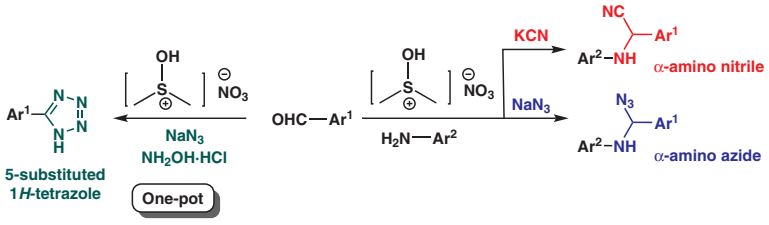
Synlett M. A. Nasseri et al. Letter

A Facile Approach to Catalyst-Free Cyanation and Azidation of Organic Compounds and a One-Pot Preparation of 5-Substituted 1*H*-Tetrazoles by Using a Dimethyl Sulfoxide–Nitric Acid Combination

Mohammad Ali Nasseri[a]
Seyyedeh Ameneh Alavi[a]
Boshra Mahmoudi[b]
Milad Kazemnejadi[*a]

[a] Department of Chemistry, Faculty of Science, University of Birjand, P. O. Box 97175-615, Birjand, Iran
miladkazemnejadi@birjand.ac.ir
[b] Research Center, Sulaimani Polytechnic University, Sulaimani 46001, Kurdistan Region, Iraq



Received: 06.09.2019
Accepted after revision: 23.10.2019
Published online: 31.10.2019
DOI: 10.1055/s-0039-1690742; Art ID: st-2019-d0469-l

Abstract In this study, cyanations or azidations of imines were performed by using hydroxy(dimethyl)-λ⁴-sulfanecarbonitrile or azido(dimethyl)-λ⁴-sulfanol, respectively, prepared in situ by treatment of potassium cyanide or sodium azide with a dimethyl sulfoxide–nitric acid combination. Furthermore, a one-pot preparation of 5-substituted 1*H*-tetrazole derivatives was carried out by using this reagent combination in the presence of an aldehyde, hydroxylamine hydrochloride, and sodium azide under mild conditions.

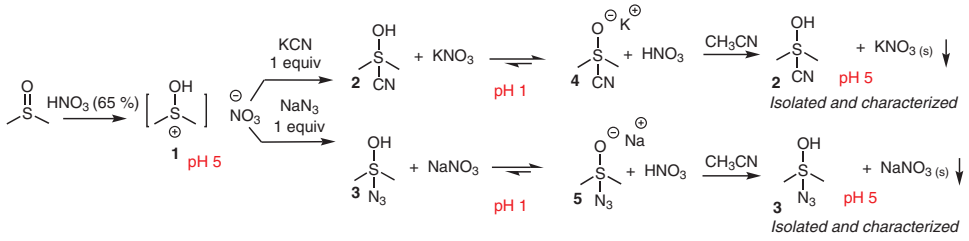
Key words dimethyl sulfoxide, nitric acid, Strecker reaction, amino nitriles, amino azides, tetrazoles

Nucleophilic addition of a cyanide or azide anion to an imine leads to the formation of an α-amino nitrile or an α-amino azide, respectively; these are two important and useful structural classes in organic synthesis. α-Amino nitriles have a wide range of applications and can be classified as cyclic or conventional α-amino nitriles.[1] They are useful precursors for the preparation of biologically active α-amino acids, heterocycles, and natural products, due to the efficient transformation of the nitrile functional group into an amide, amine, carboxylic acid, or carbonyl group.[2] The α-amino nitrile moiety is found in scaffolds of various biologically active molecules and natural compounds, such as cyanocycline (isolated from the culture broth of *Streptomyces flavogriseus*) and saframycin A (isolated from the culture broth of *S. lavendulae*), which have antitumor and antibiotic activities; phthalascidin 650, a synthetic analogue of ecteinascidin 743 (extracted from marine tunicate *Ecteinascidia turbinata*); and girgensohnine, a cyanogenic piperidine, found in *Girgensohnia oppositiflora*.[3]

The Strecker reaction provides an efficient approach to the synthesis of α-amino nitriles; this multicomponent reaction involves the treatment of an aldehyde or ketone with an amine and an alkali-metal cyanide. The reaction proceeds by nucleophilic addition of the cyanide ion onto an imine, and is catalyzed by a range of Lewis acids or bases.[4–6] Over the past decade, various homogeneous and heterogeneous catalytic systems have been developed for use with a variety of cyanide sources;[1a] these include sulfated tungstate,[7] aluminoborate molecular sieves,[1b,c] chitosan,[2a] xanthan sulfuric acid,[2b] neodymium metal–organic frameworks,[8] titanium cluster,[9a] a cobalt complex,[9b] alumina-supported tungstosilicic acid,[10] a bifunctional Lewis acid–Lewis base,[11] a biphasic solvent system,[12] lithium tetrafluoroborate,[3a] MCM-41,[3b] and $CuFe_2O_4$/chitosan.[3c] Recently, Baghery et al. reported Fe_3O_4@SiO_2@urea and Fe_3O_4@SiO_2@urethane catalysts for one-pot Strecker synthesis of α-amino nitriles.[3d]

Organic azides are also useful intermediates for the synthesis of imines (through rearrangement), N-heterocycles (triazoles and tetrazoles), or amines (through reduction). Nucleophilic substitutions of alcohols,[13] alkyl halides,[14], or imines[15] by azide provide simple and straightforward approaches to alkyl azides. C–H bond azidation, C–C bond azidation,[16] and oxyazidation and diazidation of styrenes[17] are other approaches that have been used. The use of phase-transfer catalysis with modified clays,[18] poly(4-vinylpyridine)-supported sodium azide,[14] or an acidic ionic liquid[13] have also been reported. Sharma and Hartwig[16b] and Zhu and co-workers[16a] independently developed facile C–H bond azidations with Fe or Mn salts. However, impediments such as the insolubility of inorganic azides in organic solvents, the use of expensive or unstable catalysts, and contamination arising from the use of a phase-transfer catalyst limits the general application of some of these methods.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany



Scheme 1

5-Substituted 1*H*-tetrazoles are among the most useful N-heterocyclic compounds, possessing various biological properties such as antihypertensive, antiinflammatory, antibiotic, antiallergenic, antifungal,[19] anticonvulsant, and anti-HIV activities.[20b] Furthermore, tetrazole derivatives have a wide range of applications in agriculture, photography,[21] and industry[22] and in coordination chemistry as strong ligands.[23] In materials science, they have a role in the production of explosives and propellants.[24]

A direct route for the preparation of 5-substituted 1*H*-tetrazoles, initially developed by Hantzsch and Vagt, involves a [3+2] cycloaddition of azide ion onto nitriles.[25] However, this method can suffer from complex workup procedures, high reaction temperatures, and the use of toxic solvents. Thus, efforts continue to be made to find alternative methods. Among recent developments have been the use of Pd-SMTU@boehmite (SMTU = *S*-methylisothiourea),[26] $Ni(OH)_2$ nanoparticles,[27] choline azide,[28] MCM-41@AMPD@Zn (AMPD = 2-amino-2-methylpropane-1,3-diol),[29] and Sm@*l*-MSN (*l*-MSN = large-pore mesoporous silica nanoparticles),[30] or Cu-MOF nanocatalysts.[31] De Luca et al. used a DMF–2,4,6-trichloro-1,3,5-triazine complex for the efficient transformation of oximes into nitriles under mild conditions.[32]

We have developed a straightforward, metal-free, reproducible, and reliable method for the efficient preparation of α-amino nitriles and α-amino azides by using hydroxy(dimethyl)-λ⁴-sulfanecarbonitrile or azido(dimethyl)-λ⁴-sulfanol, respectively, formed by treatment of a DMSO–HNO_3 mixture with KCN or with NaN_3. In addition, a one-pot preparation of 5-substituted 1*H*-tetrazoles from aldehydes can be carried out by using azidodimethyl-λ⁴-sulfanol.

The reaction of DMSO with HNO_3 gives the adduct **1**, with a melting point of about 40 °C.[33] By adding a salt such as potassium cyanide or sodium azide, the intermediate cyanosulfhydrin **2** and azidosulfhydrin **3** are produced, respectively, in equilibrium with the cyanosulfoxide **4** or the azidosulfoxide **5** (Scheme 1). However, at the pH of the mixture, the equilibrium is very much in favor of the former pair of products. To prove this, the equilibrium was shifted toward the latter pair of products by adding CH_3CN to precipitate potassium or sodium nitrate from the mixture.

To isolate and characterize compounds **2** and **3**, in two separate experiments, DMSO–HNO_3 intermediate **1** was treated with KCN or NaN_3. The resultant mixture was then poured into cold CH_3CN to precipitate KNO_3 or $NaNO_3$, which was subsequently removed by filtration. The solvent was removed and the crude product **2** or **3** was isolated, and immediately subjected to FTIR and ^1H NMR analysis. However, the FTIR and ^1H NMR results suggested that structures **6** (X = CN, N_3) (Figure 1) might also be possible for compounds **2** and **3**, respectively. It worth noting that the bond-dissociation energy for the S–N bond is relatively low (D°_{298} = 467 ± 24 kJ·mol^{-1}), which supports the possibility of structures **6**.

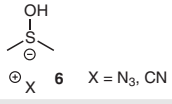
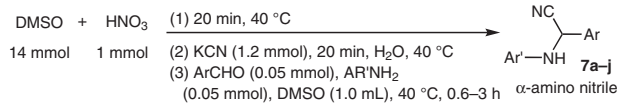


Figure 1

The optimization of the DMSO–HNO_3 ratio and the temperature was investigated by using the reaction of benzaldehyde, aniline, KCN, and DMSO–HNO_3 as a model reaction. Initially, we examined the effects of the ratio of DMSO to nitric acid and we found that the best choice was a 14:1 molar ratio. Increasing the amount of HNO_3 reduced the yield, presumably due to a lower pH. Changing the amount of DMSO had no significant effect (see Supporting Information; Table S1). Carrying out the reaction at 40 °C afforded the highest yield, whereas higher temperatures (80 °C or reflux conditions; Table S1, entries 4–6) did not improve the yield. Consequently, subsequent investigations were performed at 40 °C in the presence of DMSO–HNO_3 in a 14:1 molar ratio.

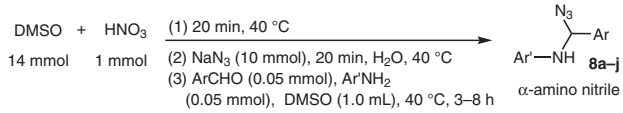
Compound **2** was then used in the preparation of a series of α-amino nitriles (Table 1), and compound **3** was used to prepare α-amino azides (Table 2). High to excellent yields were achieved for all substrates in short reaction times. Aromatic aldehydes bearing electron-donating or electron-withdrawing groups reacted equally effectively.

Table 1 One-Pot Preparation of α-Amino Nitriles by Using DMSO–HNO_3 in the Presence of KCN[34]



Entry	Ar^1	Ar^2	Time (h)	Product	Yield (%)
1	Ph	Ph	1	**7a**	90
2	4-$MeOC_6H_4$	Ph	0.6	**7b**	94
3	4-$O_2NC_6H_4$	Ph	1.5	**7c**	92
4	cinnamyl	Ph	2	**7d**	76
5	cinnamyl	Bn	2.5	**7e**	70
6	Cy	Ph	3	**7f**	84
7	Cy	Bn	3	**7g**	80
8	3-pyridyl	Ph	1.5	**7h**	94
9	2-ClC_6H_4	Bn	1	**7i**	95
10	4-ClC_6H_4	Bn	1.5	**7j**	95

Table 2 One-Pot Preparation of α-Amino Azides by Using a Mixture of DMSO and HNO_3 in the Presence of NaN_3[34]

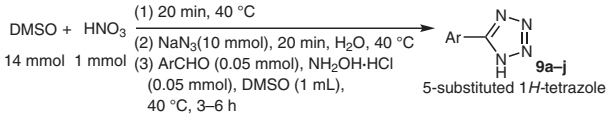


Entry	Ar^1	Ar^2	Time (h)	Product	Yield (%)
1	Ph	Ph	5	**8a**	91
2	4-$MeOC_6H_4$	Ph	4	**8b**	96
3	4-$O_2NC_6H_4$	Ph	5	**8c**	92
4	cinnamyl	Ph	6	**8d**	75
5	cinnamyl	Bn	7	**8e**	70
6	Cy	Ph	8	**8f**	85
7	Cy	Bn	8	**8g**	80
8	3-pyridyl	Ph	4	**8h**	94
9	2-ClC_6H_4	Bn	3.5	**8i**	96
10	4-ClC_6H_4	Bn	3	**8j**	94

One prominent advantage of the present method was the one-pot preparation of 5-substituted 1*H*-tetrazole derivatives by using aldehydes as starting materials rather than nitriles. Efficient transformation of aldehydes was observed in the presence of DMSO–HNO_3, $NH_2OH{\cdot}HCl$, and NaN_3, and high to excellent yields of the corresponding tetrazoles **9a–j** were obtained for all aldehydes (Table 3).

The method is limited to compounds that are not acid sensitive; no product was obtained for compounds such as furfural. However, it is worth noting that cinnamaldehyde

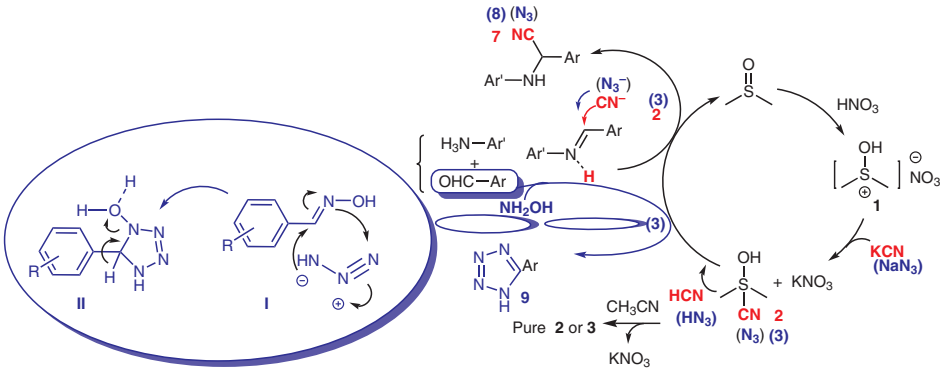
Table 3 One-Pot Preparation of 5-Substituted 1*H*-Tetrazoles by Using a Mixture of DMSO and HNO_3 in the Presence of $NH_2OH{\cdot}HCl$ and NaN_3[35]



Entry	Ar	Time (h)	Product	Yield (%)
1	Ph	4.5	**9a**	94
2	4-$MeOC_6H_4$	4	**9b**	97
3	4-$O_2NC_6H_4$	3	**9c**	95
4	4-MeC_6H_4	5	**9d**	79
5	3-$O_2NC_6H_4$	3.5	**9e**	95
6	2-naphthyl	6	**9f**	85
7	4-ClC_6H_4	3	**9g**	95
8	2-chloropyridin-4-yl	3	**9h**	95
9	4-HOC_6H_4	4	**9i**	89
10	4-$H_2NC_6H_4$	3.5	**9j**	92

afforded moderate-to-satisfactory yields of compounds **7d**, **7e**, **8d**, **8e**, and **9d**.

Based on our observations and in accordance with reports in the literature,[1a,3a,13] a plausible mechanism can be proposed for the one-pot preparation of α-amino nitriles, α-amino azides, and 5-substituted 1*H*-tetrazoles using hydroxy(dimethyl)-λ^4-sulfanecarbonitrile and azido(dimethyl)-λ^4-sulfanol (Scheme 2). First, the interaction of DMSO with HNO_3 provides intermediate **1**.[33] Cyanide or azide ion then adds to **1** to gives intermediate **2** or **3**, respectively. In the next step, α-amino nitrile **7** or azide **8** is formed in the presence of HCN or HN_3 generated from intermediate **2** or **3**, respectively. DMSO is also regenerated to reenter the next cycle. Scheme 2 also shows a proposed mechanism for the preparation of the tetrazole. An oxime formed by the reaction of the aldehyde with $NH_2OH{\cdot}HCl$ under the acidic conditions might undergo a [3+2] cycloaddition with hydrazoic acid to form intermediate **II**. Finally, the tetrazole is formed by elimination of water from intermediate **II**. To support this mechanism, intermediates **2** and **3** were isolated and characterized. Furthermore, two control experiments were conducted to gain more insight into the proposed mechanism. The reaction of aniline and benzaldehyde with KCN (or NaN_3) and the reaction of benzaldehyde, $NH_2OH{\cdot}HCl$, and sodium azide were conducted in DMSO alone at 40 °C for one hour (for the preparation of **7a**) or for five hours (for the preparation of **8a** and **9a**). No **7a** was detectable in the first experiment, and only traces of **8a** or **9a** were observed in the second control experiment. These results confirm the vital role of HNO_3 and the importance of intermediates **2** and **3**.



Scheme 2 Proposed mechanism for one-pot preparation of α-amino nitrile, α-amino azides, and 5-substituted 1*H*-tetrazoles by using hydroxy(dimethyl)-λ^4-sulfanecarbonitrile (**2**) or azido(dimethyl)-λ^4-sulfanol (**3**)

Further evidence for the proposed mechanism was obtained from the evolution of the pH of the reaction mixture with time. The pH of the reaction mixture of benzaldehyde, aniline, and KCN in the presence of DMSO– HNO_3 was monitored every ten minutes. It would be expected, based on the proposed mechanism, that HNO_3 would be consumed during the reaction, along with the production of intermediate **1**, followed by **2** or **3**. The observed results were completely in agreement with this expectation and the proposed mechanism, as the pH increased linearly with time (Supporting Information; Figure S1), reaching a pH of 6.0 at the end of the reaction.

In summary, we have developed a convenient and mild protocol for efficient cyanation or azidation with short reaction times by using a DMSO–HNO_3 combination in the presence of a cyanide or azide salt. Moreover, a one-pot preparation of 5-substituted 1*H*-tetrazoles was accomplished by using this reagent combination in the presence of an aldehyde and NH_2OH·HCl. These processes constitute reliable and attractive methods for cyanation and azidation and for the one-pot preparation of 5-substituted 1*H*-tetrazoles.

Funding Information

The authors gratefully acknowledge the financial support of this work by the Research Council of the University of Birjand.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690742.

References and Notes

(1) (a) Kazemnejadi, M.; Sardarian, A. R. *RSC Adv.* **2016**, *6*, 91999. (b) Wang, W.; Wang, Y.; Wu, B.; Cong, R.; Gao, W.; Qin, B.; Yang, T. *Catal. Commun.* **2015**, *58*, 174. (c) Yang, T.; Bartoszewicz, A.; Ju, J.; Sun, J.; Liu, Z.; Zou, X.; Wang, Y.; Li, G.; Liao, F.; Martín-Matute, B.; Lin, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 12555.
(2) (a) Dekamin, M. G.; Azimoshan, M.; Ramezani, L. *Green Chem.* **2013**, *15*, 811. (b) Shaabani, A.; Maleki, A.; Soudi, M. R.; Mofakham, H. *Catal. Commun.* **2009**, *10*, 945.
(3) (a) Desai, U. V.; Mitragotri, S. D.; Thopate, T. S.; Pore, D. M.; Wadgaonkar, P. P. *Monatsh. Chem.* **2007**, *138*, 759. (b) Eslami, M.; Dekamin, M. G.; Motlagh, L.; Maleki, A. *Green Chem. Lett. Rev.* **2018**, *11*, 36. (c) Maleki, A.; Haji, R. F.; Ghassemi, M.; Ghafuri, H. *J. Chem. Sci.* **2017**, *129*, 457. (d) Baghery, S.; Zolfigol, M. A.; Schirhagl, R.; Hasani, M.; Stuart, M. C.; Nagl, A. *Appl. Organomet. Chem.* **2017**, *31*, e3883.
(4) Takahashi, E.; Fujisawa, H.; Yanai, T.; Mukaiyama, T. *Chem. Lett.* **2005**, *34*, 318.
(5) Yadav, J. S.; Reddy, B. S.; Eeshwaraiah, B.; Srinivas, M. *Tetrahedron* **2004**, *60*, 1767.
(6) (a) Khalafi-Nezhad, A.; Foroughi, H. O.; Panahi, F. *Heteroat. Chem.* **2013**, *24*, 1. (b) Kantam, M. L.; Mahendar, K.; Sreedhar, B.; Choudary, B. M. *Tetrahedron* **2008**, *64*, 3351.
(7) Pathare, S. P.; Akamanchi, K. G. *Tetrahedron Lett.* **2012**, *53*, 871.
(8) Liu, Y.; Mo, K.; Cui, Y. *Inorg. Chem.* **2013**, *52*, 10286.
(9) (a) Seayad, A. M.; Ramalingam, B.; Chai, C. L.; Li, C.; Garland, M. V.; Yoshinaga, K. *Chem. Eur. J.* **2012**, *18*, 5693. (b) Rajabi, F.; Nourian, S.; Ghiassian, S.; Balu, A. M.; Saidi, M. R.; Serrano-Ruiz, J. C.; Luque, R. *Green Chem.* **2011**, *13*, 3282.
(10) Rafiee, E.; Rashidzadeh, S.; Joshaghani, M.; Chalabeh, H.; Afza, K. *Synth. Commun.* **2008**, *38*, 2741.
(11) Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. A. *Angew. Chem. Int. Ed.* **2000**, *39*, 1650.
(12) Gualtierotti, J. B.; Schumacher, X.; Wang, Q.; Zhu, J. *Synthesis* **2013**, *45*, 1380.
(13) Hajipour, A. R.; Rajaei, A.; Ruoho, A. E. *Tetrahedron Lett.* **2009**, *50*, 708.
(14) Zarchi, M. A. K.; Escandari, Z. *J. Appl. Polym. Sci.* **2011**, *4*, 1916.
(15) Bosmani, A.; Pujari, S. A.; Besnard, C.; Guénée, L.; Poblador-Bahamonde, A. I.; Lacour, J. *Chem. Eur. J.* **2017**, *23*, 8678.
(16) (a) Ren, R.; Zhao, H.; Huan, L.; Zhu, C. *Angew. Chem. Int. Ed.* **2015**, *54*, 12692. (b) Sharma, A.; Hartwig, J. F. *Nature* **2015**, *517*, 600.

(17) Lu, M.-Z.; Wang, C.-Q.; Loh, T.-P. *Org. Lett.* **2015**, *17*, 6110.
(18) Varma, R. S.; Naicker, K. P.; Kumar, D. *J. Mol. Catal. A: Chem.* **1999**, *149*, 153.
(19) Varadaraji, D.; Suban, S. S.; Ramasamy, V. R.; Kubendiran, K.; Raguraman, J. S. K.; Nalilu, S. K.; Pati, H. N. *Org. Commun.* **2010**, *3*, 45.
(20) (a) Malik, M. A.; Al-Thabaiti, S. A.; Malik, M. A. *Int. J. Mol. Sci.* **2012**, *13*, 10880. (b) May, B. C.; Abell, A. D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 172.
(21) Kantam, M. L.; Kumar, K. S.; Raja, K. P. *J. Mol. Catal. A: Chem.* **2006**, *247*, 186.
(22) Lang, L.; Zhou, H.; Xue, M.; Wang, X.; Xu, Z. *Mater. Lett.* **2013**, *106*, 443.
(23) Frija, L. M. T.; Ismael, A.; Santos Cristiano, M. L. *Molecules* **2010**, *15*, 3757.
(24) Fischer, D.; Klapötke, T. M.; Stierstorfer, J. *Angew. Chem. Int. Ed.* **2015**, *54*, 10299.
(25) Hantzsch, V. A.; Vagt, A. *Justus Liebigs Ann. Chem.* **1901**, *314*, 339.
(26) Moradi, P.; Ghorbani-Choghamarani, A. *Appl. Organomet. Chem.* **2017**, *31*, e3602.
(27) Halder, M.; Islam, M. M.; Singh, P.; Singh Roy, A.; Islam, S. M.; Sen, K. *ACS Omega* **2018**, *3*, 8169.
(28) Mehraban, J. A.; Azizi, K.; Jalali, M. S.; Heydari, A. *ChemistrySelect* **2018**, *3*, 116.
(29) Molaei, S.; Tamoradi, T.; Ghadermazi, M.; Ghorbani-Choghamarani, A. *Microporous Mesoporous Mater.* **2018**, *272*, 241.
(30) Samanta, P. K.; Biswas, R.; Das, T.; Nandi, M.; Adhikary, B.; Richards, R. M.; Biswas, P. *J. Porous Mater.* **2019**, *26*, 145.
(31) Salahshournia, B.; Hamadi, H.; Nobakht, V. *Appl. Organomet. Chem.* **2018**, *32*, e4416.
(32) De Luca, L.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272.
(33) Goheen, D.; Bennett, C. *J. Org. Chem.* **1961**, *26*, 1331.
(34) **Phenyl(phenylamino)acetonitrile (7a) and N-[Azido(phenyl)methyl]aniline (8a); Typical Procedure**
CAUTION: Due to the formation of HN_3 during the preparation of α-amino azides, the reactions should be performed in a well-ventilated fume hood and behind a blast shield. Cyanides present a serious risk of poisoning by inhalation, skin contact, or swallowing. A 14:1 mixture of DMSO and HNO_3 (5 mL) was stirred for 20 min at 40 °C. Then, KCN or NaN_3 (1 mmol), PhCHO (1 mmol), $PhNH_2$, (1 mmol), and H_2O (2 mL) were simultaneously added to the mixture. Upon completion of reaction (TLC), the mixture was neutralized with 01. M aq NaOH and extracted with CH_2Cl_2 (2 × 20 mL). The solvent was removed, and the crude product was purified by chromatography.
7a White solid; yield: 9.3 mg (90%); mp 74–76 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.07 (br s, 1 H, N–H), 5.48 (s, 1 H, C–H), 6.77–6.80 (m, 2 H, Ar–H), 6.92 (t, J = 7.50 Hz, 1 H, Ar–H), 7.22–7.28 (m, 2 H, Ar–H), 7.46 (d, J = 7.50 Hz, 3 H, Ar–H), 7.55–7.59 (m, 2 H, Ar–H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 50.1, 114.1, 118.1, 120.2, 127.3, 129.3, 129.5, 133.9, 144.7. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 80.67; H, 5.71; N, 13.47.
8a White solid; yield: 10.2 mg (91%); mp 82 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.03 (d, J = 5.00 Hz, 1 H, N–H), 5.44 (d, J = 5.00 Hz, 1 H, C–H), 6.77–6.88 (m, 2 H, Ar–H), 6.92 (d, J = 7.00 Hz, 1 H, Ar–H), 7.25–7.27 (m, 2 H, Ar–H), 7.29 (d, J = 7.00 Hz, 3 H, Ar–H), 7.45–7.61 (m, 2 H, Ar–H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 62.3, 114.6, 120.5, 125.3, 129.2, 130.0, 131.0, 146.1, 146.6. MS: m/z = 224 [M^+]. Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.66; H, 5.33; N, 25.07.
(35) **5-Substituted 1H-Tetrazoles 9a–j; General Procedure**
CAUTION: Due to the formation of HN_3 during the preparation of 5-substituted 1H-tetrazoles, the reactions should be performed in a well-ventilated fume hood and behind a blast shield. A 14:1 mixture of DMSO and HNO_3 (5 mL) was stirred for 20 min at 40 °C. PhCHO (1.0 mmol), $NH_2OH{\cdot}HCl$ (1.2 mmol), and H_2O (2 mL) were added, the mixture was stirred for 20 min at 40 °C, and NaN_3 (1.2 mmol) was added. Upon completion of reaction (TLC), the mixture was neutralized with 0.1 M aq NaOH and extracted with CH_2Cl_2 (2 × 20 mL). The solvent was removed, and the crude product was purified by chromatography. 5-Phenyl-1H-tetrazole (**9a**) White solid; yield: 6.8 mg (94%); mp 214–215 °C (Lit.[7] 214–215 °C). ^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.38 (s, 1 H), 7.59–7.61 (m, 3 H), 8.02–8.06 (m, 2 H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 121.1, 126.8, 129.9, 141.2, 155.0. Anal. Calcd for $C_7H_6N_4$; C, 57.53; H, 4.14; N, 38.34. Found: C, 57.57; H, 4.34; N, 38.44.