Regioselective Photocyclization of (*E*)-2-(2,3,6-Trichlorostyryl)-benzothiazole and Synthesis of 3,4-Dichloro- and 4-Chloro-benzothiazolo[3,2-*a*]quinolinium Chlorides: A Synthetic and Theoretical Study

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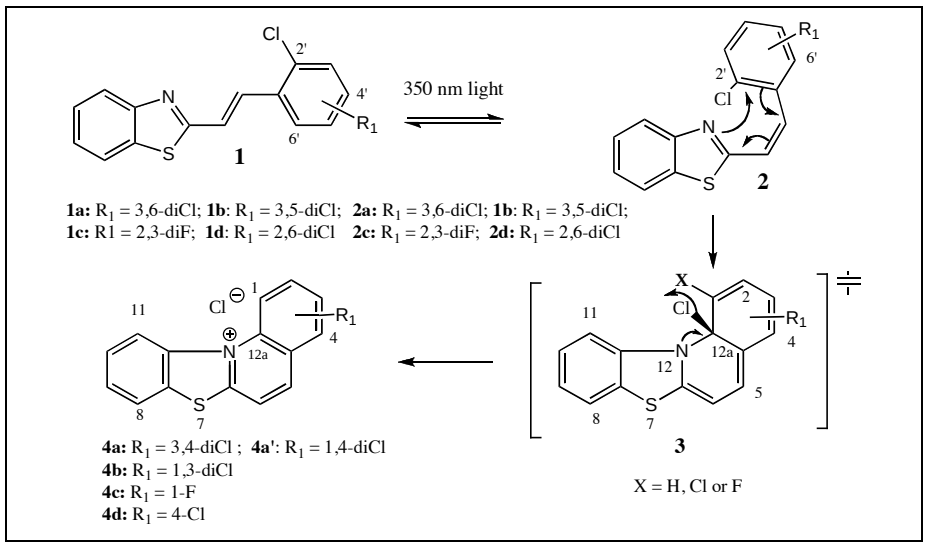

A high degree of regioselectivity is observed in the photochemically induced cyclization of (*E*)-2-(2,3,6-trichlorostyryl)benzothiazole (**1a**). According to the proposed mechanism, this compound was expected to afford two products, 3,4-dichloro- and 1,4-dichlorobenzothiazolo[3,2-*a*]quinolinium chlorides (**4a** and **4a'**, respectively). However, this reaction produced 3,4-dichlorobenzazolo[3,2-*a*]quinolinium chloride (**4a**) as the sole product. On the other hand, irradiation of (*E*)-2-(2,3,5-trichlorostyryl)benzothiazole (**1b**) failed to produce the expected 1,3-dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (**4b**). Furthermore, (*E*)-2,3-difluorostrylbenzothiazole (**1c**) also failed to give the corresponding 1-fluorobenzothiazolo[3,2-*a*]quinolinium fluoride (**4c**). Interestingly, the irradiation of 2,6-dichlorostyrylbenzothialole (**1d**) produced 4-chlorobenzothiazolo[3,2-*a*]quinolinium chloride (**4d**) in excellent yield. This paper presents the results of these investigations and a mechanistic rationale for the outcome of this reaction based on steric arguments and theoretical studies using a combination of molecular mechanics (MM+) and semiempirical quantum mechanical calculations (PM3/RHF/CI). Two-dimensional high field nmr methods were employed to make complete assignments of the proton and carbon spectra of all new compounds.

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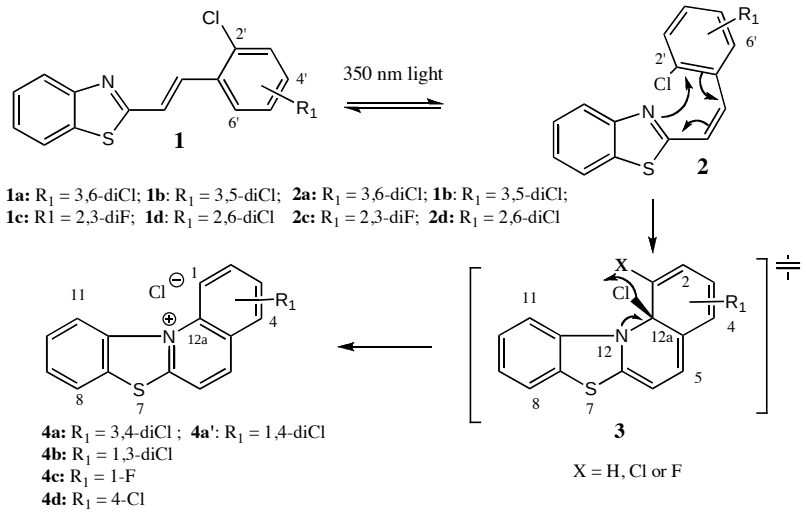
INTRODUCTION

During the past few years, work in our laboratory has been focused in the design and synthesis of benzazolo-[3,2-*a*]quinolinium salts, a new family of unnatural alkaloids that have been shown to be potent antitumor agents [1-12]. Recent work has shown that these salts exert their mechanism of action by inhibition of topoisomerase II activity [10,12]. The synthesis of these compounds is achieved *via* the photochemically induced cyclization of 2-(2-halostyryl)benzazoles [1]. The reaction is envisaged to occur in three steps, namely: (1) a *trans* to *cis* isomerization of the styryl derivative **1**, (2) a photochemically induced electrocyclic π_a^6-process to give **3**, and finally (3) ionization of the intermediate (**3**), with the loss of a chloride ion, to yield the corresponding benzazolo[3,2-*a*]quinolinium salt (**4**) derivative as final product (see Scheme 1). In an effort to assess the mechanistic details for the formation of the intermediate **3** in this sequence of reactions, we synthesized and subjected to 350 nm - irradiation the compounds (*E*)-2-(2,3,6-trichlorostyryl)-, (*E*)-2-(2,3,5-trichlorostyryl)-, (*E*)-2,3-(difluorostyryl)- and (*E*)-2,6-(dichlorostyryl)benzothiazole (**1a, 1b**, **1c** and **1d**, respectively, see Scheme 1). This paper describes the results of these investigations.

Scheme 1

Proposed mechanism for the formation of the benzazolo[3,2-*a*]quinolinium salts *via* the photocyclization of **1** derivatives.

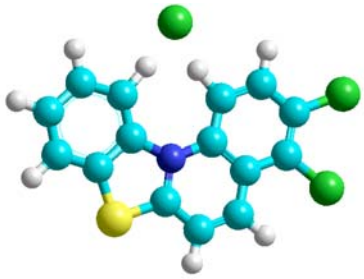
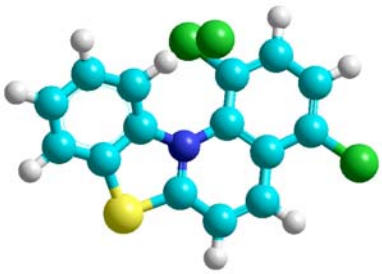
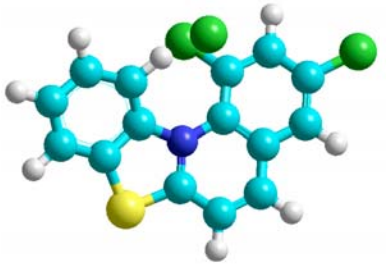


RESULTS AND DISCUSSION

The irradiation of **1a** (R_1 = 3,6-triCl) produced the quinolinium salt **4a** (R_1 = 3,4-diCl) in 45 % yield as a sole product. On the other hand, the irradiation of **1b** failed to give the expected quinolinium salt **5** (R_1 = 1,4-diCl). Likewise, irradiation of **1c** (R_1 = 2,3-diF) also failed to produce the expected benzazolo[3,2-*a*]quinolinium salt (**4c**). On the other hand, photolysis of **1d** produced 4-chlorbenzothiazolo[3,2-*a*]quinolinium chloride (**4d**) in good yield. These results are attributed to the difference in stability of the proposed intermediate **3** (X = H *vs* X = Cl or F). To corroborate this hypothesis, a mechanistic study for the outcome of the photocyclization of **1a** and **1b** was performed using a combination of molecular mechanics (MM+), semiempirical quantum mechanical calculations (PM3/RHF/CI), and *ab initio* DFT with B3LYP/6-31G(d). The results of the theoretical calculations are summarized in Figures 1 and 2. The *trans* to *cis* isomerization is not the limiting factor for the photoreaction of **1a**, since it requires an average net energy of only 3.1 kcal/mol for **2a** and **2a'**, but 4.1 kcal/mol for **2b** (data not shown). As a matter of fact, the activation energy for this isomerization in the ground state is 22.5 kcal/mol, but in the first excited state this is an exothermic process. The S0→S1 energy for *trans* **2a** is about 94.4 kcal/mol, and that for S1→*cis* **2a** is -91.3 kcal/mol. Therefore, after providing the required excitation energy by irradiation of the sample, the **2a**-S1 state decays to the **2a´**-S0 state without any further energy requirement. Moreover, the predicted "transition state" between these two systems has lower energy (121.9 kcal/mol) than the **2a**-S1 (173.0 kcal/mol). The activation energy required for the interconversion of the rotamers **2a** and **2a´** is predicted to be 10.1 kcal/mol (Fig.1). Moreover, the *ab initio* calculations predict a shorter N---Cl distance for **2a** (3.5 Å), than for **2a´** (4.6 Å) This fact gives a steric advantage to product **4a**. In the case where X = Cl, the calculated energy for the formation of the intermediates **3a'** and **3b** from the corresponding *cis*-styryl **2a'** and **2b**, was 4.5 and 5.5 kcal/mol higher than for the formation of the intermediate **3a**, respectively. In addition, both intermediates would produce the corresponding less thermodynamically stable products **4a'** (R = 1,4-diCl; ΔH_f = 95.5 kcal/mol) and **4b** (R **=** 1,3-diCl; ΔH_f = 94.9 kcal/mol) (see Figure 2). Furthermore, the enthalpy of the reaction (ΔH_{rex}), taken as the difference of the enthalpy of formation between the intermediate and the final product, shows that in the case where X = H, the formation of product **4a** (ΔH_{rex} = -0.3 kcal/mol) is energetically favored with respect to compounds **4a'** (ΔH_{rex} = 8.9 kcal/mol) and **4b** (ΔH_{rex} = 8.8 kcal/mol). These results indicate that the photocyclization of the (*E*)-styrylbenzothiazoles is also thermodynamically controlled by the formation of the intermediate **3** and subsequent reorganization to yield the corresponding benzazolo[3,2-*a*]quinolinium salt. The thermodynamic instability of these intermediates and their end products is mainly introduced by the C1-substituent, which leads to severe steric and electronic interactions between the two chlorine atoms at position C-12a, and X-1 (X = H vs Cl, see Scheme 1 and Table 1). This is shown in Table 1 in terms of the phenyl-phenyl torsional angle and the distance between the BQ nitrogen and the chlorine ion. These values show that the stability of **4a** is a result of the flattened conformation of the molecule, which forces the chlorine atom to reside near the hydrogens at a distance of 4.4 Å of the nitrogen. The next stable conformation found for this molecule has a N^+---Cl^- distance of only 2.7

Table 1.

PM3/RHF/CI theoretical parameters and most stable structures of the products and their intermediates for the reactions shown in Figures 1 and 2.

Product	Structure	ΔH_f (kcal/mol)		Torsional angle (degrees)[c]	N^+---Cl^- (Å)[d]
		3[a]	**BQS**[b]		
4a		82.1	81.8	0.1	4.4
4a'		86.6	95.5	26.9	3.8
4b		86.1	94.9	26.6	3.8

[a] formation enthalpy of the corresponding intermediate **3**. [b] BQS = benzazolo[3,2-*a*]quinolinium chloride. [c] torsional angle measured between the phenyl-phenyl planes. [d] distance between the nitrogen at BQ^+ and the Cl^-.

Å, but the torsional angle increases to 9.8 degrees and accordingly, the formation enthalpy increases to 94.7 kcal/mol. This increase in energy is attributed to the repulsion between the chloride ion and the huge electron density of the phenyl-phenyl system. The same behavior is observed for **4a'** and **4b**. Their most stable conformation given in Table 1 has a smaller N^+---Cl^- distance (3.8 Å), larger torsional angles (~27 degrees) and larger formation enthalpies (~95 kcal/mol) than in **4a**. Besides, if the chloride ion in **4a** is forced to be closer to the phenyl-phenyl system, the enthalpy increases to 105 kcal/mol, while the torsional angle decreases only to 24.9 degrees. This is due to the steric hindrance experienced by the chloro-substituent residing closer to the H-substituent and the charge repulsion mentioned before. This rationale also explains why the photolysis of **1c** (**3**, X= F) did not produce the expected product (1-fluorobenzothiazolo[3,2-*a*]quinolinium chloride (**4c**), whereas in the case of **1d** (X = H) the reaction proceeds in a normal fashion to produce **4d** in good yield.

In addition to the mechanistic study, the 2D nmr analysis (COSY, HMBC and HMQC) of **4a** and **4d** confirmed the proposed structure and allowed for a complete assignment of the ^1H and ^{13}C signals (see Tables 2 and 3). Based on previous studies [13] the downfield signal at δ 9.35 ppm in **4a** is assigned to H1 (see Tables 2 and 3). The COSY spectrum of **4a** shows a correlation of H1 with a signal at δ 8.38 ppm assigned to H2. Thus H1 and H2 constitute an AB doublet with a coupling constant J = 9.3 Hz. Likewise, the low field signal at δ 9.35 in **4d**

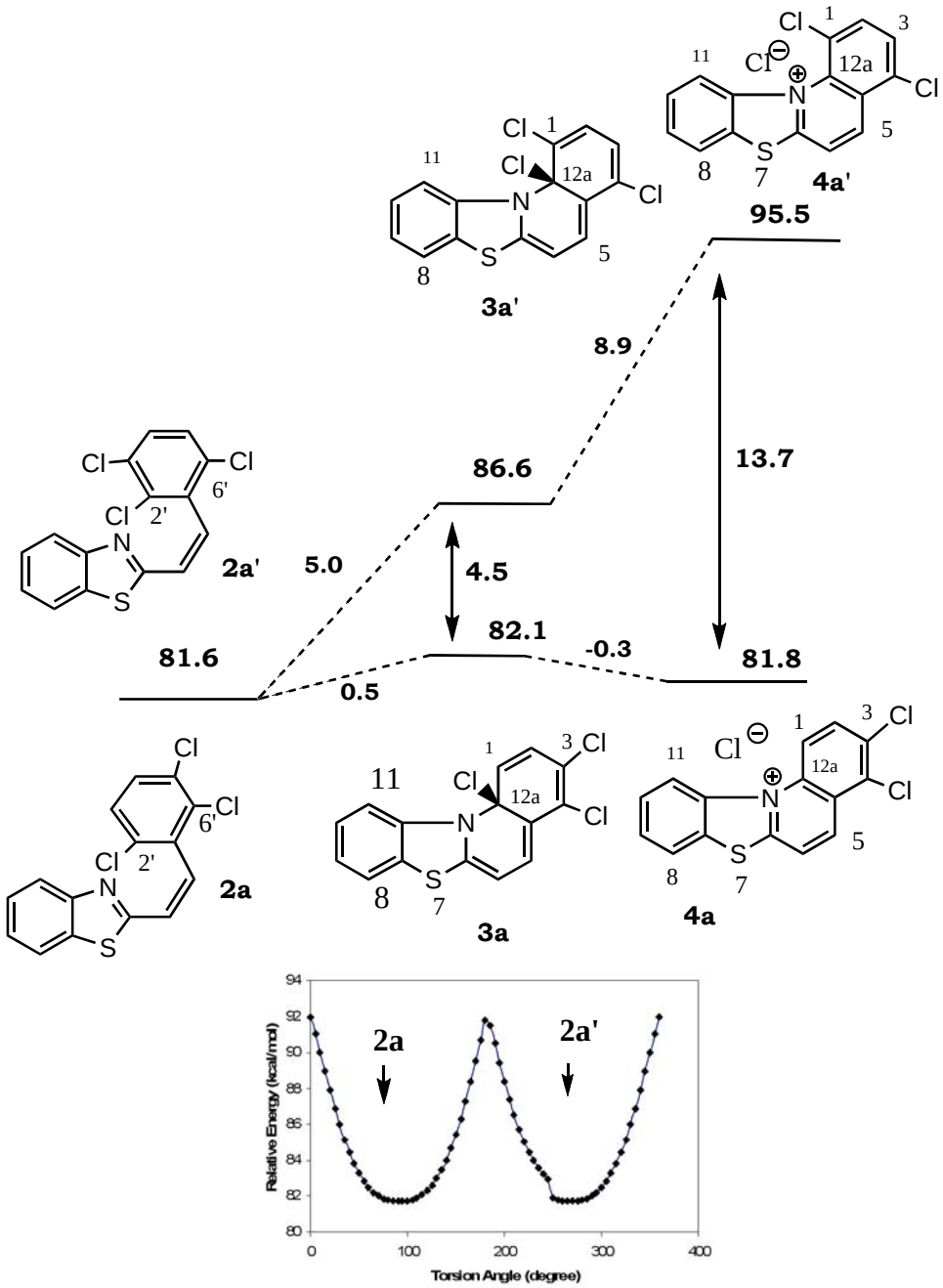


Figure 1. TOP: Theoretical enthalpies in kcal/mol, for the photocyclization of (*Z*)-2-(2,3,6-trichlorostyryl)benzothiazole (**2a** and its conformer **2a'**). The reactants, intermediates and end products are shown as solid lines, their reactions as dashed lines and their relative thermal stability with double headed arrows. BOTTOM: Potential energy for the rotamers **2a** and **2a'**.

was also assigned to H1. As expected H2 in **4d**, appears as a triplet with J = 8.3 Hz, and shows a correlation with H1 and H3 in the COSY spectrum. Once the signal corresponding to H-1 was assigned, the assignment of the remaining protons was straightforward by COSY experiments and further confirmed by HMBC experiments. The HMBC spectra of **4a** and **4d** are shown in Figures 2 and 3.

Once the proton resonances were established, the attention was focused to the assignment of the chemical shifts for all carbons at ring A. Thus, C-1 and C-2 were easily assigned by HMQC experiments at 119.9 and 133.6 ppm, respectively. These resonances are similar to those observed in **4d** (δ 118.9 and 133.8 ppm, respectively). Additionally, the HMBC experiment confirmed that irradiation of H-1 shows a correlation with C-3 and the

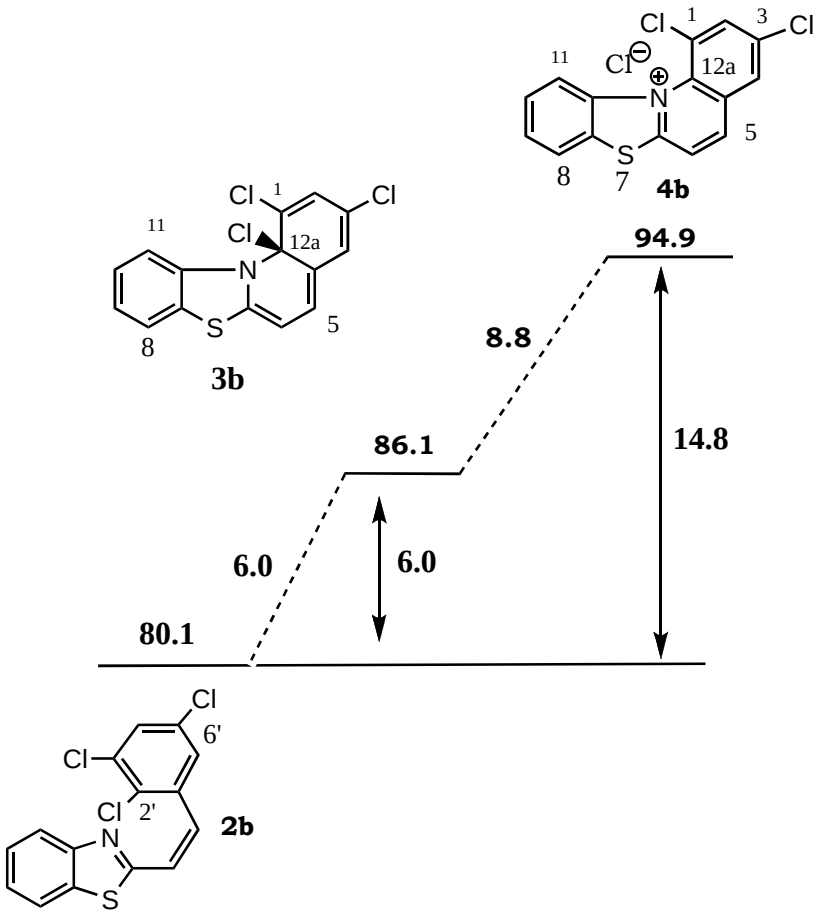


Figure 2. Theoretical enthalpies in kcal/mol for the formation of the reactants, intermediates and end products (solid lines); their reactions (dashed lines); and their relative thermal stability (double headed arrows) for the photocyclization of (*Z*)-2-(2,3,5-trichlorostyryl)benzothiazole (**2b**).

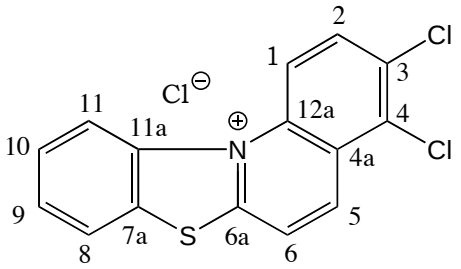
quaternary carbon C-4a. On the other hand, the irradiation of H-2 shows a correlation with the quaternary carbons C-4 and C-12a. Thus, carbons C-3, C-4, C-4a and C-12a resonate at δ 132.6, 131.0, 126.4 and 136.4 ppm, respectively. Additionally, the identification of H-1 in **4a** was supported by the observed J^1 with C-12a (see Figure 3). This J^1 coupling is not consistent with structure **4a**' because in this compound C-1 is a quaternary carbon. In conclusion, both the ^1H and the ^{13}C nmr spectral analysis summarized in Tables 2 and 3 is consistent with structures **4a** and **4d**.

CONCLUSIONS

Based on theoretical studies using a combination of molecular mechanics (MM+) and semiempirical quantum mechanical calculations (PM3/RHF/CI), it is concluded that the formation of the 3,4-dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (**4a**) is thermodynamically favored over both the 1,4-dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (**4b**) and 1,3-dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (**4c**). These results are rationalized in terms of the stability of the corresponding intermediate **3**, based on steric and electronic interactions introduced when X = H is changed for X = Cl or F. Thus, as expected, **4**a (X = H) is the sole product obtained with a good yield of 45% upon the irradiation of **1a**, while **4b** (X = Cl), **4c** (X = Cl), and **4d** (X = F) were not observed. The structure of **4a** and **4d** were secured by two-dimensional nmr experiments.

EXPERIMENTAL

General. Melting points were determined on a Melt-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Nicolet Series 6000 FT-IR spectrometer as potassium bromide pellets. The uv-*vis* spectra were measured in ethanol or acetonitrile solution on a Varian Cary Spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded using either a General Electric QE-300 MHz or a Bruker DRX500 nmr spectrometers operating at a respective observation frequency of 300.15 MHz or 500.13 MHz for ^1H nuclei and 75.0 MHz or



4a

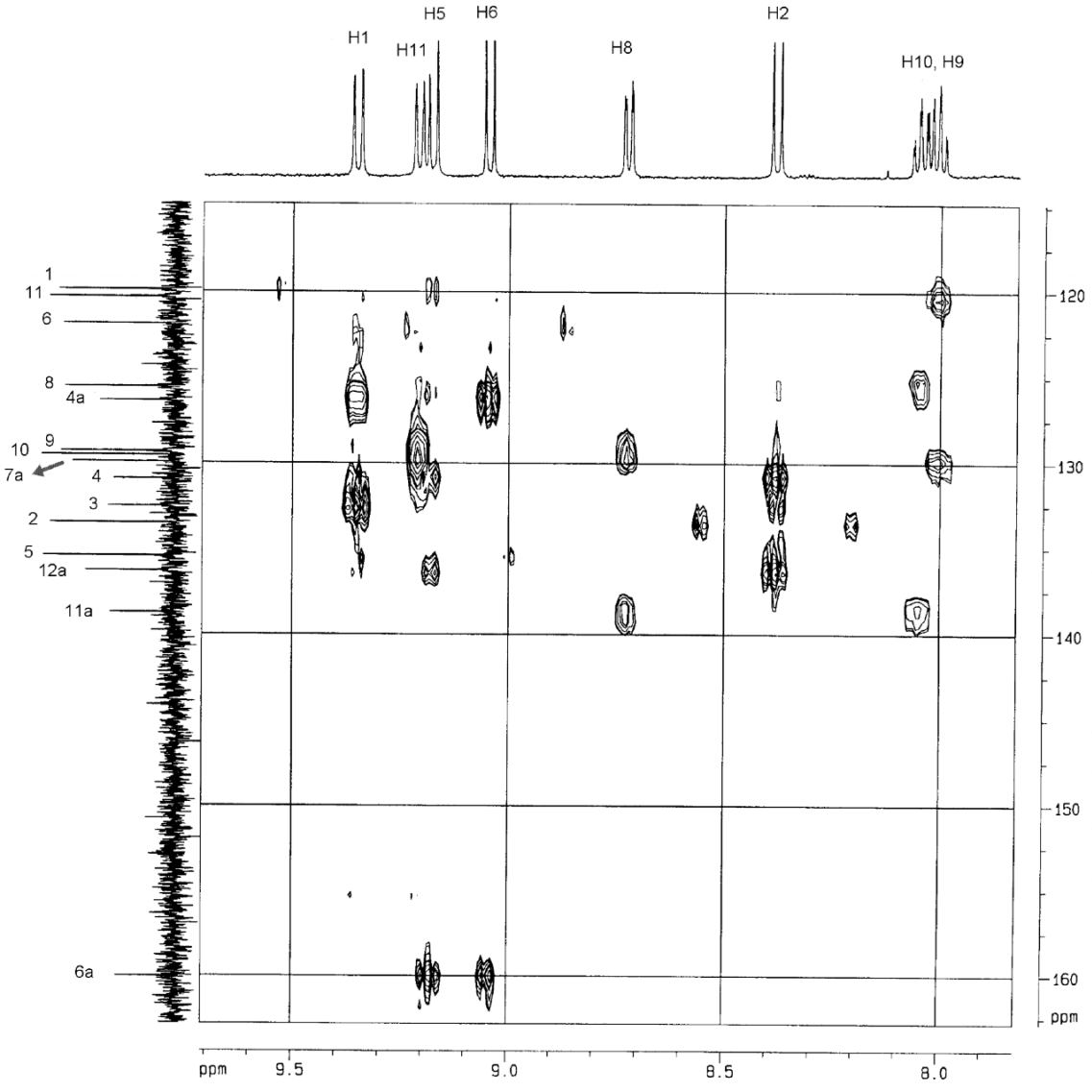
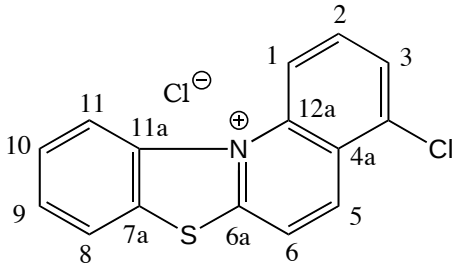


Figure 3. HMBC spectrum of 3,4-dichlorobenzothiazolo[3,2-*a*]quinolinium (**4a**).



4d

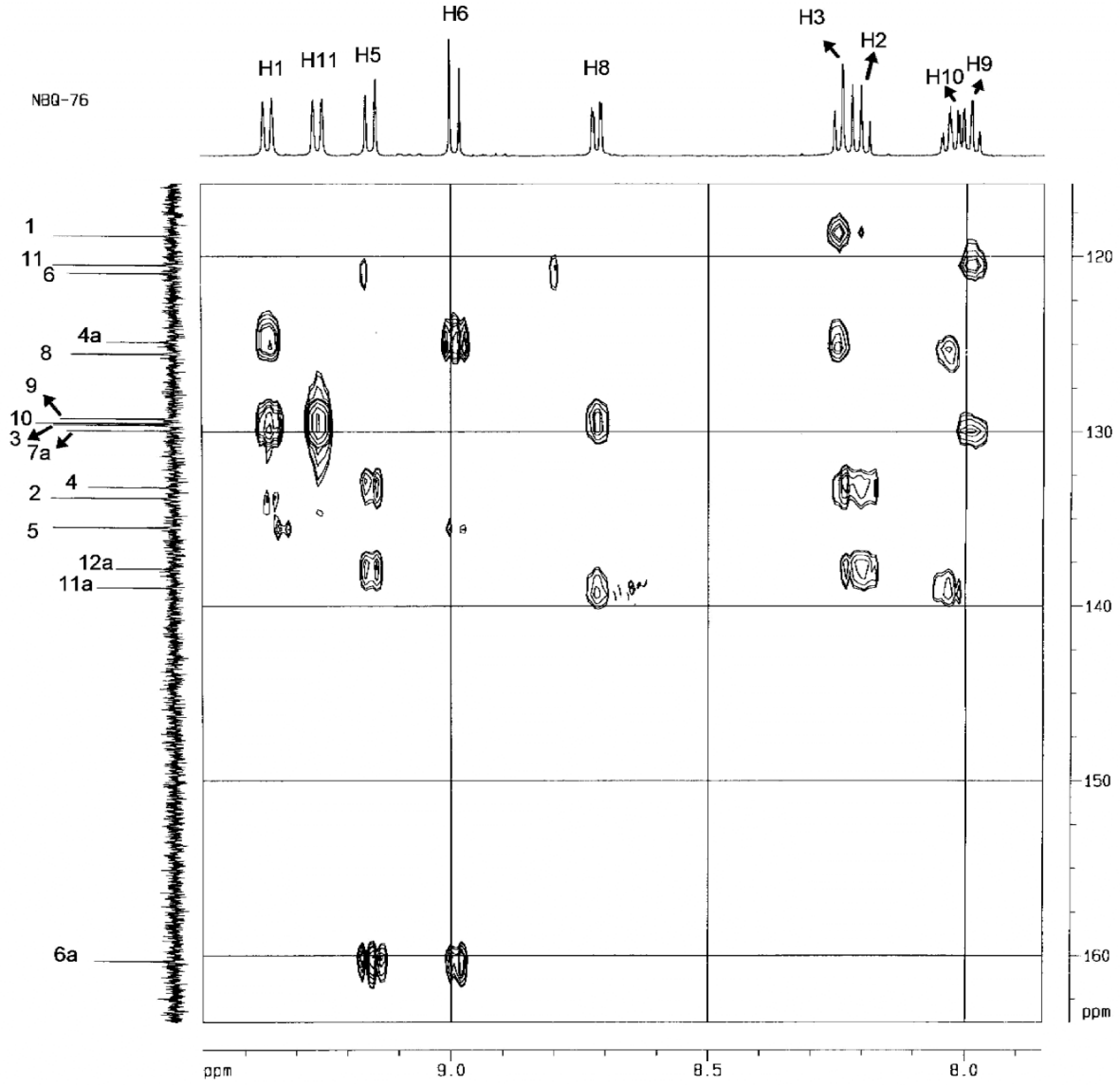
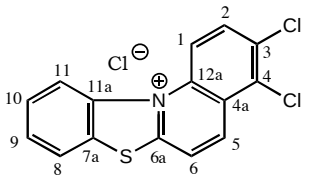


Figure 4. HMBC spectrum of 4-chlorobenzothiazolo[3,2-*a*]quinolinium chloride **4d**.

Table 2. Complete ^{1}H and ^{13}C nmr assignments of **4a.**

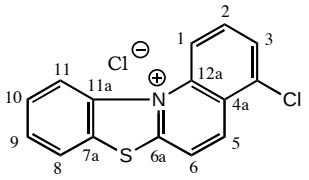


4a

Position	^{1}H (ppm), (Mult., J (Hz))[a)]	^{13}C (ppm)
1	9.35 (d, 9.3)	119.9
2	8.38 (d, 9.6)	133.6
3	---	132.6
4	---	131.0
4a	---	126.4
5	9.18 (d, 9.8)	135.5
6	9.05 (d, 9.5)	121.9
6a	---	160.1
7a	---	130.0
8	8.73 (dd, 7.9, 1.4)	125.6
9	8.05 (td, 7.9 [c], 1.4)	129.4
10	8.01 (td, 7.5, 0.7)	129.6
11	9.21 (d, 8.6)	120.4
11a	---	138.8
12a	---	136.4

[a] At 500.13 MHz with $(CD_3)_2SO$ internal standard

Table 3. ^{1}H and ^{13}C Chemical Shifts Assignments of **4d**



4d

Position	^{1}H (ppm), (Mult., J (Hz))[a)]	^{13}C (ppm)
1	9.35, d, 8.7	118.85
2	8.20, t, 8.3	133.83
3	8.25, dd, 7.5, 0.7	129.63
4	----	133.22
4a	----	124.90
5	9.15, d, 9.8	135.52
6	8.99, d, 9.4	120.99
6a	----	160.35
7a	----	138.97
8	9.25, d, 8.5	120.52
9	8.00, m	129.53
10	8.00, m	129.27
11	8.72, dd, 7.9, 1.4	125.57
11a	----	129.96
12a	----	137.88

[a] These chemical shifts were taken from one–dimensional slices of the HMQC spectrum.

125.77 MHz for ^{13}C nuclei. The proton data was referenced to either tetramethylchlorosilane (TMS) at δ 0.0 ppm, deuteriochloroform ($CDCl_3$) at δ 7.26 ppm or dimethyl sulfoxide-d_6 [$(CD_3)_2SO$] at δ 2.49 ppm. The 2D NMR experiments (COSY, HMQC and HMBC) were performed on a Bruker DRX500 NMR spectrometer. High Resolution Mass Spectra (hrms) spectra were recorded on a FISON instrument, VG Auto Spect Series using a Direct Insertion Probe (DIP). The hrms parameters were as follows: Electron-impact = 70 eV, Resolution = 1000 ppm, and Temperature ramp = 100-400 °C (30°C/min). Irradiations were carried out in a Rayonet Photochemical apparatus fitted with 350 nm lamps. Compounds 2-methylbenzothiazole and the corresponding benzaldehydes, used in the synthesis of **1a-d**, are commercially available by Aldrich-Sigma. All the solvents were HPLC grade from Aldrich or were distilled before used.

Computational Studies. The geometry optimizations using a combination of molecular mechanics (MM+), molecular dynamics and semiempirical calculations (PM3/RHF/CI) were performed with HyperChem 8.0 (HyperCube Inc., Florida) or semiempirical DT with B3LYP/6-31G(d) using Gaussian 03 at the BobSCEd cluster (Earlham College Cluster Computing Group; Richmond, IN). The optimization was done at least three times using different starting geometries. These were generated with the stimulated annealing feature of Hyperchem or by arbitrarily changing the bond lengths and/or bond angles. At the semiempirical level, the optimizations were done with the Polak-Ribiere conjugated gradient protocol ($1x10^{-5}$ convergence limit, 0.01 kCal/Å*mol RMS-limit). No restraints were required for the interaction of the chloride and benzazolo[3,2-*a*]quinolinium ions in the optimization process. The thermodynamic properties were finally obtained with PM3/RHF/CI-single point calculations starting with the most stable PM3-optimized conformation and using three occupied and three virtual orbitals. The reaction enthalpies were taken as the difference between the enthalpy of formation of the corresponding product and reactant.

Synthetic Procedures. The (*E*)-2-(2-halostyryl)benzothiazole derivatives (**1a-d)** were prepared as described [1,15]. The benzazolo[3,2-*a*]quinolinium chlorides (**4a-d**) were prepared by a modification of the procedure described by Cox *et. al*., using a 350 nm light source [1]. A representative procedure for the preparation of **1b** and **4a** is presented.

(*E*)-2-(2,3,5-Trichlorostyryl)benzothiazole (1b). This compound was prepared as described [1,14] from the condensation of 2-methylbenzothiazole (1.78 mL, 14.0 mmol) and 2,3,5-trichlorobenzaldehyde (3.00 g, 14.0 mmol) in boiling acetic anhydride (30 mL). The crude solid was collected by filtration and washed with a cold 1:1 hexane/acetone mixture. Recrystallization from a 1:1 hexane/acetone mixture produced 1.83 g (38%) of **1b** as an off-white solid: mp 150-152°C; ^1H-nmr (300.15 MHz, $CDCl_3$) δ ppm): 8.04 (dd, 1H, J= 8.3, 0.9 Hz), 7.89 (dd, 1H, J= 8.5, 0.9 Hz), 7.86 and 7.39 (AB, 2H, J= 16.2 Hz), 7.61 (d, 1H, J= 2.5 Hz), 7.50 (td, 1H, J= 7.7, 1.3 Hz), 7.47 (d, 1H, J= 2.5 Hz), 7.41 (td, 1H, J= 8.0, 1.3 Hz); ^{13}C nmr (75 MHz, $CDCl_3$ δ ppm): 165.5, 153.5, 136.8, 134.6, 134.6, 133.1, 132.1, 130.1, 130.2, 126.7, 126.5, 126.0, 125.2, 123.4, 121.6; uv (95% ethanol) λ_{max} nm (ε): 333 (22673), 224 (31717) and 200 (31350); ir (potassium bromide): 3061, 3050, 3039, 1568, 1547, 1434, 1419, 1392, 1317, 1239, 1178, 1127, 953, 856, 822, 753, 734, 722, 671 cm^{-1}; hrms: Calcd. for $C_{15}H_8Cl_3NS$ 338.944304, found M+ 338.942432 (δ 5.5 ppm). Anal. Calcd. for $C_{15}H_8Cl_3NS$: C, 52.89; H, 2.37; N, 4.11%. Found: C, 52.64; H, 2.40; N, 4.02%.

***(E)*-2-(2,3,6-Trichlorostyryl)benzothiazole (1a).** Following the general procedure this compound (1.67 g, 56%) was obtained as a white solid: mp 148-150 °C. ^1H nmr (500.13 MHz, $CDCl_3$ δ ppm): 8.05 (dd, 1H, J= 7.3, 0.6 Hz), 7.90 (dq, 1H, J= 8.0, 0.6 Hz), 7.58 and 7.51 (AB, 2H, J= 16.5 Hz), 7.50 and 7.42 (td, 2H, J= 7.7, 1.2 Hz); ^{13}C nmr (125.77 MHz, $CDCl_3$ δ ppm): 165.7, 153.9, 134.7, 134.6, 133.2, 132.8, 132.6, 131.1, 131.0, 130.9, 130.0, 129.0, 126.5, 125.9, 123.5, 121.6; uv (95% ethanol) λ_{max} nm (ε): 319 (19817), 225 (28550) and 200 (33200); hrms: Calcd for $C_{15}H_8Cl_3NS$ 338.944304, found M+ 338.943468 (δ 2.5 ppm). Anal. Calcd for $C_{15}H_8Cl_3NS$: C, 52.89; H, 2.37; N, 4.11%. Found: C, 52.99; H, 2.42; N, 4.05%.

3,4-Dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (4a). Following the general procedure [1], **1a** (0.26 g 0.66 mmol) was photocyclized to afford 0.114g (44%) of **4** as a yellow solid: mp 250-260°C (dec.); ^1H nmr (300.15 MHz, $[CD_3)_2SO]$) δ ppm): 9.36 and 8.38 (AB, 2H, J= 9.6 Hz), 9.21 (dd, 1H, J= 9.9, 1.2 Hz), 9.18 and 9.06 (AB, 2H, J= 9.6 Hz), 8.74 (dd, 1H, J= 7.8, 1.8 Hz), 8.03 (m, 2H); ^{13}C nmr (75 MHz, $[CD_3)_2SO]$ δ ppm): 160.1, 138.8, 136.4, 135.5, 133.6, 132.6, 131.0, 130.0, 129.6, 129.4, 126.4, 125.6, 122.0, 120.4, 120.0; uv: (95% ethanol) λ_{max} nm (ε) 382 (7402), 366 (8676), 263 (17038), 237 **sh** (10992) and 201 (22618). Anal. Calcd for $C_{15}H_8Cl_3NS{\cdot}2H_2O$: C, 44.23; H, 2.97; N, 3.44%. Found C, 43.89; H, 2.68; N,3.32%.

4-Chlorobenzothiazolo[3,2-*a*]quinolinium chloride (4d). Following the general procedure, (*E*)-2-(2,6-dichlorostyryl)-benzothiazole (0.6 g, 1.96 mmol) was photocyclized to give 0.30g (50%) of **4d** as a yellow solid: mp 238°C (dec.); ^1H nmr (500.13 MHz, [(CD3)2SO] δ ppm): 9.35 (d, 1H, J= 8.7 Hz), 9.25 (d, 1H, J= 8.5 Hz), 9.15 (1H, d, J= 9.8 Hz), 8.99 (1H, d, J= 9.4 Hz), 8.72 (1H, dd, , J= 7.9, 1.4 Hz), 8.25 (1H, dd, J= 7.5, 0.7 Hz), 8.20 (1H, t, J= 8.3 Hz), 8.00 (2H, m); ^{13}C nmr (125.77 MHz, $[(CH_3)_2SO]$ δ ppm): 160.35, 138.97, 137.88, 135.52, 133.83, 133.22, 129.96, 129.63, 129.53, 129.27, 125.57, 124.90, 120.99, 120.52, 118.85; uv: (ethanol, 95%), λ_{max} nm (ε): 380 (10444), 364 (10905), 259 (16538), 225 sh (12273) and 201 (23193). Anal. Calcd for $C_{15}H_9Cl_2NS{\cdot}2.5H_2O$: C, 51.47; H, 4.03; N, 4.00%. Found: C, 50.98; H, 3.54; N, 4.34%.

1,3-Dichlorobenzothiazolo[3,2-*a*]quinolinium chloride (4b). A solution of (*E*)-2-(2,3,5-trichlorostyryl)benzothiazole (**1a**) (0.50 g, 1.47 mmol) was irradiated for longer reaction time (18-46 h). No product was observed in the wall of the irradiation vessel and 60% of the starting material was recovered by vacuum evaporation of the reaction mixture, as shown by TLC and nmr analysis. The other 40% corresponds to a mixture of the starting material and unknown polymeric material.

1-Fluorobenzothiazolo[3,2-*a*]quinolinium chloride (4c). A solution of (*E*)-2-(2,3-difluorostyryl)benzothiazole (**1c**) (0.51 g, 1.87 mmol) in 3:1 benzene/dioxane mixture (200 mL) was irradiated for 18-46 h. After this long period of time no product was formed. However, a change from a yellow to a dark brown solution was observed. The ^1H nmr spectrum and TLC (80:20 hexane/ethyl acetate) of the viscous oil obtained from the vacuum evaporation of the reaction mixture were identical those of the starting material.

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