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7-Dialkylamino-1-alkylquinolinium Salts: Highly Versatile and Stable Fluorescent Probes

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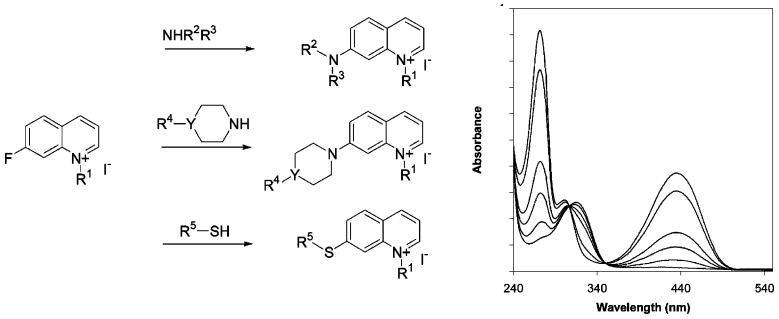

7-Dialkylamino- and 7-alkylsulfenyl-1-alkylquinolinium salts have been synthesized using a novel synthetic approach. The key intermediate, 7-fluoro-1-methylquinolinium iodide, was shown to possess high reactivity toward nitrogen and sulfur nucleophiles, and the kinetics of this nucleophilic aromatic substitution reaction was investigated. A wide variety of compounds were synthesized and characterized spectroscopically. High fluorescence quantum yields were observed, and this was attributed to the rigid molecular architecture. The thermal and photochemical stability of a number of compounds was investigated, and it was demonstrated that 7-dialkylamino-1-methylquinolinium salts have superior stability compared to a number of hemicyanine dyes and rigid charge-transfer probes. Based on the high quantum yields, the large Stokes shifts, and in particular, the high thermal and photochemical stability, it is concluded that 7-dialkylamino-1-methylquinolinium salts are excellent color-shifting, mobility-sensitive fluorescent probes for polymer characterization and other demanding applications.

Introduction

Fluorescent molecular probes are used in a wide range of applications and have become an indispensable tool in chemistry, physics, biology, and medicinal sciences.[1] The major advantage of fluorescent probes is their sensitivity. Detection of single fluorescent molecules and investigation of the interactions of these molecules with their local environment have become routinely possible, typically by the use of near-field microscopy or confocal techniques.[2] The large variation in the photophysics of the available chromophores combined with chemical modifications give fluorescent probe techniques a virtually unlimited scope for the detection of specific molecules and the investigation of intermolecular interactions on a molecular scale. One of the most developed fields in fluorescence spectroscopy is the application of fluorescent probes and labels for the characterization of (bio)chemical processes, both in vitro and in vivo. In many applications, fluorescent labels have replaced their radioactive counterparts that have the obvious disadvantages associated with radioactive materials, i.e., in regard to availability, safety, and waste disposal. Moreover, fluorescent probes can incorporate specific functions, such as the detection of glucose under physiological conditions[3] or the detection and quantification of calcium ions.[4] The sequencing of the human genome[5] was only possible because of the automated procedures using specific labeling[6] and fluorescent in situ hybridization (FISH).[7]

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Since the early 1980s, there has been growing interest in the development of mobility-sensitive fluorescent probes for application in the field of polymer science. Studies on polymerization reactions,[8−13] the detection of phase transitions[14,15] and the glass transition,[15−17] and probing physical aging of amorphous polymers[18,19] have been reported. Different types of mobility-sensitive fluorescent probes have been employed in this research field.

Well-known are probes that respond to decreases in local mobility by an increase in fluorescence quantum yield. The first examples, the malononitrile-based "rotor probes",[20] show little fluorescence in low viscous media. However, upon increasing the viscosity, intramolecular rotations are retarded due to increased steric hindrance, and this results in dramatic increases in fluorescence quantum yield. The malononitrile-based probes were shown to be sensitive to changes in free volume in glassy polymers, allowing for T_g determination[16] and the measurement of physical aging.[18] More recently, the glass transition dynamics[17] and physical aging rates[21] in ultrathin polymer films were investigated.

Other fluorescent probes detect changes in local mobility by shifts in emission wavelength, and in all cases, a decreased local mobility results in blue shift of emission. A large variety of molecules is available that can be divided, at least conceptually, into two classes of compounds: probes that undergo conformational changes in the excited state and probes that undergo changes in charge distribution upon excitation. Probes that undergo conformational changes in the excited state lower their energy contents during this process. Such probes are mobility sensitive irrespective of the medium polarity. Molecules that undergo *intramolecular* excimer formation such as 1,10-di(1-pyrenyl)decane are good examples.[12] Probes that undergo changes in charge distribution during excitation find themselves in a solvent cage tailor-made for the ground state. The medium will respond to the altered charge distribution by adapting the solvent cage, notably by rearranging dipoles. Since this process is largely due to dipole−dipole interactions, more pronounced effects are expected in polar media.

The best known, most extensively used, mobility-sensitive color-shifting fluorescent probes are the internal charge transfer (ICT) probes. Generally, these molecules consist of an electron-donating and an electron-withdrawing group linked by a π-system[9c] or an appropriate σ-system,[10] and numerous examples are known. It is worthwhile to mention that the emission of charge-transfer probes responds to changes in mobility *and* polarity of the medium, and the latter effect is known as solvatochromism. Charge resonance (CR) probes possess a D-π-A^+X^- architecture[9d,13] and form another class of mobility-sensitive color-shifting fluorescent probes. These materials show little solvatochromism and large shifts in emission wavelength with changing local viscosity, which makes them suitable probes for the study of polymerization reactions.[9d,13] Although the distinction between probes that undergo conformational changes themselves and probes that force their direct environment to respond is a fundamental one, many probes are subjected to both processes. Twisted internal charge-transfer (TICT) probes,[22] for instance, need to undergo a conformational rearrangement, generally considered to be a 90° rotation over a C−N aniline bond, prior to the formation of a charge-transfer state.

In our research, we prefer wavelength-shifting over intensity-changing probes because under many circumstances the observed emission intensity will not be proportional to Φ_f, the fluorescence quantum yield of the probe. In fact, only in the case of homogeneous samples, both in composition and geometry, the observed intensity of emission and Φ_f will be proportional. The use of emission *wavelength* instead of emission *intensity* as the parameter connected with the local viscosity is a more reliable technique to determine probe emission, and this allows for the investigation of inhomogeneous, scattering, or opaque samples of virtually any geometry. For the applications we have in mind, notably detection of glass transition temperatures, characterization of the (meso)phase behavior of polymers, and the probing of physical aging, all fluorescent probes that we examined so far were not suitable due to the lack of thermal and photochemical stability and the occurrence of conformational rearrangements in the excited state. Notably, the stilbene-containing chromophores,[9c,d,13] which are excellent materials for monitoring polymerization processes, are unsuited. Most likely, conformational rearrangements in the excited state, some of which result in *Z*/*E* isomerization[23] and subsequent photochemical cyclization,[24] and bleaching by other processes are responsible. Replacing the stilbene moiety for a rigid π-system and attaching stable donor and acceptor groups are expected to result in more stable fluorescent probes with higher fluorescence quantum yields.

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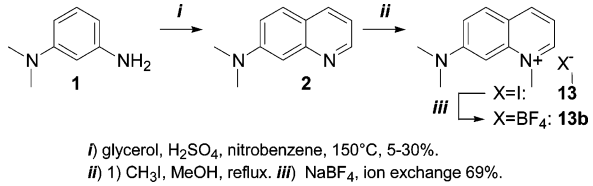
The effect of the rigidity of the π-system on the fluorescence quantum yield Φ_f was convincingly demonstrated by a direct comparison between the biphenyl compound 1-methyl-4-[4-(dimethylamino)phenyl]pyridinium tetrafluoroborate and the analogous fluorene compound 2-methyl-7-(dimethylamino)-2-azafluorenium tetrafluoroborate. In the fluorene compound, rotation over the central bond is prevented, and this has a dramatic effect on Φ_f.[25] While the fluorescence quantum yields of the biphenyl compound are around 0.05 and highly dependent on the solvent polarity, the fluorene compound has high fluorescence quantum yields in all solvents, up to a value of 0.83.

A number of ICT probes with a rigid π-system, such as the dansyl amides, coumarins, 7-substituted 4-nitrobenzodiazole (NBD) derivatives,[26] substituted naphthalenes such as 2-(dimethylamino)-6-propionyl naphthalene (PRODAN), and similar annulated aromates,[27] are known. In addition to an increased stability and a decreased conformational flexibility in the excited state, these probes also have increased fluorescence quantum yields. Charge resonance probes with rigid π-systems are rare, and most charge resonance probes are hemicyanines containing stilbazolium units. A new class of annulated hemicyanine chromophores was reported recently,[28] and the photophysical properties reported, high fluorescence quantum yields and large Stokes shifts, are promising. Unfortunately, these molecules are synthetically accessible only by an elaborate multistep synthesis.

Recently, we have reported the synthesis of 7-(dimethylamino)-1-methylquinolinium tetrafluoroborate (**13b**)[29] and have shown that this compound is an excellent fluorescent probe for nondestructive characterization of polymers. Determination of glass transition temperatures in polymers[15] and physical aging rates of amorphous polymers[19] have been reported. The high thermal and photochemical stability, along with a high quantum yield, distinguishes compound **13b** from other chromophores capable of detecting mobility by changes in emission wavelength and is critical to the successful application of this probe.

In this paper, we report the synthesis of 7-dialkylamino- and 7-alkylsulfenyl-1-methylquinolinium salts, the simplest types of charge-resonance probes in which the donor and acceptor units are connected by a rigid π-system. We have developed a highly versatile synthesis based on the classical Skraup reaction, in which the last step is a nucleophilic aromatic substitution with nitrogen and sulfur nucleophiles on 7-fluoro-1-methylquinolinium iodide (**6**). This is a highly efficient process that allows for the synthesis of a wide variety of quinolinium salts. The compounds obtained have been characterized spectroscopically, and stability tests have been performed. On the basis of these measurements, it is concluded that 7-dialkylamino-1-methylquinolinium salts meet the requirements for our applications, i.e., have large Stokes shifts, generally regarded as an indication of high sensitivity, possess high fluorescence quantum yields, and above all have excellent thermal and photochemical stability.

SCHEME 1. Synthesis of 7-(Dimethylamino)-1-methylquinolinium Tetrafluoroborate (13b)[a]



[a] Key: (i) glycerol, H_2SO_4, nitrobenzene, 150 °C, 5−30%; (ii) (1) CH_3I, MeOH, reflux; (iii) $NaBF_4$, ion-exchange 69%.

Results and Discussion

Synthesis. Our first synthetic route toward **13b**, outlined in Scheme 1,[19,29] used a traditional Skraup procedure.[30] The yields using this procedure, however, were unacceptably low, and a key issue in this respect is the limited stability of compound **2**. Another disadvantage of this procedure is the limited choice of substituents that can be attached to the quinolinium chromophore. Substituents at the amino functionality must be attached at the beginning of the reaction, and functional groups are not expected to survive the following reaction sequence. Only at the quinolinium position functionality may be introduced. To obtain reasonable yields and make functionalized derivatives of **13** accessible, another synthetic route was required.

To have a more flexible synthetic route, the amino group had to be introduced after the Skraup procedure. Therefore, we chose to synthesize 7-fluoroquinoline (**4**),[31] a compound that can be transformed to substituted 7-aminoquinolines by an aromatic nucleophilic substitution. Using a Skraup procedure on 3-fluoroaniline (**3**), 7-fluoroquinoline (**4**) and 5-fluoroquinoline (**5**) were obtained in 82% yield as a 3:1 mixture; see Scheme 2. Separation of both isomers by column chromatography or distillation was not successful, and therefore, isolation of the isomers from this mixture had to be achieved indirectly. We have developed two methods for isolating the prevalent 7-isomer. In the first approach, the mixture of **4** and **5** was converted into a mixture of the corresponding monooxalates **4a** and **5a**. The oxalate formed from the 7-isomer (**4a**) was isolated by recrystallization from 96% ethanol in a yield of 80%, based on the initial amount of **4**. From the reaction of **4** and **5** with methyl iodide in methanol, a mixture of the methylated quinolinium salts **6** and **7** was obtained from which **6** was isolated by crystallization in ethanol, once more in 80% yield. So far, attempts to isolate the 5-fluoro isomers, **5** or the oxalate **5a**, by crystallization have not been successful.[32]

The last step in the synthesis of 7-dialkylaminoquinolinium salts is the nucleophilic aromatic substitution, a reaction that has been described for 7-chloro- and 7-bromoquinoline.[30] Harsh reaction conditions and low yields make this approach unattractive, but it was anticipated that the fluoroquinoline **4** would be more reactive. When the mixture of **4** and **5** was heated to 100 °C with dimethylamine in DMF in a sealed tube, only traces of dimethylamino quinoline isomers were obtained after 160 h of heating. Transforming the quinoline **4** into the quinolinium

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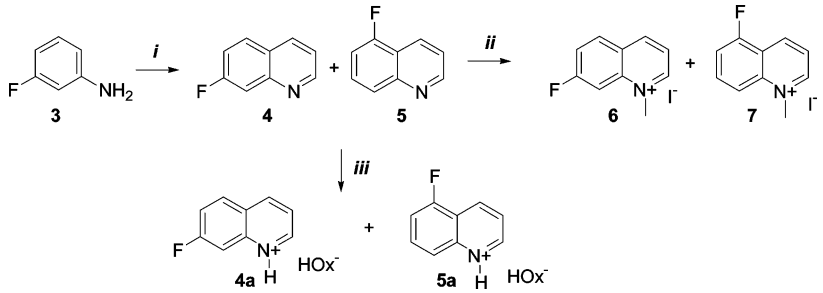
(32) Enrichment of **5a** in the mother liquor, up to 80%, was observed.

SCHEME 2. Synthesis of 7-Fluoro-1-methylquinolinium Iodide[a]



[a] Key: (i) glycerol, H_2SO_4, *m*-nitrobenzenesulfonic acid, 140 °C, 82%, **4**:**5** = 3:1; (ii) CH_3I, MeOH, reflux, 80% yield (7-isomer, **7** isolated from 96% ethanol); (iii) (1) H_2Ox, 96% ethanol (7-isomer, **4a** isolated).

salt **6** is expected to enhance the reactivity toward nucleophilic aromatic substitutions, since 4-fluoro-1-methylpyridinium salts are reported to be highly reactive toward nucleophilic aromatic substitution reactions[33] and activation of 7-haloquinolines by oxidation or protonation of the quinolinium nitrogen has also been reported.[34] However, when the reaction of **6** with dimethylamine in DMF was performed under standard conditions[35] (100 °C, K_2CO_3 as a base), a black tar was formed and no products were isolated. Fortunately, this result was a consequence of the high reactivity of **6**, presumably resulting in reactions with K_2CO_3 under the aforementioned conditions. Additional experiments have shown that **6** is so reactive that the nucleophilic aromatic substitution reaction with dimethylamine takes place in virtually all polar, nonacidic solvents at room temperature. The reaction itself could be detected by the appearance of an orange color and the onset of green fluorescence, both indicative for the formation of **13**.[36] By gentle heating, reactions could be run to completion in a matter of seconds, and in most solvents **13** crystallized from solution spontaneously.[37]

Standard nucleophilic aromatic substitutions were performed by heating **6** in the presence of 2.2 equiv of an amine in ethanol to reflux. After cooling, the corresponding 7-amino-1-methylquinolinium salts were isolated in a 60−98% yield as pure materials. The isolated yields reported do not reflect the conversion of the reaction, but merely the solubility of the product, vide infra.[38] For reactions where the amine is expensive or in scarce supply, the use of 2.2 equiv of amine may be a major disadvantage. In such cases, 1.1 equiv of amine with 1.1 equiv of triethylamine or diisopropylethylamine were added, and this gave identical yields. The reaction of **6** with the difunctional amine 1,2-diaminoethane gave the monosubstituted products **11** in high yields. Initially, a 10-fold excess of amine was used, but later experiments have shown that a high excess is not required since after addition of **6** to the diamine the second amine functionality is strongly deactivated. Further proof of a strong communication between nitrogens spaced by a dimethylene bridge, as present in compounds **11** and **22**−**24**, will be given in the spectroscopic characterization section.

The synthesis of compounds bearing other alkyl groups at the quinolinium nitrogen starts from 7-fluoroquinoline **4**, obtained from **4a**. This procedure was chosen because alkylations of the 3:1 mixture of **4** and **5** with alkylating agents other than methyl iodide were successful, but isolation of the desired alkylated 7-fluoro isomers had not been accomplished. For the alkylation of **4** with hexyl and 2-hydroxyethyl bromide, the low reactivity of alkyl bromides resulted in long reaction times. Therefore, alkylations were achieved with in situ generated hexyl iodide or iodoethanol.[39] The resulting 7-fluoroquinolonium salts were not isolated but converted to the desired 7-(dimethylamino)-1-hexylquinolinium iodide (**18**) and 7-(dimethylamino)-1-(2-hydroxyethyl)quinolinium iodide (**19**) with dimethylamine in ethanol in a one-pot procedure.

We have prepared the 7-alkylsulfenylquinolinium salts **26**−**28** by the reaction of **6** with the corresponding sulfur nucleophiles. Thiolate anions, obtained by the addition of triethylamine, were the reactive species. Satisfactory yields were obtained, and once more, the solubility of the product determined the yield. At this stage, it is worth mentioning that under the reaction conditions chosen, either in 96% ethanol or in water, addition of oxygen nucleophiles has not been observed. In contrast to other aromatic fluorides, which readily undergo nucleophilic aromatic substitution,[26b,40] **6** is extremely stable under ambient conditions.

The various 7-amino- and 7-alkylsulfenylquinolinium salts that were synthesized are summarized in Scheme 3 and Table 1. Obviously, the reaction between **6** and different nitrogen and sulfur nucleophiles may be employed for the synthesis of a large variety of quinolinium salts. It should be noted that compounds **10**, **11**, **16**, **17**, **19**, and **23** contain hydroxyl or amino functionality and may be used for further modification, for example, for fluorescent labels. Another type of modification that may be employed for these molecules is ion exchange. Substitution of iodide for an anion with a lower oxidation potential will increase probe stability. Also the fluorescence quantum yield will increase, since heavy atoms such as iodide promote intersystem crossing.[41]

Reaction Kinetics of the Nucleophilic Aromatic Substitution. The reaction between 7-fluoro-1-methylquinolinium iodide (**6**) and nucleophilic amines is expected to follow an

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(36) Compound **6** is fluorescent in most solvents. The emission maximum is however strongly shifted towards the blue compared to 7-dialkyamino compounds(λ_{max} abs = 317 nm, λ_{max} em = 395 nm in water).
(37) During the reaction of **6** with amines, 1 equiv of fluoride is formed. The 7-substituted quinolinium iodide is much less soluble in ethanol and will crystallize first.
(38) Higher yields, approaching 100%, may be achieved by another workup procedure, for instance, by crystallization from methanol/diethyl ether mixtures.
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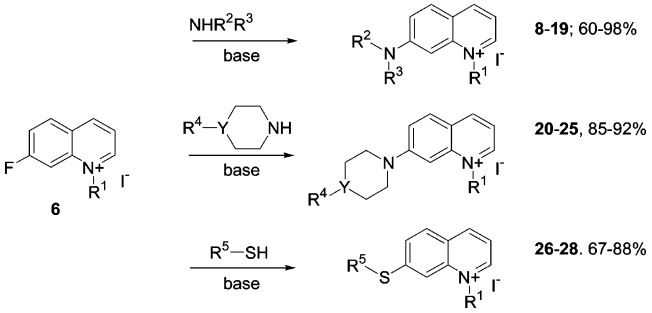
TABLE 1. Summary of the Synthesized Molecules

	R^1	R^2	R^3	R^4Y	R^5	yield (%)
8	CH_3	H	H			64
9	CH_3	H	CH_3			72
10	CH_3	H	CH_2CH_2OH			86
11	CH_3	H	$CH_2CH_2NH_2$			84
12	CH_3	H	$CH_2(C_6H_4)$-4-(CH_3O)			89
13	CH_3	CH_3	CH_3			82
14	CH_3	CH_2CH_3	CH_2CH_3			70
15	CH_3	*n*-C_6H_{13}	*n*-C_6H_{13}			60
16	CH_3	CH_3	CH_2CH_2OH			98
17	CH_3	CH_2CH_2OH	CH_2CH_2OH			89
18b	*n*-C_6H_{13}	CH_3	CH_3			71[a]
19	CH_2CH_2OH	CH_3	CH_3			47[a]
20	CH_3			H_2C		85
21	CH_3			O		90
22	CH_3			NCH_3		92
23	CH_3			NCH_2CH_2OH		91
24	CH_3			NC_6H_5		92
25	CH_3			$NCOOCH_2CH_3$		89
26	CH_3				$CH_2CH_2CH(CH_3)_2$	67
27	CH_3				CH_2CH_2 C_6H_5	74
28	CH_3				C_6H_5	88

[a] Starting from the oxalate **4a**.

SCHEME 3. Synthesis of 7-Substituted 1-Alkylquinolinium Derivatives



addition−elimination mechanism,[42] with second-order kinetics. The presence of an isolated CT absorption in all 7-amino-1-methylquinolinium dyes facilitates the study of the kinetics of this reaction using UV−vis absorption spectroscopy. The formation of the CT absorption in water is illustrated in Figure 1, and the isobestic points are indicative for the absence of stable intermediates in this reaction.

To verify the second-order reaction kinetics, experiments were performed using the pseudo-first-order approximation. Initial reaction rates were determined for series of different concentrations of **6** in water, with a fixed concentration of diethylamine, or with a fixed concentration of **6** and different concentrations of diethylamine. Linear correlations between reaction rates and reactant concentrations, both for **6** and for diethylamine, prove that these are pseudo-first-order reactions. The second-order rate constant was calculated to be 1.32×10^{-4} (l/mol·s), and rate constants for the other amines are shown in Table 2. Comparison with rate constants for the reaction of amines with Sanger's reagent, 1-fluoro-2,4-dinitrobenzene, shows a similar order of reactivity for the various amines,[40] but rate constants for the reaction with Sanger's reagent are 2−3 orders of magnitude higher. A comparison between rate constants measured for

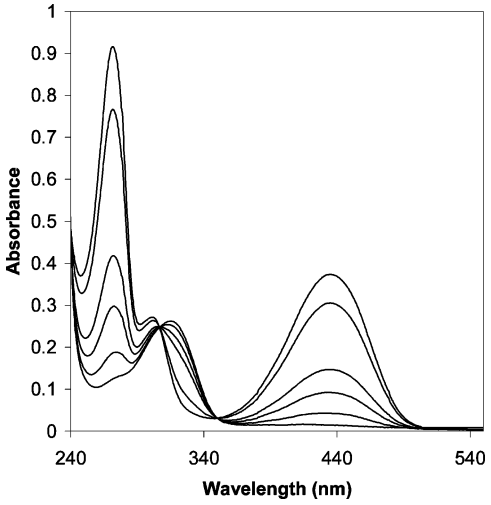


FIGURE 1. UV−vis spectra of a 0.0001 M solution of **6** and 0.2 M dimethylamine in water at 23 °C. Spectra were taken at 20, 280, 1190, 3860, and 6900 s.

TABLE 2. Rate Constants of 6 with a Selection of Amines at 23 °C

amine	product	*k* (l/mol·s) at 23 °C	relative *k*
piperidine	**20**	4.73E−03	1
dimethylamine	**13**	1.28E−03	0.27
1-methylpiperazine	**22**	7.42E−04	0.16
morfoline	**21**	5.82E−04	0.12
2-(*N*-methylamino)ethanol	**16**	4.68E−04	0.099
diethylamine	**14**	1.32E−04	0.028
2,2′-aminodiethanol	**17**	1.21E−05	0.0026

Sanger's reagent and 4-fluoronitrobenzene reveals that addition of a second nitro group results in a $\sim 10^6$ fold increase in reactivity. This suggests that **6** is 3 orders of magnitude more reactive than 4-fluoronitrobenzene and that the *N*-alkylquinolinium group is a stronger activating group than a nitro group. Reactions of 2- and 4-fluoro-1-methylpyridinium salts with amino nucleophiles[33] are reported to be fast and quantitative

(42) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry − Part B: Reaction and Synthesis*, 4th ed.; Plenum Publishing Corp.: New York, 1993.

TABLE 3. Absorption and Emission Maxima (in nm) and Stokes Shift (in cm^{-1}) of the CT Absorption of 13b, 29, and 30 in Various Solvents

solvent	Δf	λ_{abs}	**13b** λ_{em}	Stokes shift	λ_{abs}	**29** λ_{em}	Stokes shift	λ_{abs}	**30** λ_{em}	Stokes shift
chloroform	0.253	443	521	3380	503	585	2790	530	663	3780
chlorobenzene	0.262	446	525	3370	529	597	2150	567	717	3690
ethyl acetate	0.293	434	532	4240	457	593	5020	475	685	6450
tetrahydrofuran	0.308	435	530	4120	472	606	4680	490	710	6320
1,2-dimethoxyethane	0.310	432	534	4420	478	611	4550	500	710	5920
dichloromethane	0.320	442	505	2820	526	613	2700	568	707	3460
acetonitrile	0.392	443	533	3810	473	636	5420	490	716	6440
methanol	0.393	439	536	4120	476	615	4750	496	710	6080
water	0.405	435	538	4400	452	619	5970	451	716	8210
PMMA		440	522	3570	475	595	4250	495	662	5100

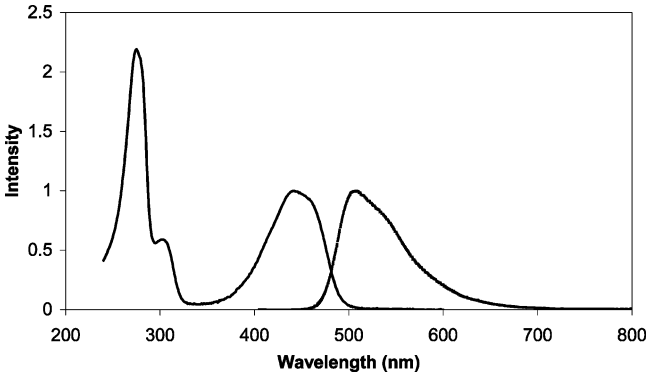


FIGURE 2. Absorption (solid line) and emission (dotted line) of **13b** in dichloromethane.

TABLE 4. Quantum Yields of 13b, 29, and 30 in Various Solvents, Relative to 9,10-Diphenylanthracene (DPA) in Cyclohexane (Quantum Yield 0.86[43]) and Corrected for Refractive Index

solvent	Δ*f*	**13b**	**29**	**30**
chloroform	0.253	0.16	0.06	0.12
chlorobenzene	0.262	0.20	0.07	0.15
ethyl acetate	0.293	0.08	0.03	0.08
tetrahydrofuran	0.308	0.05	0.05	0.06
1,2-dimethoxyethane	0.310	0.03	0.02	0.10
dichloromethane	0.320	0.68	0.09	0.26
acetonitrile	0.392	0.03	0.003	0.03
methanol	0.393	0.03	0.005	0.04
water	0.405	0.03	0.002	0.009

under mild conditions, in accordance with the previous observation. Kinetic data on these systems, however, have not been reported.

From Table 2, it is evident that 2,2′-aminodiethanol is the least reactive amine in the series. To determine whether the reaction conditions were sufficient for full conversion, the conversion versus time plot for this amine under reaction conditions identical to those used for the preparation of compounds **8**−**25** was taken. A reaction rate constant of 3.7×10^{-3} (l/mol·s) was determined, and it was calculated that full conversion (>99%) was reached after 30 min at 80 °C. On the basis of these experiments, it is concluded that most nucleophilic aromatic substitutions, performed with amines that are expected to be at least 1 order of magnitude more reactive, reach full conversion.

Spectroscopic Characterization. The absorption and emission spectra of **13b** in dichloromethane are shown in Figure 2. In this figure, the charge-transfer absorption at 442 nm and the large Stokes shift separating the absorption and the emission spectra are clearly visible. To characterize the basic chromophore, the spectral data of **13b** were compared with those of the hemicyanine analogues **29** and **30**;[43,44] see Figure 2. In this series of compounds, the same donor, acceptor, and counterion are employed, but the size and the nature of the π-system, being short and rigid in **13b** and longer and more flexible in **29** and **30**, are different.

The absorption and emission wavelengths, λ_{abs} and λ_{em}, along with the Stokes shifts of **13b**, **29**, and **30** in a number of solvents are shown in Table 3. Upon increasing the size of the π-system, λ_{abs} and λ_{em} shift to the red and the Stokes shifts increase. In contrast to charge-transfer probes, the polarity of the solvent, quantified by the solvent parameter Δ*f*,[45] does not have a profound effect on the absorption and emission spectra.[9a,46] The polarizability of the solvents, on the other hand, does affect the spectral properties, and in the chlorinated solvents dichloromethane, chlorobenzene, and chloroform, significant red shifts in absorption are observed. In emission the effects are less pronounced, and only for **13b** are observed blue shifts that are both consistent and significant. Both effects, the red shift in absorption and the blue shift in emission of **13b**, can be explained by "instant" stabilization due to a fast rearrangement of polarizable electrons *during* excitation or emission, respectively.

The quantum yields of emission are displayed in Table 4. For the flexible hemicyanines it has been reported that rotation over ϕ_1- ϕ_4 in the excited state decreases the fluorescence quantum yield due to thermal deactivation.[46−48] For compound **29**, rotation over ϕ_2 has been identified as the major deactivation route leading to low fluorescence quantum yields in all solvents.[48] In addition, an enhanced rotation over ϕ_1 is assigned as the major cause for the decrease in emission intensity observed upon increasing the solvent polarity.

For compounds **13b** all bond rotations are blocked, with the exception of the rotation over ϕ_1. Therefore, high fluorescence quantum yields, which may decrease upon increasing the solvent polarity (due to rotation over ϕ_1), are expected. The data presented in Table 4 show that the highest fluorescence quantum yields are indeed observed for compound **13b**. The order of fluorescence quantum yields, **13b** > **30** ≫ **29**, however, il-

(43) Morris, J. V.; Mahaney, M. A.; Huber, J. R. *J. Phys. Chem.* **1976**, *80*, 969.

(44) Wróblewski, S.; Trzebiatowska, K.; Jędrzejewska, B.; Pietrzak, M.; Gawinecki, R.; Pączkowski, J. *J. Chem. Soc., Perkin Trans. 2*. **1999**, 1909.

(45) The solvent parameter is defined as: $\Delta f = (\epsilon - 1)/(2\epsilon + 1) - (n^2 - 1)/4n^2 + 2$; see: Mes, G. F.; Jong, B. d.; Ramesdonk, H. J.; Verhoeven, J. W.; Warman, J. M.; Haas, M. P. d.; Dool, L. E. W. H.-v. d. *J. Am. Chem. Soc.* **1984**, *106*, 6524.

(46) Strehmel, B.; Seifert, H.; Rettig, W. *J. Phys. Chem. B* **1997**, *101*, 2232.

(47) Cao, X.; Tolbert, R. W.; McHale, J. L.; Edwards, W. D. *J. Phys. Chem. A* **1998**, *102*, 2740.

(48) Kim, J.; Lee, M. *J. Phys. Chem. A* **1999**, *103*, 3378.

TABLE 5. Spectroscopic Characterization of a Selection of 7-Substituted Quinolinium Salts[a]

	λ_{max} abs (nm)			λ_{max} em (nm)			Φ_f		
	water	CH_2Cl_2	ethyl acetate	water	CH_2Cl_2	ethyl acetate	water	CH_2Cl_2	ethyl acetate
8	397	362	ins	498	491	ins	0.63	0.031	ins
9	413	424	ins	504	471	ins	0.59	0.72	ins
10	412	427	ins	505	492	ins	0.65	0.70	ins
11[c]	416	429	ins	518	504	ins	0.043	0.32	ins
11[b]	401	421	ins	490	485	ins	0.85	0.85	ins
12	413	426	365	500	484	500	0.57	0.69	0.22
13	435	442	434	538	505	532	0.040	0.51	0.012
13b	435	443	434	538	505	532	0.030	0.68	0.08
14	439	446	434	528	509	518	0.0060	0.29	0.027
15	444	450	442	531	512	531	0.030	0.29	0.048
16	444	444	ins	540	525	ins	0.055	0.21	ins
18b	436	443	434	531	504	535	0.059	0.76	0.046
19	438	443	ins	545	523	ins	0.041	0.24	ins
20	436	451	434	553	524	536	0.011	0.39	0.043
21	415	432	ins	531	518	ins	0.036	0.31	ins
22[c]	424	441	ins	524	494	ins	0.0036	0.018	ins
22[b]	404	415	ins	498	500	ins	0.76	0.50	ins
23[c]	423	435	ins	524	503	ins	0.0022	0.034	ins
23[b]	405	413	ins	498	486	ins	0.70	0.31	ins
24[c]	422	442	ins	508	499	ins	0.00039	0.000089	ins
24[b]	405	420	ins	497	494	ins	0.094	0.16	ins
25	423	442	ins	530	521	ins	0.051	0.20	ins
26	384	404	ins	505	486	ins	0.10	0.19	ins
27	383	401	361	502	485	504	0.094	0.17	0.0035
28[c]	369	393	ins			ins			ins

[a] Quantum yields were taken relative to 9,10-diphenylanthracene (DPA) in cyclohexane (quantum yield 0.86[43]) and corrected for the refractive index [b] One drop of trichloroacetic acid solution in CH_2Cl_2 was added. [c] One drop of 1 M piperidine solution in CH_2Cl_2 was added or 1 drop of 1 M NaOH solution in water was added. It should be noted that piperidine is an effective quenching agent (±40% reduction in emission upon adding one drop of 1 M piperidine solution). [d] Nonfluorescent compound.

lustrates that a straightforward correlation between flexibility of the molecule, characterized by the *number* of deactivation pathways, 1, 4, and 6 for **13b**, **29**, and **30**, respectively, and the fluorescence quantum yield does not exist. Also, the increased quantum yield of **13b**, as compared to **29** and **30**, is not as pronounced as expected. A decrease in fluorescence quantum yield upon increasing the solvent polarity is generally found but only for **29** this effect is very significant. Increasing the solvent *polarizability* by chlorination has a more significant effect. In particular, in dichloromethane high quantum yields are observed, and the value obtained for **13b** in this solvent, 0.68, is noteworthy.

To investigate the effect of the substituents R_1-R_5 on the spectroscopic properties of quinolinium salts, spectra were recorded in ethyl acetate, water, and dichloromethane; see Table 5. These solvents were chosen to obtain data that may be representative for those in an apolar, a polar, and a highly polarizable solvent. It should be noted that, with the exception of **13b** and **18b**, all compounds are iodides, and that this has a pronounced influence on the spectroscopic properties, especially in apolar media. For example, the quantum yields of **13** and **13b** in dichloromethane are 0.51 and 0.68, respectively, which shows that iodide is an effective heavy-atom quenching agent for the quinolinium chromophore.[41] In the next section, the quinolinium salts are divided into three classes: acyclic 7-amino, cyclic 7-amino, and 7-sulfenyl compounds.

Within the series of acyclic 7-aminoquinolinium salts (**8**−**19**), a striking difference in the spectroscopic properties between those compounds that do (**8**−**12**) and those that do not have hydrogen(s) attached to the 7-amino group (**13**−**19**) has been observed. The spectroscopic properties of the last group (**13**−**19**) resemble those of **13**. Absorption and emission spectra in water and ethyl acetate are fairly similar, but in dichloromethane absorptions are red shifted and emissions are blue shifted, which results in Stokes shifts that are reduced by 30−40 nm. Extending the alkyl groups R_2 and R_3 results in red shifts of the charge-transfer absorption, due to an increased donor strength of the dialkylamino moiety. Fluorescence quantum yields are high in dichloromethane, between 0.3 and 0.7, and 1 order of magnitude lower in water and ethyl acetate. Quantum yields in ethyl acetate and to a lesser extent in dichloromethane may have decreased specifically by the presence of an iodine ion.

For the compounds that have hydrogen(s) attached to the 7-amino group (**8**−**12**), large, 30 nm blue shifts in absorption are observed, due to a decreased donor strength. Emission wavelengths are also blue-shifted, and Stokes shifts are unaffected. The most striking observation made for these compounds, however, is the strongly increased fluorescence in water, with Φ_f values up to 0.85! For compound **11**, strong fluorescence is observed in the protonated form only, due to intramolecular quenching of the free base by photoinduced electron transfer (PET).[49] The unusually high fluorescence in water and other polar solvents may be ascribed to a retarded rotation over ϕ_1 (Figure 3) caused by H-bridging interactions with the solvent.

Within the series of cyclic 7-aminoquinolinium salts **20**−**25**, the (hetero)atom Y in the exocyclic ring has a large influence. The spectra of **20** (Y = CH_2) and **21** (Y = O) are fairly similar to those of **13**. For compound **20**, the emission spectra are 10−20 nm red-shifted and for **21** the absorption spectra are 10−20 nm blue-shifted, and both effects result in larger Stokes shifts. For compounds **22**−**24**, in which Y = N-R_4, the spectroscopic properties are similar to those of **21**, except that fluorescence quantum yields are much lower. Upon addition of acid, which results in protonation of the 4-piperazine

(49) Silva, A. P. d.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.

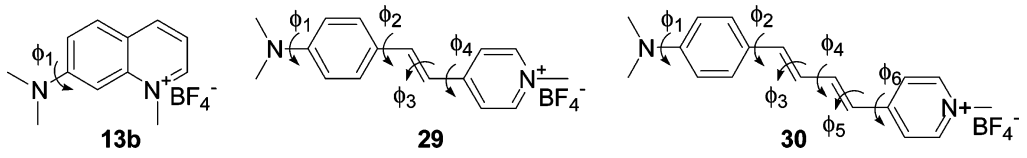


FIGURE 3. Chemical structures of QB (**13b**) and two hemicyanine dyes (**29** and **30**), along with the rotations that may lead to internal conversion.

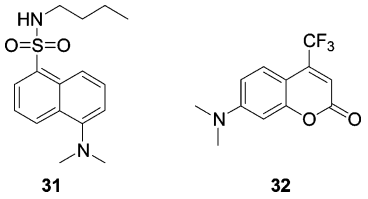


FIGURE 4. Structure of *N*-butyl-5-dimethylaminonaphthalene-1-sulfonamide (**31**, DASB) and (dimethylamino)-4-(trifluoromethyl)-coumarin (**32**, coumarin 152).

nitrogens, absorption and emission spectra shift 20 nm to the blue. The most striking observation, however, is the strong increase in emission quantum yield. For **22**−**24**, the quantum yield in water increases by a factor of 200−300 to values up to 0.76, making these compounds highly sensitive, strongly fluorescent acid−base indicators.[50] The low value of Φ_f found for compounds **22**−**24** is ascribed to intramolecular quenching by the 4-piperazine nitrogens. This effect, a strong increase in fluorescence by protonation of a nitrogen close to the donor group of a chromophore, is known as photoinduced electron transfer (PET).[49]

The spectroscopic properties of the 7-sulfenylquinolinium salts **26**−**28** deviate from those of the 7-aminoquinolinium salts because the alkylsulfenyl groups are weaker electron donors. The absorption maxima **26**−**28** are shifted 40−50 nm to the blue, and the fluorescence of **26** and **27** is also shifted to the blue by 20−30 nm. Both effects results in increased Stokes shifts, as compared to the dialkylamino compounds. In comparison with dialkylamino compounds, fluorescence quantum yields in ethyl acetate and dichloromethane are relatively low, but in water higher fluorescence quantum yields are observed. Compound **28**, however, is nonfluorescent.

Thermal and Photochemical Stability. The stability of a number of chromophores was investigated by taking UV spectra of samples that were stored at 150 °C or irradiated with 370 nm light for fixed periods of time. Probe degradation may result from chemical degradation of the donor, the acceptor, or the π-system, and all these processes will annihilate the charge-transfer absorption. Therefore, the intensity of the charge-transfer absorption was taken as a measure of probe degradation. To put the results obtained for quinolinium salts in perspective, the hemicyanines **29** and **30**, along with the well-known charge-transfer probes *N*-butyl-5-dimethylaminonaphthalene-1-sulfonamide (**31**) and (dimethylamino)-4-(trifluoromethyl)coumarin (**32**) were investigated as well (Figure 4).

Results obtained in various solvents were highly medium dependent. In addition, the reproducibility was limited and very much dependent on the exact experimental conditions. As an example, the thermal degradation of quinolinium salts in triacetin (1,2,3-propanetriol triacetate) at 150 °C is shown in Figure 5.

By comparing the results obtained in various solvents, it was concluded that 7-dialkylamino-1-methylquinolinium salts are the most stable compounds. 7-Sulfenyl compounds are markedly less stable, both thermally and photochemically, 7-piperazine salts lack thermal stability, whereas compound with long alkyl

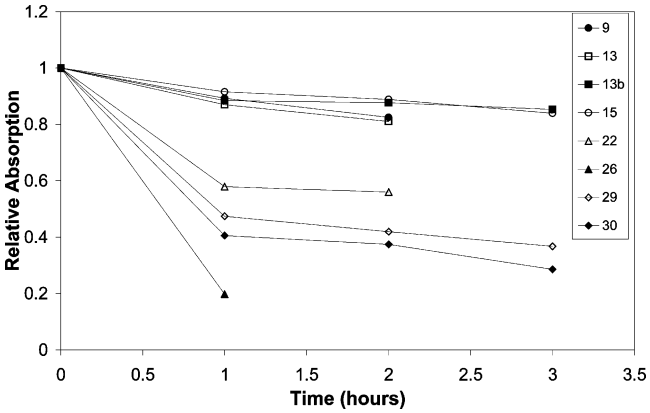


FIGURE 5. Thermal degradation at 150 °C in triacetin.

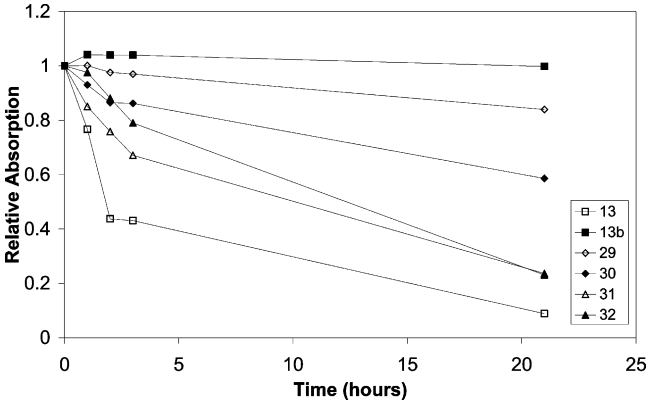


FIGURE 6. Thermal degradation at 150 °C in PMMA films.

groups at that position are photochemically unstable. A counterion effect, i.e., a lesser stability of iodides as compared to tetrafluoroborates, was observed mainly in less polar media.

The results obtained in PMMA, which are most relevant to the applications we have in mind for these fluorescent molecules, are shown in Figures 6 and 7. From the thermal degradation experiments, it is concluded that the quinolinium salt **13b**, with the tetrafluoroborate counterion, is the most stable probe. Even after 21 h at 150 °C, the extent of probe degradation is negligible. Interestingly, the hemicycanines **29** and **30**, which are notably unstable in most solvents, are fairly stable in PMMA films and rank second and third. The thermal stability of the CT compounds **31** and **32** is comparatively poor, and after 21 h, over 75% degradation has been observed. The quinolinium iodide **13** is distinctly the least stable compound.

During irradiation in PMMA films, which were performed over a period of 90 h, **13b** and **31** were the most stable probes, as is shown in Figure 7. The iodide **13** is less stable, but the

(50) (a) Gareis, T.; Huber, C.; Wolfbeis, O. S.; Daub, J. *Chem. Commun.* **1997**, 1717. (b): Kollmannsberger, M.; Gareis, T.; Heinl, S.; Breu, J.; Daub, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1333. (c): Baruah, M.; Qin, W.; Basariæ, N.; De Borggraeve, W. M.; Boens, N. *J. Org. Chem.* **2005**, *70*, 4152.

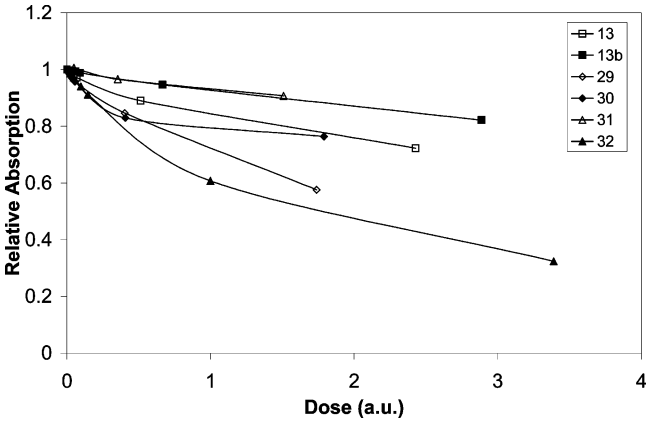


FIGURE 7. Photochemical degradation in PMMA; normalized extinction coefficient as a function of absorbed dose at 23 °C. The total irradiation time was 90 h.

effect of the counterion on the photochemical stability is limited. A lower stability was observed for the hemicyanine dyes **29** and **30**, and coumarin **32** is the least stable probe.

From the combined thermal and photochemical experiments in PMMA films it is concluded that 7-(dimethylamino)-1-methylquinolinium tetrafluoroborate **13b** is clearly the most stable probe. Thermal degradation at 150 °C is virtually absent, and the extent of photochemical degradation, even after 90 h of irradiation, is limited. The corresponding iodide **13** is markedly less stable. In particular, the thermal stability of compound **13** is very low, and most likely electron transfer from the iodide to the quinolinium ion occurs.[51] The hemicyanines **29** and **30** are clearly less stable although these compound are more stable in polymer films than in solution. Presumably, the decreased mobility in the polymer matrix retards degradation originating from the flexible π-system. For both conventional CT probes **31** and **32**, a low thermal stability was observed and this may result from the acceptor groups in both compounds. We can conclude that **13b** has a strongly improved stability as compared to the corresponding flexible hemicyanine dyes **29** and **30** and the rigid CT probes **31** and **32**.

Conclusions

We have synthesized 7-dialkylamino- and 7-sulfenyl-1-alkylquinolinium salts, charge resonance compounds that exhibit stable acceptor and donor groups and a rigid π-system. The key intermediate, 7-fluoro-1-methylquinolinium iodide (**6**), was synthesized by a Skraup reaction. Compound **6** was converted to various 7-amino- and 7-sulfenyl-1-methylquinolinium salts by a nucleophilic aromatic substitution reaction that is fast, quantitative, and takes place in virtually all nonacidic solvents, including water. The kinetics of this highly versatile reaction was investigated by UV spectroscopy. Based on the rate constants observed, it was concluded that the methylquinolinium ion is a strongly activating group for this reaction.

Spectroscopic studies have shown that 7-(dimethylamino)-1-methylquinolinium tetrafluoroborate (**13b**), the basic chromophore, has quantum yields that are substantially higher than those of the corresponding hemicyanine dyes **29** and **30**. It was also demonstrated that the iodide counterion suppresses the fluorescence quantum yield in less polar solvents. From the spectroscopic data (λ_{abs}, λ_{em}, and Φ_f) structure−property relations were derived. Absorption and emission wavelengths responded to the donor strength in the expected manner, which explains the substantial blue shifts observed for the less donating alkylsulfenyl compounds compared to the dialkylamino compounds. For most compounds, high quantum yields are observed only in chlorinated solvents. Monoalkylamino compounds, i.e., those compounds that bear one hydrogen at the 7-amino position, exhibit exceptionally high quantum yields in water and other polar solvents, and this phenomenon is not yet fully understood. For the 1-methyl-7-piperazylquinolinium compounds **22**−**24** exceptionally low emission quantum yields were observed, but protonation of the 4-piperazine nitrogens resulted in spectacular increases in quantum yields up to values of 0.76. These low emission quantum yields are ascribed to a highly efficient intramolecular quenching due to electron transfer to the amine, an effect also known as PET. This finding may be utilized for developing fluorescent pH sensors.

The thermal and photochemical stability of a number of compounds has been investigated, and it was concluded that 7-dialkylamino-1-methylquinolinium tetrafluoroborates exhibit superior stability as compared to hemicyanines **29** and **30** and the rigid CT probes **31** and **32**. The thermal *and* photochemical stability of tetrafluoroborates is significantly better than that of corresponding iodides, and the lower stability of the iodides may be explained by electron transfer from the iodide to the quinolinium ion. It was concluded that 7-(dimethylamino)-1-methylquinolinium tetrafluoroborate (**13b**), the compound we have used so far for polymer characterization, is one of the most stable quinolinium salts. Further research on the application of 7-dialkylamino-1-alkylquinolinium salts and the synthesis of related fluorescent compounds is currently underway.

Experimental Section

UV−vis Spectroscopy. UV−visible characterization of probes was performed using a quartz cell (1 cm optical path) and a double-beam spectrophotometer. Molar extinction coefficients of the fluorescent dyes were determined by dissolving precisely weighed amounts of dye (~0.5 mmol) in deionized water.

Fluorescence Spectroscopy. Fluorescence spectra were recorded with a fluorescence spectrometer equipped with a standard 90° setup. For the quantum yield determinations, a fixed excitation wavelength of 400 nm and fixed slit widths (1 nm excitation, 1 nm emission) were chosen. and a dye solution was prepared with an absorption below 0.1. The relative quantum yields were calculated from the integrated emission intensity (I_{em}) and the transmission (T) of the specific sample at 400 nm (or 470 nm for comparison of the different types of chromophore), using the following equation:

$$\Phi_{rel} = \frac{I_{em}*(1 - T_{ref})*n}{I_{ref}(1 - T)*n_{ref}} \quad (1)$$

9,10-Diphenylanthracene (DPA) in cyclohexane (quantum yield 0.86[43]) was used as reference.

Photochemical Stability Measurements. Solid PMMA films were prepared by solution casting from a solution of PMMA (2 g) and dye (0.002 g) in dichloromethane (18 mL) onto a glass plate, using a doctor blade with a 200 μm gap. The plates were left to dry for 24 h at room temperature. The films were then cut with a razor blade, and a drop of water was added to release the films from the glass. Finally, the films were dried for 48 h at 50 °C at 20 mmHg. Pieces of film (2.5 × 5 cm) were fixed to microscope glass slides with adhesive tape and placed into the carousel for

(51) Jedrzejewska, B.; Kabatc, J.; Pietrzak, M.; Paczkowski, J. *J. Polym. Sci. A* **2002**, *40*, 1433.

exposure. As light source, a 9 W low-pressure mercury lamp was used, mounted in the center of a carousel, which provided homogeneous exposure of all samples. The whole setup was placed in an aluminum-coated housing in order to maximize the exposure intensity. The effective dose was calculated by integration of the spectral overlap of the mercury lamp with the absorption spectrum of the sample, using the following equation:

$$\sum_{\nu_{start}}^{\nu_{end}}(1 - T(\nu))*I(\nu)*\Delta\nu \qquad (2)$$

where $T(\nu)$ and $I(\nu)$ are the transmission of the sample and the intensity of the mercury lamp at wavenumber ν, respectively.

Thermal Stability Measurements. Pieces of PMMA film (2.5 × 5 cm) on microscope glass slides were placed in the oven. After 1 h, the samples were removed from the oven and cooled by placing them on a copper plate. Subsequently, a UV−vis absorption spectrum was measured for each sample. This heating, cooling, and measurement procedure was then repeated.

Reaction Constant Determination. To a solution (2 mL) of aqueous amine (0.1 M) in a quartz cell was added 1 mL of aqueous **6** (20, 10, or 5 μM) solution and the resulting solution thoroughly mixed. The cell was then transferred to a spectrophotometer, and the absorbance at the absorption maximum was measured as a function of time. The room was thermostated at 23 °C.

Synthesis. TLC analysis was performed on silica gel, and ^{1}H and ^{13}C NMR spectra were measured at 300 and 75 MHz. Chemical shifts are given in ppm (δ) relative to tetramethylsilane (TMS) as internal standard..

The synthesis of **13b** according to Scheme 1 is described in ref 19.

The synthesis of 1:3 mixtures of 5- and 7-fluoroquinoline (**4** and **5**) was performed according to ref 31. Starting with 25 mL of **3**, 27 g of product was obtained.

7-Fluoro-1-methylquinolinium Iodide (6). To a solution of 5- and 7-fluoroquinoline isomers **4** and **5** (13.5 g, 92 mmol) in methanol (40 mL) was added methyl iodide (9.5 mL, 138 mmol). The reaction mixture was refluxed overnight. After being cooled to room temperature, the mixture was diluted with ether. The yellow precipitate was filtered and washed with ether (2 × 50 mL). Recrystallization from 96% ethanol gave pure **6** as yellow crystals. Yield: 22 g, 80%. Mp = 236.5−240 °C dec. ^{1}H NMR (DMSO-d_6) δ (ppm): 9.54 (1H, d, H2, $J_{2,3}$ = 5.7 Hz), 9.32 (1H, d, H4, $J_{4,3}$ = 5.7 Hz), 8.63 (1H, dd, H5, $J_{5,6}$ = 9.2 Hz, J_{H-F} = 6.1 Hz), 8.47 (1H, dd, H8, J_{H-F} = 10.8 Hz, $J_{8,6}$ = 2.1 Hz), 8.18 (1H, dd, H3, $J_{3,4}$ = 8.24 Hz, $J_{3,2}$ = 5.86 Hz), 8.06 (1H, M, H6). ^{13}C NMR (DMSO-d_6) δ (ppm): 164.9 (d, C7, J_{C-F} = 256 Hz), 150.6 (C4), 146.6 (C2), 139.7 (d, C9, J_{C-F} = 13.4 Hz), 133.5 (d, C5, J_{C-F} = 10.9 Hz), 126.4 (C10), 121.2 (C3), 120.1 (d, C8, J_{C-F} = 25.6 Hz), 105.0 (d, C6, J_{C-F} = 27.4 Hz), 45.5)N^+CH_3).

7-Fluoroquinoline Monooxalate (4a). To a solution of 5- and 7-fluoroquinoline isomers **4** and **5** (13.5 g, 92 mmol) in acetone (100 mL) was added a solution of oxalic acid dihydrate (11.6 g, 92 mmol) in acetone (100 mL) under vigorous stirring. The mixture was then concentrated in vacuo to a white solid, which was purified by recrystallized from 96% ethanol to give pure **4a** as white needles. Yield: 13 g, 80%. Mp = 152.5−156 °C dec. In DMSO, **4a** dissociates in **4** and oxalic acid as evidenced by the NMR spectra. ^{1}H and ^{1}H COSY NMR (DMSO-d_6) δ (ppm): 8.89 (1H, dd, H5, $J_{5,6}$ = 4.3 Hz, $J_{5,8}$ = 1.8 Hz), 8.39 (1H, dd, H4, $J_{4,3}$ = 7.7 Hz, $J_{4,2}$ = 0.8 Hz), 8.05 (1H, dd, H2, $J_{2,3}$ = 9.0 Hz, $J_{2,4}$ = 6.3 Hz), 7.72 (1H, dd, H8, J_{H-F} = 10.6 Hz, $J_{8,6}$ = 2.8 Hz), 7.48−7.54 (2H, M, H3 and H6) The COSY spectrum shows cross-peaks for δ (ppm): 7.52 (H3) and 8.05 (H2) and 8.39 (H4), 7.54 (H6) and 8.89 (H5). ^{13}C NMR (DMSO-d_6) δ (ppm): 168.6 (CO oxalic acid), 163.0 (d, C7, J_{C-F} = 246 Hz), 152.3 (C2), 149.2 (d, C9, J_{C-F} = 12.6 Hz), 136.8 (C4), 131.5 (d, C5, J_{C-F} = 9.5 Hz), 125.8 (C10), 121.6 (C3), 117.5 (d, C6, J_{C-F} = 25.2 Hz), 112.8 (d, C8, J_{C-F} = 20.5) Hz).

7-Amino-1-methylquinolinium Iodide (8) To 7-fluoro-1-methylquinolinium iodide (**6**) (500 mg, 1.73 mmol) were added 2 mL of 30% ammonia solution (20 equivalents) and 2 mL of 96% ethanol. The solution was heated at 60 °C for 1 h, and subsequently the solvent was evaporated. After recrystallization in 96% ethanol a yellow crystalline solid was obtained Yield: 316 mg, 64%. Mp = 118−123 °C. ^{1}H and ^{1}H COSY NMR (acetonitrile-d_3) δ (ppm): 9.30 (1H, d, H2, $J_{2,3}$ = 5.7 Hz), 9.16 (1H, d, H4, $J_{4,3}$ = 8.4 Hz), 8.50 (1H, dd, H5, $J_{5,8}$ = 9.3 Hz, $J_{5,6}$ = 6.0 Hz), 8.13 (1H, dd, H8, $J_{8,6}$ = 9.6 Hz, $J_{8,4}$ = 1.8 Hz), 8.02 (1H, dd, H3, $J_{3,4}$ = 8.4 Hz, $J_{3,2}$ = 5.7 Hz), 7.85 (1H, m, H6), 4.58 (3H, s, CH_3N^+). The COSY spectrum shows cross-peaks for δ (ppm): 7.85 (H6) and 8.50 (H5), 8.02 (H3) and 9.16 (H4) and 9.30 (H2).

General Procedure for the Synthesis of Substituted 7-Aminoquinolinium Iodides (9−25). To 7-fluoro-1-methylquinolinium iodide (**6**) (1 g, 3.46 mmol) were added 96% ethanol (10 mL) and amine (7.61 mmol, 2.2 equiv). The mixture was subsequently heated to reflux and allowed to cool slowly to room temperature. The crystalline products were collected by filtration and washed with cold absolute ethanol (2 × 5 mL) to give spectroscopically pure materials in a yield between 60 and 98%.

General Procedure for the Synthesis of Substituted 7-Sulfenylquinolinium Iodides (26−28). To 7-fluoro-1-methylquinolinium iodide (**6**) (0.5 g, 1.76 mmol) were added 96% ethanol (5 mL), triethylamine (0.28 mL, 1.1 equiv), and the thio compound (1.1 equiv). The mixture was subsequently heated to reflux and left to cool slowly to room temperature. The crystalline products were collected by filtration and washed with cold absolute ethanol (2 × 5 mL) to give spectroscopically pure materials.

7-Dimethylamino-1-hexylquinolinium Tetrafluoroborate (18b). 7-Fluoroquinoline monooxalate (**4a**) (1 g, 4.2 mmol) was dissolved in water (50 mL), and potassium carbonate (1.16 g, 8.4 mmol) was added. The aqueous solution was extracted with dichloromethane (4 × 50 mL). The combined organic layers were concentrated in vacuo and redissolved in methanol (5 mL). 1-Bromohexane (1.38 g, 8.4 mmol) and sodium iodide (1.26 g, 8.4 mmol) were added, and the mixture was refluxed overnight. After being cooled to room temperature, the mixture was concentrated in vacuo and the residue was redissolved in dichloromethane. The dichloromethane solution was washed with water (3 × 50 mL). The dichloromethane layer was concentrated in vacuo, and 20 mL of a 1 M dimethylamine solution in ethanol was added. The mixture was subsequently refluxed for 30 min. After being cooled to room temperature this solution was added slowly to a saturated solution of sodium tetrafluoroborate in water (50 mL) under vigorous stirring. **18b** crystallized as yellow crystals. Yield: 1.0 g, 71%. Mp = 144−145 °C. ^{1}H NMR (DMSO-d_6) δ (ppm): 8.96 (1H, dd, H2, $J_{2,3}$ = 6.0, $J_{2,4}$ = 1.2 Hz), 8.77 (1H, d, H4, $J_{4,3}$ = 7.5 Hz), 8.14 (1H, d, H5, $J_{5,6}$ = 9.6 Hz), 7.61 (1H, dd, H6, $J_{6,5}$ = 9.3 Hz, $J_{6,8}$ = 2.4 Hz), 7.53 (1H, dd, H3, $J_{3,4}$ = 7.8 Hz, $J_{3,2}$ = 6.3 Hz), 6.85 (1H, d, H8, J = 2.1 Hz), 4.80 (2H, t, CH_2N^+, J = 7.5 Hz), 3.27 (6H, s, $(CH_3)_2N$), 1.85−2.00 (2H, t, β-CH_2, J = 7.2 Hz),1.2−1.42 (6H, m, CH_2), 0.86 (3H, t, CH_3, J = 6.9 Hz).

7-Dimethylamino-1-(2-hydroxyethyl)quinolinium Iodide (19). 7-Fluoroquinoline monooxalate (**4a**) (1 g, 4.2 mmol) was dissolved in water (50 mL), and potassium carbonate (1.16 g, 8.4 mmol) was added. The aqueous solution was extracted with dichloromethane (4 × 50 mL). The combined organic layers were concentrated in vacuo and redissolved in methanol (5 mL). Bromoethanol (1.05 g, 8.4 mmol) and sodium iodide (1.26 g, 8.4 mmol) were added, and the mixture was refluxed overnight. The mixture was allowed to cool to room temperature, and 20 mL of a 1 M dimethylamine solution in ethanol was added. The mixture was subsequently refluxed for 30 min. After being cooled to room temperature **19** crystallized as bright yellow crystals. Yield: 0.68 g, 47%. Mp = 250 °C dec. ^{1}H NMR (DMSO-d_6) δ (ppm): 8.87 (1H, dd, H2, $J_{2,3}$ = 6.04, $J_{2,4}$ = 1.3 Hz), 8.79 (1H, d, H4, $J_{4,3}$ = 7.7 Hz), 8.15 (1H, d, H5, $J_{5,6}$ = 9.5 Hz), 7.59 (1H, dd, H6, $J_{6,5}$ = 9.33 Hz, $J_{6,8}$ = 2.19 Hz), 7.53 (1H, dd, H3, $J_{3,4}$ = 7.69 Hz, $J_{3,2}$ = 6.04 Hz), 6.94 (1H,

d, H8, $J_{8,6}$ = 2.02 Hz), 5.29 (1H, t, OH, J = 5.5 Hz), 4.92 (2H, t, CH_2N+, J = 4.92), 3.91 (2H, m, CH_2O), 3.26 (6H, s, CH3N).

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra of compounds **4a**, **6**, **13** (including ^{1}H COSY, NOESY), **17**, **22**, and **26**. UV spectra for the protonation/deprotonation of **22** and the reaction of **6** with dimethylamine. Analytical and spectroscopic data for compounds **9**−**28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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