Polish J. Chem., **75**, 1427–1440 (2001) **ORGANIC CHEMISTRY**

New Congeners of 1-Picryl-2-phenyl-2-(*para*-picramidophenyl)-diazenium Betaine whose Picramido Groups Are Replaced by 4-Cyano-2,6-dinitrophenyl Analogs

by I.C. Covaci[1*], T. Constantinescu[1*], M.T. Caproiu[2], H. Caldararu[3], P. Ionita[1] and A.T. Balaban[3,4*]

[1]*Roumanian Academy, Institute "I.G.Murgulescu" of Physical Chemistry, Laboratory of Supramolecular Chemistry and Interphase Processes, Splaiul Independentei 202, 77408, Bucharest, Roumania*
[2]*Roumanian Academy, Institute "C. D. Nenitzescu" of Organic Chemistry, Splaiul Independentei 202B, 77408, Bucharest, Roumania*
[3]*University "Polytechnica", Faculty of Industrial Chemistry, Department of Organic Chemistry, Bucharest, Roumania*
[4]*Texas A&M University at Galveston, Galveston, TX 77553-1675, USA*

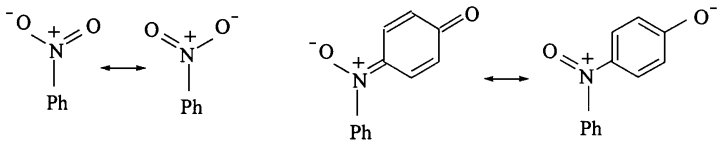
(Received April 11th, 2001)

By analogy with our previously described 1-picryl-2-phenyl-2-(*para*-picramidophenyl)-diazenium betaine (**4a**), three new congeners were synthesized in which either one, or the other, or both of the picryl groups have one 4-nitro group replaced by a cyano group. The spectral properties of these new compounds are described, and they prove that the cyanodinitrophenyl group behaves like a slightly less powerful electron-withdrawing group than a picryl group. The dipotassium salt of 1-picryl-2-phenyl-2-(4-picrylaminophenyl)-hydrazine (**5a**) forms a supramolecular complex, **13**, with 18-crown-6 ether, which can be mono- or dialkylated with methyl iodide, resulting in a monomethyl and dimethyl derivative **14** and **15**, respectively. The monomethyl derivative, **14**, has the methyl attached to the diarylamino nitrogen atom, since oxidation by potassium permanganate converts it into a stable hydrazylic radical, **17**. A byproduct in the synthesis of betaine **4a**, when an excess of DPPH is used over N-methoxypicramide, was proved to be 2-(4-methoxyphenyl)-2-phenyl-1-picrylhydrazine, **12**. In order to avoid the formation of such byproducts and to allow simpler purification procedures, it is recommended to use equimolar ratios of reactants, in the presence of potassium permanganate.

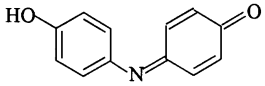
Key words: betaines, stable free radicals, crown compounds, NMR spectra, hydrazine derivatives

The betainic compound **2** can be regarded as a *para*-phenylog of nitrobenzene (**1**). Compound **2** is an isomer of indophenol, **3**. If the two oxygen atoms of **2** are replaced by electron-withdrawing pseudoatoms such as picramido groups, one obtains 1-picryl-2-phenyl-2-(*para*-picramidophenyl)-diazenium betaine (**4a**), which was described in our previous publications [1,2]

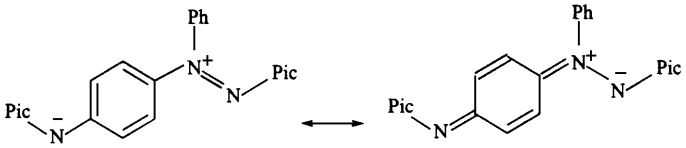
*Authors for correspondence.
E-mail:balabana@tamug.tamu.edu; E-mail for Dr. T. Constantinescu: titel@chimfiz.icf.ro



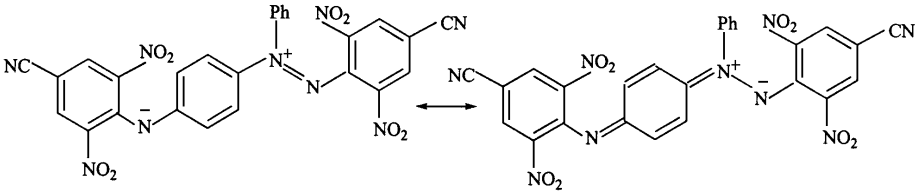
1 **2**



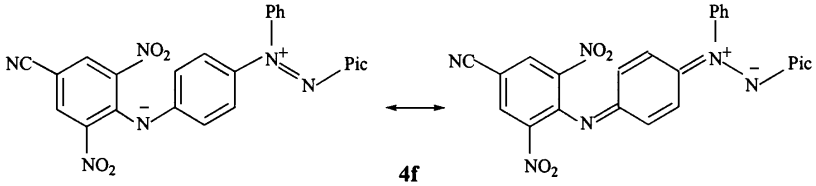
3



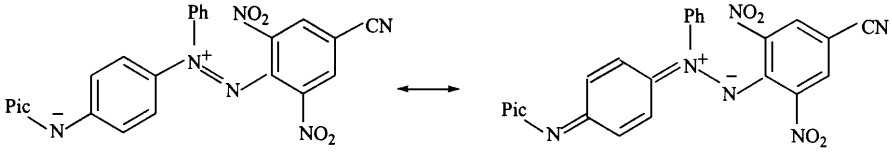
4a



4e



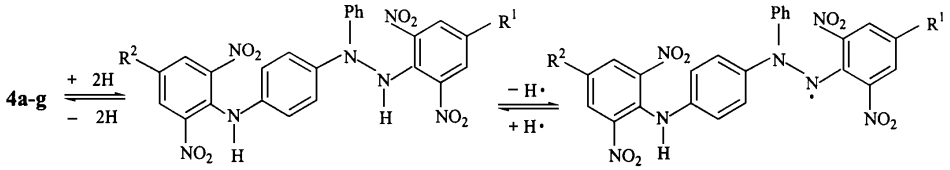
4f



4g

	R^1	R^2
a	NO_2	NO_2
b	NO_2	COOH
c	NO_2	CF_3
d	NO_2	COOMe
e	CN	CN
f	NO_2	CN
g	CN	NO_2

This paper reports the synthesis and describes the spectral properties of three new congeners of betaine **4a**, in which the 4-nitro substituent of one or both 2,4,6-trinitrophenyl, *i.e*. picryl (Pic) group(s), is/are replaced by a nitrile group, yielding the dicyano (**4e**) and the monocyano (**4f, 4g**) analogs of betaine **4a** (Scheme 1). Similarly to the betaines **4a–d** described previously [1,2], reduction of the new blue betaines **4e–g** affords the yellow hydrazine derivatives **5e–g,** which can be oxidized to stable hydrazylic free radicals **6e–g**. These radicals **6** can be further oxidized, regenerating the initial betaines **4**. The hydrazine **5a** can be alkylated with methyl iodide yielding mono- and dimethylated derivatives. A byproduct in the synthesis of betaine **4a** is the 4-methoxy-DPPH-ine **12**, and in order to avoid its formation which complicates the purification of betainic products a better synthetic procedure is recommended. Stable hydrazyl free radicals were obtained and studied by ESR spectroscopy whenever there was an N-NH-Ar group. All these results are reported in the present paper.

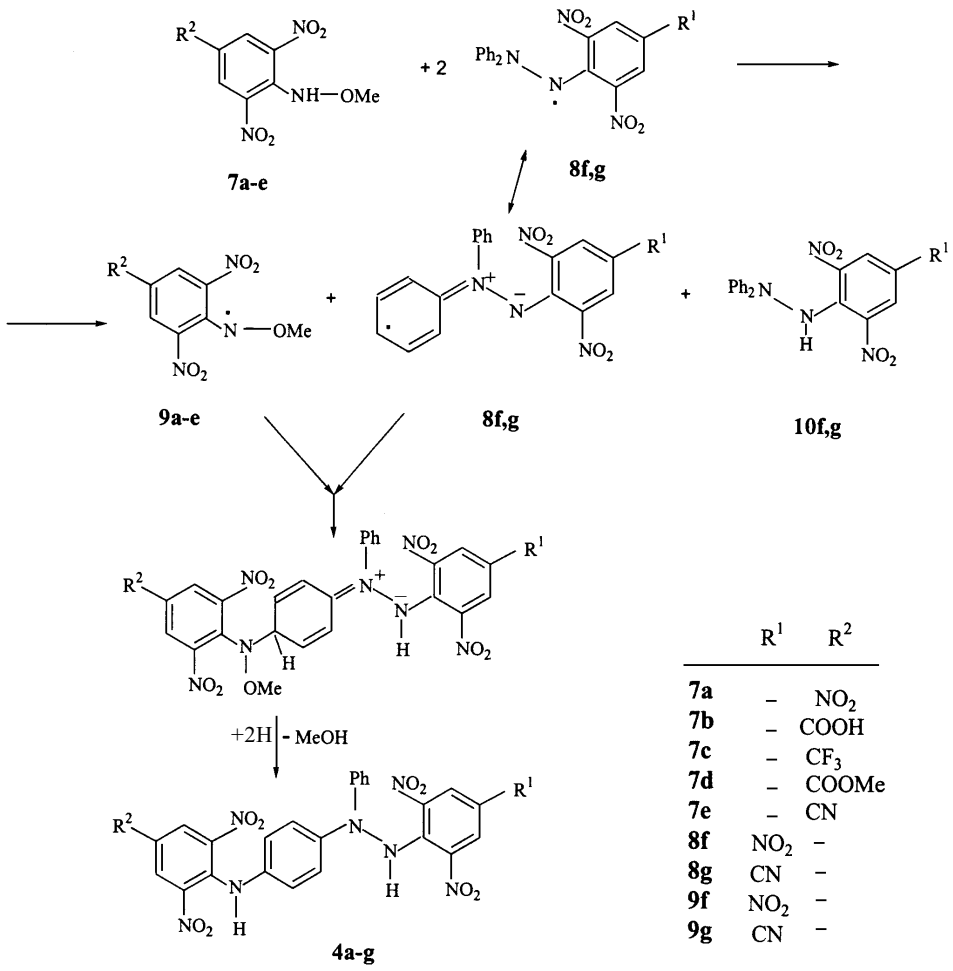


RESULTS AND DISCUSSION

Synthesis of the new betaines 4e–g: One molar equivalent of N-methoxyaniline **7** substituted with three nitro groups (N-methoxy-picramide, **7a**) or one 4-cyano and two 2,6-nitro groups (**7e**) was reacted with at least two molar equivalents of the stable free radical **8f** (2,2-diphenyl-1-picrylhydrazyl, DPPH) or its 4-cyano-2,6-dinitrophenyl analog (**8g**). Methanol is formed and eliminated, and one obtains the betaines **4e-g**, together with the hydrazine **10f** corresponding to DPPH (also called DPPH-ine or $DPPH_2$) or to its cyanodinitrophenyl analog.

One mole of the stable free radical oxidant (DPPH or cyanodinitrophenyl analog) is necessary first for forming a persistent alkoxyaminyl radical **9** from **7**; this alkoxyaminyl couples in a *para* position of a phenyl group in a second mole of DPPH or its cyanodinitrophenyl analog, by analogy with the reaction of DPPH with other free radicals such as nitrogen dioxide or bromine atoms (Scheme 1) [3–8].

Scheme 1



	R^1	R^2
7a	–	NO_2
7b	–	COOH
7c	–	CF_3
7d	–	COOMe
7e	–	CN
8f	NO_2	–
8g	CN	–
9f	NO_2	–
9g	CN	–

Some betainic structures with their opposite electrical charges concentrated mainly on nitrogen heteroatoms have found practical applications: indolic alkaloids such as serpentine and sempervirine can be used for determining cytochrome P-450 2D6 from human hepatic cells [9], and the strong oxidant TACOT (tetranitrodibenzo-1,3*a*,4,6*a*-tetraazapentalene) can be used for the determination of phenothiazinic compounds [10,11].

From Table 1 one can see that the yields of betaines **4** were higher when the molar ratio **7**:**8** was 2.5, but in this case unreacted starting material interfered in the chromatographic separation. When equimolar amounts of the two reactants were used in the presence of solid potassium permanganate (as indicated in the literature for obtaining DPPH from $DPPH_2$) [12], the yields were lower (Table 1), but TLC separation was eas-

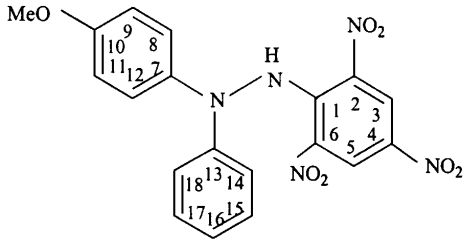
ier because one avoids byproducts with higher R_f values than those of the main products. It is likely, however, that in this case free radicalic byproducts may be formed, with lower R_f values than those of the main products, as will be shown below.

Table 1. Yields, R_f values and electronic absorption spectra of betaines **4a**, **4c–g**.

4	Yield (%)		R_f			λ_{max} (nm); log ε	λ_{max} (nm)
	I	II	A	B	C	D	E
a	80	67	0.46	0.82	0.44	579; 4.63	566
c	76	63	0.64	0.85	0.70	580; 4.70	564
d	58	45	0.20	0.66	0.25	590; 4.58	565
e	67	54	0.30	0.75	0.28	576; 4.80	557
f	63	51	0.25	0.72	0.27	583; 4.80	566
g	74	62	0.16	0.64	0.16	574; 4.69	548

I – Molar ratio **1**:**2** = 1:2.5;
II – Molar ratio **1**:**2** = 1:1;
A – Silica gel HPTLC Merck precoated plates, toluene three times;
B – Silanized silica gel GF 254 Merck, toluene one time;
C – Al_2O_3 GF 254 Merck, toluene three times;
D – Spectra in methylene chloride;
E – Spectra in adsorbed state, after TLC separation, on silica gel GF 254 Merck.

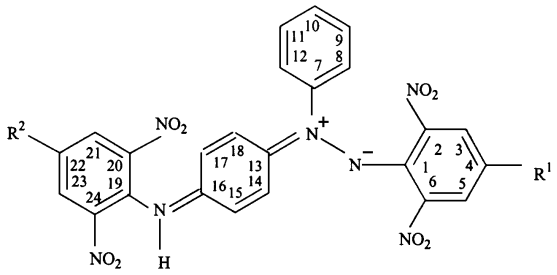
Properties and redox reactions of the new betaines 4e–g: The newly synthesized betaines **4e–g** present similar properties to those of their congeners reported earlier [1,2]: they do not melt below 300°C, but decompose above this temperature. They are insoluble in water, but dissolve in alcohols, acetone or halogenated solvents, affording solutions with intense blue-violet color. Their crystals are deep blue-violet with metallic luster. Tables 2 and 3 present the ^{1}H-NMR and ^{13}C-NMR spectra of betaines **4** obtained in this investigation, together with those of analogous products having other electron-attracting groups: instead of one 4-nitro substituent of the picryl group in N-methoxy-picramide one can have a carboxy or trifluoromethyl group (**4d** and **4c**, respectively) [13–16].



12

Tables 2. The ^{1}H-NMR comparative spectra of betaines **4a**, **4c–g** (δ values; *J* in Hz).

4	H-3,5	H-8,12	H-9,11	H-10	H-14	H-15	H-17	H-18	H-21,23
				in $CDCl_3$					
a	8.65 s	7.45 dd 1.8; 7.1	7.49 t 7.1	7.59 tt 1.8; 7.1	6.88 dd 2.6; 10	6.64 dd 1.9; 10	6.89 dd 1.9; 10	7.95 dd 2.6; 10	9.08 s
f	8.86 s	7.52 d 7.2	7.59 t 7.2	7.65 t 7.2	7.09 bd 10.2	6.87 bd 10.2	7.15 bd 10.0	8.00 bd 10.0	8.78 s
g	8.48 s	7.51 dd 1.7; 7.2	7.59 t 7.2	7.67 tt 1.7; 7.2	7.08 dd 2.6; 10.	6.83 dd 2; 10	7.12 dd 2; 10	8.01 dd 2.6; 10	9.15 s
e	8.05 s	7.43 d 7.3	7.48 t 7.3	7.57 t 7.3	6.83 dd 2.5; 10	6.58 dd 1.7; 10	6.84 dd 1.7; 9.9	7.92 dd 2.5; 9.9	8.47 s
d	8.62 s	7.43 d 7.1	7.48 t 7.1	7.57 t 7.1	6.86 dd 2.4; 9.9	6.65 dd 2.6; 9.9	6.89 dd 2.6; 10	7.90 dd 2.4; 10	8.84 s
c	8.77 s	7.52 dd 1.5; 7.1	7.58 t 7.1	7.67 tt 1.5; 7.1	7.10 dd 2.5; 10	6.89 dd 1.8; 10	7.18 dd 1.8; 10	7.99 dd 2.5; 10	8.73 q 0.7
				in $(CD_3)_2CO$					
a	8.80 s	7.53 dd 1.7; 7.0	7.59 t 7.0	7.68 tt 1.7; 7.0	7.13 dd 2.6; 10	6.88 dd 1.9; 10.	7.17 dd 1.9; 10	8.03 dd 2.6; 10	9.17 s
f	8.86 s	7.52 d 7.2	7.59 t 7.2	7.65 t 7.2	7.09 bd 10.2	6.87 bd 10.2	7.15 bd 10.0	8.00 bd 10.0	8.78 s
g	8.48 s	7.51 dd 1.7; 7.2	7.59 t 7.2	7.67 tt 1.7; 7.2	7.08 dd 2.6; 10.e	7.83 dd 2.0; 10	7.12 dd 2.0; 10	8.01 dd 2.6; 10	9.15 s
e	8.46 s	7.51 d 7.4	7.58 t 7.4	7.66 t 7.4	7.06 bd 10.4	6.82 bd 10.4	7.11 bd 10.3	7.99 bd 10.3	8.84 s
d	8.77 s	7.52 dd 1.8; 7.1	7.59 t 7.1	7.67 tt 1.8; 7.1	7.15 dd 2.4;10.2	6.87 dd 2.5; 10.2	7.09 dd 2.5; 9.9	7.99 dd 2.4; 9.9	8.84 s
c	8.77 s	7.52 dd 1.5; 7.1	7.58 t 7.1	7.67 tt 1.5; 7.1	7.10 dd 2.5; 10	6.89 dd 1.8; 10	7.18 dd 1.8; 10	7.99 dd 2.5; 10	8.73 q 0.7



4a-g

Table 3. The ^{13}C-NMR comparative spectra in acetone of betaines **4a, 4c–g**.

4	C-q	C-q	C-q	C-q	C-q	C-q	C-q	C-q
a	145.44	144.31	143.25	143.25	142.58	141.44 2C	140.25	140.25
f	144.43	144.14	143.51	143.33 2C	142.09 2C	140.40	140.17	107.92 C-22
g	145.63	144.18	142.86	142.51	142.45	141.67 2C	140.37 2C	105.75 C-4

Table 3 (continuation)

e	144.23	144.17	142.95	142.63	142.24 2C	140.36 2C	107.64 C-22	105.41 C-4
d	144.56	144.04	143.79	143.21 2C	141.68 2C	140.28	139.84	126.36 C-22
c	144.54	143.73	143.69	143.27 2C	142.09 2C	140.32	139.99	125.69

q = quaternary

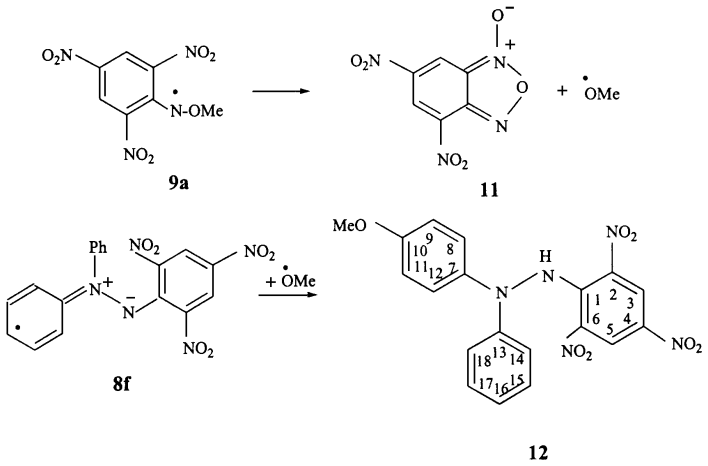
4	C-7	CH-10	2CH-9,11	2CH-8,12	CH-17	CH-14	CH-18	CH-15	2CH-21,23	2CH-3,5
a	162.49	133.81	131.44	128.23	130.40	129.42	129.29	127.80	125.48	124.79
f	162.63	133.82	131.48	128.34	130.67	129.83	129.60	128.03	134.04	124.81
g	162.53	133.74	131.43	128.23	129.93	129.41	129.23	127.18	125.45	133.22
e	162.70	133.71	131.43	128.25	130.08	129.20	129.09	127.38	133.96	133.44
d	162.55	133.74	131.44	128.29	130.54	130.42	129.00	128.12	130.78	124.61
c	162.93	133.79	131.46	128.32	129.11	129.08	128.97	127.56	127.53	124.77

The Hammett σ_p values are 0.81 for nitro and 0.70 for cyano groups. Thus, the nitro and nitrile groups are among the strongest electron acceptor substituents, but as will be seen below, the NMR chemical shifts and the electronic absorption maxima reveal subtle differences. Steric factors cannot be responsible for these differences, because only the *para*-substituents are involved. It can be observed from the proton-NMR spectra in two solvents (Table 2) that the bis-cyanodinitrophenyl derivative **4g** has the smallest chemical shifts for the H-21and H-23 protons in the marginal aryl ring connected to the isolated diarylamino nitrogen atom, and also for the H-3 and H-5 protons in the marginal ring connected to the hydrazylic nitrogen. In these betaines, a picryl group has therefore its protons more deshielded than a cyanodinitrophenyl group. In the ^{13}C-NMR spectra the CH carbon atoms are, however, less deshielded in the picryl groups (about 125 ppm) than in the cyanodinitrophenyl groups (about 134 ppm). In both cases, these carbon atoms are slightly more deshielded when they are connected to the diarylamino nitrogen than to the hydrazylic nitrogen. An interesting observation is that the hydrogen and carbon atoms of the two double bonds in the *para*-phenylene quinonoid ring are non-equivalent; this indicates that this limiting structure with the charges on the hydrazinic nitrogen atoms prevails in the resonance hybrid, preventing rotation on the NMR time scale. The electronic absorption spectra of betaines **4a, 4c–4g** were indicated in Table 1 both for their solutions in methylene chloride and in adsorbed state on silica gel, when a hypsochromic shift was noticeable. Absorption maxima of all betaines are in narrow ranges: 574–590 nm in solution, and 548–566 nm in adsorbed state. The lowest wavelengths are again for betaine **4e** with two cyanodinitrophenyl groups, and the next higher for betaine **4d** with the cyanodinitrophenyl group attached to the hydrazylic nitrogen. Surprisingly, the isomeric betaine **4f** with the cyanodinitrophenyl group attached to the diarylaminic nitrogen absorbs at a slightly higher wavelength than the betaine **4a** with two picryl groups.

Betaines **4** are readily reduced by a variety of agents such as ascorbic acid, glutathion, phenothiazine, diphenylamine, or hydroquinol, yielding the corresponding yellow-colored hydrazine derivatives **5**. An intermediate free radical **6** is involved in this reduction, but it is best obtained by oxidizing hydrazines **5** with solid potassium permanganate. The best reduction procedure involves a liquid-liquid or liquid solid biphasic process: the betaine is dissolved in methylene chloride, and the reducing agent (preferably ascorbic acid) is either solid or dissolved in water; the latter procedure is faster.

The R_f values in thin layer chromatographic separations on non-silanized (A) and silanized silica gel (B), or on alumina, are indicated in Table 1. The highest R_f values are obtained on silanized silica gel. For all three supports in TLC, the R_f values decrease in the following order: **4c** > **4a** > **4f** > **4e** > **4d** > **4g**. Thus, the 4-trifluoromethyl group of **4c** makes this betaine the most lipophilic; the bis-picryl betaine **4a** is intermediate, and all mono-picryl betaines have lower R_f values.

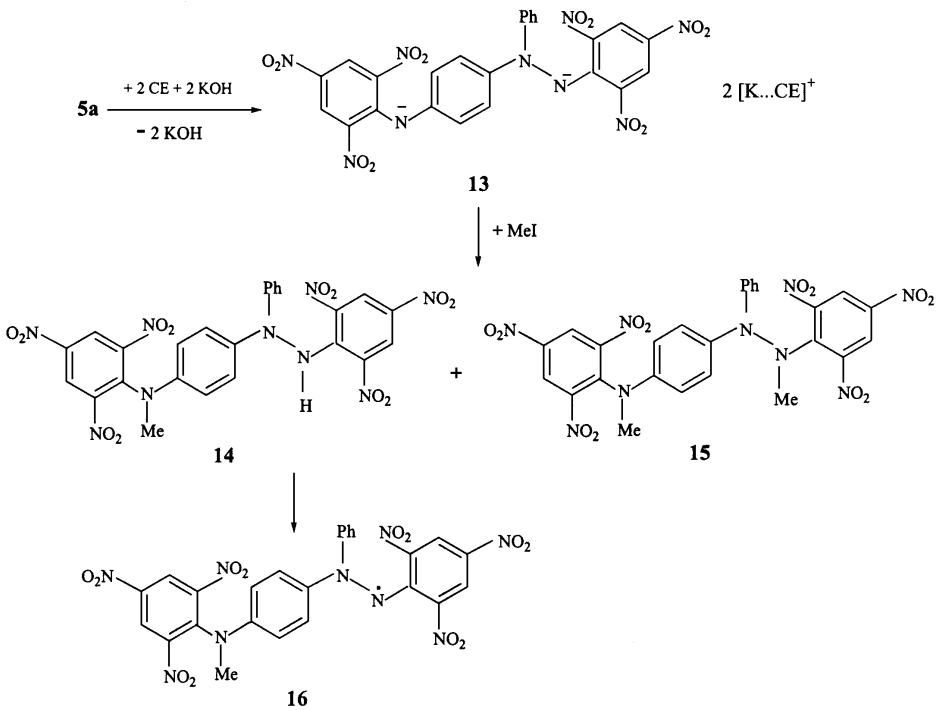
A secondary product obtained in the synthesis of betaine 4a: In order to find out what other products may result in this reaction, the synthesis of betaine **4a** from DPPH and N-methoxypicramide was reinvestigated. To the solution resulted after separating the betaine, ascorbic acid was added, the solvent was evaporated at reduced pressure, and the solid mixture was divided into smaller portions, dissolved in methylene chloride, and separated by TLC. On extracting the product with solvents that do not dissolve ascorbic acid (with $CDCl_3$ for NMR spectroscopy, or with methylene chloride followed by evaporation of the solvent for elemental analysis) it was possible to evidence the formation of 2-(4-methoxyphenyl)-2-phenyl-1-picrylhydrazine (**12**) in 30% yield when the molar ratio between DPPH and N-methoxypicramide was 2.5, and in very low yield when the ratio was 1.0. The formation of this orange-colored product, which is readily oxidized by air, indicates a homolytic reaction between DPPH and the methoxy radical. We know that methanol is eliminated during the formation of the betaine **4a**, but this secondary product **12** could not be prepared from DPPH and methanol or sodium methoxide in methylene chloride even in the



presence of the crown ether 18C6. This new compound (**12**) that affords a stable hydrazyl radical (as will be shown below) is related to 2,2-bis(4-methoxyphenyl)-1-picrylhydrazine which was obtained by synthesis [6,7]. A plausible mechanism for the generation of a methoxy free radical is *via* the splitting of the intermediate methoxyaminyl **9a** yielding also a dinitro-benzofuroxan derivative **11** (which could not yet be isolated from the complex reaction mixture).

Alkylation of hydrazines 5a and formation of stable hydrazylic free radicals: Owing to the electron-withdrawing properties of picryl and related groups, hydrazine derivatives **4** are acidic. The complexed dipotassium salt **13** of the bis-picryl hydrazine derivative **5a** can be readily obtained from **5a** with excess potassium hydroxide and 18-crown-6 ether (18C6) in methanol (molar ratios 1:2:2, as established by ^{1}H-NMR and electronic absorption spectra). This supramolecular complex **13** reacts with excess methyl iodide in methylene chloride affording a dimethylated (**15**) and a monomethylated derivative (**14**). The yield of the latter product was about twice higher in our reaction conditions. Without 18C6, methylation attempts failed.

In the monomethyl compound, it was the diarylamino nitrogen atom, and not the hydrazinic NH group that underwent methylation, as shown by NMR spectroscopy and by oxidation to a stable hydrazylic free radical, **16**, as will be shown below. Very slowly, this isolated monomethyl derivative **14** could be further methylated to the dimethyl derivative **15**, which is stable towards oxidation. The lower reactivity

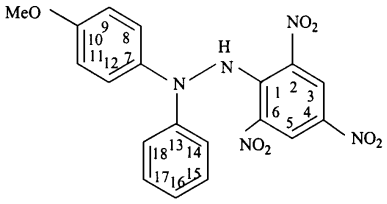


(nucleophilicity) towards alkylation of the hydrazinic nitrogen than that of the isolated nitrogen is probably due to the lower contribution of the less stabilized *para*-quinonoid resonance formula (see the two limiting structures for **4**) to the resonance hybrid.

The methylation of DPPH-ine **10f** under the same conditions affords the corresponding N-methyl derivative of DPPH-ine, **17**, which is stable towards potassium permanganate. The NMR spectra of hydrazines **12**, **14**, **15**, and **17** are presented in Table 4.

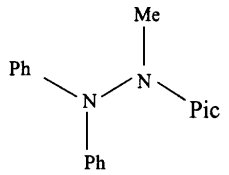
Table 4. NMR spectra of hydrazines **12**, **14, 15,** and **17**.

12	**^{1}H-NMR** ($CDCl_3$, δ ppm, *J* Hz): 10.04 (1H, bs, NH, deuterable); 9.21 (1H, s, H-3/5); 8.53 (1H, bs, H-5/3); 3.80 (3H, s, OCH_3); 6.88 (2H, d, H-9, 11, 9.1); 7.11 (2H, d, H-8, 12, 9.1); 7.01 (2H, dd, H-14, 18, 1.6, 7.5); 7.16 (1H, tt, H-16, 1.6, 7.5); 7.32 (2H, t, H-15, 17, 7.5).
14	**^{1}H-NMR** ($(CH_3)_2CO$-d_6, δ ppm, *J* Hz): 3.38 (3H, s, CH_3); 3.13 (3H, s, CH_3); 9.05 (2H, s, H-21, 23); 8.71 (2H, s, H-3,5); 7.30 (2H, dd, H-9, 11, 7.0, 8.9); 7.26 (1H, tt, H-10, 1.8, 7.0); 7.10 (2H, dd, H-8, 12, 1.8, 8.9); 7.08 (2H, d, H-15, 17, 9.0); 6.92 (2H, d, H-14, 18, 9.0).
15	**^{1}H-NMR** ($(CH_3)_2CO$-d_6, δ ppm, *J* Hz): 10.74 (1H, s, H-α); 9.03 (2H, s, H-21, 23); 8.75 (1H, bs, H-5/3); 7.31 (2H, dd, H-9, 11, 7.0, 8.8); 7.26 (1H, tt, H-10, 1.8, 7.0); 7.12 (2H, dd, H-8, 12, 1.8, 8.8); 7.18 (2H, d, H-15, 17); 6.95 2H, (d, H-14, 18, 9.1); 3.36 (3H, s, CH_3). **^{13}C-NMR** ($(CH_3)_2CO$-d_6, δ ppm): 149.00(Cq-19); 147.17 (Cq-7); 143.82 (Cq-20, 24); 142.76 (Cq-16); 141.52 (Cq-1); 140.64 (Cq-22); 140.48 (bs, Cq-2/6); 137.17 (Cq-4); 134.97 9bs, Cq-6/2); 130.67 (2CH-21, 23); 129.63 (bs, CH-3/5); 125.68 (bs, CH-3/5); 125.01(CH-10); 123.71 (2CH-8, 12); 119.92 (2CH-14, 18); 118.23 (2CH-15, 17); 40.61 (CH_3).
17	**^{1}H-NMR** ($CDCl_3$, δ ppm, *J* Hz): 8.49 (2H, s, H-3,5); 7.36 (4H, dd, H-9, 11, 15, 17, 7.2, 8.8); 7.21 (2H, tt, H-10, 16, 1.1, 7.2); 7.08 (4H, dd, H-8, 12, 14, 18, 1.1, 8.8); 3.09 (CH_3). **^{13}C-NMR** ($CDCl_3$, δ ppm, *J* Hz): 142.39 (C-7, 13); 139.95 (C-1); 136.63 (C-4); 129.36 (C-9, 11, 15, 17); 125.56 (C-10, 16); 123.68 (C-3,5); 120.63 (C-8, 12, 14, 18); 37.11 (CH_3).

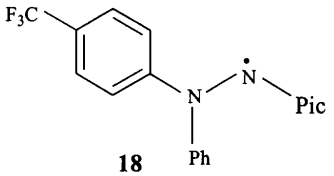


12

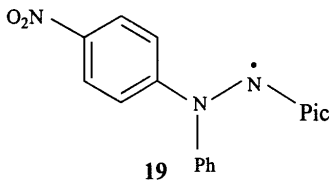
A solution of the monomethylated hydrazine **14** in methylene chloride was oxidized by solid potassium permanganate yielding a blue-violet solution containing the stable free radical **16**. Its ESR spectrum presents five broad lines (like DPPH in the same solvent) with average hyperfine coupling constant (hfc) for the two hydrazylic nitrogen atoms a_N = 8.60 Gauss, similarly to DPPH. The radical is stable in solution and in solid state, and is reduced by ascorbic acid regenerating the hydrazine **14**.



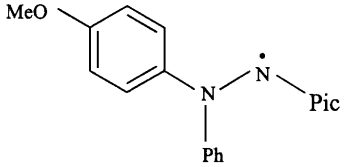
17



18



19



20

We obtained similarly a stable free radical **18** (**6g** with $R^1 = NO_2$, $R^2 = CF_3$) with an ESR spectrum also presenting five broad lines in the same conditions, due to two averaged hfc's $a_N = 8.95$ Gauss. Previously, it had been shown by ENDOR techniques [6,7,17] that the free radical obtained from hydrazine **10a** had two unequal hfc's for the two hydrazylic nitrogen atoms, namely $a_{N1} = 10.5$ Gauss and $a_{N2} = 7.07$ Gauss; the radical **19** formed from the *para*-nitro-DPPH was also shown to have two unequal hfc's [6].

Oxidation of the 4-methoxy-DPPH-ine **12** with potassium permanganate in methylene chloride afforded a stable hydrazyl **20** with five broad lines in its ESR spectrum having an average hyperfine coupling constant for the two hydrazylic nitrogen atoms $a_N = 8.80$ Gauss.

CONCLUSIONS

Three new betainic compounds (**4e-g**) were prepared. This involved replacing by a cyano group the 4-nitro group of the previously described 1-picryl-2-phenyl-2-(*para*-picramidophenyl)-diazenium betaine (**4a**). The properties of the bis-cyano-dinitro (**4e**) and the mono-cyanodinitro (**4f, 4g**) congeners are similar to those of the preceding betaines **4a-d** described previously. The cyano group behaves in electronic absorption spectra and NMR spectra as a slightly less powerful electron-withdrawing group than the nitro substituent, in agreement with the Hammett sigma-parameter scale.

A byproduct in the formation of betaine **4a** was identified as the 4-methoxy-DPPPH-ine **12**, which can be oxidized to a stable hydrazyl free radical **20**.

The dipotassium salt of hydrazine derivative **4a** forms a supramolecular complex **13** with18-crown-6 ether, which can be mono- or dialkylated with methyl iodide. The monomethyl derivative has the methyl attached to the diarylamino nitrogen atom, and oxidation by potassium permanganate converts it into a stable hydrazylic radical **16**.

EXPERIMENTAL

NMR Spectra were recorded with a Varian Gemini 300BB instrument. Electronic absorption spectra were obtained with a Specord UV-VIS Carl Zeiss (Jena) spectrophotometer. The visible absorption spectra for compounds adsorbed on silica gel were determined with a densitometer (CAMAG Software 1992 Scanner II) after developing the chromatographic plates. ESR spectra were recorded with a Jeol JES-3B instrument. The synthesis of N-methoxyaniline derivatives **7a–d** [2,18] and of hydrazine **10g** was described earlier [19]. The stable free radical DPPH (**8f**) was purchased from Fluka; radical **8g** (the *para*-cyanodinitrophenyl analog of DPPH) was prepared by oxidizing the corresponding hydrazine [20] with potassium permanganate. The hydrazine derivative **5a** was prepared by reducing the betaine **4a**. Other reagents were of analytical purity.

*General procedure for the synthesis of betaines **4e–g**. Variant A*: molar ratio **7**:**8** = 1:2.5. For obtaining betaine **4f**, the reactants (4-cyano-N-methoxy-2,6-dinitroaniline, **7e**) and **8f** (DPPH) were stirred in methylene chloride solution at room temperature for 24 hrs. The product was isolated by preparative thin layer chromatography (TLC) on silica gel Merck GF 254 (toluene, three times). The product **4f** was extracted with dichloromethane and after evaporating the solvent it crystallized (blue-violet with metallic reflexes). It does not melt below 300°C but decomposes gradually at higher temperatures. Betaines **4e** and **4g** were prepared from N-methoxyaniline derivatives **7e** and **7a**, respectively, and the *para*-cyano congener of DPPH (**8g**). The latter stable free radical **8g** was obtained by stirring the corresponding hydrazine **10g** with solid potassium permanganate in dichloromethane for 24 hrs at room temperature, and drying the solution with anhydrous sodium sulfate. Into the filtered solution of the free radical, the corresponding amount of the N-methoxyaniline derivative was added and the resulting solution was kept at room temperature for 24 hrs. The TLC purification was carried out as described above. The properties of all these betaines are similar; differences arise in R_f values, electronic absorption spectra (both in solution and in adsorbed state) and in NMR spectra, as shown in Tables 1–3.

Variant B: molar ratio **7**:**8** = 1:1. For betaine **4f**, stoichiometric amounts of **7e** and **8f** (DPPH) were dissolved in dichloromethane, solid potassium permanganate in 20-fold molar excess was added with solid anhydrous sodium sulfate (5-fold molar excess), and the mixture was stirred for 24 hrs at room temperature. After filtration, the solution was worked up as described above for variant A. For betaines **4e** and **4g**, the stable free radical **7g** was obtained *in situ* from the corresponding methoxyaniline derivative and solid potassium permanganate in methylene chloride. Hydrazine derivatives **8e** and **8g** , respectively, were added in stoichiometric amounts. Then the same procedure was followed as in variant A, but solid $KMnO_4$ and anhydrous Na_2SO_4 were present in the same molar excess as indicated above for this variant B. After stirring for 24 hrs and filtration, the resulting solution was worked up as described above for variant A. Yields for both variants A and B were presented in Table 1; the ease of TLC separations for variant B make it preferable despite the lower yields. It will be seen that in variant A, a major secondary product **12** is formed. Elemental analyses: Calc. for **4e**, $C_{26}H_{13}N_9O_8$: C, 53.88; H, 2.26; N, 21.76. Found: C, 54.00; H, 2.14; N, 21.80%. Calc. for **4f**, $C_{25}H_{13}N_9O_{10}$: C, 50.09; H, 2.19; N, 21.03. Found: C, 50.08; H, 2.20; N, 21.15 %. Calc. for **4g**, $C_{25}H_{13}N_9O_{10}$: C, 50.09; H, 2.19; N, 21.03. Found: C, 50.11; H, 2.17; N, 21.10%.

*Detection of the secondary product **12,** 2-(4-methoxyphenyl)-2-phenyl-1-picrylhydrazine in the synthesis of betaine **4a***. The mixture of DPPH (**8f**) and N-methoxypicramide (**7a**) in molar ratio 2.5 : 1 was stirred in methylene chloride for 24 hrs at room temperature. Preparative TLC on silica gel GF 254 Merck eluted with toluene three times followed by extraction with methylene chloride yielded (after adding ascorbic acid, evaporating the solvent and extraction with a solvent which does not dissolve ascorbic acid) in 30% yield the yellow-orange compound **12**, with an R_f value slightly lower than that of DPPH. It is so easily oxidized by air that it does not present an exact melting point. At a molar ratio 1:1 of the two reactants, compound **12** is detected only in traces, which makes TLC separations easier. Analysis: Calc. for $C_{19}H_{15}N_5O_7$: C, 53.65; H, 3.55; N, 16.46. Found: C, 53.79; H, 3.53; N, 16.50%. The NMR spectrum is presented in Table 4.

*General procedure for preparing the supramolecular complex **13***. The hydrazine derivative **5a** (*para*-picramido-DPPH-ine) and finely ground solid potassium hydroxide (molar ratio 1:2) were stirred in methanol till they dissolved. To the brick-red resulted solution, 18-crown-6 ether (molar ratio **5a**:18C6 = 1:2) was added, together with a minimal amount of dichloromethane for homogenizing the solution. On adding petroleum ether (30–60°) a viscous oily precipitate was formed. After decanting the solvent the

product was dissolved in methylene chloride; on adding gradually petroleum ether and scratching with a glass rod, the solid red-brown supramolecular complex **13** was obtained in practically quantitative yield. The molar ratio is 1:2:2 between the dianion of **13**, potassium cation, and 18C6, as shown by UV-VIS spectra (by acidifying an ethanolic solution of a weighed sample of the complex and determining the relative amount of hydrazine **5a**). This ratio was confirmed by NMR spectroscopy. ^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz): 8.58 (2H, s, H-21,23); 8.52 (1H, d, H-3/5, 2.6); 8.37 (1H, d, H-5/3, 2.6); 7.15 (2H, dd, H-9,11, 7.1, 8.8); 7.04 (2H, dd, H-8,12, 1.4, 8.8); 6.89 (2H, d, H-14,18, 8.8); 6.88 (1H, tt, H-10, 1.4, 7.1); 6.61 (2H, d, H-15,17, 8.8); 3.62 (48H, s, H-crown).

*General procedure for preparing methylated hydrazine derivatives using supramolecular complexes: 2-phenyl-2[4-(N-methylpicramido)phenyl]-1-picrylhydrazine (**14**), and 2-phenyl-2[4-(N-methylpicramido)phenyl]-1-methyl-1-picrylhydrazine (**15**)*. A solution of the supramolecular complex **13** in dichloromethane was treated with a 10-fold molar excess of methyl iodide at room temperature for five days. The progress of the reaction was followed by TLC (silica gel Merck GF 254, toluene, three times). The resulting solution was extracted three times with 1M hydrochloric acid, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Preparative TLC was used for separating the mon- and dimethylated products, which were extracted from the silica gel after separation into methylene chloride. Yields were 38% for the monomethyl derivative, **14**, and 20% for the dimethylated one, **15**. Unreacted starting materials from **13** were recovered in 6% yield. These hydrazine derivatives do not have definite melting points, but decompose gradually. Elemental analyses: Calc. for **14**, $C_{25}H_{17}N_9O_{12}$: C, 47.25; H, 2.70; N, 19.84. Found: C, 47.33; H, 2.77; N, 19.70%. Calc. for **15**, $C_{26}H_{19}N_9O_{12}$: C, 48.08; H, 2.95; N, 19.41. Found: C, 48.12; H, 2.93; N, 19.39%.

*Reductions **4** → **5*** were carried out either in a biphasic liquid-liquid system (with an aqueous solution of ascorbic acid in excess and a methylene chloride solution of betaines **4**), or in a biphasic solid-liquid system (with solid ascorbic acid in excess, and a methylene chloride solution of betaines **4**).

*Oxidations **5** → **4*** were performed in a biphasic solid ($KMnO_4$) – liquid system (methylene chloride solution of betaines **4**).

*Synthesis of 2,2-diphenyl-1-methyl-1-picrylhydrazine (**17**)*. The potassium salt of DPPH-ine was converted into its supramolecular complex with 18C6, as described previously [18]. Similarly to the preceding methylation of **5a**, this complex was dissolved in dichloromethane and treated with an excess of methyl iodide at room temperature for 5 weeks. The yield was practically quantitative, m.p. 151°C. No color change occurs on treatment with potassium permanganate. Elemental analysis: Calc. for $C_{19}H_{15}N_3O_6$: C, 59.84; H, 3.96; N, 11.02. Found: C, 59.80; H, 4.00; N, 11.01%.

*Preparation of stable hydrazylic free radicals **16, 18, and 20***. Methylene chloride solutions of hydrazine derivatives **14**, **4c**, and **20**, respectively, were stirred with excess solid potassium permanganate for 30 minutes at room temperature. The resulting blue-violet solutions were filtered, and the solvent was evaporated under reduced pressure. The free radicals were purified by TLC. ESR Spectra were recorded in deaerated methylene chloride solution. Hyperfine coupling constants were determined by comparison with Frémy's salt. All ESR spectra of hydrazyls **16**, **18**, and **20** were similar to that of DPPH in the same solvent, presenting five broad lines.

REFERENCES

1. Constantinescu T., Caproiu M.T., Zarna N., Caragheorgheopol A., Caldararu H., Stanciuc G., Radu M., Badescu V. and Balaban A.T., *New J. Chem*., **21**, 575 (1997).
2. Covaci I.C., Constantinescu T., Caproiu M.T., Draghici C., Ionita P., Luca C., Stanciuc G., Maganu M. and Balaban A.T., *Rev. Roum. Chim*., **44**, 333 (1999).
3. Currie P.F., Quail J.W. and Weil J.A., *Can. J. Chem*., **58**, 723 (1980).
4. Currie P.F., Quail J.W., Rusk A.C.M. and Weil J.A., *Can. J. Chem*., **61**, 1760 (1983).
5. Weil, J.A., Sane K.V. and Kinkade J.M., *J. Phys. Chem*., **65**, 710 (1961).
6. Chen M.M., Sane K.V., Walter R.I. and Weil J.A., *J. Phys. Chem*., **65**, 713 (1961).
7. Walter R.I., *J. Am. Chem. Soc*., **88**, 1923 (1966).
8. Gille I.M., Prosch T. and Stoesser R., *Radiat. Phys. Chem*., **40**, 461 (1992).
9. Strobl G.R., von Kruedener S., Stockigt J., Guengerich F.P. and Wolff T., *J. Med. Chem*., **36**, 1136 (1993).

10. Forrest J.E. and Heacock R.A., *J. Chromatogr.*, **75**, 156 (1973).
11. Carboni R.A., Kauer J.C., Hatchard W.R. and Harder R.J., *J. Am. Chem. Soc*., **89**, 2626(1967).
12. Brown K.C. and Weil J.A., *Can. J. Chem*., **64**, 1836 (1986).
13. Stanciuc G., Caproiu M.T., Caldararu H., Caragheorgheopol A., Constantinescu T. and Balaban A.T., *Z. Naturforsch*., **44b**, 1459 (1989).
14. Stanciuc G., Constantinescu T., Caproiu M.T., Zarna N., Caragheorgheopol A., Caldararu, H. and Balaban A.T., *Rev. Roum. Chim*., **41**, 395 (1997).
15. Sumi T.J., Stanciuc G., Balaban A.T. and Joela H., *Magn. Reson. Chem*., **34**, 197 (1996).
16. Sumi T.J., Stanciuc G., Kasa, S. and Joela H., *Magn. Reson. Chem*., **33**, 511 (1995).
17. Chen M. M., D'Adamo Jr. A.F. and Walter R.I., *J. Org. Chem*., **26**, 2721 (1961).
18. Covaci I.C., Constantinescu T., Caproiu M.T., Dumitrascu F., Luca C. and Balaban A.T., *Rev. Roum. Chim*., **44**, 531 (1999).
19. Luca C., Ionita P. and Constantinescu T., *Rev. Roum. Chim*., **39**, 1141 (1994).
20. Ilyasov Yu.M., Ryzhmanov, L.I. and Shatrukov L.E., *Optika Spektr.*, **15**, 340 (1963).