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A New Crown Compound with Multifunctional Capabilities

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Abstract

A new crown ether, derived from the 2,2-diphenyl-1-picrylhydrazyl free radical (DPPH) and diaza-18-crown-6 (kryptofix 22) was synthesized. The physico-chemical properties of this new compound were studied using ^{1}H- and ^{13}C-NMR, EPR, UV-Vis, and IR spectroscopy. The compound has acid-base and redox properties, each of these involving a colour change (i.e., from yellow to red-brown for acid-base processes, and from yellow to violet for redox processes). The transport properties of the compound were studied by means of biphasic (l/l or s/l) systems. Thus, by an acid-base process alkaline cations were transported into an organic phase, as well as arginine; by a redox process, short-lived free radicals such as $\cdot C_6H_5$ and $\cdot H$ were generated and observed by the EPR spin-trapping technique, using *t*-butyl-phenyl-nitrone (PBN) as spin-trap.

Introduction

DPPH and related stable free radicals have been used mainly for the determination of the antioxidant properties of amines, phenols or natural compounds (vitamins, plant extracts, medicinal drugs) and for inhibiting homolytic reactions [1–4]. Whereas DPPH is intensely violet like $KMnO_4$, its reduced counterpart, 2,2-diphenyl-1-picrylhydrazine (DPPH-H) is orange-yellow [5]. Recent work demonstrated the usefulness of DPPH and its derivatives in studying interphasic processes assisted by transport agents such as crown ethers (CEs) or cryptands [5]. The species formed by these agents are supramolecular complexes and behave as stoichiometric compounds [6–9]. One of the most interesting applications of DPPH is the generation of some short-lived free radicals by an electron transfer (ET) process, starting from an anion (A^-) transported into an organic phase as an anion pair in a supramolecular complex; it is well known that this anion is activated, due to the lack of a hydration sphere.

$$M^+A^-_{aq/s} \xrightarrow{CE} (CE \ldots M)^+A^-_{org} \xrightarrow[(ET)]{DPPH} A\cdot \xrightarrow{PBN} \text{spin-adduct.} \quad (1)$$

In an organic phase, the stable free radical DPPH abstracts one electron from the anion, giving the short-lived free radical $A^{\cdot}$, which is trapped by PBN (Equation (1)). In order to simplify these processes, we synthesized a free radical bonded to a crown moiety, as shown in Figure 1.

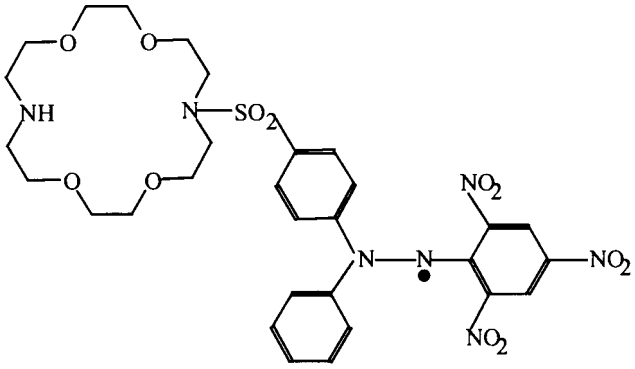

Figure 1. The new crown compound (**2**) synthesized.

Experimental

The new compound is easily synthesized, starting from the known sulphated derivative of DPPH, $NaSO_3$DPPH-H [10–11]. This reacts with thionyl sulphochloride to yield the corresponding chloro-derivative. Because kryptofix *k*-22 (1,4,10,13-tetraoxa-7,16-diaza-cyclooctadecane) is basic, even in the absence of bases, the sulfochloride reacted with kryptand *k*-22 (Equation (2)).

$$NaSO_3\text{-DPPH-H} \xrightarrow{SOCl_2} ClSO_2\text{-DPPH-H} \xrightarrow{k-22} \mathbf{1}. \quad (2)$$

Although the compounds $NaSO_3$DPPH-H and $ClSO_2$DPPH-H are known [11], we briefly mention here their synthesis. *Synthesis of $NaSO_3$DPPH-H.* 20 g freshly prepared powdered 1,1-diphenylhydrazine hydrochloride was suspended in dichloroethane (200 mL) and 6.5 mL of chlorosulfonic acid was added dropwise. Hy-

drogen chloride evolution was observed. The mixture was refluxed with stirring for 15 min., then the 1-phenyl-1-(*p*-sulfonylphenyl)hydrazine hydrochloride was filtered off and dissolved in 400 mL ethanol and 50 mL water. After adding 30 g sodium hydrogen carbonate, the solution was heated for 30 min. at 50 °C. Picryl chloride (22 g) was added, and the mixture was refluxed for two hours. After filtration, benzene was added to the solution benzene and the water was removed by azeotropic distillation at atmospheric pressure. The remaining solvent was evaporated at reduced pressure and the residue was purified by dissolution in hot methanol with charcoal, filtration, and evaporation of the solvent. The remaining solid was washed with methylene chloride, then dissolved in acetone (traces of disulfonate which is insoluble were removed by filtration), and the solvent is evaporated at reduced pressure, leaving the monosulfonate $NaSO_3$DPPH-H. *Synthesis of $ClSO_2$DPPH-H*. A suspension of $NaSO_3$DPPH-H (1 g) in 30 mL 1,2-dichloroethane was treated with 1 mL of thionyl chloride and 3–5 drops of *N*, *N*-dimethylformamide. After refluxing for 30 min. and filtration, the solution was concentrated at normal pressure for removing excess thionyl chloride, then passed over a column of silanized silica gel. The solid compound can be obtained by adding petroleum ether to the concentrated solution of $ClSO_2$DPPH-H. For UV-Vis, IR and NMR spectra, see [11].

Reaction between sulfochloride $ClSO_2$DPPH-H and kryptand k-22

Kryptand *k*-22 was added in excess to the solution of sulfochloride; after stirring for 10 min. the mixture was concentrated and petroleum ether added, when the corresponding compound **1** precipitated. By oxidation in methylene chloride with PbO_2 or solid $KMnO_4$ the persistent free radical **2** was obtained in 90% yield. M.p. (dec.) 118 ∘C. ^{1}H-NMR (chloroform-d, δ ppm, *J* Hz): 9.20 (bs, 1H, H-3/5); 8.54 (bs, 1H, H-5/3); 7.69 (d, 2H, H-9-11, 9,0); 7.43 (t, 2H, H-15-17, 7.1); 7.32 (tt, 1H, 7.1, 1.4); 7.27 (dd, 2H, H-14-18, 7.1, 1.4); 7.19 (d, 2H, H-8-12, 9.0); 3.15–3.98 (m, 24H, H-1′-6′). ^{13}C-NMR (chloroform-d, δ ppm): 149. 89 (C-q); 144.49 (C-q); 14429 (C-q); 141.70 (C-q); 139.88 (bs, C-2/6); 136.89 (C-q, C-4); 134.48 (bs, C-6/2); 130.35 (C-15-17); 128.37 (C-9-11); 128.17 (C-16); 125.23 (bs, C-3/5); 124.81 (bs, C-5/3); 124.35 (C-14-18); 116.84 (C-8-12); 70.51 (CH_2); 69.47 (CH_2); 69.26 (CH_2); 49.11 (CH_2); 48.93 (CH_2). IR (CH_2Cl_2, ν cm^{-1}): 1102 vi; 1126 vi; 1161 vi; 1348 vi; 1497 i; 1562 i; 1598 i; 1621 i; 3295 m.

The determination of the complexation ratio between compound **1** and alkali cations was performed by stirring an aqueous solution of LiOH, NaOH or KOH (0.1–0.5 M) with a solution of **1** in dichloromethane ($5 \times 10^{-5} - 5 \times 10^{-4}$). Equal volumes of aqueous and organic solutions were stirred till the equilibrium was reached, the organic phase was separated and the concentration of the anion was determined by spectrophotometry (λ_{max} 441 nm and $\epsilon = 12,000$); the slope of the plot indicated 1:1 complexation ratios.

Generation of short-lived radicals

To a solution of **2** (10^{-3} M) and PBN (10^{-3} M) in dichloromethane, solid sodium borohydride or sodium tetraphenylborate was added and the mixture stirred for about one minute by bubbling nitrogen (the colour changed from purple-violet to red-brown) and then the supernatant was used for recording the ESR spectra.

Results and discussion

The yellow product **1** has λ_{max} 294 nm in methylene chloride, in basic medium it loses the hydrazinic proton and the red-brown anion has λ_{max} 441 nm. The violet free radical **2** obtained on oxidation has λ_{max} 524 nm and a broad ESR quintet with $\_N1 \cong a_{N2} \cong 9.0$ G (Figure 2).

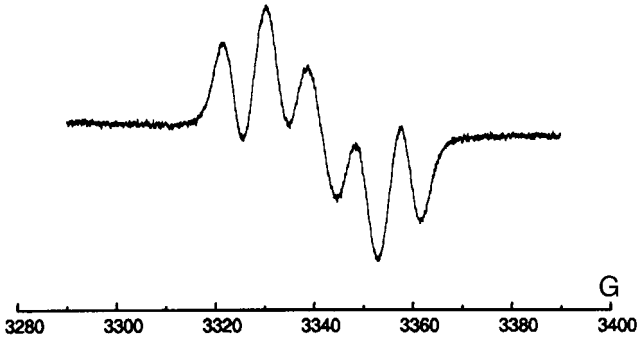

Figure 2. EPR spectrum of radical **2**.

An interesting property of compound **1** is the color variation in polar basic solvents due to ionization (λ_{max} = 410–450 nm). A zwitterionic prototropic equilibrium is possible because the molecule contains a secondary amine group and an acidic picramidic group (Figure 3).

The interphase transport properties of compound **1** were studied in a liquid-liquid system for three alkaline hydroxides (M^+HO^- with M = Li, Na, K, Equation (3)). For the system water (alkaline hydroxide)/dichloromethane (compound **1**), using the graphical method it was possible to determine the complexation ratios and the extraction constants K_{ex} (Equation (4), where *D* is the distribution ratio of the cation between the two phases) [5, 8]:

$$k22\text{-}SO_2\text{-}DPPH\text{-}H_{org} + M^+_{aq}HO^-_{aq} \rightleftharpoons (k22\ldots M)^+\text{-}SO_2\text{-}DPPH^-_{org} + HOH \quad (3)$$

$$K_{ex} = \frac{[(k22\ldots M)^+SO_2DPPH^-]_{org}}{[k22\text{-}SO_2D\ldots]_{org}[M^+]_{aq}[HO^-]_{aq}} = \frac{D}{k22\text{-}SO_2D\ldots]_{org}[HO^-]_{aq}}. \quad (4)$$

As seen from Figure 4, for all three alkali cations the slopes are about 0.9, therefore the ratio cation/ligand is 1:1. The extraction constants log K_{ex} increase from 3.42 (±0.2) for Li^+ to 5.11 (±0.4) for Na^+ and 7.45 (±0.4) for K^+.

Using the same procedure, in which arginine was used instead of alkali cations, the determined extraction constant

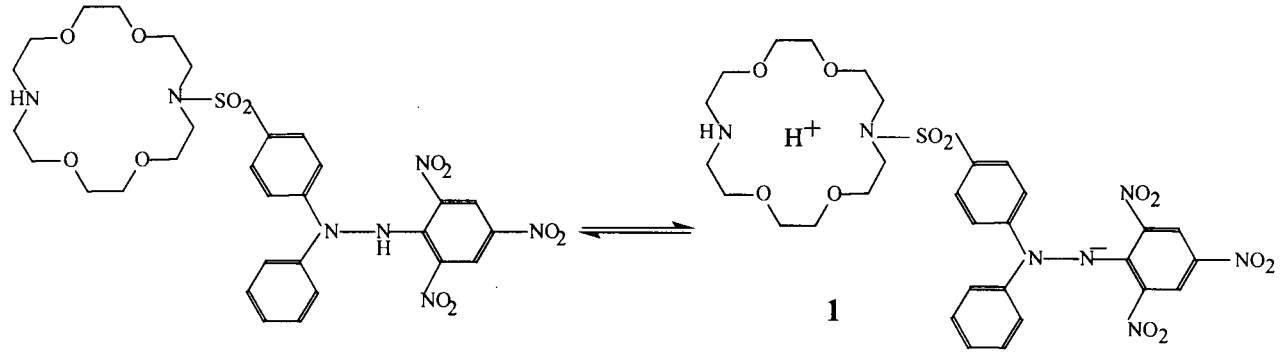

Figure 3. Compound **1** and its zwitterionic form.

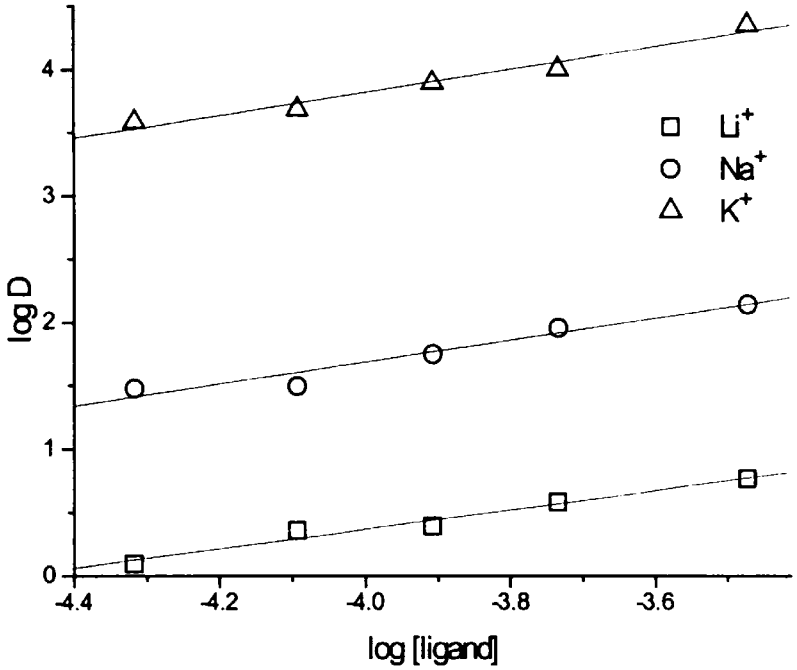

Figure 4. Plot of the ratio between concentrations of cation in the organic and aqueous phases vs. the concentration of ligand **1**.

Table 1. Hyperfine splitting constants (G) for the spin-adducts PBN-H and PBN-C6H5 (in DCM as solvent at room temperature)

Spin-adduct	aN	a_H
PBN-H	14.52	7.23
PBN-C6H5	14.52	2.74

($\log K_{ex}$) for arginine was 3.27. This amino acid can be transported into the organic phase due to its basicity ($p/$ = 10.76), which favoured the formation of the supramolecular complex by an acid-base reaction (Equation (3)). Attempts to use other amino acids (glycine, tyrozine, etc) failed.

Using a biphasic s/l system which contained in the organic phase the persistent radical **2** and a salt M^+A^- as solid phase it is possible to obtain the corresponding short-lived radicals A· [12]. In the first step the salt is transferred into the organic solvent due to the macrocyclic moiety, and the naked anion is oxidised by the persistent radical (electron transfer process, Equation (5)).

$$k22\text{-}SO_2\text{-}DPPH\cdot_{org} + M^+A^-_{s/aq} \rightarrow [(k22\ldots M)^+\text{-}SO_2\text{-}DPPH\cdot]A^-_{org} \rightarrow (k22\ldots M)^+\text{-}SO_2\text{-}DPPH^- + A\cdot\,. \quad (5)$$

If the system contains a spin-trap (PBN), the corresponding nitroxide-radical is formed and detected by EPR (Equation (1)). The EPR constants a_N and a_H thus obtained in the case of sodium borohydride and sodium tetraphenylborate are compiled in Table 1.

The short-lived radicals A· (A = H and C_6H_5) were then trapped by PBN, leading to the spin adduct PBN-A·; Figure 5 shows their EPR spectra.

Conclusions

A new crown compound, which contains a stable-free radical moiety, was synthesized. This compound can be in-

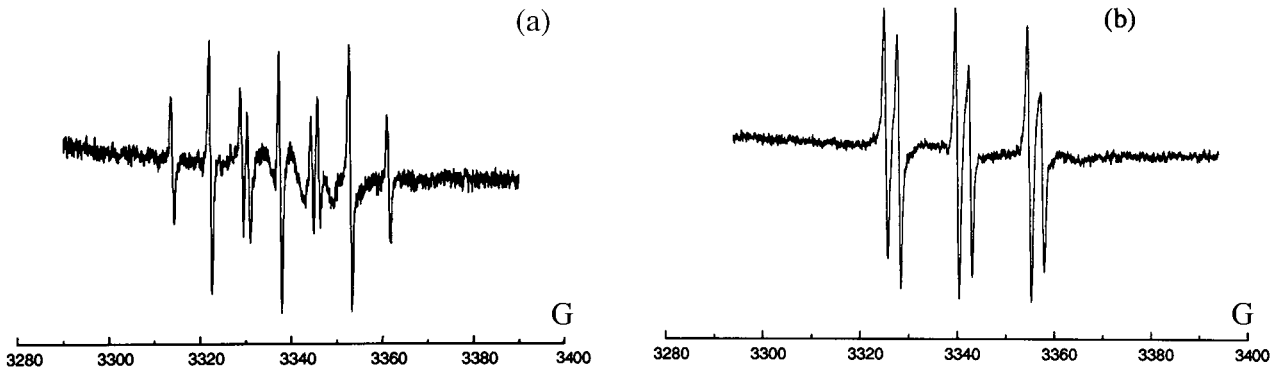

Figure 5. EPR spectra of the spin-adducts PBN-H (a) and PBN-C6H5 (b).

volved in (interphasic) acid-base or redox processes, easily monitored by the colour change.

References

1. T. Fargere, M. Abdennadher, M. Delmas and B. Boutevin: *Eur. Polym. J.* **31**, 489 (1995).
2. J. Glavind and G. Halmer: *J. Am. Oil Chem. Soc.* **44**, 539 (1967).
3. K. Emaru, H. Askal and G. Saleh: *Talanta* **38**, 1219 (1991).
4. M. Akitame and H. Hajime, *Neurosciences* **16**, 83 (1990).
5. C. Luca, P. Ionita and T. Constantinescu: *Rev. Roum. Chim.* **39**, 1141 (1994).
6. E. Weber, J.L. Toner, I. Goldberg, F. Vögtle, D.A. Laider, J.F. Stoddart, R.A. Bartsch and C.L. Liotta: In S. Patai and Z. Rappoport (eds), *Crown Ethers and Analogs*, Wiley (1989).
7. C. Luca, P. Ionita and T. Constantinescu: *Rev. Roum. Chim.* **44**, 39 (1999).
8. C. Luca, P. Ionita, M.T. Caproiu, H. Caldararu and T. Constantinescu: *Rev. Roum. Chim.* **43**, 753 (1998).
9. P. Ionita: *J. Incl. Phenom. Macrocycl. Chem.* **34**, 253 (1999).
10. G.V. Putirszkaja and T. Siladi: *Acta Chim. (Hung.)* **72**, 329 (1972).
11. P. Ionita, M.T. Caproiu and A.T. Balaban: *Rev. Roum. Chem.* **45**, 935 (2000).
12. P. Ionita. B.C. Gilbert and A.C. Whitwood: *J. Chem. Soc., Perkin Trans. 2* 2436 (2000).