Russian Journal of Organic Chemistry, Vol. 37, No. 12, 2001, pp. 1719–1722. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 12, 2001, pp. 1800–1803.
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Reductive Activation of Arenes: XIV.[*] Effect of Medium on the Products Ratio in the Alkylation of Nitrobenzene Radical Anion Sodium Salt[**]

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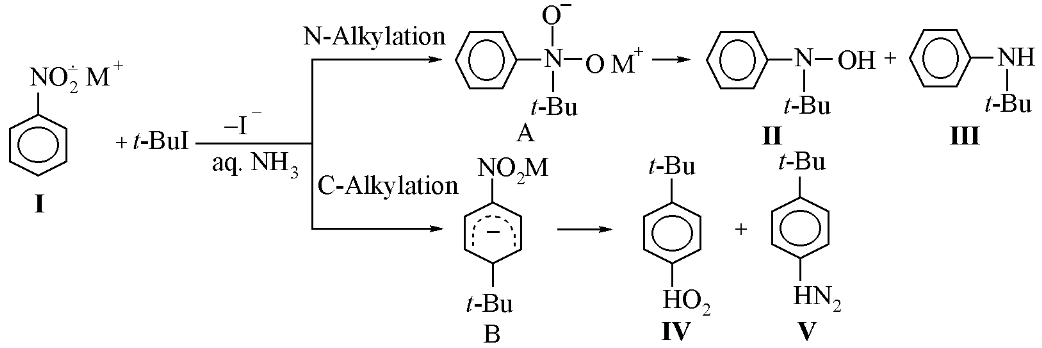
Received January 9, 2001

Abstract—The product of nitrobenzene reduction by 1 equiv of sodium reacted with tert-butyl iodide in liquid ammonia and its mixtures with tetrahydrofuran and hexamethylphosphoramide to afford a mixture of compounds alkylated either by the functional group (N-alkylation) or at the benzene ring (C-alkylation). The ratio of N- and C-alkylation products decreases in the solvents series NH_3–THF (5.7) > NH_3 (1.0) > NH_3–HMPA (0.6).

It was shown formerly [2, 3] that the reaction between alkali metal salts of nitrobenzene radical-anion (**I**) with *tert*-butyl iodide in liquid ammonia furnished products of nitrobenzene reductive alkylation both at nitrogen (N-alkylation products) and at the *para*-position of the benzene ring (C-alkylation products) (see scheme).

The ratio of N- and C-alkylation products grows with the increasing radius of the metal cation in the series Li < Na < K < Rb < Cs [3]. In the framework of the late transition state model where the transition states of the competing alkylation directions may be represented by the corresponding intermediates this fact may be rationalized as originating from increasing ion association of A and B salts in the liquid ammonia along the above series. A significant factor that to a great extent governs the character of ion association of radical-anion salts in solution is the nature of the environment. Since the excess electron density in the nitrobenzene radical-anion is located mostly on the nitro group the latter is the principal center taking part in hydrogen bonds with the solvent [4, 5–7] (specific solvation) and in association with the counterion [4, 5, 8]. Therewith the strengthening of both interactions results in still greater increase of the electron density on the nitro group [5, 6, 8–10]. In evaluation of the solvation influence on the N/C ratio it should be taken into account that the structures A and B simulating the transition states of the N- and

Scheme.



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[*] For communication XIII see [1].

[**] The study was carried out under financial support of the Russian Foundation of the Basic Research (grant no. 99-03-33111) and of Ministry of Industry and Science of the Russian Federation (grant no. 9.3.01).

1070-4280/01/3712-1719$25.00 © 2001 MAIK “Nauka/Interperiodica”

Yields of reaction products (mmol,[a] GLC) from nitrobenzene radical-anion sodium salt (**I**) and *tert*-butyl iodide[b]

Solvent	Nitro benzene	**II**	**III**	**IV**	**V**	Azo-benzene	Azoxy-benzene	Yield of alkylation products	Ratio N/C
NH_3–THF	9.55	0.06	0.11	0.02	0.01	0.02	0.08	0.20	5.67
NH_3 [2]	7.96	0.16	0.68	0.83	0.02	0.01	0.01	1.69	1.00
NH_3–HMPA	8.20	0.07	0.31	0.65	0.04	–	0.14	1.07	0.55

[a] Into the reaction was brought 10 mmol of nitrobenzene, reduced with 5 mmol of sodium metal, and 10 mmol of *tert*-butyl iodide. Concentration of reduced form 0.05 mol l^{-1}.

[b] Avereged results from 2–3 experiments. Deviations from the average do not exceed 15%.

C-alkylation respectively sharply differ since in the former one the negative charge is virtually totally localized on oxygen atoms whereas in the latter the charge is considerably delocalized. Analogously to the above this difference suggests with respect to the nitrobenzene radical-anion that the increase both in the specific solvation and ion association should stabilize stronger the A structure, and consequently in the products of *tert*-butylation of the sodium salt **I** should grow the fraction of the N-alkylation products. Thus establishing the character of solvent effect on the N/C ratio would give a possibility to prove the above statements on the nature of the transition states of the transformations under consideration. This was the target of the present study.

We investigated the reaction of salt **I** with *tert*-butyl iodide in the binary mixtures (1 : 1 by volume) of the liquid ammonia and tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) at –33°C. The selection of components for the mixtures was aimed at the widest possible variation of the solvating properties of the environment accounting also for the necessity to use the solvents where salt **I** could be generated by reduction of its precursor with alkali metal [11].

The reduction of nitrobenzene with sodium was carried out in the indicated binary mixtures with ammonia with the use of double excess of the precursor with respect to the alkali metal.

As seen from the table, in all cases formed compounds **II**–**V** and alongside these compounds were also revealed nitrobenzene, azoxybenzene, and at reaction in the THF–ammonia mixture also a little azobenzene.

The data in the table evidence that the nature of the solvent significantly affects, firstly, the overall yield of the alkylation products, and, secondly, the ratio N/C = (**II** + **III**)/(**IV** + **V**) that characterizes the competition of the two *tert*-butylation directions. For instance, in going from NH_3 to the mixture NH_3–THF the overall yield of the alkylation products is 8 times reduced, and in going to the mixture NH_3–HMPA only 1.5 times. In the former case it was in agreement with the previously found fact that in THF occurred no alkylation [11]. It is apparently due mostly to the lower solubility of the nitrobenzene radical-anion salt **I** and the stronger ion association. In keeping with the assumption on the reaction mechanism developed in [2, 3] these processes should reduce the rate of dissociative electron transfer from the radical-anion to the alkyl iodide. It should be noted that similar although not so pronounced reduction of the overall yield of the alkylation products was formerly observed [3] in carrying out the *tert*-butylation of the nitrobenzene radical-anion sodium salt in the presence of excess sodium iodide which also increased the ion association of the radical-anion salt (cf. [5]). Basically some decrease in the overall yield of alkylation products in the mixture of ammonia with THF may be ascribed to the consumption of the *tert*-butyl radical in reaction with THF (cf. [12]). However hardly it is the main reason of the decrease in the yield of the alkylation products. Firstly, the rate constant of alkyl radicals reaction with THF is considerably smaller (by 5–6 orders of magnitude) than the rate constant of their recombination with radical-anions of the aromatic compounds [12, 13]. Secondly, THF is the most commonly used solvent for reactions of radical-anions of aromatic compounds with alkyl halides following the SET mechanism. In the course of these reactions form alkyl radicals (cf., for example, [11, 13]) but the yield of the alkylation product is nearly quantitative. For instance the yields of *tert*-butylation products of nitrobenzene radical-anion salt **I** in HMPA and its mixture with THF are similar [11].

The slight decrease in the overall yield of alkylation products in going from ammonia to its mixture with HMPA may be due to increased viscosity of the medium and therewith to reduced recombination rate of the *tert*-butyl radical and nitrobenzene radical-anion. Besides the possibly decreased ion association caused by HMPA does not favor the recombination of the alkyl radical arising from the dissociative electron transfer with nitrobenzene radical-anion to yield intermediates (A) and (B) (cf. [14]); in the course of this recombination the degree of localization of the negative charge grows as compared to that in the initial nitrobenzene radical-anion.

Unlike the changes in the overall yield of the alkylation products, the N/C ratio in going from ammonia to its mixtures with THF and HMPA is altered in the opposite directions: in the presence of THF N/C grows from 1 to 5.7, and in the presence of HMPA it decreases to 0.55. Within the framework of the model of the late transition state this change in the N/C value may be attributed to the following: The intermediate of C-alkylation (B) is characterized by considerably greater delocalization of the negative charge and thus by lesser association of the counter-ions than the intermediate of N-alkylation (A). At THF addition causing decrease in the solvating power of the medium and affecting primarily the metal cation should favor due to the above key difference the formation of the more associated intermediate (A) and consequently N-alkylation. In going from NH_3 to its mixture with HMPA the opposite trend should be observed. It should be noted that the N/C value equal to 0.55 that characterizes the alkylation regio-selectivity of nitrobenzene radical-anion salt **I** in the mixture NH_3–HMPA is close to the figure obtained at *tert*-butylation in NH_3 of the lithium salt of this radical-anion [3]. Since the lithium salts in the liquid ammonia possess the most loose ion pairs among the alkali metal salts [15] it is presumable that in the NH_3–HMPA mixture the reactivity of salt **I** is due mostly to the loose ion pairs or even to the free radical-anion.

Thus it is reasonable to think that the above data are consistent with the concept on the “intermediate-like” character of the transition states of the alkyl radical recombination with the nitrobenzene radical-anion, and therefore this concept may be used in discussion of results of the future studies in this field.

EXPERIMENTAL

The reaction mixtures were analyzed by GLC on LKhM-7A instrument under the following condition: stationary phase CKTFT-50 or SKTFV-803 (15%) on the carrier Chromosorb W, oven temperature programmed from 70 to270°C at a rate 10 deg/min, carrier gas helium, flow rate 0.6 $l\,h^{-1}$, column 400×4 mm. Toluene was used as internal standard.

The liquid ammonia was purified by dissolving sodium (~2–2.5 g per 250 ml of liquid ammonia) followed by distillation of the solvent into the reaction vessel cooled to –70°C. The required amounts of THF and HMPA dried by procedures [16] and [17] respectively were preliminary charged into the reactor.

Nitrobenzene of “pure” grade was purified by method [11]. *tert*-Butyl iodide was obtained by procedure [18] and was purified just before the experiment by passing through a layer of alumina. The metallic sodium used was of the “pure” grade.

Reduction of nitrobenzene, *tert*-butylation of the reduced form, and workup of the reaction mixtures was performed as described in [2]. We used the sodium salt of the reduced form of nitrobenzene in 0.05 mol l^{-1} concentration.

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