Iodine Catalyzed One-Pot Multicomponent Synthesis of a Library of Compounds Containing Tetrazolo[1,5-*a*]pyrimidine Core

Li-Yan Zeng and Chun Cai*

Chemical Engineering College, Nanjing University of Science & Technology, Nanjing 210094, China

Received July 9, 2009

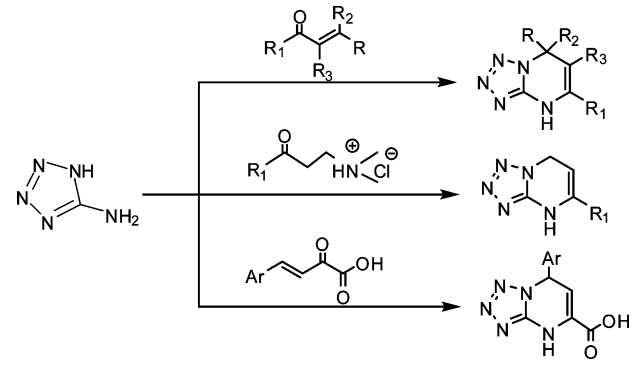
Versatile and novel reactions of 5-aminotetrazole with structurally diverse aryl aldehydes and building blocks with active methylene catalyzed by iodine were investigated in a multicomponent one-pot protocol. A series of 5,7-diaryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidines **C** and 5-methyl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylates **D** were obtained in moderate to good yields. Further exploration rapidly afforded various **E** in good to excellent yields; in addition, compound **F** was also obtained under the same condition. The structures of products were characterized by LC-MS, ^{1}H NMR, ^{13}C NMR, and elemental analysis.

Introduction

Organic compounds containing pyrimidine as a core unit are known to exhibit various biological and pharmaceutical activities,[1] the synthesis of these complex heterocyclic scaffolds is assigned as one of the most fertile areas for both organic and medicinal chemistry. Over the past decades, many procedures have been reported for the preparation of 4-aryl or 4,6-diaryl pyrimidinones;[2] however, after a detailed literature survey, we found that there were only limited publications devoted to the synthesis of azolopyrimidines, especially tetrazolopyrimidines,[3−5] wherein the 5-aminotetrazole (5-AT) with both endocyclic nitrogen and exocyclic amino group participated in the formation of the fused heterocyclic molecular as 1,3-binucleophile synthons instead of urea. To date, the most widespread pathway to these structures involved the initial synthesis of the α,β-unsaturated carbonyl skeletons,[3,4] such as chalcones, Mannich bases, or arylidenepyruvic acids in rather poor yields, followed by further cyclocondensation with 5-AT (Scheme 1). However, some flaws, namely, tedious workup procedures, poor yields, or time- and resource-wasting procedures, have occurred along with these multistage routines. Although the three-component reactions of 5-AT with methylene active compounds and aldehydes[5] have been developed and thus improved the efficiency for the synthesis of tetrazolopyrimidines, the high-temperature, long reaction time, or low yields, as well as the stoichiometric amounts of corrosive protonic acid, used in these protocols would limit the practical use in a large scale considering the demand of "Green Chemistry".

Intrigued by these facts, we surmised whether a convenient, effective, and eco-friendly process could be developed leading to a library of tetrazolopyrimidines, which might result in an entirely new complementary biological activity. Among the strategies used to construct the small molecule, Multicomponent reactions (MCRs) are ideal synthetic tools to generate multiple molecular scaffolds from the same starting materials or intermediates because of their intrinsic convergence, complexity-generating power, as well as operational simplicity, resource and energy effectivity from the viewpoint of atom-economy and sustainable technology. Moreover, MCRs have constituted an increasingly valuable approach to large libraries of structurally related drug-like compounds.[6] Meanwhile, molecule iodine, as a cheap, less-toxic and readily available mild Lewis acid, has been applied to catalyze various organic transformations.[7] Keeping in view of above points and following our continuous interest in iodine-catalyzed MCRs,[8] we initially performed an one-pot procedure based on the three-component reactions of 5-AT, pyruvic acid, and aromatic aldehydes, with the aim of examing the activity of iodine. Fortunately, this methodology provided effective access to a series of dihydrotetrazolopyrimidine carboxylic acids (Scheme 2).[9] Then, we envisioned that the scope and generality of the construction of the tetrazolopyrimidines might likewise be extended by replacing the pyruvic acid with active methylenes such as 1,3-cyclohexanedione, ethyl acetoacetate, malononitrile and so on. To our delight, further research suggested that the iodine catalyzed multicomponent cyclocondensations of 5-AT with the precursors of α,β-unsaturated unit, aldehydes and methylene active compounds proceeded excellently. In this

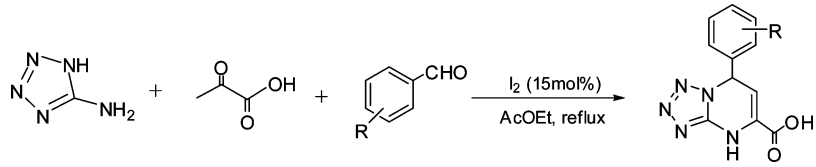
Scheme 1. Previous Methods for Synthesis of Tetrazolopyrimidines



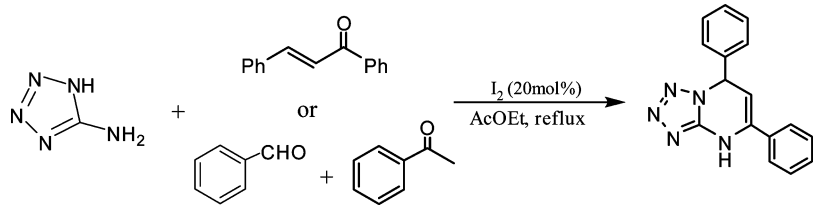
* To whom correspondence should be addressed. Phone: +86-25-84315514. Fax: +86-25-84315030. E-mail: c.cai@mail.njust.edu.cn.

10.1021/cc9000983
Published on Web 12/01/2009

Scheme 2. Iodine Catalyzed One-Pot Synthesis of the Dihydrotetrazolopyrimidine Carboxylic Acids



Scheme 3. Preparation of the 5,7-Diphenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine **C1** in Two Ways



paper, we would like to describe an efficient and mild procedure in detail that provides rapid assembly of fused tetrazolopyrimidines and tolerates a wide range of starting building blocks.

Results and Discussion

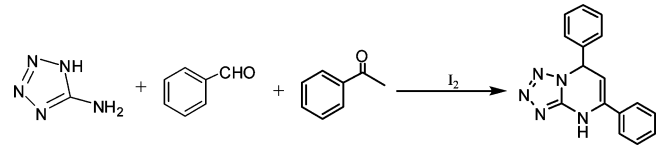
Preparation of 5,7-Diaryl-4,7-dihydrotetrazolo[1,5-a]-pyrimidines C. On the basis of our previous work,[9] as a pilot experiment, a mixture of 5-AT, chalcone, and iodine (ratio 1:1:0.2) in refluxing AcOEt was stirred (Scheme 3), the reaction was terminated after 3 h monitored by TLC, the purified product **C1** was yielded in 44% after work up. Then, we replaced the chalcone with its synthetic precursors, aldehyde and ketone, and as expected, the same product **C1** was obtained in 39% yield after treatment of benzaldehyde, acetophenone, and 5-AT under the same conditions (Scheme 3). The structure of product **C1** was unambiguously confirmed by LC-MS and ^{1}H NMR, wherein the signals recognized as arising from the pivotal elements of dihydropyrimidine ring were obviously exhibited, such as the sharp doublet signal for the 5-CH ($\delta = 6.61, 6.62$), the appearance of which as a chiral center lead to coupling of 6-CH proton signals into doublet observed at 5.31 and 5.32 ppm, the sharp singlet at 10.6 ppm for the NH without proton-exchange; and also the signals of aromatic atoms were shown at 7.37−7.67 ppm.

To our knowledge, 5,7-diphenyl-4,7-dihydrotetrazolo[1,5-*a*]-pyrimidine **C1** has been previously prepared only by multistep synthesis.[3,4b] Since we considered it to be a promising alternative procedure for the 5,7-diaryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidines, we were prompted to optimize the conditions and investigate the scope of the reaction.

As shown in Table 1, the reaction without iodine provided little product (Table 1, entry 2), and the catalyst concentration was also allowed to reduce to 10 mol %. Further screening of solvents indicated that alcohols displayed as relatively better medium while others suppressed the formation of desired product. Disappointedly, the product was formed in rather small amounts in the course of our attempts to improve the yield by adding Et_3N or K_2CO_3 as base and KI as additive.

The optimized conditions outlined above (Table 1, entry 15) were initially employed to generate 5,7-diaryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidines **C** starting from several representatives of the aldehydes and ketones. The results were collected in Table 2. Most of the substrates selected, including para-substituted benzaldehydes and meta-substituted acetophenone, participated in the reaction smoothly, and the desired products were obtained in moderate yields. Compared to electron-withdrawing group, the reaction time was slightly prolonged in the case of 4-methoxybenzaldehyde, while 4-hydroxybenzaldehyde gave lower yield, which might be caused by the particularity of hydroxyl. Unfortunately, the ortho-substituted benzaldehydes failed to provide the expected products based on the analysis of LC-MS, taking 2-chlorobenzaldehyde for example (Table 2, entry 2). The reason for this is not yet clear. Additionally, careful literature search indicated that there was no report describing the synthesis of any 5-(ortho-substituted)aryl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine before.[3,4b]

Table 1. Conditions Optimization of Iodine Catalyzed One-Pot Synthesis of 5,7-Diphenyl-4,7-dihydrotetrazolo[1,5-*a*]-pyrimidine[a]

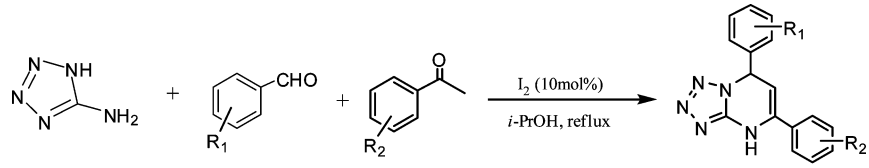


A **B1** **C1**

entry	I_2 (mol %)	solvent	*t* (h)	yield (%)[b]
1	20	AcOEt	8	39
2	0	AcOEt	24	16[c]
3	25	AcOEt	8	40
4	15	AcOEt	8	39
5	10	AcOEt	8	47
6	5	AcOEt	8	33
7	10	AcOEt	6	48
8	10	AcOEt	4	29
9	10	MeCN	6	30
10	10	H_2O	12	15
11	10		0.15[d]	32
12	10	EtOH	6	48
13	10	MeOH	6	41
14	10	DCE	6	31
15	10	*i*-PrOH	6	57
16	10	*n*-PrOH	6	51
17	10	*n*-BuOH	6	46

[a] Reaction conditions: 5-AT (5 mmol), benzaldehyde (5 mmol), acetophenone (5 mmol), refluxing temperature. [b] Isolated yields. [c] Yield based on the analysis of LC-MS. [d] The reaction mixture was solidified in 10 min.

Table 2. Iodine Catalyzed Three-Component One-Pot Synthesis of 5,7-Diaryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidines **C**[a]

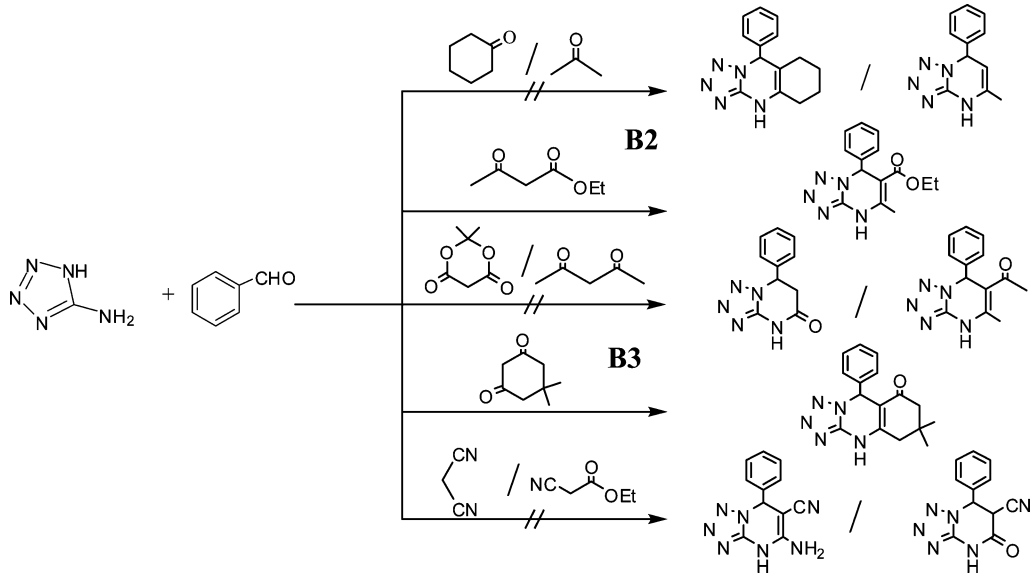


A **B1** **C**

entry	A	R_2	*t*(h)	product	yield (%)[b]
1	C_6H_5CHO	H	6	**C**1	57
2	4-ClC_6H_4CHO	H	5	**C**2	54
3	2-ClC_6H_4CHO	H	6		0[c]
4	4-$MeOC_6H_4CHO$	H	7	**C**3	56
5	C_6H_5CHO	3-Cl	5	**C**4	61
6	4-OHC_6H_4CHO	H	10	**C**5	33

[a] Reaction conditions: 5-AT (5 mmol), **A** (5 mmol), **B1** (5 mmol), iodine (0.5 mmol), refluxing temperature. [b] Isolated yields. [c] No desired product was detected.

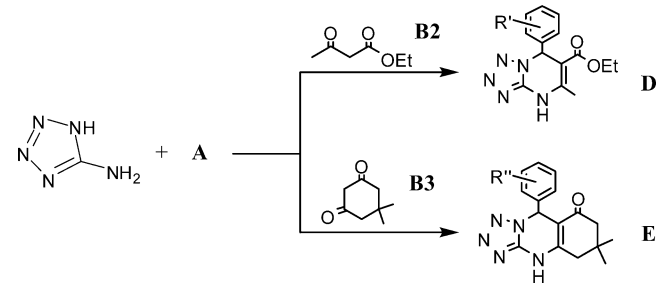
Scheme 4. Screening of the Building Blocks to Synthesize Tetrazolopyrimidines

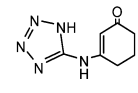


Screening of Building Blocks. With these results in hand, we were encouraged to further explore the potentiality of this protocol with other building blocks. Initially, typical building blocks (Scheme 4) with methylene active structure were anticipated to play the role of acetophenone **B1** in the reaction while benzaldehyde was chosen as representative **A**. Systematic work for screening of the activated building block **B** was subsequently carried out under the modified conditions. It can be inferred from Scheme 4 that the ketones (cyclohexanone and acetone) and the methylene active nitriles were not suitable synthons, while ethyl acetoacetate **B2** and dimedone **B3** behaved excellently. In addition, the 2,2-dimethyl-1,3-dioxane-4,6-dione and acetylacetone structurally, which are similar to dimedone and ethyl acetoacetate, respectively, did not afford the desired products. The catalytic activity of iodine was therefore settled down to furnish ethyl 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate **D1** and 6,6-dimethyl-9-phenyl-5,6,7,9-tetrahydrotetrazlo[1,5-*a*]quinazolin-8(4H)-one **E1**. A careful survey of the literature revealed that only sporadic publications reported the synthesis of tetrazoloquinazolines,[3f] and this is a unique methodology that may be adopted to form functional tetrazolopyrimidine and tetrazoloquinazoline scaffolds for their potential contribution to drug development as privileged strtuctures. Accordingly, we were attracted to apply this strategy in further investigation of the generality and limitation.

Preparation of Compounds D, E, and F. Fortunately, most of our attempts to complement the library compounds ethyl 5-methyl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylates **D** and 6,6-dimethyl-9-aryl-5,6,7,9-tetrahydrotetrazlo[1,5-*a*]quinazolin-8(4H)-ones **E** starting from building blocks **B2** and **B3**, respectively, 5-AT, and various **A** were successful. In the case of **B2**, all of the desired products obtained with moderate to good yields in 10 mol % I_2/*i*-PrOH system within 3−6 h were structurally established with the appearance of new signals at δ 1.00−1.05 ppm and δ 2.46−2.5 ppm assigned as ethyl, at δ 3.94−3.99 ppm assigned as 5-methyl and also with the disappearance of the signals for the 6-CH at δ 5.3 ppm compared to the compounds **C** in terms of the ^{1}H NMR spectra. The additional mass spectra and ^{13}C NMR measured for the samples did not contradict the product structures proposed. The results listed in Table 3 (entries 1−7) indicated that the presence of substituents at the para- and ortho-positions on the benzaldhyde had no obvious effect on the yields of the

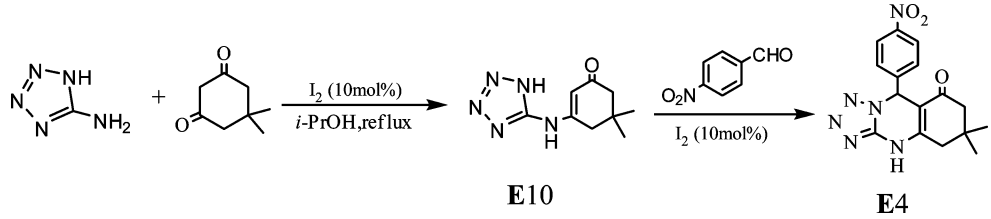
Table 3. Iodine-Catalyzed Three-Component One-Pot Synthesis of **D** and **E**[a]



Entry	**A**	**B**	*t*	Products	Yield (%)[b]
1	C_6H_5CHO	**B2**	5h	**D**1	72
2	4-ClC_6H_4CHO	**B2**	3h	**D**2	69
3	4-$MeOC_6H_4CHO$	**B2**	6h	**D**3	39
4	4-$NO_2C_6H_4CHO$	**B2**	4h	**D**4	77
5	2-$NO_2C_6H_4CHO$	**B2**	5h	**D**5	74
6	2-ClC_6H_4CHO	**B2**	3.5h	**D**6	67
7	2,4-$DiClC_6H_3CHO$	**B2**	3h	**D**7	64
8	C_6H_5CHO	**B3**	20min	**E**1	83
			2h		15[c]
9	4-ClC_6H_4CHO	**B3**	10min	**E**2	92
10	4-$MeOC_6H_4CHO$	**B3**	50min	**E**3	81
11	4-$NO_2C_6H_4CHO$	**B3**	25min	**E**4	70[d]
12	4-OHC_6H_4CHO	**B3**	20min	**E**5	76
13	4-BrC_6H_4CHO	**B3**	10min	**E**6	89
14	2-ClC_6H_4CHO	**B3**	70min	**E**7	92
15	2-$NO_2C_6H_4CHO$	**B3**	40min	**E**8	63
16	2,4-$DiClC_6H_3CHO$	**B3**	25min	**E**9	87
17	cyclohexanone	**B3**			
18	cyclopentanone	**B3**			
19	$C_6H_5COCH_3$	**B3**	5-8min		78-93[e]
20	acetone	**B3**		**E**10	
21	C_3H_7CHO	**B3**			

[a] Reaction conditions: 5-AT (5 mmol), **A** (5 mmol), **B** (5 mmol), iodine (0.5 mmol), *i*-PrOH (10 mL), refluxing temperature. [b] Isolated yields. [c] Proceeded without iodine. [d] Yield based on the LC-MS. [e] The reaction terminated in several minutes and the same product **E**10 was provided with high yields in this iodine-catalyzed system based on the analysis of LC-MS and ^{1}H NMR.

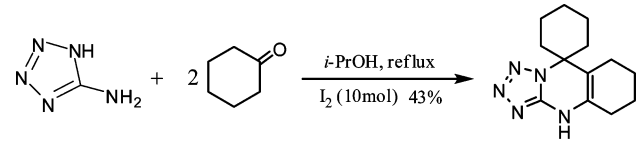
Scheme 5. Reaction Process for the Synthesis of **E4**



reaction, whereas the reaction time was slightly prolonged in the case of ortho- substituted ones ascribed to the steric effect. The electron-donating group 4-MeO afforded lower yield (39%) than electron-withdrawing substrates.

On the other hand, building block **B3** was likewise coupled with 5-AT and substituted benzaldehydes in the formation of structure **E**1-**E**9 with good to excellent yields up to 92% within rather short reaction time. However, when the ketones such as cyclohexanone, acetone, and acetophenone were considered, the intermidiate **E10** was the only product with the molecular ion peaks displayed at the same *m*/*z* values 207 by mass spectra analysis, while the ^{1}H NMR assisted to confirm the structure, any attempt to force the further cyclization of **E10** with 4-nitrobenzaldehyde was failed. The reactions were neat, and the products were isolated by simple filtration with higher purity characterized by means of LC-MS, further recrystallization would afford the analytic sample. The structures of the products were deduced from their ^{1}H NMR, LC-MS, and ^{13}C NMR. The mass spectra of these samples displayed molecular ion peaks at the appropriate *m*/*z* values, while the ^{1}H NMR spectra consisted of signals for the protons of hexatomic ring, the aromatic nuclei, the substituent, and the NH group, and did not contain the 6-CH signal. Also, the ^{13}C NMR spectra showed good agreement with the structure. The results were summarized in Table 3 (entries 8−16). Similarly, the sterically hindered substrates proceeded in rather longer time taking entries 9 and 14 for examples, and the electron-donating substituted benzaldehydes gave somewhat lower yields than electron-withdrawing ones. In addition, we noticed that the substituent $-NO_2$ presented whether on *p*- or *o*-benzaldhyde lead to a relatively lower yield. We analyzed the crude product from *p*-NO_2 one via LC-MS and found the desired product took up 70%, while an unknown compound whose molecular ion peak appeared at 414 *m*/*z* yielded in 30%. Nevertheless, a different situation was encountered during the reaction of **B3**, 5-AT, and 4-nitrobenzaldehyde. With the temperature increased, the reaction mixture turned into homophase. Normally, the product would precipitate gradually after refluxing them several minutes. In this case, however, a large amount of solid emerged suddenly after the starting materials were refluxed 5 min, and continued stirring resulted in homophase once again, and which was maintained about 12 min as far as the solid was generated gradually. Thereupon, we isolated the first emerged solid, and discovered that the intermediate **E10** was formed before the final product in high yield. Subsequently, we reacted the intermediate **E10** with 4-nitrobenzaldehyde under the same conditions with aimed to validate the reaction pathway, the contemplated product **E**4 was obtained smoothly. The reaction routine in this case was proposed as Scheme 5.

Scheme 6. Synthesis of 5′,6′,7′,8′-Tetrahydro-4′*H*-spiro[cyclohexane-1,9′-tetrazolo[5,1-*b*]quinazoline]



F

The significant results above manifested this strategy as a powerful tool for the rapid introduction and expansion of venerable tetrazolopyrimindines and tetrazoloquinazolines. However, we were always failed to apply it to the aliphatic ketones. Notably, there has been only one compound 5′,6′,7′,8′-tetrahydro-4′H-spiro[cyclohexane-1,9′-tetrazolo[5,1-*b*]-quinazoline] **F** described in literature starting from aliphatic ketone,[3f] to the best of our knowledge, which was obtained by condensation of 5-AT with cyclohexanone. Our methodology (Scheme 6), via treating 5-AT and cyclohexanone (2 equiv) under the previous modified conditions, resulted in the the target product **F** readily separating out from the homophase of the reaction mixture with the yield of 43%. However, when we employed the cyclopentanone as building block, the anticipated product was not afforded.

Conclusion

In conclusion, we have devised a versatile, convenient and cost-effective multicomponent approach to construct the structurally diverse tetrazolopyrimidines and tetrazoloquinazolines. The operational simplicity, availability of starting materials make it a rather favored alternative procedure than traditional multistep methods to prepare 5,7-diaryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidines **C**. Under the same conditions, building blocks with methylene active structure were screened, and **B2** and **B3** were found effective to perform the procedure. In this way, 5-methyl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylates **D** and 6,6-dimethyl-9-aryl-5,6,7,9-tetrahydrotetrazlo[1,5-*a*]quinazolin-8(4H)-ones **E** were rapidly synthesized for the first time in good to excellent yields and structurally confirmed by means of LC-MS, ^{1}H NMR, ^{13}C NMR, and elemental analysis, and the reaction route for the synthesis of **E**4 was observed according to the experiment results. In addition, compound **F** was also prepared in the same way. The facility, generality, and ecologically benign nature of this methodology made itself a competent lead candidate to furnish compounds containing tetrazolopyrimidine core as potential privileged medicinal scaffolds.

Supporting Information Available. Experimental methods, general procedures, spectral assignments, and copies of

^{1}H NMR and ^{13}C NMR spectra for all previous unreported products. This information is available free of charge via the Internet at http://pubs.acs.org/.

References and Notes

(1) (a) Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937, and references cited therein. (b) Sharma, A. K.; Jayakumar, S.; Hundal, M. S.; Mahajan, P. M. *J. Chem. Soc., Perkin Trans. 1* **2002**, 774. (c) Sasaki, S.; Cho, N.; Nara, Y.; Harada, M.; Endo, S.; Suzuki, N.; Furuya, S.; Fujino, M. *J. Med. Chem.* **2003**, *46*, 113.

(2) For selected examples, see: (a) Khosropour, A. R.; Baltork, I. M.; Ghorbankhani, H. *Catal. Commun.* **2006**, *7*, 713. (b) Gholap, A. R.; Venkatesan, K.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *Green Chem.* **2004**, *6*, 147. (c) Yadav, J. S.; Reddy, B. V. S.; Reddy, K. B.; Raj, K. S.; Prasad, A. R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1939. (d) Heravi, M. M.; Ranjbar, L.; Derikvand, F.; Alimadadi, B. *Mol. Diversity* **2008**, 191, and references cited therein.

(3) (a) Orlov, V. D.; Kolos, N. N.; Kiroga, K.; Desenko, S. M. *Khim. Geterotsikl. Soedin.* **1988**, 962. (b) Orlov, V. D.; Desenko, S. M.; Potekhin, K. A.; Struchkov, Y. T. *Khim. Geterotsikl. Soedin.* **1988**, 229. (c) Desenko, S. M.; Kolos, N. N.; Tueni, M.; Oriov, V. D. *Khim. Geterotsikl. Soedin.* **1990**, 938. (d) Gein, V. L.; Gein, L. F.; Tsyplyakova, E. P.; Panova, O. S. *Russ. J. Org. Chem.* **2007**, *43*, 1382. (e) Orlov, V. D.; Desenko, S. M.; Pivnenko, N. S. *Khim. Geterotsikl. Soedin.* **1988**, 1489. (f) Desenko, S. M.; Gladkov, E. S.; Komykhov, S. A.; Shishkin, O. V.; Orlov, V. D. *Khim. Geterotsikl. Soedin.* **2001**, 811.

(4) (a) Chebanov, V. A.; Desenko, S. M.; Sakhno, Y. I.; Panchenko, E. S.; Saraev, V. E.; Musatov, V. I.; Konev, V. F. *Fiziol. Akt. Rechov.* **2002**, 10. (b) Annan, N.; Paris, R.; Jordan, F. *J. Am. Chem. Soc.* **1999**, *111*, 8895. (c) Tsuda, Y.; Mishina, T.; Obata, M.; Araki, K.; Inui, J.; Nakamura, T. U. S. Patent 4 918 074, 1990. (d) Chebanov, V. A.; Sesenko, S. M.; Gurley, T. W. Six-Membered Azaheterocycles Based on 1,3-Binucleophiles; In *Azaheterocycles Based on α,β-Unsaturated Carbonyls*; Springer: Berlin Heidelberg, 2008, pp 83−107. (e) Desenko, S. M. *Khim. Geterotsikl. Soedin.* **1995**, 147.

(5) (a) Chebanov, V. A.; Sakhno, Y. I.; Desenko, S. M.; Shishkina, S. V.; Musatov, V. I.; Shishkin, O. V.; Knyazeva, I. V. *Synthesis* **2005**, 2597. (b) Gladkov, E.; Sirko, S.; Khanetskii, B.; Lukinova, E.; Desenko, S. *Chem. Pap.* **2007**, *61*, 146. (c) Drizin, I.; Holladay, M. W.; Yi, L.; Zhang, H. Q.; Gopalakrishnan, S.; Gopalakrishnan, M.; Whiteaker, K. L.; Buckner, S. A.; Sullivan, J. P.; Carroll, W. A. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1481. (d) Yao, C. S.; Lei, S.; Wang, C. H.; Yu, C. X.; Tu, S. J. *J. Heterocycl. Chem.* **2008**, *45*, 1609.

(6) (a) Weber, L. *Curr. Med. Chem.* **2002**, *9*, 2085. (b) Zhu, J. *Eur. J. Org. Chem.* **2003**, 1133. (c) Orru, R. V. A.; de Greef, M. *Synthesis* **2003**, 1471. (d) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168. (e) Lee, D.; Sello, J. K.; Schreiber, S. L. *Org. Lett.* **2000**, *2*, 709.

(7) For selected examples, see: (a) Togo, H.; Iida, S. *Synthesis* **2006**, 2159. (b) Ren, Y. M.; Cai, C. *Synth. Commun.* **2007**, *37*, 2209. (c) Ren, Y. M.; Cai, C. *Catal. Lett.* **2007**, *118*, 134. (d) Ren, Y. M.; Cai, C. *Tetrahedron Lett.* **2008**, *49*, 7110.

(8) (a) *Multicomponent Reaction*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, Germany, 2005. (b) Ren, Y. M.; Cai, C. *Catal. Commun.* **2008**, *9*, 1017. (c) Ren, Y. M.; Cai, C. *Monatsh. Chem.* **2009**, *140*, 49.

(9) Zeng, L. Y.; Ren, Y. M.; Cai, C. Unpublished work.

CC9000983