Tricholoroisocyanuric Acid as a Useful Reagent in Microwave-assisted Aromatization of 1,3,5-Trisubstituted 2-Pyrazolines

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An efficient aromatization of 1,3,5-trisubstituted 2-pyrazolines to their corresponding pyrazoles has been performed by tricholoroisocyanuric acid [**TCCA**] under microwave irradiation in excellent yields. It has been observed that the reactions occur more rapidly under microwave irradiation conditions, and the amount of the reagent **TCCA** consumed is considerably reduced to afford better yields when compared with conventional thermal conditions at the same temperature.

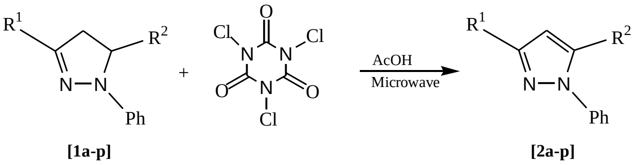
Keywords: 2-Pyrazolines; Pyrazoles; Oxidation; Aromatization; Microwave irradiation; Tricholoroisocyanuric acid; [**TCCA**].

INTRODUCTION

The use of microwave irradiation as a non-conventional energy source has become of considerable interest in organic chemistry. The frequency of publications and reviews during the last few decades has substantiated the advantages and versatility of microwave irradiation in easy and high yielding oxidation of organic compounds. This novel method is therefore a fast growing and clean practice in organic synthesis which has several advantages over classical thermal conditions in providing increased reaction rates, simplicity and improved yields.[1] The oxidative aromatization of 1,3,5-trisubstituted 2-pyrazolines to pyrazoles is biologically important, since many pyrazole derivatives possess analgesic, anti-inflammatory, antipyretic, antiarrhythmic, muscle relaxant, psychoanaleptic, antidiabetic and antibacterial activities.[2] 1,3,5-Trisubstituted 2-pyrazolines can be conveniently prepared from hydrazines and chalcone intermediates.[3] Therefore, oxidative aromatization of 2-pyrazolines by oxidizing agents should provide an efficient method for the preparation of pyrazole derivatives. A variety of oxidants such as $Zr(NO_3)_4$,[4] Pd/C,[5] carbon-promoted oxygen,[6] Co(II) and oxygen,[7] iodobenzene diacetate,[8] lead tetraacetate,[9] MnO_2,[10] and $KMnO_4$,[11] have been previously reported; most suffer from the use of excess reagent, longer reaction times, higher temperatures, acidic media, formation of side products and toxicity due to the presence of toxic transition metal cations like Co(II), Pb(IV), Hg(II), Mn(IV and VII), Ag(I), Zr(IV) within the structural formula of the reagents employed. Following our previously reported protocols on the oxidative aromatization of pyrazolines,[12] we report herein on a facile microwave-accelerated oxidation of 2-pyrazolines to pyrazoles by tricholoroisocyanuric acid [**TCCA**] under microwave irradiation. Our objective in this work focused on some interesting features such as (a) the rapid reaction rates (b) higher yields of products and cleaner reaction conditions and (c) the low consumption of the oxidant.

The reaction of 1,3,5-trisubstituted 2-pyrazolines with **TCCA** under microwave irradiation afforded pyrazoles with no side products (Scheme I).

Scheme I



The results obtained from the conversion of various 1,3,5-trisubstituted 2-pyrazolines **1a-p** into their corresponding pyrazoles **2a-p** are summarized in Tables 1 and 2.

EXPERIMENTAL

All the melting points were determined on a Büchi 530 melting point apparatus and reported uncorrected. IR spectra

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were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets). ^{1}H-NMR and ^{13}C-NMR spectra were obtained using a 90 MHz JEOL FT NMR spectrometer. The CHN analyses were performed in the Iranian Petroleum Research Center (Ray City, Tehran).

Table 1. Substrates **1a-p** and their corresponding products **2a-p**

Substrate	Product	R^1	R^2
1a	**2a**	2-Naphthyl	*o*-$CH_3C_6H_4$
1b	**2b**	Ph	Ph
1c	**2c**	*p*-$CH_3C_6H_4$	*m*-$CH_3C_6H_4$
1d	**2d**	*p*-$CH_3OC_6H_4$	*o*-$CH_3C_6H_4$
1e	**2e**	*p*-$CH_3OC_6H_4$	*m*-$CH_3C_6H_4$
1f	**2f**	*p*-$CH_3OC_6H_4$	Ph
1g	**2g**	*p*-$CH_3OC_6H_4$	*p*-ClC_6H_4
1h	**2h**	2-Naphthyl	*m*-$CH_3C_6H_4$
1i	**2i**	2-Naphthyl	*p*-ClC_6H_4
1j	**2j**	2-Naphthyl	*o*-ClC_6H_4
1k	**2k**	*m*-$CH_3C_6H_4$	*p*-$(CH_3)_2NC_6H_4$
1l	**2l**	*p*-$CH_3OC_6H_4$	*o*-ClC_6H_4
1m	**2m**	2-Naphthyl	Ph
1n	**2n**	*o*-$CH_3C_6H_4$	*p*-$(CH_3)_2NC_6H_4$
1o	**2o**	Ph	*p*-BrC_6H_4
1p	**2p**	Ph	*m*-ClC_6H_4

Table 2. Oxidative aromatization of 1,3,5-trisubstituted 2-pyrazolines (1 mmol) by **TCCA** in CH_2Cl_2 at room temperature [**I**] and under microwave irradiation conditions [**II**]

Substrate	Product[a]	Reagent (mmol)		Time (min)		Yield (%)[b]	
		I	**II**	**I**	**II**	**I**	**II**
1a	**2a**	1.25	1.00	50	5	90	96
1b	**2b**	1.25	1.00	45	4	85	94
1c	**2c**	2.25	1.50	50	3	85	96
1d	**2d**	3.25	2.75	30	3	90	96
1e	**2e**	2.75	2.50	30	4	92	94
1f	**2f**	2.00	1.25	35	4	92	92
1g	**2g**	2.25	2.25	35	4	70	92
1h	**2h**	2.25	2.00	55	5	85	94
1i	**2i**	3.50	2.75	50	4	82	96
1j	**2j**	3.25	2.50	50	4	78	92
1k	**2k**	2.50	2.00	30	4	82	92
1l	**2l**	2.50	2.00	30	3	90	96
1m	**2m**	1.25	1.25	50	5	92	94
1n	**2n**	2.50	2.00	30	3	85	96
1o	**2o**	2.50	1.75	45	5	74	90
1p	**2p**	2.75	2.25	50	5	80	90

[a] All the isolated products were characterized on the basis of their physical properties and spectra and by direct comparison with literature data.[12]

[b] Isolated yields.

Procedure for oxidation of 1,3,5-trisubstituted 2-pyrazolines by TCCA

To a stirred solution of acetic acid (5 mL) was added the substrate **1a-p** (1 mmol) and **TCCA** in appropriate amounts (Table 2). The resulting mixture was then placed in an alumina bath inside an MW oven (900 W) and irradiated for 3-5 min. After the complete conversion of the substrate as monitored by TLC, the solvent was evaporated under reduced pressure and the products were extracted with dicholoromethane. The solid residue was purified by flash chromatography (using n-hexane/ethyl acetate 10:1) to give the corresponding pyrazoles **2a-p** (Table 2).

Received April 25, 2005.

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