Synthesis and Photochemical Evaluation of Iodinated Squarylium Cyanine Dyes

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Several (multiply) iodinated squarylium cyanine dyes of type **1** and **8** (see *Scheme* and *Table*), derived from 1,3-benzothiazole and 6-iodo-1,3-benzothiazole, were synthesized as potential new photosensitizers, with absorptions in the 700-nm region. Their ability to generate singlet oxygen ($^1O_2$) was assessed by luminescence-decay measurement in the near-IR. Some of these new dyes show interesting photophysical properties, and may be potentially used in photodynamic therapy (PDT).

Introduction. – Photodynamic therapy (PDT) is a fast-developing therapeutic modality that allows the selective destruction of diseased tissue, especially for the treatment of cancer [1]. PDT involves the administration of a photosensitizing drug that is preferentially taken up or retained by neoplastic cells. The drug itself is harmless and has no effect on either healthy or abnormal tissue. However, when the tissue that contains the photosensitizer is irradiated with light of appropriate wavelength, the sensitizer is excited to a short-lived singlet state, which, after intersystem crossing (ISC), relaxes to the more-stable, longer-lived triplet state. This triplet-activated sensitizer can then interact with a suitable biological substrate, by proton or electron transfer, leading to radical formation (type-I reaction), or transfer its energy directly to ground-state oxygen ($^3O_2$), generating highly reactive singlet oxygen ($^1O_2$) in a type-II reaction. Both processes may lead to damage or destruction of cellular components, and, eventually, cause cell death restricted to the illuminated area [2]. It is widely believed that $^1O_2$, resulting from the conversion of dissolved ground-state triplet oxygen ($^3O_2$), is the primary cytotoxic agent responsible for tumor-cell inactivation [3].

So far, hematoporphyrin derivatives have been the most commonly and widely used drugs for medical applications of PDT, but several disadvantages of these 'first-generation' photosensitizers – namely chemical heterogeneity, relatively poor photo-efficiency, and prolonged skin photosensitivity – have led, in recent years, to great efforts in the search for other classes of sensitizers with improved medical properties [4]. Besides selectivity for cancer cells and the lack of collateral toxic and phototoxic effects, any potential PDT drug candidate must fulfill several other multidisciplinary

requirements such as *1*) strong absorption ($\varepsilon > 10^5$ M^{-1} cm^{-1}) within the so-called 'phototherapeutic window' (600–1000 nm), in which light is only weakly scattered by living tissue, and where its penetration depth increases; and *2*) the ability to generate cytotoxic $^1O_2$ [5].

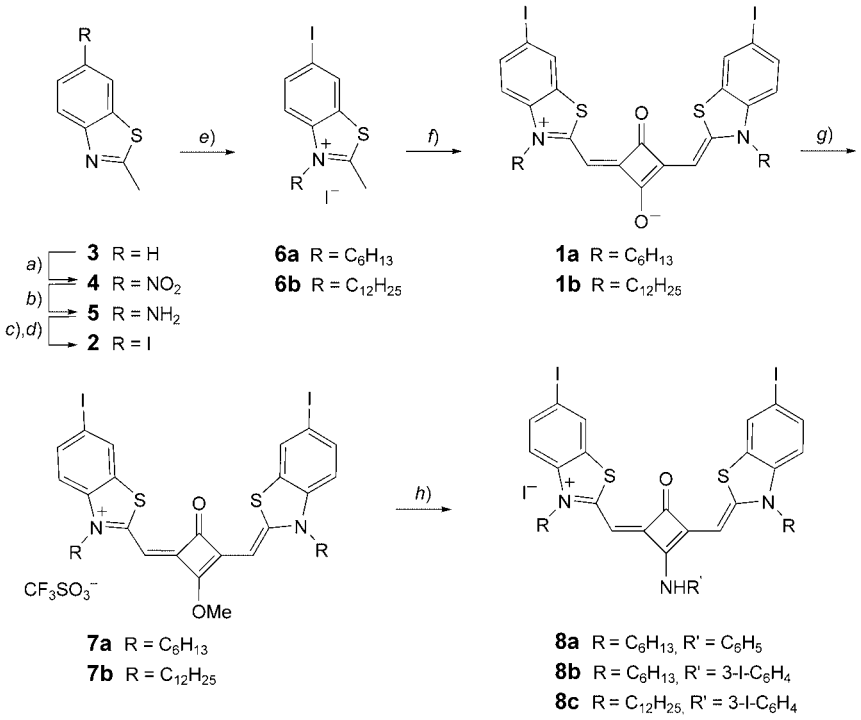
We have recently explored the $^1O_2$ production efficiency of several squarylium cyanines [6], a particular class of the large family of squarylium dyes. Despite their special properties, such as sharp and intense absorption in the VIS and near-IR region, as well as considerable thermo and photostability, which have turned them into particularly attractive substrates for technological applications in the domain of photonics [7], they have been scarcely studied with regard to PDT [8]. Our previously obtained, encouraging results [6] prompted us to improve the capacity of this type of dyes for $^1O_2$ generation. The introduction of heavy atoms (such as iodine) in the aromatic moiety of the dye seemed to be a straightforward way of increasing the ISC from the singlet to the triplet state of the sensitizer through enhancement of spin–orbital coupling, and, consequently, the efficiency of $^1O_2$ production.

Herein, we report the synthesis and photophysical properties (quantum yields of $^1O_2$ production) of several iodinated squarylium cyanine dyes that readily absorb within the 'phototherapeutic window'. Some non-halogenated analogues were also prepared, and their $^1O_2$ quantum yields were compared with the quantum yields of the halogenated analogues. Thereby, preference was given to aminosquarylium dyes, since the incorporation of amino moieties usually induces a convenient bathochromic shift in the absorption maximum of the compound relative to the unsubstituted, neutral parent squarylium dyes [9]. Also, amino groups offer a convenient way of linking the dye to biological substrates, and the *cationic* nature of these dyes may also be an advantage, since cationic cyanines seem to be potential sensitizers for PDT [10].

Results and Discussion. – 1. *Synthesis.* Our strategy for the synthesis of iodinated squarylium dyes with amino functions started with (the unsuccessful) attempt of direct iodination of the cyanine **1c** with ICl, a method recently described for the iodination of squarylium hemicyanines [8c]. Since **1c** is a relatively valuable substrate, further efforts on either direct or multistep iodination seemed not to be worthwhile, and we, thus, used as starting compound 6-iodo-2-methyl-1,3-benzothiazole (**2**), which was easily prepared through classical aromatic iodo-dediazotation (*Scheme*). Thus, nitration of 2-methyl-1,3-benzothiazole (**3**) with HNO_3/H_2SO_4, followed by reduction of the resulting nitro compound **4** with 10% Pd/C in the presence of HCO_2NH_4 yielded the aromatic amine **5**. The latter was converted to **2** in good overall yield through diazotation with $NaNO_2$, followed by *in situ* treatment with aqueous KI.

Quaternization of the free base **2** with an excess of hexyl or dodecyl iodide provided the salts **6a** and **6b**, respectively, which were then condensed with squaric acid (= 3,4-dihydroxycyclobut-3-ene-1,2-dione) to the corresponding squarylium cyanine dyes **1** in refluxing BuOH/pyridine. Methylation of **1** with 'methyl triflate' ($=CF_3SO_3Me$) afforded the intermediary methyl ethers **7**, whose MeO groups could be substituted with different aromatic amines to afford the desired iodinated dyes **8a**–**8c**. The non-halogenated analogues **8d** and **8e** (for structures, see *Table* below) were similarly prepared from the corresponding non-iodinated analogues of **7** according to [9a].

Scheme



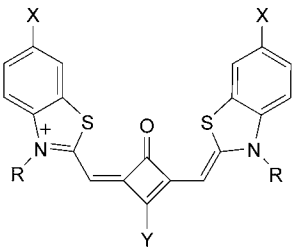
a) HNO_3, H_2SO_4. *b*) 10% Pd/C, HCO_2NH_4, MeOH/THF 2:1. *c*) $NaNO_2$, aq. HCl, 0°. *d*) aq. KI, 0° → 30 to 40°. *e*) $C_6H_{13}I$ or $C_{12}H_{25}I$, MeCN, reflux. *f*) Squaric acid, BuOH, pyridine, reflux. *g*) CF_3SO_3Me, CH_2Cl_2. *h*) Aniline ($C_6H_5NH_2$) or 3-iodobenzene-amine (3-I-C_6H_4-NH_2), CH_2Cl_2.

2. *Photophysical Properties.* The iodinated squarylium cyanine dyes **1a**,**b** and **8a**–**c** exhibit absorptions within the 'phototherapeutic window', with high molar absorption coefficients ε. As can be seen from the *Table*, these compounds, upon irradiation at 337 nm, produce singlet oxygen ($^1O_2$) in variable quantum yields ϕ. In contrast to alkylamino- and (dialkylamino)-substituted squarylium cyanines [9], the presence of *aromatic* residues at the central, four-membered ring had a negligible effect (or no effect at all) on the VIS spectrum, when compared to that of the corresponding unsubstituted compound. However, the introduction of I-atoms at the termini of the chromophoric, heteroaromatic system caused a bathochromic shift of *ca.* 12–15 nm (compare λ_{max} value of **1a** with that of **1c** [6a] in the *Table*; see also *Fig. 1*).

As expected, all the iodinated dyes produced $^1O_2$ more efficiently than the corresponding non-halogenated analogues. Among the dyes with the same carbon skeleton, the compounds with the highest numbers of I-atoms invariably gave rise to the highest efficiency.

The relative enhancement in $^1O_2$ quantum yields ϕ of the aminosquarylium dyes **8** due to the 'internal heavy-atom effect' depends on the previous presence of I-atoms in the molecule. In fact, while iodination of the non-halogenated substrate **8d** (to formally

Table. *UV/VIS Spectral Data, Yield of Singlet Oxygen* ($^1O_2$) *Production, and Quantum Yield for Compounds* **1** *and* **8**. In CH_2Cl_2 at ambient temperature; excitation wavelength 337.1 nm (or 355 nm; see *Exper. Part*).



	R	X	Y	Counter ion
1a	C_6H_{13}	I	O^-	none
1b	$C_{12}H_{25}$	I	O^-	none
1c	C_6H_{13}	H	O^-	none
8a	C_6H_{13}	I	NH-C_6H_5	I^-
8b	C_6H_{13}	I	NH-(3-I-C_6H_4)	I^-
8c	$C_{12}H_{25}$	I	NH-(3-I-C_6H_4)	I^-
8d	C_6H_{13}	H	NH-C_6H_5	I^-
8e	C_6H_{13}	H	NH-(3-I-C_6H_4)	I^-

Compound	λ_{max} [nm] (log ε)	Yield [%]	Quantum yield
1a	684 (5.47)	62	0.32 ± 0.02
1b	684 (5.46)	47	0.22 ± 0.02
1c[a])	672 (5.39)	76	0.26 ± 0.02
8a	678 (5.35)	90	0.46 ± 0.03
8b	675 (5.20)	83	0.66 ± 0.05
8c	675 (5.28)	34	0.33 ± 0.02
8d	663 (5.29)	60	0.32 ± 0.02
8e	660 (5.19)	65	0.39 ± 0.03

[a]) Data from [6a].

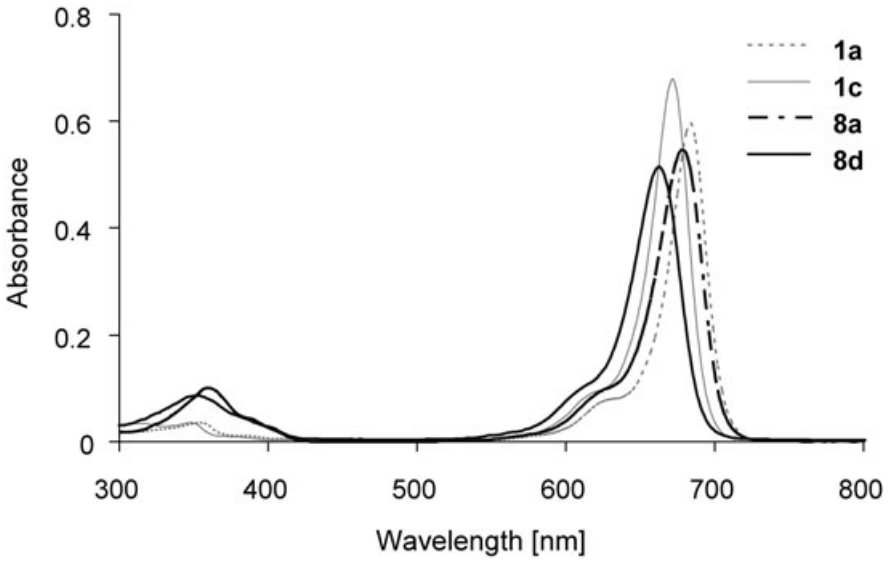


Fig. 1. *UV/VIS Absorption spectra of selected squarylium cyanine dyes.* In CH_2Cl_2 at ambient temperature.

produce **8a** and **8e**) results in a consistent contribution to ϕ of 0.07 per I-atom, additional iodination of **8a**,**e** to **8b** induces an increment in ϕ that is more pronounced with the introduction of iodine in aniline (0.20) than in the heteroaromatic ring (0.135 per I-atom).

In general, amino-substituted squarylium cyanine dyes show quantum yields for $^1O_2$ generation superior to those of the parent, unsubstituted compounds. In spite of the possibility that an eventual enhancement is originated by the '*external* heavy-atom effect', which is absent in the zwitterionic squarylium dyes **1**, a possibly higher degree of rigidification in compounds **8** (due to restricted rotation about the C–N bond) may also contribute to the observed difference. Restriction to free rotation eventually leads to a decrease of the efficiency of the non-radiative decay by photo-isomerization. As a consequence, there is an increase of the efficiency of ISC and $^1O_2$ production.

Hindered rotation of the amino group in **8** was also suggested by the two very broad, separated ^{1}H-NMR signals for the methine H-atoms at ambient temperature, indicating non-equivalence of chemical environments and local field inhomogeneity. Upon recording the same spectra at 60–70°, the two signals collapsed to a slightly broadened *singlet* of intermediate chemical shift.

We have reported before that related squarylium cyanine dyes derived from benzothiazole and containing pendant *N*-hexyl groups give rise to enhanced $^1O_2$ quantum yields compared to those of the *N*-ethyl analogs [6b]. Interestingly, in all of the new dyes, increasing the *N*-alkyl chain from C_6H_{13} to $C_{12}H_{25}$ diminished the $^1O_2$ quantum yields (*Table*). For shorter *N*-alkyl chains (less than six C-atoms), the increase in chain length decreases the relative importance of the non-radiative pathways of deactivation (photo-isomerization) [6]. However, for longer alkyl chains (more than six C-atoms), the major effect is probably the increase of internal conversion (associated with vibrational relaxation), which becomes more important in this case relative to photo-isomerization and ISC processes.

In conclusion, taking into consideration the absorption and quantum yields for $^1O_2$ generation, some of the newly synthesized dyes could be tested as PDT sensitizers.

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Experimental Part

General. All reagents were purchased from *Sigma-Aldrich* and used without further purification. Solvents were of anal. grade. All reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm Al-backed silica gel plates (*Merck 60 F_{254}*). Melting points (m.p.) were measured in open capillaries on a *Büchi 530* melting-point apparatus; uncorrected. IR Spectra were recorded on a *Mattson 5000* FT-IR spectrophotometer; in cm^{-1}. UV/VIS Spectra were recorded on a *Perkin-Elmer Lambda-6* instrument; λ_{max} in nm (log ε). ^{1}H- and ^{13}C-NMR spectra were recorded on *Bruker ACP-250*, *ARX-300*, and *ARX-400* spectrometers; chemical shifts δ in ppm rel. to residual solvent signals or Me_4Si, coupling constants *J* in Hz. Fast-atom-bombardment electron-impact mass spectra (FAB-EI-MS) were recorded on *Micromass AutoSpec-M* and *AutoSpec-Q* spectrometers operating at 70 eV, using a 4-nitrobenzyl alcohol as matrix; in *m/z*.

2-Methyl-6-nitro-1,3-benzothiazole (**4**). To an ice-cooled soln. of 2-methyl-1,3-benzothiazole (**3**; 5.87 g, 39 mmol) in H_2SO_4 (23 ml) was slowly added a mixture of HNO_3 (4.7 ml) and H_2SO_4 (3.5 ml). The mixture was stirred for 3 h at r.t., poured on ice, and left overnight. The resulting precipitate was collected by filtration, washed several times with cold H_2O, and recrystallized from MeOH to afford **4** (4.86 g, 64%). Yellowish crystals. M.p. 166.5–167.5° (lit. 168–170° [11]). IR (KBr): 3097*w*, 3066*w*, 1600*w*, 1569*m*, 1506*s*, 1436*m*, 1332*s*, 1267*s*,

1238*m*, 1174*m*, 1116*m*, 1037*w*, 993*w*, 916*w*, 902*m*, 821*m*, 752*m*, 717*m*, 671*w*, 647*w*, 547*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.91 (*s*, 3 H); 8.02 (*d*, *J* = 9.0, 1 H); 8.32 (*dd*, *J* = 2.3, 9.0, 1 H); 8.76 (*d*, *J* = 2.3, 1 H). FAB-MS: 195 ($[M + H]^+$).

6-Amino-2-methyl-1,3-benzothiazole (**5**). To a soln. of **4** (2.0 g, 10 mmol) in THF (40 ml) and MeOH (20 ml), 10% Pd/C (750 mg) and $HCOONH_4$ (9.74 g, 150 mmol) were added, and the mixture was stirred at r.t. for 3 d. The mixture was filtered through a bed of *Celite*, washing with hot MeOH. The filtrate was evaporated to dryness, the resulting residue was dissolved in $CHCl_3$, and extracted with brine. The org. layer was dried (Na_2SO_4), filtered, and evaporated *in vacuo* to afford **5** (1.55 g, 92%).White crystals. M.p. 119–120° (lit. 125–126° [12]). IR (KBr): 3376*m*, 3315*m*, 3207*m*, 1637*m*, 1604*s*, 1560*m*, 1517*m*, 1465*s*, 1432*m*, 1288*m*, 1228*s*, 1166*s*, 1049*w*, 829*m*, 817*m*, 728*w*, 649*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.74 (*s*, 3 H); 3.70 (br. *s*, 2 H, exchanging with D_2O); 6.78 (*dd, J* = 2.3, 8.6, 1 H); 7.05 (*d*, *J* = 2.3, 1 H); 7.69 (*d*, *J* = 8.6, 1 H). FAB-MS: 165 ($[M + H]^+$).

6-Iodo-2-methyl-1,3-benzothiazole (**2**). To an ice-cooled soln. of **5** (1.48 g, 9.02 mmol) in conc. HCl (4 ml) and H_2O (4 ml), a soln. of $NaNO_2$ (1.14 g, 16 mmol) in H_2O (5.2 ml) and, 30 min later, a soln. of KI (2.59 g, 16 mmol) in H_2O (3 ml), were added dropwise. After stirring for 10 min., the mixture was allowed to gradually reach r.t., and then heated at 30–40° for 15 min. The resulting dark cake was dissolved in CH_2Cl_2 and washed with 5% aq. $NaHSO_3$ soln., until a pale yellow color was obtained. The org. layer was dried (Na_2SO_4) and evaporated *in vacuo*, and the resulting residue was recrystallized from EtOH to afford **2** (1.70 g, 79%). White crystals. M.p. 140–141° (lit. 140–141° [13]). IR (KBr): 1511*m*, 1430*s*, 1390*w*, 1371*w*, 1297*w*, 1268*m*, 1238*m*, 1178*m*, 1166*m*, 858*w*, 817*s*, 740*w*, 665*w*, 651*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.81 (*s*, 3 H); 7.65–7.73 (*m*, 2 H); 8.14 (*d*, *J* = 1.5, 1 H). FAB-MS: 276 ($[M + H]^+$).

General Procedure for the Synthesis of the Quaternary Ammonium Salts **6**. A soln. of **2** (1.0 mmol) and 1-iodohexane or 1-iodododecane (3.0–5.0 mmol) in MeCN (25 ml) was heated at reflux for 5 d. After cooling, Et_2O was added, the precipitated ammonium salt was collected by vacuum filtration, washed several times with Et_2O, and dried *in vacuo* to afford spectroscopically pure **6**. The combined etheral filtrates were evaporated *in vacuo*, and the remaining residue, consisting mainly of unreacted starting materials, was heated at reflux for another 5 d, followed by the same workup as described above. This process was repeated three times to achieve suitable yields of **6** (see below).

3-Hexyl-6-iodo-2-methyl-1,3-benzothiazol-3-ium Iodide (**6a**). Yield: 64%. White crystals. M.p. 202–203°. IR (KBr): 3050*w*, 2952*w*, 2923*w*, 2852*w*, 1565*w*, 1513*w*, 1452*w*, 1382*s*, 1319*w*, 823*w*. ^{1}H-NMR (400 MHz, $CDCl_3$/CD_3OD): 0.79 (*t*, *J* = 6.9, 3 H); 1.24–1.28 (*m*, 4 H); 1.36–1.40 (*m*, 2 H); 1.81–1.85 (*m*, 2 H); 3.68 (*s*, 3 H); 4.64 (*t*, *J* = 7.9, 2 H); 7.70 (*d*, *J* = 8.9, 1 H); 8.03 (*dd*, *J* = 1.4, 8.9, 1 H); 8.48 (*d*, *J* = 1.3, 1 H). FAB-MS: 360 (M^+).

3-Dodecyl-6-iodo-2-methyl-1,3-benzothiazol-3-ium Iodide (**6b**). Yield: 20%. White crystals. M.p. 191–193°. IR (KBr): 2915*s*, 2848*s*, 1569*w*, 1511*w*, 1465*w*, 1450*w*, 1382*m*, 1326*w*, 802*w*, 719*w*, 557*w*, 530*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (*t*, *J* = 6.8 Hz, 3 H); 1.23–1.34 (*m*, 16 H); 1.43–1.47 (*m*, 2 H); 1.90–1.93 (*m*, 2 H); 3.39 (*s*, 3 H); 4.78 (*t*, *J* = 7.8, 2 H); 7.76 (*d*, *J* = 8.9, 1 H); 8.04 (*dd*, *J* = 1.3, 8.8, 1 H); 8.66 (*d*, *J* = 1.4, 1 H). FAB-MS: 444 (M^+).

General Procedure for the Synthesis of Squarylium Dyes **1**. The novel squarylium dyes **1** were prepared, in analogy to a literature procedure [14], by condensing the iodides **6** with squaric acid (= 3,4-dihydroxycyclobut-3-ene-1,2-dione) in BuOH/pyridine at reflux.

(4Z)-4-[(3-Hexyl-6-iodo-1,3-benzothiazol-3-ium-2-yl)methylidene]-2-[(Z)-(3-hexyl-6-iodo-1,3-benzothiazol-2(3H)-ylidene)methyl]-3-oxocyclobut-1-en-1-olate (**1a**)[1]). Yield: 62%. Metallic, green crystals. M.p. 261° (dec.). UV/VIS (CH_2Cl_2): 684 (5.47). IR (KBr): 2921*w*, 2848*w*, 1641*w*, 1590*w*, 1573*w*, 1459*s*, 1431*s*, 1355*w*, 1243*s*, 1187*w*, 1093*m*, 1074*w*, 954*w*, 755*w*, 514*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (br. *t*, *J* = 6.8, 6 H); 1.31–1.42 (*m*, 12 H); 1.67–1.77 (*m*, 4 H); 4.02 (br. *t*, *J* = 7.4, 4 H); 5.96 (br. *s*, 2 H); 6.86 (*d*, *J* = 8.5, 2 H); 7.63 (*d*, *J* = 8.6, 2 H); 7.78 (*s*, 2 H). HR-FAB-MS: 797.0220 ($[M + H]^+$, $C_{32}H_{35}I_2N_2O_2S_2^+$; calc. 797.0230).

(4Z)-4-[(3-Dodecyl-6-iodo-1,3-benzothiazol-3-ium-2-yl)methylidene]-2-[(Z)-(3-dodecyl-6-iodo-1,3-benzothiazol-2(3H)-ylidene)methyl]-3-oxocyclobut-1-en-1-olate (**1b**)[1]). Yield: 47%. Metallic, red crystals. M.p. 250° (dec.). UV/VIS (CH_2Cl_2): 684 (5.46). IR (KBr): 2921*m*, 2850*w*, 1666*w*, 1587*m*, 1571*m*, 1459*s*, 1432*s*, 1388*m*, 1369*s*, 1353*m*, 1330*m*, 1241*s*, 1143*w*, 1099*s*, 1076*m*, 1031*w*, 960*w*, 784*w*, 761*w*, 738*w*, 520*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (br. *t*, *J* = 6.6, 6 H); 1.25–1.39 (*m*, 36 H); 1.74–1.76 (*m*, 4 H); 3.99 (br. *t*, *J* = 7.5, 4 H); 5.84 (br. *s*, 2 H); 6.84 (*d*, *J* = 8.7, 2 H); 7.61 (*d*, *J* = 8.6, H); 7.76 (*s*, 2 H). HR-FAB-MS: 965.2073 ($[M + H]^+$, $C_{44}H_{59}I_2N_2O_2S_2^+$; calc. 965.2108).

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[1]) Since the chromophore is fully delocalized, the systematic name of only *one* resonance structure is given (the one shown in the *Scheme* or *Table*).

General Procedure for the Synthesis of the Methylated Squarylium Dyes **7**. To a soln. of **1** (*ca.* 0.5 mmol) in anh. CH_2Cl_2 (50 ml), vigorously stirred under N_2 atmosphere, $CF_3SO_3CH_3$ (4 equiv.) was added at r.t. After 3–5 h, the mixture was quenched with cold 5% aq. $NaHCO_3$ soln. The org. layer was dried (Na_2SO_4) and evaporated, and the resulting residue was recrystallized from CH_2Cl_2/MeOH.

*3-Hexyl-2-[(Z)-{3-[(Z)-(3-hexyl-6-iodo-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-methoxy-4-oxocyclobut-2-en-1-ylidene}methyl]-6-iodo-1,3-benzothiazol-3-ium Trifluoromethanesulfonate* (**7a**)[1]). Yield: 99%. Metallic, green crystals. M.p. 250° (dec.). UV/VIS (CH_2Cl_2): 655 (5.48). IR (KBr): 2927*w*, 2865*w*, 1650*w*, 1575*w*, 1500*w*, 1421*s*, 1351*m*, 1322*w*, 1243*s*, 1209*s*, 1145*s*, 1114*s*, 1025*m*, 806*w*, 744*w*, 636*w*, 518*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (br. *t*, *J* = 6.6, 6 H); 1.30–1.41 (*m*, 12 H); 1.76–1.82 (*m*, 4 H); 4.33 (br. *t*, *J* = 7.0, 4 H); 4.61 (*s*, 3 H); 5.98 (br. *s*, 2 H); 7.11 (*d*, *J* = 8.7, 2 H); 7.75 (*d*, *J* = 8.6, 2 H); 7.91 (*s*, 2 H). HR-FAB-MS: 811.0361 (M^+, $C_{33}H_{37}I_2N_2O_2S_2^+$; calc. 811.0380).

*3-Dodecyl-2-[(Z)-{3-[(Z)-(3-dodecyl-6-iodo-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-methoxy-4-oxocyclobut-2-en-1-ylidene}methyl]-6-iodo-1,3-benzothiazol-3-ium Trifluoromethanesulfonate* (**7b**)[1]). Yield: 89%. Metallic, red crystals. M.p. 222–224°. UV/VIS (CH_2Cl_2): 655 (5.51). IR (KBr): 2921*w*, 2850*w*, 1654*w*, 1577*w*, 1502*w*, 1425*s*, 1353*m*, 1243*s*, 1209*m*, 1143*s*, 1025*w*, 746*w*, 636*w*, 516*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (br. *t*, *J* = 6.7, 6 H); 1.22–1.39 (*m*, 36 H); 1.79 (br. *s*, 4 H); 4.33 (br. *s*, 4 H); 4.61 (*s*, 3 H); 5.97 (br. *s*, 2 H); 7.11 (*d*, *J* = 8.8, 2 H); 7.75 (*d*, *J* = 8.6, 2 H); 7.90 (*s*, 2 H). HR-FAB-MS: 979.2237 (M^+, $C_{45}H_{61}I_2N_2O_2S_2^+$; calc. 979.2264).

General Procedure for the Synthesis of the Aminosquarylium Dyes **8**. The appropriate aromatic amine (sixfold excess) was added to a soln. of **7** (*ca.* 0.4 mmol) in anh. CH_2Cl_2 (40 ml) under N_2 atmosphere, and the mixture was stirred at r.t. for 6 d in the presence of catalytic amounts of Et_3N and DMAP (= 4-(dimethylamino)pyridine). The mixture was extracted with cold H_2O, the org. layer was separated by decantation, dried (Na_2SO_4), and evaporated *in vacuo*. The resulting residue was dissolved in MeOH, and to this soln. was added 14% aq. KI soln. (approximately the same volume). After 2 h, the precipitated dye, bearing the iodide counter-ion, was collected by filtration, washed with H_2O, and recrystallized from CH_2Cl_2/MeOH/Et_2O to afford **8a–c**. Compounds **8d** and **8e** were prepared analogously, but starting from the corresponding non-iodinated dyes (*Table*).

*3-Hexyl-2-[(Z)-{3-[(Z)-(3-hexyl-6-iodo-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-(phenylamino)-4-oxocyclobut-2-en-1-ylidene}methyl]-6-iodo-1,3-benzothiazol-3-ium Iodide* (**8a**)[1]). Yield: 90%. Violet crystals. M.p. 270° (dec.). UV/VIS (CH_2Cl_2): 678 (5.35). IR (KBr): 3457*w*, 2925*w*, 2852*w*, 1631*w*, 1594*w*, 1542*w*, 1492*m*, 1434*s*, 1349*m*, 1247*s*, 1172*m*, 1147*m*, 1076*w*, 1024*w*, 983*w*, 796*w*, 759*w*, 518*w*. ^{1}H-NMR (400 MHz, CD_2Cl_2): 0.89 (br. *s*, 6 H); 1.30–1.52 (*m*, 14 H); 1.83 (br. *s*, 2 H); 3.71 (br. *s*, 2 H); 4.53 (br. *s*, 2 H); 5.02 (br. *s*, 1 H); 6.95–7.11 (*m*, 2 H); 7.31–7.44 (*m*, 6 H); 7.46–7.95 (*m*, 4 H); 10.92 (*s*, 1 H, exchanging with D_2O). ^{13}C-NMR (62.5 MHz, (D_6)DMSO, *T* = 60°): 13.4; 21.5; 25.3; 26.6; 30.4; 46.3; 87.0; 88.4; 114.9; 124.2; 126.4; 129.0; 129.5; 130.6; 136.1; 140.2; 160.3; 177.6. HR-FAB-MS: 872.0690 (M^+, $C_{38}H_{40}I_2N_3OS_2^+$; calc. 872.0702).

*3-Hexyl-2-[(Z)-{3-[(Z)-(3-hexyl-6-iodo-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-[(3-iodophenyl)amino]-4-oxocyclobut-2-en-1-ylidene}methyl]-6-iodo-1,3-benzothiazol-3-ium Iodide* (**8b**)[1]). Yield: 83%. Purple crystals. M.p. 242° (dec.). UV/VIS (CH_2Cl_2): 675 (5.20). IR (KBr): 3434*w*, 2925*w*, 2854*w*, 1637*w*, 1579*w*, 1529*w*, 1492*m*, 1463*m*, 1444*s*, 1347*m*, 1267*m*, 1247*m*, 1170*m*, 1149*w*, 1066*w*, 987*w*, 802*w*, 771*w*, 520*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO, *T* = 60°): 0.87 (br. *t*, *J* = 6.5, 6 H); 1.26 (br. *s*, 12 H); 1.62 (br. *s*, 4 H); 4.13 (br. *s*, 4 H); 5.70 (br. *s*, 2 H); 7.33–7.52 (*m*, 4 H); 7.72–7.86 (*m*, 4 H); 8.40 (*s*, 2 H); 10.71 (br. *s*, 1 H, exchanging with D_2O). ^{13}C-NMR (62.5 MHz, (D_6)DMSO, *T* = 60°): 13.6; 21.8; 25.5; 26.8; 30.6; 46.5; 87.1; 88.7; 94.6; 115.1; 123.3; 129.6; 130.7; 130.9; 132.2; 135.0; 136.2; 137.6; 140.3; 159.8; 174.9. HR-FAB-MS: 997.9641 (M^+, $C_{38}H_{39}I_3N_3OS_2^+$; calc. 997.9669).

*Dodecyl-2-[(Z)-{3-[(Z)-(3-dodecyl-6-iodo-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-[(3-iodophenyl)amino]-4-oxocyclobut-2-en-1-ylidene}methyl]-6-iodo-1,3-benzothiazol-3-ium Iodide* (**8c**)[1]). Yield: 34%. Blue crystals. M.p. 240° (dec.). UV/VIS (CH_2Cl_2): 675 (5.28). IR (KBr): 3434*w*, 2921*w*, 2850*w*, 1635*w*, 1579*w*, 1533*w*, 1442*s*, 1382*w*, 1347*w*, 1247*m*, 1174*w*, 1149*w*, 1064*w*, 981*w*, 761*w*, 518*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (br. *s*, 6 H); 1.23 (br. *s*, 34 H); 1.53 (br. *s*, 4 H); 1.88 (br. *s*, 2 H); 3.80 (br. *s*, 2 H); 4.61 (br. *s*, 2 H); 5.03 (br. *s*, 1 H); 6.89 (br. *s*, 1 H); 7.13 (*t*, *J* = 7.7, 2 H); 7.53–7.90 (*m*, 8 H). HR-FAB-MS: 1166.1571 (M^+, $C_{50}H_{63}I_3N_3OS_2^+$; calc. 1166.1547).

*2-[(Z)-{3-[(Z)-(3-Hexyl-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-4-oxo-2-(phenylamino)cyclobut-2-en-1-ylidene}methyl]-3-hexyl-1,3-benzothiazol-3-ium Iodide* (**8d**)[1]). Yield: 60%. Blue crystals. M.p. 260–262°. UV/VIS (CH_2Cl_2): 663 (5.29). IR (KBr): 3444*w*, 2927*w*, 2856*w*, 1634*w*, 1545*w*, 1495*w*, 1442*s*, 1355*w*, 1258*s*, 1175*w*, 1156*w*, 1137*w*, 983*w*, 750*w*, 505*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO/$CDCl_3$): 0.89 (br. *s*, 6 H); 1.31–1.86 (*m*, 16 H); 3.82 (br. *s*, 2 H); 4.39 (br. *s*, 2 H); 5.00 (br. *s*, 1 H); 6,61 (br. *s*, 1 H); 7.36–7.53 (*m*, 11 H); 7.70 (br. *s*, 2 H); 10.63 (br. *s*, 1 H, exchanging with D_2O). ^{13}C-NMR (75 MHz, (D_6)DMSO/$CDCl_3$): 13.5; 21.9; 25.7; 27.1; 30.8;

46.7; 87.3; 112.1; 121.9; 124.0; 124.8; 126.2; 127.4; 128.6; 135.9; 140.1; 160.2; 175.0. HR-FAB-MS: 620.2774 (M^+, $C_{38}H_{42}N_3OS_2^+$; calc. 620.2769).

*2-[(Z)-{3-[(Z)-(3-Hexyl-1,3-benzothiazol-2(3*H*)-ylidene)methyl]-2-[(3-iodophenyl)amino]-4-oxocyclobut-2-en-1-ylidene}methyl]-3-hexyl-1,3-benzothiazol-3-ium Iodide* (**8e**)[1]). Yield: 65%. Blue crystals. M.p. 254–256°. UV/VIS (CH_2Cl_2): 660 (5.19). IR (KBr): 3435*w*, 2858*w*, 2921*w*, 1635*w*, 1581*w*, 1536*w*, 1444*s*, 1353*w*, 1254*s*, 1176*w*, 1156*m*, 1138*w*, 986*w*, 747*w*, 506*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO/$CDCl_3$): 0.89 (*t*, *J* = 6.7, 6 H); 1.29 (br. *s*, 12 H); 1.67 (br. *s*, 4 H); 4.14 (br. *s*, 4 H); 5.05 (br. *s*, 1 H); 6.40 (br. *s*, 1 H); 7.26–7.38 (*m*, 4 H); 7.48–7.52 (*m*, 4 H); 7.67–7.69 (*m*, 2 H); 7.84 (*d*, *J* = 7.8, 2 H); 10.65 (br. *s*, 1 H, exchanging with D_2O). ^{13}C-NMR (75 MHz, (D_6)DMSO/$CDCl_3$): 13.6; 21.9; 25.7; 27.0; 30.7; 46.4; 87.1; 94.1; 112.7; 122.3; 122.7; 124.8; 127.4; 127.5; 130.3; 131.9; 134.5; 137.4; 140.1; 159.2; 175.0. HR-FAB-MS: 746.1737 (M^+, $C_{38}H_{41}IN_3OS_2^+$; calc. 746.1736).

Quantum Yields ϕ *of Singlet Oxygen* ($^1O_2$) *Generation*. Experiments were performed at r.t. with a *PTI-PL2300* N_2 laser (337.1 nm, 0.60 ns pulses, 1.1 mJ/pulse) with air-equilibrated samples. The emission from $^1O_2$ was detected at 90° to the incident laser beam – after passing through a 1270-nm interference filter (*Corion*) or a combination of the interference filter with a long-wave pass filter (1200 nm; *CVI Laser Corp.*) to reduce scattered radiation from the laser (shortly after the laser pulse) as much as possible – by means of a 5-MHz Ge photodiode (*Judson J16-8SP-R05 M-HS*). The signal was amplified with a pre-amplifier (*Oriel 70732*, 350 MHz; and *Thorn EMI Electron Tubes A1* and/or *A2*).

Decay curves were obtained with the help of an 8-bit AD-converter/recorder system (*Fast TR50*; 50 MHz), and each curve was the average of at least 50 decays. Decays were fitted with a single-exponential function to obtain the initial luminescence intensity at time $t = 0$ (or the intensity at any other time t) after the laser pulse (*Fig. 2*) [15]. Phenazine in CH_2Cl_2 ($\phi = 0.89$) [15a], with an absorbance A of 0.30 [15c] at the wavelength of excitation (337.1 nm), was used as a reference. Deoxygenated solns. were obtained by bubbling N_2 for *ca.* 20 min. Accurate calibration curves, with linear dependence of $^1O_2$ emission intensity *vs.* laser energy were obtained by placing neutral density filters in the excitation laser path length. A comparison of the slopes for the test samples and the reference yielded the quantum yield ϕ in a straightforward manner (*Fig. 2*).

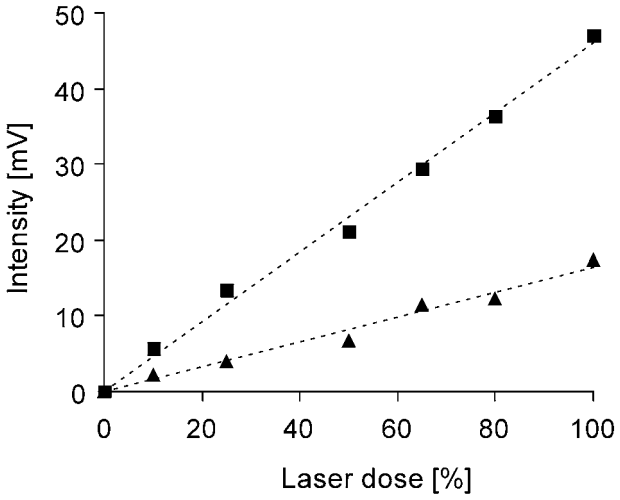

Fig. 2. *Plots of initial singlet oxygen* ($^1O_2$) *luminescence intensity* vs. *laser dose for optically matched samples of compound* **1a** (▲) and phenazine (■). In CH_2Cl_2 at ambient temperature; excitation wavelength: 337.1 nm. The quantum yield ϕ was derived from the ratio of slopes ($\phi = 0.32 \pm 0.02$ for **1a**).

The third harmonic (355 nm, *ca.* 6-ns FWHM, 2–15 mJ/pulse) of a Nd-YAG laser (*Thomson-CSF Sagsa 12-10*) could also be used as an excitation source. In this case, $NaNO_2$ solns. were used to attenuate the excitation energy and to ensure that the emission intensity was a linear function of the laser energy. The results obtained independently with the two lasers were the same within experimental error, and most work was, thus, performed with the N_2 laser.

There was no dye aggregation in CH_2Cl_2 at $A = 0.30-0.50$ for all dyes under study, as carefully verified by ground-state absorption studies at $10^{-6}-10^{-5}$ M. There was also no dependence on concentration of the quantum yield of $^1O_2$ production in this range for both excitation wavelengths (337 and 355 nm; see above). The $^1O_2$ phosphorescence lifetime for air-equilibrated solns. of phenazine in CH_2Cl_2 (at $A_{337} = 0.30$) was 88 ± 2 μs. For all other compounds under study, a similar lifetime was observed for $^1O_2$ emission.

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