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Synthesis of new substituted tetrazines: electrochemical and spectroscopic properties

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Original tetrazines substituted by heterocyclic rings have been prepared. Their syntheses, as well as their electrochemical and spectroscopic features, are described. Calculations have also been made on the cation radicals, anion radicals and neutral compounds and are in correct agreement with the experimental results. All compounds are electroactive, both in oxidation and reduction, and display two absorption bands in the UV and visible regions of the spectrum. Reduction potentials and maximum wavelengths are correlated with the electron-rich character of the heterocyclic substituent on the tetrazine ring. None of these compounds gives good quality polymers upon electro-oxidation, which was unexpected, especially for the bis(2-pyrrolyl) tetrazine. This latter result can be explained by the occurrence of a self-deprotonation equilibrium in the cation radical.

Introduction

The search for new optically and electroactive compounds is still active, given their potential in fields such as sensors.[1–4] With regard to such aims, fluorescence and electroactivity are particularly interesting properties, because fluorescent and/or electroactive molecules may constitute the active component of a device. In this respect, the tetrazine family appears as a very promising and fascinating one. Tetrazines are highly coloured and electroactive heterocycles, displaying the following special properties. (1) They have a very high electron affinity, which makes them easily reducible (actually they are the electron poorest C–N heterocycles).[5] (2) They have a low lying π* orbital, resulting in a n-π* transition in the visible light range.[6]

These properties make tetrazine based molecules and materials attractive targets for devices targeted for optical and/or electrochemical applications. In addition, low band gap polymers could be expected from structures alternating tetrazine rings and any electron-rich moiety like an oligothiophene, since molecules and supramolecules providing alternating electron-rich and electron-poor structures have become desirable targets for the achievement of such properties.[7–11]

In this article, we report one of the first syntheses of pyrrole and thiophene substituted tetrazines,[12] in addition to a pyrrole-pyrazole substituted tetrazine (see Fig. 1). We also report their electrochemical and absorption properties.

Experimental

Synthesis of the monomers

The synthetic approach followed in our work for tetrazines **2** and **3** is detailed in Scheme 1. The synthesis of bis(thien-2-yl)-tetrazine (**4**) and bis(pyrrol-2-yl)tetrazine (**5**) was performed following a separate route.

Synthesis of bis(*N*-pyrrolyl)tetrazine and (*N*-dimethylpyrazolyl-*N*-pyrrolyl)tetrazine. Bis(dimethylpyrazol-1-yl)tetrazine (**1**; 2.57 g, 2 mmol), prepared according to ref. 13, was dissolved in 50 cm^3 of dry THF and 4 mmol of pyrrolyl lithium (prepared by reaction of 2 mmol of pyrrole with 2 mmol of

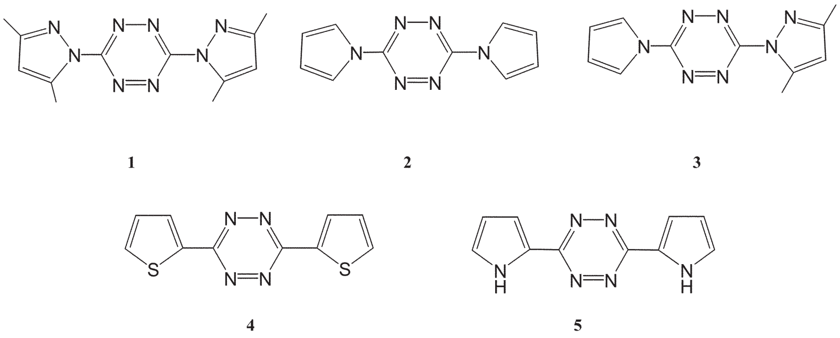
1 2 3 4 5

Fig. 1 Formulae of the tetrazine compounds investigated.

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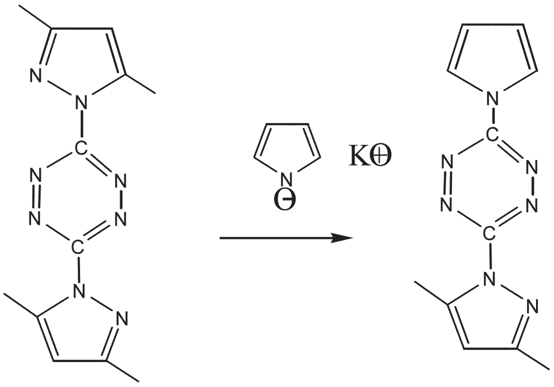


Scheme 1 Synthesis of compounds **2** and **3**.

butyllithium in 20 cm^3 THF) was added at 0 °C. After 15 min stirring and warming to room temperature, the THF was evaporated, the mixture taken up in dichloromethane (DCM) and chromatographed (eluant DCM–petroleum ether 2:1) The first orange product was bis(*N*-pyrrolyl)tetrazine (**2**), yield 30–35%. The second product was (*N*-dimethylpyrazolyl-*N*-pyrrolyl)-tetrazine (**3**), yield 15–20%.

2. ^{1}H NMR ($CDCl_3$): 7.86 (4H, t, $J = 2.6$ Hz, α-pyrrolic-H); 6.51 (4H, t, $J = 2.6$ Hz, β-pyrrolic-H); ^{13}C: 158.09 (tetrazine), 118.86, 114.33, (pyrrole). Anal. calcd: C 56.56, H 3.79, N 39.60; found: C 56.43, H 4.29, N 37.09.

3. ^{1}H NMR ($CDCl_3$): 7.89 (2H, t, $J = 2.5$ Hz, α-pyrrolic-H); 6.51 (1H, t, $J = 2.5$ Hz, β-pyrrolic-H); 6.20 (1H, s, pyrazole); 2.71 (3H, s, methylpyrazole), 2.40 (3H, s, methylpyrazole); ^{13}C: 160. 67, 158.07 (tetrazine), 154.77, 143.99, 119.66, 115.17, 112.32 (pyrazole and pyrrole), 15.21, 14.56 (methylpyrazole). Anal. calcd: C 54.76, H 4.58, N 40.64; found: C 55.25, H 4.64, N 38.80.

Synthesis of bis(thien-2-yl)tetrazine and bis(pyrrol-2-yl)tetrazine. The syntheses were performed *via* the dihydrotetrazine route, but this intermediate, which is moderately stable in the case of thiophene and quite unstable in the case of pyrrole, was not isolated but immediately aromatised into tetrazine.

Preparation of the dihydrotetrazine. To 2.5 g of 2-cyanopyrrole or 3 g of 2-cyanothiophene ($\sim 2.7 \times 10^{-2}$ mol), dissolved in 8 mL of absolute ethanol, was added 0.42 g of powdered sulfur (sulfur flower, 1.3×10^{-2} mol in sulfur) and 2 mL of fresh hydrazine monohydrate (4×10^{-2} mol). The mixture was refluxed for 1.5 h and produced hydrogen sulfide (***CAUTION!*** use a well-ventilated hood). The mixture was cooled to room temperature where the dihydrotetrazine crystallised and was quickly filtered off, dried *in vacuo* and quickly used for the next step (approx. yields 60–70%).

Syntheses of the tetrazines **4** *and* **5**. The dihydrotetrazines (1 g) were dissolved in ethanol (200 mL). In the case of **4**, excess sodium nitrite (about one mass equivalent relative to the substrate) was added to the solution, which was stirred overnight. In the case of **5**, the solution was simply stirred at 50 °C in the presence of air. In both cases the tetrazines slowly crystallised upon cooling of the solution to room temperature and were recovered in several successive crops (150–250 mg each). Overall yield 60–70%.

4. ^{1}H NMR ($CDCl_3$): 8.31 (2H, dd, β2-H); 7.73 (2H, dd, α-H); 7.31, (2H, dd, β3-H), $J_{\alpha\beta2} = 1.29$ Hz, $J_{\alpha\beta3} = 5.06$ Hz, $J_{\beta2\beta3} = 3.95$ Hz; ^{13}C: 161.66 (tetrazine), 136.12, 132.59, 131.08, 129.13 (thiophene). Anal. calcd: C 48.72, H 2.44, N 22.74; found: C 48.82, H 2.42, N 22.67.

5. ^{1}H NMR (DMSO-d6): 12.22 (1H, s, NH) 7.16 (2H, m, β-pyrrolic-H); 6.34 (1H, q, α-pyrrolic-H); ^{13}C: 157.89 (tetrazine), 124.89, 124.72, 112.79, 110.74 (pyrrole). Anal. calcd: C 56.56, H 3.79, N 39.60; found: C 56.43, H 4.29, N 37.09.

Electrochemistry and spectroscopy measurements

The electrochemical studies were performed using an EG&G PAR 273 potentiostat, interfaced to a PC computer.

For CV measurements, the reference electrode used was an AgCl/Ag electrode. This reference electrode was checked *vs.* ferrocene as recommended by IUPAC. Potential values are thus given with respect to ferrocene. Triethyl phosphate (Fluka puriss.) was used, assuming the same potential for ferrocene.

Tetrabutylammonium perchlorate was purchased from Fluka (puriss). Acetonitrile (Aldrich, 99.8%), dichloromethane (SDS, 99.9%) and toluene (Aldrich 99.5%) were used as received. All solutions were deaerated by bubbling argon gas for a few minutes prior to electrochemical measurements.

Transmission spectra were recorded on a dual beam spectrometer (Perkin Elmer Lambda 9). UV-vis spectroelectrochemistry was performed using a homemade cell; the working electrode was made of ITO coated on glass. Platinum and silver wires were used, respectively, as counter and pseudo-reference electrodes and were located on the cell sides in order not to disturb the beam. A double UVIKON 923 (Bio-Tek Kontron) spectrophotometer was used for the spectral acquisition.

Theoretical modelling

The calculations were performed using the Gaussian 98 package[14] for density functional and solvation calculations. Gas phase geometries and electronic energies were calculated by full optimisation without imposed symmetry of the conformations using the B3LYP density functional with the 6-31G* basis set,[15,16] starting from preliminary optimisations performed with semi-empirical methods. The quality of the obtained minima was checked by running frequency calculations. We also checked that the spin contamination remained low ($s^2 < 0.78$) for all the open-shell B3LYP calculations (cation and anion radical). Solvation free energies were calculated on the gas-phase-optimised conformations according to the SCRF (self consistent reaction field) method using the IPCM method[15] and the B3LYP density functional in acetonitrile ($\varepsilon = 36.64$). In this method, the solvent is treated as a continuum of uniform dielectric constant in which the solute is placed into a cavity defined as an isodensity surface of the molecules. The value for the isodensity surface was chosen as 0.001 electron $bohr^{-1}$,[16] as used in previous published calculations.

Results and discussion

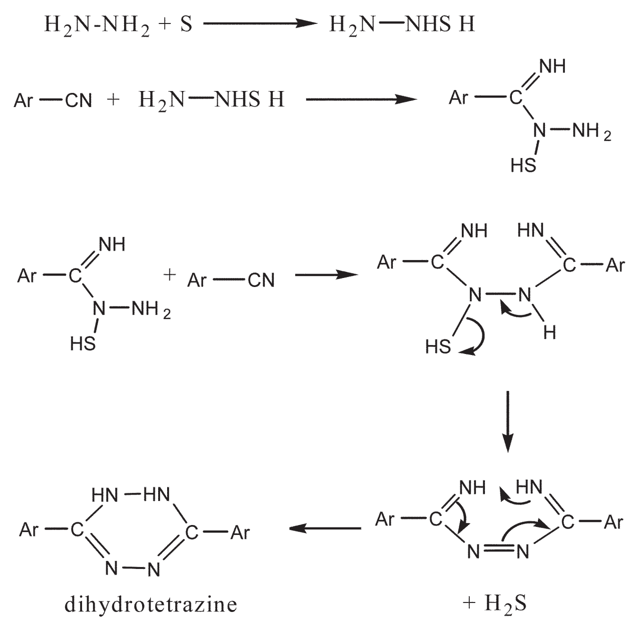
Synthesis of the monomers

The first part of the synthetic scheme followed in our work is based on the beautiful synthetic work of Hiskey *et al.*,[13,17–19] who devised a very efficient synthesis of our basic starting compound: bis(dimethylpyrazolyl)tetrazine **1**. It should, however, be pointed out that the reaction involved had been discovered before,[20] while **1** itself had been prepared for the first time even earlier, although in low yields.[21] The pyrazolyl groups may act as soft leaving groups, allowing a nice range of heterocyclic substituents to be introduced on the tetrazine ring, provided that the basic character of the entering nucleophile is not too strong and its hardness of medium strength. This has been done in particular with hydrazine and ammonia,[13,17–19] and we show here that the pyrrolyl anion is also able to enter the tetrazine ring (Scheme 1), to give mono- and disubstitution products. However, we noticed that this is not the case for the much more reactive thiophene based anions, where only tars are obtained.

Therefore, in order to prepare the more potentially interesting bis(α-heterocyclic)tetrazines another strategy, based on previously published work, has been employed. It had been shown in the past that sometimes hydrazine, alone[12] or preferably in the presence of sulfur,[22] could lead to the formation of dihydrotetrazine from aromatic nitriles. Nevertheless, the reaction requires highly concentrated conditions, as well as a neat excess of hydrazine in many cases. No mechanism was suggested by the previous authors; however, we have observed that: (1) the colourless solution turns immediately light orange as soon as the sulfur is added and (2) vigorous hydrogen sulfide emission takes place throughout the reaction.

On the basis of these observations, we propose that the active nucleophile in the solution be the fast addition product of hydrazine to sulfur, namely H$_2$N–NH–SH, with the following mechanism as shown in Scheme 2.

The regiochemistry, as well as the preference (relative to the other nucleophiles still present like excess hydrazine) of both nucleophilic attacks are consistent with the ''alpha effect'' exerted by both the sulfur and the second nitrogen atom linked to the nitrogen responsible for the nucleophilic attack. If this mechanism were to be right, only 1/2 equiv. of sulfur would be required (relative to the starting material) to form again one half of the first intermediate, which can react further with the remaining nitrile. The previous authors used an undefined stoichiometry (they described a general procedure with only masses indicated, with the stoichiometry falling roughly between 1 and 1/2) but we noticed that indeed the required sulfur amount was 1/2 equiv.



Scheme 2 Synthesis of compounds **4** and **5**.

Electrochemical behaviour of the tetrazine derivatives

All tetrazines are reducible, either in acetonitrile or in dichloromethane, according to their solubility. Most of them give well-defined cyclic voltammograms, as exemplified on Fig. 2. On a few occasions, the voltammograms are not fully reversible, showing that the anion radical undergoes chemical evolution. The most likely process for this is probably the coupling of two anion radicals, since it appears to be relatively general and not limited to the compounds having an acidic hydrogen. However, it is not possible to perform a mechanistic study, because of the too-narrow scan rate range underwhich a reaction occurs.

The potentials are given in Table 1 and correlate well with the electron-rich or -poor character of the heterocycle substituted on the tetrazine, since the highest reduction potential is displayed by the bis(dimethylpyrazolyl)tetrazine **1** and the lowest by the bis(α-pyrrolyl)tetrazine **5**.

All the tetrazines bearing electron-rich heterocycles can also be oxidised, although they do not give polymers except for **2**, which gives a very poor quality polymer. The potential values are given in Table 2 and will be discussed in the next part, in the light of the molecular modelling results.

Molecular modelling on tetrazine compounds and their derived charged species

The geometries of the prepared tetrazines were calculated. Except for compound **1**, which is slightly twisted in the neutral form, all the investigated tetrazines are completely planar, indicating that there is electron delocalisation and therefore charge transfer between the tetrazine ring and the electron-rich heterocycle, which enhances the interest of using tetrazine as an attracting ring in designing NLO-active molecules. Similarly, we found that the bonds connecting the heterocycle (pyrrole or thiophene) to the tetrazine ring are shorter than the values corresponding to the similar single bond: for example, in **2** the N–C bond length is equal to 1.38 Å and in **5** to 1.44 Å, again showing a good conjugation between the heterocycle and the tetrazine. This confirms that the electronic connection is rather strong in all compounds, and correlates well with the results of the electrochemical studies showing the potential dependence on the substituents.

Calculations were also performed on the charged species (anion and cation radicals) to predict where the unpaired electron will be localised after electron transfer.[23] Two examples are shown in Fig. 3 for the spin densities in the pyrrolyl

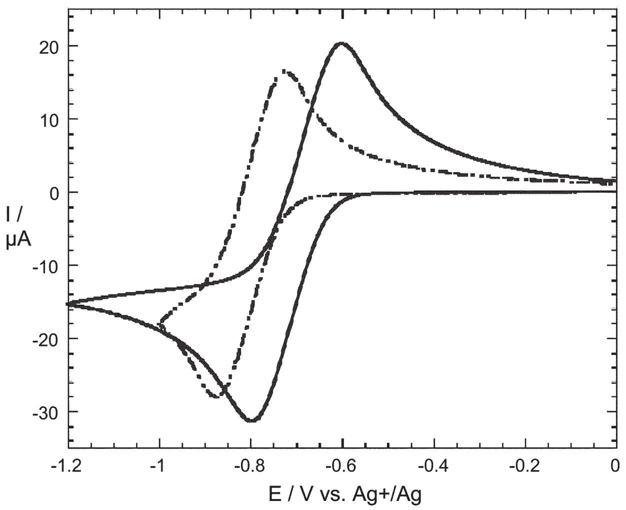


Fig. 2 Cyclic voltammograms of bis-substituted tetrazines in dichloromethane (+0.1 M TBAP) on a platinum electrode: bis(*N*-pyrrolyl)tetrazine **2** (solid line) and bis(thienyl)tetrazine **4** (dashed line).

Table 1 Standard potentials (in V *vs.* ferrocene) for the tetrazine reduction in acetonitrile (AN) and dichloromethane (DCM)

	E°(AN)/V *vs.* Fc	E°(DCM)/V *vs.* Fc
1	−0.96	Not fully rev.
2	−1.07	−1.01
3	−0.97	−1.02
4	−1.22	−1.21
5	−1.22	−1.25

Table 2 Experimental and B3LYP/6-31G* estimated oxidation potentials of the various tetrazine compounds

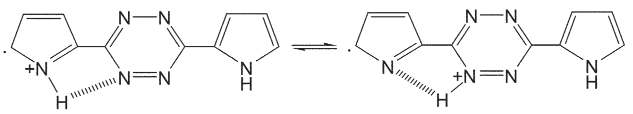
	Calcd[a]	E_p/V *vs.* Ag/Ag$^+$
1	1.02	> 1.8 (ill-defined peak)
2	0.73	1.27
3	0.80	1.45
4	0.62	> 1.8 (ill-defined peak)
5	0.0	0.60 (resp. 0.90[b])

[a] In volt. Bis(2-pyrrolyl)tetrazine (compound **5**) is taken as an internal reference in the B3LYP calculations. [b] In the presence of acetic acid.

compounds. In the radical anion, the unpaired electron is localised in the centre of the molecule (namely on the tetrazine ring) contrarywise to the radical cation where the unpaired electron is mainly present on the 2-positions of the pyrrole moieties [this is especially true in the case of bis(1-pyrrolyl) tetrazine, **2**]. This localisation should in principle help the oxidative polymerisation, indicating that the difficulties encountered in the polymer formation are mainly due to other factors than the electronic properties of the radical cation.

B3LYP calculations generally allow good predictions of the variation trends for a family of molecules. We performed such calculations using the IPCM methods to estimate the solvation free energies.[24] These estimations are gathered in Table 2: the values of the oxidation peak potentials display a good agreement between the expected and experimental data, especially in the case where well-defined peaks could be obtained, because the relative differences are quasi-constant (of course, the absolute values from the calculations do not correlate, because they depend on an arbitrary choice of internal reference). The trend in the variation of E_{ox} is correctly predicted by the calculations, especially for the pyrrole family, while there is some disagreement for the thiophene derivative **4**. We note that compounds **4** and **5**, both connected in the 2-positions, seem much easier to oxidise, indicating a greater stabilisation of the electrogenerated radical cations.

The question why **2** and, more surprisingly, **5** do not polymerise is therefore still open to discussion and of particular interest. The case of **5** is particularly surprising, because in addition its oxidation occurs at a very low potential (Table 2). However, this potential rises noticeably when one adds a moderate acid such as acetic acid to the solution (Fig. 4). This behaviour would be in accordance with the existence of a self deprotonation equilibrium, *in the cation radical species*, according to the following equation:[25]



It is known that deprotonated pyrrole cation radicals in general do not polymerise (some work has shown that pyrrole polymerisation is not possible in the presence of non-nucleophilic strong bases[26,27]). The cation radical of **5**, due to the smaller charge on the ring associated with the delocalised character, should not be able to polymerise. This would also account for the unusually low peak potential, which would be shifted towards lower values because the internal protonation-deprotonation equilibrium would stabilise the oxidised form.

Spectroscopic features of the tetrazine derivatives

The UV-visible spectra of all the compounds have been obtained in dichloromethane and are displayed on Fig. 5; the corresponding maxima are listed in Table 3. They all display a very strong band in the UV region, corresponding to the π-π* allowed transition, and a much less intense band in the visible region, corresponding to the n-π* transition, which is responsible for the colour of the compounds.[28] The wavelength of the UV band correlates clearly with the donor-acceptor balance of the substituted heterocycle, as it could be expected, while this is less obvious in the case of the visible band. This shows clearly that the donor character of an α-pyrrole is considerably higher than that of a N-pyrrole, due to the complete conjugation in the former case, as previously suggested by the theoretical calculations.

While there is little influence of the heterocycle on the visible band, one should, however, notice that the case of the α-pyrrole compound **5** lies apart, since it displays a strong bathochromic absorption shift relative to the other four compounds. This may also be in relation with the fact that the proton born by the pyrrole rings may also be linked to the nearest nitrogen of the neighbour tetrazine ring.

We have attempted to perform spectroelectrochemistry on ITO at the first reduction potential of tetrazine **4** (−1.4 V); unfortunately, as evidenced by the CV in Fig. 6(a), the anion radical is no longer stable when generated on an ITO electrode. The spectra recorded at this potential show the emergence of two new bands [see Fig. 6(b)]: one at shorter

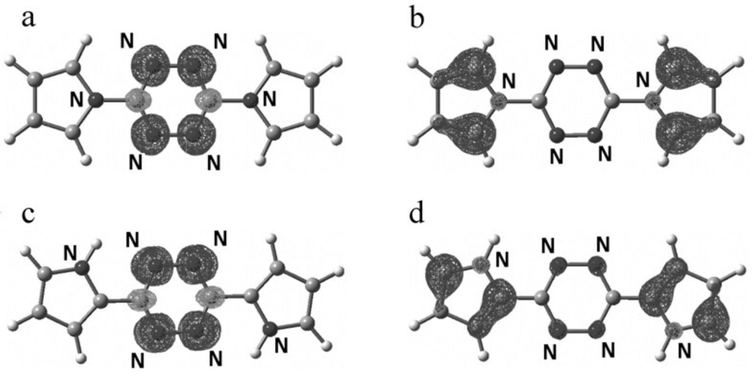


Fig. 3 Spin density (isodensity at 0.004 a.u.) from B3LYP calculations for radical anions (a and c) and radical cations (b and d) of **2** (top) and **5** (bottom).

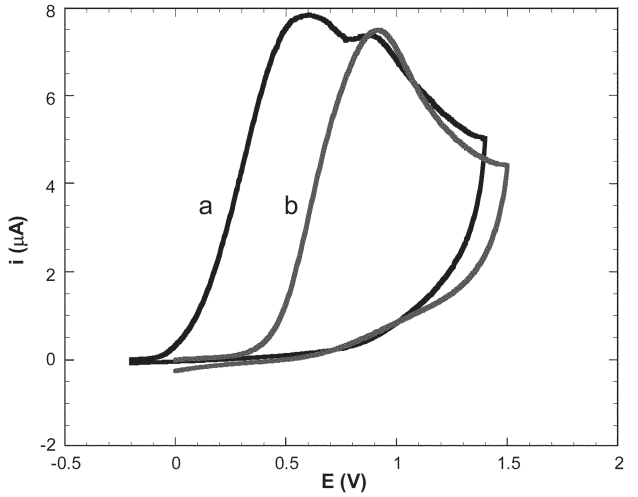


Fig. 4 Cyclic voltammograms (v = 100 mV s^{-1}) of 0.01 M bis(α-pyrrole)-*s*-tetrazine **5** in triethylphosphate–0.1 M tetrabutylammonium perchlorate. Reference Ag/Ag^+ (CH_3CN): (curve a) without acetic acid and (curve b) in the presence of acetic acid (25% relative to the same electrolyte solvent).

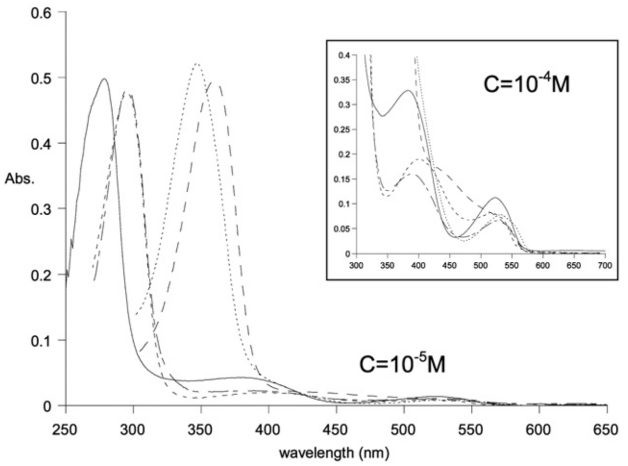


Fig. 5 UV-vis absorption spectra of compounds **1** (–), **2** (---), **3** (–·–), **4** (······) and **5** (—).

Table 3 Spectroscopic[a] features of the tetrazine derivatives

	λ_{max}/nm	ε/L mol^{-1} cm^{-1}
1	278	49 800
2	295	47 750
3	295	48 300
4	347	52 230
5	360	49 530

[a] All spectra recorded in dichloromethane except for **5** whose spectrum is recorded in acetonitrile

wavelengths that can probably be ascribed to dihydrotetrazine (this yellow compound has an absorption maximum in the UV with a bandtail up to 480 nm), and another one at longer wavelengths, which is probably due to oligomers resulting from coupling reactions.

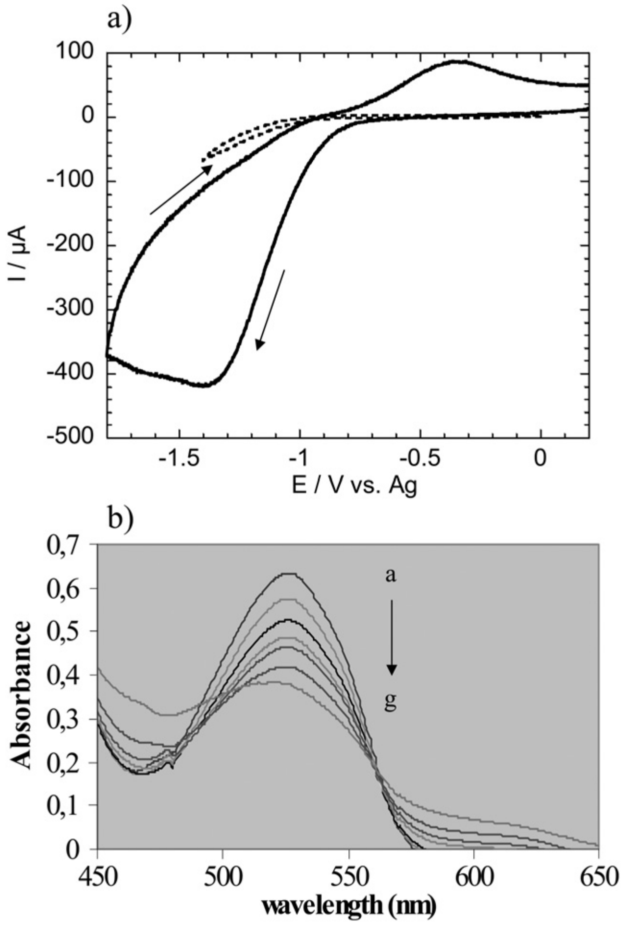


Fig. 6 CV and spectroelectrochemistry of **4** in acetonitrile (+TBAP) on an ITO electrode. (a) CV (full line) at 100 mV s^{-1}. The dotted line shows the background current in the absence of substrate on the same electrode. Potentials are given with respect to a bare Ag wire quasi-reference. (b) Spectra recorded at −1.4 V after the following waiting times: (curve a) a few s, (curve b) 1.5 min, (curve c) 3 min, (curve d) 5.5 min, (curve e) 7 min, (curve f) 9 min, (curve g) 11 min.

Concluding remarks

In this article, we have described the properties of a few new heterocycle substituted tetrazines, which display high to very high reduction potentials. Although they do not polymerise, they constitute an intriguing family of molecules that may find applications in various fields of physical chemistry such as the previously mentioned NLO materials. The third-order NLO properties are currently under investigation for this family and beyond.

References

1 F. Bédioui, J. Devynck and C. Bied-Charreton, *J. Mol. Catal. A: Chem.*, 1996, **92**, 1411.
2 G. Bidan, B. Divisia-Blohorn, M. Lapkowski, J. M. Kern and J. P. Sauvage, *J. Am. Chem. Soc.*, 1992, **114**, 598.
3 R. P. Kingsborough and T. M. Swager, *Prog. Inorg. Chem.*, 1999, **48**, 123.
4 J. P. Lang, H. Kawaguchi and K. Tatsumi, *Inorg. Chem.*, 1997, **36**, 6447.
5 A. R. Katritzky, *Handbook of Heterocyclic Chemistry*, Pergamon Press, Oxford, 1986.
6 W. Kaim, *Coord. Chem. Rev.*, 2002, **230**, 127.
7 J. Roncali, *Chem. Rev.*, 1997, **97**, 173.
8 L. Groenendaal, M. J. Bruining, E. H. J. Hendrickx, A. Persoons, J. A. J. M. Vekemans, E. E. Havinga and E. W. Meijer, *Chem. Mater.*, 1998, **10**, 226.
9 J. Kürsti, P. R. Surjan, M. Kertesz and G. Frapper, *Synth. Met.*, 1993, **55–57**, 4338.

10 G. Zotti, S. Zecchin, G. Schiavon, A. Berlin, G. Pagani, M. Borgonovo and R. Lazzaroni, *Chem. Mater.*, 1997, **9**, 2876.

11 J. Cao, J. W. Kampf and M. D. Curtis, *Chem. Mater.*, 2003, **15**, 404.

12 (*a*) (1-Bithienyl)-*s*-tetrazine was claimed to have been prepared in a recent paper, but characterisation of the molecule was not provided: F. Bentiss, M. Lagrenée, M. Traisnel, B. Mernari and H. El Attari, *J. Heterocycl. Chem.*, 1999, **36**, 149; (*b*) While this work was being reviewed, a very recent article describing the synthesis of pyrrole and thiophene substituted tetrazines was published: J. Soloducho, J. Doskocz, J. Cabaj and S. Roszak, *Tetrahedron*, 2003, **59**, 4761.

13 D. E. Chavez, R. D. Gilardi and M. A. Hiskey, *Angew. Chem., Int. Ed.*, 2000, **39**, 1791.

14 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, *GAUSSIAN 98 (Revision A.11)*, Gaussian, Inc., Pittsburgh, PA, 2001.

15 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.

16 P. C. Hariharan and J. A. Pople, *Chem. Phys. Lett.*, 1972, **16**, 217.

17 D. E. Chavez and M. A. Hiskey, *J. Energet. Mater.*, 1999, **17**, 357.

18 D. E. Chavez and M. A. Hiskey, *J. Heterocycl. Chem.*, 1998, **35**, 1329.

19 M. D. Coburn, G. A. Buntain, B. W. Harris, M. A. Hiskey, K. Y. Lee and D. G. Ott, *J. Heterocycl. Chem.*, 1991, **28**, 2049.

20 R. N. Butler, F. L. Scott and R. D. Scott, *J. Chem. Soc. C*, 1970, 2510.

21 C.-H. Lin, E. Lieber and J. P. Horwitz, *J. Am. Chem. Soc.*, 1954, **76**, 427.

22 M. O. Abdel-Rahman, M. A. Kira and M. N. Tolba, *Tetrahedron Lett.*, 1968, 3871.

23 Hybrid density functional methods with the 6-31G* base have been used previously for calculations on neutral and radical cations of hetorocycles containing sulfur atoms and found to give a good qualitative description of their properties.(*a*) V. Hernández, H. Muguruma, S. Hotta, J. Casado and J. T. López Navarrete, *J. Phys. Chem. A*, 2000, **104**, 735; (*b*) T. Keszthelyi, M. M.-L. Grage, J. F. Offersgaard, R. Wilbrandt, C. Svendsen, O. S. Mortensen, J. K. Pedersen and H. J. A. Jensen, *J. Phys. Chem. A*, 2000, **104**, 2808.

24 (*a*) J. B. Foresman, T. A. Keith, K. B. Wiberg, J. Snoonian and M. J. Frisch, *J. Phys. Chem.*, 1996, **100**, 16 098; (*b*) For a general review about solvation methods, see: J. Cramer and D. G. Truhlar, *Chem. Rev.*, 1999, **99**, 216.

25 There is no p*K* data for the *s*-tetrazines, besides the known fact that a strong acid is required to protonate the relatively electron-deficient nitrogens in polyazines where the number of nitrogens is greater than 3.[5] Similarly, there are no data on the pyrrole cation radical, which could be, however, slightly above 1, since pyrrole polymerises with some difficulty in pure water, but not at all as soon as an even very weak base is added. When the pyrrole bears an attracting moiety (like the tetrazine in the present case), it should be even lower, which renders the aforementioned proposition on the protonation equilibrium acceptable. (See ref. 5, p. 153).

26 M. Zhou and J. Heinze, *J. Phys. Chem.*, 1999, **103**, 8451.

27 L. Guyard, P. Hapiot, M. Jouini, J. C. Lacroix, C. Lagrost and P. Neta, *J. Phys. Chem.*, 1999, **103**, 4009.

28 J. Waluk, J. Spanget-Larsen and E. W. Thulstrup, *Chem. Phys.*, 1995, **200**, 201.