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## Synthesis of 5-(4-nitrophenoxy)-1H-tetrazole

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### ABSTRACT

Reaction of phenol and its derivatives (4-nitrophenol) with cyanogen bromide afforded aryl cyanate in the presence of triethylamine aryl cyanate then reacted with sodium azide by 1,3-dipolar cycloaddition reaction, acidified with concentrated HCl were obtained 5-aryloxy tetrazoles in good yield. The proposed reaction mechanism is discussed. All structures were characterized by <sup>1</sup>H, <sup>13</sup>C NMR, IR and elemental analysis.

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### KEYWORDS

 Tetrazole;  
 Derivative;  
 Synthesis;  
 Characterization.

### INTRODUCTION

The tetrazole moiety exhibits a wide and growing number of applications. This nitrogen-rich ring system is used in propellants<sup>[1]</sup>, explosives<sup>[2]</sup>, and pharmaceuticals<sup>[3]</sup>. Practicing medicinal chemists who may be interested in an evaluation of more comprehensive tabular surveys may also consult some of the review materials listed in this bibliography<sup>[4-8]</sup>. Synthesis of tetrazoles has been reported since the mid-century, there is still a dearth of efficient processes. Tetrazoles are an increasing popular functionality<sup>[9]</sup>. With wide-ranging applications. Structural elucidation of tetrazoles involved is helpful in understanding how and why they own these functions. For tetrazole and its 5-substituted derivatives, tautomeric and ring-chain isomerisms are known (Scheme 1)<sup>[10]</sup>.

To date, reports on mass spectrometric investigations of 5-substituted tetrazoles are scarce<sup>[11-15]</sup>. In those case, loss of N<sub>2</sub> upon electron impact is observed mainly

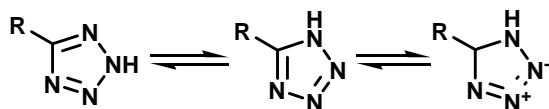
and loss of N<sub>3</sub>· is only of minor importance. In continuation of our studies on organic reactions, we report here an efficient method for the synthesis of tetrazole via reaction of 5-(phenoxy)-1H-tetrazole with acid nitric in the presence of solvent. Tetrazole derivative were synthesized and characterized by using elemental analyses, FT-IR, NMR.

### EXPERIMENTAL

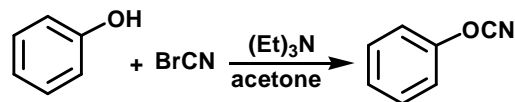
#### Materials and general methods

The reagents and solvents were of analytical grade. Sodium azide, phenol, and other material were purchased from Merck Company. <sup>1</sup>H and <sup>13</sup>C NMR spectra of deuterated chloroform (CDCl<sub>3</sub>) and solutions of the compounds were registered on a Bruker WM-300 spectrometer (300 MHz) using tetramethylsilane as internal standard. The infrared spectra of the compounds as KBr-disks were recorded in the range of 400–

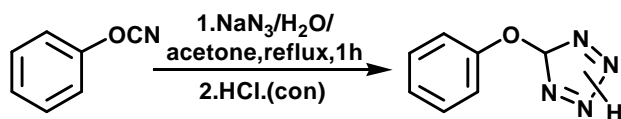
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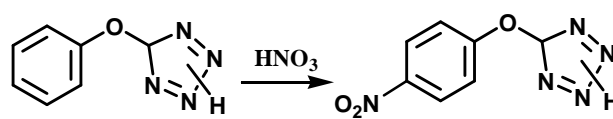
Scheme 1 : Tautomeric and ring-chain isomerisms of tetrazole



Scheme 2 : Synthesis of phenyl cyanate



Scheme 3 : Synthesis of 5-(phenoxy)-1H-tetrazole



Scheme 4 : Synthesis of 5-(4-nitrophenoxy)-1H-tetrazole

4000  $\text{cm}^{-1}$  with a Mattson 1000 FT spectrometer.

### Synthesis of phenyl cyanate

17.6 g of the crude phenol were dissolved in 70 ml of acetone. The solution was cooled to  $-30^{\circ}\text{C}$  and 19.8g of liquefied cyanogen bromide were added under stirring. Within a period of 60 min a solution of 26 ml of triethyl amine in 20 ml of acetone was added dropwise. During the addition the temperature of the reaction solution was maintained between  $-30^{\circ}\text{C}$  and  $-20^{\circ}\text{C}$ . The solution was then stirred for further 60 min at room temperature to complete the reaction. These operations were carried out under appropriate safety precautions in a well-ventilated hood. After filtration the reaction solution was concentrated in vacuo. The oily residue was chromatographed over a silica gel column using n-hexane/ethyl acetate (vol. ratio 10:3) as eluent (Scheme 2). IR (KBr,  $\text{cm}^{-1}$  film on NaCl disc): 2974, 2277, 2239, 1602, 1501, 1459, 1167, 1086, 1012, 761, 687  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (DMSO- $d_6$ , 300MHz):  $\delta$  (ppm) 6.73-7.28.

### Synthesis of 5-(phenoxy)-1H-tetrazole

A three-necked 50 ml flask was equipped with a distillation head, a dropping funnel. 1.4 g sodium azide in 10 ml water placed in the flask. After loading the dropping funnel with 2.4 g of the phenyl cyanate, the distillation apparatus was heated in an oil bath thermostatted at  $150^{\circ}\text{C}$ . The contents of the dropping funnel were dropped into the heated flask over a period of 30 min. The solution was cooled to  $-30^{\circ}\text{C}$  and 0.5g of HCl was added under stirring. The precipitate are combined and washed three times with 300 ml portions of water and then dried over polyphosphoric anhydride (Scheme 3). 5-(phenoxy)-1H-tetrazole recrystallized from methanol. IR (KBr,  $\text{cm}^{-1}$ ): 3060, 2901-2281, 1621, 1577, 1488, 1276, 1189, 1055, 977, 853, 781, 687, 611, 482.  $^1\text{H}$  NMR (DMSO- $d_6$ , 300MHz):

$\delta$  (ppm) 7.743 (m, 2H), 7.252 (m, 3H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 75MHz): 166.80, 154.50, 130.52, 126.09, 119.38.

### Synthesis of 5-(4-nitrophenoxy)-1H-tetrazole

In a 50 ml beaker, 14 g of 5-(phenoxy)-1H-tetrazole is dissolved in 60-50 ml acid nitric. The beaker is placed in an ice-salt bath and cooled to  $0-5^{\circ}\text{C}$  whilst stirring vigorously. Then ice-salt bath was removed and temperature of the solution is allowed to rise above  $40^{\circ}\text{C}$ . The precipitate are combined and washed with water and then dried over polyphosphoric anhydride (Scheme 4). Compound recrystallized from chloroform. IR (KBr,  $\text{cm}^{-1}$ ): 3113, 2892-2476, 1928, 1584, 1543, 1487, 1351, 1201, 1165, 1061, 864.62, 738, 687, 649.  $^1\text{H}$  NMR (DMSO- $d_6$ , 300MHz):  $\delta$  (ppm) 8.3 (d,  $J=9\text{Hz}$ , 2H) 7.53 (d,  $J=9.3\text{ Hz}$ , 2H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 75MHz):  $\delta$  (ppm) 166.79, 159.17, 144.70, 126.44, 119.70.

## RESULTS AND DISCUSSION

Phenyl cyanate was readily converted to 5-(phenoxy)-1H-tetrazole by treating them with sodium azide and hydrochloric acid in water. Infrared spectrum of compound 5-(phenoxy)-1H-tetrazole showed a sharp absorption and at  $3060\text{ cm}^{-1}$  which is attributed to secondary amino group. The synthesized compound 5-(4-nitrophenoxy)-1H-tetrazole showed absorption bands  $3113, 2892-2476\text{ cm}^{-1}$  which are attributed to proton tetrazole ring. Characteristic absorption bands were observed for nitro group and aromatic region of the synthesized compound.  $^1\text{H}$ -NMR spectra of the synthesized 5-(4-nitrophenoxy)-1H-tetrazole showed doublet at 7.53 ppm two protons ortho and doublet at 8.28 ppm two protons meta. 1-H (NH) proton of the tetrazole is undetectable in NMR spectra.

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### CONCLUSION

The method described in this paper, allows the preparation of unique substituted tetrazoles from commercial and available phenol and easy to prepare from sodium azides and various nitration agents. The important aspects of this protocol, are mild reaction conditions, availability of the purity of the obtained products with no further crystallization.

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