Pergamon

Tetrahedron Letters 43 (2002) 8925–8927

TETRAHEDRON
LETTERS

Amines addition to α-nitrohydrazones: application to amidrazones and triazoles formation

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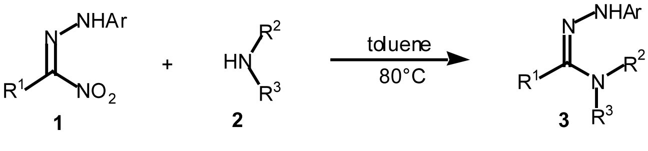
Accepted 27 September 2002

Abstract—Primary nitro compounds can be easily converted into amidrazone by addition of amines. The best yields for primary amines are obtained with a large excess of amine as oxidation products are formed. These additions were applied to the selective formation of triazole (Buzykin reaction) and pyrrole. © 2002 Elsevier Science Ltd. All rights reserved.

Since the first additions of aryldiazonium salts to nitro compounds and apart from the [3+2] cycloadditions first reported by Huisgen, few synthetic applications have emerged from the resulting α-nitrohydrazones.[1–9] In a previous study, we have explored the electrophilic behaviour of these hydrazones by reporting an Arbuzov-type reaction between α-nitrohydrazones and triethylphosphite.[10] In spite of the early report by Ponzio on ammonia addition to α-nitrohydrazones,[11] the only relevant addition of amines to α-nitrohydrazones can be found in the work of Shawali et al.[12] In this study only a single example (morpholine addition to a diarylnitrohydrazone) is however presented.[12] The scope and utility of these additions still needed to be defined.

Amines **2** add to α-nitrohydrazones **1** (amine/nitro = 3/1) when heated in toluene to form amidrazones **3** in good to moderate isolated yields (Scheme 1, Table 1, method A). The NMR analyses of the crudes indicate usually much higher yields as the products partially decompose on silica.

With these conditions much lower yields are nevertheless obtained with various primary amines as triazoles **4** are formed as side products (Scheme 2). To raise the yield, the reaction was then conducted with the amine as solvent when possible; evaporation of the amine and fast filtration on silica then gave the new amidrazone **3** in quantitative yield for all amines tested (Table 1, method B).



Scheme 1.

The formation of **4** can be associated to the triazole synthesis first reported by Buzykin[13] and further improved by Paulvannan.[14] Different oxidising agents for the transformation of amidrazones to triazoles were evaluated and best conditions obtained with silver carbonate in acetonitrile.[14] Though the use of nitrite anion as oxidizing agent is not classical in a basic medium, we analyzed this triazole formation as an oxidation assisted by the nitrite anion released in the medium. This was confirmed with triazole **4a** by the following experiments: benzylamine (3 equiv.) addition to hydrazone **1a** gives amidrazone **3e** (54% isolated yield) along with triazole **4a** (26%); if sodium nitrite (4 equiv.) and TEBA are added at the end of the reaction and the mixture further heated for several hours, triazole **4a** is now recovered in a 76% isolated yield (Scheme 2).

These oxidation conditions can be used for the straightforward conversion of nitrohydrazones **1** to triazoles **4**. The nitro derivative **1a** was first converted to amidrazone **3** by heating in the amine as solvent; evaporation of the amine followed by addition of toluene, sodium nitrite and TEBA give the new triazole **4** after several hours heating (Table 2). A control experiment without added sodium nitrite revealed that the amidrazone was also consumed forming triazole **4** but with a lower overall yield.

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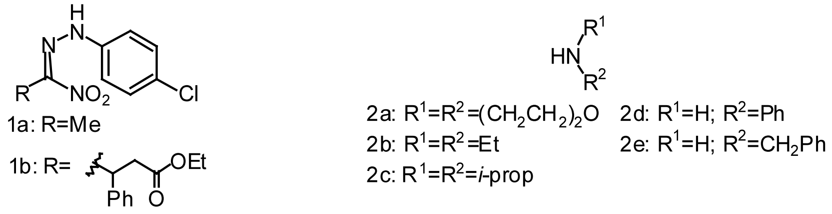
PII: S0040-4039(02)02188-3

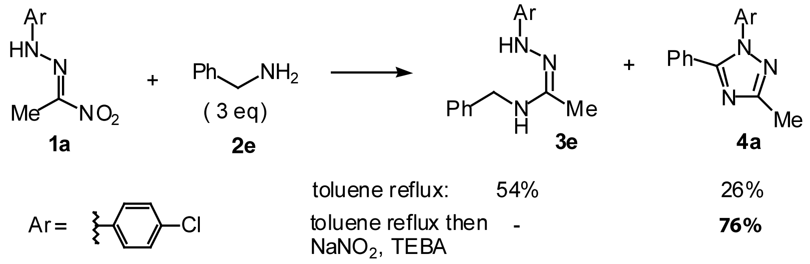
Table 1. Formation of amidrazones **3** from **1**



Entry	Starting **1**	Amine **2**	Product (procedure)	Yield (%)
1	**1a**	**2a**	**3a** (A)[a]	50
2	**1a**	**2a**	**3a** (B)[b]	Quant.
3	**1b**	**2b**	**3b** (B)	Quant.
4	**1b**	**2c**	**3c** (B)	Quant.
5	**1b**	**2d**	**3d** (A)	63
6	**1a**	**2e**	**3e** (A)	54

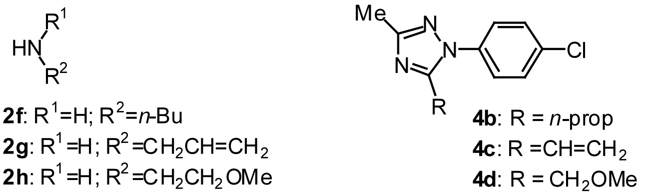
[a] *Method A*: A 0.2 M solution of **1** in toluene was heated (80°C) with 3 equiv. of amine **2** until completion to give **3** after evaporation of the solvent and chromatography on silica gel.

[b] *Method B*: A 0.2 M solution of **1** in **2** was refluxed for 1–3 h to give **3** in quantitative yield after evaporation and fast filtration on silica gel.



Scheme 2.

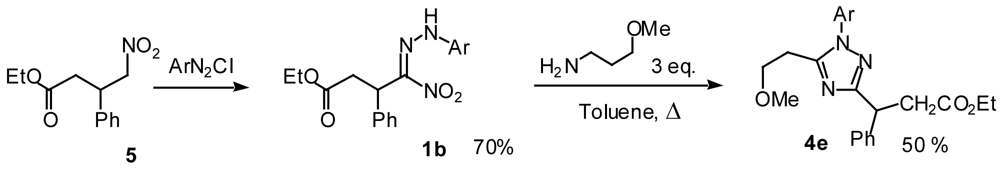
Table 2. Triazole **4** from **1**



Entry	Starting **1**	Amine **2**	Triazole **4**	Yield (%)[a]
1	**1a**	**2f**	**4b**	55
2	**1a**	**2g**	**4c**	52
3	**1a**	**2h**	**4d**	65

[a] A 0.2 M solution of nitrohydrazone **1a** in amine **2** (5 ml) was refluxed for 3 h; evaporation of excess amine followed by addition of toluene (5 ml), sodium nitrite (4 equiv.) and TEBA give after reflux triazole **4** which was purified on silica gel.

Amidrazones **3** are classically obtained by the addition of amines to α-halogenohydrazones; they have found important applications in the preparation of nitrogen heterocyclic compounds.[15] Although the first formation of amidrazones from nitrohydrazones was reported about a century ago,[16] the potential of these addition–elimination processes remained largely underestimated. We believed that the flexibility offered by nitro chemistry coupled with easy diazonium additions and nucleophilic displacements should guarantee a larger use of this methodology in heterocyclic synthesis. We have thus performed an easy preparation of the functionalized triazole **4e** from the Michael adduct of nitromethane with ethyl cinnamate **5**. Diazotation followed by addition of 3-methoxypropylamine in toluene permit the formation of the triazole without any prior condensation of the ester with the hydrazone (Scheme 3).



Scheme 3.

These preliminary trials are illustrative of the manifold chemistry offered by α-nitrohydrazones; we are currently studying the use of other functionalised nitro and amino compounds.

Acknowledgements

We thank Professor A. S. Shawali for the warmth of his reception in Cairo and discussions on hydrazones.

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