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Note

Dedicated to Professor Alexandru T. BALABAN on the occasion of his 90th anniversary

SYNTHESIS AND CHARACTERIZATION OF A NEW HYDRAZYL FREE RADICAL, A FORMYL-DERIVATIVE OF DPPH

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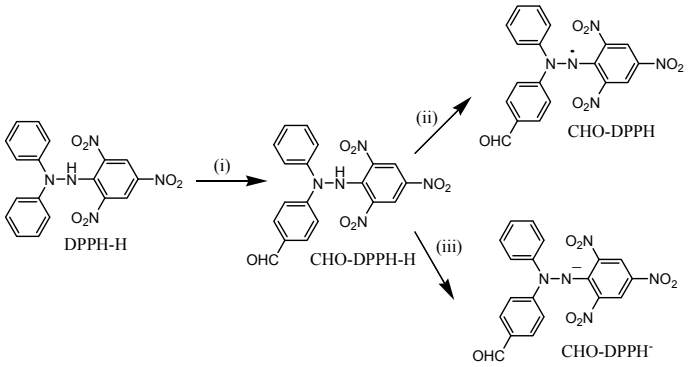
Starting from 2,2-diphenyl-1-(2,4,6-trinitropheyl)hydrazine and urotropine in the presence of trifluoracetic acid it was obtained a formyl derivative as a yellow solid, that can form under oxidative condition the persistent hydrazyl free radical 2-(*p*-formyl-phenyl)-2-phenyl-1-(2,4,6-trinitrophenyl)hydrazyl having a violet colour. The same formyl hydrazine derivative in the presence of a base forms the corresponding anion with a red-brown colour. The new compounds were characterized by appropriate means, like NMR, IR, UV-VIS, ESR.



INTRODUCTION

Hydrazyl free radicals are an interesting topic in chemistry, since the discovery, about 100 years ago, of the so called DPPH free radical (2,2-diphenyl-1-(2,4,6-trinitropheyl)hydrazyl).[1] Meantime, many other derivatives and congeners were synthesized and their properties studied.[2-5] Their stability was a subject of high debate, and it can be mentioned the pioneering work of Prof. Balaban and collaborators that pinpoint the factors affecting the stability and equilibria of such nitrogen centered free radicals.[6,7]

Some *p*-phenyl derivatives of DPPH are known, containing methyl-, hydroxyl-, bromo-, or nitro-groups (Figure 1).[8,9] The substitution of a H-atom from the *p*-phenyl position usually induce a strong change in the physical and chemical behavior. For example, addition a nitro-group in the *p*-phenyl position of DPPH changes the following: in visible spectroscopy, the absorption wavelength from about 524 to 495 nm; in ESR, the hyperfine coupling constants from almost equivalent nitrogen atoms with hyperfine coupling constants $a_{N1}=a_{N2} \sim 9$ G to about $a_{N1}= 10.43$ G and $_{aN2} = 6.95$ G;[8,10] in the case of the reduced counterpart of DPPH, usually denoted as DPPH-H, the acidity constant of the NH group is lowered from 8.54 to 7.35 pK$_a$ units.[11]

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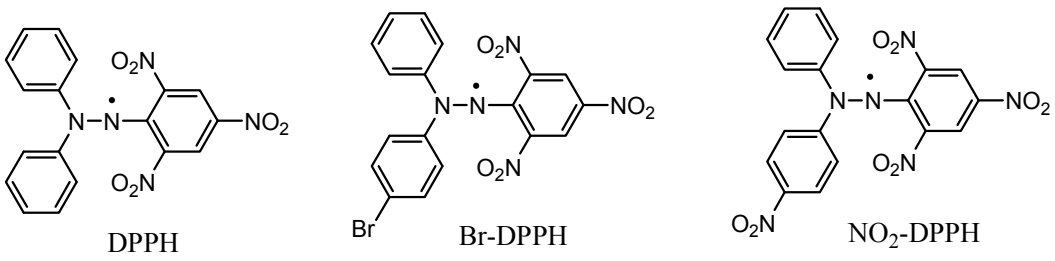

Fig. 1 – Structure of DPPH and some *p*-phenyl derivatives.

In the quest of finding new hydrazyl stable free radicals with interesting properties that can be pursued in novel applications,[12] this work deals with the synthesis and characterization of a new compound derived from DPPH, in which a formyl group was inserted into the *para*-position of a phenyl ring.

RESULTS AND DISCUSSION

The synthesis of *p*-phenyl derivatives of DPPH usually follows two routes.[8] In the first one, the starting material is a substituted *p*-diphenyl amine, that undergoes reaction of nitrosation, reduction to the corresponding hydrazine and coupling with picryl chloride (1-chloro-2,4,6-trinitrobenzene); the picryl-hydrazine thus obtained is further oxidized to the hydrazyl free radical using solid potassium permanganate, lead dioxide or silver oxide. For the second route, DPPH or its reduced counterpart DPPH-H reacts in a radical reaction with specific regents, like bromine or nitrogen dioxide and forms directly the corresponding *p*-substituted derivative.[2,3,9,13] Although the second way seems simpler, it can be used only for these specific reagents that are or can form free radicals. As an example, *p*-nitrophenyl derivative of DPPH (usually denoted in literature as NO_2-DPPH) cannot be obtained using the first route, as nitro-group will be reduced during synthesis steps; however, this compound is selectively obtained through a radical + radical coupling, from DPPH and NO_2.[10]

Introduction of a formyl group can be achieved is a single step for aromatic compounds using urotropine (hexamethylenetetramine) and trifluoroacetic acid.[14] This procedure was found to work in the case of DPPH-H, while another classical one (DMF and $POCl_3$)[15] didn't work. Therefore, starting from DPPH-H the formyl-derivative CHO-DPPH-H (Figure 2) was obtained. The compound of interest was separated from a complex mixture using column chromatography or preparative TLC (see Experimental).

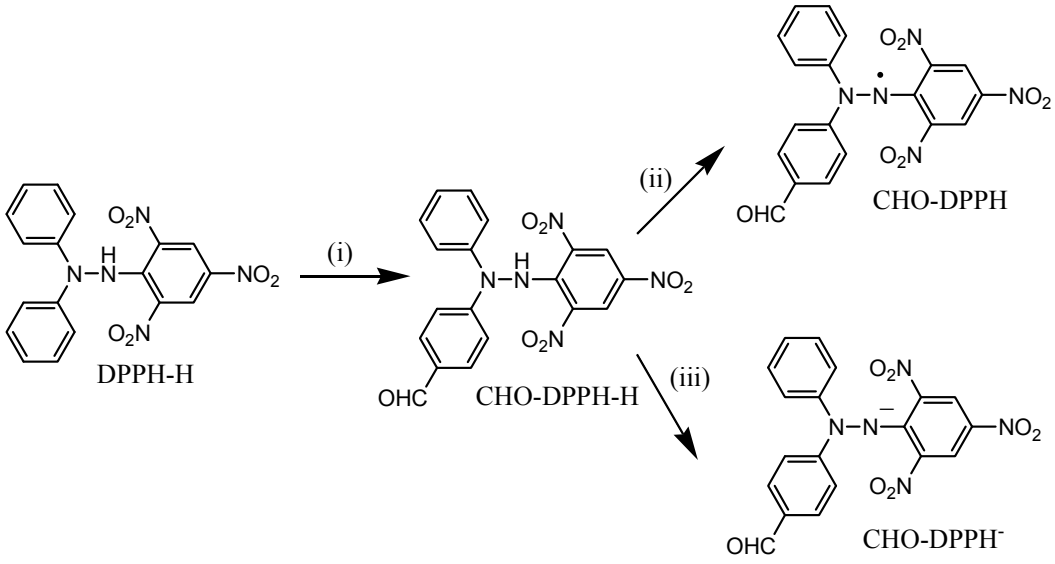

Fig. 2 – Synthesis of CHO-DPPH: i) urotropine/TFA; ii) PbO_2; iii) KOH.

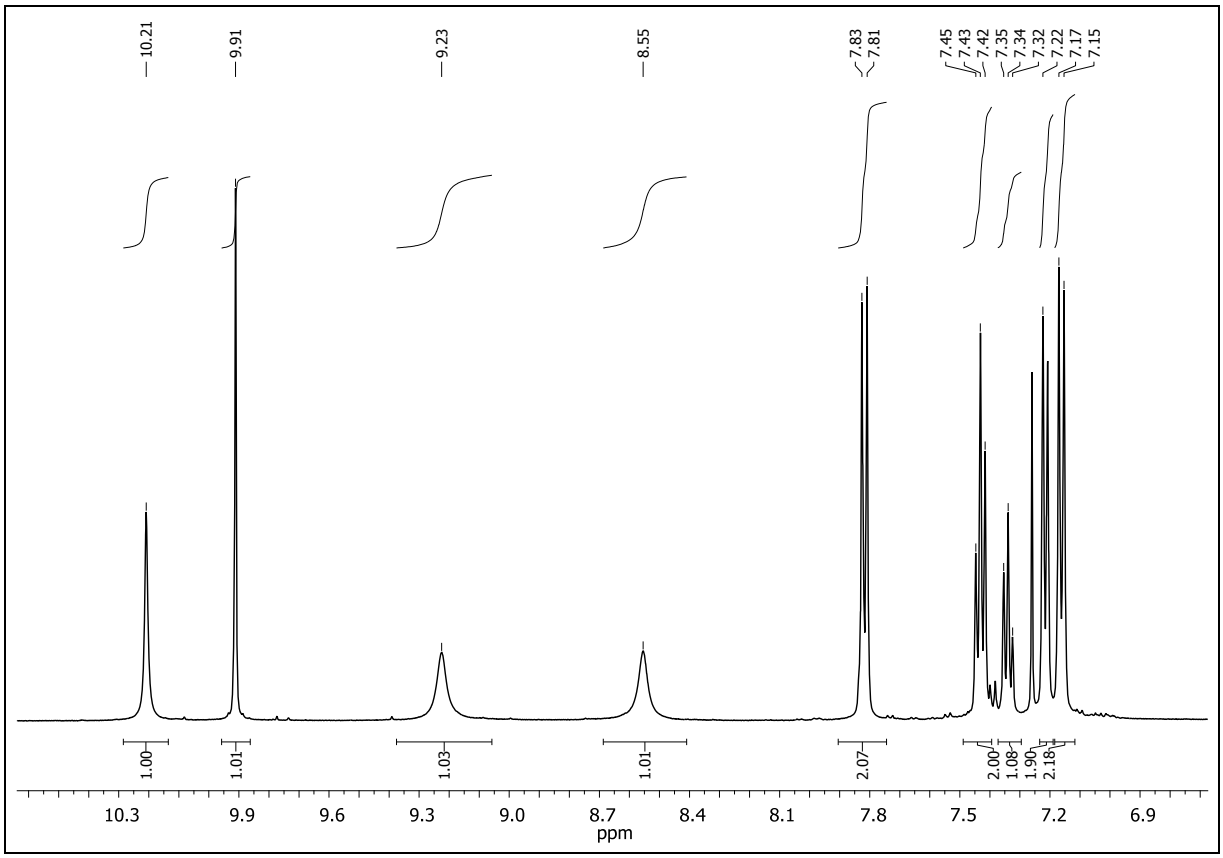

Fig. 3 – ^{1}H-NMR spectrum of CHO-DPPH-H in $CDCl_3$.

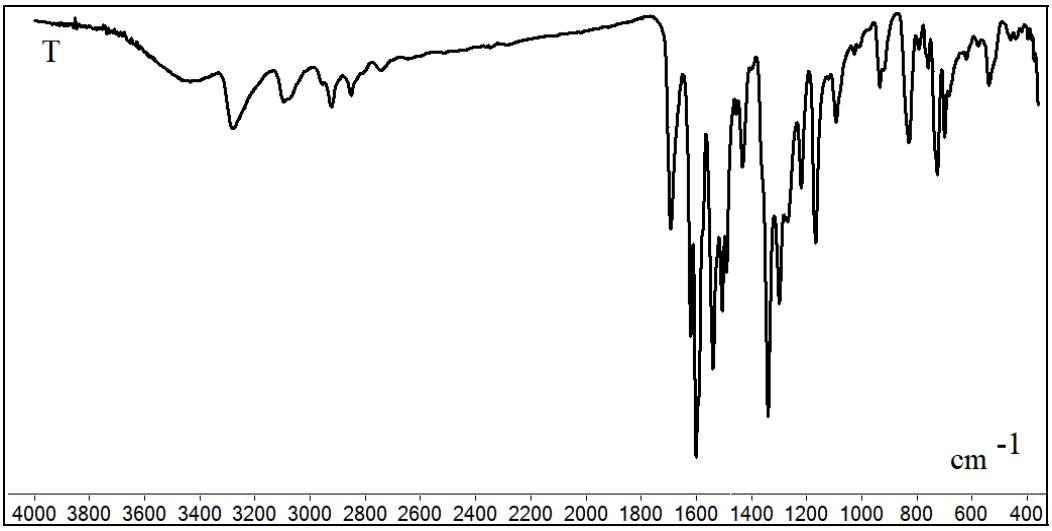

Fig. 4 – IR spectrum of CHO-DPPH-H.

Characterization of the CHO-DPPH-H was performed using several techniques. Thus, in the ^{1}H-NMR spectrum (Figure 3) there is noticed the N*H* proton at 10.21 ppm, followed by the C*H*O one at 9.91 ppm. The two C*H* from the picryl moiety appear as different singlets at 9.23 ppm and 8.55 ppm. The *H*-nuclei from the two phenyls ring are located between 7.9-7.1 ppm, with the corresponding splitting. In the ^{13}C-NMR spectrum it is necessary to mention the *C*HO peak at 190.63 ppm, thus confirming the proposed structure.

In the IR spectrum (Figure 4), the most intense band is noticed at 1601 cm^{-1}, being due to the formyl group; other groups are present as amino (3279 cm^{-1}), nitro (1339 and 1539cm^{-1}), and aromatic rings (3094 cm^{-1}), supporting the proposed structure.

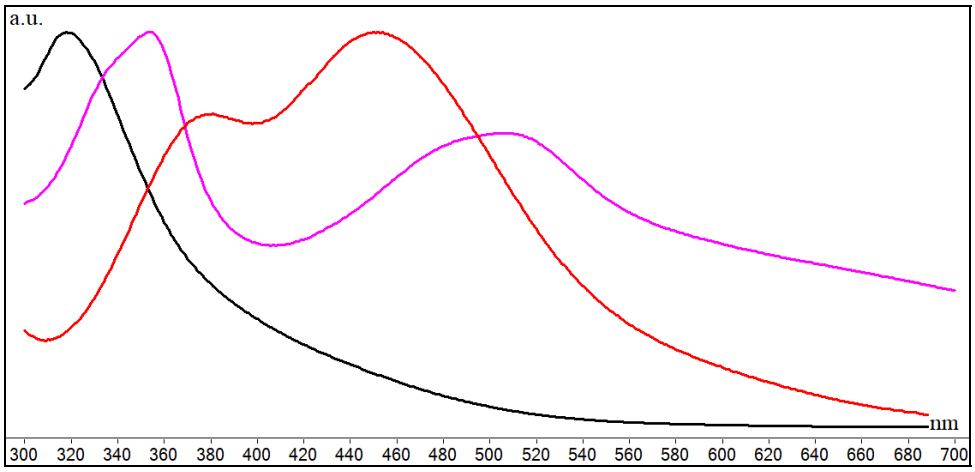

Fig. 5 – UV-VIS spectra of CHO-DPPH-H hydrazine (black), CHO-DPPH free radical (violet) and the corresponding anion CHO-DPPH$^-$ (red).

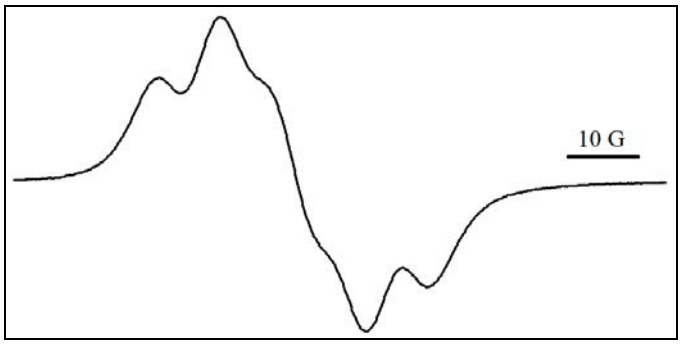

Fig. 6 – ESR spectrum of CHO-DPPH free radical.

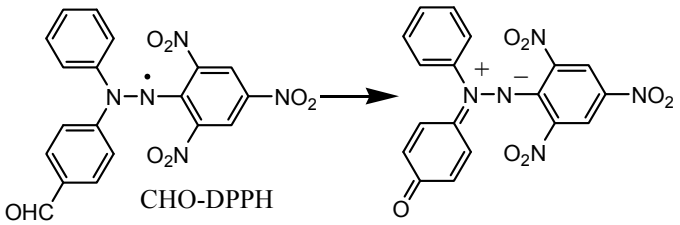

Fig. 7 – Over-oxidation of CHO-DPPH free radical.

An interesting and well-known property of such derivative is their colour change, process that can be simply followed by UV-Vis (Figure 5). Thus, the hydrazine CHO-DPPH-H has a l_{max} = 318 nm, being yellow in colour, while the free radical CHO-DPPH has a l_{max} = 506 nm and is violet; the corresponding anion CHO-DPPH$^-$ has a l_{max} = 451 nm, with a red-brown colour.

ESR spectrum shown in Figure 6 is that one undoubtedly confirming the free radical structure of CHO-DPPH. The measured hyperfine coupling constants are about a_{N1} = 10.5 G and a_{N2} = 8.5 G. Regarding the shape of the spectrum, it can be observed five peaks with large linewidth, commonly recorded for DPPH derivatives.

Although the CHO-DPPH free radical can be regarded as a stable or persistent hydrazyl type free radical, an interesting behaviour was observed checking by TLC the progress of the oxidation reaction from CHO-DPPH-H to CHO-DPPH (oxidation performed in DCM with lead dioxide). It was found that in time the CHO-DPPH free radical undergoes an interesting transformation, yielding the previously known quinonoid derivative (Figure 7).[9]

At this time the mechanism for this transformation (Figure 7) is not clear and further investigations are necessary. It can be only supposed that *p*-formyl-group is also oxidized in a first instance to a carbonyl radical that undergoes

stabilization by pairing with the free hydrazyl electron altogether with CO or CO_2 elimination.

In conclusion, synthesis of novel hydrazyl free radicals with specific properties and containing groups that can be easily converted into other moieties of interest is still an attractive subject in this area. The new derivative of DPPH can be further be involved in many other organic processes of interest due to the high reactivity of formyl group.

EXPERIMENTAL

All chemicals and materials, including solvents, were purchased from Merck or Chimopar. NMR spectra were recorded in $CDCl_3$ on a Bruker Avance III 500 MHz. IR spectrum was recorded on a FT-IR Bruker Vertex 70 spectrometer. UV-Vis spectra were recorded in methanol on a double-bean UVD-3500 spectrometer. ESR spectrum was recorded in toluene on a JES-FA 100 apparatus.

Synthesis of CHO-DPPH-H, 2-(*p*-formyl-phenyl)-2-phenyl-1-(2,4,6-trinitrophenyl)hydrazine or 4-(1-phenyl-2-(2,4,6-trinitrophenyl)hydrazynyl)benzaldehyde, $C_{19}H_{13}N_5O_7$. 200 mg DPPH-H (0.5 mmol) and 560 mg urotropine (4 mmol) were suspended in about 2 mL DCM to which under stirring was added dropwise 2 mL trifluoroacetic acetic and the mixture left overnight. Next day were added about 50 mL DCM and 50 mL of water and under vigorous stirring was added also solid sodium hydrogen carbonate till the aqueous solution reach pH 8. The organic phase was separated, dried over anhydrous sodium sulphate and the solvent removed using a rotavap. The residue was chromatographied on silica gel using DCM as eluent. Yields 35%. R_f 0.50 (DCM/silica gel). l_{max} = 318 nm (ethanol); in the presence of KOH l_{max} = 451 nm (1 mg compound dissolved in 10 mL methanolic solution of KOH (1 mg KOH/mL methanol)). ^{1}H-NMR (ppm, $CDCl_3$): 10.21 (s, 1H, N*H*), 9.91 (s, 1H, C*H*O), 9.23 (s, 1H, C*H*-picryl), 8.55 (s, 1H, C*H*-picryl), 7.82 (d, *J* = 8.5 Hz, 2H, C*H*-benzaldehyde), 7.43 (t, *J* = 7.8 Hz, 2H, C*H*-phenyl), 7.34 (t, *J* = 7.4 Hz, 1H, C*H*-phenyl), 7.21 (d, *J* = 8 Hz, 2H, C*H*-phenyl), 7.16 (d, *J* = 8.6 Hz, 2H, C*H*-benzaldehyde). ^{13}C-NMR (ppm, $CDCl_3$): 190.63, 150.98, 144.62, 141.67, 140.11, 137.17, 134.23, 132.20, 132.17, 131.09, 130.56, 130.46, 128.37, 126,27, 125.09, 124.12, 116.82. IR (cm^{-1}): 3435; 3279; 3094; 2922; 1692; 1619; 1601; 1539; 1506; 1431; 1339; 1298; 1166; 1092; 924; 828; 726; 538.

The CHO-DPPH persistent free radical was obtained by oxidation of a DCM solution of CHO-DPPH-H (5 mg in 2 mL solvent) with lead dioxide (200 mg). R_f 0.58 (DCM/silica gel). UV-VIS: l_{max} = 506 nm (ethanol). ESR (toluene): a_{N1}= 10.5 G and $_{aN2}$ = 8.5 G. Over-oxidation affords the *p*-quinonoid (betainic) compound described earlier.[9]

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