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A New Family of 2(3*H*)-Thiazolone Azines as Precursors to Air-Stable Radical Cations

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A Novel 2(3*H*)-thiazolone azines family having R_F substituents on the 4,4′-positions were efficiently prepared in good yield. The two-step synthesis involves the preparation of *N*,*N*′-dialkyl-1,2-hydrazinedicarbothioamides and their reaction with bromomethyl perflooroalkyl ketone, resulting in double ring closure. All the members prepared in this new family of compounds form stable radical cations, which enables them to be considered as ideal candidates for electrochemical tuning of light absorption as in electrochromic windows or displays and as redox indicators or mediators.

The viologen type redox couples ($X^{2+} \Leftrightarrow X^{\bullet +} \Leftrightarrow X^{\circ}$) have been extensively studied[1–5] in recent years, mostly for their potential application in electrochromic devices. While all di-cations based on quaternized 4,4′-bipyridines and homologues show perfectly reversible redox behavior, the potential at which the highly colored radical mono-cations form is too negative for stability in air. Since complete prevention of oxygen ingress in electrochromic devices based on redox dyes is illusory, especially for the appealing flexible devices using ITO-on-plastic substrates (retrofit on existing windows), the achievement of air/moisture stability is essential. Separating the pyridine moieties by the electronegative –N=N– bridge shifts the potential by $\approx +200$ mV, which is still insufficient. 2(3*H*)-Benzo-thiazolone azines discovered by Hünig,[6,7] which were made water soluble by sulphonation, give mono- and dication radicals at (0.67 V and 1.19 V vs Ag/AgCl), and are used to test peroxidases (laccases).[8,9] These compounds, however, are difficult to prepare and are mutagenic. In addition, the di-sulfonate is insoluble in aprotic solvents and polymer electrolytes, possibly including gelled, of interest for electrochromic devices. The pristine molecule itself shows poor solubility due to extensive "π" stacking of this large multi-ring system.

The simple 2(3*H*)-thiazolone azines have received far less attention.[10,11] Their potential is not strong enough (170 mV), and the neutral molecule is already highly colored (yellow to red) due to the chromogenic azo linkage.[12]

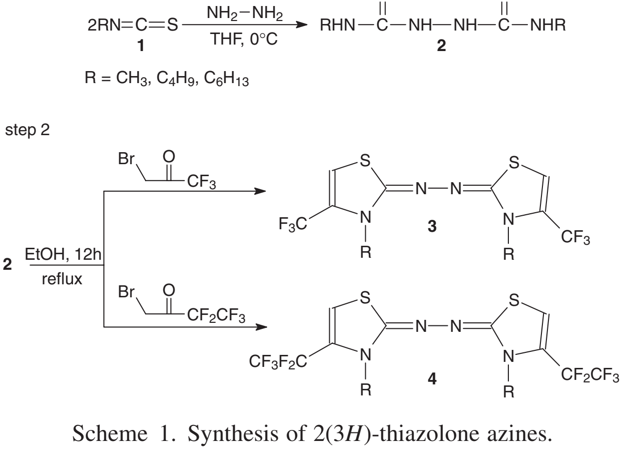
Results and Discussion

In this paper, we report a new family of 2(3*H*)-thiazolone azines in which a perfluoroalkyl substituent is introduced on each ring. This strategy was used to raise the redox potential, influenced by the electron-withdrawing effect of the perfluoro moieties, resulting also in a non-absorbing neutral state: ($N_{\text{colorless}} \Leftrightarrow X^{\bullet +}_{\text{absorbing}} \Leftrightarrow X^{2+}_{\text{weakly absorbing}}$). These new molecules have been characterized in terms of electrochemistry, structure, and absorbance.

The title molecules were prepared in two steps: i) addition of an alkyl isothiocyanate to hydrazine (quantitative) to produce the symmetrical *N*,*N*′-dialkyl-1,2-hydrazinedicarbothiioamides, ii) formation of the thiazole moieties by ring closure using halomethyl perfloroalkyl ketone.

The synthesis[13,14] of compounds **3** and **4** is straightforward (Scheme 1), and the availability of various isothiocyanates[15] allows for the manipulation of their lipophilic character and the introduction of various functionalities. They were prepared in two steps. The first step was the synthesis of *N*,*N*′-dialkyl-1,2-hydrazinedicarbothiioamides **2** by direct addition of the corresponding isothiocyanate **1** to hydrazine in a 2:1 ratio. The reaction takes place in THF at 0 °C, with a quantitative yield. Then, the target compounds **3** and **4** were obtained by addition of 2 molar amounts of bromomethyl trifluoromethyl ketone and bromomethyl pentafluoroethyl ketone, respectively, in refluxing ethanol. Compounds **3** and **4** were obtained in good yields (70–75%; Table 1). Recrystallization from ethanol gave analytically pure samples.

For each product, a single crystal suitable for X-ray diffraction studies was grown by cooling an ethanol solution of compound **3**. All 2(3*H*)-thiazolone azines form colorless rectangular prismatic crystals, easily isolated and characterized. The



Scheme 1. Synthesis of 2(3*H*)-thiazolone azines.

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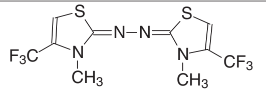
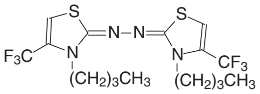
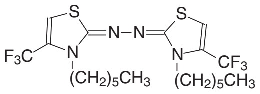
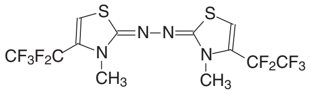
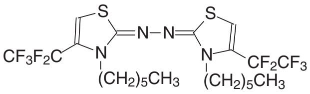
Table 1. Yields Obtained for 2(3*H*)-Thiazolone Azines

2(3*H*)-Thiazolone azines		Yield/%
	**3a**	73
	**3b**	75
	**3c**	70
	**4d**	78
	**4e**	75

rings are co-planar with the two perfluoroalkyl groups in the eclipsed conformation. For **3b**, the hexyl side-chains chose a trans-gauche-trans-trans conformation. The planearity of the rings conjugated through the azino linkage is almost a prerequisite for stable radicals.

The azinodi-4-thiazolines previously described in the literature are yellow compounds, resembling in this respect azo-pyridines, a measure of electron density on the N–N bridge. The immediate effect of the presence of two perfluoroalkyl groups ($\sigma^*_{CF_3} = 2.6$), reducing the electron density, is the formation of colorless derivatives with an absorption shifted to the UV region. **3a**–**4e** are strictly insoluble in water, especially those with the longest perfluoroalkyl and/or *N*-alkyl groups. They dissolve easily in most organic solvents, however.

All compounds prepared in this study exhibit a well-behaved electrochemical response in MeCN with a one electron oxidation of the neutral form to the radical cation ($E^\circ = 0.68$ and 0.71V for **3** and **4**) of intense blue coloration, followed by a second electron abstraction leading to the dicationic species (pale yellow-green) at 1.2 V vs Ag°/AgCl. The radical cations thus prepared where found not only to be air stable, due to their redox potential, which is above that of oxygen, but also water stable, the redox reaction, taking place before the oxidation of the latter- and especially light-fast.

When the counter-anion is hydrophobic (e.g., $[(CF_3SO_2)_2N]^-$), the radical salt is water insoluble, but soluble in polar organic solvents (Ac, MeCN, CH_2Cl_2…). On the other hand, hydrophilic counter-anions (e.g., Cl^-, Br^-, $CF_3CO_2^-$) yield water soluble salts. The electrochemistry of such materials will be presented in detail elsewhere.

Conclusions

The new family of 2(3*H*)-thiazolone azines bearing R_F substituents can be easily synthesized from readily available precursors. The choice of R_F and R allows for fine-tuning of the properties of the molecules compared to the 2(3*H*)-thiazolone azine. Their solubility in ordinary organic solvents is excellent while their redox potentials are similar. The most striking change resulting from the introduction of the R_F group is the shift in absorption to a colorless starting molecule. The materials, in molecular form or as polymers, are ideal candidates for electrochemical tuning of light absorption, as in electrochromic windows and displays. They offer an interesting alternative to the 2(3*H*)-thiazolone azines in terms of solubility and stability of the radical cation as redox shuttles and mediators (indirect oxygen bleaching …), and for laccases assays.

Experimental

Material. All chemicals used were reagent grade. A 1 M (= 1 mol dm^{-3}) solution of hydrazine in THF (Aldrich) was used as the source of the anhydrous base. Isothiocyanates, bromomethyl trifluoromethyl ketone and 1-bromo-3,3,4,4,4-pentafluoro-2-butanone were obtained from Lancaster (UK) or TCI (Japan) and were used as received. All reactions were conducted under dry a argon atmosphere.

General. ^{1}H, ^{13}C and ^{19}F spectra were recorded on a Bruker 400 MHz spectrometer in THF-d_8 solution. Chemical shifts are reported in ppm with internal reference to TMS. Mass spectra (MS) were recorded on a Micromass 1212 spectrometer. Infrared (IR) spectra were recorded in the range 4000–600 cm^{-1} using a Perkin-Elmer 298 infrared spectrometer. Spectra were taken with KBr disks. Melting points (mp) were determined with a capillary tube Thomas Hoover melting point apparatus and are reported as uncorrected values.

Synthesis of Dicarbothiothioamides (Compounds 2a–2e). A 1.0 M hydrazine solution in anhydrous THF (10 mL, 10 mmol, 320 mg contained N_2H_4) was added dropwise over 30 min to a solution of alkyl isothiocyanate (20 mmol, 1.462 mg for CH_3NCS, resp. 2.865 mg for $C_6H_{13}NCS$) in anhydrous THF (35 mL), at 0 °C under dry argon. After 1 h of vigorous stirring a white precipitate appeared. Stirring was maintained for 3 h. Then, the solvent was removed under reduced pressure, and the crude product was washed with cold THF to obtain a white powder in pure form and quantitative yield.

General Procedure for the Synthesis of Compounds 3a–c and 4d–e. *N*,*N′*-dialkyl-1,2-hydrazinedicarbothiioamides (3 mmol. 534.8 or 859.5 mg for C_1 resp. C_6) were dissolved in 60 mL anhydrous ethanol at 50 °C over 30 min, 7.5 mmol (1336 or 1807 mg for CF_3 resp. C_2F_5) of bromomethyl trifluoromethyl ketone or 1-bromo-3,3,4,4,4-pentafluoro-2-butanone were added slowly at 50 °C over 30 min. The mixture was refluxed overnight. A white precipitate separated when the mixture was cooled to 0 °C. The precipitates were filtered and recrystallized from ethanol to obtain colorless tubular crystals.

3-Methyl-4-trifluoromethyl-2(3*H*)-thiazolone Azine 3a: 73% yield; mp 181 °C; IR (KBr) 3412, 3182, 3103, 2953, 1742, 1607, 1445, 1397, 1332, 1305, 1259, 1198, 1157, 1000, 861, 826, 754 cm^{-1}; ^{1}H NMR (THF-d_8) 6.83 (s, 2H, CH), 3.40 (s, 6H, CH_3); ^{13}C NMR (THF-d_8) 164.9, 132.7, 110.8, 124.6 (q, $J_{CF} = 269$ Hz), 36.3; ^{19}F NMR (THF-d_8) −60.2 (CF_3); HRMS calcd for $C_{10}H_8F_6N_4S_2$ 362.009, found 362.008.

3-Butyl-4-trifluoromethyl-2(3*H*)-thiazolone Azine 3b: 75% yield; mp 104 °C; IR (KBr) 3412, 3173, 3114, 2973, 2940, 2881, 2345, 1602, 1583, 1452, 1425, 1375, 1329, 1290, 1272, 1214, 1126, 846 cm^{-1}; ^{1}H NMR (THF-d_8) 6.81 (s, 2H, CH), 3.78 (m, 4H, NCH_2), 1.85 (m, 8H, CH_2CH_2), 0.97 (m, 6H, CH_3); ^{13}C NMR (THF-d_8) 160.0, 128.4, 106.6, 120.4 (q, $J_{CF} = 269$ Hz), 48.5, 21.1, 20.8, 11.4; ^{19}F NMR (THF-d_8) −59.3 (CF_3); HRMS calcd for

$C_{16}H_{20}F_6N_4S_2$ 446.102, found 446.103.

3-Hexyl-4-trifluoromethyl-2(3*H*)-thiazolone Azine 3c: 70% yield; mp 102 °C; IR (KBr) 3122, 2959, 2858, 1603, 1582, 1471, 1452, 1423, 1378, 1332, 1270, 1233, 1185, 1155, 1121, 1011, 988, 857 cm^{-1}; ^1H NMR (THF-d_8) 6.81 (s, 2H, CH), 3.82 (m, 4H, NCH_2), 1.81 (m, 4H, CH_2), 1.38 (m, 12H, CH_2), 0.92 (m, 6H, CH_3); ^{13}C NMR (THF-d_8) 164.2, 132.5, 110.1, 124.8 (q, $J_{CF} =$ 269 Hz), 51.2, 36.6, 32.0, 18.7; ^{19}F NMR (THF-d_8) −61.2 (CF_3); HRMS calcd for $C_{20}H_{28}F_6N_4S_2$ 502.166, found 502.167.

3-Methyl-4-pentafluoroethyl-2(3*H*)-thiazolone Azine 4d: 78% yield; mp 218 °C; IR (KBr) 3414, 3158, 3095, 1593, 1439, 1392, 1332, 1305, 1198, 1140, 1097, 1053, 952, 850, 761, 737, 692, 594 cm^{-1}; ^1H NMR 6.89 (s, 2H, CH), 3.43 (s, 6H, CH_3); ^{13}C NMR 165.3, 131.0 (m), 113.6, 115.1 (m), 125.2, 37.3; ^{19}F NMR (THF-d_8) −79.6 (CF_3), −106.9 (CF_2); HRMS calcd for $C_{12}H_8F_6N_4S_2$ 462.003, found 462.001.

3-Hexyl-4-pentafluoroethyl-2(3*H*)-thiazolone Azine 4e: 75% yield; mp 53 °C; IR (KBr) 3156, 2958, 2931, 2859, 1599, 1576, 1460, 1413, 1377, 1321, 1309, 1165, 1141, 1098, 1079, 953, 824, 735 cm^{-1}; ^1H NMR 6.86 (s, 2H, CH), 3.52 (m, 4H, NCH_2), 2.44 (m, 4H, CH_2), 1.67 (m, 4H, CH_2), 1.30 (m, 8H, CH_2), 0.92 (m, 6H, CH_3); ^{13}C NMR 160.3, 126.5 (m), 109.5, 111.4 (m), 120.9 (m), 47.5, 32.5, 27.6, 27.3, 23.4, 14.3; ^{19}F NMR (THF-d_8) −79.5 (CF_3), −106.3 (CF_2); HRMS calcd for $C_{22}H_{28}F_6N_4S_2$ 602.159, found 602.158.

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