Mild Oxidation of 1,3,5-Trisubstituted Pyrazolines with N-Bromo-sulphonamides

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1,3,5-Trisubstituted pyrazolines to pyrazoles are carried out efficiently in the presence of new reagents *N*,*N*,*N*′,*N*′-tetrabromo-benzene-1,3-disulfonylamine **[TBBDA]** and *N*,*N*′-dibromo-*N*,*N*′-1,2-ethanediylbis-(*p*-toluenesulphonamide) **[BNBTS]** in solvent-free conditions with catalytic amounts of SiO_2 under microwave irradiation in high yields.

Keywords: Pyrazolines; Oxidation; Aromatization; **BNBTS**; **TBBDA**.

INTRODUCTION

The oxidation of 1,3,5-trisubstituted pyrazolines to pyrazoles is an important transformation in organic synthesis and because of its significant role, it often has been used commercially for its analgesic, anti-inflammatory, antipyretic, antiarrhythmic, tranquilizing, muscle relaxant, psychoanaleptic, anticonvulsant, monoamineoxidase inhibitor, antidiabetic and antibacterial activities.[1] Therefore, oxidative aromatization of pyrazolines[2] with oxidizing reagents should provide an efficient method for the preparation of pyrazole derivatives. For this oxidative conversion of pyrazolines, a limited number of reports exist in the literature which include $Zr(NO_3)_4$,[3] Pd/C,[4] Co(II) and oxygen,[5] iodobenzene diacetate,[6] lead tetraacetate,[7] MnO_2,[8] potassium permanganate[9] and NBS,[10] but most of them suffer from the use of excess reagent, longer reaction times, higher temperatures, formation of side products, solvents and difficulty in removing the reagent from the sensitive pyrazoles.

RESULTS AND DISCUSSION

Herein, we report on a simple and efficient procedure for oxidative aromatization of 1,3,5-trisubstituted pyrazolines to pyrazoles using *N*,*N*,*N*′,*N*′-tetrabromo-benzene-1,3-disulfonylamine **[TBBDA]** and *N*,*N*′-dibromo-*N*,*N*′-1,2-ethanediylbis(*p*-toluenesulphonamide) **[BNBTS]**[11] (Fig. 1) in solvent-free conditions with catalytic amounts of SiO_2 under microwave irradiation.

The advantages of **BNBTS** and **TBBDA** are as follows:

1. The preparation of **BNBTS** and **TBBDA** are easy.

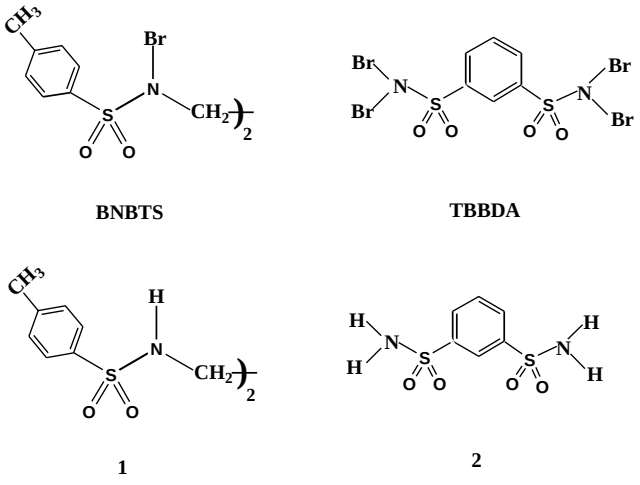
2. **BNBTS** and **TBBDA** are stable for two to three months under atmospheric conditions.

3. After completion of the reaction, the sulphonamide is recovered and can be reused many times without decreasing the yield.

The reaction of 1,3,5-trisubstituted pyrazolines with **BNBTS** or **TBBDA** afforded pyrazoles without side products (Scheme I).

The results of the conversion of various 1,3,5-trisubstituted pyrazolines to their corresponding pyrazoles in the presence or absence SiO_2 are presented in Tables 1 and 2.

It was found that the best result is obtained in the presence of SiO_2 (Tables 1 and 2), because silica absorbed the microwave radiation and caused enhanced chemical reac-



BNBTS **TBBDA**

1 **2**

Fig. 1.

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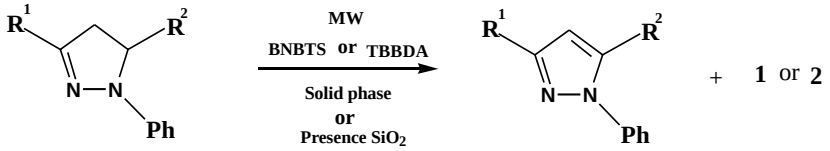
Scheme I



3 **4**

Table 1. Oxidative aromatization of 1,3,5-trisubstituted pyrazolines with **BNBTS** in solvent-free conditions with catalytic amounts of SiO_2 under microwave irradiation

Substrate	Product[a]	R^1	R^2	Reagent/Product	Time (min) I[b] (II)[c]	Yield (%) I[b] (II)[c]
1a	2a	2-Naphthyl	2-$CH_3C_6H_4$	4	11 (7)	70 (86)
1b	2b	Ph	Ph	4	10 (4)	68 (78)
1c	2c	4-$CH_3C_6H_4$	3-$CH_3C_6H_4$	5	12 (5)	71 (82)
1d	2d	3-$CH_3C_6H_4$	4-ClC_6H_4	5	10 (4)	62 (76)
1e	2e	4-$OCH_3C_6H_4$	Ph	4.25	8 (6)	72 (90)
1f	2f	4-$OCH_3C_6H_4$	2-$CH_3C_6H_4$	4.5	14 (5)	70 (90)
1g	2g	4-$OCH_3C_6H_4$	3-$CH_3C_6H_4$	4.25	12 (5)	64 (82)
1h	2h	2-Naphthyl	3-$CH_3C_6H_4$	5	14 (8)	72 (78)
1i	2i	2-Naphthyl	2-ClC_6H_4	5	11 (7)	66 (78)
1j	2j	2-Naphthyl	4-ClC_6H_4	5.5	15 (10)	70 (88)
1k	2k	3-$CH_3C_6H_4$	4-$N(CH_3)_2C_6H_4$	5	11 (5)	64 (88)
1l	2l	4-$OCH_3C_6H_4$	2-ClC_6H_4	4.5	14 (6)	58 (73)

[a] Products were characterized by their physical properties, comparison with authentic samples, and by spectroscopic methods.
[b] In the absence of SiO_2.
[c] In the presence of SiO_2 (1 mmol of reagent/0.02 mmol of SiO_2).

Table 2. Oxidative aromatization of 1,3,5-trisubstituted pyrazolines with **TBBDA** in solvent-free conditions with catalytic amounts of SiO_2 under microwave irradiation

Substrate	Product[a]	R^1	R^2	Reagent/Product	Time (min) I[b] (II)[c]	Yield (%) I[b] (II)[c]
1a	2a	2-Naphthyl	2-$CH_3C_6H_4$	2.75	14 (6)	78 (88)
1b	2b	Ph	Ph	2.75	12 (4)	75 (82)
1c	2c	4-$CH_3C_6H_4$	3-$CH_3C_6H_4$	3.75	14 (5)	80 (90)
1d	2d	3-$CH_3C_6H_4$	4-ClC_6H_4	3.5	15 (6)	70 (84)
1e	2e	4-$OCH_3C_6H_4$	Ph	3	13 (7)	89 (90)
1f	2f	4-$OCH_3C_6H_4$	2-$CH_3C_6H_4$	3.25	15 (5)	70 (90)
1g	2g	4-$OCH_3C_6H_4$	3-$CH_3C_6H_4$	3	14 (6)	72 (84)
1h	2h	2-Naphthyl	3-$CH_3C_6H_4$	3.75	14 (7)	80 (84)
1i	2i	2-Naphthyl	2-ClC_6H_4	3.5	12 (4)	72 (88)
1j	2j	2-Naphthyl	4-ClC_6H_4	4	16 (8)	70 (76)
1k	2k	3-$CH_3C_6H_4$	4-$N(CH_3)_2C_6H_4$	3.75	14 (7)	72 (82)
1l	2l	4-$OCH_3C_6H_4$	2-ClC_6H_4	3	12 (5)	76 (79)

[a] Products were characterized by their physical properties, comparison with authentic samples, and by spectroscopic methods.
[b] In the absence of SiO_2.
[c] In the presence of SiO_2 (1 mmol of reagent/0.014 mmol of SiO_2).

tions.[12,13] Of course, this reaction was examined with SiO_2 in the absence of *N*-bromosulfonamide, and the progress of the reaction was not observed.

In conclusion, the presented method is an efficient and selective protocol for aromatization of 1,3,5-trisubstituted pyrazolines to pyrazoles. Thus, microwave irradiation could be used for the oxidation of a wide variety of pyrazoline derivatives with **BNBTS** and **TBBDA** in the presence of a catalytic amount of SiO_2. Also, the results show that the mole of SiO_2 in **TBBDA** is approximately 50% that of in **BNBTS**.

EXPERIMENTAL

IR and NMR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and a 90 MHz Jeol FT-NMR spectrometer, respectively. A Butane Industrial Co. microwave (220 v, 1000 w) was used for the microwave irradiations.

Procedure for preparation of benzene-1,3-disulfonylamide

To benzene-1,3-disulfonyl acid sodium salt (0.016 mol) was added PCl_5 (0.0165 mol) as chlorination agent. For starting the reaction, the vessel should be heated (40-50 °C), then the reaction completes spontaneously. After complete conversion (2 h), crushed ice (100 g) was added; the product was separated from inorganic materials by chloroform. Then to the solution was added NH_3 (l) (400 mL); the reaction mixture was stirred with a mechanical stirrer. After complete addition, removal of the solvent under reduced pressure gave the crude product. The pure product (90%, m.p. 228-230 °C) was obtained by crystallization with ethanol. IR spectrum (KBr pellets): 3320, 3090, 1600, 1320, 1130 cm^{-1}. ^1H NMR (acetone-d^6): δ 6.7 (s, 4H), 7.7 (t, 1H), 8.1 (d, 2H), 8.3 (s, 1H). ^{13}C NMR: 124.2, 130.6, 129.8, 124.2.

Procedure for preparation of *N,N,N′,N′*-Tetrabromobenzene-1,3-disulfonylamide [TBBDA]

N,*N*,*N′*,*N′*-Tetrabromo-benzene-1,3-disulfonylamide (0.003 mol) was dissolved in a slight molar excess of chilled sodium hydroxide solution (3 M) at room temperature and was the solution transferred to a beaker. Then bromine (0.0584 mol) was added to the solution with vigorous stirring, and immediately precipitate was formed. The product was collected on a buchner funnel, and it was washed with 30 mL distilled cold water and then dried in a vacuum desicator at room temperature for 6 h. The yield of pure TBBDA, m.p. 267-270d °C, was 90%. The reagent was identified by NMR, IR spectroscopies. IR spectrum (KBr pellets): 3070, 1620, 1310, 1130 cm^{-1}. ^1H NMR (acetone-d^6): δ 7.9 (t, 1H), 8 (d, 2H), 8.3 (s, 1H). ^{13}C NMR spectrum (acetone): δ 123.4, 128.7, 127.9, 122.3.

General procedure for oxidation of 1,3,5-trisubstituted pyrazoline with TBBDA or BNBTS

A mixture of 1,3,5-trisubstituted pyrazoline **3** (1 mmol), **BNBTS** or **TBBDA** (1 mmol) and SiO_2 (0.014-0.02 mmol) was introduced in a flask and was irradiated in a microwave oven at a power output of 1000 W for the appropriate time as indicated in Tables 1 and 2. After irradiation and monitoring on TLC (hexan:aceton, 10:1), the product is extracted with carbon tetrachloride; K_2CO_3 (0.5 g) was added and stirred for 0.5 h, and the insoluble sulfonamide **1** or **2** was removed by filtration and washed with cold carbon tetrachloride (10 mL). Removal of the solvent under reduced pressure gave the crude product. The pure product **4** was obtained by recrystalization with methanol/H_2O (10:1).

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