Recl. Trav. Chim. Pays-Bas 114, 311-315 (1995)

Hydrocarbons and chloroaromatics from anilines and *n*-butyl nitrite.

Angelo G. Giumanini *, Giancarlo Verardo, Fausto Gorassini and Paolo Strazzolini

Department of Chemical Sciences and Technologies, University of Udine, I-33100 Udine, Italy (Received October 4, 1994)

Abstract. A single reagent, *i.e.* n-butyl nitrite, can be used to oxidize an aromatic amine, or the corresponding N-methylene derivative, to a diazo compound followed by its subsequent reduction to hydrocarbon in a single batch. Alternatively, a chloro derivative can be obtained if carbon tetrachloride is used as the solvent. The reactions appear to be general and complete product identification was accomplished.

Introduction

Diazotation of primary aromatic amines (1) was first accomplished in an aqueous medium and chemists have been reluctant to recognise, in books and authoritative reviews¹, that aprotic media may offer interesting and useful variations on this theme, especially with respect to the frequent fate of the obtained diazo derivative (i.e., of being eventually transformed into an ArX). Perhaps it is time that the pioneering work of Friedman² on the aprotic diazotation of 2-aminobenzoic acid to generate in situ benzine, may be developed to its full potential. One of the aims of exploiting aprotic diazotation is certainly the elimination of the annoying need to separate the diazonium salts from selected and often costly anions (e.g. BF_4^-) in order to perform the desired subsequent aromatic substitution.

$$\operatorname{ArNH}_2$$
 + HNO_2 \longrightarrow $\operatorname{ArN}_2^{\oplus}$ $\xrightarrow{X^{\oplus}}$ $\operatorname{ArN}_2^{\oplus}$ X^{\oplus} $\xrightarrow{Y^{\oplus}}$ ArY

Almost as important is the wish to eliminate the use of carefully chilled solutions of NaNO₂ acidified with a mineral acid or, perhaps worse, acetic acid and an alkyl nitrite. Previous attempts to carry out the full sequence in a single step (not only a single batch!) were not crowned with success, perhaps due to some unfortunate choices of experimental conditions. The development of new techniques will involve a re-assessment of the X carrier.

The aim of this contribution is to describe some experimental variations of the overall Sandmeyer reactions.

Results and discussion

Our first observations arise from our recent study³ of the reaction between alkyl nitrites and N-methylene aromatic amines. Monomeric N-methylene-2,6-di-isopropylaniline (2) surprisingly did not add *n*-butyl nitrite (3) across the CN double bond but, after prolongued reflux, was partly transformed into 1,3-diisopropyl-benzene (4a); chlorine from the solvent (CH_2Cl_2) ended up in the other compound, i.e. 1,3-diisopropyl-2-chlorobenzene (5a), accounting for a complete material balance of the transformation of 2. On a shorter refluxing time 2,6-diisopropylaniline (1a) was also detected.

Two possible initial pathways may be invoked for the observed result. In one, 2,6-diisopropyl-N-methyleneaniline (2) is slowly hydrolyzed to the amine 1a and is eventually aprotically diazotized to 6a. 6 may be in equilibrium with the products of its ionic (7 and 8) and radical (9 and 10) dissociation, the prevalence of any particular form strongly depending on the temperature, pH and nature of the solvent (Scheme 1).

Radicals 9 and 10 may react with each other to yield the diazene 13, an intrinsically unstable species, undergoing fast nitrogen elimination to 4. Decomposition to aryl radicals 9 is the only step which is expected to give the aryl chloride 5 by chlorine abstraction from the solvent. The alternative pathway is a reaction not previously described which leads to the unstable intermediate 16 as the result of the addition of n-butyl nitrite (3) across the double bond of 2, followed by an internal rearrangement and cleavage.

$$2 + 3 \longrightarrow Ar - N \longrightarrow CH_2 - Pr \xrightarrow{-CH_2O} N \equiv N \longrightarrow O - Bu$$

The water required for the initiation of the hydrolysis of 2 comes from the slow decomposition of 3 into butanal (12) and monomeric hyponitrous acid, the latter quickly dimerizing and producing dinitrogen oxide and water. BuO-NO ---- NOH

+

PrCHO

2 NOH \longrightarrow N₂O₂H₂ \longrightarrow N₂O н,0 +

Once some amine 1a is formed, the additional water required is produced from its diazotation by 3; the use of aged 3, although indistinguishable from the fresh product by GC-MS, ¹H-NMR and IR spectroscopy, resulted in faster initial reactions, probably because of higher initial concentrations of water. That the chlorine present in 5a was captured from the solvent by the aryl radical via a radical abstraction was confirmed by the fact that a similar reaction occurred in CCl₄. On the other hand, when no solvent was used, the only product was the hydrocarbon 4a. Reduction of diazotized aromatic amines by alcohol (ethanol) by a radical mechanism is a well-established



Scheme 1.



process⁴. Aprotic diazotations of aromatic amines under a variety of conditions have been described in the literature, using nitrosyl halides⁵, alkyl nitrite with bases⁶, acids⁴ and aprotic media⁷⁻⁹, and alkyl thionitrite^{10,11}. Addition of copper halides to the reaction mixture caused the production of aryl halides by a radical process^{9,10}, whereas the addition of some organic hydrogen donors⁸ allowed reduction to the corresponding hydrocarbon. The use of *n*-butyl nitrite (3) allows a single reagent to be used in a one-batch operation, both for the reductive deamination reaction without solvent, and the deamination-chlorination reaction in CCl₄.

The intermediacy of a species like 6, having a detectable lifetime in the reaction mixture under the present condi-tions, was ruled out by ¹H-NMR analysis at convenient intervals before any work-up. When any volatile material was removed from the reaction mixture by vacuum distillation and the mixture was treated with hot aqueous sodium hydrogen carbonate, gas-chromatographic analysis of the residual organic material did not show any of the corresponding 2,6-diisopropylphenol (17a): this fact was taken as an indication that the lifetime of any diazotized species was very short. The imine 2 reacted with 3 in the absence of any chlorinated solvent to yield the amine 1a and hydrocarbon 4a: once again, no n-butoxy derivative was formed. When the reaction solvent was CCl₄ or CH_2Cl_2 , the outcome was quite similar to that obtained on reacting arylamines with alkyl thionitrites in the presence of CCl_4^{14} . The hypothesis that the amine 1a was the intermediate precursor of the diazotized species was confirmed by the direct reaction of 1a with 3, yielding the hydrocarbon 4a and the chloro derivative 5a in CH_2Cl_2 , but only 4a (82%) when the chlorine donor was absent. This reactivity pattern was found to be absolutely general: 4-chloroaniline (1b), treated with 3 without solvent, yielded chlorobenzene (4b, 70%) accompanied by minor amounts of 3,4'- and 4,4'-dichlorobiphenyls (14b and 14'b). When CCl₄ was used as the solvent, chlorine-atom donation to the diazotized substrate was dominant, producing 1,4-dichlorobenzene (5b, 53%). Analogous behaviour was found using 4-tert-butylaniline (1c): reduction to tert-butylbenzene (4c) was smooth and extensive (48%), whereas the presence of CCl₄ caused the production of 1-tert-butyl-4chlorobenzene (5c, 58%). The sterically hindered amine 1a was transformed into the chloride (5a, 38%) by the

same reaction. Curiously, the produced hydrocarbon 4c underwent partial nitration to 1-*tert*-butyl-3- and -4nitrobenzene (18 and 19). In addition, a minor amount of 4,4'-di-*tert*-butylazobenzene (15c) was formed in the reactions of 1c, thus giving further support to the radical course of the reaction.



The product **20**, formed from attack of a 4-*tert*-butylphenyl radical on the preformed chloro derivative 5c, was also observed; arylation of aromatics by the alkyl-nitrite/aromatic-amine system, is a well established process¹².



The reactions in CCl_4 were invariably carried out at ca. 60°C; heating was interrupted if the reaction became too rapid. The disappearance of **1a** was much slower than that of the other tested substrates. Incidentally, we noticed the inherent instability of the product **5c** in the presence of excess **3**; when the heating time was prolonged, **5c** underwent transformation into the ether **11c** and nitrophenol **21**. This behaviour may be rationalized as shown in Scheme 2.

Nitric acid may be slowly formed by hydrolysis of 3 and the nitration of 4-*tert*-butylphenol (11c) could be performed both by the nitric acid and, perhaps, by the nitrite itself. It should be noticed that, when CCl_4 was not present, the formation of 11c was barely noticeable. Similar behaviour was observed in the experiments with 1a. Anilines were found to undergo partial nitration by the action of 3^{13} . In an attempt to force the possibly compet-



ing ionic pathway of the diazotized-product decomposition, we carried out the diazotation of 1a by 3 in the presence of *n*-butanol: the greater quantities of 11a were formed although the overall reaction was much slower. This fact allowed the butanal (12) formed to react with 1a to yield N-butylidene-2,6-diisopropylaniline (22).

The rationalization offered in Scheme 1 for the reductive path of the reaction between aromatic amines (1) and *n*-butyl nitrite (3) foresees the production of butanal (12). But, surprisingly, this compound could never be detected in the reaction mixtures, where invariably we found its n-butyl acetal 23. The fact clearly showed that reduction could not possibly come only from hydrogen abstraction from the butoxy radical: 3 and hydrogen-containing solvents and reagents could also be sources of hydrogen. Moreover, the formation of 23 under these acid-free conditions was not expected. In the absence of positive experimental confirmation, we suggest that 3 acts as a catalyst, as shown in Scheme 3.

Conclusions

These preliminary observations on a limited number of aromatic amines allow us to make some interesting remarks. Aprotic diazotation may be conducted without the need for special reducing agents and added acids. The radical decomposition of the diazotized amines, which does not need any special catalyst, may be due to the abstraction of chlorine atoms from alkyl halides, thus eliminating the need for copper chloride or other metal halides, a definitive advantage for nature-friendlier reactions and permitting the elimination of some cumbersome unit operations in possible industrial applications. The overall processes appear to represent a real step forward in the replacement of the original Sandmeyer conditions.

Experimental

Materials

Primary aromatic amines were obtained from a commercial source (Aldrich, Milano, Italy). *n*-Butyl nitrite¹⁴ (3) and *N*-methylene-2,6-di-isopropylaniline¹⁵ (4) were prepared as previously described.

Product analyses

Preliminary identification of the components of the intact reaction mixtures was made by ¹H-NMR spectroscopy (Bruker Mod. AC-F 200 spectrometer) and GC-MS spectrometry (Fisons TRIO 2000 apparatus), using MS library data and direct comparison with commercially available materials whenever possible. Work-up consisted of a preliminary reduced-pressure evaporation of volatile materials, followed by GC-MS analysis of the residue. Pure products were obtained by fractional distillation at suitable pressures. Confirmatory structural evidence on the major products was obtained by IR (Jasco Mod. DS-702-G spectrophotometer) and ¹H-NMR spectroscopy¹⁶ Product yields were determined on the reaction mixtures after the elimination of 3 by conventional distillation using 1-bromo-4methoxybenzene as internal standard and appropriate calibration factors.

Reaction procedure and analysis: N-methylene-2,6-diisopropylaniline (2) and n-butyl nitrite (3)

A. The imine 2 (2.38 mmol) and n-butyl nitrite (3, 9.52 mmol) were kept at 40°C in argon atmosphere under stirring. Monitoring of the reaction course by GC-MS showed that, in addition to a small quantity of amine 1a, the only product formed was the hydrocarbon 1,3-diisopropylbenzene (4a, 70% at 20 h), which could be isolated by conventional distillation under reduced pressure after acid-base separation from a large-scale experiment. 4a: MS (70 eV) m/z: 162 (M⁺, 30), 147 (100), 119 (63), 105 (38), 91

(40), 77 (12), 43 (57) and 41 (25).

B. An experiment was carried out as described above in solution of CH₂Cl₂ (1.5 ml). After 20 h, two products were formed in practically the same concentrations, namely the hydrocarbon 4a (25%) and 2-chloro-1,3-diisopropyl-benzene (5a, 25%).

5a: b.p. 54°C at 20 Pa. MS (70 eV) m / z: 198 (M⁺, 8), 196 (M⁺, 21), 183 (30), 181 (100), 161 (4), 153 (6), 139 (10), 117 (28), 91 (17), 77 (10), 43 (40) and 41 (18). ¹H-NMR (CDCl₃): δ 1.24 (d, 12H; J 6.9 Hz), 3.49 (sept, 2H; J 6.9 Hz) and 7.05-7.27 (m, 3H). IR (NaCl): 2960vs, 2920s, 2862s, 1458s, 1418s, 1379m, 1358m, 1248m, 1054m, 1023m, 787s and 729s cm-

C. When CCl_4 was replaced by CH_2Cl_2 the prevalent product in the mixture was 5a (25%, 60 h, 60°C), which was separated by fractional distillation in a larger-scale experiment. Beside the unreacted imine 2 (40%), minor components of the reaction mixture were la (6%) and 4a (3%).

2,6-Diisopropylaniline (1a) and n-butyl nitrite (3)

A. A solution of 1a (2.88 mmol) and 3 (8.65 mmol) was kept at 60°C for 5 h in an inert atmosphere: the hydrocarbon 4a was the only GC-volatile component of the mixture (82%).

B. A similar experiment in CCl_4 (1.5 ml) gave a mixture at 5 h, containing the aryl chloride 5a as the prevalent product (58%); the amine was totally consumed and some 2-butoxy-1,3-diisopropyl-benzene (11a, 10%) was formed. Only a trace of 4a was present.

11a: b.p. 72°C at 20 Pa. MS (70 eV) m/z: 234 (M⁺, 24), 178 (32), 163 (100), 135 (12), 117 (10), 91 (18), 57 (11), 43 (13) and 41 (28). ¹H-NMR (CDCl₃): δ 0.99 (t, 3H; J 7.2 Hz), 1.23 (d, 12H; J 6.9 Hz), 1.48–1.63 (m, 4H), 3.33 (sept, 2H; J 6.9 Hz), 3.74 (t, 2H; J 6.5 Hz) and 7.07–7.12 (m, 3H). IR (NaCl): 2958vs, 2921s, 2860s, 1650m, 1452s, 1322m, 1250m, 1183s, 1064m, 790m and 757m cm⁻¹.

C. The amine 1a (3.45 mmol), 3 (6.90 mmol) and n-butanol (10.40 mmol) were kept at 60°C in an inert atmosphere for 22 h. The reaction mixture still contained a considerable proportion of 1a (44%) along with 4a (36%), 2-butoxy-1,3-diisopropyl-benzene (11a, 8%) and the N-butylidene-2,6-diisopropylaniline (22, ca. 12%). The latter component was identified on the basis of its mass spectrum. 22: MS (70 eV) m / z: 231 (M⁺, 15), 216 (8), 188 (67), 174 (18), 146 (100), 132 (14), 91 (10), 43 (10) and 41 (14).

4-Chloroaniline (1b) and n-butyl nitrite (3)

A. The amine 1b (2.36 mmol), 3 (7.01 mmol), and diethyl ether (1 ml, to insure total solubility) were refluxed for 2 h. The main product was chlorobenzene (5b, 70%), accompanied by two minor coupling products 14b and 14'b, tentatively identified as 3,4'-dichlorobiphenyl and 4,4'-dichlorobiphenyl on the basis of their mass spectra. The original mixture contained a large quantity of 1,1-dibutoxybutane (23).

14b: MS (70 eV) m/z: 226 (M⁺, 10), 224 (M⁺, 61), 222 (M⁺, 100), 186 (10), 152 (77), 93 (12), 76 (11) and 75 (14).

B. The same experiment carried out using CCl_4 (1 ml) instead of ether (60°C, 1 h) gave 1,4-dichlorobenzene (5b, 53%) as the main product, accompanied by the reduced product chlorobenzene (4b, 38%) and small amounts of 14b and 14'b. 1,1-Dibutoxybutane (23) was also produced in large quantities.

4-tert-Butylaniline (1c) and n-butyl nitrite (3)

A. The amine 1c (2.88 mmol) and 3 (8.66 mmol) were kept at 60°C for 3 h to yield tert-butylbenzene (4c, 48%) together with two nitro derivatives identified as 1-tert-butyl-3- and -4-nitrobenzene (18, ca. 6% and 19 ca. 18%) from their mass spectra and GC retention properties and the coupling product 4,4'-di-tert-butylbiphenyl (14c, ca. 12%).

14c: MS (70 eV) 266 (M⁺, 27), 251 (100), 223 (4), 118 (11), 104 (11), 90 (30), 57 (63) and 41 (21).

B. An experiment carried out as above in CCl_4 (2 ml) for 30 min gave a 58% yield of 1-tert-butyl-4-chlorobenzene (5c); no amine survived. The following other products accounted for the material balance: 4c (14%), 4-tert-butyl-2-nitrophenol (21, ca. 10%), 1-butoxy-4-tert-butylbenzene (11c, ca. 10%) and 4,4'-di-tert-butylazobenzene (15c, ca. 4%). Also present was a moderate amount of 23. Products 21 and 11c and 15c were identified tentatively on the basis of their spectral patterns.

21: MS (70 eV) m / z: 195 (M⁺, 16), 180 (100), 152 (16), 134 (19), 133 (5), 105 (6), 91 (7), 77 (12) and 41 (8).

11c: MS (70 eV) m/z: 206 (M⁺, 20), 191 (61), 135 (100), 107 (22), 91 (10), 77 (5) and 41 (20).

15c: MS (70 eV) m/z: 294 (M⁺, 15), 161 (13), 133 (100), 118 (8), 105 (13), 91 (17) and 57 (7).

Acknowledgments

This work was supported in part by grants to AGG (CNR 92.00391CT03, CNR 93.03024CT03, MURST 1990 and 1992, 60%), to PS (MURST 1991 and 1992, 40% and 60%) and to GV (MURST 1990–1992, 60%). FG is the recipient of a postdoctoral scholarship from the Department of Agriculture of the Autonomous Region of Friuli-Venezia Giulia.

References and Notes

- ¹ J. March, "Advanced Organic Chemistry-Reactions, Mechanisms and Structure", 4th edn, John Wiley & Sons, New York, 1992; S.H. Pine, J.B. Hendrickson, D.J. Cram and G.S. Hammond, "Organic Chemistry", 4th edn, McGraw-Hill, New York, 1980; R.O.C. Norman and J.M. Coxon, "Principles of Organic Synthesis", Blakie Academic & Professional, London, 1993; K. Schank, "The Chemistry of Diazonium and Diazo Groups", Part 2, Chapter 14, S. Patai, ed., John Wiley & Sons, New York, 1978; B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, "Vogel's-Textbook of Practical Organic Chemistry", 5th edn, Longman Scientific & Technical, New York, 1989; R. Putter, "Methoden der Organischen Chemie (Houben Weyl)", Vol. X/3, R. Stroh, ed., Georg Thieme Verlag, Stuttgart, 1965, p. 32; C. Sübing, "Methoden der Organischen Chemie (Houben Weyl)", Vol. X/3, R. Stroh, ed., Georg Thieme Verlag, Stuttgart, 1965, p. 710.
- ² L. Friedman and F.M. Logullo, J. Am. Chem. Soc. 85, 1549 (1963).
- ³ G. Verardo, A.G. Giumanini, F. Gorassini and P. Strazzolini, Bull. Chem. Soc. Jpn., in press.
- ⁴ P. Putter, "Methoden der Organischen Chemie (Houben-Weyl)", Vol. 10/XI3, R. Stroh, ed., Georg Thieme Verlag, Stuttgart, 1965, p. 115.

- ⁵ E. Muller, "Methoden der Organischen Chemie (Houben-Weyl)", Vol. X1/2, R. Stroh, ed., Georg Thieme Verlag, Stuttgart, 1968, p. 214.
- p. 214. ⁶ E. Bamberger and E. Rust, Chem. Ber. 33, 3511 (1950); A.E. Tschitschibabin and M. Rjasanzev, Khim. 47 II, 1571 (1950).
- ⁷ L. Friedman and J.F. Chlebowsky, J. Org. Chem. 33, 1636 (1968); M.S. Newman and W.M. Hung, J. Org. Chem. 39, 1317 (1974).
- ⁸ J.I.G. Cadogan and G.A. Molina, J. Chem. Soc., Perkin Trans. I, 541 (1973); *M.P. Doyle*, J.F. Dellaria Jr., B. Siegfried and S.W. Bishop, J. Org. Chem. **42**, 3494 (1977).
- ⁹ M.P. Doyle, B. Siegfried and J.F. Dellaria Jr., J. Org. Chem. 42, 2426 (1977).
- ¹⁰ S. Oae, K. Shinhama and Y.H. Kim, Bull. Chem. Soc. Jpn. 53, 1065 (1980).
- ¹¹ S. Oae, K. Shinhama and Y.H. Kim, Bull. Chem. Soc. Jpn. 53, 2023 (1980).
- R. Putter, "Methoden der Organischen Chemie (Houben-Weyl)", Vol. X/3, R. Stroh, ed., Georg Thieme Verlag, Stuttgart, 1965, p.
 150.
- ¹³ G. Verardo, A.G. Giumanini and P. Strazzolini, Tetrahedron 46, 4303 (1990).
- ¹⁴ B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, "Vogel's-Textbook of Practical Organic Chemistry", 5th edn, J. Wiley & Sons, New York, 1989, p. 414.
- ¹⁵ A.G. Giumanini, G. Verardo and M. Poiana, J. Prakt. Chem. 330, 161 (1988).
- ¹⁶ EI-positive mass spectra at 70 eV ionization energy were secured for all quantitatively significant peaks in the GC profiles of all the whole reaction mixtures. IR and ¹H-NMR spectra were recorded for all separated products. These properties were compared with those of authentic specimens in spectral collections, whenever feasible: a) *C.J. Pouchert*, "The Aldrich Library of FT-IR Spectra", Aldrich Chemical, Milwaukee, 1985; b) *C.J. Pouchert* and *J. Behnke*, "The Aldrich Library of ¹³C and ¹H FT-NMR Spectra", Aldrich Chemical, Milwaukee, 1992; c) MS library present in the data system of the Fisons TRIO 2000 from NIST, London 1992 (65 000 spectra).

Spectral data are not replicated here in those cases, but only for compounds which were not found in the above sources.