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Aluminium–isopropanol reduction of *tert*-nitronitriles: an unusual structure of the reduction products

Andrei V. Stepanov and Electron A. Mistryukov*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: + 7 499 135 5328; e-mail: step@ioc.ac.ru

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The reduction of γ-nitronitriles with aluminium–isopropanol results in a cyclic product, strongly O-nucleophilic iminonitronium, which is resistant to further reduction.

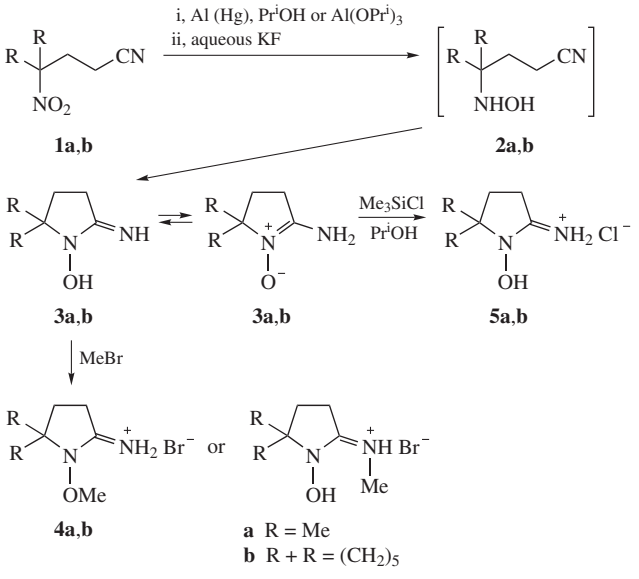
A convenient procedure for the synthesis of *tert*-nitronitriles using imidazolium salt catalysis of Michael addition of acrylates to *sec*-nitroalkane has been reported.[1] As these nitronitriles are of interest as starting compounds for biologically active aminobutyric acids and derivatives, methods for nitro group conversion into an amino substituent deserve attention.

This work is devoted to a method for nitro group reduction with aluminium amalgam–protic solvent.

Corey *et al.*[2] developed a method, which was extensively used[3–5] to prepare primary amines from primary or secondary nitro aliphatic derivatives. In respect to a particular case of *tert*-nitronitriles with nitro function at the quaternary carbon, we encountered an interesting deviation of the reaction pathway connected with the position of nitro and nitrile groups in the molecule. All details of the reduction procedure were optimised for nitronitriles **1a**,**b**.[†]

When **1a** or **1b** in isopropanol were stirred with a calculated quantity of amalgamated aluminium foil (1.33 mol per mole of nitronitrile, *i.e.*, 4 electrons per one nitro group) and the temperature was 30–40 °C, the dissolution of the metal occurred (with no hydrogen evolution) and the reduction product was formed. This product was a partially reduced compound rather than the expected amine.

Of particular experimental importance is the separation of the reduction product from aluminium isopropylate by forming complexes with potassium fluoride. The continuation of stirring after 5–7 min produced a surprising effect of complete separation of clear solution of the reduction product and the thick precipitate of aluminium complex. Evaporation of the organic solution gives pure free bases **3a**,**b**.



Interestingly, the yield of these products always exceeds the theoretical value on a consumed aluminium basis. This indicates additional pathways from **1** to **3**. Really, when the mixture of **1**, aluminium isopropylate and isopropanol was heated, TLC indicated the formation of reduction product **3**.

† *Typical procedure.* The reaction flask with an overhead stirrer (1300 or 2800 rpm) was loaded with 0.15 mol of aluminium foil cut into small strips and 0.3 g of mercury chloride and purged with argon. Then, 100 ml of isopropanol was added and after 10 min of stirring (to form amalgam) by small portions 0.1 mol (13.15 ml) of nitronitrile **1a** was added. By external cooling the temperature of the reaction mixture was controlled below 30 °C for 1 h. Then, the temperature was increased to 50 °C. After 3 h of stirring to the reaction mixture cooled to room temperature 25 ml of saturated aqueous potassium fluoride was added. With a small exothermal effect (temperature rise to ~40 °C), the mixture became solid and when intense stirring was prolonged (5–7 min) the clear upper phase and the precipitate were separated. The solution was decanted and rotary evaporated. The crystalline product was transferred to a filter, washed with acetone or tetrahydrofuran and dried to give 10.9 g (85%) of **3a**; subl. at 200–205 °C (decomp.). ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.3 (s, 6H, Me), 1.8 (t, 2H), 2.7 (t, 2H), 7.6 (br. s, 2H). ^{13}C NMR (75 MHz, D_2O) δ: 23.89, 23.98, 31.07, 67.64, 150.64.

Compound **3b** was prepared (starting from **1b**) analogously to **3a**; mp 175–180 °C (decomp.).

Methyl bromide adduct **4a**. The suspension of 0.62 g of **3a** in 5 ml of acetonitrile was saturated with methyl bromide. The initial dissolution was followed after some time by crystallization of 0.82 g of bromide **4a**, mp 192–193 °C. ^{1}H NMR (200 MHz, CD_3CN) δ: 1.41 (s, 6H, Me), 2.05 (t, 2H, CH_2, J 7.5 Hz), 3.00 (t, 2H, CH_2, J 7.5 Hz), 4.00 (s, 3H, OMe), 8.72 (br. s, 1H, NH), 9.75 (br. s, 1H, NH). ^{13}C NMR (50 MHz, CD_3CN) δ: 25.22 (Me), 25.80 [C(3)], 32.40 [C(4)], 66.88 (OMe), 69.57 [C(5)], 164.87 [C(2)].

Methyl bromide adduct **4b** was obtained analogously to **4a**; mp 198–200 °C. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.0–2.0 (m, 14H), 3.34 (s, 3H, OMe), 6.30 (br. s, 2H).

Cloride **5a** was prepared by the action of Me_3SiCl on solution of **3a** in isopropanol; mp 170 °C. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.3 (s, 6H, Me), 1.9 (t, 2H), 2.8 (t, 2H), 8.7 (s, 1H), 9.4 (s, 1H), 11.4 (s, 1H). ^{13}C NMR (75 MHz, D_2O) δ: 23.70, 24.41, 24.45, 30.87, 67.76, 162.32.

Chloride **5b**. The raw product **3b** was dissolved in 70 ml of isopropanol and to this solution 1 mol of Me_3SiCl was added with cooling. After standing overnight the crystals of **3b** were filtered off, washed with acetone and dried to yield 17.1 g (60%) of **5b**; mp 195–197 °C. Evaporation of the filtrate gave additional 4.8 g of **5b** (total yield 93%). ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.0–2.0 (m, 10H), 2.0 (t, 2H), 2.85 (t, 2H), 9.5 (br. s, 2H).

The most interesting are observations concerning the structure of reduction products **3a** or **3b**. For **3a**, elemental analysis and mass spectra gave results consistent with the structure of **2a** with the CN function. But the ^{13}C NMR spectrum of **3a** is inconsistent with the presence of nitrile function in the molecule of the reduction product. In the ^{13}C NMR spectrum of **1a**, there is no resonances typical of the CN group (δ 120 ppm) but a signal at δ 151 ppm appears.

Therefore, the resonance nitrone–hydroxyamine structure seems to fit the properties of reduction product **3**. In addition, the salt-like behaviour of **3a**,**b** is in agreement with this structure: both compounds are high melting solids as is typical of compounds with strong hydrogen bonds of intra–intermolecular types. Both compounds formed salts with acids (**5a**,**b**) and alkyl bromides. Of the two possible structures of alkyl salts (O-alkyl or N-alkyl), the first structure is in agreement with the ^{13}C NMR spectral data. This O-alkylation is uncommon for imine structures and resembles more that of O-alkylations of dialkylamides. In favour of O-alkyl structure of the reaction products of **3** with alkyl halides are the UV spectra. The absorption of **3a** at 232 nm was shifted to 221 nm in the free base of alkylated product **4**. This shift obviously is connected with the disruption of the conjugation in the nitronium resonance structure **3** by O-alkylation.

The partial reduction of *tert*-nitroalkanes is in contrast with the behaviour of the less substituted nitro derivatives, which give amines as the products under similar reduction conditions.[2] This difference may be connected with the participation of oximes as intermediates in the reduction process in case of primary or secondary nitroalkanes. For *tert*-nitroalkanes in the reduction with aluminium where the nitroso–oximino isomerization is impossible for steric reasons, in the nitro–nitroso–hydroxyamino reaction sequence the last intermediate is intercepted by the nitrile function with the formation of reduction resistant end product **3**. These cyclic products **3a**,**b** are of special interest as lipophilic complexing reagents solubilizing metal (Cu, Ni, Co, Fe, Pd) salts in organic solvents (methylene chloride, acetonitrile and tetrahydrofuran).

Note that products like compound **3** were obtained by the Raney nickel hydrogenation of **1** in 1947.[6] But the present reduction procedure is more effective in time/yield/cost factors.

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