



Pergamon

Tetrahedron Letters 40 (1999) 8291–8293

TETRAHEDRON
LETTERS

Single electron transfer reductive cleavage of the aryl–nitrogen bond in phenyl-substituted dimethylanilines

U. Azzena, F. Dessanti, G. Melloni * and L. Pisano

Dipartimento di Chimica, Università di Sassari, Via Vienna 2, I-07100 Sassari, Italy

Received 3 August 1999; revised 6 September 1999; accepted 14 September 1999

Abstract

By treatment with Li metal in THF at room temperature the three isomeric *N,N*-dimethylaminobiphenyls and *N,N*-dimethyl-2,6-diphenylaniline underwent 100% regioselective reductive cleavage of the aryl–N bond, affording biphenyl and *meta*-terphenyl, respectively, in various yields. © 1999 Published by Elsevier Science Ltd. All rights reserved.

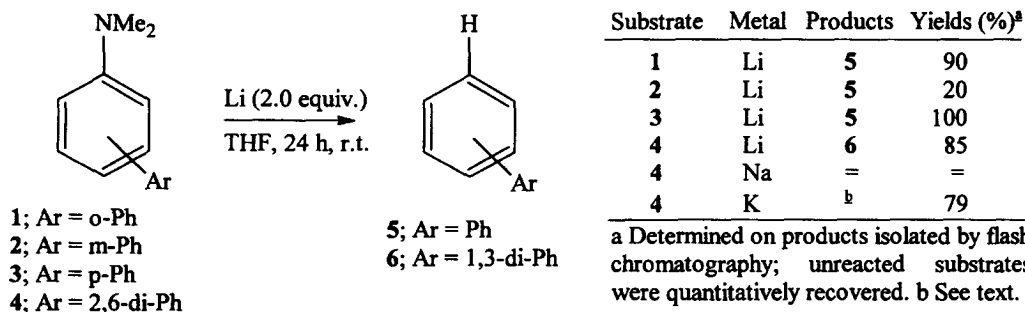
Keywords: reduction; electron transfer; bond cleavage; regioselectivity; deamination.

The cleavage of strong covalent bonds by reductive single electron transfer (SET) is an object of present interest,¹ focused on both its mechanistic aspects² and synthetic usefulness,³ as well as on the discovery of hitherto unknown fragmentations. As an extension of our study of mechanisms^{2g,h,4} and synthetic applications⁵ of the SET reductive cleavage of C–O bonds in aryl alkyl ethers, in which we have shown that under appropriate conditions the scission of the aryl–O bond in anisole and many substituted anisoles may compete favorably with that of the Me–O bond, we took into consideration the possibility of obtaining scission of C–N bonds of aromatic amines. This subject has received little attention, likely due to the low electron affinity of such substrates; only a few reports can be found in the literature.^{6–9}

We wish to report here that by simple treatment with Li metal in THF at room temperature the three isomeric *N,N*-dimethylaminobiphenyls **1–3** and 2,6-diphenyl-*N,N*-dimethylaniline **4** underwent exclusive Ar–N bond cleavage to afford biphenyl **5** and *meta*-terphenyl **6**, respectively (Scheme 1).

The reductive cleavage was carried out as follows. Li metal (30% wt dispersion in mineral oil, 2 equiv.) was placed under Ar in a two-necked flask equipped with reflux condenser and magnetic stirrer, washed with THF (3×10 mL), and suspended in anhydrous THF (25 mL). To this well stirred suspension a solution of the appropriate substrate **1–4** (2.5 mmol) in THF (5 mL) was added dropwise. The mixture was stirred at room temperature for 24 h and then quenched by slow dropwise addition of H₂O (10 mL) (caution). Extraction with Et₂O and standard workup afforded products **5** or **6**, which were identified by GC–MS and purified by flash chromatography (hexane/EtOAc).

* Corresponding author. Tel: +39 079 229547; fax: +39 079 229559; e-mail: melloni@ssmain.uniss.it

Scheme 1. Reductive cleavage of phenyl-substituted *N,N*-dimethylanilines 1–4

All the reactions were carried out for 24 h for comparison purposes, since we were interested, at this exploratory stage of the research, to check the regioselectivity of the cleavage rather than to obtain better conversion yields. Reductions of substrate 4 were also carried out with Na and K metals. In the case of Na, no reaction occurred; in the case of K, a complex, tarry mixture of products corresponding to 79% consumption of the starting material was obtained, mostly composed of products of partial reduction of the aromatic ring(s) and/or degradation. Analysis of this mixture by ¹H NMR permitted us to ascertain a partial loss of the dimethylamino group but gave no evidence of cleavage of the Me–N bond; owing to its complexity, the mixture was not analyzed further. The results are reported in Scheme 1. Experiments were also carried out with Li metal on *N,N*-dimethylaniline 7 and *ortho*- and *para*-*N,N,N',N'*-tetramethylphenylenediamines 8 and 9 under the same conditions as above. However, no evidence for electron transfer was obtained, as indicated by no metal consumption and lack of the usual intense colors accompanying formation of radical anions or other intermediates during SET reduction of aromatic substrates.

Taken as a whole, our results indicate that, in order for the electron transfer to occur to these electron-rich substrates, strongly electropositive metals are needed, as well as structures allowing extensive delocalization of a negative charge. A second comment regards the 100% regioselective scission of the Ar–N bond observed for substrates 1–4. This is at variance with what has been observed in the reductive cleavage of C–O bonds of aryl alkyl ethers bearing the same substituents, i.e., phenyl- and diphenyl-substituted anisoles,^{2g,h} where the Me–O fragmentation represents an important pathway and in some cases becomes the exclusive process. At the present stage of the research we are not able to offer a rationale for the observed exclusive fragmentation of the Ar–N bond, which represents a further example of the remarkable ease with which a strong bond can be broken under electron transfer reductive conditions. It has to be stressed that, assuming that fragmentation might occur at the level of either a radical ion or a dianion, cleavage of the Ar–N bond corresponds to the departure of a very poor leaving group, the anion Me₂N[–]. These points are under active investigation in our laboratory.

Acknowledgements

This work was carried out in the framework of the Italian National Project 'Radicali Liberi e Radicali Ioni nei Processi Chimici e Biologici' supported by the Ministero della Ricerca Scientifica e Tecnologica (MURST), Rome, and by the University of Sassari. Financial support from the Italy–Spain Joint Project 'Azioni Integrate' (HI 1998-0138) is also acknowledged.

References

1. Reviews: (a) Maercker, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 972; (b) Chanon, M.; Rajzmann, M.; Chanon, F. *Tetrahedron* **1990**, *46*, 6193; (c) Maslak, P. *Top. Curr. Chem.* **1993**, *168*, 1; (d) Savéant, J.-M. *Acc. Chem. Res.* **1993**, *26*, 455; idem *Tetrahedron* **1994**, *50*, 10117.
2. Recent literature: (a) Maslak, P.; Narvaez, J. N.; Vallombroso Jr., T. M. *J. Am. Chem. Soc.* **1995**, *117*, 12373 and references cited therein; (b) Guthrie, R. D.; Patwardhan, M.; Chateaufneuf, J. E. *J. Phys. Org. Chem.* **1994**, *7*, 147; (c) Maslak, P.; Chapman Jr., W. H. *J. Org. Chem.* **1996**, *61*, 2647; (d) Maslak, P.; Theroff, J. *J. Am. Chem. Soc.* **1996**, *118*, 7235; (e) Marquet, J.; Cayón, E.; Martin, X.; Casado, F.; Gallardo, I.; Moreno, M.; Lluch, J. M. *J. Org. Chem.* **1995**, *60*, 3814; (f) Gonzalez-Blanco, R.; Bourdelande, J. L.; Marquet, J. *J. Org. Chem.* **1997**, *62*, 6903; (g) Azzena, U.; Casado, F.; Fois, P.; Gallardo, I.; Pisano, L.; Marquet, J.; Melloni, G. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2563; (h) Casado, F.; Pisano, L.; Farriol, M.; Gallardo, I.; Marquet, J.; Melloni, G. *J. Org. Chem.* submitted for publication.
3. (a) Azzena, U.; Demartis, S.; Melloni, G. *J. Org. Chem.* **1996**, *61*, 4913; (b) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1996**, *52*, 8545; (c) Azzena, U.; Carta, S.; Melloni, G.; Sechi, A. *Tetrahedron* **1997**, *53*, 16205; (d) Azzena, U.; Pilo, L. *Synthesis* **1999**, 664; (e) Schmaltz, H. G.; Koning, C. B.; Bernicke, D.; Siegel, S.; Pfletschinger, A. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 1620.
4. (a) Azzena, U.; Denurra, T.; Melloni, G.; Fenude, E.; Rassa, G. *J. Org. Chem.* **1992**, *57*, 1444; (b) Azzena, U.; Denurra, T.; Melloni, G.; Fenude, E. *Gazz. Chim. Ital.* **1996**, *126*, 141.
5. (a) Azzena, U.; Melloni, G.; Pisano, L. *J. Chem. Soc., Perkin Trans. 1* **1995**, 261; (b) Azzena, U.; Melloni, G.; Nigra, C. *J. Org. Chem.* **1993**, *58*, 6707; (c) Azzena, U.; Melloni, G.; Piroddi, A. M.; Azara, E.; Contini, S.; Fenude, E. *J. Org. Chem.* **1992**, *57*, 3101; (d) Azzena, U.; Denurra, T.; Melloni, G.; Piroddi, A. M. *J. Org. Chem.* **1990**, *55*, 5386 and 5522.
6. Birch, A. J.; Hextall, P.; Sternhell, S. *Aust. J. Chem.* **1954**, *7*, 256.
7. Eisch, J. *J. Org. Chem.* **1963**, *28*, 707.
8. Bartmann, E. *J. Organomet. Chem.* **1985**, *284*, 149.
9. Gilman, H.; Dietrich, J. *J. Org. Chem.* **1957**, *22*, 851; *J. Am. Chem. Soc.* **1958**, *80*, 380.