ELSEVIER

Dyes and Pigments 40 (1999) 205–209

DYES AND PIGMENTS

Studies on the selective synthesis of N-monoalkyl aromatic amines

Xiaojian Zhou *, Zuwang Wu, Li Lin, Guijuan Wang

Department of Fine Chemicals, Dalian University of Technology, Dalian 116012, People's Republic of China

Received 30 April 1998; accepted 16 June 1998

Abstract

The intermediate Schiff base was detected by GC–MS in the reductive alkylation of nitro aromatic compounds catalysed by Raney nickel, supporting the proposed reaction mechanism. The influence of substituents and alkylating agents-alcohols on the reaction were studied and the results showed that both the position and properties of the substituents and the structures of the alcohols used have a significant effect on the N-alkylation. Steric hindrance is the main factor which inhibits N-alkylation and causes side reactions. High yields of N-monoalkyl arylamines were obtained with nitro compounds having *para-* or *meta-* substituents and with straight chain alcohols, except for methanol. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: N-alkylation; Schiff base; Substituent effect; Alcohol influence; Steric hindrance; Raney nickel

---

1. Introduction

With the emphasis on environmental protection, studies on environmentally friendly processes for the chemical industry are of increasing importance. Thus, the synthesis of aromatic amines from nitro compounds is, or will be mainly effected using catalytic hydrogenation instead of the traditional iron powder reduction or sodium sulfide reduction. N-alkylation of aromatic amines is a typical consecutive reaction, but selectivity control is still a big challenge, for the synthesis of N-monoalkyl arylamines [1], and many methods such as N-alkylation with a hydrogenation catalyst and reductive alkylation [2,3], or with zeolite and solid acid as catalyst [4] have been studied [5].

With Raney nickel as a catalyst, nitro compounds as start material and ethanol as alkylating agent, the novel process gives high conversion and selectivity for *N*-ethyl-arylamines [6]. The effect of substituents in the phenyl ring and the influence of alcohols as alkylating agents on the reaction were studied. The Schiff base proposed as an intermediate in this reaction was detected by GC–MS.

2. Experimental: general procedure

First, 0.05 mol Nitro aromatic compound, 0.25 mol of the appropriate alcohol and 0.58 g Raney nickel were placed into a 200 ml autoclave and the system purged three times with nitrogen

---

* Corresponding author at present address: Laboratory of Technical Chemistry, ETH-Zentrum, 8092 Zurich, Switzerland

PII: S0143-7208(98)00054-0

and then three times with hydrogen. Hydrogenation was carried out under 2.0 MPa hydrogen pressure at 90°C for about 2 h. When the residual hydrogen was exhausted below 50°C, alkylation was complete at 140°C over 18 h. The obtained products were analysed by an HP 6890 Series GC or a Shimadzu QP-5000 GC–MS. All products were purified by fractional distillation or recrystallization and characterized by NMR FX90Q JEOL.

3. Results and discussion

3.1. Detection of Schiff base by GC–MS

The mechanism of the N-alkylation of aromatic amines with an alcohol catalysed by Raney nickel has been proposed to occur via a Schiff base [3] [Eqs. (1–3)].

$$RCH_2OH \overset{RaneyNi}{\rightleftharpoons} RCHO + H_2 \quad (1)$$

$$RCHO + ArNH_2 \rightleftharpoons RCH = NAr + H_2O \quad (2)$$

$$RCH = NAr + H_2 \overset{RaneyNi}{\rightarrow} RCH_2NHAr \quad (3)$$

Detection of the Schiff base in this reaction has been rarely reported. In this present work, for the reduction and alkylation of nitrobenzene with isopropanol and isobutyl alcohol, the respective Schiff bases were detected by GC–MS in the final products, which therefore supports the suggested mechanism (Fig. 1).

3.2. Effect of substituents on the reaction

3.2.1. Effect of the position of the methyl group on the reduction–alkylation of nitrotoluenes.

With ortho, meta and para-nitrotoluene as starting material and ethanol as alkylating agent, the reduction–alkylation products were analysed by GC using the area normalisation method. The composition and yield of products are shown in Table 1.

For the reaction of meta and para-nitrotoluene, the results are quite similar. *N,N*–Diethyl-*p*-toluidine is only slightly increased since the basicity of *para*-toluidine is a little higher. The yield of *N*-ethyl-ortho-toluidine is low. Even when the alkylation was carried out at 160°C and with four times Raney nickel, the yield of the product was only 70%. This result could not only be attributed to the relatively low basicity of *ortho*-toluidine, but mainly to the steric hindrance of the *ortho*-methyl group, which prevents not only the formation of the Schiff base, but also hydrogenation of Schiff base. Since acetaldehyde, formed from dehydrogenation of ethanol [Eq. (1)] always has a low concentration in the reaction, and catalytic hydrogenation occurs only at the surface of Raney nickel, the absorption of the Schiff base in the catalyst causes increased steric hindrance.

3.2.2. Effect of para-substituents on the reaction

The nitro compounds with different para–substituents were used as starting material and ethanol as alkylating agent; all reactions were carried out under the same conditions as above Table 2.

Since $COOC_2H_5$ is a strong electron acceptor, the reduction product ethyl *p*-aminobenzoate is a very weak base, conversion to N-alkylation is low, while the selectivity to N-monoethylation is excellent. When the ethylation was completed at 150°C for 24 h with three times Raney nickel, 95.3% yield of ethyl *p*-ethylaminobenzoate was obtained. This reaction shows both high conversion and excellent selectivity. The other three substituents are electron donor groups, and conversion of the aromatic amines are quite similar, but the amounts of *N,N*-diethylarylamines are increased with the decrease of the Hammett constants of the substituents and the increase in the basicity of the corresponding aromatic amines. The results also show, that alkylation should be carried out under mild conditions. According to observed by-product content, side reactions such as ring-hydrogenation might also be affected by the substituents [6].

3.3. Influence of alcohols as alkylating agents

Ethanol as alkylating agent is widely used in N-alkylation, especially when acid is used as a catalyst,

Table 1
Effect on the position of the methyl group

Nitro-toluene	pK_b of toluidine	Toluidine (%)	N-ethyl-toluidine (%)	N,N-diethyl-toluidine (%)	By-products (%)	Yield of N-ethyl-toluidine (%)
Ortho	9.56	44.40	53.40	0.00	2.20	46.20
meta	9.28	1.60	92.20	0.90	5.30	89.70
para	8.90	0.37	91.00	2.60	6.03	89.10

Table 2
Effect of *para* substituents on the reaction

R	Hammett constant σ	pK_b of p-$RC_6H_4HN_2$	Yield of p-$RC_6H_4NHC_2H_5$(%)
$COOC_2H_5$	0.502	11.50	74.0
H	0.000	9.40	85.9
CH_3	−0.170	8.90	89.1
OCH_3	−0.268	8.66	85.8

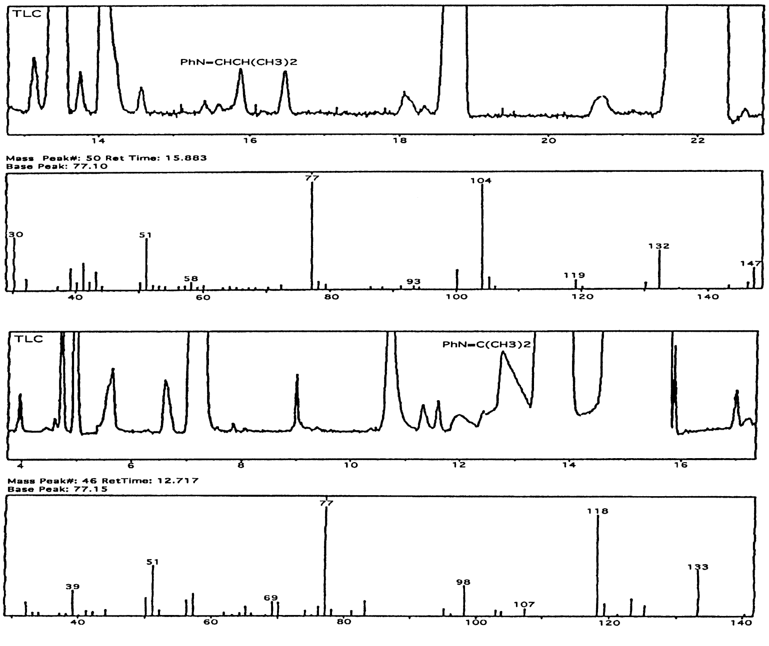


Fig. 1. GC-MS spectrum of Schiff base $PhN{=}CHCH(CH_3)_2$ and $PhN{=}C(CH_3)_2$.

but this results in low N-monoalkylating selectivity. The mechanism of the reaction catalysed by Raney nickel is totally different with that by acid, and the influence of the alcohol on the reaction might thus be different. Seven different alcohols were used Table 3.

Except for methanol, all straight chain alcohols gave high conversion and selectivity to the aimed products. When the methylation of aniline was carried out at 160°C for 32 h and with 50% more Raney nickel, there was still only 44.11% N-methylaniline in the final products with 42.46% aniline.

Table 3
Influence of alkylating agents-alcohols to the reaction

Nitroaromatic compound	Alkylating agent alcohol	Amine (%)	N-alkylamine (%)	By-products (%)	Yield of N-alkyl-arylamine (%)
$C_6H_5NO_2$	CH_3OH	89.26	8.38	2.36	10.1
$C_6H_5NO_2$	C_2H_5OH	0.73	86.70	12.57	85.1
$C_6H_5NO_2$	*n*-C_3H_7OH	0.20	80.90	18.90	84.4
$C_6H_5NO_2$	*n*-C_4H_9OH	0.76	77.70	21.54	83.2
$C_6H_5NO_2$	*n*-$C_8H_{17}OH$	0.74	88.30	10.96	84.9
m-$CH_3C_6H_4NO_2$	C_2H_5OH	1.60	92.20	6.20	89.7
m-$CH_3C_6H_4NO_2$	*n*-C_4H_9OH	0.21	87.00	12.79	85.9
$C_6H_5NO_2$	*i*-C_3H_7OH	22.64	25.62	51.74	26.7
$C_6H_5NO_2$	*i*-C_4H_9OH	55.70	15.00	29.30	12.0

Table 4
Kp value of the dehydrogenation of alcohols at 140°C

Alcohol	CH_3OH	C_2H_5OH	n-C_3H_7OH	i-C_3H_7OH
Kp	1.00×10^{-5}	5.00×10^{-3}	1.77×10^{-3}	1.33×10^{-1}

There are two feasible explanations for the difficult methylation of aniline catalysed by Raney nickel at reflux temperature with methanol. Rice and Kohn thought no formaldehyde could be formed by catalysis with Raney nickel at this temperature [3], and Ainsworth concluded that the formed formaldehyde would easily undergo the Cannizzaro reaction [7].

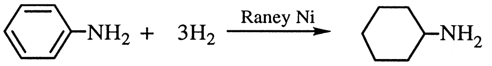
$$2HCHO + H_2O \rightarrow CH_3OH + HCOOH \qquad (4)$$

By calculation of the equilibrium constant (*Kp*) of the dehydrogenation of the alcohol at 140°C, it was found that the *Kp* values were quite different (Table 4)

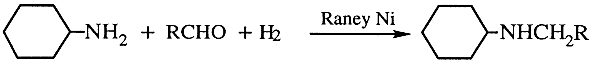
$$RCH_2OH(g) \rightleftharpoons RCHO(g) + H_2(g) \qquad (5)$$

The difficult dehydrogenation of methanol is suggested to be the main reason for the low yield of N-methylation, and this result also supports the mechanism via a Schiff base. The relative higher yields of alkylation of *m*-toluidine than that of aniline suggests that the methyl group might partly prevent side reactions.

Only very low yields of the intended products were obtained, together with large amount of by-products and unreacted aniline, when branched chain alcohols were used as alkylating agent. Here the dehydrogenation of isopropanol is easier than that of *n*-propanol according to thermodynamic data (Table 4), but due to the steric hindrance of acetone, the formation of the Schiff base from aniline and acetone and the hydrogenation of the Schiff base is difficult, and this becomes the control step of the whole reaction. The hydrogen formed would be in favour of side reactions such as ring-hydrogenation [Eqs. (6) and (7)].

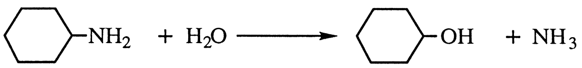


(6)

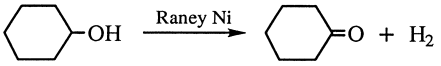


(7)

In all experiments, cyclohexanol and cyclohexanone, or derivatives of these compounds with corresponding substituents were detected by GC–MS or GC; the formation of these products might proceed through the following reactions [Eqs. (8) and (9)].



(8)



(9)

4. Conclusion

The mechanism of the reductive alkylation of nitro compounds with alcohols as alkylating agents and catalysed by Raney nickel was shown to occur via a Schiff base process. Para-electron donor substituents favoured N-alkylation, while para-electron acceptors inhibited the reaction. An *ortho*-group in the aromatic amine results in steric hindrance to N-alkylation. Higher conversions and selectivity for N-monoalkyl arylamines were achieved if straight chain alcohols, except methanol, were used; the low conversion of methylation was due to the difficult dehydrogenation of methanol to formaldehyde. The low conversions and poor selectivity of the reaction with branched chain alcohols were also attributed to steric hindrance.

References

[1] Verardo G, Giumanini AG, Strazzalini P, Poiana M. Synthesis 1993;1:121.
[2] Immel O, Schwarz H-H, Braden R. DE 3840194, 1990.
[3] Rice RG, Kohn EJ. J Am Chem Soc 1955;77:4052.
[4] Klug G, Buysch HJ, Puppe L. DE 3803661, 1989.
[5] Zhou XJ, Wu ZW. Progress of Chemical Industry 1996;1:5 (in Chinese).
[6] Zhou XJ, Wu ZW, Lin L., et al. Dyes and Pigments 1998;36(4):365.
[7] Ainsworth C. J Am Chem Soc 1956;78:1635.