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Electron paramagnetic resonance and cyclic voltammetry of new alkylsulfanyl pyrroles. Models of stable radical cations

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Received (in Cambridge, UK) 28th March 2000, Accepted 28th March 2000

β-Functionalization with alkylsulfanyl groups in pyrroles contributes to stabilizing their radical cations by a mesomeric effect, as demonstrated by the presence of a reversible redox pair in their cyclic voltammetry diagrams and, when they are chemically oxidized, the detection of strong signals in electron paramagnetic resonance (EPR) spectroscopy.

A collection of EPR spectra of the radical cations derived from neutral pyrroles in solution has been reported in the literature, all of them can be simulated with the electronic structure based on the principle that the unpaired electron is located in a ψ_A orbital showing large coupling constant values at the 2- and 5-positions and small values at the 3- and 4-positions, the pyrrole nitrogen being situated in the nodal plane of ψ_A and showing a small splitting with the unpaired electron.[1]

In our research project focused on the preparation of magnetic materials based on the incorporation of pyrroles into stable organic free radicals derived from (4-amino-2,6-dichlorophenyl)bis(2,4,6-trichlorophenyl)methyl radical,[2] we are searching for stable pyrrole radical cations to generate ground triplet states as a consequence of electronic spin–spin interactions between the unpaired electron centered in the trivalent carbon atom and the radical cation generated by smooth oxidation of the heterocycle.[3] One promising approach to this goal to be tested is the introduction of alkylsulfanyl substituents into the pyrrole ring since sulfur atoms stabilize the radical cations by a mesomeric effect.[4]

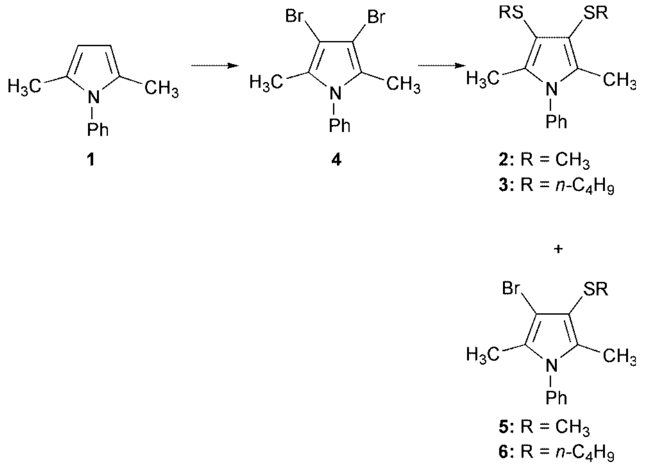
We now report the synthesis of two new alkylsulfanyl derivatives of pyrrole, 3,4-bis(methylthio)- (**2**) and 3,4-bis(butylthio)-2,5-dimethyl-1-phenylpyrrole (**3**), as good models to study the influence of the substituents into the generation and stability of their radical cations by cyclic voltammetry (CV) and EPR spectroscopy.

Two different methodologies have been used to prepare pyrroles **2** and **3**. According to Scheme 1, 2,5-dimethyl-1-phenylpyrrole (**1**) was reacted with *N*-bromosuccinimide to yield the 3,4-dibromo derivative **4**[5] in quantitative yield. Pyrrole **2** was formed in moderate yield (30%) by treatment of **4** with *n*-BuLi and then with dimethyl disulfide.[6]† Pyrrole **3** was prepared according to Klinsberg's method, by treatment of **4** with copper(I) *n*-butanethiolate in a mixture of quinoline and pyridine to give **3** (33%).[7]‡ In both cases, the monosubstituted derivatives **5** and **6** were obtained as intermediates.

EPR spectra of good quality were obtained for the radical cations **1**$^{\cdot+}$,[8] **2**$^{\cdot+}$ and **3**$^{\cdot+}$ in trifluoroacetic (TFA) acid solution, those of **2**$^{\cdot+}$ and **3**$^{\cdot+}$ being much stronger than that of **1**$^{\cdot+}$ as a consequence of the additional stability provided by alkylsulfanyl substituents. However, it is always necessary to rigorously degas the solutions by bubbling an inert gas, because oxygen drastically diminishes the signals. Species **1**$^{\cdot+}$ were generated when TFA acid solutions of the parent compound **1** in the presence of thallium(III) trifluoroacetate were irradiated with light from a high-pressure mercury lamp. The more persistent **2**$^{\cdot+}$ and **3**$^{\cdot+}$ species were easily detected in the absence of the oxidative reagent and without UV light, but their signals increased when small amounts of thallium(III) trifluoroacetate were added. The spectrum of **2**$^{\cdot+}$ and its computer simulation[9] are shown in Fig. 1 and the spectral parameters for the three radical cations are summarized in Table 1. It is worth noting the much shorter hyperfine coupling constants with 2,5-methyl protons and with nitrogen in **2**$^{\cdot+}$ and **3**$^{\cdot+}$ than in **1**$^{\cdot+}$, the splitting observed with α-hydrogens of the alkylsulfanyl groups in the β-position, whose values are of the same order as those observed for β-hydrogens in **1**$^{\cdot+}$, and the larger *g*-values in **2**$^{\cdot+}$ and **3**$^{\cdot+}$ due to spin-orbit coupling with sulfur atoms. Spin densities have been evaluated (Table 2) by using the UHF/6-31G(d) level,[10] and the method corroborates the displacement of spin densities from C2, C5 and N to C3 and C4 in **2**$^{\cdot+}$.

Table 1 EPR parameters for radical cations **1**$^{\cdot+}$, **2**$^{\cdot+}$ and **3**$^{\cdot+}$

Radical species	*g*	$a_{(\alpha)}$/G	a(N)/G	$a_{(\beta)}$/G
1$^{\cdot+}$	2.0023	16.6 (6H)	4.40	3.60 (2H)
2$^{\cdot+}$	2.0055	9.4 (6H)	1.62	3.12 (6H)
3$^{\cdot+}$	2.0055	9.12 (6H)	1.37	2.87 (4H)



Scheme 1

Cyclic voltammetry (CV) at a platinum disk electrode in rigorously anhydrous CH_2Cl_2 (alumina suspended in the voltammetric solution) (~10^{-3} M) containing TBAP (0.1 M) gave an irreversible oxidation peak with a peak potential ($E_p{}^a$) of 1.0 V *vs.* SSCE for **1**, and one remarkably reversible couple with a standard potential ($E°$) of 0.95 and 0.90 V *vs.* SSCE for **2** and **3**, respectively. Moreover, **2** and **3** also showed a second

DOI: 10.1039/b002478n

Table 2 Calculated spin densities in the SOMO of $\mathbf{1}^{\bullet+}$ and $\mathbf{2}^{\bullet+}$ at the UHF/6-31G(d) level

Radical species	ρ(N1)	ρ(C2)	ρ(C3)	ρ(S)
$\mathbf{1}^{\bullet+}$	0.158	0.498	0.058	—
$\mathbf{2}^{\bullet+}$	0.114	0.423	0.284	0.154

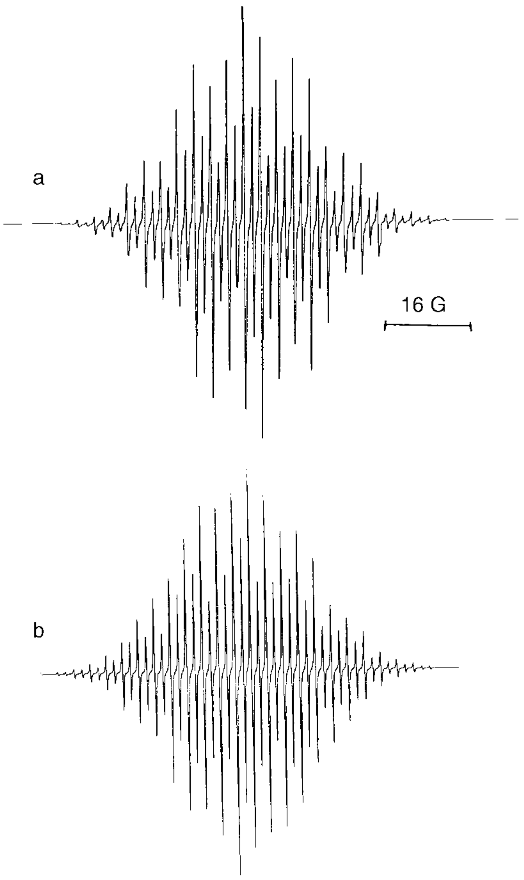


Fig. 1 (a) EPR spectrum of $\mathbf{2}^{\bullet+}$ in trifluoroacetic acid solution and (b) its computer simulation.

irreversible peak with $E_p{}^a = 1.47$ and 1.53 V at a sweep rate (v) of 100 mV s^{-1}, respectively. These results indicate a marked stability of the radical cations $\mathbf{2}^{\bullet+}$ and $\mathbf{3}^{\bullet+}$ on the CV time scale at any sweep rate from $v = 20$ mV s^{-1}.

The electronic spectra of **2** and **3** in CH_2Cl_2 have bands at 254 nm. In trifluoroacetic acid solutions the largest wavelength bands are bathochromically shifted to 416 and 425 nm, respectively. If thallium(III) trifluoroacetate is added to these solutions, new bands at 485 and 482 nm appeared in the spectra which were attributed to π–π* bands of $\mathbf{2}^{\bullet+}$ and $\mathbf{3}^{\bullet+}$, respectively.

All these results corroborate the influence of β-functionalization with alkylsulfanyl groups in pyrroles in stabilizing their radical cations sufficiently to make these heterocycles more attractive to incorporate to stable free radicals and test the spin interaction between unpaired electrons. Moreover, analysis of their radical cations by EPR confirms the displacement of the spin density to C3 and C4 due to the presence of sulfur atoms, the splitting values due to protons of SCH_3 in $\mathbf{2}^{\bullet+}$ and of SCH_2R in $\mathbf{3}^{\bullet+}$ being considerable.

Acknowledgements

Support of this research by DGICYT of MEC (Spain) through project PB96-0836 is gratefully acknowledged. The authors express their gratitude to the EPR service of Centre d'Investigació i Desenvolupament (CSIC) in Barcelona.

Notes and references

† *Synthesis of* **2**: A stirred solution of **4** (1.0 g; 3.04 mmol) in THF (25 mL) under an argon atmosphere was cooled to −78 °C. A 1.6 M solution of *n*-BuLi in hexane (4.2 mL; 6.72 mmol) was added, and the brown solution was further stirred at −78 °C for 35 min. Then, dimethyl disulfide (0.69 g; 7.39 mmol) was added dropwise and stirred for 1 h. The reaction solution was poured into water and the resulting mixture extracted with diethyl ether. The organic solution was dried over anhydrous Na_2SO_4, and the solvent evaporated at reduced pressure. The residue was purified by flash chromatography on silica gel (3 : 1, CCl_4 : $CHCl_3$ and 1 : 1, CCl_4 : $CHCl_3$) to afford **5** (0.41 g; 45%) as a colorless oil: δ_H ($CDCl_3$, 200 MHz) 2.02 (s, 3H), 2.12 (s, 3H), 2.27 (s, 3H), 7.52–7.15 (m, 5H); δ_C ($CDCl_3$, 75 MHz) 11.87, 11.92, 19.97, 101.92, 126.58, 127.99, 128.41, 128.46, 129.41, 132.57, 138.40; Exact mass calcd. for $C_{13}H_{14}BrNS$: 295.0030, found: 295.0027. The second product was **2** (0.24 g; 30%), obtained as a colorless oil: δ_H ($CDCl_3$, 200 MHz) 2.12 (s, 6H), 2.32 (s, 6H), 7.49–7.17 (m, 5H); δ_C ($CDCl_3$, 75 MHz) 11.51, 20.60, 114.11, 127.87, 128.14, 129.20, 132.64, 138.52. Exact mass calcd. for $C_{14}H_{17}NS_2$: 263.0802, found: 263.0805.

‡ *Synthesis of* **3**: A mixture of **4** (0.5 g; 1.52 mmol) and copper(I) butanethiolate (0.48 g; 3.19 mmol) in a mixture of quinoline (6 mL) and pyridine (2 mL) was heated at 180 °C with stirring for three days. The crude product was poured into water–HCl and the resulting mixture extracted with diethyl ether. The organic solution was dried over anhydrous Na_2SO_4 and the solvent evaporated at reduced pressure. The residue was purified by flash chromatography on silica gel (CCl_4) to afford recovered **4** (0.022 g, 4%) and compound **6** (0.054 g; 10.5%) as a colorless oil; δ_H ($CDCl_3$, 200 MHz) 0.89 (t, *J* 7.2, 3H), 1.48 (m, 4H), 1.99 (2,m 3H), 2.08 (2, 3H), 2.63 (t, *J* 7.2, 2H), 7.14–7.18 (m, 2H), 7.44–7.49 (m, 3H); δ_C ($CDCl_3$, 75 MHz) 10.69, 11.67, 13.74, 21.74, 31.63, 35.94, 114.02, 124.54, 128.04, 128.32, 128.37, 129.31, 132.58, 138.30. Exact mass calcd. for $C_{16}H_{20}BrNS$: 337.0499, found: 337.0505. The third product was **3** (0.175 g; 33%) as a colorless oil; δ_H ($CDCl_3$, 200 MHz) 0.90 (t, *J* 7, 6H), 1.47 (m, 8H), 2.10 (s, 6H), 2.71 (t, *J* 7.1, 4H), 7.15–7.19 (m, 2H), 7.40–7.49 (m, 3H); δ_C ($CDCl_3$, 75 MHz) 11.83, 13.77, 21.87, 31.69, 36.58, 113.05, 128.00, 128.12, 129.22, 133.39, 138.85. Exact mass calcd. for $C_{20}H_{29}NS_2$: 347.1741, found: 347.1747.

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7 While this method is well known in homoaromatic systems: R. Adams and A. Ferretti, *J. Am. Chem. Soc.*, 1959, **81**, 4927; *The Chemistry of the Thiol Group, Part 1*, ed. S. Patai, Wiley, New York, 1974, pp. 235–237, no report is known on the introduction of alkyl thiolate by direct nucleophilic substitution of bromines in pyrroles so far.

8 A good spectrum of $\mathbf{1}^{\bullet+}$ was reported in ref. 1(*b*), generated by photolysis of a trifluoroacetic acid solution of **1** in the presence of mercury(II) trifluoroacetate.

9 WINSIM program provided by D. Dulog, Public EPR Software Tools, National Institute of Environmental Health Sciences, Bethesda, MD, 1996.

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