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Application of Primary Allylamines from Morita–Baylis–Hillman Adducts: Cyanogen Azide Mediated Synthesis of Substituted 5-Aminotetrazoles and Their Attempted Transformation into Tetrazolo[1,5-*a*]pyrimidinones[‡]

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A general protocol for the synthesis of substituted 5-aminotetrazoles by treating cyanogen azide with primary allylamines afforded either by S_N2 or S_N2' reactions of Morita–Baylis–Hillman acetates of acrylate has been developed. The base-promoted intramolecular cyclizations of these tetrazoles afford highly substituted 2-azidopyrimidin-4(3*H*)-ones instead of the expected tetrazolopyrimidinone due to azide–tetrazole tautomerism. Nevertheless it has been discovered that substituted tetrazolo[1,5-*a*]pyrimidin-7(4*H*)-ones could be isolated in pure form from a methanolic solution of the respective 2-azidopyrimidin-4(3*H*)-ones through crystallization. The structure of tetrazolo[1,5-*a*]pyrimidin-7(4*H*)-one was unambiguously assigned by X-ray crystallography. The existence of azide–tetrazole tautomerism in this class of compounds has been supported through NMR spectroscopic studies.

Introduction

Tetrazoles are structural cores of many compounds with wide-ranging applications. In coordination chemistry[1] they serve as ligands, whereas in material chemistry they serve as structural elements of high energy-density materials.[2] Besides, the therapeutic potential of tetrazole derivatives is of major interest, as they serve as metabolically stable surrogates for carboxylic acids[3] and have shown to display antiallergic, antiasthmatic,[4] antiviral, antibiotic,[5] anti-inflammatory,[6] antineoplastic,[7] and cognition enhancing activities.[8] In our program focused at the construction of tetrazole-fused frameworks from intermediates derived from Morita–Baylis–Hillman chemistry (MBH),[9] we report herein the synthesis of substituted 5-aminotetrazoles from primary allylamines by using cyanogen azide and a base-promoted intramolecular cyclization leading to 2-azido-pyrimidin-4(3*H*)-ones instead of the expected tetrazolo[1,5-*a*]pyrimidin-5(4*H*)-ones. Nevertheless the azido derivatives display azide–tetrazole tautomerism in solution to furnish the corresponding tetrazolo[1,5-*a*]pyrimidin-7(4*H*)-ones, which were isolated by crystallization from methanol.

Owing to the propensity to deliver densely functionalized products amenable to a variety of manipulations, the MBH reaction has become very popular in synthetic organic chemistry.[10] The synthetic intermediates afforded from adducts provide a versatile platform for developing novel approaches to a variety of heterocyclic frameworks.[10b,11] One such derivative is the primary allylamine, which is an effective precursor to different azaheterocycles.[12] Although MBH-acetate, in principle, has the potential to afford two variants of primary allylamines as depicted in Figure 1, a general route to primary allylamines of only type II has been developed.[13] To the best of our knowledge, a general and practical method for synthesizing primary allylamines of type I is not know, and henceforth, their synthetic potential remains unexplored. Although Xu et al. reported the isolation of such amines as hydrochloride salts through deprotection of aza-MBH adducts prepared from *N*-dithiophosphoryl imine and activated alkenes, the scope of the methodology was not investigated.[14]

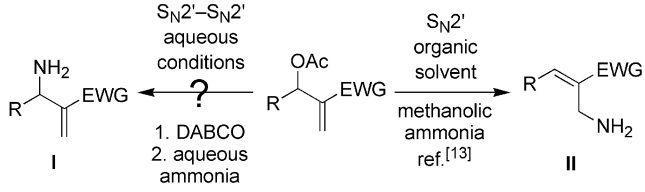

Figure 1. MBH acetate as viable precursors to primary allylamines (**I** and **II**).

It occurred to us that like any other S_N2'–S_N2' displacement reaction, treatment of the DABCO salt of MBH acetate with ammonia under aqueous conditions would furnish amine I. On the basis of literature precedence we envisaged

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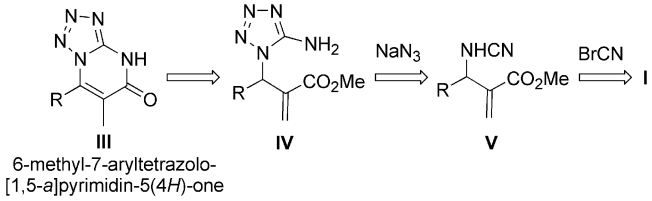
that treatment of this amine with cyanogen bromide will lead to cyanamide.[15] Reaction of cyanamide with sodium azide would result in the substituted 5-aminotetrazole, which may undergo concomitant intramolecular cyclization with the ester group to afford the annulated tetrazole. Our reasoning was supported by the retrosynthetic evaluation as presented in Scheme 1.

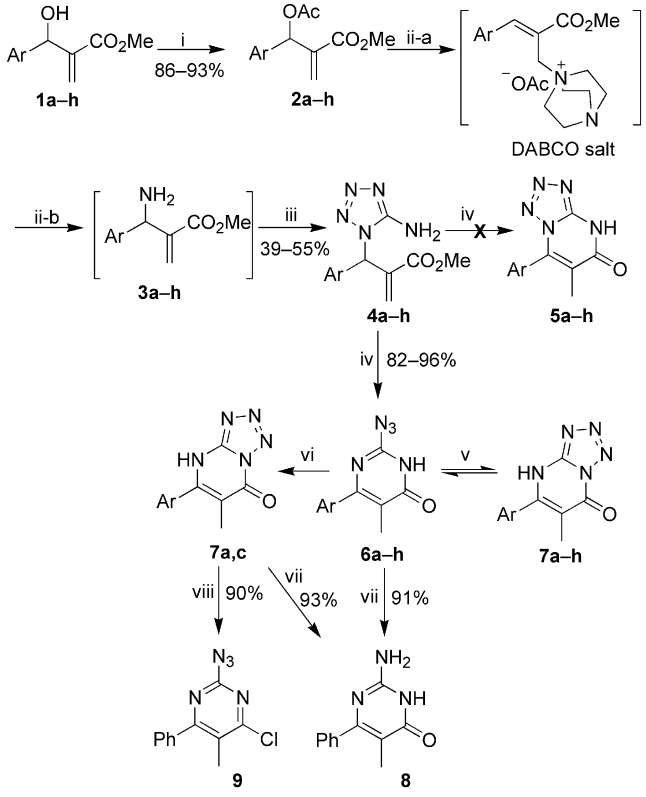


Scheme 1. Retrosynthetic scheme for the synthesis of annulated tetrazole from amine **I**.

Results and Discussion

The first objective of the present study was to develop a general synthesis for primary allylamine **I** from the DABCO salt of the MBH acetate of acrylate. Accordingly, we synthesized acetate **2a** from **1a** and utilized it as model substrate to optimize the synthesis of the amine. Treating **2a** with DABCO in THF/water at room temperature gave the DABCO salt, which was treated with aqueous ammonia under different conditions with respect to time and temperature. Notably, the aqueous medium essential for the formation of the DABCO salt influenced our decision to explore aqueous ammonia for introducing the amino functionality. It was pleasing to note that treatment of the DABCO salt of **2a** with aqueous ammonia (30%) for 30 min at 15 °C followed by workup with dichloromethane resulted in required amine **3a** (Scheme 2). Attempts to purify **3a** by column chromatography or even leaving it unattended at room temperature for a couple of hours, however, resulted in polymerization. As a consequence, freshly prepared **3a** was immediately treated with cyanogen bromide and $NaHCO_3$ in ethanol at a temperature below 10 °C for 1 h followed by addition of sodium azide. The reaction mixture was then acidified by the slow addition of dilute HCl (1:1) at 0 °C. The reaction was continued for 2 h at the same temperature and then heated at 90 °C for another 3 h, following a literature procedure.[14] Contrary to the reported method, the reaction in our hands was not clean, and TLC analysis displayed a mixture of several nonpolar spots. This led us to seek an alternate route for the synthesis of the 5-aminotetrazole from amine **3a**.

Recently, Shreeve and co-workers demonstrated that cyanogen azide is an excellent reagent for generating tetrazoles directly from hydrazines and primary and secondary amines at low temperature, though safety methods for handling this reagent are necessary for a successful outcome.[16] Nevertheless the low stability and short shelf life of **3a** prompted us to examine cyanogen azide for achieving the synthesis of the desired 5-aminotetrazole. An additional



Scheme 2. Reagents and conditions: (i) AcCl (1.5 equiv.), pyridine (1.3 equiv.), CH_2Cl_2, 0 °C to room temp., 2 h; (ii) a) DABCO (1.0 equiv.), THF/H_2O, room temp., 15 min; b) aq. NH_3 (30%), 10–20 °C, 30 min; (iii) N_3CN (2.0 equiv.), MeCN, 0–10 °C, 8 h; (iv) a) NaH (2.5 equiv., 60% in oil), THF, room temp., 15 min; b) aq. HCl (2 N, to pH 2); (v) equilibration in solution of MeOH, CD_3OD, [D_6]acetone, [D_5]pyridine, or [D_6]DMSO; (vi) crystallization from a solution of MeOH; (vii) Zn (3.0 equiv.), AcOH, 80 °C, 2 h; (viii) $POCl_3$, PCl_5 (catalytic), 110 °C, 1 h.

advantage of using this reagent was that no anhydrous conditions were required to perform the reaction. As a consequence, crude **3a** was treated with cyanogen azide in acetonitrile at low temperature, which in turn was freshly prepared by treating cyanogen bromide with sodium azide in dry acetonitrile at 0 °C. Workup and purification of the reaction mixture gave a product in 46% yield. On the basis of spectral analysis, this product was established to be 1-substituted 5-aminotetrazole **4a**. Perhaps the lower stability of **3a** could be one of the reasons for the low yield. Unexpectedly, no intramolecular cyclization was observed during this reaction.

With substituted the 5-aminotetrazole in hand, we then examined base-mediated intramolecular cyclization of **4a** to achieve the synthesis of tetrazolopyrimidinone. Accordingly, **4a** was treated with NaH in THF at room temperature for 15 min to furnish a product that could be isolated only after acidifying the reaction mixture to pH 2.0 with 2 N HCl. The isolated crude product upon triturating with diethyl ether furnished the pure product as a solid, which appeared as a black spot under UV light (254 nm) in TLC analysis. The IR spectrum of the product displayed peaks for the azide and amide groups, whereas the ^1H NMR spec-

trum recorded in [D_6]DMSO indicated the product to be a mixture of two compounds with similar proton disposition. There were two signals for methyl groups in the ^{1}H NMR spectrum at δ = 1.89 and 1.92 ppm in a ratio of 2:1, whereas in the ^{13}C NMR spectrum the corresponding peaks were observed at δ = 12.4 and 12.9 ppm. The origin of the methyl group in the product was attributed to the isomerization of the exocyclic double bond to the endocyclic position in the presence of base.[17] This result invoked us to perform TLC analysis with the recovered NMR sample, which revealed the presence of two spots. One of the spots corresponded to the initial black spot, whereas the second was observed to be a more polar fluorescent violet spot that had appeared after the solution was prepared. Thus, we considered TLC analysis of the product at different time intervals. It was observed that when spotted immediately after preparation of the solution, the product appears as a single black spot, but after a short interval, a new violet spot starts to appear. Essentially, to provide additional support, the NMR spectrum of a freshly prepared solution of the isolated product in [D_6]DMSO was recorded. Notably, this time we could observe the presence of a single compound, wherein a signal for the methyl group was present at δ = 1.89 ppm and 12.9 ppm in the ^{1}H and ^{13}C NMR spectrum, respectively. However, after a time gap of 1.0 h, a new peak at δ = 1.92 ppm in the ^{1}H NMR spectrum started to appear. As monitored by ^{1}H NMR spectroscopy, the percentage of this peak increased with time, and after 24 h, the ratio of the two products stabilized to 2:1; this ratio did not change even after 48 h (see Supporting Information). In the ^{13}C NMR spectrum, the appearance of a peak at δ = 12.4 ppm corresponded to this new compound. These results inferred that in solution the product generated through reaction of **4a** with NaH equilibrated with a compound having similar disposition of protons.

It is widely reported that annulated tetrazoles display ring-chain tautomerism to exist in the azido form in solution, but this process is reversible.[18] Hence, it was assumed that the isolated product is 2-azido-5-methyl-6-phenylpyrimidin-4(3*H*)-one (**6a**), which tautomerized in solution to coexist as 6-methyl-7-phenyltetrazolo[1,5-*a*]pyrimidin-5(4*H*)-one (**5a**). Nevertheless, to arrive at the structure of the isolated product unambiguously, colorless crystals suitable for X-ray studies were obtained by slow evaporation of its saturated methanolic solution. To our surprise, analysis revealed the structure to be 6-methyl-5-phenyltetrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**7a**) instead of envisaged product **5a** (Figure 2).[19] The spot for the crystalline product on TLC corresponded to the fluorescent violet spot. Moreover, the IR spectrum of the crystalline compound recorded as KBr disc displayed a peak for the amide group, but the characteristic peak for the azide group was absent. Subjecting a freshly prepared sample of **7a** to NMR spectroscopic analysis showed the signal of the methyl group at δ = 1.92 ppm in the ^{1}H NMR spectrum and at δ = 12.4 ppm in the ^{13}C NMR spectrum. These signals matched the new signals appearing over time in the NMR spectra of **6a** (Figure 3). However, repeated NMR spectroscopic analysis of the same sample of **7a** after 24 h showed it too tautomerizes to coexist with **6a**. Thus, we concluded that the compound isolated as a solid from the reaction mixture is azidopyrimidinone **6a**, which tautomerizes to tetrazolopyrimidinone **7a** in solution to reach an equilibrium in approximately 24 h. Importantly, however, **7a** can be isolated in pure form by crystallization from methanol. To chemically ascertain the presence of the azido form, **6a** was subjected to reduction in the presence of Zn in AcOH to furnish a single product in 91% yield that was delineated to be 2-amino-5-methyl-6-phenylpyrimidin-4(3*H*)-one (**8**). On the other hand, even pure **7a** upon treatment with Zn in AcOH resulted in **8** in

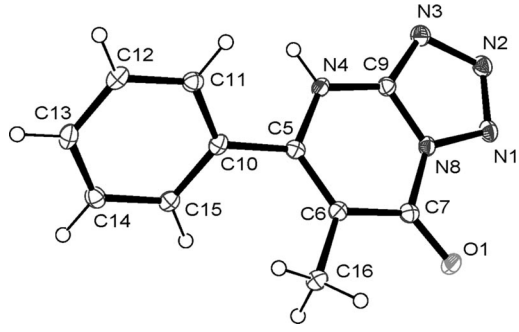


Figure 2. ORTEP diagram of **7a** at 35% probability level.

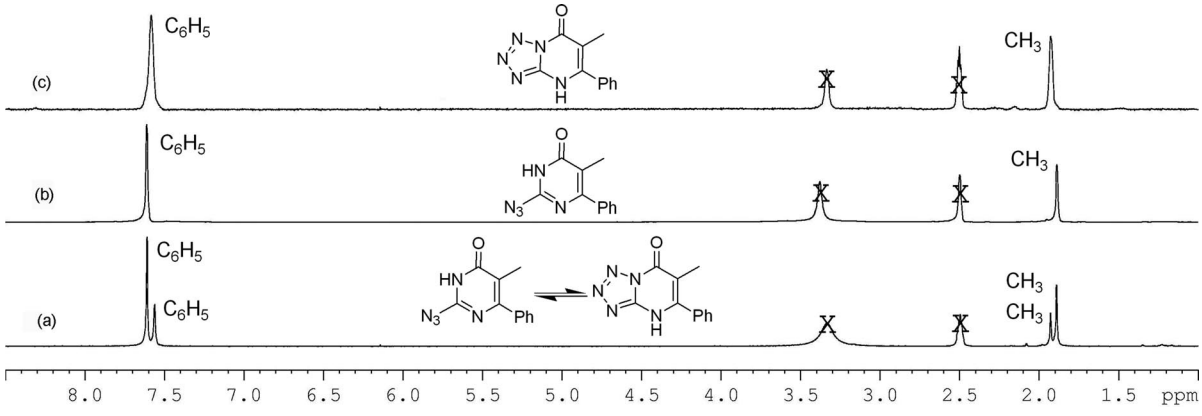


Figure 3. ^{1}H NMR spectra ([D_6]DMSO) of (a) an equilibrated mixture of **6a** and **7a**, (b) pure **6a**, and (c) pure **7a**.

93% yield.[20] The formation of **8** from **7a** was rationalized on the basis of the conversion of **7a** into **6a** under acidic conditions followed by reduction. Additional support for this assumption came from the reaction of **7a** with $POCl_3$ in the presence of a catalytic amount of PCl_5, which resulted in the formation of chloride **9**. The IR spectrum of **9** displayed the characteristic peak for the azido group, thereby confirming the opening of the tetrazole subunit under acidic conditions.

In view of the results achieved by Zn/AcOH reduction of **6a** and **7a**, we considered it worthwhile to study the effect of acidic and basic conditions on **6a** and **7a** independently by NMR spectroscopic experiments. As a consequence, samples for both compounds were prepared in [D]TFA and [D_5]pyridine. The ^{1}H NMR spectra of **6a** and **7a** in [D]TFA were found to be identical whether recorded immediately or after 24 h. The chemical shifts of these spectra corresponded to the one observed for the azido form. This observation was in agreement with the literature, which documents the existence of the azido form in acidic medium, and in particular TFA.[21] On the other hand, the ^{1}H NMR spectra of **6a** and **7a** in [D_5]pyridine recorded immediately displayed the azido and tetrazolyl forms, respectively, but repetition of the ^{1}H NMR spectroscopic experiments of the same samples after 24 h showed both forms equilibrating, wherein the azido and tetrazolyl forms were present in a 3:2 ratio.

To assess the generality of the protocol, we examined MBH acetates **2b**–**h** for similar series of reactions, and the results have been illustrated in Table 1. In all cases primary allylamines **3b**–**h** were formed, which were subsequently transformed into 5-aminotetrazoles **4b**–**h** in moderate yields. Gratifyingly, reactions of **4b**–**h** with NaH yielded the respective substituted 2-azido-pyrimidin-4(3*H*)-ones **6b**–**h** in good yields. Crystallization of **6c** from MeOH resulted in isolation of corresponding tetrazole form **7c**.

Table 1. Isolated yields of substituted 5-aminotetrazoles **4** and azidopyrimidinones **6**.

Compd. no.	Ar	% Yield of **4**	% Yield of **6**
a	Ph	46	96
b	2-ClC_6H_4	50	93
c	2-FC_6H_4	39	95
d	4-ClC_6H_4	53	90
e	4-FC_6H_4	48	92
f	4-MeC_6H_4	51	95
g	2,4-$Cl_2C_6H_3$	55	92
h	2-thienyl	45	82

On the basis of the findings it is speculated that the NaH-mediated intramolecular cyclization proceeds by the pathway delineated in Figure 4. Initially, intramolecular cyclization involving the free amino and the ester moiety takes place in tetrazole **A** to furnish intermediate **B**, which immediately stabilizes as **C**. Acid workup of the reaction mixture yields azido derivative **D**, which in solvent equilibrates with tetrazole form **E**.

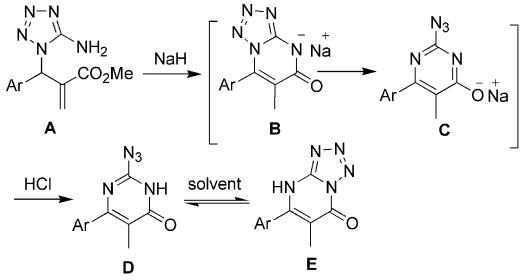
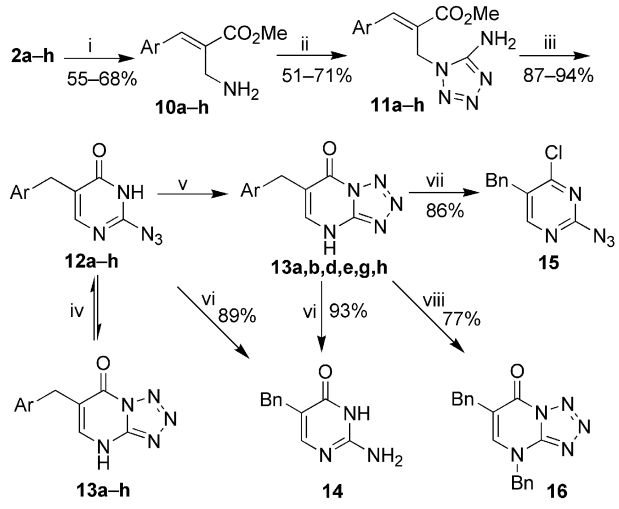


Figure 4. Plausible mechanism for the isolation of azide derivative **6** through acidic workup during NaH-promoted intramolecular cyclization.

Encouraged by the success of the protocol with primary allylamine **I**, we decided to extend its application to primary allylamine **II**, which is rather easily accessible from the MBH acetate.[12] Accordingly, we selected allylamine **10a** for initial optimization studies, which was readily obtained from acetate **2a** by following a reported procedure. Treating **10a** with freshly prepared cyanogen azide for 8 h afforded required substituted 5-aminotetrazole **11a** in 61% yield (Scheme 3). Intramolecular cyclization in the presence of NaH in THF was complete in 15 min to afford a product after acidic workup. Similar to the preceding section, TLC analysis of the product carried out immediately displayed a single nonpolar spot, whereas analysis of the same solution after different time intervals showed the appearance of a violet spot in addition to the original black spot, which increased in intensity with time. The IR spectrum of the isolated product displayed the presence of a peak for the azido and amide groups, whereas the ^{1}H NMR spectrum recorded immediately after preparing the sample in [D_6]-DMSO showed the presence of one compound with a char-



Scheme 3. Reagents and conditions: (i) NH_3/MeOH, room temp. 1 h; (ii) N_3CN (2.0 equiv.), MeCN, 0–10 °C, 8 h; (iii) a) NaH (2.5 equiv., 60% in oil), THF, room temp., 15 min; b) aq. HCl (2 N, to pH 2); (iv) equilibration in solution of MeOH, CD_3OD, [D_6]acetone, [D_5]pyridine, or [D_6]DMSO; (v) crystallization from MeOH; (vi) Zn (3.0 equiv.), AcOH, 80 °C, 2 h; (vii) $POCl_3$, PCl_5 (catalytic), 110 °C, 1 h; (viii) benzyl bromide (1.2 equiv.), NaH (2.5 equiv., 60% in oil), DMF, room temp., 6 h.

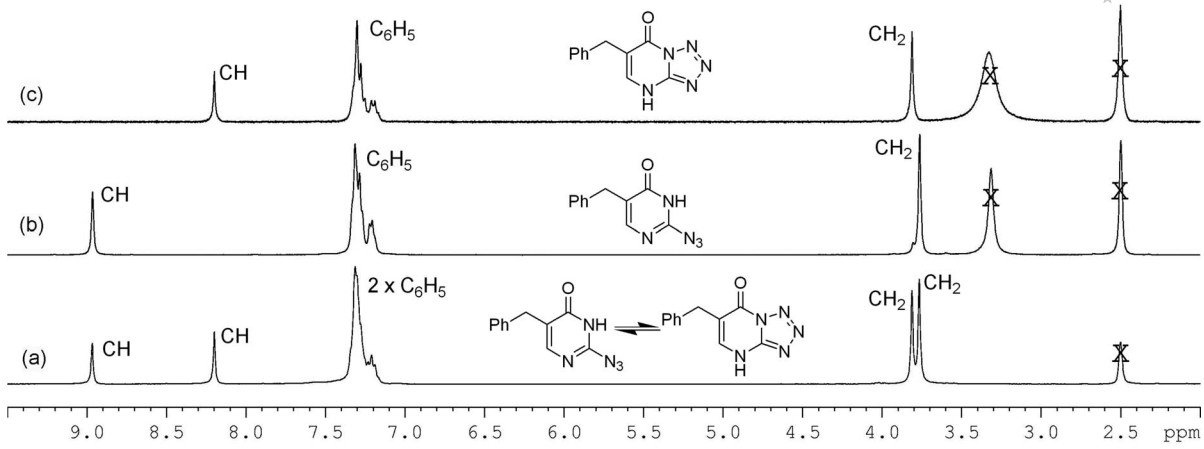


Figure 5. ^{1}H NMR spectra ([D$_6$]DMSO) of (a) an equilibrated mixture of **12a** and **13a**, (b) pure **12a**, and (c) pure **13a**.

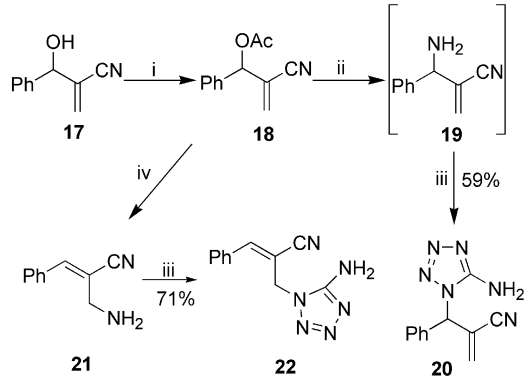
acteristic peak for the =CH proton appearing at δ = 8.96 ppm. Therefore, the structure of the product was assigned as 2-azido-5-(phenylmethyl)pyrimidin-4(3*H*)-one (**12a**). In line with earlier observations, recording of the NMR spectrum of the sample after 24 h displayed it to be a mixture of two products, but the ratio was observed to be 5:6. Moreover, TLC analysis of the recovered sample showed the presence of a new violet spot besides the original one. Fortunately, we were able to crystallize the more polar compound corresponding to the fluorescent violet spot from a saturated methanolic solution as tetrazolyl form **13a**. In the ^{1}H NMR spectrum of pure **13a** the chemical shift of the =CH proton was observed to be δ = 8.21 ppm. This chemical shift was identical with the chemical shift of the peak that had appeared in the NMR spectrum of **12a** recorded after a gap of 24 h. For the sake of clarity, a comparison of the ^{1}H NMR spectra of **12a** and **13a** has been provided in Figure 5. Chemically, the reduction of either **12a** or **13a** in the presence of Zn/AcOH resulted in the formation of **14**. Furthermore, reaction of **13a** with $POCl_3$ in the presence of a catalytic amount of PCl_5 led to the isolation of azido derivative **15** in 86% yield.

With the desire to understand the general trend of our methodology for these substrates, allylamines **10b**–**h** were examined, and the results are presented in Table 2. Amines **10b**–**h** successfully furnished the respective 5-aminotetrazoles **11b**–**h**. Subsequent treatment of **11b**–**h** with NaH followed by acidic workup provided azido compounds **12b**–**h** in good yields. Further crystallization of **12b**,**d**,**e**,**g**,**h** from methanol successfully led to isolation of a crystalline compound in each case, and the structures of each was delineated to be corresponding tetrazoles **13b**,**d**,**e**,**g**,**h**. Unfortunately, crystals of none of the compounds were found to be suitable for X-ray analysis. Thus, to ascertain the structure of **13a** unambiguously, we embarked on a detailed NOESY experiment of **16**, which was realized through benzylation of **13a**. The NOE of the =CH proton of the pyrimidinone ring with protons of both of the benzylic group confirmed the assigned structure.

Table 2. Isolated yields of substituted 5-aminotetrazoles **11** and azidopyrimidinones **12**.

Compd. no.	Ar	% Yield of **11**	% Yield of **12**
a	Ph	61	93
b	2-ClC_6H_4	65	87
c	2-FC_6H_4	66	91
d	4-ClC_6H_4	70	94
e	4-FC_6H_4	59	92
f	4-MeC_6H_4	71	91
g	2,4-$Cl_2C_6H_3$	69	90
h	2-thienyl	51	89

Having utilized the primary allylamines from the MBH acetate of acrylates we decided to investigate the scope of the strategy with the corresponding amines generated from the MBH acetate of acrylonitrile. Accordingly, allylamine **19** was first generated from adduct **17** and was then subjected to reaction with cyanogen azide as outlined above. This resulted in the formation of substituted 5-aminotetrazole **20** (Scheme 4). However, attempts to carry out intramolecular cyclization by using different bases failed to



Scheme 4. Reagents and conditions: (i) AcCl (1.5 equiv.), pyridine (1.3 equiv.), dry CH_2Cl_2, 0 °C to room temp.; (ii) a) DABCO (1.0 equiv.), THF/H_2O, room temp., 15 min; b) aq. NH_3, 10–20 °C, 30 min; (iii) N_3CN, MeCN, 0–10 °C, 8 h; (iv) NH_3/MeOH, room temp., 1 h.

yield the desired annulated tetrazole. Simultaneously, amine **21** was also prepared and subjected to reaction with cyanogen azide to yield required 5-aminotetrazole **22** in good yield. Unfortunately, **22** also failed to undergo intramolecular cyclization to furnish the annulated tetrazole derivative.

Conclusions

In summary, we have developed a benign and general protocol for the synthesis of primary allylamines through S_N2'–S_N2' displacement reactions of MBH acetates. We demonstrated the utility of primary allylamines generated from the MBH acetates of acrylates for the synthesis of substituted 5-aminotetrazoles by reaction with cyanogen azide. The base-promoted intramolecular cyclization of these tetrazoles resulted in isolation of highly substituted azidopyrimidinones instead of the expected tetrazolo[1,5-*a*]-pyrimidin-5(4*H*)-ones. Nevertheless, we could successfully isolate the tetrazolo[1,5-*a*]pyrimidin-7(4*H*)-one form in pure state through crystallization of the azido derivative from methanolic solution. We have further studied the scope of the strategy and found that the primary allylamines from the MBH acetate of acrylonitrile furnished the 5-aminotetrazoles but failed to undergo intramolecular cyclization to furnish the fused tetrazole system. This work signifies the usefulness of MBH chemistry for achieving the synthesis of important heterocyclic motifs.

Experimental Section

General: Melting points were determined in capillary tubes with a Precision melting point apparatus containing silicon oil. IR spectra were recorded by using a Perkin–Elmer RX I FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with either a Bruker DPX-200 FT or a Bruker Avance DRX-300 spectrometer by using TMS as an internal standard. Mass spectra (ESI) were recorded with a MICROMASS Quadro-II LC–MS system. HRMS (EI) spectra were recorded with a JEOL system and DART-HRMS (recorded as ESI+) were recorded with a JEOL-AccuTOF JMS-T100LC mass spectrometer having a DART (direct analysis in real time) source. Elemental analyses were performed with a Carlo Erba 108 or an Elementar Vario EL III microanalyzer. Room temperature varied between 20 and 35 °C. The ^{13}C NMR spectra of fluoro-substituted derivatives display extra peaks due to C–F couplings. For all final compounds where the azido and tetrazolyl forms were isolated, individual spectroscopic data for the pure state along with the data of solution containing both forms have been provided. For all azide derivatives where the corresponding tetrazoles were not isolated, spectroscopic data for the azide and the mixture containing both tautomeric forms have been provided.

General Procedure for the Synthesis of 3a–h and 19 as Exemplified for 3a: To a solution of acetate **2a** (1.60 g, 6.84 mmol) in THF/H_2O (1:1, 20 mL) was added DABCO (0.77 g, 6.84 mmol), and the reaction mixture was stirred for 15 min at room temperature. After the reaction mixture became clear, aqueous ammonia (30%, 10 mL) was added at 15 °C, and the reaction was continued at the same temperature. After 30 min, CH_2Cl_2 (10 mL) was added, and the organic phase was separated. The aqueous phase was further extracted with CH_2Cl_2 (10 mL). The combined organic layer was diluted with acetonitrile (40 mL), and the volume of the solution was evaporated under reduced pressure at low temperature (below 10 °C). The concentrated solution containing allylamine **3a** was instantly used for further reaction without any purification.

General Procedure for the Synthesis of 4a–h, 11a–h, 20, and 22 as Exemplified for 4a: At 0 °C, cyanogen bromide (1.45 g, 13.68 mmol) was dissolved in dry acetonitrile (25 mL) to which sodium azide (2.67 g, 41.04 mmol) was added. The reaction mixture was stirred at 0–10 °C for 4 h. The inorganic salt was filtered off (*Caution!* After filtering, the salt must be dissolved in cold water quickly). The solution of amine **3a** in acetonitrile was diluted with water (6 mL) and stirred at 0 °C. To this solution was added the filtrate containing cyanogen azide at the same temperature. After stirring for 8 h at 10 °C, reaction mixture was concentrated under reduced pressure, and the residue was diluted with water (20 mL). The mixture was extracted with ethyl acetate (3 × 20 mL). The organic layers were pooled, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification of the crude product by column chromatography over silica gel (ethyl acetate/hexanes, 1:1) furnished pure product **4a** as a white solid (0.81 g, 46%).

Methyl 2-[(5-Amino-1*H*-1,2,3,4-tetraazol-1-yl)(phenyl)methyl]acrylate (4a): R_f = 0.43 (ethyl acetate/hexanes, 4:1). M.p. 170–171 °C. IR (KBr): $\tilde{\nu}$ = 1648 (C=N), 1724 (CO_2Me), 3324 (NH_2) cm^{-1}. ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ = 3.64 (s, 3 H, OCH_3), 5.26 (d, J = 1.3 Hz, 1 H, CH), 6.45 (s, 1 H, =CH_2), 6.56 (s, 1 H, =CH_2), 6.90 (s, 2 H, exchangeable with D_2O, NH_2), 7.21–7.25 (m, 2 H, ArH), 7.35–7.44 (m, 3 H, ArH) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 53.1, 59.0, 129.0, 129.4, 129.6, 130.0, 136.5, 139.0, 156.1, 165.8 ppm. MS (ESI+): *m*/*z* (%) = 259.9 (100) [M + 1]$^+$, 175.1 (12) [M – 84]$^+$. $C_{12}H_{13}N_5O_2$ (259.1069): calcd. C 55.59, H 5.05, N 27.01; found C 55.73, H 4.85, N 27.25.

General Procedure for the Synthesis of 6a–h and 12a–h as Exemplified for 6a: To a solution of **4a** (0.25 g, 0.97 mmol) in anhydrous THF (15 mL) was added NaH (60% in mineral oil, 0.05 g, 2.00 mmol) at 0 °C, and the reaction mixture was stirred at ambient temperature for 15 min. Thereafter, the reaction mixture was quenched with MeOH and concentrated under reduced pressure. The residue was acidified with 2 N HCl to pH 2, and the resulting solution was extracted with Et_2O (3 × 15 mL). The combined organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain a residue, which upon trituration with Et_2O yielded product **6a** as a white solid (0.21 g, 96%).

2-Azido-5-methyl-6-phenylpyrimidin-4(3*H*)-one (6a): R_f = 0.34 (ethyl acetate/hexanes, 4:1). M.p. 207–209 °C. IR (KBr): $\tilde{\nu}$ = 1679 (C=N and CO), 2148 (N_3), 3447 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.89 (s, 3 H, CH_3), 7.61 (s, 5 H, ArH) ppm. ^{1}H NMR (300 MHz, [D]TFA): δ = 2.32 (s, 3 H, CH_3), 7.54 (d, J = 7.0 Hz, 2 H, ArH), 7.62–7.75 (m, 3 H, ArH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 12.9, 117.5, 129.1, 130.1, 131.0, 141.2, 149.8, 162.0 ppm. ^{13}C NMR (300 MHz, [D]TFA): δ = 9.8, 113.8, 128.1, 128.5, 129.4, 132.6, 155.9, 157.3 ppm. MS (ESI+): *m*/*z* (%) = 228.1 (100) [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_9N_5O$ 227.0807; found 227.0876.

General Procedure for Isolation of 7a,c and 13a,b,d,e,g,h: Tetrazolopyrimidinones **7a**,**c** and **13a**,**b**,**d**,**e**,**g**,**h** were obtained by crystallizing the corresponding azidopyrimidinones **6a**,**c** and **12a**,**b**,**d**,**e**,**g**,**h** from methanol.

6-Methyl-5-phenyl[1,2,3,4]tetraazolo[1,5-*a*]pyrimidin-7(4*H*)-one (7a): Obtained as a white solid by crystallizing **7c** from methanol. R_f = 0.14 (ethyl acetate/hexanes, 4:1). M.p. 210–212 °C. IR (KBr): $\tilde{\nu}$ = 1679 (C=N and CO), 3446 (NH) cm^{-1}. ^{1}H NMR (200 MHz,

[D_6]DMSO): δ = 1.92 (s, 3 H, CH_3), 7.58 (s, 5 H, ArH) ppm. ^{1}H NMR (300 MHz, [D_5]pyridine): δ = 2.11 (s, 3 H, CH_3), 7.55 (s, 3 H, ArH), 7.67–7.70 (s, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 12.5, 106.4, 129.4, 129.6, 130.3, 131.1, 131.3, 133.2, 150.8, 156.2 ppm. MS (ESI+): *m*/*z* (%) = 228.1 (100) [M + 1]$^+$. HRMS (EI): calcd. for $C_{11}H_9N_5O$ 227.0807; found 227.0796.

Supporting Information (see footnote on the first page of this article): Additional experimental details and spectroscopic data and stacked ^{1}H NMR spectra showing the tautomeric equilibration.

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[19] Crystal data of compound **7a** (crystallized from MeOH): $C_{11}H_9N_5O$, *M* = 227.23, monoclinic, $P\bar{1}$, *a* = 7.378(3) Å, *b* =

12.501(2) Å, c = 10.971(2) Å, α = 90.00, β = 103.934(2)°, γ = 90°, V = 982.1(5) Å^3, Z = 4, $D_{calcd.}$ = 1.537 g cm^{-3}, μ(Mo-K_α) = 0.107 mm^{-1}, F (000) = 472 yellow block, dimension 0.20 × 0.20 × 0.20 mm, 5244 reflections measured (R_{int} = 0.0607), 1916 unique, wR_2 = 0.1249, conventional R = 0.0494 on F^2 values of 1916 reflections with $I > 2\sigma(I)$, $(\Delta/\sigma)_{max}$ = 000), S = 1.108 for all data and 156 parameters. Unit cell determination and intensity data collection (2θ = 50°) were performed with a Bruker P4 diffractometer at 293(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: XSCANS (Siemens Analytical X-ray Instrument Inc., Madison, WI, USA, 1996) for data collection and data processing; SHELXTL-NT (Bruker AXS Inc., Madison, Wisconsin, USA, 1997) for structure determination, refinements, and molecular graphics. CCDC-773490 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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