

Two New Classes of Fluorescent Dyes
Chin H. Chen*, John L. Fox and Joseph L. Lippert

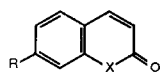
Corporate Research Laboratories, Eastman Kodak Company,
Rochester, New York 14650
Received December 29, 1986

The synthesis of two new classes of phosphorous-containing coumarin dyes is described and their fluorescent properties are compared with those of known coumarin dyes.

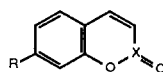
J. Heterocyclic Chem., **24**, 931 (1987).

Although there are numerous documented heterocoumarins in which the lactonic oxygen is replaced by a hetero atom such as nitrogen [2(1*H*)-quinolinone] [1] or sulfur (2*H*-1-benzopyran-2-ones) [2] systems, depicted in **1**, to our knowledge no attempt has been made to synthesize coumarins in which a heteroatom is substituted in place of the α -pyronyl carbon as shown in **2**. This paper describes the synthesis and properties of the first such ring system in which a phosphorus atom is incorporated in place of the lactonic carbon with a carboxylic ester substituted at C-3 as depicted in **3**. We call this new class of compounds *phosphacoumarins*, since they are basically heterocyclic analogs of coumarins [3].

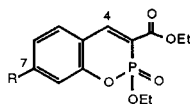
During the course of our research, we also isolated and identified another class of highly fluorescent coumarins in which an electron-withdrawing phosphoryl ester function is substituted at the C-3 position of the coumarin nucleus as shown in **4**. To differentiate this substitution pattern from that of **3**, we call these new derivatives *phosphonocoumarins* [3,4].



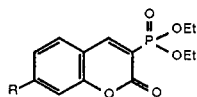
1 (X = NR', S)



2



3



4

To design a good organic laser dye, it is essential to have a donor substituent R, preferably bearing nitrogen or oxygen at C-7, as shown. Thus, for the synthesis of *phosphono-* and *phosphacoumarins*, we chose to use the 4-methoxy-, diethylamino-, and julolidyl-substituted salicylaldehydes and triethyl phosphonoacetate. The standard conditions for the condensation/lactonization (a procedure using piperidine in refluxing ethanol) gave only poor yields of the desired products. However, 10 mole% of freshly prepared piperidinium acetate in refluxing toluene

gave the desired mixture of phosphacoumarin **3** and phosphonocoumarin **4**. The mixtures are easily separated by flash chromatography. The reaction conditions and yields are summarized in Table I.

Starting Salicylaldehyde	Δ (hour)	Yield (%)	
		3	4
R = OMe (a)	12	21	69
R = NEt ₂ (b)	12	17	58
R = julolidyl (c)	6	18	54

These hetero-substituted coumarins can be distinguished on the basis of the $^3J_{P-H}$ coupling constants. The $^3J_{P-H}$

Compound	Absorption λ -max (ethanol)	Fluorescence λ -max (ethanol)	Stokes $\Delta \lambda$ -max - λ -max (nm)	Shift ϵ_a (cm ⁻¹ M ⁻¹) [a]	Φ_f (%) [b]
4a	340	395	55	17,750	16
3a	332	395	63	19,550	9
4b	406	455	49	34,500	4
3b	400	457	57	45,600	5
4c	423	473	50	36,600	70
3c	420	478	58	41,000	62
5	436	480	44	47,000	68

[a] ϵ_a = Extinction coefficient at maximum absorption.

[b] Φ_f = Fluorescence quantum efficiency

Table III

Compound	Molecular Formula	Elemental Analysis						FDMS m/e (M ⁺)	¹ H NMR (Deuteriochloroform/TMS)
		Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N		
3a	C ₁₄ H ₁₇ O ₆ P	53.9	5.5		53.7	5.3		312	δ 1.43 (t, 3), 1.45 (t, 3), 3.88 (s, 3), 4.3-4.5 (m, 4), 6.68 (d, 1), 6.73 (dd, 1), 7.35 (d, J = 8 Hz, 1), 8.16 (d, J _{PCH} = 37 Hz, 1)
4a	C ₁₄ H ₁₇ O ₆ P	53.9	5.5		54.1	5.1		312	δ 1.4 (t, 6), 3.9 (s, 3), 4.17-4.27 (m, 4), 6.8 (d, 1), 6.86 (dd, 1), 7.45 (d, J = 8 Hz, 1), 8.43 (d, J _{PCH} = 15 Hz, 1)
3b	C ₁₇ H ₂₄ NO ₅ P	57.8	6.8	4.0	57.5	6.8	3.8	353	δ 1.18 (t, 6), 1.32 (t, 3), 1.35 (t, 3), 3.37 (q, 4), 4.2-4.4 (m, 4), 6.30 (d, 1), 6.40 (dd, 1), 7.18 (d, J = 8 Hz, 1), 8.12 (d, J _{PCH} = 37 Hz, 1)
4b	C ₁₇ H ₂₄ NO ₅ P	57.8	6.8	4.0	57.6	6.5	4.1	353	δ 1.19 (t, 6), 1.33 (t, 3), 3.41 (q, 4), 4.1-4.3 (m, 4), 6.42 (d, 1), 6.56 (dd, 1), 7.3 (d, J = 9 Hz, 1), 8.34 (d, J _{PCH} = 16 Hz, 1)
3c	C ₁₉ H ₂₄ NO ₅ P	60.5	6.4	3.7	60.2	6.4	4.0	377	δ 1.35-1.46 (m, 6), 1.95 (m, 4), 2.65-2.9 (m, 4), 3.3 (m, 4), 4.1-4.4 (m, 4), 6.79 (s, 1), 8.0 (d, J _{PCH} = 37 Hz, 1)
4c	C ₁₉ H ₂₄ NO ₅ P	60.5	6.4	3.7	60.5	6.3	3.9	377	δ 1.39 (t, 6), 1.99 (m, 4), 2.76 (t, 2), 2.87 (t, 2), 3.32 (q, 4), 4.2 (m, 4), 6.88 (s, 1), 8.21 (d, J _{PCH} = 15 Hz, 1)

coupling constant between the endocyclic phosphonate and the proton in the 4-position is ~37 Hz, which is consistent with the range of 35-50 Hz reported [5] for the *trans* configuration. Likewise, the ³J_{P-H} coupling constant of 15-16 Hz for the exocyclic phosphonate is also consistent with reported values for the *cis* configuration between the phosphorous and the 4H proton.

The absorption and fluorescence properties of phosphacoumarins **3** and phosphonocoumarins **4** in ethanol are shown in Table II. The only hetero-substituted coumarins having a quantum yield of fluorescence comparable to that of corresponding laser coumarin dye **5** are the julolidyl derivatives **3c** and **4c**. Although the extinction coefficients of phosphorous-substituted coumarins are lower than that of **5**, their Stokes shifts are consistently larger. The larger Stokes shift could favor an increased lasing efficiency because of the decrease in overlap between the absorption and emission spectra.

EXPERIMENTAL

The ¹H nmr spectra were recorded on Varian EM-390 and Bruker WH 270-MHz spectrometers, with TMS as the internal standard. Field-desorption mass spectra were recorded on a Varian MAT-731 spectrometer. Microanalyses were done by the Analytical Sciences Division, Kodak Research Laboratories. Absorption and fluorescence spectra were obtained on Perkin-Elmer 330 and LS-5 spectrophotometers.

A description of the general procedure for the synthesis of phosphacoumarins **3** and phosphonocoumarins **4** follows.

To a 100-ml one-necked, round-bottomed flask, equipped with a Dean Stark trap and a reflux condenser, was added 100 mmoles of substituted salicylaldehyde, 2.0 ml (10 mmoles) of triethyl phosphonoacetate, 60 mg (1 mmole) of acetic acid, and 85 mg (1 mmole) of piperidine. The solution was refluxed for the specified time (6-12 hours) and the water was slowly collected in the Dean Stark trap (~1.8 ml). The reaction mixture was cooled to room temperature and filtered through a ¼-inch pad of silica gel, which was then washed with ethyl acetate until the yellow color had all been eluted. The eluant was concentrated and the yellow oily residue was purified by flash chromatography (ethyl acetate, silica gel, 1 ½ x 15") to yield the phosphacoumarin **3** as the first fraction and the phosphonocoumarin **4** as the second. Isolated yields are shown in Table I and elemental analyses and spectral data are tabulated in Table III.

REFERENCES AND NOTES

- [1] A. Weissberger in "The Chemistry of Heterocyclic Compounds", Vol **32**, John Wiley & Sons, New York, 1977, pp 93-318.
- [2] O. Meth-Cohn and B. Tarnowski, *Adv. Heterocyclic Chem.*, **26**, 116 (1980).
- [3] Following a nomenclature generally accepted in heterocyclic organophosphorus chemistry, a prefix *phosphono* indicates that the *phosphorus* is substituted *outside* the ring system, rather than inside.
- [4] During the preparation of this manuscript, a paper describing the preparation of diethylcoumarin-3-phosphonates without the nitrogen-bearing substituents at C-7 was published: R. K. Singh and M. D. Roger, *J. Heterocyclic Chem.*, **22**, 1713 (1985).
- [5] L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd Ed, Pergamon Press, New York, 1969, p 352.