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Accelerated synthesis of 3,5-disubstituted 4-amino-1,2,4-triazoles under microwave irradiation

Fouad Bentiss,[a] Michel Lagrenée [a] and Didier Barbry [b,*]

[a]*Laboratoire de Cristallochimie et Physicochimie du Solide, CNRS UPRESA 8012, ENSCL, B.P. 108,*
F-59652 Villeneuve d'Ascq Cedex, France
[b]*Laboratoire d'Ingénierie Moléculaire, UPRES EA 2699, Université des Sciences et Technologies de Lille,*
F-59655 Villeneuve d'Ascq Cedex, France

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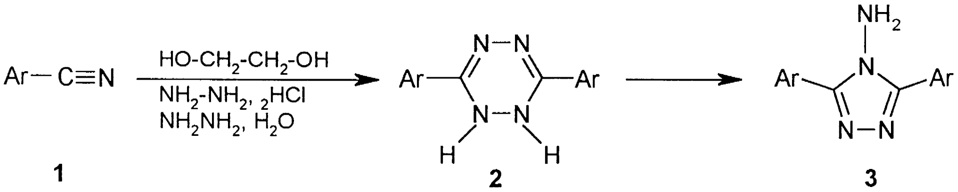
Abstract

A number of symmetrically 3,5-disubstituted 4-amino-1,2,4-triazoles are quickly prepared by the reaction of aromatic nitriles on hydrazine dihydrochloride in the presence of an excess of hydrazine hydrate in ethylene glycol under microwave irradiation. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: 4-amino-1,2,4-triazoles; microwave irradiation.

4-Amino-1,2,4-triazoles **3** are potentially good corrosion inhibitors.[1,2] These compounds can be prepared by the nucleophilic attack of hydrazine derivatives on nitriles.[3–9] The initial product, in each case, is the 1,2-dihydro-1,2,4,5-tetrazine **2** which rearranges at elevated temperatures or on treatment with acid to the corresponding 4-amino-1,2,4-triazole **3**. One of these methods[8] involves the reaction between 2-cyanopyridine **1h** and hydrazine hydrate. The reaction product was 3,6-bis(2-pyridyl)-1,2-dihydro-1,2,4,5-tetrazine **2h**. This compound was rearranged by further treatment with hydrochloric acid to 3,5-bis(2-pyridyl)-4-amino-1,2,4-triazole **3h**. Recently, a one-step synthesis of 3,5-disubstituted 4-amino-1,2,4-triazoles by direct reaction of hydrazine derivatives on nitriles bearing a variety of substituted aromatic rings or heteroatoromatic has been reported.[10]



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[*] Corresponding author. Fax: (33) 03 20 43 49 74; e-mail: didier.barbry@univ-lille1.fr (D. Barbry)

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Table 1
Data for the synthesis of 3.5-diaryl-4-amino-1,2,4-triazoles **3a–i** under microwave irradiation

Compound	Ar	Microwave Irradiation		Classical Heating		Mp (°C)
		Time (min)	Yield (%)	Time (min)	Yield (%)	
3a	C_6H_5	4	92	60	97	263
3b	4-$CH_3C_6H_4$	6	66	60	67	294
3c	4-$H_2NC_6H_4$	4	70	45	67	226
3d	4-HOC_6H_4	10	96	45	87	295
3e	3-CH_3O, 4-OHC_6H_3	6	79	60	86	228
3f	4-$CH_3OC_6H_4$	6	73	45	83	277
3g	4-ClC_6H_4	5	63	45	61	290
3h	2-pyridyl	5	95	45	85	186
3i	4-pyridyl	6	58	45	75	340

This method allows the synthesis of the solely symmetrically 3,5-disubstituted 4-amino-1,2,4-triazoles. We report that this reaction takes place in good yields and rapidly under microwave irradiation (Table 1). This technique has been applied with success to a number of reactions proceeding with or without solvent.[11,12]

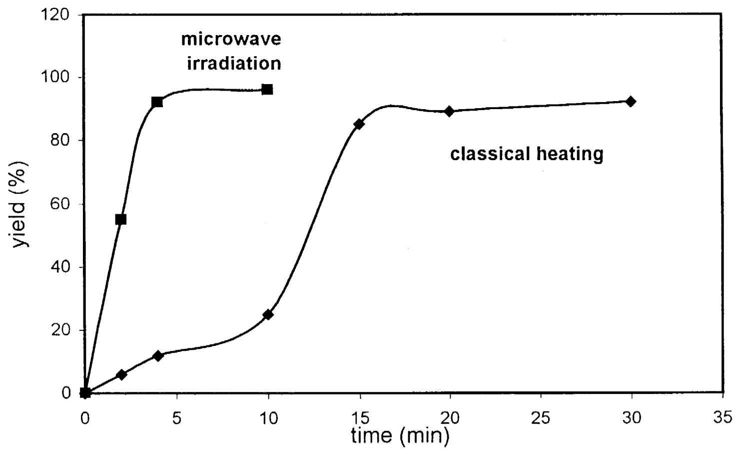

Fig. 1. Yield versus time for 3,5-diphenyl-4-amino-triazole at 130°C

The initial product, in each synthesis of aminotriazoles, is the orange-coloured, dihydro-1,2,4,5-tetrazine **2** which rearranges on treatment under acidic conditions into the corresponding 4-amino-1,2,4-triazole **3**. Addition of hydrazine dihydrochloride or sulfate was used to generate protons which promoted the rearrangement of **2** into the triazole **3**. Without using hydrazine dihydrochloride, the main reaction product was **2**. For example, using the same conditions, a mixture of benzonitrile **1a** and hydrazine hydrate, heated in ethylene glycol, leads to a mixture of **2** and **3** with about 70% of **2** (estimated by integration of the nitrogen protons in ^{1}H NMR). Compound **2** can be differentiated from **3** by oxidation of the former to the red-coloured tetrazine. However, a further reliable basis of differentiaton is their ^{1}H

NMR spectra. The nitrogen protons of dihydrotetrazine appeared at a much lower field (δ=9.1 ppm) than did those of 4-amino-1,2,4-triazoles (δ=6.4 ppm).

Under classical heating in a high boiling polar solvent such as ethylene or diethylene glycol obtention of compounds **3** in good yield required much longer reaction times (45–60 min) at 130°C depending on starting compounds **1** of the reaction.[10] With microwave irradiation some reactions were complete after just 4 min (compounds **3a** and **3c**) and did not exceed 10 min (compound **3d**). The rates of formation of 3,5-diphenyl-4-aminotriazole at 130°C with classical heating and under microwave irradiation have been compared (Fig. 1). Superheating of the solvent under microwave irradiation may lead to the observed rate enhancement.[14]

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