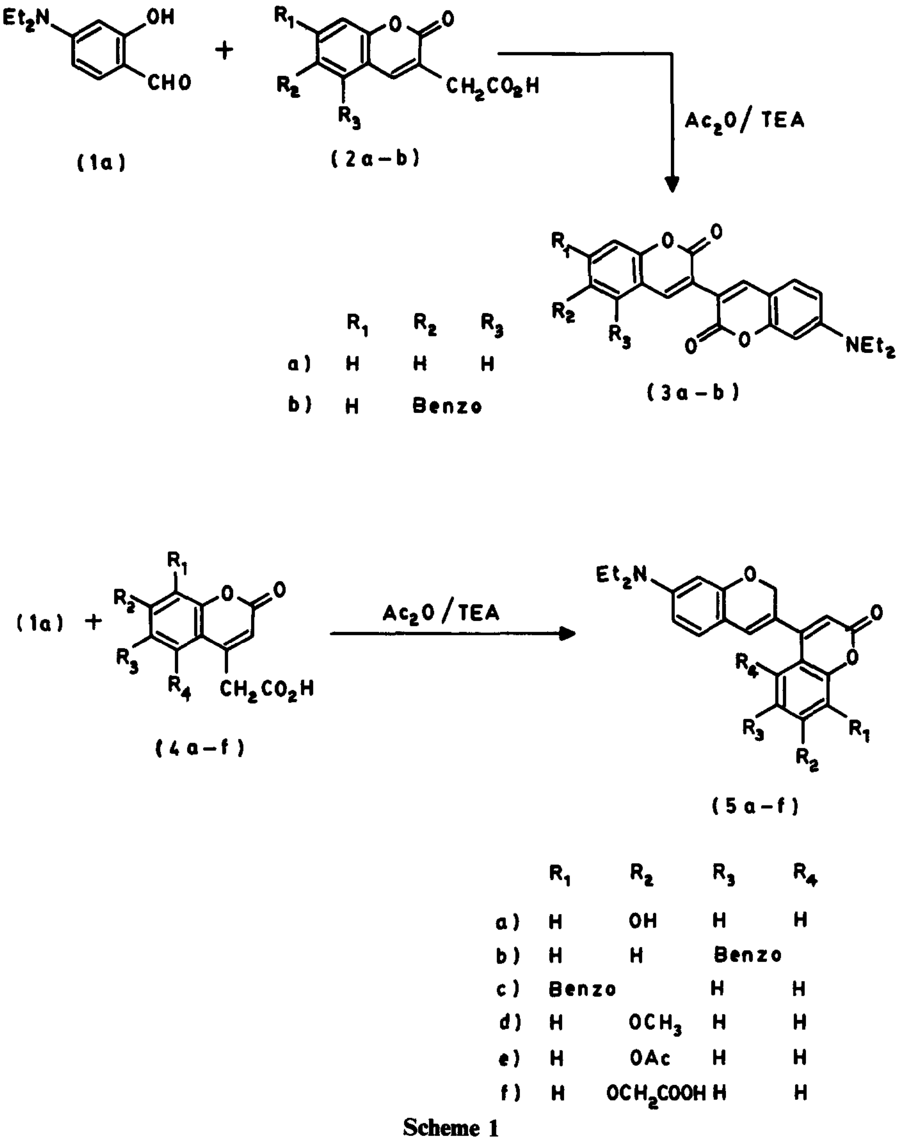
In a similar fashion, coumarin-4-acetic acids (**4a–f**) were also condensed with **1a** to give 3,4′-biscoumarins (**5a–f**). The structures were clearly established on the basis of elemental analysis, UV spectra, increased fluorescence and PMR spectrum (**5c**).

Under the reaction conditions 7-hydroxycoumarin-4-acetic acid (**4a**) gave rise to two compounds: (i) 7-diethylamino-7′-hydroxy-3,4′-biscoumarin (**5a**) and (ii) 7′-acetoxy-7-diethylamino-3,4′-biscoumarin (**5e**). The acetoxy derivative (**5e**) was prepared by carrying out the reaction at reflux and its structure was confirmed by elemental analysis data and mass spectrum (M^+ at *m/e* 419). 7′-Hydroxybiscoumarin (**5a**) was obtained when the reaction was carried out using ammonium acetate. The structure was established on the basis of elemental analysis, UV and PMR spectral data. Scheme 1 shows the reactions employed.

The strong fluorescence of the biscoumarins described above led us to study the properties of 3,3′-biscoumarinyl ketones. The synthesis of such compounds was accomplished by the condensation of salicylaldehyde derivatives (**1a, b**) with diethyl acetonedicarboxylate (**6**). The condensation could be carried out either in a single-step operation using two moles of the aldehyde leading to symmetrical compounds or in a two-step operation wherein the intermediate β-ketoesters (**7a, b**) were isolated in moderate yields and then condensed with different salicylaldehyde derivatives to obtain a range of unsymmetrical compounds. The structures of the ketones were established on the basis of elemental analysis and spectral data.

The biscoumarinyl ketones are coloured only when at least one of the coumarin moieties contains a diethylamino function at the 7-position.

Reaction of the ketoester (**7, b**) with *m*-diethylaminophenol (**8**) under modified Pechmann conditions[5] (Scheme 2) gave 3,4′-biscoumarins (**9a, b**), which were not previously accessible because of the difficulty in synthesising 7-diethylaminocoumarin-4-acetic acid. The structures were confirmed by elemental analysis, chemical properties (insolubility in dilute alkali and no colouration with ferric chloride) and PMR spectrum

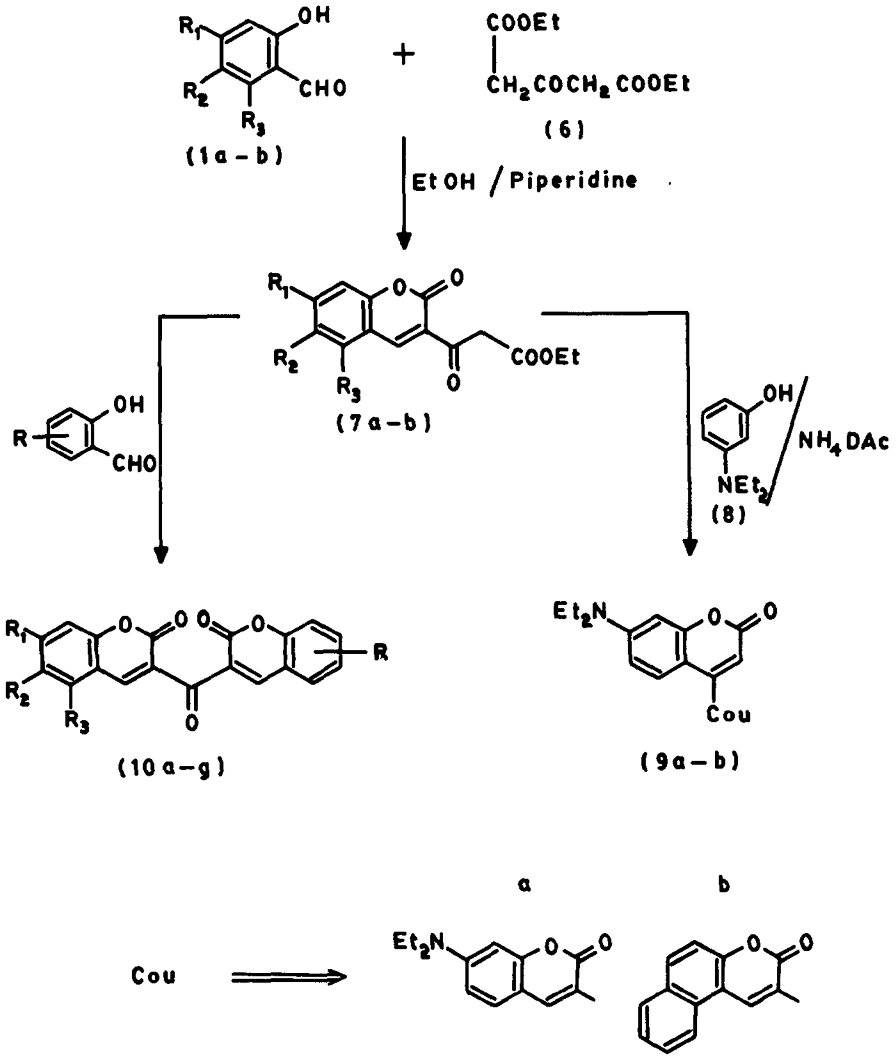


	R$_1$	R$_2$	R$_3$
a)	H	H	H
b)	H	Benzo	

	R$_1$	R$_2$	R$_3$	R$_4$
a)	H	OH	H	H
b)	H	H	Benzo	
c)	Benzo		H	H
d)	H	OCH$_3$	H	H
e)	H	OAc	H	H
f)	H	OCH$_2$COOH	H	H

Scheme 1

(**9b**). A comparison of the PMR spectrum of **9b** with that of its starting material in $CDCl_3$ clearly revealed that C_4 of the ketoester is involved in bond formation (disappearance of low-field sharp singlet at δ 9·4 due to proton at C_4). The biscoumarins (**9a, b**) did not show much fluorescence and were all dull red compounds.



Scheme 2

In view of the attractive colours and strong fluorescence properties the various compounds synthesised were evaluated as disperse dyes (greenish yellow to reddish yellow) on polyester and the evaluation data are set out in Table 3. Colouration properties varied from very good to poor and lightfastness of the dyeings was generally very low. Some of the biscoumarinyl ketones have been described[6] with respect to their photosensitisation properties and the strong fluorescence of the biscoumarins has led to a detailed study of their fluorescence and dye laser properties which have been reported[7] by our co-workers.

3. EXPERIMENTAL

All melting points are uncorrected. UV–visible spectra were recorded on Beckmann-DK 2 and Unicam SP-8000 spectrophotometers, PMR spectra on a Varian EM-360L spectrophotometer using TMS as the internal standard and mass spectra on a Varian CH-7 instrument.

Coumarin-3-acetic acids (**2a, b**),[1] coumarin-4-acetic acids (**4a–d, 4f**),[3,4] salicyladehyde derivatives (**1a**,[8] **1b**,[9] **1c**[10]) and the β-ketoester (**7b**)[11] were prepared following the reported procedures.

Preparation of 3-(ω-carbethoxyacetyl)-7-diethylaminocoumarin (7a)

A mixture of **1a** (0·01 mol) and diethyl acetonedicarboxylate (**6**) (0·011 mol) in ethanol (30 ml) was refluxed with a few drops of piperidine for 3–4 h. The bright yellow solid which separated on cooling the reaction mixture was filtered and crystallised from ethanol. Yield 72%, m.p. 108–110°C; reported m.p. (CH_3CN) 112–114°C.[6]

Preparation of 3,3′ and 3,4′-biscoumarins from acetic acid derivatives (3a, b, 5b–d, 5f)

General procedure

A mixture of **1a** (0·02 mol) and coumarin-3/4-acetic acid derivative (0·025 mol) in Ac_2O (5–6 ml) and triethylamine (1 ml) was slowly warmed on a waterbath at 80 °C for 2–3 h. The cooled reaction mixture was slowly poured into ice-cold water containing ethanol and the product which separated was collected. The yield, m.p., crystallisation solvent, molecular formula and various spectral data are given in Table 1; UV absorption–emission and evaluation of dyeings are given in Table 3.

Preparation of 7′-acetoxy-7-diethylamino-3,4′-biscoumarin (**5e**)

A mixture of **1a** (0·01 mol) and **4a** (0·011 mol) in Ac_2O (4 ml) containing Et_3N (1 ml) was refluxed for 2 h. The product obtained after the usual work-up was crystallised from $CHCl_3$–DMF (4:1). Yield 80%, m.p.

TABLE 1
Physical Data of the Biscoumarins

Compound	*Yield (%)*	*M.p. (°C)*	*Crystallisation solvent*	*Molecular formula*[a]	*MS M$^+$*	*PMR δ (ppm)*
3,3'-Biscoumarins						
3a	72	223	CHCl$_3$	$C_{22}H_{19}NO_4$	361	—
3b	70	268	CHCl$_3$	$C_{26}H_{21}NO_4$	—	—
3,4'-Biscoumarins						
5b	70	254	EtOH–DMF (1:1)	$C_{26}H_{21}NO_4$	—	—
5c	66	264	CHCl$_3$–DMF (10:1)	$C_{26}H_{21}NO_4$	—	CDCl$_3$: 1·1–1·4 (t, 6H, $\underline{CH}_3$), 3·4–3·7 (q, 4H, —$\underline{CH}_2$), 6·6–7·9 (m, 11H, aromatic)
5d	75	218	CHCl$_3$	$C_{24}H_{21}NO_7$	—	—
5f	70	265	CHCl$_3$–DMF	$C_{24}H_{21}NO_7$	—	—
9a	48	>300	HOAc	$C_{26}H_{28}N_2O_4$	—	—
9b	58	158–160	EtOH	$C_{26}H_{21}NO_4$	—	CDCl$_3$:1·2(t, 6H, —$\underline{CH}_3$), 3·5 (q, 4H, —$\underline{CH}_2$), 6·1–8·8 (m, 10H aromatic)

[a] Satisfactory elemental analysis data were obtained.

262 °C. Mass spectrum: 419 (M$^+$). Found: N, 3·7; $C_{24}H_{21}NO_6$ requires N, 3·4%.

Preparation of 7-diethylamino-7'-hydroxy-3,4'-biscoumarin (**5a**)
7-Hydroxycoumarin-4-acetic acid (**4a**) (0·011 mol), **1a** (0·01 mol) and NH_4OAc (5 g) were thoroughly mixed and fused in an oil-bath at 130 °C for 1 h. The reaction mixture was poured into water and neutralised. The product was obtained in 60% yield and was crystallised from CHCl$_3$, m.p. 240 °C. PMR(DMSO-d_6): δ 1·1–1·4 (q, 6H, -N-(CH$_2\underline{CH}_3)_2$), δ 3·0–3·4 (t, 4H, -N($\underline{CH}_2CH_3)_2$), δ 6·0–7·9 (m, 9H, aromatic) and δ 10·5 (s, OH proton).

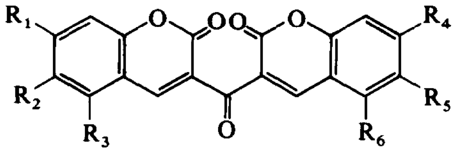
Preparation of the biscoumarinyl ketones

General procedure

A mixture of the ketoester (**7a, b**) (0·005 mol) and the corresponding

TABLE 2

Physical Data of the Biscoumarinyl Ketones



Compound	R_1	R_2	R_3	R_4	R_5	R_6	*M.p. (°C)*	*Yield (%)*	*Molecular formula*[a]	*MS* M^+
10a	NEt_2	H	H	NEt_2	H	H	205 (EtOH)	65	$C_{27}H_{28}N_2O_5$[b]	460
10b	NEt_2	H	H	H	H	H	284 (DMF)	89	$C_{23}H_{19}NO_5$	389
10c	NEt_2	H	H	H	Benzo		229 ($CHCl_3$–C_6H_6)	65	$C_{27}H_{21}NO_5$	—
10d	NEt_2	H	H	OH	H	H	223 (dec.) (EtOH)	62	$C_{29}H_{19}NO_6$	—
10e	H	Benzo		H	H	H	254–257 (DMF)	70	$C_{23}H_{12}O_5$	368
10f	H	Benzo		H	Benzo		>355 (DMF)	55	$C_{27}H_{14}O_5$	—
10g	H	Benzo		OH	H	H	268–270 (EtOH–DMF)	70	$C_{23}H_{12}O_6$	—

[a] Satisfactory elemental analyses were obtained.

[b] PMR spectrum in $CDCl_3$: δ 1·3 (t, 12H, CH_3), δ 3·5 (q, 8H, CH_2), δ 6·5–8·3 (m, 8H, aromatic).

salicylaldehyde derivative (0·006 mol) was refluxed with piperidine in ethanol (DMF as solvent in the case of **10f**; a fusion reaction between **7a** and resorcylaldehyde at 120 °C in the case of **10d**). The product which separated was filtered, dried and recrystallised. Physical characteristics are given in Table 2.

Preparation of the biscoumarins (**9a, b**)

An equimolar mixture of the ketoester (**7a, b**) (0·005 mol) and *m*-diethylaminophenol (**8**; 0·005 mol) was heated in an oil-bath at 80 °C with a pinch of ammonium acetate as catalyst for 3–4 h. The reaction mixture was cooled and ethanol was added. The solid which separated was filtered and dried. Physical data of the coumarins are given in Table 1.

TABLE 3
Absorption–Emission and Dyeing Evaluation Data

Compound	λ_{max} *(absorption)* *(nm)*	*log E*	λ_{max} *(emission)* *(nm)*	*P.U.*[a]	*Xeno*[b]	*Thermo*[c]
3a	410	4·23	528	—	—	—
3b	410	4·23	556	1	1	3
5a	393	4·1	502	—	—	—
5b	390	4·1	510	—	—	—
5c	385	4·25	502	1	1	4
5d	390	4·11	498	1	4	3–4
5e	390	4·21	505	1	2	4
5f	390	4·2	498	—	—	—
7a	440	4·72	484	2	< 1	2
10a	458	4·82	—	4	< 1	3
10b	450	4·69	—	2	< 1	2
10c	450	4·71	—	3	< 1	4
10d						
10e	385	4·23	—	1	2	3
10g	390	4·30	—	—	—	—

[a] P.U.: Pick-up
5 = 2 × standard (excellent)
4 = standard (very good)
3 = $\frac{1}{2}$ × standard (good)
2 = $\frac{1}{3}$ × standard (moderate)
1 = $\frac{1}{6}$ × standard (poor)

[b] Xeno: Lightfastness
8 = outstanding
7 = excellent
6 = very good
5 = good
4 = fairly good
3 = fair
2 = poor
1 = very poor

[c] Thermo: Sublimation fastness
5 = excellent
4 = good
3 = fair
2 = poor
1 = very poor

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REFERENCES

1. N. K. Chodankar and S. Seshadri, *Dyes and Pigments*, **6**, 313 (1985).
2. N. K. Chodankar and S. Seshadri, *Dyes and Pigments*, **6**, 331 (1985).
3. B. S. Burton and H. von Pechmann, *Ann. Chem.*, **261**, 151 (1891).
4. B. B. Dey, *J. Chem. Soc.*, **107**, 1606 (1915).
5. T. Kappe and C. Mayer, *Synthesis*, 524 (1981).
6. D. P. Specht, P. A. Matric and S. Fadrid, *Tetrahedron*, **38**, 1203 (1982).
7. M. R. Padhye, T. S. Varadarajan and A. V. Deshpande, presented and published in the Symposium on Quantum Electronics, held at Poona, January 1981.
8. General Aniline and Film Corpn., US Patent 2 789 125; *Chem. Abstr.*, **51**, 13410 (1957).
9. A. Russell and L. B. Lockhard, in *Organic synthesis*, Coll. Vol. 3, E. C. Horning, New York, Wiley (1962) p. 463.
10. M. Lorenzo, *Ann. Chem.*, **48**, 930 (1958).
11. E. Knoevenagel and E. Langensiepen, *Ber.*, **37**, 4492 (1904).