Synthesis and Reactivity of a New Nonacarbon Chain Carboxonium Salt − Access to a New Class of Streptocyanine Dyes

Albert Izquierdo,[a] Valérie Guieu,[a] Heinz Gornitzka,[b] Yves Madaule,[a] and Corinne Payrastre*[a]

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A new highly reactive nonacarbon chain carboxonium salt **1** was synthesized. It leads, by action of various amines and hydrazone, to a new class of symmetrical nonacarbon chain streptocyanine dyes **3–5**.

Introduction

Polymethinium dyes are cationic conjugated organic compounds containing a chain made up of an odd number of carbon atoms between two nitrogen atoms. They are called cyanine dyes if the nitrogen atoms are part of a conjugated heterocycle, and streptocyanine dyes if not. Among their numerous applications[1] (dyes, photographic sensitizers, recordable laser discs, nonlinear optics and drugs), compounds that absorb in the near-infrared region are increasingly used as biological fluorescent probes.[2−5] Their peculiar spectral properties in this range (600−1000 nm) allow for the avoidance of autofluorescence from biomolecules, which is a great advantage for bioanalytical purposes.[6,7]

We had previously developed the synthesis of the pentacarbon (named 5-C)[8] and heptacarbon (named 7-C)[9] chain carboxonium salts (Figure 1).

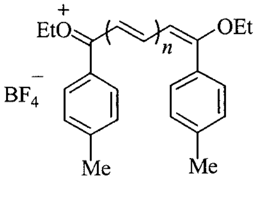

Figure 1. 5-C (*n* = 1) and 7-C (*n* = 2) carboxonium salts

These salts react with various nitrogen nucleophiles to give 5-C and 7-C streptocyanines, with the maximum absorbance falling in the range 435 to 720 nm.[8,9]

Results and Discussion

We have attempted the synthesis of a new nonacarbon chain (9-C) carboxonium salt in order to increase the wavelength. We have noted that in 1995, Narayanan et al.[10] have discussed the synthesis of symmetrical or nonsymmetrical nonacarbon chain cyanines, in one step, starting with a quaternary salt of a heterocyclic base containing an activated methyl group compound, and an unsaturated bisaldehyde, 2-chloro-3-(hydroxymethylene)cyclohexene-1-carboxaldehyde.[11] Therefore, we used this bisaldehyde with 4-methylphenylethanone, tetrafluoroboric acid and triethoxymethane to obtain the 9-C carboxonium salt **1** (Scheme 1).

The 9-C carboxonium salt differs from the 5-C and 7-C carboxonium salts by the presence of a chlorine atom that would allow further functionalization,[12,13] and by a central ring structure in the chromophore that increases the stability of the dyes in solution, both chemically and towards light.[12]

A study which involved varying the stoichiometry of triethoxymethane showed that the best conditions for the formation of the 9-C carboxonium salt **1** were when the stoichiometry was 1:2:1:4 (bisaldehyde:4-(methylphenyl)ethanone:tetrafluoroboric acid:triethoxymethane) (Scheme 1).

Analysis of the ^{1}H NMR spectrum shows the presence of a product identified as the 1,9-diketone **2**, together with the carboxonium salt **1**, with a molar ratio of 1:9, respectively. Two equivalents of triethoxymethane was used to isolate the 1,9-diketone **2**; when three to five equivalents were

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[a] Laboratoire de Synthèse et Physicochimie de Molécules d'Intérêt Biologique, UMR 5068, Université Paul-Sabatier,
118, route de Narbonne, 31062 Toulouse cedex 04, France
Fax: (internat.) +33-561556011
E-mail: payrastr@chimie.ups-tlse.fr
[b] Laboratoire d'Hétérochimie Fondamentale et Appliquée, UMR 5069, Université Paul-Sabatier,
118, route de Narbonne, 31062 Toulouse cedex 04, France
E-mail: heinz@chimie.ups-tlse.fr

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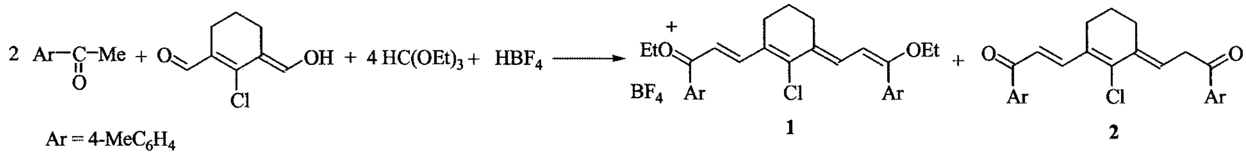


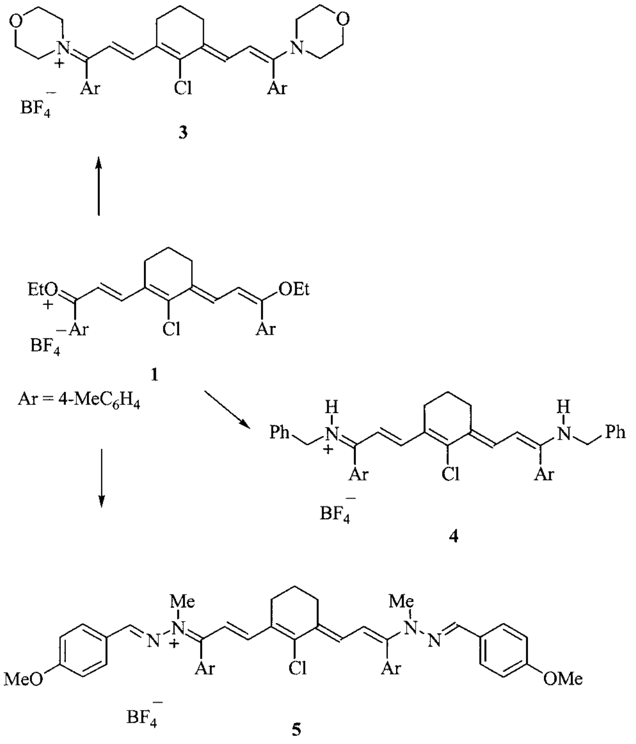
Scheme 1. Synthesis of 9-C carboxonium salts

used, a mixture of the 9-C carboxonium salt **1** and the diketone **2** was obtained; and when more than five equivalents were used, a mixture of the 9-C carboxonium salt and the 5-C carboxonium salt was obtained, at the expense of **2**. It was impossible to eliminate **2** by purification.

The 1,9-diketone **2** could arise as a result of the hydrolysis of **1**, or it could be an intermediate in the reaction for the formation of **1**. Mezheritskii[14] postulated that a 1,5-diketone was the intermediate produced in the reaction for the formation of 5-C carboxonium salt.

Moreover, **1** was obtained from **2** by the action of two equivalents of triethoxymethane and one equivalent of tetrafluoroboric acid in anhydrous chloroform at room temperature after three hours (with the same molar ratio, 9:1).

We have synthesized the symmetrical streptocyanines **3–5** from two equivalents of morpholine, benzylamine, and 4-(methoxyphenyl)methylene-*N*-methylhydrazone (Scheme 2). The diketone **2** does not react with the nucleophiles and can be filtered off as it is weakly soluble in acetonitrile (used as the solvent), and can be completely removed by recrystallization of the streptocyanine.



Scheme 2. Syntheses of symmetrical streptocyanine dyes **3–5**

The structures of all the products were unambiguously determined by ^1H and ^{13}C NMR spectroscopy, mass spectrometry (electrospray, DCI/NH_3), and that of **3** by X-ray diffraction (Figure 2).

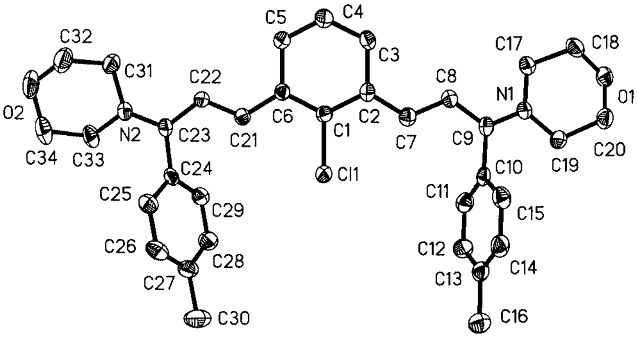


Figure 2. X-ray crystal structure of **3**; selected bond lengths [Å] and angles [°]: N1–C9 1.351(3), C9–C8 1.399(3), C8–C7 1.397(3), C7–C2 1.392(3), C2–C1 1.410(3), C2–C3 1.516(3), C1–C6 1.399(3); C9–N1–C17 121.9(1), C1–C6–C21 121.3(2), C9–N1–C19 122.6(2), C22–C21–C6 126.7(2), C17–N1–C19 112.6(2), N2–C23–C22 122.2(2), C7–C8–C9 121.8(2), C23–N2–C33 124.7(2), C2–C7–C8 126.1(2), C33–N2–C31 111.3(2), C7–C2–C1 122.1(2), C23–N2–C31 123.7(2); deviation of the chain carbons from the mean plane: 0.346 Å

The structure of **3** reveals an "*all-trans*" conjugated carbon chain, which is almost planar, with angles of about 120°. The C–C and C–N bond lengths of the conjugated system have intermediate values between those of single and double bonds, and the aryl groups are almost perpendicular to the chain.

An average bathochromic effect of about 140 nm is observed for the new nonacarbon chain streptocyanines relative to the heptacarbon chain streptocyanines[9] (Table 1).

Table 1. Absorbance and fluorescence data of the 9-C streptocyanines (CH_2Cl_2, 23 °C) (in brackets, values for the corresponding 7-C compound)

	$\lambda_{max.abs}$ nm	$\lambda_{max.em}$ nm	Stokes shift nm [cm^{-1}]	ε_{max} M^{-1} cm^{-1}
3	706	743	37 [705]	186000
	(566)	(606)	(40 [1166])	(183600)
4	696	728	32 [631]	105000
	(552)	(592)	(40 [1224])	(118000)
5	819	843	24 [348]	210000
	(679)	(720)	(41 [839])	(137000)

Compounds **3−5** show large molar extinction coefficients and Stokes shifts of the fluorescence emission maximum of about 30 nm.

Conclusion

The synthesis of a new 9-C carboxonium salt was achieved. Its reactivity towards amines and hydrazone was identical to those of the 5-C and 7-C carboxonium salts. Thus, a new class of near-infrared absorbing streptocyanine dyes was synthesized.

Experimental Section

General Remarks: All experiments were performed under dry conditions (argon atmosphere, anhydrous solvents) to avoid degradation of the carboxonium salt.

Melting points were determined with a Büchi capillary apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC 250 or AM 400 WB spectrometers. Chemical shifts are given in ppm from TMS. Mass spectra were obtained on a Nermag R10−10H apparatus for Electrospray and DCI. Ultraviolet-visible spectra were obtained on a Hewlett−Packard 8453 UV/Vis spectrophotometer. Excitation and fluorescence emission spectra were obtained using a Perkin−Elmer LS 50B spectrofluorimeter fitted with a Xenon-pulsed lamp (20 kW, flash-time 8 µs) and a Hamamatsu R 928 photomultiplier, except for compound **5** where a PTIQM1 spectrofluorimeter fitted with Xenon lamp (75 W) and a R 928P photomultiplier was used. Elemental analyses were performed at the Microanalysis Interuniversitary Service of the Chemistry School of Toulouse (ENSIACET).

5-Chloro-1,9-diethoxy-1,9-bis(4-methylphenyl)-4,6-(propane-1,3-diyl)nona-1,3,5,7-tetraenylium Tetrafluoroborate (1): A mixture of 4-methylphenylethanone (0.33 mL, 2.33 mmol) and 54% tetrafluoroboric acid in diethyl ether (0.16 mL, 1.17 mmol) was added dropwise to a mixture of 2-chloro-3-(hydroxymethylene)cyclohexene-1-carboxaldehyde[11] (0.202 g, 1.17 mmol) and triethoxymethane (0.78 mL, 4.67 mmol) that was partially dissolved in diethyl ether (2 mL). The mixture was stirred for 10 minutes, and the color became progressively purple, and the solution solidified. Diethyl ether (200 mL) was then added and the solution stirred for at least 1 hour, after which it became green. The solid was filtered off and dried under reduced pressure to give a purple powder (0.378 g). The ^{1}H NMR spectrum also showed the presence of a by-product identified as the 1,9-diketone **2** (molar ratio of 9:1 for **1**:**2**). The estimated yield of **1** was 48%. ^{1}H and ^{13}C NMR spectral data of **1** were evaluated using the spectra of the mixture of **1** (90%) and **2** (10%), by the abstraction of the signals corresponding to the pure diketone **2**.

1: ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): δ = 1.55 (t, ^{3}J = 6.9 Hz, 6 H, CH_3CH$_2$O), 1.96 (q, 2 H, ^{3}J = 5.7, H$^{5'}$), 2.43 (s, 6 H, CH$_3$Ar), 2.76 (t, ^{3}J = 5.7 Hz, 4 H, H$^{4'-6'}$), 4.50 (q, ^{3}J = 6.9 Hz, 4 H, CH$_3$CH_2O), 6.52 (d, 2 H, ^{3}J = 13.0 H$^{2-8}$), 7.30 and 7.48 (AB syst., 8 H, ^{3}J = 8.1, H$_{\mathrm{arom}}$), 8.24 (d, ^{3}J = 13.0 Hz, 2 H, H$^{3-7}$) ppm. ^{13}C NMR Jmod ^{13}C{^{1}H} (63 MHz, CDCl$_3$, 25 °C): δ = 14.4 (CH$_3$CH$_2$O), 20.4 (C$^{5'}$), 21.8 (CH$_3$Ar), 26.9 (C$^{4'-6'}$), 69.3 (CH$_3$$CH_2$O), 108.0 (C$^{2-8}$), 129.6 (C$_{\mathrm{arom}}$), 130.6 (C$^{4-6}$), 130.8 (C$_{\mathrm{arom}}$), 133.6 ($C_{\mathrm{arom}}$−C$^{1-9}$), 144.6 (C$_{\mathrm{arom}}$−CH$_3$), 156.4 (C$^{3-7}$), 160.1 (C^{5}−Cl), 182.6 (C$^{1-9}$) ppm.

5-Chloro-1,9-bis(4-methylphenyl)-4,6-(propane-1,3-diyl)nona-2,4,6-trien-1,9-dione (2): A mixture of 4-methylphenylethanone (0.78 mL, 5.55 mmol) and 54% tetrafluoroboric acid in diethyl ether (0.38 mL, 2.78 mmol) was added dropwise to a mixture of 2-chloro-3-(hydroxymethylene)cyclohexene-1-carboxaldehyde[11] (0.480 g, 2.78 mmol) and triethoxymethane (0.93 mL, 5.56 mmol) that was partially dissolved in diethyl ether (2 mL). After 15 minutes of stirring, 100 mL of diethyl ether was added. The solution was stirred for one hour and it progressively turned from pink to orange. The solid was filtered off and dried under reduced pressure to give an orange powder which was recrystallized from acetonitrile.

2: Orange crystals (30%). M.p.: 214−216 °C (dec.). ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 1.82 (q, 2 H, ^{3}J = 6.2, H$^{5'}$), 2.39 (s, 6 H, CH$_3$Ar), 2.52 (2t, 4 H, ^{3}J = 6.2, H$^{4'-6'}$), 3.85 (d, ^{3}J = 7.2 Hz, 2 H, H^{8}), 6.63 (t, ^{3}J = 7.2 Hz, 1 H, H^{7}), 7.00 (d, ^{3}J = 15.6 Hz, 1 H, H^{2}), 7.25 and 7.83 (AB syst., 8 H, ^{3}J = 8.2, H$_{\mathrm{arom}}$), 8.18 (d, ^{3}J = 15.6 Hz, 1 H, H^{3}) ppm. ^{13}C NMR Jmod ^{13}C{^{1}H} (100 MHz, CDCl$_3$, 25 °C): δ = 21.1 (C$^{5'}$), 21.8 (CH$_3$Ar), 27.3 and 27.4 (C$^{4'-6'}$), 38.7 (C^{8}), 124.0 (C^{2}), 124.8 (C^{7}), 128.6, 128.8, 129.4 and 129.6 (C$_{\mathrm{arom}}$), 131.8 (C^{4}), 134.2 (C_{arom}−C$^{1-9}$), 135.8 (C^{6}), 138.2 (C^{5}−Cl), 142.2 (C^{3}), 143.6 and 144.4 (C−$_{\mathrm{arom}}$CH$_3$), 190.5 (C^{1}), 196.5 (C^{9}) ppm. MS (DCI/NH$_3$): m/z (%) = 405 (100) [MH]$^{+}$ and 407 (37.7) [MH + 2]$^{+}$. C$_{26}$H$_{25}$ClO$_2$ (404.93): calcd. C 77.12, H 6.22; found C 76.95, H 6.23. UV/Vis (23 °C, CH$_2$Cl$_2$): $\lambda_{\max}$ nm ($\varepsilon_{\max}$ M^{-1} cm^{-1}) 349 (24000). Fluorescence spectrometry (23 °C, CH$_2$Cl$_2$): $\lambda_{\mathrm{ex}}/\lambda_{\mathrm{em}}$: 349/396 nm.

Preparation of 3 and 4: The amine (morpholine, benzylamine) (2.08 mmol) was added drop by drop to **1** (0.571 g, 1.04 mmol) in 100 mL of acetonitrile. After stirring for 24 h, the solution was filtered off to eliminate the diketone. The solvent was then removed under reduced pressure. The crude streptocyanine was recrystallized from ethanol.

5-Chloro-1,9-bis(4-methylphenyl)-1,9-dimorpholino-4,6-(propane-1,3-diyl)nona-1,3,5,7-tetraenylium Tetrafluoroborate (3): Green crystals (49%). M.p.: 255−257 °C (dec.). ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 1.79 (q, 2 H, ^{3}J = 6.0, H$^{5'}$), 2.36 (s, 6 H, CH$_3$−Ar), 2.53 (t, ^{3}J = 6.0 Hz, 4 H, H$^{4'-6'}$), 3.54 (t, ^{3}J = 4.5 Hz, 8 H, CH$_2$N), 3.78 (t, ^{3}J = 4.5 Hz, 8 H, CH$_2$O), 6.23 (d, ^{3}J = 13.2 Hz, 2 H, H$^{2-8}$), 7.13 (part A from an AB syst., 4 H, ^{3}J = 7.8, H$_{\mathrm{arom}}$), 7.21 (d, ^{3}J = 13.2 Hz, 2 H, H$^{3-7}$), 7.23 (part B from an AB syst., 4 H, ^{3}J = 7.8, H$_{\mathrm{arom}}$) ppm. ^{13}C NMR Jmod ^{13}C{^{1}H} (100 MHz, CDCl$_3$, 25 °C): δ = 21.1 (C$^{5'}$), 21.6 (CH$_3$−Ar), 26.9 (C$^{4'-6'}$), 50.9 (CH$_2$N); 66.8 (CH$_2$O), 108.0 (C$^{2-8}$), 127.5 (C$^{4-6}$), 129.5 (C$_{\mathrm{arom}}$), 129.8 (C$_{\mathrm{arom}}$), 130.1 (C_{arom}−C$^{1-9}$), 141.2 (C_{arom}−CH$_3$), 149.5 (C$^{3-7}$), 150.1 (C^{5}−Cl), 168.1 (C$^{1-9}$) ppm. MS (Electrospray): m/z (%) = 543.2 (100) [M]$^{+}$, 545.2 (44) [M + 2]$^{+}$. C$_{34}$H$_{40}$BClF$_4$N$_2$O$_2$ (630.96): calcd. C 63.81, H 6.46, N 4.38; found C 63.63, H 6.00, N 4.26. UV/Vis (23 °C, CH$_2$Cl$_2$): $\lambda_{\max}$ nm ($\varepsilon_{\max}$ M^{-1} cm^{-1}), shoulder at 656, 706 (186000). Fluorescence spectrometry (23 °C, CH$_2$Cl$_2$): $\lambda_{\mathrm{ex}}/\lambda_{\mathrm{em}}$: 649/743 nm

5-Chloro-1,9-bis(benzylamino)-1,9-bis(4-methylphenyl)-4,6-(propane-1,3-diyl)nona-1,3,5,7-tetraenylium Tetrafluoroborate (4): green spangles (63%). M.p.: 210 °C (dec.). ^{1}H NMR (250 MHz, CDCl$_3$, 25 °C): δ = 1.77 (m, 2 H, H$^{5'}$), 2.37 (s, 6 H, CH$_3$−Ar), 2.42 (m, 4 H, H$^{4'-6'}$), 4.58 (large s, 4 H, CH$_2$−Ar), 6.05 (m, 2 H, NH), 7.22−7.32 (m, 20 H, H$_{\mathrm{arom}}$ and H$^{2-8}$), 7.58 (d, ^{3}J = 13.2 Hz, 2 H, H$^{3-7}$) ppm. ^{13}C NMR Jmod ^{13}C{^{1}H}, (63 MHz, CDCl$_3$, 25 °C): δ = 20.9 (C$^{5'}$), 21.5 (CH$_3$−Ar), 26.6 (C$^{4'-6'}$), 49.9 (CH$_2$−Ar), 125.4 (C$_{\mathrm{arom}}$), 127.7 (C$_{\mathrm{arom}}$), 128.0 (C$^{2-8}$), 129.0 (C$_{\mathrm{arom}}$), 129.3 (C$^{3-7}$), 129.6 (C$_{\mathrm{arom}}$), 136.1 (C$_{\mathrm{arom}}$), 142.0 (C$_{\mathrm{arom}}$), 150.7 (C^{5}−Cl) ppm. IR (KBr pellet): $\tilde{\nu}$ =3306 cm^{-1} (ν_{NH}). MS (DCI/NH$_3$): m/z (%) = 584

(3.8) $[M]^+$, 586 (1.8) $[M + 2]^+$, 547 (100) $[M - Cl]^+$. $C_{40}H_{40}BClF_4N_2$ (671.02): calcd. C 71.60; H 6.01; N 4.17; found C 71.65, H 6.05, N 4.12. UV/Vis (23 °C, CH_2Cl_2): λ_{max} nm (ε_{max} M^{-1} cm^{-1}): 346 (10000), 427 (18000), shoulder at 641, 696 (105000). Fluorescence spectrometry (23 °C, CH_2Cl_2): $\lambda_{ex}/\lambda_{em}$: 682/728 nm.

5-Chloro-1,9-bis[*N*-methyl-*N'*-(4-methoxyphenyl)methylenehydrazono]-1,9-bis(4-methylphenyl)-4,6-(propane-1,3-diyl)nona-1,3,5,7-tetraenylium Tetrafluoroborate (5): 4-*N*-[(dimethylamino)phenyl]methylene-*N'*-methylhydrazone (0.905 g, 5.11 mmol) and triethylamine (0.1 mL, 3.57 mmol) were added to 1 (1.402 g, 2.55 mmol) in 200 mL of anhydrous acetonitrile. After 48 hours of stirring, the solution was filtered off and the solvent was removed under reduced pressure. The crude product was dissolved in dichloromethane, precipitated from petroleum ether, filtered and dried. The precipitate was dissolved in dichloromethane and washed with distilled water. The organic phase was dried on $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was recrystallized from toluene/acetonitrile (3:1) to give green crystals with gold glints (9%). M.p.: 214−216 °C (dec.). ^1H NMR (250 MHz, $[D_6]$DMSO, 25 °C): δ = 1.86 (m, 2 H, $H^{5'}$), 2.40 (s, 6 H, $CH_3{-}Ar$), 2.63 (m, 4 H, $H^{4'-6'}$), 3.42 (s, 6 H, NCH_3), 3.81 (s, 6 H, OCH_3), 6.96−7.09 (m, 6 H, H_{arom} and H^{2-8}), 7.22−7.30 (m, 10 H, H_{arom} and H^{3-7}), 7.70 (m, 4 H, H_{arom}), 8.30 (s, 2 H, CHN) ppm. ^{13}C NMR Jmod $^{13}C\{^1H\}$ (63 MHz, $[D_6]$DMSO, 25 °C): δ = 20.5 ($C^{5'}$), 21.0 ($CH_3{-}Ar$), 26.3 ($C^{4'-6'}$), 37. 5 (CH_3N), 55.1 (CH_3O), 110.2 (C^{2-8}), 114.3 (C_{arom}), 126.0 ($C_{arom}{-}CH{=}N$), 127.4 (C^{4-6}), 129.0 (C_{arom}), 129.3 (C_{arom}), 129.4 ($C_{arom}{-}C_{1-9}$), 129.7 (C_{arom}), 140.3 ($C_{arom}{-}CH_3$), 147.5 (N=CH), 147.9 (C^{3-7}), 148.8 ($C^5{-}Cl$), 161.7 ($C_{arom}{-}OCH_3$), 163.8 (C^{1-9}) ppm. MS (Electrospray): *m*/*z* (%) = 697 (100) $[M]^+$, 699 (52) $[M + 2]^+$. $C_{44}H_{46}BClF_4N_4O_2$ (785.13): calcd. (+ 1 mol of water) C 65.80, H 6.02, N 6.98; found C 65.99, H 5.82, N 6.85. UV/Vis (23 °C, CH_2Cl_2): λ_{max} nm (ε_{max} M^{-1} cm^{-1}): 290 (29000), 421 (25000), shoulder at 751, 819 (210000). Fluorescence spectrometry (23 °C, CH_2Cl_2): $\lambda_{ex}/\lambda_{em}$: 827/843 nm.

X-ray Crystallographic Study of 3: $C_{34}H_{40}BClF_4N_2O_2$, $M = 630.94$, triclinic, $P\bar{1}$ $a = 11.328(3)$ Å, $b = 11.720(3)$ Å, $c = 12.378(3)$ Å, $\alpha = 85.860(5)°$, $\beta = 85.050(5)°$, $\gamma = 77.654(5)°$, $V = 1596.8(6)$ Å^3, $Z = 2$. 8253 reflections (5390 independent, $R_{int} = 0.0284$) were collected at low temperatures ($T = 173(2)$ K) using an oil-coated shock-cooled crystal on a Bruker-AXS CCD 1000 diffractometer with Mo-K_α radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods (SHELXS-97)[15] and all non hydrogen atoms were refined anisotropically using the least-squares method on F^2.[16] Largest electron density residue: 0.319 e·Å^{-3}, R_1 (for $I > 2\sigma(I)$) = 0.0462 and $wR_2 = 0.1094$ (all data) with $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

CCDC-226535 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] A. Mishra, R. K. Behera, P. K. Behera, B. K. Mishra, G. B. Behera, *Chem. Rev.* **2000**, *100*, 1973−2011 and references cited therein.

[2] S. R. Mujumdar, R. B. Mujumdar, C. M. Grant, A. S. Waggoner, *Bioconjugate Chem.* **1996**, *7*, 356−362.

[3] A. L. Ellis, J. C. Mason, H. W. Lee, L. Strekowski, G. Patonay, H. Choi, J. J. Yang, *Talanta* **2002**, *56*, 1099−1107.

[4] K. Licha, C. Hessenius, A. Becker, P. Henklein, M. Bauer, S. Wisniewski, B. Wiedenmann, W. Semmler, *Bioconjugate Chem.* **2001**, *12*, 44−50.

[5] Y. Lin, R. Weissleder, C. H. Tung, *Bioconjugate Chem.* **2002**, *13*, 605−610.

[6] N. Narayanan, G. Little, R. Raghavachary, G. Patonay, *Proc. SPIE -Int. Soc., Opt. Eng.* **1995**, *2388*, 6−15.

[7] G. Patonay, M. D. Antoine, *Anal. Chem.* **1991**, *63*, 321−327A.

[8] N. Obaya, C. Payrastre, Y. Madaule, *Tetrahedron* **2001**, *57*, 9137−9147, and references cited therein.

[9] A. Izquierdo, C. Payrastre, H. Gornitzka, Y. Madaule, *Eur. J. Org. Chem.* **2003**, 2371−2374.

[10] N. Narayanan, G. Patonay, *J. Org. Chem.* **1995**, *60*, 2391−2395.

[11] G. A. Reynolds, K. H. Drexhage, *J. Org. Chem.* **1977**, *42*, 885−888.

[12] L. Strekowski, M. Lipowska, T. Gorecki, J.C. Mason, G. Patonay, *J. Heterocyclic. Chem.* **1996**, *33*, 1685−1688 and references cited therein.

[13] L. Strekowski, M. Lipowska, G. Patonay, *J. Org. Chem.* **1992**, *57*, 4578−4579.

[14] A. L. Pikus, V. M. Feigel′man, V. V. Mezheritskii, *Zh. Org. Khim.* **1989**, *25*, 2333−2337.

[15] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467−473.

[16] SHELXL-97, *Program for Crystal Structure Refinement*, G. M. Sheldrick, University of Göttingen, **1997**.

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