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CHEMICAL KINETICS AND CATALYSIS

Reduction of Nitrotoluenes in Supercritical Isopropanol over Al_2O_3 in a Flow Reactor

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Abstract—The reduction of *o*-, *m*-, and *p*-nitrotoluenes in supercritical isopropanol over Al_2O_3 in a flow reactor is studied. It is shown that corresponding toluidines are major reaction products. Aromatic ring alkoxylation and *N*-alkylation products make a considerable contribution to the composition of reaction mixtures.

Keywords: nitrotoluene, toluidine, supercritical isopropanol, aluminum oxide, reduction, hydride transfer, alkoxylation.

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INTRODUCTION

It is well known that *o*-, *m*-, and *p*-toluidines are widely used as intermediate compounds in the production of dyes, pigments, pesticides, herbicides, vulcanization accelerators in the production of rubber, polymeric hardeners, corrosion inhibitors, and pharmaceuticals [1]. A basic method for the synthesis of toluidines is the reduction of corresponding nitrotoluenes. In addition to catalytic hydrogenation with hydrogen [1], some systems based on the transfer of hydrogen from other molecules are currently being considered as a safer alternative. Among the proposed systems are reduction with hydrazine hydrate in the presence of Fe_2O_3–MgO [2] and systems based on isopropanol as a reducer converting into acetone in the presence of $LaFeO_3$ [3] or ruthenium nanoparticles stabilized with montmorillonite clay [4].

We recently discovered that using supercritical alcohols as hydrogen sources in the presence of Al_2O_3 enables the efficient reduction of nitrobenzene (**1**) into aniline (**2**) in a flow reactor at temperatures of 270–340°C and a contact time of less than 6 min (Fig. 1) [5]. The reduction of halide-containing nitrobenzenes gives corresponding haloanilines with high yields and selectivities. At the same time, the reactivity of nitroaromatic compounds containing other substituents has yet to be studied under these conditions.

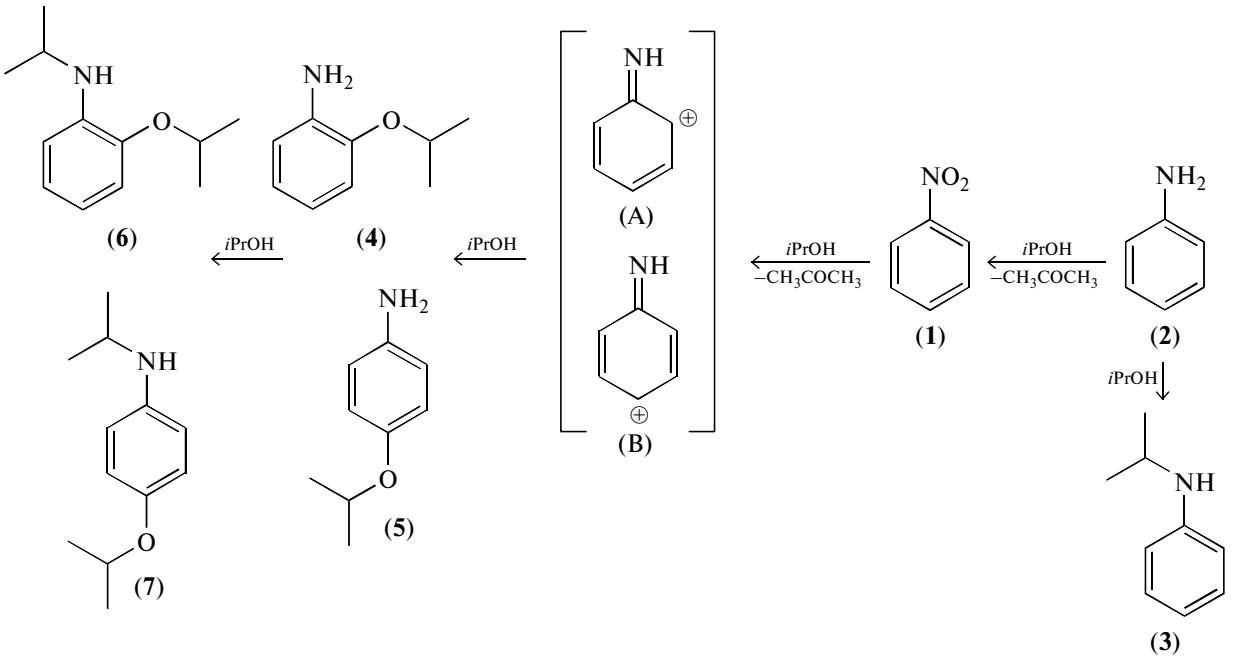
The aim of this work was to study the conversions of substituted nitrobenzenes (*o*-, *m*-, and *p*-nitrotoluenes) in a flow reactor using the *sc*-isopropanol/Al_2O_3 reducing system.

EXPERIMENTAL

Our studies were performed using *o*-, *m*-, and *p*-nitrotoluenes (Aldrich) and Al_2O_3 (Macherey-Nagel; pH 7 ± 0.5; 50–200 μm; BET free surface area, ~130 m^2/g). The reactions were experimentally studied under supercritical solvent conditions on a laboratory unit [6, 7] using a tubular reactor (6.0 × 0.8 mm; length, 3.0 m) loaded with granular Al_2O_3 (42 cm^3, 39.1 g). The reaction mixture was fed into the reactor as two flows. The first flow (supercritical isopropanol, 7 mL/min) was fed with a syringe pump into a mixer placed at the inlet of the reactor through a heat exchanger, in which it was heated to the reaction temperature. The second flow (1% solution of *o*-, *m*-, *p*-nitrotoluenes in isopropanol, 3 mL/min) was fed into the same mixer with a piston pump without preliminary heating.

The reaction mixture contact time (τ) was calculated as the ratio of the catalyst volume in the reactor (V_C, cm^3) to the total mixture flow rate at the inlet of the reactor (Q, cm^3/s). It proved to be ~4.2 min at a flow rate of 10 mL/min. The reactions were performed within the temperature range of 270–320°C at pressure $p \approx 200$ atm. The reactor temperature and pressure that ensured supercritical conditions for the reaction mixture were selected on the basis of thermodynamic calculations and phase diagrams.

The reaction mixture at the outlet of the reactor was cooled and sampled for analysis. The mixture of reaction products was analyzed by gas chromatography/mass spectrometry on an Agilent 6890N gas chromatograph equipped with an Agilent 5973N quadrupole mass analyzer as a detector. An HP-5MS quartz column (5% diphenyl–95% dimethylsyloxane copol-



Scheme 1. Reduction of nitrobenzene (**1**) in *sc*-*i*PrOH over Al_2O_3 [5].

ymer) with a length of 30 m, an inner diameter of 0.25 mm, and a stationary phase film thickness of 0.25 μm was used in our analysis. The range of mass : charge ratio $m : z$ was 29 : 500.

The percentage composition of mixtures was calculated from the surface areas of peaks in chromatograms with no correcting coefficients. Qualitative analysis of reaction products was performed by comparing the retention times of components and their full mass spectra to the NIST and Wiley 7 library data. To confirm the structure of some compounds unavailable in the NIST and Wiley 7 libraries, we preliminarily separated these compounds from their reaction mixtures. The structures of compounds **10**–**12**, **15**, **17**, **21**, and **22** was established from ^{1}H and ^{13}C NMR data. The structures of compounds **16**, **18**, and **23** were determined by analyzing their mass spectra and comparing them to the mass spectra of compounds whose structures were established from NMR data.

The ^{1}H and ^{13}C NMR spectra of compounds were recorded on a Bruker DRX-500 spectrometer (working frequencies, 500.13 MHz for ^{1}H and 125.76 MHz for ^{13}C) as $CDCl_3$ solutions. The signals of chloroform ($\delta_H = 7.24$ and $\delta_C = 76.90$ ppm) were used as internal standards. The structures of the synthesized compounds were established by analyzing the ^{1}H NMR spectra along with ^{1}H–^{1}H double resonance spectra, ^{13}C NMR *J*-modulated (JMOD) spectra, and two-dimensional ^{13}C–^{1}H heteronuclear correlation spectra with direct spin–spin coupling constants (C–H COSY, $^1J_{C,H} = 160$ Hz).

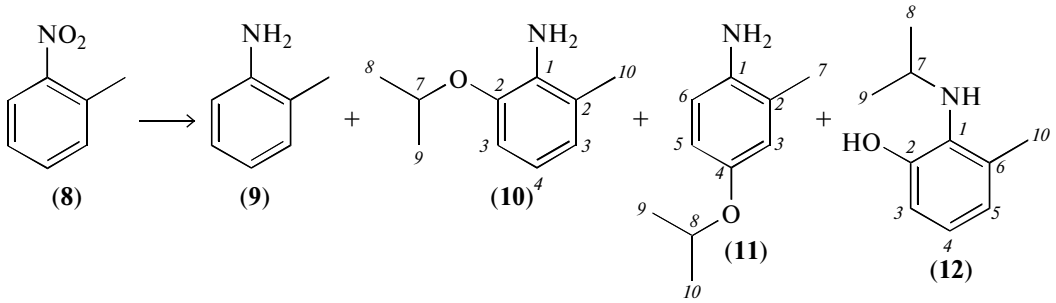
The mixtures obtained via the conversion of *o*-, *m*-, and *p*-nitrotoluenes at 320°C were separated by column chromatography on SiO_2. Hexane with an ethyl acetate gradient of 0 to 100% was used as the eluent with the addition of 1% NEt_3.

The products (0.10 g) obtained via the reduction of *o*-nitrotoluene (**8**) were separated into 2-isopropoxy-6-methylaniline (**10**, 0.008 g) and mixtures of 4-isopropoxy-2-methylaniline (**11**) with 2-(isopropylamino)-3-methylphenole (**12**) at ratios of 1 : 2.3 (0.028 g).

Compound 10. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 d (C^8H_3, C^9H_3, $J_{8(9),7} = 6.0$ Hz), 2.15 s ($C^{10}H_3$), 4.50 septet (H^7, $J_{7,8(9)} = 6.0$ Hz), 6.61 dd (H^4, $J_{4,3} = J_{4,5} = 7.7$ Hz), 6.67 bd (H^5, $J_{5,4} = 7.7$ Hz), 6.68 dd (H^3, $J_{3,4} = 7.7$ Hz, $J_{3,5} = 1.3$ Hz). ^{13}C NMR Spectrum ($CDCl_3$), δ, ppm: 135.28 s (C^1), 144.96 s (C^2), 111.13 d (C^3), 117.37 d (C^4), 122.45 d (C^5), 122.82 s (C^6), 70.60 d (C^7), 22.27 q (C^8, C^9), 17.20 q (C^{10}).

Compound 11. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.26 d (C^9H_3, $C^{10}H_3$, $J_{9(10),8} = 6.1$ Hz), 2.12 s (C^7H_3), 4.34 septet (H^8, $J_{8,9(10)} = 6.1$ Hz), 6.57 d (H^6, $J_{6,5} = 8.5$ Hz), 6.60 dd (H^5, $J_{5,6} = 8.5$ Hz, $J_{5,3} = 2.5$ Hz), 6.64 d (H^3, $J_{3,5} = 2.5$ Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 138.22 s (C^1), 123.84 s (C^2), 119.34 d (C^3), 150.67 s (C^4), 115.07 d (C^5), 115.88 d (C^6), 17.52 q (C^7), 70.91 d (C^8), 22.09 q (C^9, C^{10}).

Compound 12. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10 d (C^8H_3, C^9H_3, $J_{8(9),7} = 6.3$ Hz), 2.26 s ($C^{10}H_3$), 3.22 septet (H^7, $J_{7,8(9)} = 6.3$ Hz), 6.66 bd (H^5, $J_{5,4} = 7.8$ Hz), 6.74 dd (H^3, $J_{3,4} = 7.8$ Hz, $J_{3,5} = 1.3$ Hz), 6.91 dd (H^4, $J_{4,3} = J_{4,5} = 7.8$ Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 131.45 s, 134.15 s (C^1,



Scheme 2. Conversions of *o*-nitrotoluene (**8**) in *sc*-*i*PrOH.

C^6), 153.20 s (C^2), 111.51 d (C^3) 125.49 d (C^4), 121.49 d (C^5), 49.16 d (C^7), 23.10 q (C^8, C^9), 17.52 q (C^{10}).

The products (0.11 g) obtained via the reduction of *m*-nitrotoluene (**13**) were separated into 2-isopropoxy-5-methylaniline (**15**, 0.013 g) and 2-isopropoxy-*N*-isopropyl-5-methylaniline (**17**, 0.024 g).

Compound 15. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 d (C^8H_3, C^9H_3, $J_{8(9),7}$ = 6.1 Hz), 2.20 s ($C^{10}H_3$), 4.43 septet (H^7, $J_{7,8(9)}$ = 6.1 Hz), 6.47 ddq (H^4, $J_{4,3}$ = 8.1 Hz, $J_{4,6}$ = 2.2 Hz, $J_{4,10}$ = 0.7 Hz), 6.53 d (H^6, $J_{6,4}$ = 2.2 Hz), 6.67 d (H^3, $J_{3,4}$ = 8.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 137.15 s (C^1), 138.54 s (C^2), 114.10 d (C^3), 118.59 d (C^4), 130.65 s (C^5), 116.14 d (C^6), 70.92 d (C^7), 22.23 q (C^8, C^9), 20.62 q (C^{10}).

Compound 17. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.21 d (C^8H_3, C^9H_3, $J_{8(9),7}$ = 6.3 Hz), 1.31 d ($C^{11}H_3$, $C^{12}H_3$, $J_{11(12),10}$ = 6.1 Hz), 2.25 s ($C^{13}H_3$), 3.59 septet (H^7, $J_{7,8(9)}$ = 6.3 Hz), 4.42 septet (H^{10}, $J_{10,11(12)}$ = 6.1 Hz), 6.38 ddq (H^4, $J_{4,3}$ = 8.1 Hz, $J_{4,6}$ = 2.2 Hz, $J_{4,13}$ = 0.7 Hz), 6.43 d (H^6, $J_{6,4}$ = 2.2 Hz), 6.66 d (H^3, $J_{3,4}$ = 8.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 138.41 s (C^1), 142.73 s (C^2), 113.33 d (C^3), 115.86 d (C^4), 130.75 s (C^5), 111.64 d (C^6), 43.84 d (C^7), 23.01 q (C^8, C^9), 71.14 d (C^{10}), 22.26 q (C^{11}, C^{12}), 21.12 q (C^{13}).

The products (0.10 g) obtained via the reduction of *p*-nitrotoluene **19** were separated into 2-isopropoxy-4-methylaniline (**21**, 0.005 g) and 2-isopropoxy-*N*-isopropyl-4-methylaniline (**22**, 0.011 g).

Compound 21. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 d (C^8H_3, C^9H_3, $J_{8(9),7}$ = 6.1 Hz), 2.23 s ($C^{10}H_3$), 3.60 bs (NH_2), 4.49 septet (H^7, $J_{7,8(9)}$ = 6.1 Hz), 6.56 ddq (H^5, $J_{5,6}$ = 7.8 Hz, $J_{5,3}$ = 1.7 Hz, $J_{5,10}$ = 0.7 Hz), 6.60 d (H^6, $J_{6,5}$ = 7.8 Hz), 6.61 bd (H^3, $J_{3,5}$ = 1.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 134.65 s (C^1), 145.35 s (C^2), 114.73 d (C^3), 127.84 s (C^4), 121.29 d (C^5), 115.26 d (C^6), 70.62 d (C^7), 22.26 q (C^8, C^9), 20.83 q (C^{10}).

Compound 22. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19 d (C^8H_3, C^9H_3, $J_{8(9),7}$ = 6.3 Hz), 1.32 d ($C^{11}H_3$, $C^{12}H_3$, $J_{11(12),10}$ = 6.1 Hz), 2.22 s ($C^{13}H_3$), 3.55 septet (H^7, $J_{7,8(9)}$ = 6.3 Hz), 4.47 septet (H^{10}, $J_{10,11(12)}$ = 6.1 Hz), 6.51 d (H^6, $J_{6,5}$ = 8.1 Hz), 6.60 bd (H^3, $J_{3,5}$ = 1.8 Hz), 6.63 ddq (H^5, $J_{5,6}$ = 8.1 Hz, $J_{5,3}$ = 1.8 Hz, $J_{5,13}$ = 0.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 136.20 s (C^1), 144.99 s (C^2), 114.20 d (C^3), 125.33 s (C^4), 121.35 d (C^5), 111.07 d (C^6), 44.26 d (C^7), 23.00 q (C^8, C^9), 70.82 d (C^{10}), 22.27 q (C^{11}, C^{12}), 20.72 q (C^{13}).

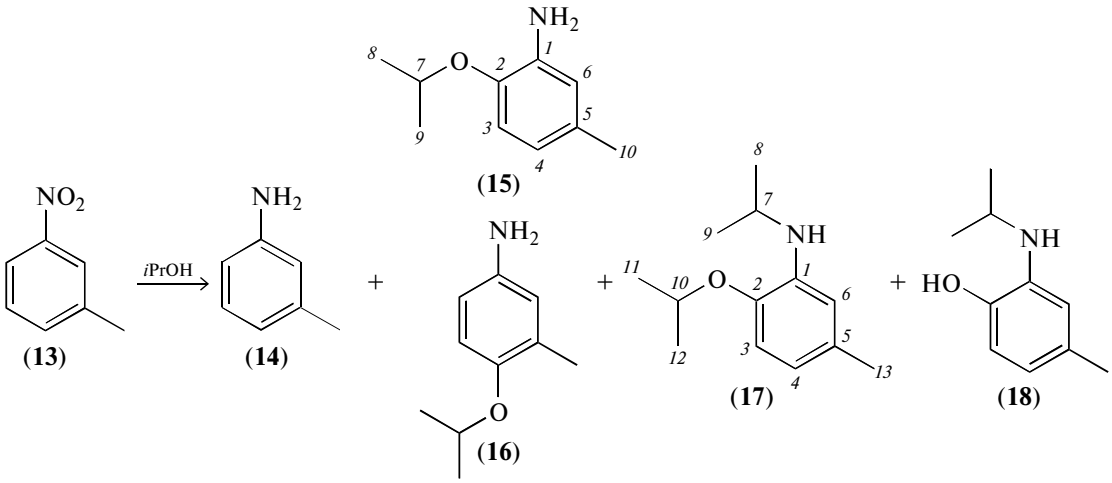
Table 1. Conversion of *o*-nitrotoluene (**8**) in *sc*-*i*PrOH

T, °C	Conversion, %	Selectivity, %			
		9	**10**	**11**	**12**
270	2	100	–	–	–
300	20	66	12	13	9
320	100	62	13	12	13

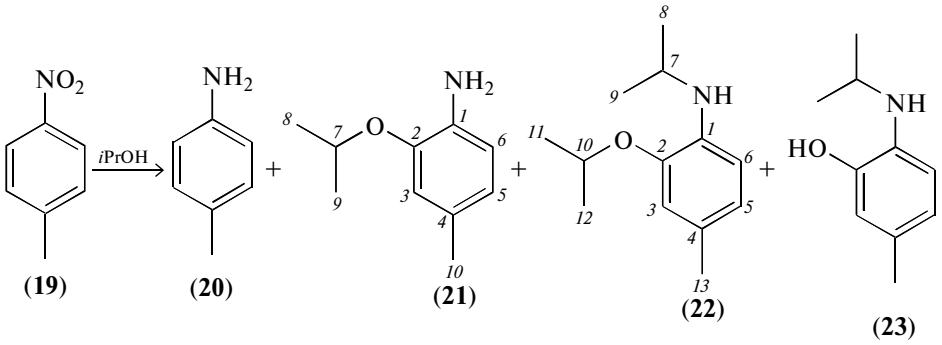
RESULTS AND DISCUSSION

In studying the processes that occur during the reduction of nitrobenzene (**1**) over Al_2O_3 in a flow reactor in supercritical alcohols, we found [5] that the reaction mixture contained products of *N*-alkylation (**3**), alkoxylation (**4** and **5**), and both these processes (**6** and **7**) in addition to aniline (**2**), a key product, independently of the composition of the supercritical solvent and the reaction temperature (Scheme 1). It seems that compounds **4** and **5** result from the reaction of intermediately formed iminium cations *A* and *B* with isopropanol. This route of the formation of compounds **4**–**7** was confirmed by the absence of alkoxylation products for aniline **2** allowed to stand under reaction conditions [5]. It was noteworthy that introducing a halide atom into the aromatic ring almost completely blocked the process of alkoxylation [5].

We began our study of the conversion of nitrotoluenes with *o*-nitrotoluene (**8**, Scheme 2). Conversion was 2% at 270°C, and *o*-toluidine (**9**) proved to be the only product (Table 1). After the temperature was raised to 300°C, conversion grew to 20%, and the selectivity to *o*-toluidine (**9**) reached 66%. It should be noted that the conversion of nitrobenzene under the same conditions was slightly higher [5] than for *o*-nitrotoluene. Comparing the conversions of *o*-chloronitrobenzene [5] and *o*-nitrotoluene (**8**) under the same conditions, we may conclude that *ortho*-halogenated nitrobenzene is more reactive than *o*-nitrotoluene.



Scheme 3. Conversions of *m*-nitrotoluene (**13**) in *sc*-*i*PrOH.



Scheme 4. Conversions of *p*-nitrotoluene (**19**) in *sc*-*i*PrOH.

Raising the temperature further to 320°C enabled quantitative conversion, but the selectivity to compound **9** fell slightly to 62%. The by-products of these conversions were the products of alkoxylation (**10** and **11**) and phenol (**12**) that was probably formed via the reaction of iminium cations *A* and *B* (Scheme 1) with water liberated in the process of reduction. Note that we did not observe the formation of aminophenols in studying the conversion of nitrobenzene (**1**). As would be expected from the mechanism shown in Scheme 1, substitution occurred in the *ortho*- and *para*-positions relative to the amino group.

When *m*-nitrotoluene (**13**) was used as the initial compound, the conversion at 300°C was slightly higher than for *o*-nitrotoluene (**8**) and equal to 46% at 89% selectivity to *o*-toluidine (**14**, Scheme 3, Table 2). Raising temperature to 320°C reduced the selectivity to compound **14** to 78% due to the greater amount of by-products. As for the reduction of compound **8**, all of the by-products proved to be products of alkoxylation (some with subsequent *N*-alkylation) or hydroxylation.

Table 2. Conversion of *m*-nitrotoluene (**13**) in sc-*i*PrOH

T, °C	Conversion, %	Selectivity, %				
		14	**15**	**16**	**17**	**18**
300	46	89	7	–	–	4
320	100	78	4	5	8	5

Since only the *ortho*-position in *p*-nitrotoluene (**19**) is free for the addition of an oxygen-containing reagent (isopropanol or water), the composition of the reaction mixture in the reduction of this compound could be expected to simplify. Indeed, the reaction mixture at 300°C contained only two products: *p*-toluidine (**20**) and 2-isopropoxy-4-methylaniline (**21**), with selectivities of 83 and 17%, respectively, at 35% conversion (Scheme 4, Table 3). After the temperature was raised to 320°C, 2-isopropoxy-*N*-isopropyl-4-methylaniline (**22**) and phenol (**23**) were also revealed in the reaction mixture.

Table 3. Conversion of *p*-nitrotoluene (**19**) in sc-*i*PrOH

T, °C	Conversion, %	Selectivity, %			
		20	**21**	**22**	**23**
300	35	83	17	–	–
320	100	60	11	15	14

CONCLUSIONS

We showed that *o*-, *m*-, and *p*-nitrotoluenes are subject to reduction with supercritical isopropanol over Al_2O_3 in a flow reactor at contact times of less than 5 min, and the total conversion of initial compounds was in all cases reached at 320°C. The key products at this temperature proved to be the corresponding toluidines with selectivities of 60 to 78%. Almost all of the by-products were ethers or phenols resulting from the reaction between alkoxylation and isopropanol with subsequent partial *N*-alkylation or from reactions with water, respectively.

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