Transformations of *myo*-inositol hexa-*O*-nitrate under the action of amines

V. E. Kuznetsov,[a]* *N. L. Sukhov,*[b] *F. V. Pichugin,*[a] *and B. G. Ershov*[b]

[a]*Institute of Chemistry and Chemical Technology, National Academy of Sciences of Kyrghyz Republic,*
720071 Bishkek, Kyrghyz Republic
[b]*Institute of Physical Chemistry, Russian Academy of Sciences,*
117915 Moscow, Russian Federation.
Fax: 007 (095) 952 7514

Reactions of *myo*-inositiol hexa-*O*-nitrate with ammonia and primary amines yield tetrahydroxy-1,4-benzoquinone derivatives, *viz.*, its tetraammonium salt and its diimines, respectively. Reactions with secondary and tertiary amines give salts of rhodizonic acid, which are converted into salts of croconic acid under certain conditions. The reactions with secondary amines involve intermediate formation of radical species, which were dectected by ESR spectroscopy. A scheme for the chemical transformations of *myo*-inositol hexa-*O*-nitrate under the action of amines was proposed.

Key words: *myo*-inositol hexanitrate, amines, salts of rhodizonic and croconic acid, tetrahydroxy-1,4-benzoquinone derivatives, scheme of reaction.

Transformations of nitrates under the action of bases have been reported in the literature; however, reactions with amines have not yet been adequately studied.[1] The behavior of nitrates of cyclic polyols in reactions with amines has not been investigated.

When dilute solutions of *myo*-inositol hexa-*O*-nitrate (IHN) in EtOH (10^{-2} mol L^{-1}) were treated with an excess of a highly basic secondary or tertiary amine (piperidine, diethylamine, and triethylamine), intense red coloration appeared (λ_{max} 440, 480 nm). The intensity of the color decreased with time, and the solution turned light-yellow (λ_{max} 360 nm). This suggests that the process involves at least two steps. Analysis of the ^1H NMR spectra of IHN—amine mixtures showed that the signals corresponding to protons of the starting nitrate disappeared in the early moments of the process; nitrite ions (λ_{max} 358 nm) were detected in the reaction mixture by UV spectroscopy. When Et_2NH was added to a 0.2 *M* solution of IHN in MeOH (at a molar ratio of 2 : 1 or 1 : 1), a colorless precipitate formed; on subsequent stirring, this precipitate rapidly dissolved. The UV spectrum of the precipitate exhibited an absorption maximum at 358 nm. On heating, the precipitate turned into a yellow liquid whose odor was typical of nitrosamines and the boiling point was equal to that of diethylnitrosamine (174—175 °C). Apparently, this transformation can be described by Scheme 1.

Scheme 1

$$Et_2NH_2{}^{+}NO_2{}^{-} \longrightarrow Et_2N{-}NO + H_2O$$

When saturated solutions of IHN in methanol were treated with the amines mentioned above, red-orange products with λ_{max} 440 and 480 nm precipitated. Their IR spectra contained no absorption bands due to the nitrate groups of the starting hexanitrate (1680, 1295, and 840 cm^{-1}),[2] but instead they exhibited an intense broad absorption band at 1500 cm^{-1}; according to the published data,[3] the latter is typical of $C_nO_n{}^{m-}$ aromatic anions. The ^1H NMR spectra of these products contained only signals corresponding to the protons of the starting amines. Analysis of the ^{13}C NMR spectra showed that the products contain carbonyl groups (δ 178.2), $C{-}O^-$ groups (δ −343.0), and amine fragments. The elemental analysis and spectroscopic data indicate that the products isolated are previously unknown salts of rhodizonic acid with organic cations (**1—3**) (Scheme 2).

When we attempted to grow crystals of diethylammonium rhodizonate from a saturated solution in aqueous methanol (3 : 1) for X-ray diffraction analysis, we found that the rhodizonate $C_6O_6{}^{2-} \cdot 2Et_2NH_2{}^+$ is converted into the croconate of the composition $C_5O_5{}^{2-} \cdot 2Et_2NH_2{}^+$ (m.p. > 250 °C, decomp.; IR, ν/cm^{-1}: 1500 (C=O, $C{-}O^-$); 2300—2700 ($NH_2{}^+$); UV, λ_{max} 360 nm). The structure of the croconate was confirmed by X-ray diffraction data.[4] Triethylammonium rhodizonate was converted into the corresponding croconate under similar conditions. Transformations of this type are known to occur when oxygen is passed through alkaline aqueous solutions of rhodizonates.[5]

Apparently, the enhancement of the coloration occurring in the first stage in treatment of dilute solutions of IHN with amines is due to accumulation of

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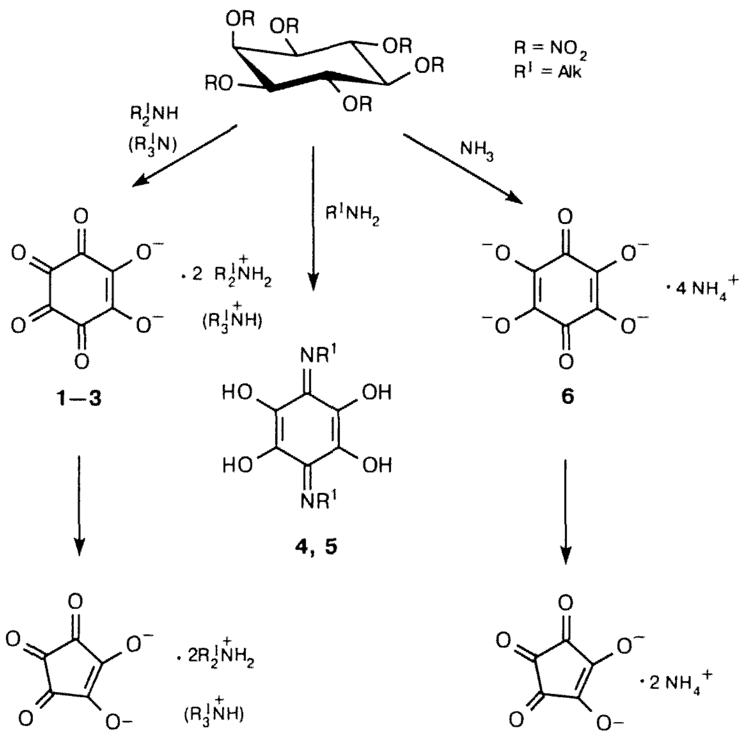
Scheme 2



rhodizonate (λ_{max} 440, 480 nm) in the reaction mixture, whereas the decrease in the intensity of the color is caused by transformation of the rhodizonate into the croconate (λ_{max} 360 nm). This transformation was monitored by UV spectroscopy (Fig. 1). It is probably accompanied by a benzyl type rearrangement giving[6] carbanions, which apparently follows from the presence of an adsorption maximum at 270 nm in the UV spectrum.

When IHN was treated with an excess of a highly basic primary amine (benzylamine, methylamine), tetrahydroxy-1,4-benzoquinonimines (**4** and **5**) were isolated from the reaction mixture.

When excess ammonia was passed through a saturated solution of IHN, a previously unknown tetraammonium salt of tetrahydroxy-1,4-benzoquinone (THBQ) **6** precipitated from the solution.

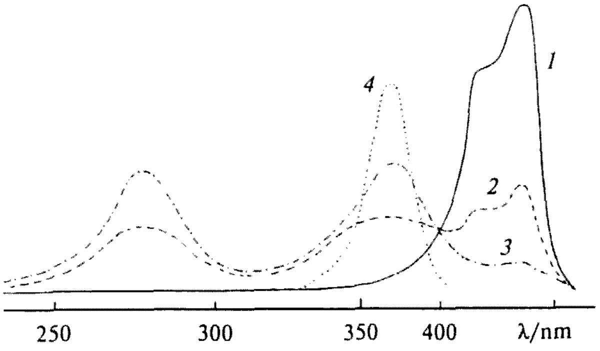


Fig. 1. Time dependence of the optical density of a 0.01 *M* aqueous solution of diethylammonium rhodizonate in the presence of diethylamine: the starting rhodizonate (*1*), 15 min later (*2*), 30 min later (*3*), the croconate (*4*).

The structures of the diimines and the tetraammonium salt of THBQ were confirmed by converting them into THBQ and into *N*,*N'*-diphenyltetrahydroxy-1,4-benzoquinonimine.[7—9]

When an ethanolic solution of ammonia was added to a 0.2 *M* solution of IHN, changes in the color of the reaction mixture were observed, similar to those accompanying treatment of IHN with secondary and tertiary amines. In this case, in addition to the maximum in the region of 440 and 480 nm typical of products **1—6**, the UV spectrum exhibited maxima at 270 and 360 nm. The maxima at 440 and 480 nm diminished with time, whereas those at 270 and 360 nm continued to increase; later, the maximum at 270 nm disappeared, while that at 360 nm still increased. The final light yellow solution exhibited one absorption maximum at 360 nm. Apparently, simultaneously with the formation of product **6**, its transformation to ammonium croconate occurs, probably according to the known[3] scheme.

Scheme 3

$$C_6O_6^{4-} \longrightarrow C_6O_6^{2-} \longrightarrow C_5O_5^{2-}$$

The reactions of IHN with piperidine and diethylamine yield radicals which were detected by ESR spectroscopy. A typical ESR spectrum is shown in Fig. 2.

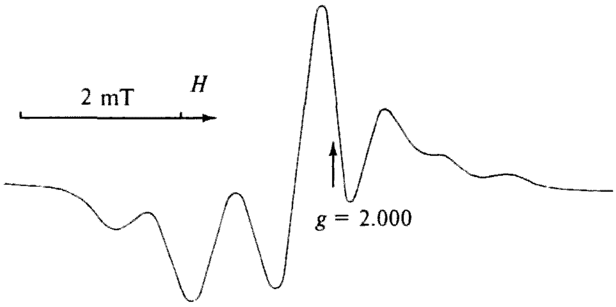
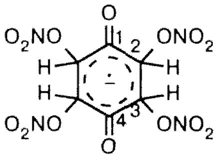


Fig. 2. ESR spectrum of a mixture of *myo*-inositol hexanitrate—piperidine. a_{HFC} = 1.07 mT. g = 2.003.

This is a quintet with a component ratio close to binomial (1 : 4 : 6 : 4 : 1). The *g*-factor of the signal is 2.003. Some asymmetry of the spectrum (the widths of its components and their arrangement are asymmetric with respect to the center) is probably due to anisotropic coupling, *i.e.*, to the anisotropy of the *g*-factor and hyperfine coupling. The HFC constant can be estimated as being equal to 1.07 mT.

The ESR signal discussed above corresponds to a radical species in which the unpaired electron interacts with four protons. In all probability, this is the following radical anion



In the intermediate stages of the process, radical anions of various natures can arise. However, the species observed corresponds to the most stable form.

The frequency of transfer of the unpaired electron is lower than the HFC constant expressed in frequency units. This accounts for the equivalence of all four protons. The unpaired electron density is evenly divided between positions 1 and 4. Therefore, the constant of the HFC with β-protons should be approximately half the constant, which should be expected if the unpaired electron was localized only in position 1 or 4. The splitting constants at the β-protons in radicals containing polar substituents are normally[10] 1.8—2.2 mT.

Thus, the transformation of *myo*-inositol hexa-*O*-nitrate under the action of amines is determined by the structure of the amine. The formation of products is accompanied by the appearance of species of a radical nature.

Experimental

The IR spectra were recorded for pellets with KBr on UR-20 and Specord 75 IR spectrophotometers; the UV spectra were obtained on a Specord M-40 instrument. The ^1H and ^{13}C NMR spectra were recorded using Bruker WM-250 (250 MHz) and Tesla BS-567A (100 MHz) instruments and HMDS as the internal standard.

The ESR spectra were made on an RE-1306 radiospectrometer at 77 K. The magnetic field was calibrated with $^{55}Mn^{2+}$ in MgO (a_{HFC} = 8.73 mT). The *g*-factor was determined from the position of the DPPH signal (*g* = 2.0036).

The ESR studies were carried out using a saturated solution of IHN in acetone. Solutions of amines in acetone were prepared in such a way that they contained 8 moles of amine per 1 mole of IHN. The solutions of the reactants were purged with argon, mixed, and then quickly frozen by liquid nitrogen.

IHN were prepared by nitration of *myo*-inositol in acetic anhydride according to a known procedure.[11] The purities of the starting nitrate and the transformation products were confirmed by elemental analysis and by spectroscopy. The amines and solvents were purified by standard procedures.[12]

Piperidinium rhodizonate (1). Anhydrous piperidine (8 mL) was slowly added with intense stirring to a solution of IHN (4.148 g, 9.2 mol) in 20 mL of dioxane. The precipitate formed was filtered off and recrystallized from aqueous methanol (1 : 1). Yield 2.15 g (75 %), m.p. > 250 °C (decomp.). Found (%): C, 56.30; H, 7.20; N, 8.25. $C_{16}H_{24}N_2O_6$. Calculated (%): C, 56.47; H, 7.08; N, 8.23. IR, ν/cm^{-1}: 1510 (C=O), C—O$^-$); 2300—2570 (NH_2^+). ^{13}C NMR (H_2O), δ: −342.99 (C—O$^-$); 178.22 (C=O); 45.87, 23.53, 22.82 (C(2,6), C(3,5) C(4) in $C_5H_{10}NH_2^+$).

Diethylammonium rhodizonate (2). Anhydrous diethylamine (7.5 mL) was slowly added with intense stirring to a saturated solution of IHN (4.28 g, 9.5 mmol) in methanol. The precipitate formed was filtered off and recrystallized from aqueous methanol (1 : 1). Yield 2.64 g (88%), m.p. > 250 °C (decomp.). Found (%): C, 56.42; H, 7.93; N, 8.83. $C_{14}H_{24}N_2O_6$. Calculated (%): C, 53.16; H, 7.59; N, 8.86. IR, ν/cm^{-1}: 1510 (C=O, C—O$^-$); 2300—2700 (NH_2^+).

Triethylammonium rhodizonate (3). Anhydrous triethylamine (5.5 mL) was slowly added with intense stirring to a saturated solution of IHN (2.25 g, 5 mmol) in methanol. The precipitate formed was filtered off and recrystallized from aqueous methanol (1 : 1). Yield 1.56 g (84.3%), m.p. > 250 °C (decomp.). Found (%): C, 58.30; H, 8.72; N, 7.34. $C_{18}H_{32}N_2O_6$. Calculated (%): C, 58.06; H, 8.60; N, 7.52. IR, ν/cm^{-1}: 1520 (C=O, C—O$^-$); 2300—2750 (NH^+).

***N,N'*-Dimethyltetrahydroxy-1,4-benzoquinonimine (4).**[7] Dry methylamine (8 mol per mole of the nitrate) was passed with stirring in a saturated solution of IHN (4.5 g, 10 mmol) in methanol. The precipitate formed was filtered off and washed with methanol. Yield 1.62 g (82 %), m.p. > 250 °C (decomp.). Found (%): C, 48.50; H, 5.12; N, 14.01. $C_8H_{10}N_2O_4$. Calculated (%): C, 48.48; H, 5.05; N, 14.14. IR, ν/cm^{-1}: 1670 (C=N).

A solution of compound **4** (1.62 g) in 20 mL of 2 *M* HCl was cooled to 0 °C. The crystals that precipitated were filtered off, washed with cold water, and dried *in vacuo* to give **tetrahydroxy-1,4-benzoquinone** (1.28 g, 91%), m.p. > 300 °C (decomp.). Found (%): C, 40.10; H, 2.61. $C_6H_4O_6$. Calculated (%): C, 40.69; H, 2.32. IR, ν/cm^{-1}: 1650 (C=O).

***N,N'*-Dibenzyltetrahydroxy-1,4-benzoquinonimine (5).** Anhydrous benzylamine (6.5 mL) was slowly added with vigorous stirring to a saturated solution of IHN (4.5 g, 10 mmol) in methanol. The precipitate formed was filtered off and washed with methanol. Yield 2.45 g (70 %), m.p. > 250 °C (decomp.). Found (%): C, 68.27; H, 5.32; N, 8.15. $C_{20}H_{18}N_2O_4$. Calculated (%): C, 68.57; H, 5.14; N, 8.00. IR, ν/cm^{-1}: 1670 (C=N).

Tetraammonium salt of tetrahydroxy-1,4-benzoquinone (6). Dry ammonia (10 moles per mole of the nitrate) was passed with stirring in a saturated solution of IHN (2.25 g, 5 mmol) in dioxane. The precipitate formed was filtered off and washed with ethanol. Yield 0.98 g (81.6 %), m.p. > 250 °C (decomp.). Found (%): C, 30.00; H, 4.24; N, 24.78. $C_6H_{16}N_4O_6$. Calculated (%): C, 30.00; H, 6.66; N, 23.33. IR, ν/cm^{-1}: 1680 (C=O); 1520 (C—O$^-$); 2600—2800, 1400 (NH_4^+).

***N,N'*-Diphenyltetrahydroxy-1,4-benzoquinonimine dihydrate**.[8] A 2 *M* solution of HCl (15 mL) and aniline (0.8 mL) were added with heating and stirring to a saturated solution of compound **6** (0.98 g). The precipitate formed on cooling was filtered off and washed with water and aqueous methanol. Yield 0.93 g (63 %), m.p. > 250 °C (decomp.). Found (%): C, 61.02; H, 4.73; N, 7.71. $C_{18}H_{14}N_2O_4 \cdot 2H_2O$. Calculated (%): C, 60.33; H, 5.02; N, 7.82.

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