

## Some problems of nitroxyl chemistry\*

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**Abstract** - The development of chemistry of free nitroxyl radicals puts a number of new problems before the researchers. It is possible to subdivide nitroxyl radicals into two independent groups: nitroxides and iminoxyls, due to pronounced difference in their reactivity. To specify the concept of stability of a substance it is necessary to reconsider the ideas concerning the discovery of the first stable free radical.

### INTRODUCTION

Unlike other classes of free radicals, nitroxyl radicals are extremely popular in various fields of science and technology. Since the time of the first monographs on nitroxyl radicals (ref. 1,2) a great number of scientific papers had been presented as well as patents for their application as inhibitors in free radical processes, e.g., polymerization reactions of acrylonitrile, acrylic esters, vinylacetate, vinylchloride, styrene, divinylacetylene, vinylacetylene, divinyl, neoprene, isoprene and furfural (ref. 3). Nitroxyl radicals and their diamagnetic precursors are employed to improve quality of anaerobic sealants, technical amines, alcohols, fats, oils, lubricants, detergents, liquid crystals, carotenes, fodder, rubber, epoxyresins, cellulose acetate and other polymeric materials (ref. 4). Two-sided reactivity of nitroxyl radicals makes possible their use as promoters and initiators to intensify technological processes such as aromatic hydrocarbon alkylation, polymerization of monomers and olefin oxide production.

Nitroxyl radicals are efficient inhibitors for the development of certain malignant formations in laboratory animals, they are attenuated mutagenic effect of benzopyrene derivatives and used in production of cigarette filters and metalation of polymeric films. Nitroxyl radicals won wide popularity in biology and medical science as spin labels, spin-immunology probes, enzyme inhibitors (ref. 5). They can be used in designs of nuclear precession magnetometers with high sensitivity, accuracy, and absolute readings independent of temperature, pressure and sensor orientation. Due to narrowed electron resonance spectra of deuterium-substituted nitroxyl radicals, they were suggested as working media for such magnetometers (ref. 6). Unlike tritium oxide and other conventional indicators used in the development of oil-fields, nitroxyl radicals are ecologically harmless and can be successively applied to monitor the migration of in-strata fluids (ref. 7). Further progress in this and other application is essentially hampered by relatively high market price for pure nitroxyl paramagnetics.

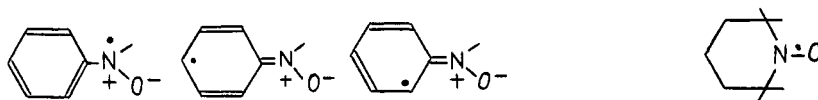
### THE PROBLEM OF UNIFICATION

The current literature on pure and applied chemistry of nitroxyls is a complex entanglement of terms, notions, concepts and regularities borrowed from

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\* After having sent the manuscript in advance of the symposium, the lecturer was subsequently unable to attend the meeting to present it in person.

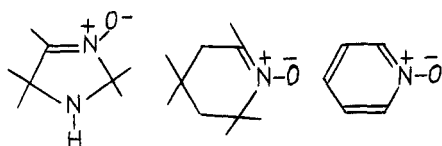
classical organic chemistry and quantum mechanics. The situation apparently doesn't help the progress of nitroxyl chemistry and is a permanent source of curious misunderstandings. This problem can be partly solved through a stricter and unambiguous systematization of accumulated data and unification of existing terms and symbols. Specific features of electronic structure and reactivity of nitroxyls enable us to divide this class of neutral organic paramagnetics into nitroxides (anachronism doesn't fit modern definition of a free radical) and iminoxyls. While the reactions with the free valency transfer (the free valency transfer within the paramagnetic particle) is peculiar to nitroxides, such transfers are evidently forbidden for iminoxyls:



classical paramagnetic nitroxides

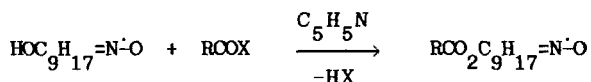
iminoxyls

Unlike the first group of radicals with pronounced delocalized spin density, free iminoxyls are characterized with free valency localized on the (=N-O) bond, and the contribution of nitroxide valence bond structures to the total resonance hybrid is negligible. The difference is even deeper if we taken into account that the most nitroxides have no relation to free radicals at all, e.g.



nonparamagnetic nitroxides

Unlike paramagnetic nitroxides, free iminoxyl radicals due to the presence of localized reaction centre can enter regioselective reactions without involving the unpaired electron (ref. 8), e.g. nonradical reactions of free radicals:



where  $\text{HOC}_9\text{H}_{17}=\text{N}^{\cdot}\text{O}$  is 2,2,6,6-tetramethyl-4-hydroxypiperidine-1-oxyl (ref. 9).

Nitroxides mistaken for iminoxyls may result in misunderstanding (ref. 10).

## ELECTRON SPIN EXCHANGE PHENOMENA

A stable biradical with localized paramagnetic centres was first isolated and studied 25 years ago (ref. 11). With this biradical they observed a paradoxical phenomenon of electron exchange between both paramagnetic centres at their complete structural isolation (the exchange integral being much higher the value of the isotropic hyperfine coupling constant). The electron resonance spectrum of a iminoxyl biradical consist of five lines (as with diphenylpicrylhydrazyl) due to equal exchange interactions of unpaired electrons with two nitrogen atoms. Research has proved that the exchange was not though single chemical bonds ( $\sigma$ -bonds) but by nearing localization centres of unpaired electrons as the result of deformation oscillations of paramagnetic particle skeleton. The phenomenon is highly temperature dependent.

The development of nonradical reactions of free radicals in the authors' laboratory enable us to obtain all possible paramagnetic esters of benzene carboxylic derivatives:  $\text{C}_6\text{H}_5\text{CO}_2\text{C}_9\text{H}_{17}=\text{N}^{\cdot}\text{O}$ ,  $\text{C}_6\text{H}_4(\text{CO}_2\text{C}_9\text{H}_{17}=\text{N}^{\cdot}\text{O})_2$  - (three isomers),  $\text{C}_6\text{H}_3(\text{CO}_2\text{C}_9\text{H}_{17}=\text{N}^{\cdot}\text{O})_3$  - (three isomers),  $\text{C}_6\text{H}_2(\text{CO}_2\text{C}_9\text{H}_{17}=\text{N}^{\cdot}\text{O})_4$  -

(three isomers),  $C_6H(CO_2C_9H_{17}=N^{\cdot}O)_5$ ,  $C_6(CO_2C_9H_{17}=N^{\cdot}O)_6$ , where  $C_9H_{17}=N^{\cdot}O$  is 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl fragment. The comparison of ESR spectra of polyradicals in these series shows, that the discovered biradical paradox is the result of consecutive "relay race" spin-to-spin transference disturbances through pairwise interactions of localized paramagnetic centres (Fig. 1).

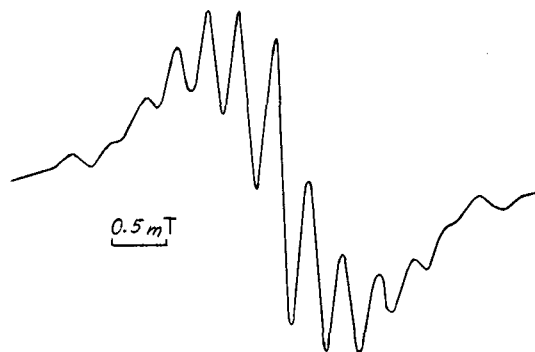


Fig. 1. The electron resonance spectrum of the hexaradical  $C_6(CO_2C_9H_{17}=N^{\cdot}O)_6$  in solution.

The comparative study of ESR spectra of iminoxyl radicals with various structures shows vividly the essential difference from paramagnetic nitroxides (ref. 12). Though until now the problem of experimental studies of electron spin exchange in gaseous media is not solved, the discovered phenomenon proved to be useful in solving various structural and analytical problems.

#### PARAMAGNETIC PARTICLES AND SUBSTANCES

It seems obvious, that for further progress in the field of nitroxyl chemistry the unbiased analyses is necessary for the data accumulated on the terms of modern concepts of paramagnetic substances (bodies) and particles (free radicals). It is unbelievable but many researchers dealing with the matter of chemical structure even now have these fundamental notions mistaken. From the physicist's view point there is no reason to classify chemical particles into molecules and radicals, since he is not interested in chemical transformations of the particles. In that case any chemical particle (molecule, ion, radical or atom) is a relatively stable formation, consisting of nuclei and electrons.

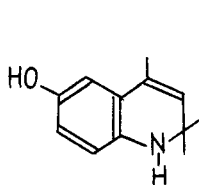
Chemistry is most interested in the particulars of electronic structure of chemical particles and processes of electron redistribution between them (chemical reactions) with formation of new particles. From the chemist's view point there are principal differences between free radicals (odd valent electron) and molecules (even valent electron). Proceeding on this assumption chemists agreed for free radical denomination to use terms "yl" suffix, e.g., hydroxyl, methyl, phenyl, hydrazyl, iminoxyl, phenoxy, nitroxyl and so on. The term nitroxide which physicists borrowed from old chemical literature does not point to the free radical character of particles. Deliberate introduction of ambiguous terminology into chemistry would hardly assist in solution of the problem of operative information exchange between specialists.

Quantum mechanics certainly makes the theoretical basis of paramagnetic particles (radicals) interaction in elementary acts of chemical transformations. Quantum statistics and thermodynamics make the theoretical basis in studies of pure paramagnetics (macroscopic aggregates of free radicals). Thus we find principal difference between separate chemical

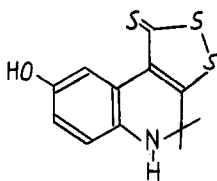
particle (free radical) and chemically pure paramagnetic substance (body) consisting of free radicals. Free radicals (chemical particles with unpaired electrons) while interacting under normal conditions can produce chemically pure substance consisting of identical paramagnetic particles. If the substance is stable enough, it can be identified and described with physical constants. Such a substance (paramagnetic) is certainly a stable radical with a definite semiconversion period under normal conditions (under the conditions the experimenter is in).

If paramagnetic particles interactions result in transformation products (usually nonparamagnetic substances) it is useless to consider radical stability. In the laboratory practice chemists deal mostly with radical substances and not with individual paramagnetic particles. A chemist is first of all interested in the properties of solid, liquid and gaseous paramagnetics, therefore he is to realize which problems of structure and reactivity can be solved on the basis of structure theory, quantum mechanics, quantum statistics and thermodynamics. There is a curious view point popular among chemists that the stability of radical (substance) can be assessed by the stability of radicals (particles) in solid and liquid solutions. However the stability of chemical particle and that appropriate substance are absolutely different notions and make the matters for consideration by different sciences (chemical physics and organic chemistry). In other words the stability of solvated paramagnetic particles and the stability of chemically pure substances consisting of these particles are determined by absolutely different factors.

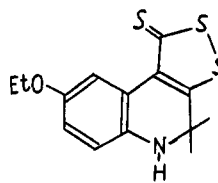
Strictly speaking neither Gomberg radical nor Fremy anion radical are stable ones, since they do not exist as chemically pure entities. These and many other instances only allow the idea of stability of solvated radicals (radicals in solutions). Such approach reduces considerably the number of real (true) stable radicals described in chemical literature and leads to the necessity to reconsider a number of priority matters in the organic chemistry of free radicals. For instance, Gomberg radical have never been obtained free of solvent. Actually it was not Gomberg, but Pyloty and Schwerin two German chemists who in 1901 pioneered in isolation of the first stable nitroxyl with the unpaired electron: pure crystalline sample of free imidazolinic nitroxide (ref. 13). The equilibrium in solution depends apart of solvation factors of mesomeric and steric properties of the paramagnetic particles. The structure of porphyraxide radical particles can be presented with a combination of eight valent tautomeric structures which permits to consider Pyloty-Schwerin's radical as the first representative of paramagnetic nitroxides with highly delocalized charge and spin density. Author started in his laboratory the investigation of paramagnetic nitroxides of aromatic and heterocyclic series many years ago (ref. 14). Nitrogen-substituted tocopherol analogues were of special practical interest. However, in spite of relative availability of the 2,2,4-trimethyl-6-hydroxydihydroquinoline derivatives I, e.g., II and III:



I



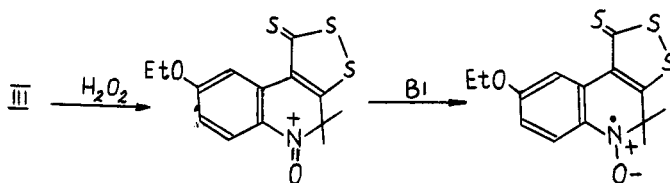
II



III

their paramagnetic products of oxidation had not been practically studied with ESR until today.

These compounds were oxidized with  $H_2O_2$  in ether or tetrahydrofuran to produce appropriate cation radicals. For instance, in the case of oxidation I the ESR spectrum is a triplet (1:1:1) with  $a_N = 1.17$  mT. Other magnetic nuclei do not exhibit hyperfine splitting, because of line broadening ( $\Delta H \approx 0.6$  mT). ESR spectra of sulfur containing cation radicals are quadruples (1:2:2:1). In the case of the cation radical corresponding to II  $a_N = a_H(NH) = 0.74$  mT, quadruple lines are subplit into doublets with  $a_H(OH) = 0.28$  mT. In electrochemical oxidation II the cation radical splits the proton off and converts to the appropriate phenoxyl (the cathode branch of a cyclic voltammogram). The ESR spectrum is a triplet (1:1:1) with  $a_N = 0.72$  mT, whose each lines is subsplit into a doublet with  $a_H(NH) = 0.40$  mT. In the case of the cation radical corresponding to III  $a_N = 0.75$  mT and  $a_H = 0.50$  mT, here the subsplitting of the quadruple lines is caused by interactions of the unpaired electron with protons of methyl groups ( $a_H(CH_3) = 0.14$  mT). The paramagnetic nitroxide corresponding to III is obtained as follows:



The ESR spectrum of the nitroxyl radical obtained after oxidation of III is a multiplet with  $a_N = 1.65$  mT and  $a_H(CH_3) = 1.13$  mT (Fig. 2).

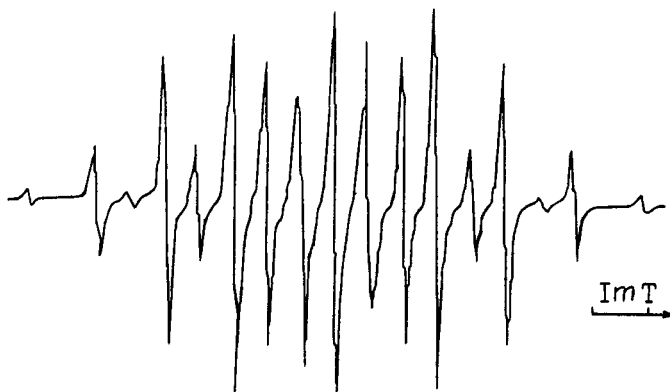


Fig. 2. The ESR spectrum of the nitroxyl ("the nitroxide") obtained after oxidation of III.

Unfortunately the existence of the above paramagnetic nitroxides in a solution does not prove a thing, since the problem of isolation of these radicals in a chemically pure state is not solved yet. At least now I don't know, if it is possible to treat these radicals as stable substances indeed.

#### RADICALS AND DIAMONDS

It is well known that the strength of solid essentially depends on the condition of its surface. The problem of nondestructive test always occurs in

surface quality estimation for smaller natural and synthetic diamonds of various geometry. We have managed to solve this problem in principle by means of nitroxyl radicals (ref. 15), which can be directly registered in microcavities, fissures and other surface dislocations of diamond crystals without damaging. The new method is very simple: ESR signals from radicals in dislocations are continuously compared to the signals of standard sample in the process of radical diffusion from the surface of the diamond into a pure solvent. By processing the experimental data they obtain information on the quality of the diamond tested. In other words for quality diagnostics the tested diamond is first immersed into the solution of a stable iminoxyl radical and then put into a flow cell in the ESR cavity through which they pump with constant velocity organic solvent eluted radicals from diamond surface cavities. They record continuously the decreasing content of free radicals in diamond surface cavities and on the basis of kinetic data estimate the width and depth of these cavities.

For instance, natural diamonds intended for cutting tools are washed in chloroform and dried at 70°C to remove solvent from microcavities. Then the sample is immersed into 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl solution and 3 minutes later is transferred into a flow cell in the ESR cavity through which the solvent elutes with constant velocity. The changes in ESR signal intensity for spin-labeled sample are automatically registered, and the resulting information is used for plotting curves of  $\ln(I/I_0)$  vs time. In model experiments to plot calibration curves they use glass capillaries of various lengths and diameters. The inflexion points on  $\ln(I/I_0)$  vs time curves correspond to various types of crystal surface defects. Computer analysis of experimental curves provides complete information on the character of microcavities (shallow, deep, narrow, wide), their geometry and volumes, and enables fast selection of reference samples for various technical purposes. Recently it has been established that the new method of quality diagnostics for raw diamonds and finished products of superhard materials can be applied to evaluate the quality of gems.

## REFERENCES

1. E.G. Rozantsev, Free Nitroxyl Radicals, Plenum Press, New York (1970).
2. E.G. Rozantsev, Free Iminoxyl Radicals, Khimiya, Moscow (1970).
3. E.G. Rozantsev, M.D. Goldfein, A.V. Trubnicov, Usp. Khim. **55**, 1881-1897 (1986).
4. E.G. Rozantsev, E.S. Kagan, V.D. Scholle, V.B. Ivanov, V.A. Smirnov, In Polymer Stabilization and Degradation (P.P. Klemchuk, ed.), pp. 11-35, ACS, Symposium Series 280, Washington D.C. (1985).
5. Nitroxyl Radicals. Synthesis, Chemistry and Applications (E.G. Rozantsev, R.N. Zhdanov, eds.), Nauka, Moscow (1987).
6. E.G. Rozantsev, A.P. Stepanov, In Geofizicheskaya Apparatura, **29**, pp. 35-41, Nedra, Leningrad (1966).
7. I.I. Bukin et al., Neftepromysl. Delo **8**, 3 (1978).
8. E.G. Rozantsev, Izv. Akad. Nauk. SSSR, Ser. Khim. **9**, 1669-1672 (1963).
9. E.G. Rozantsev, Izv. Akad. Nauk. SSSR, Ser. Khim. **12**, 2187-2191 (1964).
10. E.G. Rozantsev, M.B. Neiman, Zh. Org. Khim. **7**, 1337-1338 (1965).
11. E.G. Rozantsev, V.A. Golubev, M.V. Neiman, Izv. Akad. Nauk. SSSR, Ser. Khim. **2**, 393-394 (1965).
12. E.G. Rozantsev, W.D. Szolle, Chemia Organiczna Wolnych Rodnikow, PWN, Warszawa (1985).
13. O. Pyloty, B. Schwerin, Ber. **34**, 1880 (1901), *ibid.* **36**, 1286 (1903).
14. E.G. Rozantsev, A.A. Medzhidov, M.B. Neiman, Izv. Akad. Nauk. SSSR, Ser. Khim. **10**, 1713-1717, 1876-1877 (1963).
15. I.I. Bukin, I.F. Kagarmenov, E.G. Rozantsev et al., Sverkhтвердые Materialy, **6** (27), 23-25 (1983).