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Unprecedented two-step synthesis of symmetrical diarylamines from 2-alkyl-1,3-dinitropropanes

Roberto Ballini,[a,*] Luciano Barboni,[a,*] Cristina Femoni,[b] Guido Giarlo[a] and Alessandro Palmieri[a]

[a]*Dipartimento di Scienze Chimiche dell'Università di Camerino, Via S. Agostino 1, 63032 Camerino, Italy*
[b]*Dipartimento Chimica Fisica e Inorganica, Università di Bologna, Viale Risorgimento 4, 40136 Bologna, Italy*

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Abstract—This letter reports a new, two-step synthesis of symmetrical diarylamines from 1,3-dinitropropanes, by their reaction with acrolein under basic conditions (Al_2O_3, neat), followed by aromatisation of the obtained 2,4-dinitrocyclohexanols, through their treatment with four equivalents of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), in acetonitrile as a solvent, and warming overnight at 60 °C.

Arylamines are found in pharmaceuticals,[1,2] materials with important electronic properties,[3–15] and ligands for early metal catalysts.[16] Despite the simplicity of the arylamine moieties, the synthesis of these compounds is often difficult.[17] Procedures involving nitration, reduction or substitution are incompatible with many functional groups and often comprise protection and deprotection steps. Reductive amination, which implicates formation of an imine from an arylamine and subsequent reduction of the imine, needs two steps, a preformed C–N bond in an aniline, an excess of the amine, and sluggish reductions.[18–21] On the other hand, copper-mediated (Ullmann) substitutions demand high temperatures,[22–25] while direct nucleophilic substitution of aryl halides typically requires a large excess of reagent, high temperature or highly activated aryl halides.[26,27] Alternatively, transition metal–arene complexes[28] or palladium acetates (Buchwald–Hartwig procedure)[29] have been employed, but stoichiometric amounts of the metal complex are required or low chemoselectivity is observed. Anyway, all the above procedures need the presence of a preformed aromatic system.

Aromatization of acyclic precursors is undoubtedly a useful reaction in the synthesis of highly substituted aromatic rings,[30] and several methods are known for this purpose.[31] In this context, nitroalkane derivatives have emerged, over the last years, as versatile precursors for the synthesis of a variety of aromatic systems.[32–34]

During our efforts devoted to the use of nitroalkanes as versatile precursors for the preparation of aromatic structures,[32,33] we have now discovered a new, two-step synthesis of symmetrical diarylamines, starting from 1,3-dinitropropanes.[35]

Thus, the reaction of 1,3-dinitroalkanes **1** with acrolein, under basic conditions (basic Al_2O_3, neat) affords the nitrocyclohexanols **2** in a one-pot sequence[36] (Scheme 1), through tandem Michael/nitroaldol (Henry) reactions. After extraction, treatment of the crude **2**, with 4 equiv of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), in acetonitrile as a solvent, and warming overnight at 60 °C, directly produces the diarylamines **3** in satisfactory overall yields (32–45%, Table 1).

Some spectral features conducted us to the structure of compounds **3**: (i) the high molecular weights indicate that two molecules of the starting material are included in **3** and, since the molecular weights are odd, an odd number of N-atoms are present; (ii) ^{1}H NMR spectra indicate **3** as symmetric molecules and the presence of one exchangeable proton around 5.5 ppm is compatible with symmetric secondary amines. The ^{1}H NMR spectra also show the 1,2,3-substitution of the nitroaromatic

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* Corresponding authors. Tel.: +39 0737402270; fax: +39 0737402297; e-mail: roberto.ballini@unicam.it

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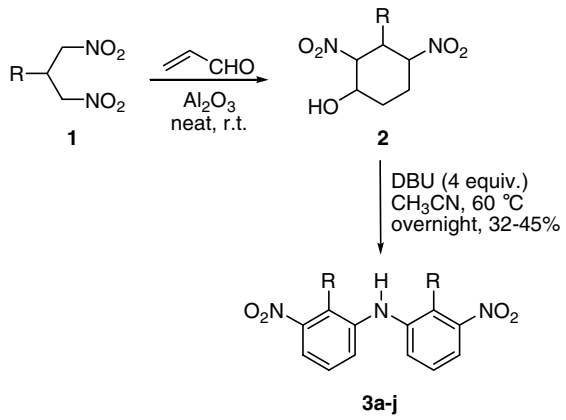

Scheme 1.

Table 1. Symmetrical diarylamines **3**

Entry	R	Reaction time **1** to **2** (h)	Yield (%)[a] from **1**
a	Ph	4	42
b	*p*-$CF_3C_6H_4$	5	36
c	*p*-$MeOC_6H_4$	18	37
d	$PhCH_2CH_2$	6	36
e	$CH_3(CH_2)_4CH{=}CH(CH_2)_2$	5	35
f	*i*-Pr	9	32
g	*n*-Pr	5	36
h	$CH_3(CH_2)_4$	5	38
i	$CH_3(CH_2)_7$	6	36
j	*c*-C_6H_{11}	6	45

[a] Yields of pure, isolated compounds.

moieties. Because the formation of **3** seemed to us quite surprising, the structures of two selected products (**3b** and **3j**) were confirmed by X-ray analysis.[37]

The mechanism of the conversion of **2** to **3** is not clear at the moment and the formation of **3** is an unexpected behaviour of compound **2** under our reaction conditions. A possible pathway could be (i) firstly, the conversion of the intermediate **2** into a 2-alkyl-1,3-dinitroaromatic system (in the same way as for mono-nitrocyclohexanols),[32,33] (ii) followed by reductive coupling reaction (with loss of NO_2),[38] that leads to the diarylamine derivatives **3**. Anyway, independently from the mechanism, the reaction represents an unprecedented, reproducible, and useful method for the preparation of a variety of symmetrical diarylamines from acyclic precursors. Additionally, in our procedure, by making an appropriate choice of the starting 1,3-dinitroalkane **1**, a multiplicity of alkyl groups in the *ortho*-position can be easily introduced, including aryls, and both cyclic and acyclic alkyls. Besides, other peculiarities can be seen in our approach, such as the one-pot preparation of trisubstituted aromatics with the avoidance of *ortho–meta–para* mixture formation common in conventional aromatic synthesis methods. In fact, our method appears as a regiodefinited synthesis of a new class of symmetrical *m*-nitro-*o*-alkyldiarylamines very difficult to obtain by other routes. Moreover, the reported synthesis permits the insertion of several *n*-alkyl groups without the isomerization problems typical of the classical Friedel–Crafts alkylation. It should be noted that the synthesis of substituted biphenyls (compounds **3b**,**c**) can also be accomplished.

In conclusion, the simplicity of execution, the ready availability of the substrates, the broad range of potential products, the avoidance of a workup, since the crude mixture can be directly charged to a chromatographic column for the immediate purification, make this synthetic strategy very attractive for academic research and practical applications. For the time being we are aiming to verify the mechanism of the reaction and to enlarge the potential of our discovery.

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Supplementary data

Method of preparation and spectral data of compounds **3**, X-ray structures of compounds **3b** and **3j**, X-ray data collection procedure, and ^{13}C NMR spectra of compounds **3a**–**3j**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.02.027.

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37. Crystallographic data (excluding structure factors) for the structures **3b** and **3j** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-279183 and CCDC-279184, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk]. See also the Supplementary data.
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