J.Sci.Soc.Thailand, 22 (1996) 71-74

SHORT REPORTS

A SIMPLE PROCEDURE FOR THE SYNTHESIS OF AMINOOXADIAZOLE+

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(Received Jauary. 7, 1995)

ABSTRACT

A simple precedure for the synthesis of aminooxadiazole is described. Yields of 80-85% are obtained.

INTRODUCTION

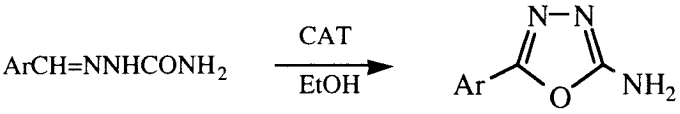
Substituted oxadiazoles have been reported to act as fluorescent whiteners, as herbicides, as fungicides, as hypnotics and as sedatives.[1] These compounds also showed analgesic, anti-inflammmatory, anticonvulsive, diuretic and antimitotic activity.[2] Aminooxadiazoles are useful photographic sensitizers and act as muscle relaxants. The usual synthesis of oxadiazoles involves the oxidative cyclization of hydrazone or semicarbazone[3] with bromine in glacial acetic acid or with bromine or iodine in aqueous sodium carbonate. Though there are methods for their synthesis, the yields are low (50 to 70%)[4] or side reactions may predominate.[5] Thus new procedures for the synthesis of aminooxadiazoles remain a topic of interest.

METHODS AND REAGENTS

Our success in converting aldoximes to nitrile oxides[6] and aldehyde hydraxones to nitrilimines[7] with N-chloro-N-sodio-p-toluene sulfonamide (CAT) prompted us to devise a simple and versatile procedure for the synthesis of aminooxadiazoles by heating an equimolar mixture of semicarbazones 1 and CAT trihydrate in ethanol at reflux for 3 hours. In general aminooxadiazoles (2a to 2e see Table 1 and 2) were obtained in 80-85% yield.

* Chloramine-T in Organic Synthesis. For previous paper Rai.K.M.L., Linganna.N, Hassner.A and Anjanamurthy.C, (1992), Org,Prep.Proced.Inst., **24**, 91.

Structure proof for the aminooxadiazoles were provided by mass ^{1}H NMR and ^{13}C NMR. Unfortunately, the yield of products from the cyclization of aliphatic aldehydes ranged from 2 to 4% yield.



1 2

a) Ar = Ph ; b) Ar = 4-$MeOC_6H_4$; c) Ar = 3,4-$(MeO)_2C_6H_3$
d) Ar = 3,4-$(OCH_2O)C_6H_3$ e) Ar = 2,4,6-$(MeO)_3C_6H_2$

TABLE 1. Yield and Physical Data of Aminooxadiazoles.

Product	Yield %	mp (°C)	lit. mp (°C)	Elemental analysis (Found) C	H	N
2a	82	238-240	241-243[8]	59.63	4.35	26.09
				(59.59)	(4.25)	(29.01)
2b	85	242-246	248-249[9]	56.54	4.71	21.99
				(56.41)	(4.59)	(21.81)
2c	82	213-215	-	54.29	4.90	19.00
				(54.21)	(4.86)	(18.87)
2d	83	247-250	-	52.68	3.41	20.49
				(52.59)	(3.30)	(20.38)
2e	80	197-200	-	52.59	5.18	16.73
				(52.50)	(5.11)	(16.62)

TABLE 2. Spectral Data of Aminooxadiazole (2).

Product ppm (δ)	1H NMR (CDCl3)	13C NMR (CDCl3) ppm (δ)	Mass spectra m/z (relative intensity)
2a	3.34 (bs, 2H, NH_2), 7.52 (m, 2H, ArH), 7.80 (m, 3H, ArH),	124.30 (s, C-1'), 124.92 (d, C-2', 6'), 129.08 (d, C-3', 4'), 157.24 (s, C-5), 163.75 (s, C-2)	162(M+1, 100) 161(M+, 81)
2b	3.36 (bs, 2H, NH_2), 3.82 (s, 3H, OMe), 7.15 (d, 2H, 3', 5'-H) 7.72 (d, 2H, 2', 4'-H)	55.31 (q, OMe), 114.61 (d, C-3', 5'), 116.95 (s, C-1') 126.94 (d, C-2', 6'), 157.29 (s, C-5), 160.79 (s, C-4'), 163.47 (s, C-2)	192 (M+1, 100), 191 (M+, 12)
2c	3.33 (bs, 2H, NH_2), 3.83 (s, 6H, OMe), 7.12 (m, 2H, ArH), 7.31 (m, 1H, ArH)	-	222 (M+1, 100), 221 (M+, 9)
2d	3.33 (bs, 2H, NH_2), 6.12 (s, 2H, OCH_2O), 7.02 (d, 1H, ArH), 7.29 (m, 2H, ArH)	101.70 (t, $O\underline{C}H_2O$), 104.97 (d), 108.87 (d,), 118.23 (d), 147.88 (s), 149.03 (s), 157.12 (s, C-5), 163.48 (s, C-2)	206 (M+1, 100), 205(M+, 8)
2e	3.36 (bs, 2H, NH_2), 3.38 (s, 3H, MeO), 4.02 (s, 6H, MeO), 7.02 (s, 2H, ArH).	252 (M+1, 100), -	251 (M+, 10)

EXPERIMENTAL SECTION

NMR spectra were recorded on a Bruker MHz spectrometer in $CDCl_3$ solution. The ^1H NMR spectra were measured at 300 MHz, Me_4Si was used as an internal standard, and chemical shifts are expressed in ppm (δ). the 13C NMR spectra were measured at 75 MHz and the values are in parts per million downfield from Me_4Si. Mass spectra were obtained on a Finnigan 4021 mass spectrometer. Chromatographic separations were carried out on a silica gel (70-230 mesh, Merck) column using chloroform-acetone (7:1) as the eluent.

Preparation of Aminooxadiazole (2). Typical Procedure

A mixture of semicarbazone 1b (2 g, 10.36 mmol) and CAT.$3H_2O$ (Loba Chemie Indo-Austranal Co., INDIA, 3 g, 10.67 mmol) in ethanol (20 ml) was heated to reflux with stirring for 3 hrs. The sodium chloride formed in the reaction was filtered off and washed with ethanol. The combined filtrate and washings were evaporated in vacuo and the residue was extracted with 10 % HCl (15 ml) and washed thoroughly with dichloromethane (2x29 ml). The aqueous layer on neutralization with 10 % sodium hydroxide (15 ml) gave 2 as white solids which was collected, washed and dried. Recrystallization from ethanol gave 1.67 g (85 %) of aminooxadiazole 2b as a white crystalline solid.

ACKNOWLEDGEMENT

We wish to thank Dr. Gottlieb.H.E. and Dr. Miriam Cojocaru, Bar-Ilan University, Israel for their valuable assistance with NMR and Mass spectra.

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