J IRAN CHEM SOC
DOI 10.1007/s13738-013-0279-4

ORIGINAL PAPER

Cross-linked poly (4-vinylpyridine) supported azide ion as a versatile and recyclable polymeric reagent for synthesis of 1-substituted-1*H*-1,2,3,4-tetrazoles

Mohammad Ali Karimi Zarchi · Fatemeh Nazem

Received: 26 January 2013 / Accepted: 22 May 2013

Abstract Cross-linked poly (4-vinylpyridine) supported azide ion, $[P_4\text{-VP}]N_3$, is easily prepared and used as an efficient polymeric reagent for synthesis of 1-substituted-1*H*-1,2,3,4-tetrazoles via condensation reaction of azide ion, primary aromatic amines, and triethyl orthoformate in glacial acetic acid. After optimization of the reaction conditions, a wide variety of primary aromatic amines were also subjected to preparation of the corresponding 1-aryl-1*H*-1,2,3,4- tetrazoles using $[P_4\text{-VP}]N_3$ under heterogeneous conditions. In this method, the reaction times were very short and the isolated yields were excellent (90–98 %). 1-Aryl-1*H*-1,2,3,4- tetrazole products were characterized by Fourier transform infrared (FT-IR) and some of them were also characterized by proton nuclear magnetic resonance (^{1}H NMR) spectroscopy, and physical properties were compared with the literature values of known compounds. The spent polymeric reagent were regenerated quantitatively and reused for several cycles without significant loss of their activity.

Keywords 1-Substituted-1*H*-1,2,3,4-tetrazoles · Polymer-supported azide ion · Aromatic amine · Triethyl orthoformate

Introduction

The problems associated with classical multi-step synthesis in solution may overcome by a modified technique that was introduced by Merrifield [1]. This technique has been used in the production of large amounts of products. However, recently the chemistry of functional polymers has received great attention and has become a practical method for the efficient preparation of novel chemical libraries [2–4]. Polymer-supported reagents particularly anion exchange resins have been widely applied in organic synthesis [2–16]. These polymeric reagents have been used in the production of large number of products in single step reactions. The advantages of this technique over conventional classical methods are mild reaction conditions, safe handling, rapid, and very simple work-up. On the other hand, usually the spent polymeric reagents can be regenerated and reused for several times without significant loss of their activity.

In recent years, the number of publications and patents describing the synthesis and investigations of the structural and physicochemical properties of tetrazoles has grown intensely. This is due to the wide range of practical applications of these compounds. For example, 1-substituted tetrazoles have been used in different application in many important field such as medicinal chemistry [17], coordination chemistry [18, 19], color photography couplers [20], agriculture [21], and high energy density materials with high nitrogen contents [22, 23].

In general, the most direct and versatile method of the synthesis of tetrazoles is the cycloaddition between nitriles, cyanates and cyanamides, and azides [24–29].

1-Substituted tetrazoles are generally synthesized by the reaction of isocyanides with large excess amounts of dangerous and harmful hydrazoic acid [30, 31] or trimethylsilyl azide [32].

Other methods of a tetrazole ring synthesis include addition of primary amines or their salts to sodium azide and orthocarboxylic acid ester in acetic acid or trifluoroacetic acid [33, 34]. Recently, 1-substituted tetrazoles were

M. A. Karimi Zarchi (✉) · F. Nazem
Department of Chemistry, College of Science,
Yazd University, P. O. Box 89195-74, Yazd, Iran
e-mail: makarimi@yazd.ac.ir

Published online: 19 June 2013

prepared in ionic liquids [35, 36]. Habibi et al. [37] have reported silica sulfuric acid as an efficient heterogeneous catalyst for the solvent-free synthesis of 1-substituted 1*H*-1,2,3,4-tetrazoles. Habibi et al. [38] have also reported the synthesis of 1-substituted 1*H*-1,2,3,4-tetrazoles in the presence of Natrolite zeolite. Su et al. [39] have reported 1-substituted 1*H*-1,2,3,4-tetrazoles using Yb (OTf).

All of these known methods suffered from some limitation such as low yields; tedious work-up procedures; the use of expensive and toxic metal catalysts; the use of high boiling point solvent such as dimethyl formamide (DMF); and complex isolation and recovery procedures. Therefore, it is desirable to develop a convenient method for the synthesis of 1-substituted 1*H*-1,2,3,4-tetrazoles.

Although there are numerous applications of polymeric reagents in literature, there are only a few reports in the literature based on polymer-supported azide ion and there is only one report on the synthesis of 5-substituted 1-H-tetrazoles based on polymer-supported azide ion [29]. Hassner et al. [40] have reported the use of the polymeric quaternary ammonium azide for synthesis of alkyl azides from alkyl halides or esters. Previously, we have reported the synthesis and application of cross-linked poly (4-vinylpyridine) supported azide ion, $[P_4\text{-VP}]N_3$, for synthesis of alkyl azides from alkyl halides [41]. Recently, we also used this polymeric reagent for synthesis of 5-substituted 1-H-tetrazoles [40], diazotization–azidation of primary aromatic amines [42, 43], and synthesis of acyl azides from acyl halides [44].

In continuation of our studies on the development of application of cross-linked poly (4-vinylpyridine) supported azide ion, $[P_4\text{-VP}]N_3$, in organic synthesis [29, 41–44], herein, we wish to report an efficient and easy method for preparation of 1-substituted 1-*H* tetrazoles using $[P_4\text{-VP}]N_3/ArNH_2/CH(OEt)_3$/AcOH at 100 °C.

Experimental

Materials

Chemicals were either prepared in our laboratory or were purchased from Fluka (Buchs, Switzerland), Aldrich (Milwaukee, WI, USA), and Merck chemical companies. Poly (4-vinylpyridine) cross-linked with 2 % divinyl benzene (DVB), $[P_4\text{-VP}]$ 2 % DVB, was purchased from Fluka company (Buchs, Switzerland) and $[P_4\text{-VP}]N_3$, was prepared according to our reported procedure [29].

The reactions were monitored by thin layer chromatography (TLC) using silica gel Poly Gram SIL G/UV 254 plates. All products were characterized by comparison of their Fourier transform infrared (FT-IR), proton nuclear magnetic resonance (^{1}H-NMR) spectra, TLC, and physical data with pure compounds. All yields refer to the isolated products. FT-IR and NMR spectra were run on a Bruker Equinox (model 55) and Bruker AC 500, respectively, Aveance DPX spectrophotometer at 500 MHz for ^{1}H-NMR in $CDCl_3$, and DMSO solution (using tetramethylsilane as internal reference).

Preparation of $[P_4\text{-VP}]N_3$

Poly (4-vinylpyridine) cross-linked with 2 % DVB (white powder, 100–200 mesh) (1.0 g) was added to a solution of methyl iodide (20 mmol, 3.24 g) in acetonitrile (10 mL), and the mixture was stirred slowly for 24 h at room temperature. The yellow quaternized polymer, $[P_4\text{-VP}]I$, was filtered and washed with acetone (3 × 5 mL). It was then dried under vacuum in the presence of P_2O_5 at 40 °C overnight.

The obtained $[P_4\text{-VP}]I$ was added to 40 mL of a 3 mol L^{-1} aqueous solution of sodium azide and was stirred slowly for 24 h. The prepared resin, $[P_4\text{-VP}]N_3$, was filtered off and was washed with distilled water. It was then washed with diethyl ether (5 mL) and dried under vacuum in the presence of P_2O_5 at 40 °C overnight. The capacity of the polymer was determined by potentiometric titration of the filtrates with a 0.1 mol L^{-1} aqueous solution of silver nitrate, and it was found to be 3.4 mmol per gram of the polymer.

General procedure for synthesis of 1-substituted 1-H-1,2,3,4-tetrazoles

A suspension of a primary aromatic amine (1 mmol), triethyl orthoformate (2.5 mmol), and $[P_4\text{-VP}]N_3$ (2.5 mmol) in glacial acetic acid (5 mL) was stirred for appropriate time as indicated in Table 2 (shown later) at 100 °C. The progress of reaction was monitored by TLC (*n*-hexane/ethyl acetate: 9/1). After completion of the reaction, ethanol (8 mL) was added to the reaction mixture and heated at 70 °C for 5 min. The reaction mixture was filtered off and was washed with hot ethanol. Then, the solution was cooled to room temperature and 4 mL of 4 mol L^{-1} aqueous solution of HCl was added. The precipitated product was filtered, washed with water, and dried to obtain the pure product. When further purification was needed, column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate: 9/1) was applied and highly pure product was obtained.

Preparation of 1-(4-chlorophenyl)-1H-1,2,3,4-tetrazole: a typical procedure

A suspension of 4-chloroaniline (1 mmol), triethyl orthoformate (2.5 mmol), and $[P_4\text{-VP}]N_3$ (2.5 mmol) in glacial acetic acid (5 mL) was stirred for 10 min at 100 °C (The

progress of reaction was monitored by TLC; *n*-hexane/ethyl acetate: 9/1). After completion of the reaction, ethanol (8 mL) was added to the reaction mixture and heated at 70 °C for 5 min. The reaction mixture was filtered off and was washed with hot ethanol. Then, the solution was cooled to room temperature and 4 mL of 4 mol L^{-1} aqueous solution of HCl was added. The precipitated product was filtered, washed with water, and dried to obtain the pure product.

Yield: 178 mg (98 %), white solid; mp: 160–162 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.62 (2H, d, J = 8.7 Hz), 7.73 (d, J = 8.7 Hz, 2H), 9.2 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-Phenyl-1H-1,2,3,4-tetrazole

Yield: 131 mg (98 %), white solid; mp: 63–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.32 (t, J = 7.4 Hz, 1H), 7.63 (t, J = 7.6 Hz, 2H), 7.76 (d, J = 7.8, 2H), 9.07 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Bromophenyl)-1H-1,2,3,4-tetrazole

Yield: 143 mg (98 %) white solid; mp: 180–181 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.64 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H), 9.23 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,125, 1,493, 1,383, 1,270, 1,210, 1,194, 1,178, 992, 815.

1-(4-Iodophenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 196–197 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.52 (d, J = 6.9 Hz, 2H), 7.98 (d, J = 6.9 Hz, 2H), 9.03 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Hydroxy phenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 210–211 °C; ^{1}H NMR (500 MHz, DMSO-d_6, 298 K): δ (ppm) = 6.98 (d, J = 8.9 Hz, 2H), 7.68 (d, J = 8.9 Hz, 2H), 9.91 (s, 1H), 10.11 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Ethylphenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 77–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.33 (t, J = 7.6 Hz, 3H), 2.79 (q, J = 7.6 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 9.00 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Methylphenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 93–94 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 3.02 (s, 3H), 7.40 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 9.02 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Methoxyphenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 117–118 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 3.82 (s, 3H), 7.00 (d, J = 8.9 Hz, 2H), 7.58 (d, J = 8.9 Hz, 2H), 9.04 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Acetylphenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 174–175 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 2.61 (s, 3H), 7.89 (d, J = 8.9 Hz, 2H), 8.12 (d, J = 8.9 Hz, 2H), 9.37 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(4-Nitrophenyl)-1H-1,2,3,4-tetrazole

Yellow solid; mp: 191–193 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 8.06 (d, J = 8.9 Hz, 2H), 8.38 (d, J = 8.9 Hz, 2H), 9.64 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

1-(3-Nitrophenyl)-1H-1,2,3,4-tetrazole

White solid; mp: 108–110 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.78 (t, J = 8.2 Hz, 1H), 8.21 (d,

Table 1 Optimization of the reaction conditions for synthesis of 1-(4-chlorophenyl)-1*H*-1,2,3,4-tetrazole (1 mmol) using [P_4-VP]N_3/$CH(OEt)_3$/AcOH

Entry	[P_4-VP]N_3 (mmol)	$CH(OEt)_3$ (mmol)	Reaction time (min)	Reaction temp. (°C)	Isolated yield (%)
1	3.4	3	10	100	98
2	2.5	3	10	100	98
3	2	3	30	100	98
4	2.5	2	60	100	51
5	2.5	2.5	10	100	98
6	2.5	2.5	60	r.t	0
7	2.5	2.5	60	65	50
8	2.5	2.5	60	75	78

Table 2 Synthesis of 1-Aryl 1 *H*-1,2,3,4-tetrazoles using $ArNH_2$/[P_4-VP] N_3/$CH(OEt)_3$ in glacial acetic acid at 100 °C

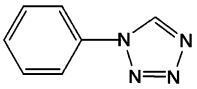
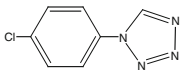
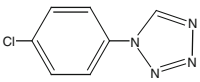
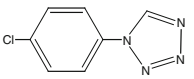
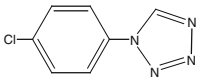
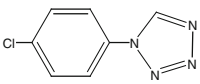
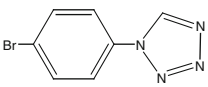
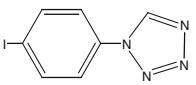
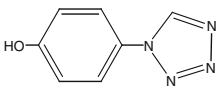
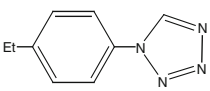
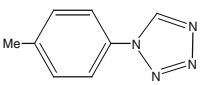
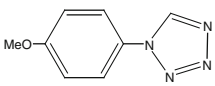
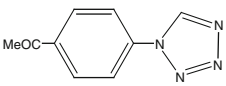
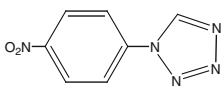
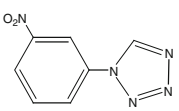
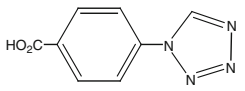
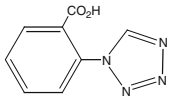
Entry	Substrate ($ArNH_2$)	Product	Time (min)	Yield (%)[a]	m.p. (°C)	Ref.
1	$C_6H_5NH_2$		25	90	63–65	35, 36, 37, 39, 45
2[b]	4-$ClC_6H_4NH_2$		10	98	160–162	35, 36, 37, 39, 45
	4-$ClC_6H_4NH_2$		10	98	160–162	35, 36, 37, 39, 45
3[b] 4[b]	4-$ClC_6H_4NH_2$		10	95	160–162	35, 36, 37, 39, 45
5[b]	4-$ClC_6H_4NH_2$		10	92	160–162	35, 36, 37, 39, 45
6[b]	4-$ClC_6H_4NH_2$		10	92	160–162	35, 36, 7, 39, 45
7	4-$BrC_6H_4NH_2$		15	98	180–181	37
8	4-$IC_6H_4NH_2$		15	97	196–197	–
9	4-$OHC_6H_4NH_2$		5	96	210–211	–
10	4-$EtC_6H_4NH_2$		25	95	77–78	–
11	4-$MeC_6H_4NH_2$		20	95	93–94	35, 36, 37, 39, 45
12	4-$OMeC_6H_4NH_2$		15	98	117–118	35, 36
13	4-$MeCOC_6H_4NH_2$		10	97	174–175	36
14	4-$NO_2C_6H_4NH_2$		10	98	191–193	37
15	3-$NO_2C_6H_4NH_2$		15	95	108–110	45

Table 2 continued

Entry	Substrate ($ArNH_2$)	Product	Time (min)	Yield (%)[a]	m.p. (°C)	Ref.
16	4-$CO_2HC_6H_4NH_2$		10	98	196–197	–
17	2-$CO_2HC_6H_4NH_2$		15	92	194–195	–

[a] Isolated yields based on amines

[b] The entries 3-6 refer to the use of the $[P_4\text{-VP}]N_3$ that is recycled first, second, third, and fourth time, respectively, under identical conditions

$J = 8.1$ Hz, 1H), 8.30 (d, $J = 8.1$, 1H), 8.72 (s, 1H), 9.67 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

4-(1H-1,2,3,4-Tetrazol-1-yl)benzoic acid

White solid; mp: 196–197 °C; ^{1}H NMR (500 MHz, DMSO-d_6, 298 K): δ (ppm) = 8.08 (d, $J = 8.6$ Hz, 2H), 8.19 (d, $J = 8.6$ Hz, 2H), 10.21 (s, 1H), 13.34 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2,211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

2-(1H-1,2,3,4-Tetrazol-1-yl)benzoic acid

White solid; mp: 194–195 °C; ^{1}H NMR (500 MHz, DMSO-d_6, 298 K): δ (ppm) = 7.72 (d, $J = 7.8$ Hz, 1H), 7.79 (t, $J = 7.6$ Hz, 1H), 7.86 (t, $J = 7.4$, 1H), 8.10 (d, $J = 7.8$, 1H), 9.83 (s, 1H), 13.69 (s, 1H); FT-IR: ν_{max} (cm^{-1}) = 3,105, 2211, 1,500, 1,461, 1,385, 1,205, 1,174, 1,085, 1,040, 995, 822.

Regeneration of [P4-VP]N3

The spent cream-colored polymer (1 g) was added to a 40 mL of a 3 mol L^{-1} aqueous solution of sodium azide and was stirred slowly for 24 h. The mixture was filtered and washed with distilled water (3 × 8 mL) and dried under vacuum in the presence of P_2O_5 at 40 °C overnight. The capacity of the regenerated polymer was determined, and it was found that it had the same capacity as the original form (3.4 mmol of azide ion per gram of polymer). The regenerated polymer was reused several times, without losing its activity and the results are given in Table 2, entries 3–6 (shown later).

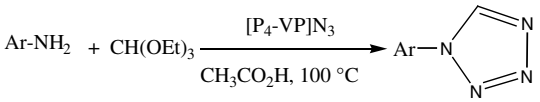
Results and discussion

Cross-linked poly (4-vinylpyridine) supported azide ion, $[P_4\text{-VP}]N_3$, was easily prepared according to our previously reported procedure [29] and used as an efficient procedure for synthesis of 1-substituted 1-*H* tetrazoles using $[P_4\text{-VP}]N_3/ArNH_2/CH(OEt)_3$ in glacial acetic acid. It is important to note that this polymeric reagent is stable and can be stored for long time (months), without losing its activity and can be readily used in condensation reaction with primary aromatic amines and triethyl orthoformate in glacial acetic acid for synthesis of different 1-substituted 1-*H* tetrazoles. We disclose a less hazardous and practical synthesis of 1-aryl 1-*H* tetrazoles from their corresponding aryl amines using a stable and nonexplosive polymeric reagent, $[P_4\text{-VP}]N_3$. A good range of available primary aromatic amines were also subjected to synthesis of 1-aryl 1-*H* tetrazoles under heterogeneous conditions (Scheme 1).

To increase the yield of tetrazole compounds, optimization of the reaction conditions was accomplished. 4-Chloroaniline (1 mmol) was chosen as a model substrate and was treated with different molar ratio of $[P_4\text{-VP}]N_3/CH(OEt)_3$, and the results are given in Table 1. It was observed that the 2.5/2.5 molar ratio of $[P_4\text{-VP}]N_3/CH(OEt)_3$ at 100 °C were the best conditions to achieve the highest yield of the product. With increasing the temperature and also with increasing the amounts of $[P_4\text{-VP}]N_3$ and $CH(OEt)_3$ result in bouts of higher yields and lower reaction times (Table 1).

We then applied these conditions for synthesis of various 1-aryl- 1-*H* tetrazoles and the results are given in Table 2. Various aromatic amines, with electron withdrawing groups as well as electron donating groups, were transformed into 1-aryl-1 *H* tetrazoles in high to excellent yields (90–98 %, Table 2).

It was observed that under similar conditions, a wide range of anilines containing electron withdrawing groups as well as electron donating groups such as Cl, Br, I, OH, CH_3CO, CO_2H OMe, Et, Me, and NO_2 easily underwent condensation with triethyl orthoformate and azide ion



Scheme 1 Preparation of 1-substituted 1 *H*-1,2,3,4-tetrazoles

Table 3 Comparison of different methods for synthesis of 1-substituted-1*H*-1,2,3,4-tetrazoles

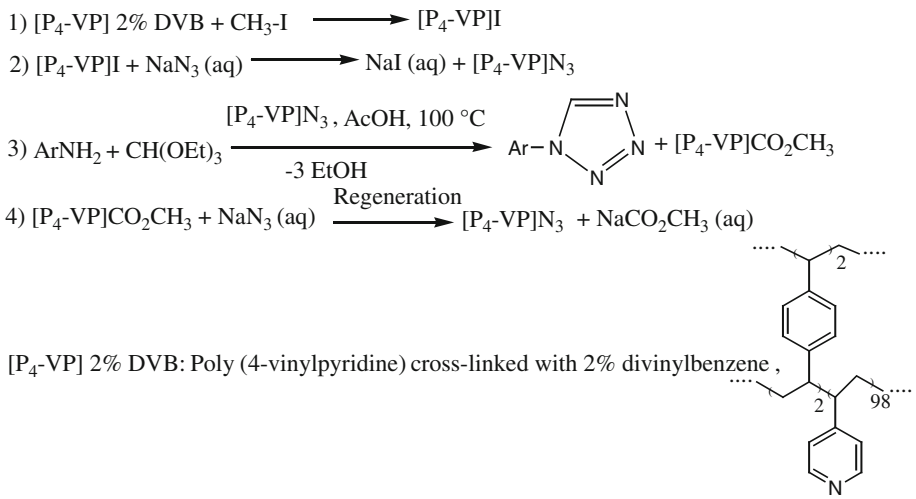
Entry	Reagents and reaction conditions	Time	Isolated yield (%)	Ref. (%)
1	$RNH_2/[P_4\text{-}VP]N_3/CH(OEt)_3$, AcOH, 100 °C	10–25 min	90–98	a
2	$RNH_2/NaN_3/CH(OEt)_3$, IL/DMSO, 30 °C	1–1.5 h	85–91	35
3	$RNH_2/NaN_3/CH(OEt)_3$, $[Hbim]BF_4$[b], 100 °C	15–35 min	85–91	36
4	$RNH_2/NaN_3/CH(OEt)_3$, SSA, 120 °C, solvent-free	2.5–8 h	88–96	37
5	$RNH_2/NaN_3/CH(OEt)_3$,Natrolite zeolite, 120 °C	4 h	80–94	38
6	$RNH_2/NaN_3/CH(OEt)_3$, $Yb(OTf)_3$, 100 °C	6–9 h	71–91	39
7	$RNH_2/NaN_3/CH(OMe)_3$, $In(OTf)_3$	1.5–3.5 h	70–90	45

IL/DMSO ionic liquids/dimethyl sulfoxide, *SSA* silica sulfuric acid

[a] Present method (Table 2)

[b] $[Hbim]BF_4$: 1-*n*-butylimidazolium tetrafluoroborate

Scheme 2 Preparation stages of $[P_4\text{-}VP]N_3$ and the plausible reaction pathway of tetrazole synthesis and regeneration of the polymeric reagent



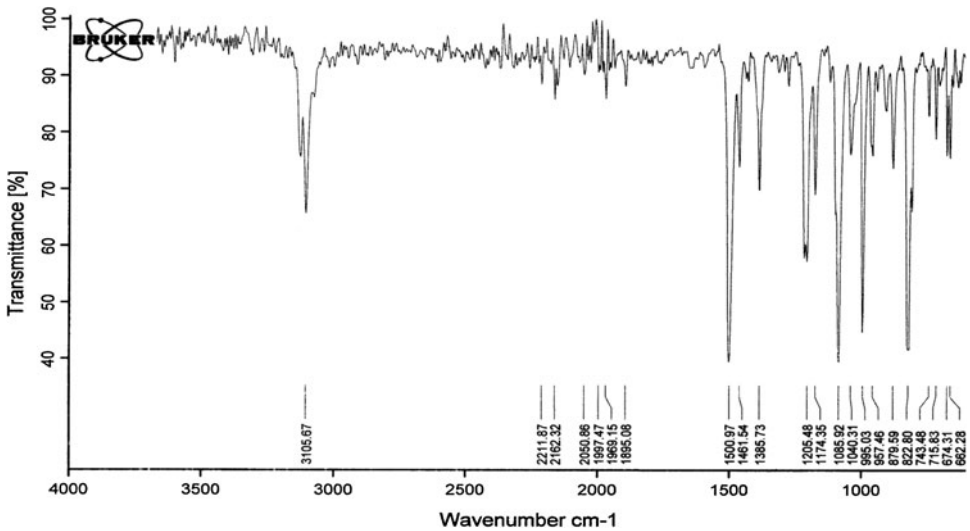


Fig. 1 The FT-IR of 1-(4-chlorophenyl)-1*H*-1,2,3,4-tetrazole

(supported on polymer) to give 1-substituted-1*H*-1,2,3,4-tetrazoles in very short reaction times (10–25 min) with excellent isolated yields (90–98 %, Table 2).

This polymeric reagent is used in single step reaction; its main advantage over non-polymeric reagents is its insolubility in the reaction medium and consequently, its easier work-up by a simple filtration. The reactions can be driven to completion using excess amounts of reagent without the fear of separation of the excess of reagent from the products. On the other hand, one of the most disadvantages of the polymeric reagents is their expensive, but in this case, appropriate chemistry is available (Scheme 2, step 4) and

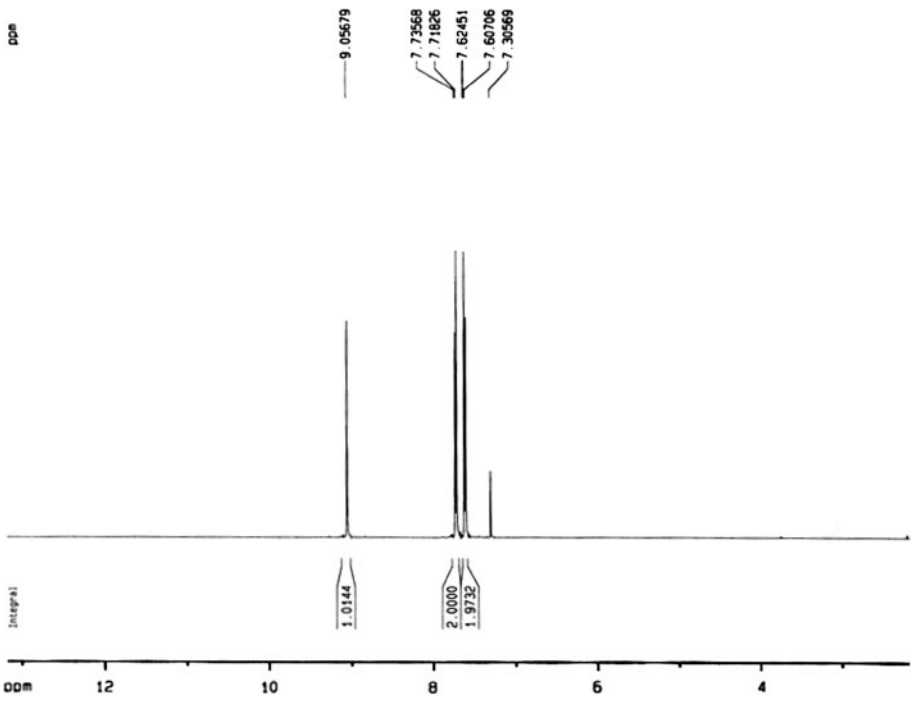


Fig. 2 The ^{1}H NMR of 1-(4-chlorophenyl)-1*H*-1,2,3,4-tetrazole

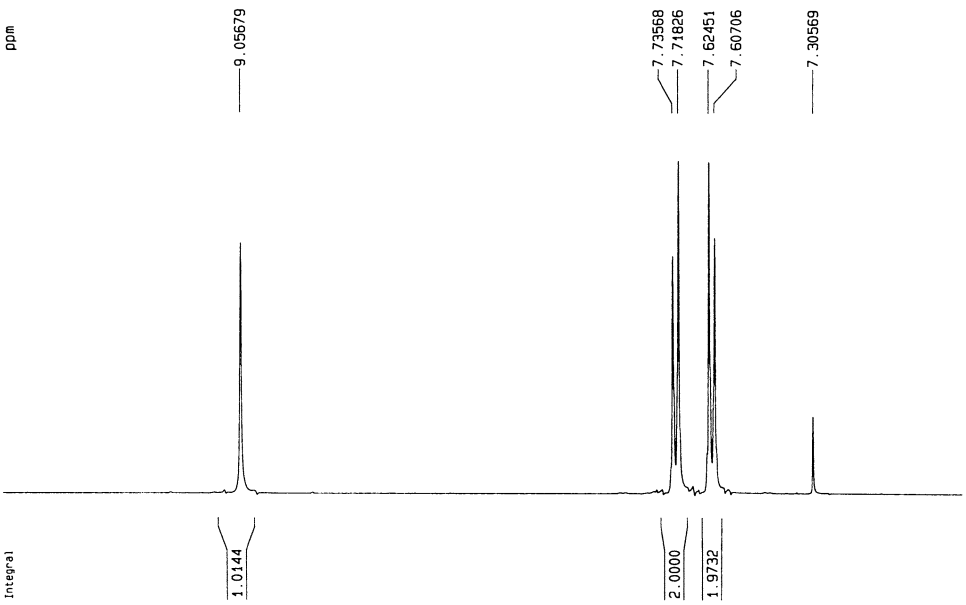


Fig. 3 The expanded ^{1}H NMR of 1-(4-chlorophenyl)-1*H*-1,2,3,4-tetrazole

the spent polymeric reagents can in principle be recycled many times (Table 2, entries 3–6). In Scheme 2, preparation stages of $[P_4\text{-VP}]N_3$, the plausible reaction pathway of tetrazole synthesis, and regeneration of the polymeric reagent are shown.

We have also successfully applied this new method on a rather large scale. For example, up to 15 mmol of 4-chloroaniline (Table 2, Entry 2) could be converted into 1-(4-chlorophenyl)- 1*H*- 1,2,3,4-tetrazole without any loss of efficiency.

The methods reported so far for the synthesis of 1-substituted tetrazoles required highly polar solvents such as 2-methoxyethanol, DMF, or methanol and very harsh reaction conditions such as refluxing for 6–24 h followed by very tedious work-up procedures involving distillation of high boiling solvents under reduced pressure. Compared to the reported methods, our method is convenient, fast, safe, and easy to work-up. In Table 3, the present method is compared with other reported methods [35–39]. As Table 3 reveals in this procedure, the reaction times are shorter than previously reported methods and the isolated yields are higher. This can probably be attributed to the local concentration of azide ion species inside the pores.

1-Substituted 1H-tetrazole products were characterized by FT-IR and ^{1}H-NMR spectroscopy, and physical properties were compared with the literature values. For example, the FT-IR and ^{1}H NMR spectra of 1-(4-chlorophenyl)-1*H*-1,2,3,4-tetrazole are shown in Figs. 1, 2, and 3, respectively. On the other hand, in Fig. 4, the FT-IR spectra of [P_4-VP] 2 % DVB, [P_4-VP]I, [P_4-VP]N_3 and regenerated polymer were compared (a, b, c, and d, respectively). The pyridine pendent groups of the polymer chain of [P_4-VP] 2 % DVB exhibit strong C=C stretching at 1,554 cm^{-1} and C=N stretching at 1,414 cm^{-1} (a). When [P_4-VP] 2 % DVB was treated with methyl iodide and the pyridine, rings of the polymer chains were quaternized; this peaks were shifted to 1,634 and 1,460 cm^{-1} (b). Also when [P_4-VP]I was converted to [P_4-VP]N_3 by an ion exchange reaction with NaN_3 (aq.), these peaks were also shifted to 1,638 and 1,463 cm^{-1} and the appearance of a new peak at 2,005 cm^{-1} indicates that the N_3^{-1} ion was supported on the polymer. This interaction increases the stiffness of the associated ring and consequently, more energy is required to deform the aromatic cycle, reflected in a higher wave number value. Figure 4 reveals that the FT-IR spectra of [P_4-VP]N_3 (c) and regenerated polymer (d) are similar.

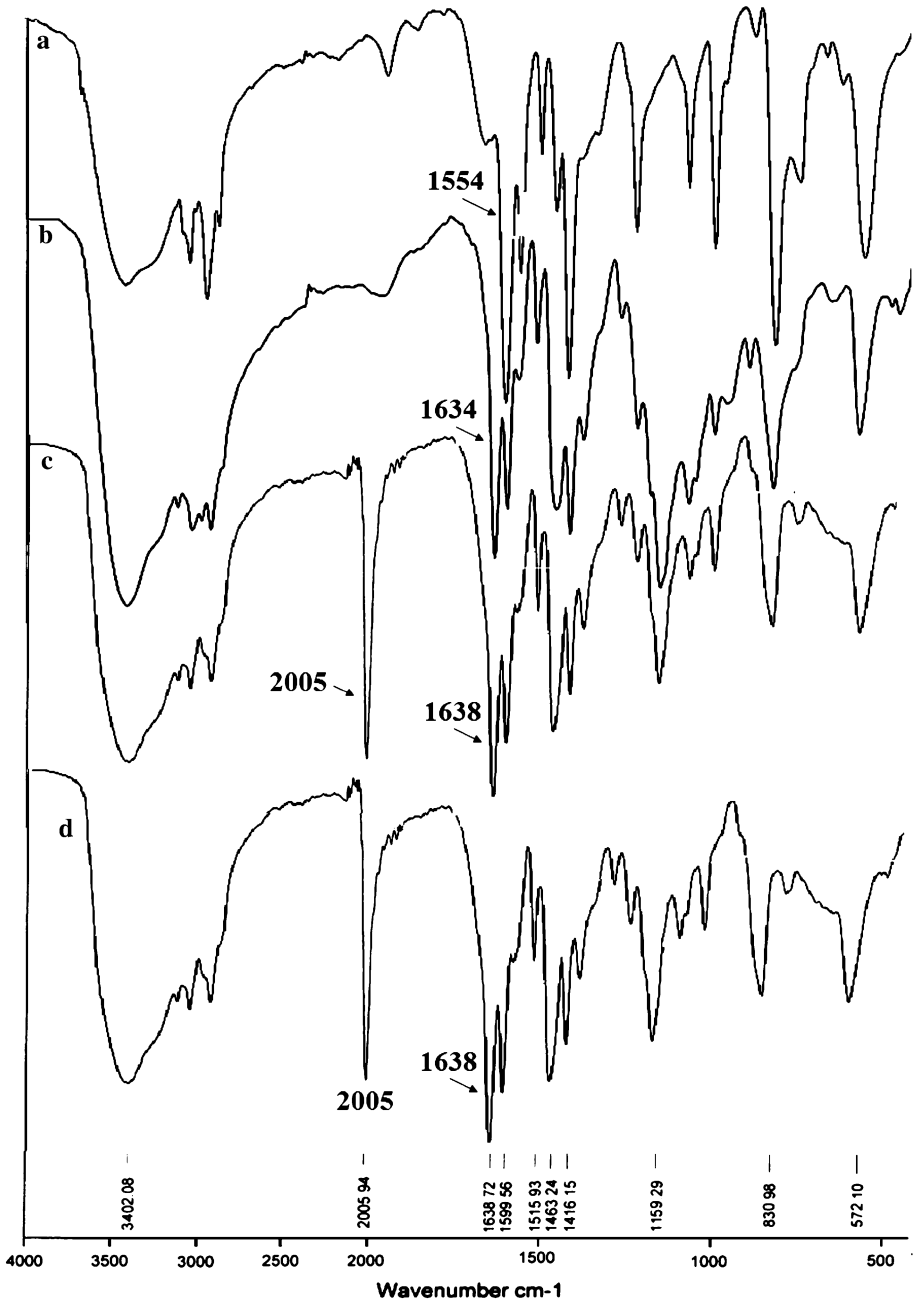


Fig. 4 The FT-IR spectra of [P_4-VP] 2 % DVB (**a**), [P_4-VP]I (**b**), [P_4-VP]N_3 (**c**), and regenerated polymer (**d**)

The advantages of this method over conventional classical methods are separation of the supports from the reaction mixture by simple filtration, low reaction time, and excess of a polymeric reagent can be readily used without incurring complication in work-up. In addition, there is current research and general interest in heterogeneous systems because these systems have importance in industry and in developing technologies [46].

Conclusions

In conclusion, we have developed a mild, convenient, and efficient method for the synthesis of 1-aryl-1H-1,2,3,4-tetrazoles via condensation reaction of azide ion, primary aromatic amines, and triethyl orthoformate in glacial acetic acid under heterogeneous conditions in excellent yields. The present method has the advantages of operational simplicity, mild reaction conditions, ready availability, fast reaction rates, and simple reaction work-up. The spent polymeric reagents can be recovered by simple filtration and after regeneration with sodium azide, reused several times without significant loss of their activity. The product can also be obtained by simple filtration and evaporation of the solvent.

References

1. R.B. Merrifield, J. Am. Chem. Soc. **85**, 2149 (1963)
2. A. Akelah, D.C. Sherrington, Polymer **24**, 1369 (1983)
3. D.C. Sherrington, P. Hodge, Synthesis and separations using functional polymers, Ch. 4. (Wiley, New York, 1988). pp. 149–179
4. S.V. Ley, I.R. Baxendale, R.N. Bream, P.S. Jackson, A.G. Leach, D.A. Longbottom, M. Nesi, J.S. Scott, R.I. Storer, S.J. Taylor, J. Chem. Soc. Perkin Trans **1**, 3815 (2000)
5. M.A. Karimi Zarchi, A. Zarei, J. Chin. Chem. Soc. **52**, 309 (2005)
6. M.A. Karimi Zarchi, J. Noei, J. Appl. Polym. Sci. **104**, 1064 (2007)
7. M.A. Karimi Zarchi, J. Noei, J. Appl. Polym. Sci. **114**, 2134 (2009)
8. M.A. Karimi Zarchi, M. Karimi, J. Appl. Polym. Sci. **120**, 538 (2011)
9. M.A. Karimi Zarchi, M. Karimi, J. Appl. Polym. Sci. **120**, 2762 (2012)
10. M.A. Karimi Zarchi, F. Rahmani, J. Appl. Polym. Sci. **120**, 2830 (2012)
11. M.A. Karimi Zarchi, F. Rahmani, J. Appl. Polym. Sci. **121**, 582 (2011)
12. M.A. Karimi Zarchi, N. Ebrahimi, J. Appl. Polym. Sci. **121**, 2621 (2011)
13. M.A. Karimi Zarchi, N. Ebrahimi, J. Appl. Polym. Sci. **124**, 2807 (2012)
14. M.A. Karimi Zarchi, N. Ebrahimi, Iran. Polym. J. **21**, 591 (2012)
15. M.A. Karimi Zarchi, N. Ebrahimi, J. Appl. Polym. Sci. **125**, 2163 (2012)
16. M.A. Karimi Zarchi, N. Ebrahimi, Phosphorous Sulfur **187**, 1226 (2012)
17. L. Myznikov, A. Hrabalek, G. Koldobskii, Chem. Heterocycl Com. **43**, 1 (2007)
18. E.A. Popova, R.E. Trifonov, V.A. Ostrovskii, Arkivoc **1**, 45 (2012)
19. H. Zhao, Z.R. Qu, H.Y. Ye, R.G. Xiong, Chem. Soc. Rev. **37**, 84 (2008)
20. O.E. Alawode, C. Robinson, S. Rayat, J. Org. Chem. **76**, 216 (2011)
21. R.J. Nachman, G.M. Coast, K. Kaczmarek, H.J. Williams, J. Zabrocki, Biopolymers **75**, 412 (2004)
22. A. Hammerl, M.A. Hiskey, G. Holl, T.M. Klapoetke, K. Polborn, J. Stierstorfer, J.J. Weigand, Chem. Mater. **17**, 3784 (2005)
23. A. Hammerl, G. Holl, T.M. Klapötke, P. Mayer, H. Nöth, H. Piotrowski, M. Warchhold, Eur. J. Inorg. Chem. **2002**, 834 (2002)
24. F.R. Benson, The Chemistry of the tetrazoles. Chem. Rev. **41**, 1 (1947)
25. G.I. Koldobskii, V.A. Ostrovskii, V.S. Popavskii, Chem. Heterocycl. Compd. **17**, 965 (1981)
26. A.R. Katritzky, B.V. Rogovoy, K.V. Kovalelko, J. Org. Chem. **68**, 4941 (2003)
27. D. Habibi, M. Nasrollahzadeh, Synth. Commun. **40**, 3159 (2010)
28. M. Nasrollahzadeh, Y. Bayat, D. Habibi, S. Moshaee, Tetrahedron Lett. **50**, 4435 (2009)
29. M.A. Karimi Zarchi, F. Nazem, J. Appl. Polym. Sci. **123**, 1977 (2012)
30. D.M. Zimmerman, R.A. Olofason, Tetrahedron Lett. **10**, 5081 (1969)
31. F.G. Fallon, R.M. Herbst, J. Org. Chem. **22**, 933 (1957)
32. T. Jin, S. Kamijo, Y. Yamamoto, Tetrahedron Lett. **45**, 9435 (2004)
33. Y. Satoh, N. Marcopulos, Tetrahedron Lett. **36**, 1759 (1995)
34. A.K. Gupta, C.H. Song, C.H. Oh, Tetrahedron Lett. **45**, 4113 (2004)
35. S.N. Dighe, K.S. Jain, K.V. Srinivasan, Tetrahedron Lett. **50**, 6139 (2009)
36. T.M. Potewar, S.A. Siddiqui, R.J. Lahoti, K.V. Srinivasan, Tetrahedron Lett. **48**, 1721 (2007)
37. D. Habibi, H. Nabavi, M. Nasrollahzadeh, J. Chem. **2013**, 4 (2012). Article ID 645313
38. D. Habibi, H. Nabavi, M. Nasrollahzadeh, A.T. Kamali, Green Chem. **13**, 3499 (2011)
39. W.K. Su, Z. Hong, W.G. Shan, X.X. Zhang, Eur. J. Org. Chem. **2006**, 2723 (2006)
40. A. Hassner, M. Stern, Angew. Chem. Int. Ed. Engl. **25**, 478 (1986)
41. M.A. Karimi Zarchi, Z. Escandari, J. Appl. Polym. Sci. **121**, 1916 (2011)
42. M.A. Karimi Zarchi, R. Nabaei, S. Barani, J. Appl. Polym. Sci. **123**, 788–795 (2012)
43. M.A. Karimi Zarchi, R. Nabaei, J. Appl. Polym. Sci. **124**, 2362 (2012)
44. M.A. Karimi Zarchi, S. Barani Chin. J. Polym. Sci. **31**, 1002 (2013)
45. D. Kundu, A. Majee, A. Hajra, Tetrahedron Lett. **50**, 2668 (2009)
46. N.J. Turro, Tetrahedron **43**, 1589 (1987)