Scientific report 2011-2016

for the project PN-II-ID-PCE-2011-3-0408

The project PN-II-ID-PCE-2011-3-0408, entitled ‘Multifunctional organic stable radicals in supramolecular high-spin architectures and materials’, has as main objective the synthesis and structural characterization of new free radicals, which can be involved in a multitude of processes.

1. Synthesis of new (poly)radicals

The synthesis of all the compounds used in this work, namely stable monoradicals **1a-e**, diradicals **2a-d**, and triradical **3a** (Fig. 1) was performed practically in one or two steps, starting from commercially available compounds. Thus, 4-amino-tempo reacts with selected halogen-reactive derivatives (*via* a nucleophilic substitution) to yield compound **1a**, **1e** and **2d**. A key intermediate in the synthesis of the other compounds was 4-isocyanato-tempo, obtained from 4-amino-tempo, as literature data showed. 4-Isocyanato-tempo easily reacts with selected amine yielding urea derivatives **1b-d** and **2a-c**. Both types of reactions occur with good yields.

All the thus obtained derivatives were characterized by elemental analysis, ESI-MS, UV-Vis and IR spectrometry, and EPR. For the derivatives **1a** and **1c,** obtained as crystals, X-ray diffraction has been also employed to characterize their structures. All analyses confirmed the purity and the structure of the obtained (poly)radicals.

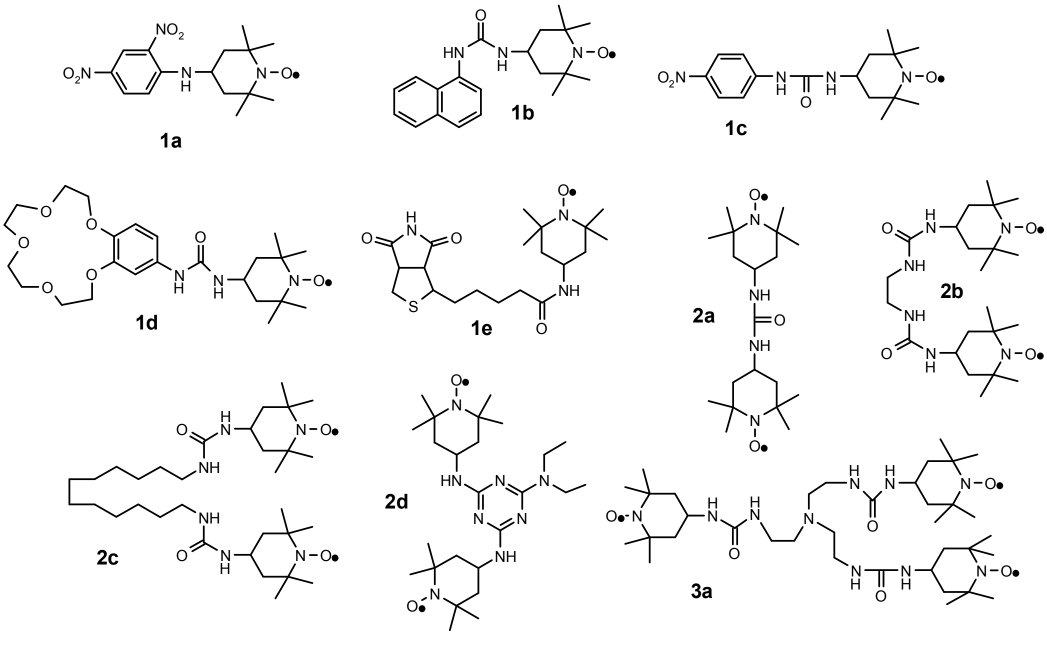


Fig. 1. Structure of the new free radicals.

2. Thermal analysis of some stable free radicals

Polynitroaromatic compounds (including explosives) are well studied derivatives, due to their high economical and environmental impact. Literature data is scarce in details about the thermal decomposition of hydrazyl free radicals. In this work the compounds shown in Fig. 2, together with their corresponding hydrazines, were studied by means of differential thermal analysis (DTA) and thermogravimetric analysis (TG). A mechanism of thermal decomposition is proposed based on the identification of some known products found in the residue after the thermal decomposition.

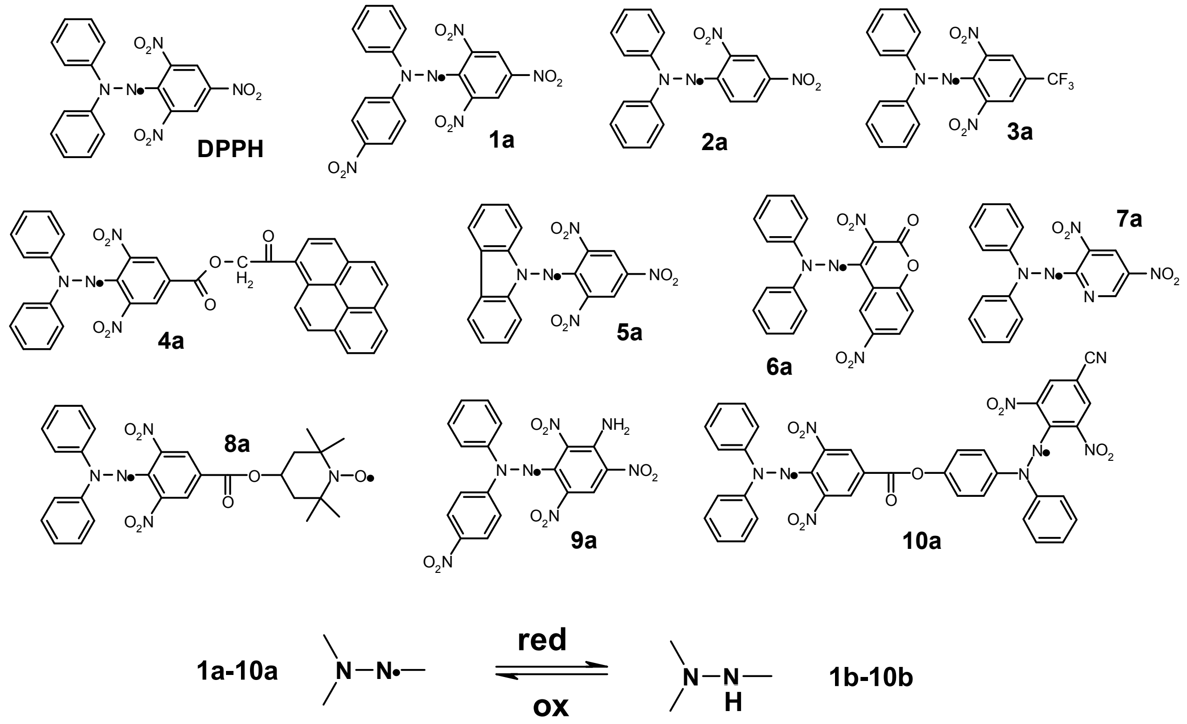


Fig. 2. Chemical structure of the stable free radical DPPH, its congeners **1a-10a** and hydrazines **1b-10b**

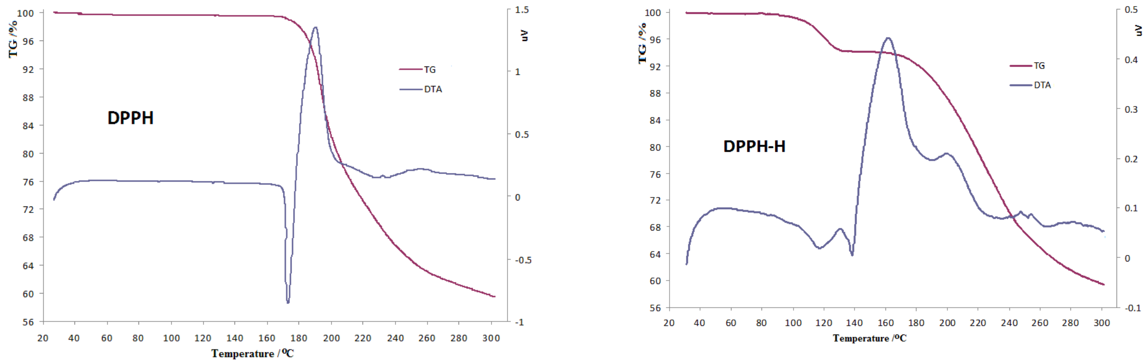
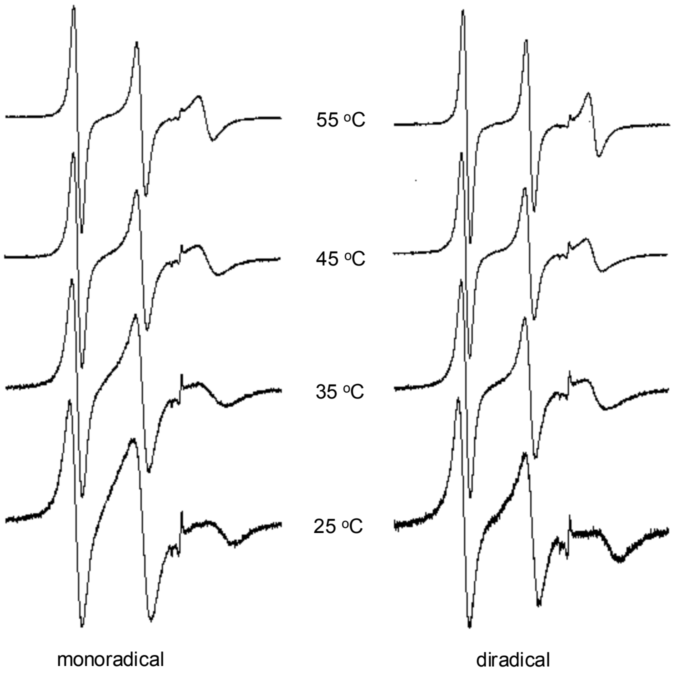


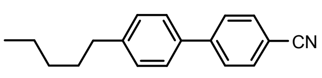
Fig. 3. DTA/TG analysis for DPPH and DPPH-H

3. Polyradicals in liquid crystals

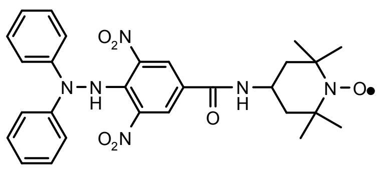
Liquid crystals are molecular materials with very high impact in many fields of science; for example, they have anisotropic properties and can be orientated under magnetic or electric fields, making them extremely attractive compounds for different types of applications (most known being the light modulating properties used in displays).

Stable organic mono- and poly-radicals have been also used as novel molecule-based organic magnetic materials with multi-functionality; spin systems with magnetic properties depending on external stimuli such as heat and light are also present in literature. Di- and poly-radicals were studied as well; for example, the EPR of ground state triplets in liquid crystals solutions have been studied since 60's. Those studies showed that it is possible to align planar molecules with their plans parallel to the magnetic field using a nematic liquid crystals as solvent.





5CB



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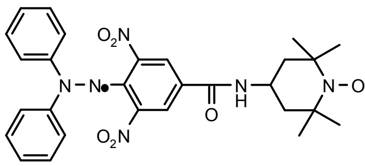


2

Fig. 4. ESR spectra of a diradical at different temperatures

4. Synthesis of a betaine-diradical of imino-nitroxide type

Betainic compounds derived from the DPPH stable free radicals are known since 1997; these are intense coloured compounds with multifunctional properties, such are redox and acid-base. In this work is shown a multistep synthesis which finally led to the obtaining of a betainic imino-nitroxide stable free diradical, with multifunctional properties.

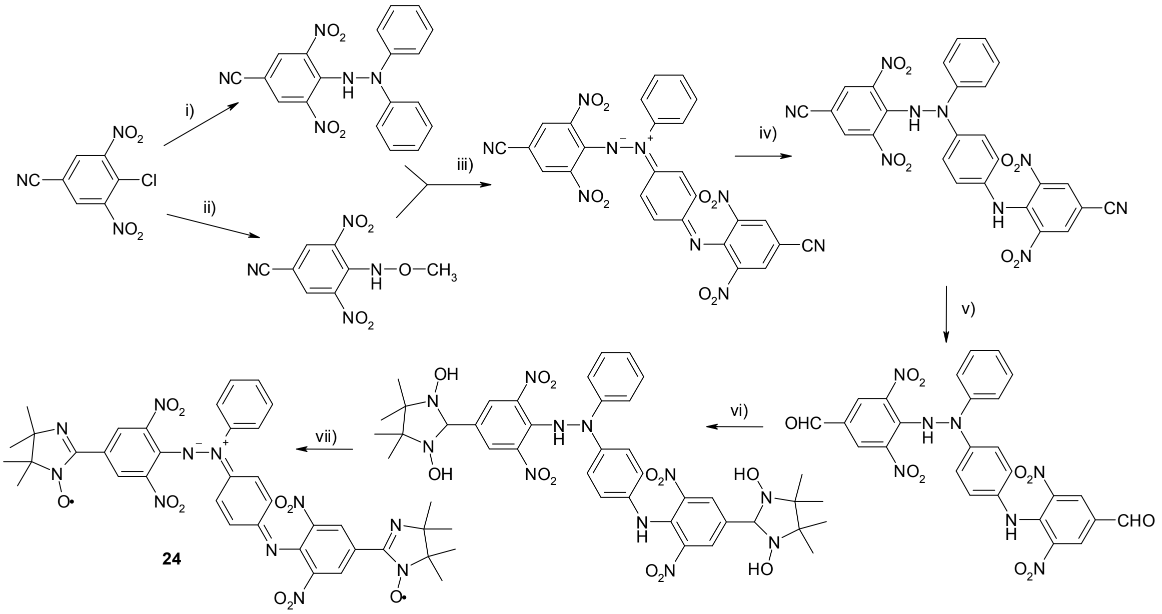


Fig. 5. Reactions scheme for the obtaining of the diradical **24**

One of the most interesting properties of the betainic diradical is its intense blue colour. UV-Vis spectrum showed a maximum absorption at 552 nm (Fig. 6), due to the extended conjugation system. Reduction with ascorbic acid or sodium ascorbate led to the corresponding hydrazine-hydroxylamine derivative, with a yellow colour, having a maximum absorption at 405 nm, and of course no ESR signals. This type of interconversion of such species is well known and can be used to study or monitor redox reactions (by reduction the ESR signals disappears, but can be restored by oxidation).

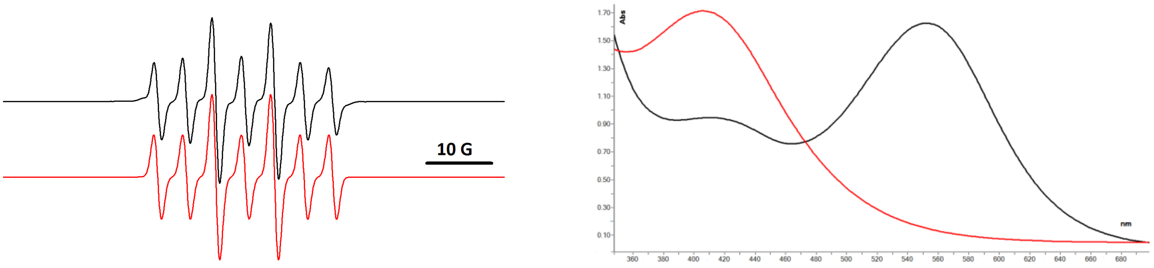


Fig. 6. ESR spectra and UV-Vis measurements

5. Synthesis of some biological active compounds (including free radicals)

Design and synthesis of novel medicines is a quite long and expensive process, requesting a tremendous amount of work. Besides, the chosen chemical as a prospective medicine has to pass a huge number of tests, in which all the aspects of the possible chemical and biological factors has to be carefully addressed.

Benzocaine (and antypyrine), an anesthetic, a simple chemical compound that induces pain relief, is used in topical, dermal and mucous formulations; because its low water solubility, benzocaine cannot be used in parenteral administration. As any medicine, benzocaine has advantages and week issues, therefore new derivatives containing as substructure the benzocaine moiety are always of interest.

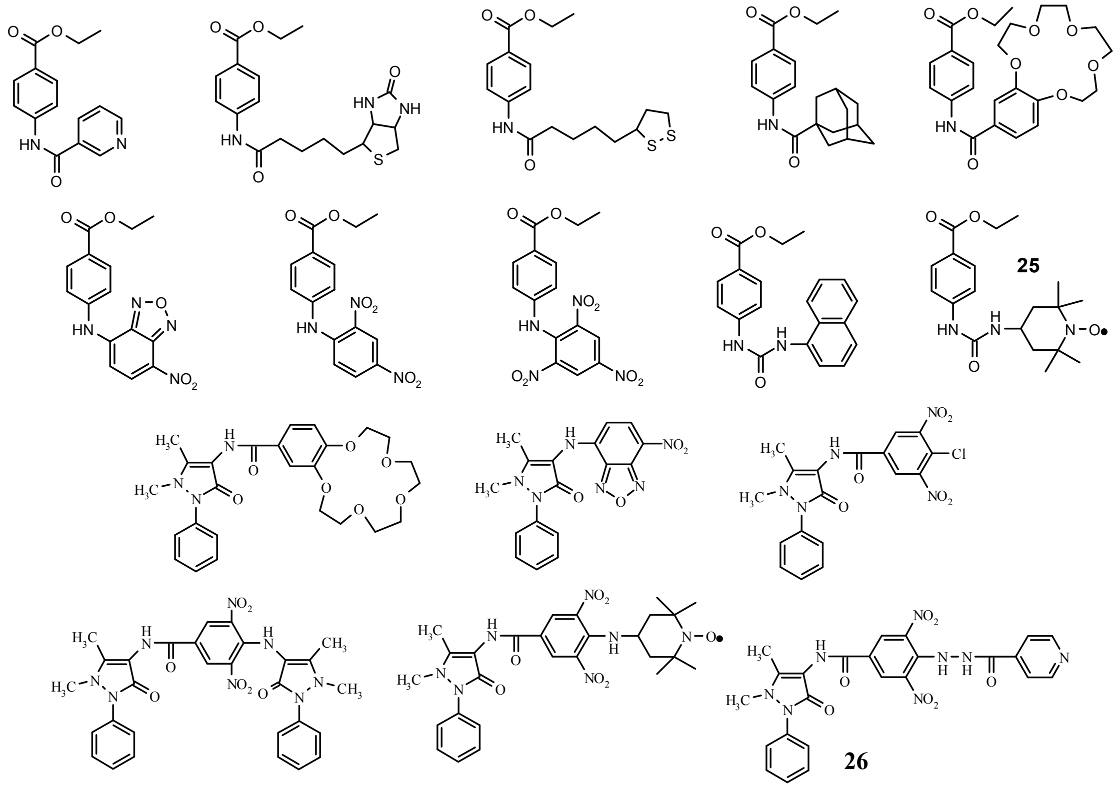


Fig. 7. The new compounds synthesized

Starting from benzocaine or antypyrine, all the compounds were obtained practically in a single step, coupling benzocaine with the desired compound. Thus, to obtain the desired compounds, the coupling reactions between benzocaine and the required carboxylic acids have been tried in three different types of reactions, to get the highest yields: *i*) coupling using DCC; *ii*) coupling using EEDQ; *iii*) coupling using the corresponding acid chloride of the carboxylic acid. It was shown that the higher yields were obtained by using the corresponding acid chloride of the carboxylic acid; between EEDQ and DCC, EEDQ is a better coupling agent.

6. Acid-base interaction between two types of nanoparticles

Producing nanomaterials with new properties by simple combination of two types of NPs has the potential to develop new materials and applications. For a reversible property, the main problem which arises is the way to obtain a homogenous material and to stabilize the mixture by non-covalent bonds.

Formation of hydrogen bonds leads to strong interactions, and moreover, they may be tuned by pH. Acid-base interaction between an amino group and the carboxyl group can be regarded as a particular case of hydrogen bond formation. Amino- or carboxyl- terminated protected NPs are well known in literature for their straightforward functionalization; dissociable assemblies of these different types of NPs may be thus easily formed and pH controlled.

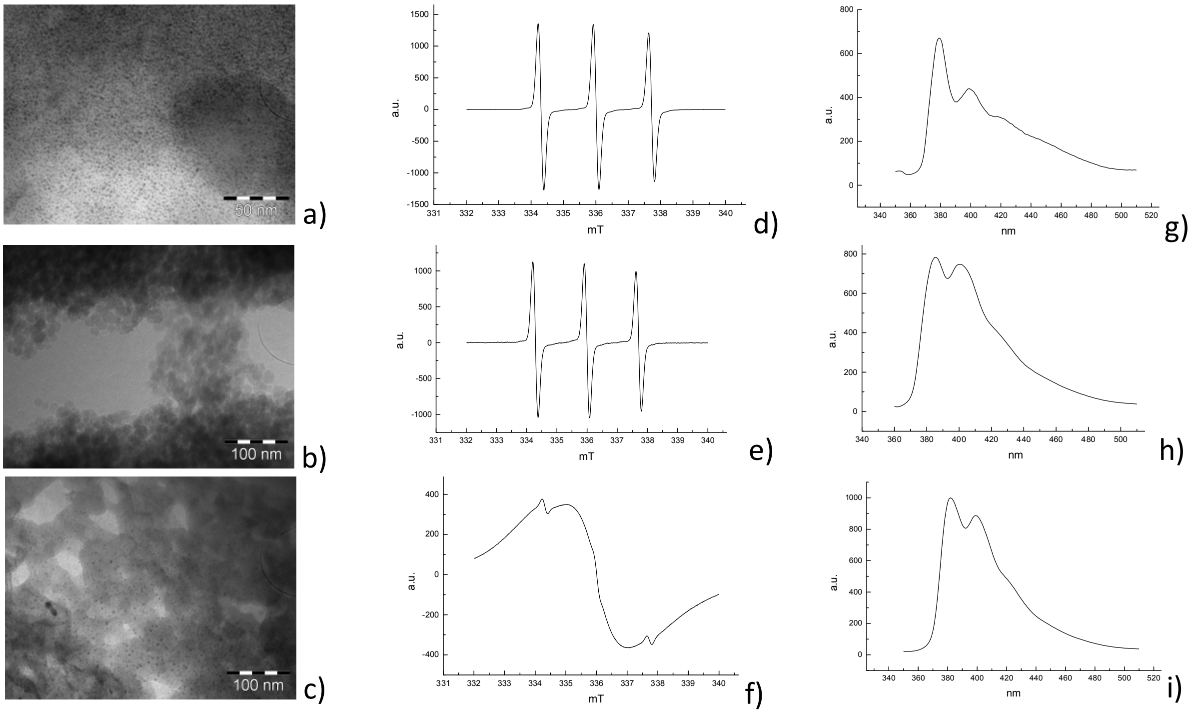


Fig. 8. TEM images (a-c), ESR spectra (d-f) and fluorescence measurements (g-i) for gold and silica nanoparticles

Our test experiments showed indeed that the aggregation is reversible, so by a simple pH change (adding a strong acid or a base to the mixture), the aggregates dissolute. pH measurements indicated that at around pH 4 or below, or at pH 10 or higher, the aggregates start to dissolute (they are stable as aggregates only in a pH range of 5-9). It is worth to mention that at extreme low pH Tempo moiety is unstable; as well, at extreme high pH silica NPs are destroyed; however, those changes occurs in a harmless range of pH values.

7. Detection of some nitroderivatives using free radicals processes

The procedure described below is based either on the exclusion of nitro groups from explosives as nitrite (alkaline way), using a strong base (like sodium or potassium hydroxide), or on the thermal exclusion of nitro groups from explosives as nitrogen dioxide (thermal way). In the case of nitrite anions, these in acid environments and in the presence of air forms nitrogen dioxide, and this, generated in either ways, converts ABTS into its extremely intense colored radical cation (Figure 2). The detection of nitrogen dioxide using ABTS is also known in literature.

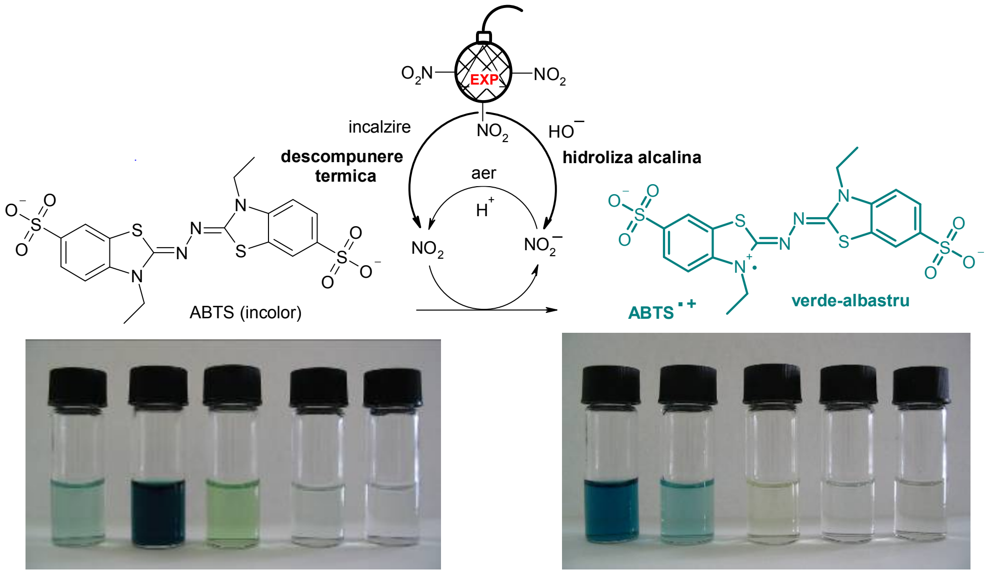


Fig. 9. Identification of explosives

The most important issue in the processes described is the formation of nitrogen dioxide and its catalytic task. Indeed, in the first way of work, nitrite anions expulsed by the alkali hydroxide are converted in acid media to nitrogen oxides (NO_x), such are nitric oxide (NO) and nitrogen dioxide (NO_2), and the open air process help the formation of the later. NO_x are known to play an important biological role, as oxidant and transmitter, and ABTS is also known as a dye that is used in biochemistry to detect cell regions with high nitric oxide concentration, as well in catalysts screening of NO_x decomposition. As Figure 2 shows, nitrogen dioxide obtained in both ways oxidises ABTS to the corresponding colored radical cation $ABTS^{\cdot+}$, re-generating the nitrite anions, which enter into the catalytic cycle, thus enhancing the formation of the dye.

In this work were tested five nitro-explosives, namely NG, RDX, TNT, dinitrotoluene (DNT) and trinitrophenol or picric acid (TNP), using both ways (alkaline and thermal) to generate eventually nitrogen dioxide, which subsequently oxidizes a colorless solution of ABTS to its intense blue-green colored radical cation $ABTS^{\cdot+}$

8. Catalytic oxidation of alcohols by TEMPO

First, inspired by the use of some soluble TEMPO derivatives as catalyst and sodium nitrite as cocatalyst in the presence of an acid, a similar experimental model system was set up. Commercially available silica supported TEMPO (as insoluble solid, with a loading of 0.7 mmol/g, named herein *catalyst A*) has been chosen as catalyst (5-20 mol %), sodium nitrite as cocatalyst (5-20 mol %), and DCM-acetic acid (9-1 v/v) as solvent; as model substrates for the oxidation reaction, benzylic alcohol, 1-phenylethanol and diphenylcarbinol have been used. The reactions were performed under air atmosphere (balloon) or oxygen (balloon).

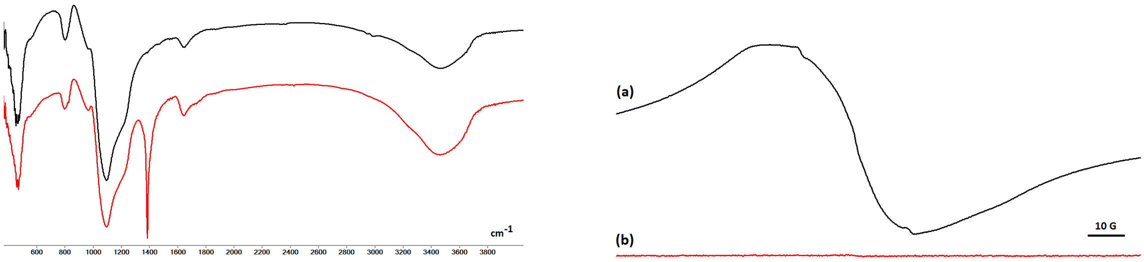


Fig. 10. IR and ESR spectra of the catalyst

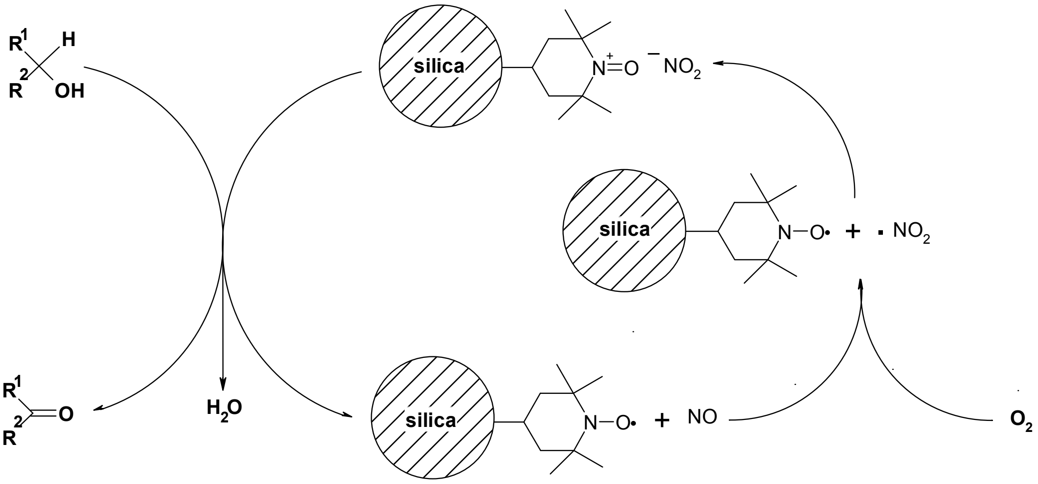
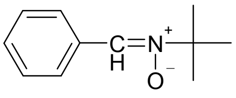


Fig. 11. Catalytic processes

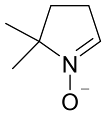
Therefore, the genuine active specie in the system used in this work can be either the oxoammonium ion (formed by the oxidation of TEMPO by NO_2) or an organic nitrate mediator (formed by a radical + radical coupling reaction). It is worth to mention that there are not literature reports on the formation of inorganic esters (nitrate or nitrite) of alcohols in the systems that employ TEMPO derivatives as catalyst. Therefore ere it is proposed a novel versatile bifunctional catalyst for alcohols oxidation, using a simpler and greener TEMPO/NOx system; based on experimental evidences, a new mechanistic pathway of oxidation is proposed, in which supported TEMPO acts as a generator and scavenger of NO_2. The method does not require the presence of a cocatalyst or an acid and can be used in solvent free reactions, with very high yield.

9. Free radicals in cigarette smoke

Tobacco smoking represents a source of exposure of humans to the reactive radicals which are considered responsible for chronic diseases. In this work we present the evidence of reactive radicals' formation in tobacco smoke using the electron paramagnetic resonance (EPR) spin-trapping method. Four types of commercially available cigarette were used. In each case the cigarette was smoked a quarter, half and totally, and the smoke was passed through a filter into a toluene solutions of the spin traps α-phenyl-N-*t*-butylnitrone (PBN) and 5,5-dimethyl-1-pyrroline-N-oxide (DMPO). The analysis of the spin-adducts spectra evidenced the formation of different free radicals with short lives (C•, CO•, O• and HO•). The ratio between these radical species depends on the cigarette characteristics (tar and nicotine) and the cigarette length consumption. It was found that the cigarette tar gives also an EPR signal, corresponding to quinone type radicals.



PBN



DMPO

Using the type **A** cigarettes and DMPO as spin-trap, no EPR signals were detected. Therefore, in this case the free radicals obtained from cigarette smoke cannot be identified. This might be correlated with the low amount of tar and nicotine in the light cigarette smoke.

For the smoke collected from a whole **B** type cigarette (menthol cigarette), an EPR spectrum with a high intensity was recorded which correspond to adduct of DMPO. This spectrum show a dominant component characterized by six lines (Figure 3). Simulation of the EPR spectrum obtained for B type cigarette revealed the presence of O-centered radicals in a large proportion.

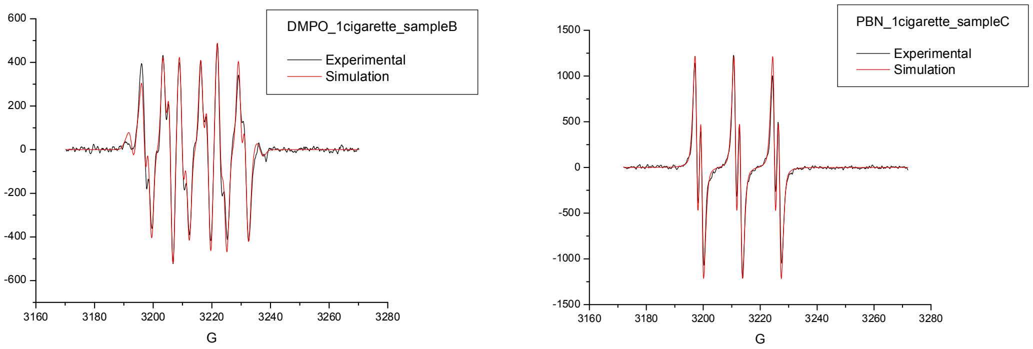


Fig. 12. ESR spectra and values

Free radical	***a**$_N$*	***a**$_H$*	***g***
-C•	13.81-14.62	21.18-22.02	2.0056-2.0063
-CO•	12.71-13.8	16-16.9	2.0062-2.0073
-O•	12.37-13.8	6.39-7.6 1.72-1.85	2.0058-2.0066
HO•	14.9	14.9	2.0072-2.0077
decomposition	13.71-13.75	-	2.0057-2.0074

10. The influence of the gold nanoparticles on the Tempo labelled silica

The next objective of the grant was to study the influence of the supported gold nanoparticles on Tempo functionalized silica nanoparticles. Several methods of synthesis were employed for the obtaining of the silica nanoparticles, using starting materials that allow organic derivatization, such is aminopropylsilica. To these amino groups Tempo moieties were covalently bound.

These materials were first characterized by physic-chemical means and then tested as catalyst in oxidation of activated alcohols. We tested also them as catalyst in the oxidative coupling, with the aim to get directly an ester starting from an alcohol (Fig. 13).

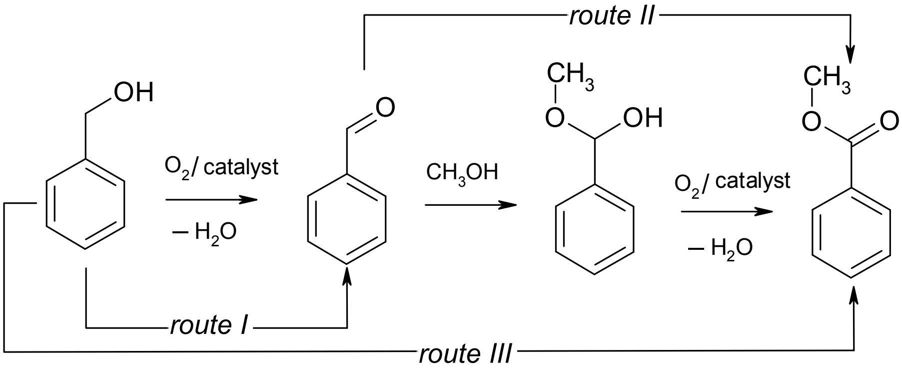


Fig. 13. Oxidative processes catalysed by the newly synthesised materials

Thus, using sol-gels methods, four materials were obtained, named A-D; A was obtained by linking 4-hydroxy-Tempo on silica, while C was obtained by linking 4-amino-Tempo; the B and D materials are in fact A and C to which gold nanoparticles were deposited.

This work started after we noticed an unusual high activity of such composite materials, that also fitted some literature data. Moreover, oxidative coupling reactions are in high demand as they simplify a two step process and skip a lot of labour.

The A-D nanocomposites were fully characterized by IR, TEM, BET, TGA, and ESR where appropriate. Thus, Fig. 14 shows the TEM analysis, being an evidence of the nanoparticles size of 20 nm for silica, while the gold nanoparticles have about 20-50 nm.

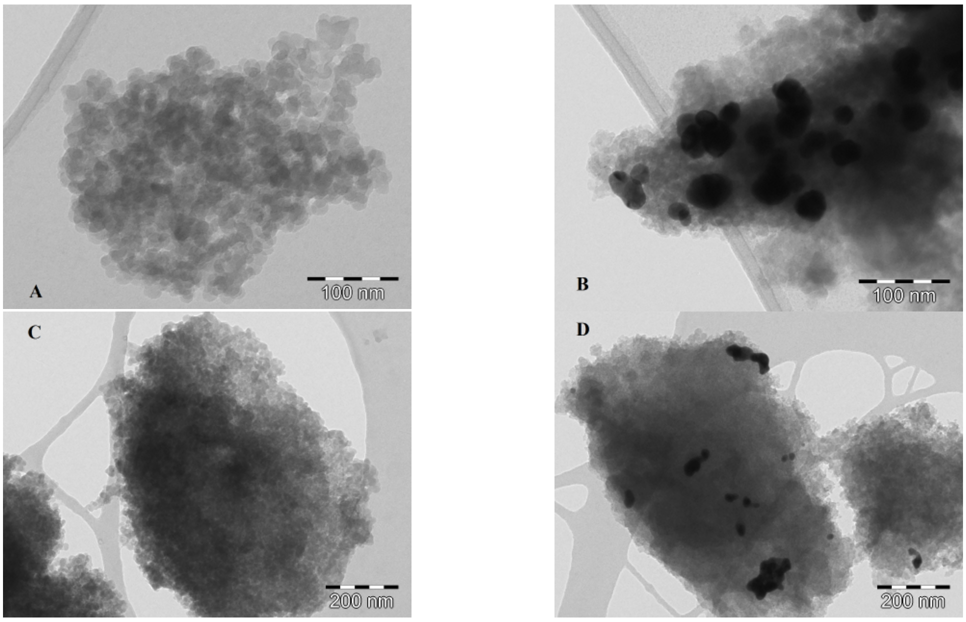


Fig. 14. TEM micrographs of samples A-D

IR analysis showed the presence of the bands at 3100-3500 cm^{-1}, due to NH and OH groups; Si-O bonds appear at 1200-1400 cm^{-1}, while C-H at 1350-1450 cm^{-1}. The other measurements are compiled in Table 1.

Table 1. Characterization of samples A-D

	Cat. A	Cat. B	Cat. C	Cat. D
BET surface (m^2/g)	323	257	26	17
Pore diameter (nm)	3.6	6.1	5.6	5.8
Pore volume	0.41	0.50	0.05	0.03
Organic material (%)	20	30	5	6
TEMPO (mmol/g)	0.11	0.10	0.23	0.22
Gold (%)	0	5	0	5

TGA and ESR analyses are showed in Fig. 15 and Fig. 16.

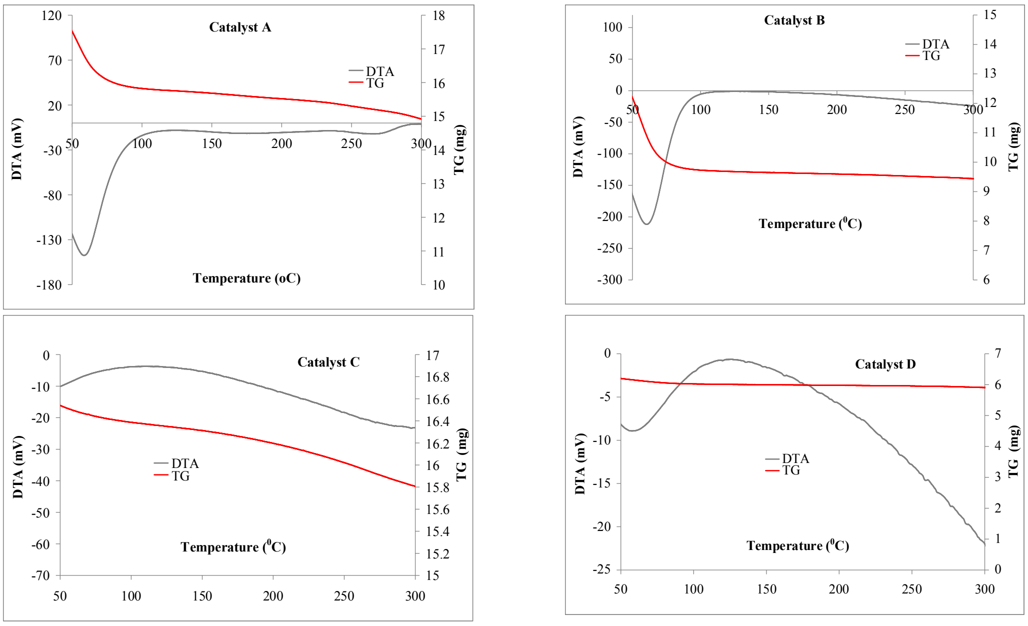


Fig. 15. TGA for samples A-D

It is easily noticed that there is a big difference between samples A-B and C-D, the organic content lost up to 300 °C being 20% and 30% for the first two samples, while for the last two the values are only 5% and 6%.

ESR analyses showed without doubt that the Tempo free radicals are attached to the nanoparticles. The ESR spectra were recorded as dry solids or suspended nanoparticles in DCM- small changes are visible in the last case.

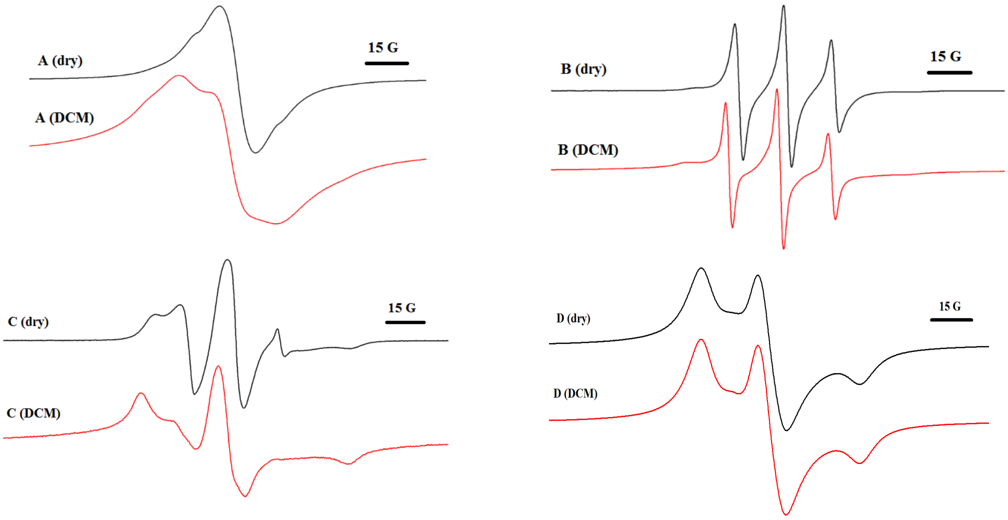
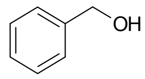
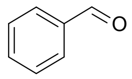
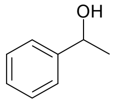
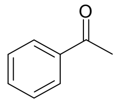
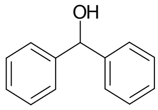
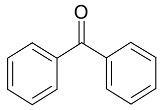
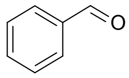
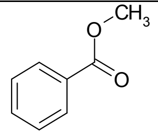
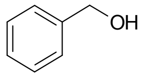
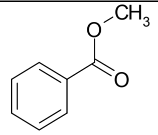


Fig. 16. ESR spectra for samples A-D

As usual, samples A-D were tested as catalyst in the oxidation of three alcohols; the results thus obtained are compiled in Table 2.

Table 2. Yields of oxidation of the alcohols in the presence of A-D catalyst

Reactant	Product	Cat. A	Cat. B	Cat. C	Cat. D
Method I (solvent DCM)					
		100	95	99	53
		100	55	83	66
		70	85	87	69
Method II (solvent methanol)					
		0 (0)*	13 (10)*	0 (2)*	0 (4)*
Method III (solvent methanol)					
		0 (0)*	0 (0)*	0 (0)*	0 (0)*

These results showed that the hybrid materials synthesized can work as catalyst in oxidative processes. Catalyst A demonstrated a high efficiency in such oxidation reactions, while B was the only one that was able to act in oxidative coupling reaction.

The proposed mechanism is depicted in Fig. 17. In principle, two catalytic cycles are acting together to make the process possible.

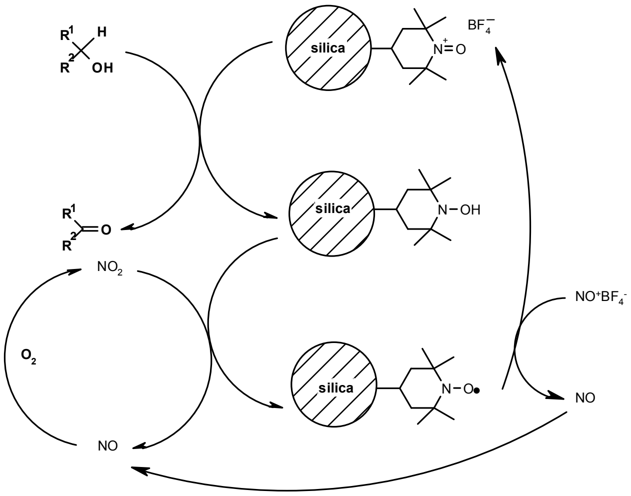


Fig. 17. Proposed mechanism of alcohol oxidation

11. Tempo grafted on graphene oxide

Graphene oxide is a material known since 150 years ago, but it found important applications only nowadays. This can be considered a 2D material, containing mostly carbon atoms; however, mainly on the edges, it contains functional groups, like carboxyl and hydroxyl. These allow further derivatization, either by covalent bonds or by other types of interactions (ionic, *van der Walls*).

Graphite (G) is easily converted into graphene oxide (GO) via a strong oxidation procedure. Two methods are used, the Hummers methods and an improved one, yielding the samples named herein GO and iGO.

Covalent functionalization make use of standard coupling reactions; in this way many derivatives of GO were obtained, containing, ferocen, polymers, porphirins and so on.

These hybrid materials have new and interesting properties, which can be chemically tuned. In this way new materials for electrochemistry, catalysis or energy conversion and storage were obtained.

As mentioned before, oxidation reactions have important industrial applications. Normally, such processes are generating a huge amount of toxic waste, as transition metal ions are in fact the active oxidant; therefore, more benign or green methods are of high interest.

Free radicals that can activate oxygen were used lately as a good variant in the oxidation of alcohols. In this part of the project we grafted Tempo stable free radicals on graphene oxide and used this hybrid material as catalyst.

For grafting, it was necessarily to activate the carboxyl groups from GO by converting them into the carbonyl chloride (Fig. 18), and then the reaction with 4-amino-Tempo afforded the desired material. Following this procedure, two solid black materials were obtained, namely GO-T and iGO-T.

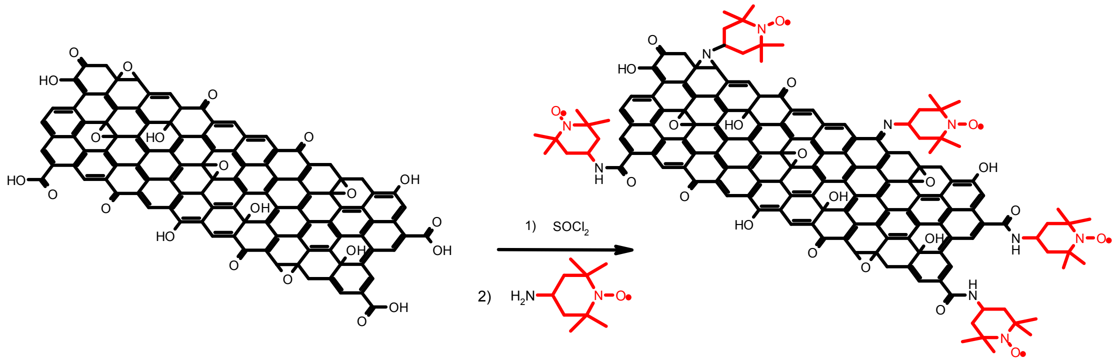


Fig. 18. Tempo functionalization of graphene oxide

All these hybrid materials were characterized by elemental analysis, IR, RAMAN, TGA, ESR and SEM. ESR spectra are shown in Fig. 19, while IR ones in Fig. 20.

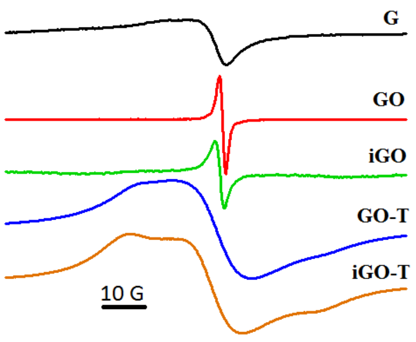


Fig. 19. ESR spectra for graphite (G), graphene oxide (GO si iGO) and Tempo functionalized GO (GO-T si iGO-T)

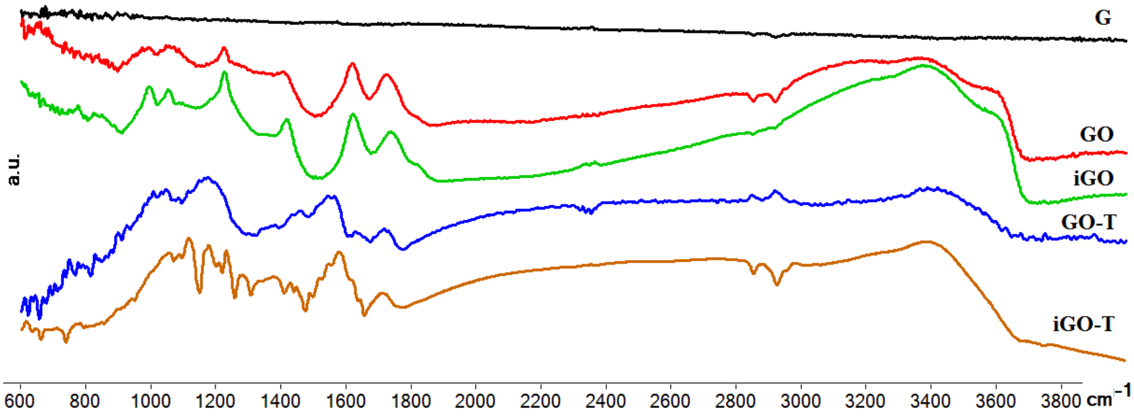
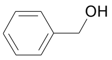
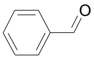
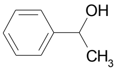
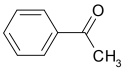
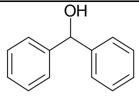
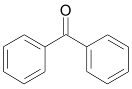
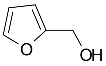
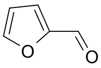
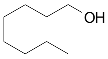
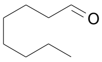


Fig. 20. IR spectra for graphite (G), graphene oxide (GO si iGO) and Tempo functionalized GO (GO-T si iGO-T)

For applicative purposes, the resulting materials were tested as well in oxidation reactions. Table 3 shows the yields of oxidation obtained under different working conditions. The best yield (99%) was obtained by the iGO-T sample.

Table 3. Oxidation yields for functionalized graphenes

	Reactant	Product	Cat	Co-cat	Yield
1			-	$NaNO_2$	trace
2			G		<1
3			GO		<1
4			iGO		<1
5			GO-T		42
6			iGO-T		46
7			G	NO_2	trace
8			GO-T		57
9			**iGO-T**		**99**
10			iGO-T	$NaNO_2$	9
11			iGO-T	NO_2	12
12			iGO-T	$NaNO_2$	9
13			iGO-T	NO_2	25
14			iGO-T	$NaNO_2$	5
15			iGO-T	NO_2	11
16			iGO-T	$NaNO_2$	3
17			iGO-T	NO_2	10

As was before mentioned, a similar catalytic pathway is proposed (Fig. 21).

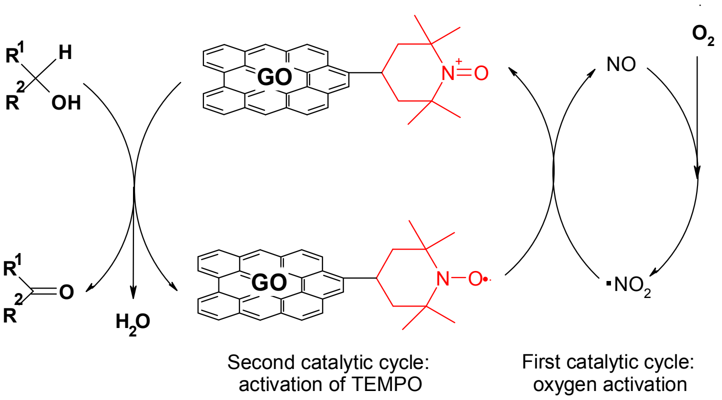


Fig. 21. Oxidation processes in the presence of GO-T (two catalytic circles)

In conclusion, this grant allowed the publication of 15 scientific papers, as follows.

Summary of the published papers that acknowledges the UEFISCDI grant:

15. Covalently grafted TEMPO on graphene oxide: a composite material for selective oxidations of alcohols, A. J. Shakir, D. C. Culita, J. C. Moreno, A. Musuc, O. Carp, G. Ionita, P. Ionita, *Carbon*, **2016**, 105, 607-614.

14. Synthesis of novel TEMPO stable free (poly)radicals derivatives and their host-guest interaction with cucurbit[6]uril, G. Ionita, A. M. Madalan, A. M. Ariciu, A. Medvedovici, P. Ionita, *New J. Chem*., **2016**, 40, 503-511.

13. Exploring porous nanosilica-TEMPO as heterogeneous aerobic oxidation catalyst. The influence of supported gold clusters, A. Shakir, M. Florea, D. C. Culita, G. Ionita, C. Ghica, C. Stavarache, A. Hanganu, P. Ionita, *J. Porous. Mat*., **2016**, 23, 247-254.

12. A convenient alternative for the oxidation of various alcohols by silica supported TEMPO free radical using nitrosonium tetrafluoroborate as cocatalyst, A. Shakir, C. Paraschivescu, M. Matache, M. Tudose, A. Mischie, F. Spafiu, P. Ionita, *Tetrahedron Let*., **2015**, 56, 6878-6881.

11. Silver azide nanoparticles embedded into silica as energetic nano-materials, C. Ghica, R. Damian, D. Culita, I. Turcu, P. Ionita, *Mat. Sci*., **2015**, 21, 329-332.

10. An EPR spin-trapping study of free radicals in cigarette smoke, A. M. Ariciu, P. Ionita, G. Ionita, *Rev. Roum. Chim*., **2014**, 59, 781-789.

9. Thermal behavior of several stable hydrazyl free radicals and of their parent hydrazines, M. Marinescu, C. Zalaru, M. Florea, P. Ionita, *J. Thermal Analysis Calorim*., **2014**, 116, 259-263.

8. A QSPR Study on Some Hydrazyl Radicals and Congeners, M. Marinescu, C. Zalaru, P. Ionita, *Sci. Bull*., **2014**, 76, 175-184.

7. A mechanistic glimpse on the oxidation of alcohols using TEMPO/NO_x catalytic systems: towards a greener bifunctional catalyst**,** P. Ionita**,** *RSC Advances*, **2013**, 3, 21218-21221.

6. Synthesis and structural characterization of a stable betaine imino-nitroxide free diradical, A. Paun, I. Zarafu, M. T. Caproiu, P. Ionita, *Arkivoc,* **2013**, iv, 144-151.

5. Synthesis and microbiological evaluation of several benzocaine derivatives, A. Paun, I. Zarafu, M. T. Caproiu, C. Draghici, M. Maganu, A. I. Cotar, M. C. Chifiriuc, P. Ionita, *Comptes Rendu Chimie*, **2013**, 16, 665-671.

4. An enhanced colorimetric chemosensor for the detection of various nitro-explosives, P. Ionita, *Tetrahedron Let*., **2012**, 53, 7143-7146.

3. Reversible aggregation between nanoparticles induced by acid-base interactions, G. Ionita, C. Ghica, I. Turcu, P. Ionita, *Chem. Phys. Let*., **2012**, 546, 133-135.

2. EPR spectra of a mono- and a hetero di-radical in nematic and isotropic phases, G. Ionita, I. Zarafu, A. Paun, P. Ionita, *Mol. Cryst. Liq. Cryst*., **2012**, 562, 141-146.

1. Chemical and biological evaluation of some new antipyrine derivatives with particular properties, C. Remes, A. Paun, I. Zarafu, M. Tudose, M. T. Caproiu, G. Ionita, C. Bleotu, L. Matei, P. Ionita, *Bioorganic Chemistry*, **2012**, 41-42, 6-12.