ESR and electrochemical studies of 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines

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Abstract

The ESR spectra of radicals obtained by electrolytic reduction of 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines were measured in dimethylsulfoxide (DMSO) and analyzed by quantum chemical calculations. The electrochemistry of these compounds was characterized using cyclic voltammetry, in DMSO solvent. The results showed a two step reduction mechanism, first wave was assigned to the generation of the correspondent free radical species, and the second wave was assigned to the dianion derivatives. AM1 and DFT calculations were performed to obtain the optimized geometries, theoretical hyperfine constants, and spin distributions, respectively. The theoretical results are in complete agreement with the experimental ones.

Keywords: 2-Acylpyridines; 6,6′-Diacyl-2,2′-bipyridines; ESR; Cyclic voltammetry; DFT

1. Introduction

In general, chemical or electrochemical reduction of ketones yields alcohols [1]. More specifically, in aprotic media electrochemistry reductions give primarily dianions through radical–radical, radical–ketone or ion–ketone coupling [2]. Pyridine-based aromatic ketones have the same electrochemistry behaviour.

2-Pyridyl ketone [$(py)_2CO$] have been used as ligand which have three potential donor group, the two pyridyl nitrogens and the central oxygen [3–5]. However, there is a chemical characteristic of the $(py)_2CO$ that make this ligand special; this is its carbonyl group. Ketones (R_2CO) can undergo hydration, with the first step of the reaction involving of nucleofilic attack of water on the carbonyl group [6]. The tetrahedral intermediate is trapped by reaction with a proton to yield the hydrated form of the ketone, the germinal diol.

Perlepes et al. have developed several work using $(py)_2CO$ as ligand in with many metals. The structural diversity of these complexes stems from the ability of the singly and doubly deprotanated anions of the gem diol form of the $(py)_2CO$ and its derivatives to exhibits a variety of the coordination modes [7–9].

On the other hand, some related compounds of $(py)_2CO$ as 4-acyl- and 4-benzoylpyridinium cations are reduced, generated a radical stable species, which are characterized by electron spin resonance (ESR) spectroscopy [10,11]. These kinds of compounds could de considered for applications as redox mediator or electrochromic compounds [12–14].

In the present work, we analyze the electrochemistry mechanism of $(py)_2CO$ and the other 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines (Fig. 1) and compare

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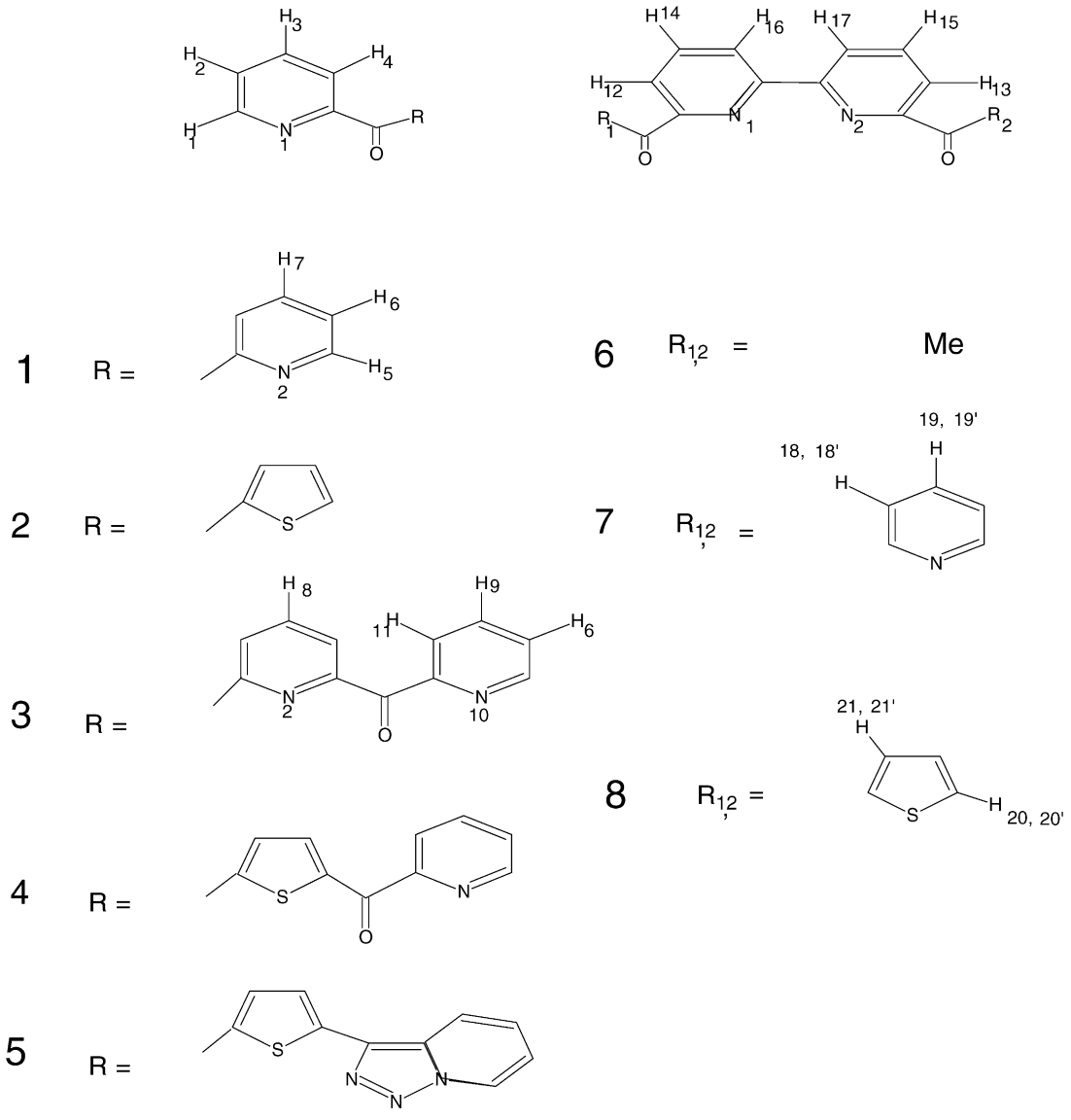

Fig. 1. Chemical structure of the 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines.

the reduction mechanism with that of 4-acyl- and 4-benzoylpyridinium cations family.

We report electrochemical and ESR studies of these families in dimetylsulfoxide (DMSO).

To estimate the theoretical hyperfine constants, DFT calculations were carried out. The geometry of each compound in both spin-paired and free radical forms was fully optimized by the AM1 methodology.

2. Experimental and theoretical methods

2.1. Samples

Compound **1** is commercial, compounds **2** [15], **3**, **7**, **8** [16] and **6** [17] are synthesized as described. Compounds **4** and **5** are new compounds synthesized as follows.

*2.1.1. 2-Pyridyl-5-(2-pyridylcarbonyl)-tien-2-ylmethanona (**4**)*

To a solution of *n*-BuLi in hexane (93 ml, 1.6 M, 148.5 mmol) a solution of thiophen in dry THF (50 ml) was added slowly (5.0 g, 59.4 mmol) at 0 °C under argon. The stirring was continued at 0 °C for 2 h, a violet colour developed. Then, a solution of 2-pyridylcarbaldehyde (15.9 ml, 148.5 mmol) in THF (50 ml) was added. The mixture was stirred overnight at room temperature. Hydrolised with an aquoeus solution of NH_4Cl (100 ml) and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated to give a reaction crude (17.73 g) that was disolved in CH_2Cl_2 (400 ml) and added to a solution of pyridinium chlorocromate (25 g, 118.84 mmol) in CH_2Cl_2 (400 ml). The suspension was heated to reflux 10 h, then filtered, concentrated, and purified by column chromatography, eluting with

AcOEt/hexane (2:1). The first fraction was a yellow oil identified as 2-pyridyl-2-tienylmethanone (**2**) (1.84 g, 17%), the second fraction a yellow solid identified as 2-pyridyl-5-(2-pyridylcarbonyl)-tien-2-ylmethanone (**4**) (2.36 g, 27%). M.P., 150 °C (AcOEt). HRMS (EI) found for M^+ 294.0467; $C_{16}H_{10}N_2O_2S_2$ requires 294.0463. ^{1}H NMR (250 MHz) δ ($CDCl_3$) 8.80 (d, J = 4.0 Hz, 2H); 8.36 (s, 2H); 8.21 (d, J = 7.5 Hz, 2H); 7.91 (dd, J_1 = 7.8, J_2 = 7.5 Hz, 2H); 7.54 (dd, J_1 = 7.8, J_2 = 4.0 Hz, 2H). ^{13}C NMR (62.9 MHz) δ ($CDCl_3$) 184.33 (CO); 153.40 (C); 148.41 (CH); 146.79 (C); 137.19 (CH); 135.36 (CH); 127.09 (CH); 123.83 (CH). IR KBr $\upsilon_{máx}$ (cm^{-1}) 1690 (CO); 1480; 1306; 1241; 1137; 927; 840.

2.1.2. 2-Pyridyl-5-([1,2,3]triazolo[1,5-a]pyridin-3-yl)-tien-2-ylmethanone (**5**)

A mixture of 2-pyridyl-5-(2-pyridylcarbonyl)-tien-2-ylmethanone (**4**) (1.00 g, 3.4 mmol) and hydrated hydrazine (8 ml, 98%) was heated to reflux 3 h, cooled and extracted with ether. The organic layer was dried, concentrated and evaporated giving a mixture of mono- and dihydrazone of 2-pyridyl-5-(2-pyridylcarbonyl)-tien-2-ylmethanone. The hydrazone's mixture without purification (1.17 g) was dissolved in dry $CHCl_3$ (100 ml), MnO_2 (1.26 g, 14.5 mmol) was added and the mixture was heated to reflux 10 h. The suspension was filtered and the solvent evaporated giving a reaction crude that was purified by column chromatography eluting with AcOEt/hexane (1:1) to give 2-pyridyl-5-([1,2,3]triazolo[1,5-*a*]pyridin-3-yl)-tien-2-ylmethanone (**5**) (0.30, 29%). M.P., 162–163 °C (AcOEt/hexane). HRMS (EI) found for M^+ 306.0579; $C_{16}H_{10}N_4OS$ requires 306.0573. ^{1}H NMR (250 MHz) δ ($CDCl_3$) 8.73 (d, J = 4.7 Hz, 1H); 8.70 (d, J = 6.9 Hz, 1H); 8.65 (d, J = 4.0 Hz, 1H); 8.15 (d, J = 7.7, 1H); 8.02 (d, J = 9.1 Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H); 7.62 (d, J = 4.0 Hz, 1H); 7.46 (dd, J_1 = 7.7, J_2 = 4.7 Hz, 1H); 7.36 (dd, J_1 = 9.1, J_2 = 6.9 Hz, 1H); 7.1 (t, J = 6.9, 1H). ^{13}C NMR (62.9 MHz) δ ($CDCl_3$) 183.00 (CO); 153.75 (C); 148.23 (CH); 144.13 (C); 138.04 (C); 137.55 (CH); 137.13 (CH); 132.83 (C); 130.33 (C); 126.88 (CH); 126.74 (CH); 125.80 (CH); 123.91 (CH); 123.63 (CH); 118.32 (CH); 115.81 (CH).

2.2. Reagents

Dimethylsulfoxide (spectroscopy grade) and tetrabutylammonium perchlorate (TBAP), used as supporting electrolyte, was supplied from Fluka.

2.3. Cyclic voltammetry

Cyclic voltammetry was carried out using a Weenking POS 88 instrument with a Kipp Zenen BD93 recorder, in DMSO (ca. 1.0×10^{-3} mol dm^{-3}), under a nitrogen atmosphere, with TBAP (ca. 0.1 mol dm^{-3}), using three-electrode cells. A hanging drop mercury electrode (HDME) was used as the working electrode, a platinum wire as the auxiliary electrode, and saturated calomel (SCE) as the reference electrode.

2.4. ESR spectroscopy

ESR spectra were recorded in the X band (9.85 GHz) using a Bruker ECS 106 spectrometer with a rectangular cavity and 50 kHz field modulation. The hyperfine splitting constants were estimated to be accurate within 0.05 G. ESR spectra of the anion radicals derivatives were obtained in the electrolysis solution. The ESR spectra were simulated using the program WINEPR Simphonia 1.25 Version.

2.5. Theoretical calculations

Full geometry optimizations of the compounds in spin-paired and free radical forms were carried out by AM1 methodology. The theoretical hyperfine constants were obtained using B3LYP 6-31G* level.

3. Results and discussion

3.1. Cyclic voltammetry

Table 1 lists the values of voltammetric peaks and the anodic and cathodic currents for all compounds. All compounds display comparable voltammetric behaviour, showing two well-defined reduction waves in DMSO.

Table 1
Cyclic voltammetric parameters of 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines families in DMSO vs. calomel electrode

Compound	E_{pc1}/V	E_{pa1}/V	ΔE/V	ip_a/ip_c	E_{pc2}/V	E_{pa2}/V	ΔE/V	ip_a/ip_c
1	−1.47	−1.27	0.20	0.94	−1.67	–	–	–
2	−1.53	−1.34	0.19	0.90	−1.72	–	–	–
3	−1.18	−1.12	0.06	0.98	−1.43	−1.27	0.16	0.94
4	−0.92	−0.83	0.09	0.97	−1.34	−1.24	0.10	0.90
5	−1.31	−1.20	0.11	0.92	−1.56	–	–	–
6	−1.63	−1.56	0.07	0.98	−1.81	−1.57	0.24	0.90
7	−1.44	−1.27	0.17	0.95	1.65	–	–	–
8	−0.72	−0.66	0.06	0.98	−0.90	–	–	–

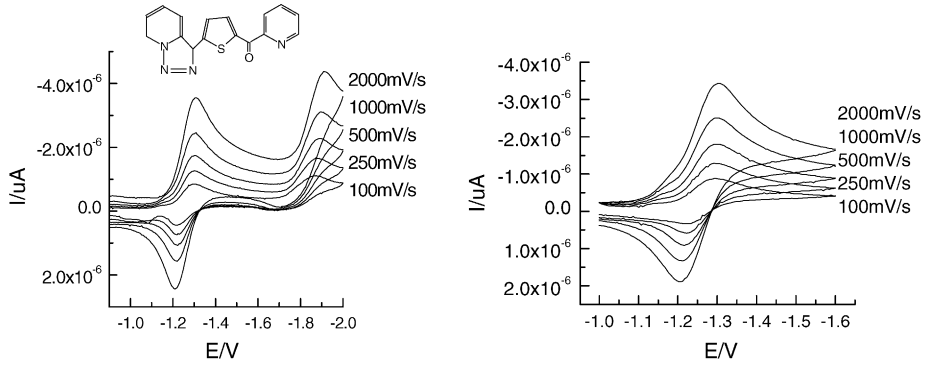

Fig. 2. Cyclic voltammetry and first couple of compound **5** in DMSO obtained at the following sweep rates: 2000, 1000, 5000, 250 and 100 mV s^{-1}.

The first wave corresponds to a reversible one-electron transfer in DMSO to compounds **3**, **6** and **8**. The reverse scan showed the anodic counterpart of the reduction waves. The breadth of cathodic wave at its half intensity has a relatively constant value of 60 mV. The intensity ratio ip_a/ip_c has a value close to one. According to the standard reversibility criteria this couple corresponds to a reversible diffusion-controlled one-electron transfer [18]. However, the first wave corresponds to a quasirreversible process to compounds **1**, **2**, **4**, **5** and **7**. This couple was attributabled to the reduction of a ketone to a stable anion radical at room temperature. The second cathodic peak is irreversible in the whole range of sweep rates used (50–2000 mV s^{-1}) to compounds **1**, **2**, **5**, **7** and **8** and quasirreversible process to compounds **3**, **4** and **6**. We can attribute this wave to the production of the corresponding anion derivative. Fig. 2 shows the voltamogram of compound **5**.

3.2. ESR

The electrochemical reductions (in situ) to the radical forms in DMSO were carried out applying the potential corresponding to the first wave from the cyclic voltammetry experiments to each compound.

The interpretation of the ESR spectra by means of a simulation process led to the determination of the experimental

Table 2
Experimental and theoretical hyperfine splittings (Gauss) and *g* values for the 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines anion radicals

Molecule	a_H	a_H	a_H	a_N	a_N	*g* value
1	(H6)	(H2, H7)	(H5, H4)	(N1, N2)		2.0067
EXP[a]	4.8	2.0	0.61	2.65		
DFT	6.9	2.39, 2.72	0.94, 0.99	3.20, 2.80		
2						2.0063
EXP						
DFT						
3	(H8)	(H6, H2)	(H11, H4)	(N1, N2, N10)		2.0060
EXP[a]	1.80	2, 5	1.5	1.8		
DFT	1.4	2.15, 2.18	1.00, 1.20	1.50, 2.30, 1.45		
4						2.0058
EXP						
DFT						
5						2.0060
EXP						
DFT						
6	(R1, R2CH_3)	(H12, H13)	(H16, H17)	(N1, N2)		2.0065
EXP[a]	3.8, 3.6	5.2	3.5	1.0		
DFT	3.5, 3.0	4.68, 5.67	3.44, 3.64	1.06, 1.13		
7	(H16, H17)	(H12, R1H18, H19)	(H13, R2H18′, H19′)	(N1, R1N)	(N2, R2N)	2.0063
EXP[a]	4, 7	3.5	3.0	4.0	1, 6	
DFT	3.8, 3.9	2.4, 2.3	2.9, 3.0, 3.2	3.2, 3.5	1.2, 1.3	
8	(H16, H17)	(R1, H20, R20′)	(R1, H21, R2H21′)	(N1, N2)		2.0058
EXP[a]	1.2	3.0	2.4	2.0		
DFT	0.90, 1.0	2.80, 2.70	2.3, 2.5	1.56, 1.59		

[a] Average data.

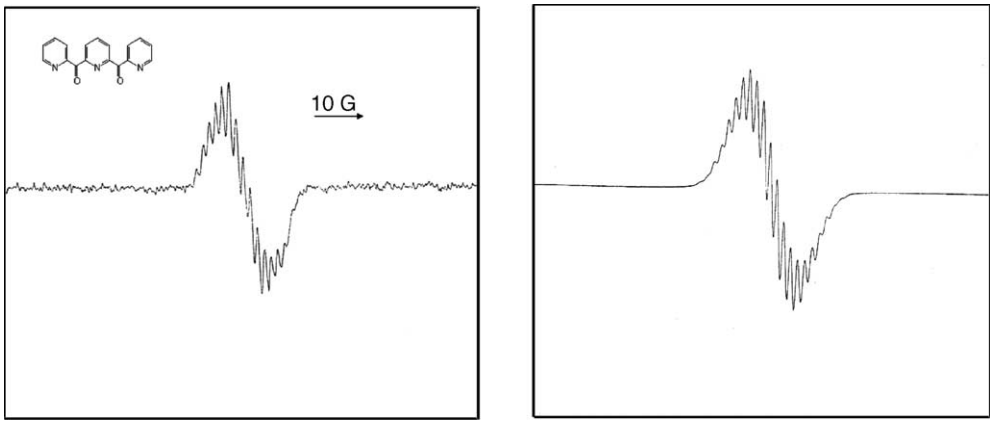

Fig. 3. ESR experimental spectrum of the radical–anion of compound **3** in DMSO and computer simulation of the same spectrum. Spectrometer conditions: microwave frequency, 9.68 GHz; microwave power, 20 mW; modulation amplitude, 0.2 G; scan rate, 1.25 G s^{-1}; time constant, 0.5 s; number of scans, 15. Spectrum was simulated using the following parameters: line width = 0.7 G, ratio Lorentzian/Gaussian = 0.8 and hyperfine constants included in Table 2.

coupling constants for the magnetic nuclei observed, confirmed by theoretical calculation obtained from the DFT calculations. The optimization of the geometries showed a direct dependence of the structure's conformation on the hyperfine pattern. The hyperfine constants are listed in Table 2.

Compound **1** was analyzed and simulated in term a quintuplet that could be assigned to the two equivalent nitrogen atoms of the pyridines two triplets of were accounted for by two hydrogens H2, H7 and H5, H4 of each pyridine, respectively, and doublet due to one hydrogen of the one pyridine ring (H6). This hyperfine pattern shows that the pyridine rings are not equivalent. Chemical calculations of this molecule indicated that in the optimized structure of the radical species, both pyridines are out of the plane defined by the carbonyl carbon (almost 45° between rings), which is in agreement with an electron localization mainly in one pyridine ring.

Compound **3** was analyzed and simulated in term a septet due to the three equivalent nitrogen atoms of the pyridines, two triplets of were accounted for two equivalent hydrogen atoms group H6, H12 and H11, H14 and one doublet due to one hydrogen of the pyridine center ring (date found by theoretical calculations). This hyperfine pattern and theoretical calculations indicated that the spin electron density was delocalized in all aromatic rings (Fig. 3).

Compounds **2**, **4** and **5** showed only one broad line in all of them. These results are in according with the theoretical structures which showed that the thiophene group are almost in the same plane of pyridine and triazolopyridine ring, which provoke that spin electron density are delocalized in all rings.

Compound **6** was analyzed and simulated in term a two quartet due to the equivalent hydrogens of methyl groups, two triplets due to hydrogens H16, H17 and H12, H13, respectively, and one quintet due to two equivalent nitrogen of pyridine rings.

Compound **7** was analyzed and simulated in term a two quintet due to the N1 and the nitrogen belongs to the R1 pyridine ring, and N2 and nitrogen belongs to the R2 pyridine ring, respectively, being the hyperfine coupling different for both groups. Two quartet due to three equivalent hydrogens (see Table 2 and Fig. 4) and one triplet due to H16 and H17.

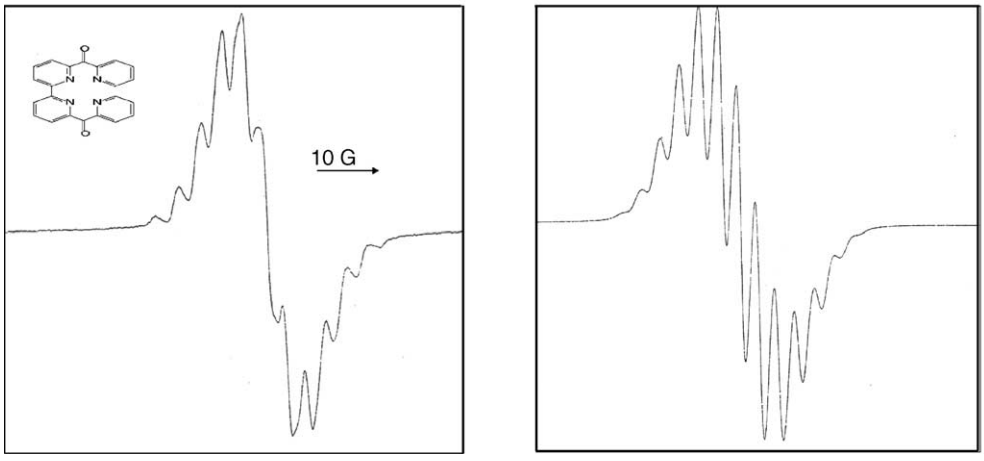

Fig. 4. ESR experimental spectrum of the radical–anion of compound **7** in DMSO and computer simulation of the same spectrum. Spectrometer conditions: microwave frequency, 9.68 GHz; microwave power, 20 mW; modulation amplitude, 0.2 G; scan rate, 1.25 G s^{-1}; time constant, 0.5 s; number of scans, 15. Spectrum was simulated using the following parameters: line width = 0.1 G, ratio Lorentzian/Gaussian = 1.0 and hyperfine constants included in Table 2.

Finally, compound **8** was analyzed and simulated in term a one quintet due to N1 and N2 (see Fig. 1), one triplet due to hydrogens H16 and H17 and two triplet due to two equivalent hydrogens of each thiophene ring.

4. Theoretical calculations

We fully optimized the geometries for the electron-paired and anion radical molecules at AM1 level. All radicals structures showed small distortion, respect to the neutral analogues molecules.

B3LYP 6-31G* calculations were performed in order to obtain the theoretical hyperfine constants, using the geometries from AM1 calculations. Table 2 shows both the experimental and calculated hyperfine constants. These results are in agreement with the assignment of the hyperfine constants.

The radicals structures optimized are in agreement with experimental hyperfine coupling. Compounds **6** and **8** have not the pyridine in the same plane (around 39° between rings), however, molecule **7** showed 59° between these rings in agreement with hyperfine pattern which indicated that spin density are mainly localized in moiety of this molecule.

Respect to compounds **2**, **4** and **5**, theoretical structures showed that the thiopheme ring are almost in the same plane of pyridine ring which are in agreement with the ESR spectra.

5. Concluding remarks

The results obtained from the electrochemical studies showed a two step reduction mechanism for the 2-acylpyridines and 6,6′-diacyl-2,2′-bipyridines. The first wave was assigned to the generation of the correspondent free radical species, and the second wave was assigned to the dianion derivatives. These reduction mechanism was also found in the of 4-acyl- and 4-benzoylpyridinium cations family which suggest that $(py)_2CO$ and derivatives compounds could be considered for applications as redox mediators or electrochromic compounds.

Stable free radicals were generated using electrochemical reductions at potential corresponding to first wave obtained from the voltammetric experiments.

The theoretical results are in complete agreement with the experimental ones and helped to rationalize the small difference in the hyperfine constants.

Acknowledgements

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References

[1] L.-G. Feoktistov, in: M.M. Baizer, H. Lund (Eds.), Organic Electrochemistry, second ed., Marcel Dekker, New York, 1983, pp. 315–320.
[2] (a) J.H. Stocker, R.M. Jenevein, D.H. Kern, J. Org. Chem. 43 (1969) 2807–2810;
(b) E.J. Rudd, B. Conway, Trans. Faraday Soc. 67 (1971) 440–447;
(c) L. Nadjo, J.M. Saveant, J. Electroanal. Chem. 44 (1973) 327–366;
(d) W.J.M. van Tilborg, D.J. Smit, J. R. Neth. Chem. Soc. 98 (1979) 532–536;
(e) J.E. Swartz, T.J. Mahachi, E. Kariv-Miller, J. Am. Chem. Soc. 110 (1988) 3622–3628;
(f) J.M. Tanko, R.E. Drumright, J. Am. Chem. Soc. 114 (1992) 1844–1854;
(g) L. Mattiello, L. Rampazzo, J. Chem. Soc., Perkin Trans. (1993) 2243–2247;
(h) E. Liotier, G. Mousset, Can J. Chem. 73 (1995) 1488–1496.
[3] G. Yang, S. Zheng, X. Chen, H.K. Lee, Y. Zhou, Inorg. Chim. Acta 303 (2000) 86–93.
[4] A.C. Deveson, S.L. Heath, C.J. Harding, A.K. Powell, J. Chem. Soc., Dalton Trans. (1996) 3173–3178.
[5] S.O. Sommerer, B.L. Westcott, J.A. Jircitano, A.K. Abboud, Acta Crystallogr., Sect C 52 (1996) 1426–1428.
[6] E.C. Constable, Metal and Ligand Reactivity, VHC, Weinheim, Germany, 1996, pp. 46, 47, 57–59.
[7] A. Thoso, B. Dionyssopoulou, C. Raptopoulou, A. Terzis, E. Bakalbassis, S. Perlepes, Angew. Chem. Int. Ed. 38 (1999) 983–985.
[8] G. Papaefstathiou, S. Perlepes, Comments Inorg. Chem. 23 (2002) 249–274.
[9] A. Boudalis, B. Donnadieu, V. Nastopoulos, J. Clemente-Juan, A. Mari, Y. Sanakis, J.P. Tuchagues, S. Perlepes, Angew. Chem. Int. Ed. 43 (2004) 2266–2270.
[10] (a) E.M. Kosower, E.J. Poziomek, J. Am. Chem. Soc. 86 (1964) 5515–5523;
(b) L. Grossi, F. Minisci, G.F. Pedulli, J. Chem. Soc., Perkin Trans. 2 (1977) 943–947;
(c) L. Grossi, F. Minisci, G.F. Pedulli, J. Chem. Soc., Perkin Trans. 2 (1977) 948–952.
[11] P. Neta, L.K. Patterson, J. Phys. Chem. 78 (1974) 2211–2217.
[12] N. Leventis, X. Gao, J. Phys. Chem. B 103 (1999) 5832–5836.
[13] Y. Nakamura, N. Kamon, T. Hori, Chem. Soc. Jpn. 62 (1989) 551–557.
[14] D.C. Bookbinder, M.S. Wrighton, J. Electrochem. Soc. 130 (1983) 1080–1085.
[15] R.J. Mohsbacher, V. Paraqaurian, E.L. Larson, B.M. Prunce, C.R. Rasmussen, J.A. Meschimo, G.I. Poos, J. Org. Chem. 31 (31) (1966) 2149–2159.
[16] B. Abarca, R. Ballesteros, M. Elmasnaoui, Tetrahedron 54 (1998) 15287–15292.
[17] G. Jones, M.A. Pitman, E. Lunt, D.J. Lythgoe, B. Abarca, R. Ballesteros, M. Elmasnaowi, Tetrahedron 53 (1997) 8257–8262.
[18] R. Nicholson, I. Shain, Anal. Chem. 36 (1964) 706–723.