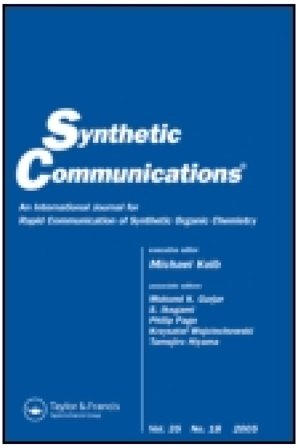

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Facile Synthesis of Benzotriazole Derivatives Using Nanoparticles of Organosilane-Based Nitrite Ionic Liquid Immobilized on Silica and Two Room-Temperature Nitrite Ionic Liquids

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FACILE SYNTHESIS OF BENZOTRIAZOLE DERIVATIVES USING NANOPARTICLES OF ORGANOSILANE-BASED NITRITE IONIC LIQUID IMMOBILIZED ON SILICA AND TWO ROOM-TEMPERATURE NITRITE IONIC LIQUIDS

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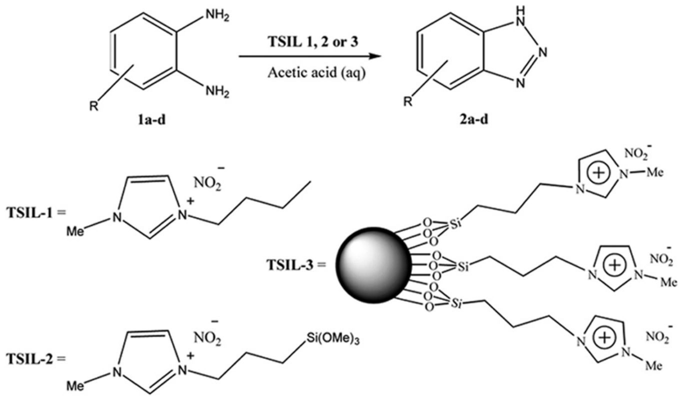
GRAPHICAL ABSTRACT



Abstract *Nanoparticles of organosilane-based nitrite ionic liquid immobilized on silica, 1-butyl-3-methylimidazolium nitrite, and 1-(3-trimethoxysilylpropyl)-3-methylimidazolium nitrite were used as effective reagents for the preparation of benzotriazole derivatives from 1,2-diaminobenzenes at room temperature under mild solvent-free conditions. These ionic liquids play as nitrosonium sources in this procedure.1,2-Diaminobenzene derivatives have been treated with ionic liquids to give the related diaminobenzenes in very good to excellent yields in short reaction times.*

Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications® *for the full experimental and spectral details.*

Keywords Benzotriazole; nanoparticles; nitrite ionic liquid; task-specific ionic liquid

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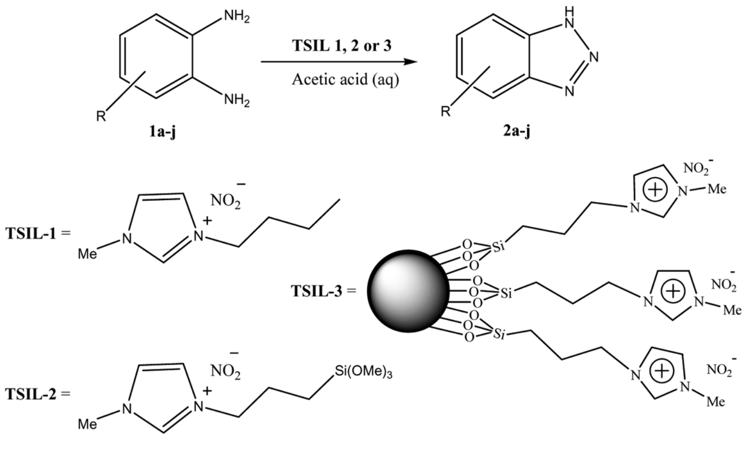
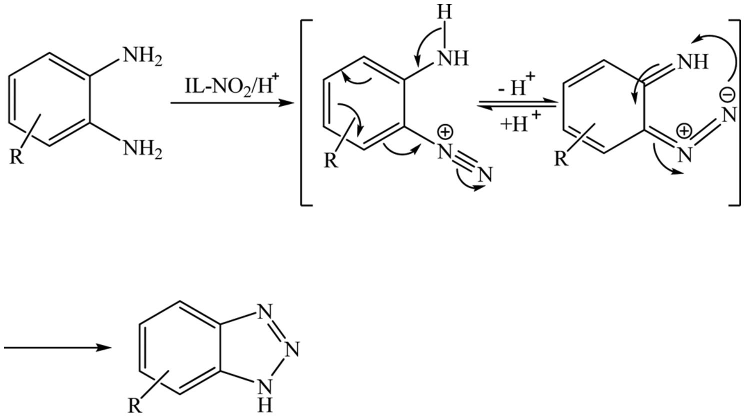
INTRODUCTION

Heterocyclic compounds containing nitrogen atoms are some of the most effective antimicrobial drugs used for cancer therapy.[1,2] Benzotriazole and 1,2,4-benzotriazole derivatives are an interesting class of heterocycles[3] and have become the most rapidly expanding group of antifungal compounds because of the advantage of low toxicity, high oral bioavailability, and broad-spectrum activity.[4–6] Moreover, several benzotriazoles inhibit the growth of some microorganisms, and some benzotriazole derivatives show anti-inflammatory properties.[7] The diazotization of 1,2-diaminobenzenes in an acidic solution is the major route to synthesis of benzotriazoles. There are some reports on synthesis of benzotriazoles from 1,2-diaminobenzene as the main precursor in the literature.[8,9] In addition, Wan et al. reported that some benzotriazole derivatives exhibiting antibacterial activity.[10] Ionic liquids have attracted chemists' interest because of their physical and chemical properties.[11,12] Many of these compounds, known as task-specific ionic liquids (TSILs), are able to play multiple roles as catalyst and/or reagent and solvent. TSILs contain functional groups that are covalently bonded to cation or anion in these compounds. TSILs have been increasingly used in synthetic organic chemistry.[13–17] Wang et al. reported the synthesis of *N*-(α-alkoxyalkyl) benzotriazoles using acidic ionic liquid as catalyst at room temperature.[18] Shi and coworkers synthesized a variety of substituted benzotriazolesvia the [3 + 2] annulation click reaction of benzynes and azides.[19] The biological significances of these classes of heterocycles and important features of ionic liquids for the synthesis of organic compounds impelled us to synthesize benzotriazole derivatives using TSILs. Herein, we report our preliminary results on the synthesis of benzotriazoles **2a–j** using task-specific nitrite ionic liquids. Three ionic liquids (1-butyl-3-methylimidazolium nitrite, 1-(3-trimethoxysilylpropyl)-3-methylimidazolium nitrite, and nanoparticles of organosilane-based nitrite ionic liquid immobilized on silica) were used in this procedure (Scheme 1).



Scheme 1. Synthesis of benzotriazoles using TSILs.

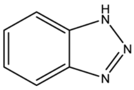
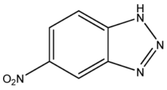
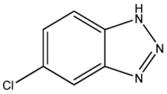
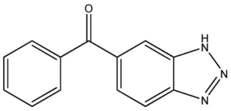
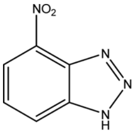
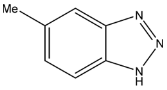
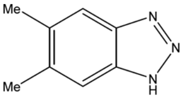
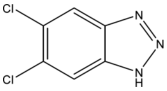
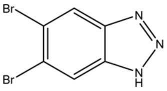
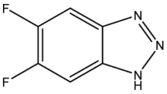


Scheme 2. Proposed mechanism for synthesis of benzotriazolesfrom 1,2-diaminobenzene using TSILs as nitrosonium sources.

RESULTS AND DISCUSSION

We started our investigation using equimolar amounts of 1,2-diaminobenzene, 1-butyl-3-methylimidazolium nitrite, **IL-1**, and AcOH at 0–5 °C without using any solvent. Benzotriazole **2a** was synthesized in 42% yield. The reaction was examined in several protic and aprotic solvents such as EtOH, MeOH, dimethylformaide (DMF), dimethylsulfoxide (DMSO), $CHCl_3$, and CH_3CN at different temperatures. The best result was achieved in protic solvents at 0–70 °C. Other acids such as hydrochloric acid and p-toluenesulfonic acid produced the product in a moderate yield. The best result was obtained when the reaction was carried out in the presence of 25 mol% acetic acid. In the absence of acid, no formation of the desired product was observed. Acetic acid (25 mol%) was required as the optimum amount of catalyst and increasing the amount of catalyst did not improve the yields but decreasing the amount of catalyst decreased the yield. The reaction was also carried out in AcOH/H_2O at 0–70 °C. Good yield (77%) of product was achieved under this condition, and the best ratio of aromaticdiamine and **IL-1** was found to be 1:1.3. These conditions were chosen as optimum for this reaction. To demonstrate the generality, we next tested different aromatic diamine precursors under these optimized reaction conditions, and the results are summarized in Table 1. As can be seen, the reaction shows good compatibility with different aromatic diamine precursors. All of these substrates gave clean reactions under mild conditions. However, aromatic diamines containing electron-withdrawing groups afforded related benzotriazoles in greater yields in shorter reaction times. Very recently we reported two TSILs as nitrosonium sources for the nitrosation and diazotization reactions.[13,14,20] We examined these TSILs as a nitrosonium sources in the described reaction and compared the results (Table 1). We examined the effectiveness of these ionic liquids as nitrosonium sources in this procedure under optimized conditions. The results showed that the synthesis of 1,2,3-benzotriazoles in the presence of nanoparticles of organosilane-based nitrite ionic liquid immobilized on silica was occurred in greater yields and in shorter reaction times in comparison with other examined TSILs. The proposed mechanism is shown in Scheme 2.

Table 1. Synthesis ofbenzotriazoles using TSILs

			M.P (°C)		Time (min)			Yield[a] (%)		
Entry	Product	Product number	Found	Reported [Ref.]	IL-1	IL-2	IL-3	IL-1	IL-2	IL-3
1		**2a**	95–96	96–97 [21]	35	30	29	77	80	85
2		**2b**	207–208	209 [22]	35	35	24	83	81	88
3		**2c**	156–157	157–159 [22]	35	30	25	81	83	86
4		**2d**	129–130	132–133 [23]	32	30	28	83	83	87
5		**2e**	228–230	228–229 [25]	33	35	30	81	78	88
6		**2f**	136–138	136–138 [23]	33	35	32	75	75	80
7		**2 g**	156–158	156–157 [26]	30	30	30	73	74	78
8		**2 h**	263–265	264–266 [27]	30	30	30	82	80	85
9		**2i**	246–248	248–250 [28]	35	35	30	80	78	86
10		**2j**	182–184	183–184 [29]	35	35	30	87	80	89

[a] Isolated yield.

CONCLUSIONS

In conclusion, it was found that immobilized nitrite ionic liquid and two room-temperature task-specific nitrite ionic liquids are convenient reagents for the synthesis of 1,2,3-benzotriazoles under solvent-free conditions. These ionic liquids are efficient nitrisonium sources. Our methodology offers several advantages including mild reaction conditions, cleaner reaction, good yields of products, and a simple experimental and isolated procedure, which make it a useful and attractive process for the synthesis of benzotriazoles.

EXPERIMENTAL

All reagents were purchased from Merck Company and used without further purification. Infrared (IR) spectra were recorded in KBr and were determined on a Perkin Elmer FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance AC 400-MHz instrument using dimethylsulfoxide (DMSO-d$_6$) or $CDCl_3$ as the deuterated solvents and tetramethylsilane (TMS) as internal standard. All melting points measured in open glass capillaries using a Stuart melting a point apparatus.

General Procedure

Aromatic diamine (50 mmol) and freshly prepared 1-butyl-3-methylimidazolium nitrite,[14] 1-(3-trimethoxysilylpropyl)-3-methylimidazolium nitrite,[20] or nanoparticles of organosilane-based nitrite ionic liquid immobilized on silica[24] (65 mmol) were added to water (5 mL) and mixed thoroughly at 0–5 °C. Then glacial acetic acid (25 mol%) was added to the mixture continuously and the temperature rose rapidly to 70–80 °C. The mixture was stirred at this temperature for a time as shown in Table 1. In the case of using IL-1 and IL-2 the precipated products were filtered and washed three times with cold water to afford the crude benzotriazole derivative. In the case of IL-3, after filtration of the mixture, the remained solid was washed with chloroform or acetone and then the organic solvent was evaporated. The crude products were recrystallized with charcoal from ethanol or ethyl acetate–hexane.

1H-Benzo[d][1,2,3]triazole (2a)

Mp 95–96 °C, 96–97 °C[21]; FT-IR (KBr, cm^{-1}): 1208 (N=N), 1575 (C=C), 1624 (C=C), 3083 (=C-H), 3146 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.50 (d, $J = 6.75$ Hz, 2H), 7.98 (d, $J = 6.75$ Hz, 2H), 13.92 (s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 113.3, 127.0, 139.8 (6C, Ph).

5-Nitro-1H-benzo[d][1,2,3]triazole (2b)

Mp 207–208 °C, 209 °C[22]; FT-IR (KBr, cm^{-1}): 1219 (N=N), 1354 (N=O), 1490 (N=O), 1521 (C=C), 1624 (C=C), 3093 (=C-H), 3577 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.38 (dd, $^3J = 8.21$ Hz and $^4J = 1.86$ Hz, 1H), 8.12 (d, $J = 8.21$ Hz, 1H), 8.38 (d, $J = 1.86$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 123.65, 123.80, 126.8, 127.1, 133.0, 146.5.

5-Chloro-1H-benzo[d][1,2,3]triazole (2c)

Mp 156–157 °C, 157–159 °C[22]; FT-IR (KBr, cm^{-1}): 1204 (N=N), 1558 (C=C), 1626 (C=C), 3039 (=C-H), 3448 (N-H); ^{1}H NMR (400 MHz, DMSO-d^6) δ (ppm): 7.47 (dd, ${}^3J = 8.8$ Hz and ${}^4J = 1.6$ Hz, 1H), 7.99 (d, $J = 8.8$ Hz, 1H), 8.06 (s, 1H);^{13}C NMR (100 MHz, DMSO-d^6) δ (ppm): 115.2, 117.0, 126.1, 130.3, 138.3, 139.4.

5-Benzoyl-1H-benzo[d][1,2,3]triazole (2d)

Mp 129–130 °C, 132–133 °C[23]; FT-IR (KBr, cm^{-1}): 1205 (N=N), 1608 (C=C), 1629 (C=C), 1662 (C=O), 3127 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29–8.45 (m, 8H, Ar), 12.64 (s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 116.8, 128.7 (2C, Ar), 129.5, 130.0 (3C, Ar), 132.7, 139.7 (2C, Ar), 145.6 (2C, Ar), 195.1 (C=O).

4-Nitro-1H-benzo[d][1,2,3]triazole (2e)

Mp 228–230 °C, 228–229 °C[25]; FT-IR (KBr, cm^{-1}): 1210 (N=N), 1348 (N=O), 1524 (N=O), 1630 (C=C), 3025 (=C-H), 3172 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.72 (t, $J = 8.21$ Hz, 1H), 8.38 (dd, ${}^3J = 8.20$ Hz and ${}^4J = 1.84$ Hz, 1H), 8.48 (dd, ${}^3J = 8.23$ Hz and ${}^4J = 1.84$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 122.61, 122.86, 127.0, 127.1, 131.5, 147.5.

5-Methyl-1H-benzo[d][1,2,3]triazole (2f)

Mp 136–138 °C, 136–138 °C[23]; FT-IR (KBr, cm^{-1}): 1201 (N=N), 1626 (C=C), 3083 (=C-H), 3188 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.35 (s, 3H), 7.31 (dd, ${}^3J = 8.19$ Hz and ${}^4J = 1.79$ Hz, 1H), 8.09 (d, $J = 8.19$ Hz, 1H), 8.38 (d, $J = 1.79$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 22.43, 120.15, 122.8, 125.8, 128.1, 135.0, 146.5.

5,6-Dimethyl-1H-benzo[d][1,2,3]triazole (2g)

Mp 156–158 °C, 156–157 °C[26]; FT-IR (KBr, cm^{-1}): 1215 (N=N), 1615 (C=C), 2905 (aliphatic C-H), 3089 (=C-H), 3193 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.33 (s, 3H), 2.36 (s, 3H), 7.35 (s, 1H), 7.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 22.54, 23.89, 121.25, 124.8, 126.1, 128.8, 137.5, 145.4.

5,6-Dichloro-1H-benzo[d][1,2,3]triazole (2h)

Mp 263–265 °C, 264–266 °C[27]; FT-IR (KBr, cm^{-1}): 1212 (N=N), 1625 (C=C), 3079 (=C-H), 3184 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.68 (s, 1H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 123.2, 126.6, 127.7, 130.8, 137.9, 146.5.

5,6-Dibromo-1H-benzo[d][1,2,3]triazole (2i)

Mp 246–248 °C, 246–250 °C[28]; FT-IR (KBr, cm^{-1}): 1211 (N=N), 1640 (C=C), 3065 (=C-H), 3181 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.65 (s, 1H), 7.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 122.2, 125.6, 126.7, 130.6, 136.8, 146.1.

5,6-Diflouro-1H-benzo[d][1,2,3]triazole (2j)

Mp 182–184 °C, 183–184 °C[29]; FT-IR (KBr, cm^{-1}): 1216 (N=N), 1618 (C=C), 3071 (=C-H), 3184 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.81 (s, 1H), 7.87 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 126.2, 127.6, 128.1, 131.6, 139.0, 147.9.

SUPPORTING INFORMATION

Melting points, FT-IR, and ^{1}H and ^{13}C NMR spectra are available online.

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