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Synthesis and Optical Properties of New Coumarin Derivatives Based on 2-(2-Chlorobenzylidene)malononitrile

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Abstract—A procedure has been developed for the conversion of the CS gas [2-(2-chlorobenzylidene)-malononitrile] to new 3-cyanocoumarin derivatives, 4-(2-chlorophenyl)-2-oxo-2*H*-chromene-3-carbonitriles. Study of the optical properties of the synthesized compounds has revealed strong fluorescence in the violet and blue regions.

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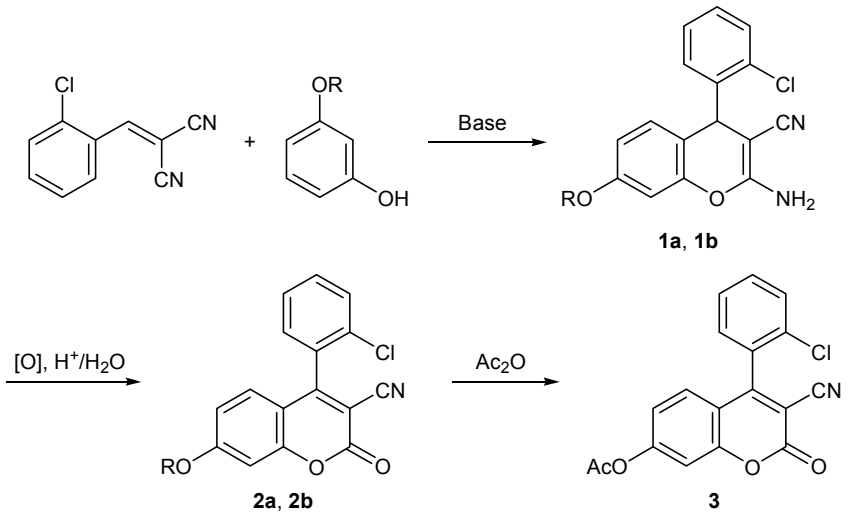
Coumarin derivatives are known as organic fluorophores [1]. They have found wide application as optical bleaching agents [2], active media of tunable lasers [3], and luminescent labels [4]. Furthermore, many coumarin derivatives exhibit anti-inflammatory [5, 6], antitubercular [7], and anticoagulant activity [8].

We have recently developed a new synthetic approach to coumarin derivatives, which is based on oxidation of cyano-substituted 4*H*-chromenes [9]; the latter can be prepared in turn by reaction of benzylidenemalononitriles with activated phenols [10]. In continuation of studies in this line, herein we propose a procedure for the disposal of 2-(2-chlorobenzylidene)-malononitrile (CS gas). This compound is a complex action irritant produced on a large scale. Due to its teratogenic properties [11], the use of CS as a riot control agent is restricted in some countries. Therefore, development of efficient methods for utilization of CS is a topical problem.

Herein, we propose a procedure for the synthesis of 2-amino-4-(2-chlorophenyl)-4*H*-chromene-3-carbonitriles **1** by reaction of 2-(2-chlorobenzylidene)-

Scheme 1.



R = H (**a**), Me (**b**).

Table 1. Solvent effect on the electronic absorption and fluorescence spectra of compound **2a**

Solvent	λ_{abs}, nm	A_{max}	ε_{max}	λ_{fl}, nm	φ_F[a]
Ethanol	375, 429	0.3354, 0.2886	14581, 12547	482	0.47
Ethyl acetate	353	0.2920	12696	415	0.22
Benzene	355	0.3876	16854	416	0.16
Acetonitrile	354	0.4326	18809	414	0.27
Acetic acid	356	0.4560	19825	417	0.43
Pyridine	366, 448	0.4073, 0.2257	17707, 9814	502	0.08

[a] The fluorescence quantum yields were determined using 4-methylumbelliferone (4-Me-umb) as reference.

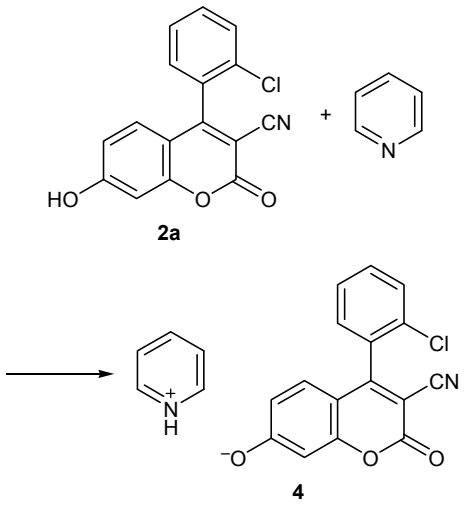
Table 2. Optical properties of compounds **2** and **3** in ethanol

Compound	λ_{abs}, nm	A_{max}	ε_{max}	λ_{fl}, nm	φ_F
4-Me-umb	358	0.3713	15469	447	0.63
2a	375, 429	0.3354, 0.2886	14581, 12547	482	0.47
2b	358	0.3632	15793	418	0.42
3	305, 341	0.2839, 0.2640	12345, 11478	410	0.49

malononitrile with resorcinol or its monomethyl ether (Scheme 1). The subsequent oxidation of compounds **1a** and **1b** with chromium(VI) oxide gave 4-(2-chlorophenyl)-2-oxo-2*H*-chromene-3-carbonitriles **2a** and **2b** in 68 and 74% yield, respectively. The acylation of **2a** with acetic anhydride afforded 88% of 4-(2-chlorophenyl)-3-cyano-2-oxo-2*H*-chromen-7-yl acetate (**3**). The structure of chromenes **1** and coumarins **2** and **3** was confirmed by spectral data.

Of particular interest are optical properties of coumarins [1–4] which are known to absorb in the UV region and show fluorescence. Therefore, we examined the absorption and luminescence spectra of coumarin derivatives **2** and **3**. Table 1 contains parameters of the electronic absorption and fluorescence spectra of **2a** in different solvents. Polar protic solvents such as ethanol and acetic acid ensured the maximum fluorescence quantum yield of **2a** as compared to aprotic and nonpolar solvents. Pyridine induced fluorescence quenching and change of the color of the solution and absorption region, presumably as a result of formation of pyridinium salt **4** (Scheme 2).

Scheme 2.



The spectral properties of **2** and **3** were studied in ethanol (Table 2; Figs. 1, 2). It is seen (Table 2) that the substituent on C^8 strongly affects the positions of the absorption and emission maxima, but the fluorescence quantum yield almost does not change.

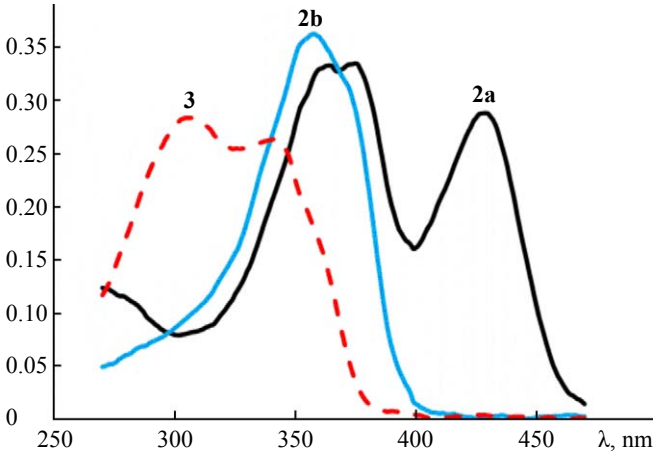


Fig. 1. Electronic spectra of compounds **2** and **3** in ethanol.

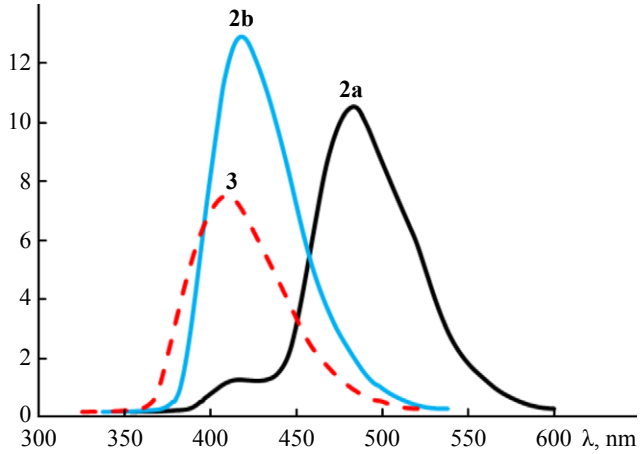


Fig. 2. Fluorescence spectra of compounds **2** and **3** in ethanol.

In summary, we have synthesized some coumarin derivatives on the basis of CS gas and studied their optical properties.

EXPERIMENTAL

The IR spectra were recorded on an FSM-1202 spectrometer with Fourier transform from samples dispersed in mineral oil. The ^{1}H NMR spectra were recorded on a Bruker DRX-500 instrument from solutions in DMSO-d_6 using tetramethylsilane as internal standard. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 mass spectrometer. The elemental compositions were determined with a Vario Micro cube CHN analyzer. The melting points were measured with an OptiMelt MPA100 automated melting point apparatus. The progress of reactions and the purity of products were monitored by TLC on Sorbfil PTSKh-AF-A-UF plates using ethyl acetate as eluent; spots were visualized under UV light, by treatment with iodine vapor, or by thermal decomposition.

2-Amino-4-(2-chlorophenyl)-7-hydroxy-4*H*-chromene-3-carbonitrile (1a). A suspension of 0.188 g (1 mmol) of 2-(2-chlorobenzylidene)malononitrile, 0.110 g (1 mmol) of resorcinol, 0.101 g (1 mmol) of triethylamine, and 0.046 g (0.15 mmol) of OKSIPAV AP in a mixture of 2.5 mL of water and 2.5 mL of ethanol was vigorously stirred for 2 h at room temperature. The mixture was then neutralized with 5% aqueous HCl, and the precipitate was filtered off, washed with 10 mL of water, recrystallized from ethanol, and dried in a vacuum desiccator. Yield 0.275 g (92%), mp 187–189°C (decomp.); published data [12]: mp 188–190°C (decomp.).

2-Amino-4-(2-chlorophenyl)-7-methoxy-4*H*-chromene-3-carbonitrile (1b) was synthesized in a similar way. Yield 94%, mp 179–181°C (decomp.); published data [13]: mp 178–180°C (decomp.).

4-(2-Chlorophenyl)-7-hydroxy-2-oxo-2*H*-chromene-3-carbonitrile (2a). A suspension of 0.299 g (1 mmol) of compound **1a** in 5 mL of acetic acid was heated to 60°C, 0.100 g (1 mmol) of chromium(VI) oxide was added in portions with stirring over a period of 10 min, and the mixture was stirred for 30 min at that temperature. The mixture was cooled and diluted with 15 mL of water, and the precipitate was filtered off, washed with 10 mL of water, recrystallized from water–propan-2-ol, and dried in a vacuum desiccator. Yield 0.202 g (68%), mp 239–240°C (decomp.). IR spectrum, ν, cm^{-1}: 3385 (OH), 2218 (C≡N), 1730 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.86 d.d (1H, CH, J = 2.2, 8.8 Hz), 6.90 d (1H, CH, J = 2.1 Hz), 6.92 d (1H, CH, J = 9.3 Hz), 7.56 d.d (1H, C_6H_4, J = 1.6, 7.5 Hz), 7.62 t (1H, C_6H_4, J = 7.4 Hz), 7.67 t.d (1H, C_6H_4, J = 1.6, 8.1 Hz), 7.77 d (1H, C_6H_4, J = 8.0 Hz), 11.47 s (1H, OH). Mass spectrum, m/z (I_{rel}, %): 299 (31) $[M]^+$, 297 (100) $[M]^+$, 262 (93) $[M - 35]^+$. Found, %: C 64.74; H 2.62; N 4.76. $C_{16}H_8ClNO_3$. Calculated, %: C 64.55; H 2.71; N 4.71. M 297.69.

4-(2-Chlorophenyl)-7-methoxy-2-oxo-2*H*-chromene-3-carbonitrile (2b) was synthesized in a similar way. Yield 74%, mp 175–176°C. IR spectrum, ν, cm^{-1}: 2227 (C≡N), 1735 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.93 s (3H, OCH_3), 6.98 d (1H, CH, J = 9.0 Hz), 7.01 d.d (1H, CH, J = 1.8, 9.0 Hz), 7.25 d (1H, CH, J = 1.7 Hz), 7.57 d (1H, C_6H_4, J = 7.3 Hz), 7.64 t (1H, C_6H_4, J = 7.4 Hz), 7.68 t (1H, C_6H_4, J = 7.4 Hz), 7.78 d (1H, C_6H_4, J = 8.0 Hz). Mass spectrum, m/z (I_{rel}, %): 313 (35) $[M]^+$, 311 (100) $[M]^+$, 276 (55) $[M - Cl]^+$. Found, %: C 65.58; H 3.29; N 4.40. $C_{17}H_{10}ClNO_3$. Calculated, %: C 65.50; H 3.23; N 4.49. M 311.72.

4-(2-Chlorophenyl)-3-cyano-2-oxo-2*H*-chromen-7-yl acetate (3). A solution of 0.298 g (1 mmol) of compound **2a** in 2 mL of acetic anhydride was refluxed for 2 h. The solvent was distilled off, the residue was ground with 5 mL of propan-2-ol, and the precipitate was filtered off, washed with propan-2-ol, and dried in a vacuum desiccator. Yield 0.299 g (88%), mp 193–194°C. IR spectrum, ν, cm^{-1}: 2229 (C≡N), 1747 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.33 s (3H, CH_3), 7.59 d (1H, CH, J = 8.7 Hz), 7.23 d.d (1H, CH, J = 2.2, 8.7 Hz), 7.55 d (1H, CH, J = 2.2 Hz), 7.59 d.d (1H, C_6H_4, J = 1.8, 7.5 Hz), 7.66 t.d (1H, C_6H_4, J = 1.0, 7.5 Hz), 7.70 t.d (1H, C_6H_4, J = 1.8, 7.6 Hz), 7.80 d (1H, C_6H_4, J = 7.9 Hz). Mass spectrum, m/z (I_{rel}, %): 341 (5) $[M]^+$, 339 (12) $[M]^+$, 299 (100) $[M - 32]^+$, 297 (30) $[M - 32]^+$. Found, %: C 63.75; H 3.05; N 4.02. $C_{18}H_{10}ClNO_4$. Calculated, %: C 63.64; H 2.97; N 4.12. M 339.73.

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REFERENCES

1. Fourati, M.A., Maris, Th., Skene, W.G., Bazuin, C.G., and Prud'homme, R.E., *J. Phys. Chem. B*, 2011, vol. 115, p. 12362.

2. *The Chemistry of Synthetic Dyes*, Venkataraman, K., Ed., New York: Academic, 1971, vol. 5, p. 535.
3. Jones, G. and Rahman, M.A., *J. Phys. Chem*., 1994, vol. 98, p. 13028.
4. Vemula, V., Ni, Zh., and Fedorova, M., *Redox Biol*., 2015, vol. 5, p. 195.
5. Kontogiorgis, Ch.A. and Hadjipavlou-Litina, D.J., *J. Med. Chem*., 2005, vol. 48, p. 6400.
6. Witaicenis, A., Seito, L.N., da Silveira Chagas, A., de Almeida, L.D., Jr., Luchini, A.C., Rodrigues-Orsi, P., Cestari, S.H., and Di Stasi, L.C., *Phytomedicine*, 2014, vol. 21, p. 240.
7. Keri, R.S., Sasidhar, B.S., Nagaraja, B.M., and Santos, M.A., *Eur. J. Med. Chem*., 2015, vol. 100, p. 257.
8. *Coumarin Anticoagulant Research Progress*, Edardes, J.P., Ed., New York: Nova Biomedical Books, 2008.
9. Bardasov, I.N., Alekseeva, A.U., Ershov, O.V., Surazhskaya, M.D., Churakov, A.V., and Grishanov, D.A., *Tetrahedron Lett*., 2015, vol. 56, p. 6145.
10. Kolla, S.R. and Lee, Y.R., *Tetrahedron*, 2011, vol. 67, p. 8271.
11. Bauchinger, M. and Schmid, E., *Mutat. Res*., 1992, vol. 282, p. 231.
12. Dekamin, M.G., Eslami, M., and Maleki, A., *Tetrahedron*, 2013, vol. 69, p. 1074.
13. Han, G., Du, J., Chen, L., and Zhao, L., *J. Heterocycl. Chem*., 2014, vol. 51, p. 1094.