

Fouad Bentiss, Michel Lagrenée *

Laboratoire de Cristallographie et Physicochimie du Solide, CNRS UPRESA 8012, ENSCL, BP.108, F-59652 Villeneuve d'Ascq Cedex, France

Hervé Vezin

Laboratoire de Chimie Organique et Macromoléculaire, CNRS UPRESA 8009, USTL Bât C3, F-59655 Villeneuve d'Ascq Cedex, France

Marya Bouanis, Bouchaib Mernari

Laboratoire de Chimie de Coordination et d'Analytique, Université Chouaib Doukkali, Faculté des Sciences, BP.20, M-24000 El Jadida, Morocco

Received July 2, 2001

A number of symmetrical 3,5-disubstituted-4*H*-1,2,4-triazoles have been synthesized in good yields by deamination of the corresponding 4-amino-1,2,4-triazoles *via* reductive diazotation of these amino compounds in the presence of hypophosphorous acid. Analytical, spectral data and theoretical calculations confirmed the structures of the new triazole derivatives.

J. Heterocyclic Chem., **39**, 93 (2002).

Introduction.

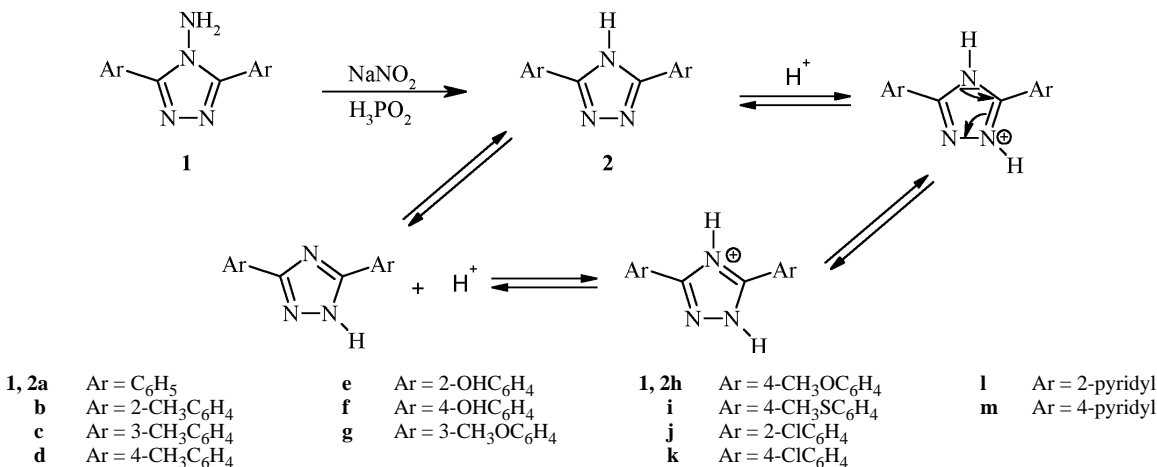
Stemming from an interest in the use of heterocyclic compounds as corrosion inhibitors, we have synthesized new triazole derivatives. Most organic corrosion inhibitors act by adsorption on the metal surface. It is well known that heterocyclic compounds containing nitrogen atoms are good corrosion inhibitors for many metals and alloys in aggressive media [1-4]. For example, benzotriazole is efficient for the protection of copper and iron. 4-Amino-1,2,4-triazoles are also very good corrosion inhibitors [5-7] but in some cases, and especially for the utilization as anticorrosion additives in paints, the amino group reacts with other constituents and must be eliminated.

3,5-Disubstituted-1,2,4-triazoles can be prepared by the reaction of an aromatic acid hydrazide, an aromatic nitrile and

dry methanol under anhydrous conditions [8]. However, this direct synthesis is both time consuming and somewhat hazardous for the preparation of large quantities. The product must be purified by repeated crystallization and chromatographed on basic alumina. On the other hand, 3,5-disubstituted-4-amino-1,2,4-triazoles are easily synthesized by a simple one step process starting with aromatic nitriles [9]. Hence, their conversion to triazoles in a practical manner is of interest. Treatment of 3,5-di(2-pyridyl)-4-amino-1,2,4-triazole with nitrous acid in aqueous nitric acid can be used to convert this compound to 3,5-di(2-pyridyl)-1,2,4-triazole [10]. Unfortunately, this procedure leads to poor yields of impure triazoles and substantial amounts of other side products.

We describe here an improved procedure for the deamination of 3,5-disubstituted-4-amino-1,2,4-triazoles by diazotation of these amino compounds in the presence of

Scheme 1



hypophosphorous acid. The 4H compounds are being tested as corrosion inhibitors [11].

Results and Discussion.

The synthesis of the 1,2,4-triazoles is shown in Scheme 1. This method involves the diazotation of the 4-amino-1,2,4-triazole in the presence of hypophosphorous acid, so that the diazonium salt is reduced almost as rapidly as it is formed. Consequently no large concentration of diazonium salt is present. The yields obtained by this method (Table 1) are better than those obtained in procedures where the 1,2,4-triazole is diazotized, in aqueous hydrochloric or nitric acid solution, prior to reaction with hypophosphorous acid. The latter method leads to significantly lower yields of triazoles along with substantial amounts of other compounds. Elemental analysis (Table 1) and mass spectra were used to identify compounds **2a-m**. The melting points of the known triazoles are in good agreement with those reported elsewhere (Table 1). The new triazole derivative structures were confirmed by NMR data. ^1H and ^{13}C NMR data are given in Tables 2 and 3. Chemical shifts of signals are in accordance with the proposed structures.

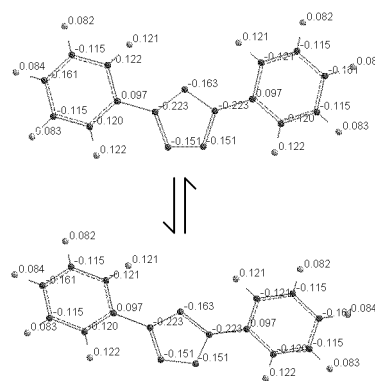
The 3,5-symmetrically disubstituted 1,2,4-triazole ring has three nitrogen atoms making possible two tautomeric forms possible as shown in Scheme 1. It is known that in 3,5-disubstituted 1,2,4-triazoles, substituents in position 3 and 5 have additive effects on the chemical shifts of *N*-methyl groups, so that the chemical shifts of the *N*-methyl groups of such compound can be calculated. In this way, it was possible to assign the peaks of mixtures of *N*-methylated derivatives obtained by methylation of 1,2,4-triazoles [12].

The methylation reaction was effectuated on **2a**. A mixture of methyl iodide and ethanol was added to a solution of **2a** in a dilute aqueous solution of sodium hydroxyde. After 24 hours the product was extracted with chloroform. Evaporation of the solvent gave a product that was recrystallized from ethanol. The ^1H nmr spectra of this product gave a simple methyl peak at 4 ppm indicating that no appreciable amount of 4-methyl derivative was observed in methylation of **2a**, which is in good agreement with the results of S. Kubota *et al.* [12].

These two possible tautomeric forms have been studied by theoretical calculations using semi-empirical PM3 formalism. The results show that these two forms have essentially the same energy of formation that is 100.28 kcal/mol for the 1H position and 99.38 kcal/mol for the 4H position, respectively. This result leads us to conclude that both tautomeric forms should exist in a 50/50 ratio. Calculation were also performed on the anionic intermediate in order to explain the methylated isomer formed. Since this methylation occurred from a nucleophilic substitution we have analyzed the Mulliken charge population analysis of the anion derived **2a** (Scheme 2) and the HOMO distribution along the molecule **2a** (Scheme 3). We can see, for

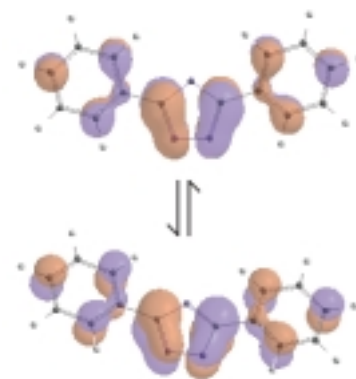
both intermediates, that the Mulliken charge values are identical for the two structures with the more negative charge centered at the 4H position. This finding suggests that methylation at the 4 position should be favored. However Scheme 3 shows that HOMO is only distributed on the nitrogen 1 and 2 and completely absent for the nitrogen 4. Assuming a nucleophilic substitution reaction for the methylation it should be governed by the HOMO distribution and indicate, despite of a higher negative charge on the 4N position, that the methylation occurs on N1 position to yield the 1-methyl-3,5-diphenyl-1,2,4-triazoles.

Scheme 2



Mulliken distribution charge on the anion derived from **2a**

Scheme 3



Distribution of the HOMO energy along **2a**

EXPERIMENTAL

Melting points were determined with a Digital melting point apparatus of IA 9000 series and are uncorrected. Elemental analyses of C, H and N were performed by the Elemental Analysis service of CNRS, Vernaison, France. ^1H and ^{13}C NMR spectra were recorded with a Bruker F.T. AC 200 spectrometer in DMSO-d_6 with TMS as internal standard. Mass spectra were obtained using a Finnigan MAT Vision 2000 MALDI-TOF spectrometer (Laser

Table 1
 3,5-Diaryl-4*H*-1,2,4-triazoles **2a-m**

Compound No.	Ar	Yield %	Lit Yield %	Mp °C	Lit Mp °C	Molecular Formula	Analysis (%)			Ref.	
							Found/(Calcd.)				
							C	H	N		
2a	C ₆ H ₅	99	14	191	189-190	C ₁₄ H ₁₁ N ₃	75.78 (76.02)	5.04 (4.98)	19.08 (19.00)	[13]	
2b	2-CH ₃ C ₆ H ₄	91	14	192	190-191	C ₁₆ H ₁₅ N ₃	77.07 (77.11)	6.18 (6.02)	16.85 (16.87)	[13]	
2c	3-CH ₃ C ₆ H ₄	80		288		C ₁₆ H ₁₅ N ₃	77.25 (77.11)	5.98 (6.02)	16.79 (16.87)		
2d	4-CH ₃ C ₆ H ₄	99	9	245	245-246	C ₁₆ H ₁₅ N ₃	77.19 (77.11)	6.16 (6.02)	16.75 (16.87)	[14]	
2e	2-OHC ₆ H ₄	76		295		C ₁₄ H ₁₁ N ₃ O ₂	66.89 (66.40)	4.21 (4.37)	16.12 (16.59)		
2f	4-OHC ₆ H ₄	98		293		C ₁₄ H ₁₁ N ₃ O ₂	66.75 (66.40)	4.46 (4.37)	16.21 (16.59)		
2g	3-CH ₃ OC ₆ H ₄	99		217		C ₁₆ H ₁₅ N ₃ O ₂	68.59 (68.33)	5.18 (5.34)	14.15 (14.95)		
2h	4-CH ₃ OC ₆ H ₄	99	14	197	196-197	C ₁₆ H ₁₅ N ₃ O ₂	68.47 (68.33)	5.22 (5.34)	14.32 (14.95)	[14]	
2i	4-CH ₃ SC ₆ H ₄	79		200		C ₁₆ H ₁₅ N ₃ S ₂	61.42 (61.34)	4.91 (4.79)	13.28 (13.42)		
2j	2-ClC ₆ H ₄	84		150		C ₁₄ H ₉ N ₃ Cl ₂	57.83 (57.95)	3.02 (3.10)	14.39 (14.49)		
2k	4-ClC ₆ H ₄	98		252		C ₁₄ H ₉ N ₃ Cl ₂	57.75 (57.95)	3.16 (3.10)	14.31 (14.49)		
2l	2-pyridyl	81	5	207	206	C ₁₂ H ₉ N ₅	64.69 (64.57)	3.97 (4.03)	31.51 (31.40)	[15]	
2m	4-pyridyl	76	45	263	264	C ₁₂ H ₉ N ₅	64.36 (64.57)	3.95 (4.03)	31.28 (31.40)	[15]	

Table 2

¹H NMR (200 MHz) data (δ values, dimethyl-d₆ sulfoxide) for 3,5-Diaryl-4*H*-1,2,4-triazoles **2a-m**

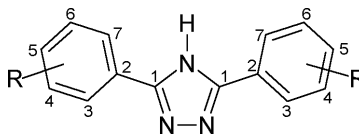
Compound No.	Aromatic signals	Substituent
2a	7.52 (m, 6H), 8.08 (m, 4H)	—
2b	7.38 (m, 4H), 7.71 (m, 2H), 7.99 (2H, m)	2.45 (s, 6H, CH ₃)
2c	7.07 (d, 2H, <i>J</i> = 7.8 Hz), 7.44 (s, 2H), 7.69 (4H, m)	2.39 (s, 6H, CH ₃)
2d	7.35 (d, 4H, <i>J</i> = 8.0 Hz), 8.02 (d, 4H, <i>J</i> = 8.0 Hz)	2.38 (s, 6H, CH ₃)
2e	7.01 (d, 2H, <i>J</i> = 7.7 Hz), 7.36 (m, 4H), 8.02 (d, 2H, <i>J</i> = 7.7 Hz)	—
2f	6.95 (d, 4H, <i>J</i> = 8.5 Hz), 7.90 (d, 4H, <i>J</i> = 8.5 Hz)	—
2g	7.05 (d, 2H, <i>J</i> = 8.0 Hz), 7.44 (t, 2H, <i>J</i> = 8.0 Hz), 7.69 (m, 4H)	3.85 (s, 6H, OCH ₃)
2h	7.04 (d, 4H, <i>J</i> = 8.5 Hz), 7.94 (d, 4H, <i>J</i> = 8.5 Hz)	3.77 (s, 6H, OCH ₃)
2i	7.41 (d, 4H, <i>J</i> = 8.1 Hz), 7.98 (d, 4H, <i>J</i> = 8.1 Hz)	3.34 (s, 6H, SCH ₃)
2j	7.50 (m, 4H), 7.61 (d, 2H, <i>J</i> = 8.0), 7.88 (d, 2H, <i>J</i> = 7.7 Hz)	—
2k	7.56 (d, 4H, <i>J</i> = 8.8 Hz), 8.01 (d, 4H, <i>J</i> = Hz)	—
2l	7.51 (t, 2H, <i>J</i> = 7.7 Hz), 7.98 (t, 2H, <i>J</i> = 7.7 Hz), 8.16 (d, 2H, <i>J</i> = 5.0 Hz), 8.71 (d, 2H, <i>J</i> = 7.9 Hz)	—
2m	8.28 (d, 4H, <i>J</i> = 6.0 Hz), 8.84 (d, 4H, <i>J</i> = 6.0 Hz)	—

desorption). All starting materials were of reagent grade and used as purchased. All quantum theoretical calculations were performed with SPARTAN Pro software package for PC (Irvine Inc.) using semi-empirical PM3 method at RHF (Restricted Hartree Fock) level, starting without any geometry constraints for full geometry optimisations. The HHON keyword was employed for hydrogen repulsion term.

3,5-Diaryl-4*H*-1,2,4-triazoles **2a-m**.

To a stirred solution of aminotriazole **1a-m** (0.01 mole) in an aqueous solution of 50 % hypophosphorous acid (30 ml), an aqueous solution of sodium nitrite (3.45 g, 0.05 mole in 10 ml of water) was added slowly. Vigorous nitrogen evolution was observed during this addition and the mixture was stirred at room

Table 3
 ^{13}C NMR (60 MHz) data (δ values, dimethyl- d_6 sulfoxide) for
 3,5-Diaryl-4H-1,2,4-triazoles **2a-m**



Numbered Structure for Parent 4H-Triazol

Compound No.	C ₁	C ₂	C ₃	C ₄	C ₅	C ₆	C ₇	Substituent
2a	159.1	126.8	129.3	129.7	130.7	129.7	129.3	
2b	156.6	127.1	136.8	131.1	129.6	129.4	126.0	20.9
2c	157.9	130.3	126.6	138.1	129.1	128.6	123.3	21.0
2d	154.0	124.5	129.0	128.1	139.1	128.1	129.0	20.9
2e	158.3	114.5	155.2	118.9	133.2	122.4	126.7	—
2f	157.8	121.3	125.6	116.8	157.7	116.8	125.6	—
2g	158.0	122.9	111.2	159.6	115.7	130.7	118.7	55.3
2h	159.2	122.1	128.9	115.5	161.5	115.5	128.9	56.3
2i	154.9	125.4	128.5	126.0	140.4	126.0	128.5	14.3
2j	158.4	129.2	132.4	131.5	129.8	128.4	128.3	—
2k	157.3	127.9	127.3	128.6	133.7	128.6	127.3	—
2l	147.1	148.9	—	148.2	124.6	137.8	122.8	—
2m	152.6	135.3	122.5	147.8	—	147.8	122.5	—

temperature for 1 hour. The powdery precipitate was collected, recrystallized from ethanol and dried. Yields and melting points are given in Table 1.

REFERENCES AND NOTES

* Corresponding author. E-mail: Michel.Lagrenée@ensc-lille.fr Fax: +33 3 20 43 68 14.

- [1] F. Zucchi, G. Trabanelli and G. Brunoro, *Corros. Sci.*, **33**, 1135 (1992).
 [2] J. O'M. Bockris and Bo Yang, *J. Electrochem. Soc.*, **138**, 2237 (1991).
 [3] F. B. Growcock and V.R. Lopp, *Corros. Sci.*, **28**, 397 (1988).
 [4] F. Bentiss, M. Lagrenée, M. Traisnel and J. C. Hornez, *Corros. Sci.*, **41**, 789 (1999).

- [5] P. G. Fox and Bradley, *Corros. Sci.*, **20**, 643 (1980).
 [6] G. Lewis, *Br. Corrosion J.*, **16**, 169 (1981).
 [7] K. Aramaki, T. Kiuchi, T. Sumiyoshi and H. Nishihara, *Corros. Sci.*, **32**, 593 (1991).
 [8] Neelima and A. P. Bhaduri, *Ind. J. Chem.*, **22B**, 79 (1983).
 [9] F. Bentiss, M. Lagrenée, M. Traisnel, B. Mernari and H. Elattari, *J. Heterocyclic Chem.*, **36**, 149 (1999).
 [10] J. F. Gueldart and F. Lions, *J. Org. Chem.*, **30**, 318 (1965).
 [11] M. Lagrenée, B. Mernari, M. Bouanis, M. Traisnel and F. Bentiss, *Corros. Sci.*, **44**, 573 (2002).
 [12] S. Kubota, M. Uda and T. Nakagawa, *J. Org. Chem.*, **12**, 855 (1975).
 [13] D. R. Liljegren and K. T. Potts, *J. Chem. Soc.*, 518 (1961).
 [14] A. Spasov and S. Robev, *Chem. Bul.*, **98**, 928 (1965).
 [15] S. Kubota and M. Ohtuska, *Yakugaku Kenkyu Nempo*, **9**, 15 (1960).