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PII: S0040-4039(13)01290-2
DOI: http://dx.doi.org/10.1016/j.tetlet.2013.07.122
Reference: TETL 43320

To appear in: *Tetrahedron Letters*

Received Date: 27 June 2013
Revised Date: 19 July 2013
Accepted Date: 23 July 2013

Please cite this article as: Jalani, H.B., Pandya, A.N., Pandya, D.H., Sharma, J.A., Sudarsanam, V., Vasu, K.K., An efficient one-pot synthesis of functionally diverse 2-aminothiazoles from isothiocyanates, amidines/guanidines and halomethylenes, *Tetrahedron Letters* (2013), doi: http://dx.doi.org/10.1016/j.tetlet.2013.07.122

An efficient one-pot synthesis of functionally diverse 2-aminothiazoles from isothiocyanates, amidines/guanidines and halomethylenes†

Hitesh B. Jalani, Amit N. Pandya, Dhaivat H. Pandya, Jayesh A. Sharma, V. Sudarsanam, Kamala K. Vasu*

Department of Medicinal Chemistry, B. V. Patel Pharmaceutical Education and Research Development (PERD) Centre, Sarkhej-Gandhinagar Highway, Thaltej, Ahmedabad-380 054, Gujarat, India.

† Communication Ref. No.: PERD-130613

*Corresponding author. Tel.: +91 79 27439375; Fax: +91 79 27450449;
e-mail: kamkva@gmail.com,

Abstract: An efficient one-pot method for the synthesis of 2-aminothiazoles using simple starting materials like isothiocyanates, amidines/guanidines and various halomethylenes is reported. The synthesis of 2-aminothiazoles involves reactions such as nucleophilic addition, S-alkylation and intramolecular nucleophilic substitution in which amines departs as the leaving group.

Keywords: 2-aminothiazoles, isothiocyanates, amidines, guanidines, one-pot reaction.

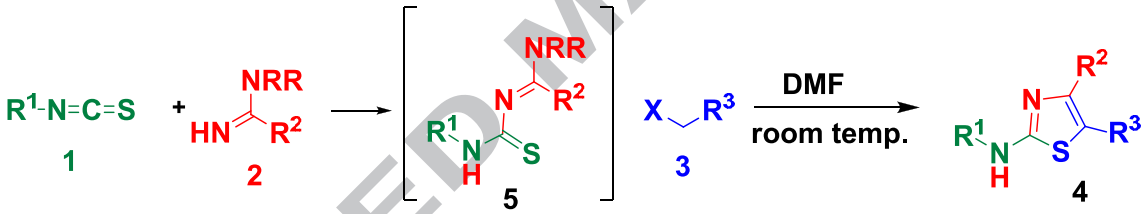
2-Aminothiazole is an important and classic heterocyclic scaffold used in the drug discovery programs. The broad spectrum biological activities exhibited by this structure include anticancer,[1] antiviral,[2] antibacterial,[3] antiprion,[4] and psychotropic activities[5] that assign it as an indispensible heterocyclic feature in drug design. In addition to this, recently, our group has successfully employed 2-aminothiazole scaffolds in the design of anti-inflammatory agents[6] as well as adenosine receptor antagonist.[7] Recently, 2-aminothiazole analogues have been identified as druglike candidates in the treatment of diabetes[8] and *mycobacterium tuberculosis*.[9] Apart from biological properties, films of conjugated polyaminothioazole have recently been demonstrated to have electrochemical properties with high thermal stability.[10] All the above described biological and physico-chemical properties of aminothioazole are probably due to its small ring structure with π excessive and π deficient properties, due to nitrogen atom behaving as hydrogen bond acceptor site.

In view of diverse biological and physico-chemical properties by 2-aminothiazoles scaffold, many synthetic protocols have been reported for their synthesis, which includes Hantzsch's cyclocondensation of thiourea with α-haloketones/α-tosylketone[11] and the reactions of α-thiocyanate carbonyl compounds with aromatic or aliphatic amine hydrochlorides.[12] 2-aminothiazoles are also synthesized by one-pot reaction of enolizable ketones with a mixture of N-bromosuccinimide, thiourea, and benzoyl peroxide,[13] as well as through the reaction of amidinothioureas with halomethylenes[6] in multistep synthesis.

In continuation of our work on the development of efficient protocols for the synthesis of various biologically interesting heterocyclic compounds from simple starting materials like isothiocyanates and amidines/guanidines,[14,15] we have been working on the reaction of various isothiocyanates with amidines/guanidines to produce functionally diverse adducts, known as amidinothioureas and guanidinothioureas. These amidinothioureas and guanidinothioureas adducts were further explored for the synthesis of thiazole,[16] imidazole,[17] triazine,[18] triazole[19] and recently 1,2,4-oxadiazole[20] using either multistep or one-pot synthesis. Earlier, we reported multistep process for the preparation of substituted thiazoles and their use as potential anti-inflammatory agents.[6,21] Despite of some methods published which are mild and high yielding,[22] the present protocol describes one-pot synthesis with structural diversity. In order to simplify the process and to obtain new derivatives of 2-aminothiazoles, we wish to demonstrate the extended development of highly functionalized 2-aminothiazoles in a one-pot, multicomponent process from simple starting materials which proceeds in good to excellent yields.

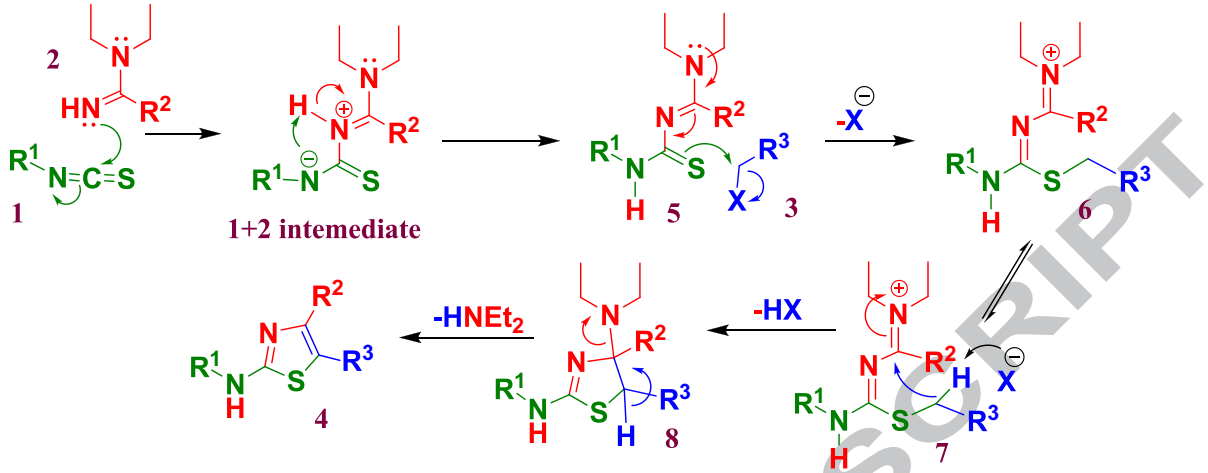
We report herein, a sequential multicomponent reaction leading to diverse 2-aminothiazoles **4**, by reacting different isothiocyanates **1** with amidines/guanidines **2** and halomethylene compounds **3** in one-pot to furnish **4** with good to excellent yields (Scheme 1).

Scheme 1. One-pot synthesis of 2-aminothiazoles.



In order to check the feasibility of thiazole formation in one-pot manner, we carried out the sequential reaction of phenyl isothiocyanate **1a** and benzamidine **2a** in DMF at ambient temperature, which resulted in the intermediate amidinothiourea **5.** This intermediate was further reacted with phenacyl bromide **3a** to give the desired 2-aminothiazole **4a**, which has different R_f value from starting materials as well as characteristic yellow spot on thin layer chromatography. Further work-up of this reaction gave the yellow solid[23]. The structure of this compound was confirmed by ^{1}H-NMR, and mass spectroscopy (Table 1). The present protocol, useful for the synthesis of various trisubstituted thiazoles bearing amino group at the 2nd position, is quite efficient (high yield) and concise (one-pot, as compared to our earlier reported protocol[6,7]) to furnish the functionally diverse 2-aminothiazoles compounds library.

Scheme 2. Plausible reaction mechanism of 2-aminothiazole formation



The plausible reaction mechanism for the formation of these trisubstituted thiazoles are described in Scheme 2. The synthesis of various isothiocyanates and amidine/guanidines **2** are well documented in the literature.[20] Nucleophilic addition of amidines **2** to the isothiocyanate results into the formation of adduct known as amidinothioureas **5** (in the case of guanidine it is referred to as guanidinothioureas). The intermediate **5** being a thiourea derivative, has one dominant nucleophilic (C=S) site and one electrophilic (C-NEt_2) site. The highly polar C-Br bond of phenacyl bromide is facile towards the nucleophilic attack of sulfur resulted into S-alkylation to give species **6**. Now the methylene group being acidic in nature attacks the electron deficient imine carbon (to which electron pulling quaternary nitrogen is attached and thus this carbon a strong electrophile) to give the intermediate **7**. This intermediate further undergoes cyclization to **8** in a *5-exo-trig* manner. This intermediate now could be stabilized by gaining the aromatic property through the removal of diethyl amine and hydrogen bromide resulting into the desired 2-aminothiazoles **4**. During the course of study, it was observed that the reaction of bromomethylenes furnished good yield (**4b, c, d, l, t**).

INSERT TABLE-1 HERE

In conclusion, we have demonstrated an efficient one-pot method for the synthesis of disubstituted-2-aminothiazoles from simple starting materials like aryl and alkoxyl isothiocyanate, amidine/guanidine and various halomethylenes to produce the tri-substituted thiazoles in good to excellent yields. The present method is attractive due to its facile conditions suggesting this protocol could be an alternative to other protocols. The product can be isolated very easily with or without the use of chromatography. Being characterized by three points of diversity, the novel chemotypes are rapidly assembled in just one operationally friendly step and the methodology proved to be general and tolerates a wide range of functional groups.

Acknowledgements

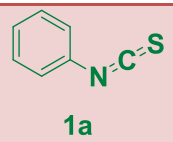
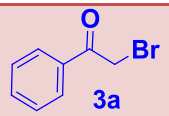
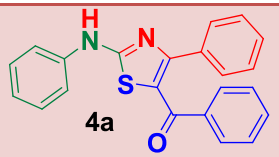
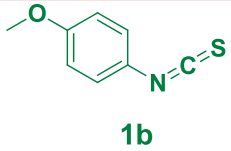
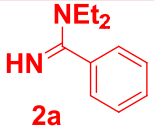
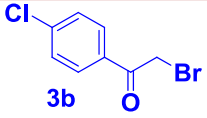
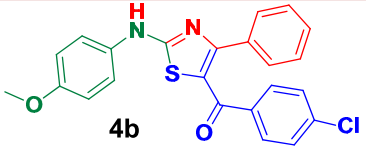
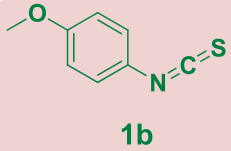
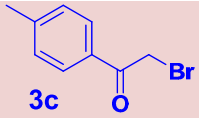
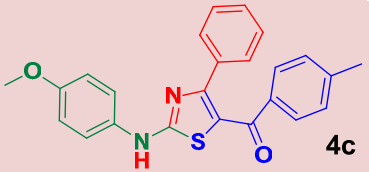
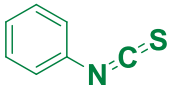
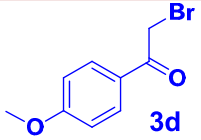
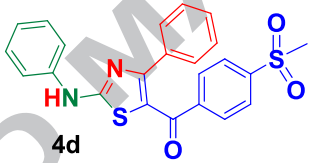
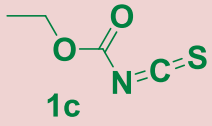
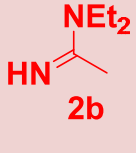
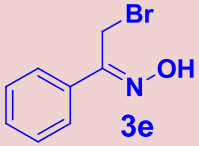
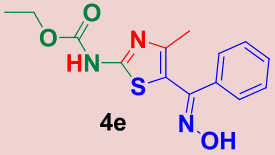
We gratefully acknowledge the financial support for this work from B.V. Patel PERD centre. H. B. J thanks the Industrial Commissioner (IC) of Gujarat for the grant provided to carry out research work. We thank Dr. Manish Nivsarkar and Prof. C.J. Shishoo Directors of B.V. Patel PERD centre, for their constant encouragement and support.

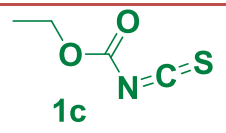
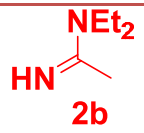
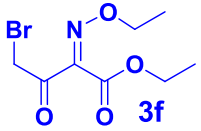
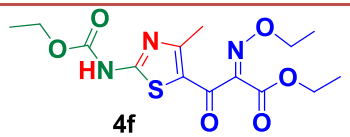
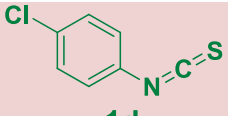
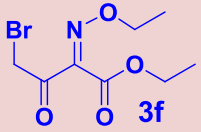
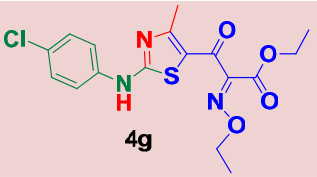
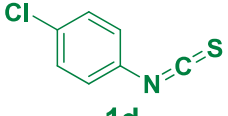
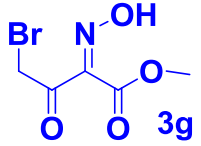
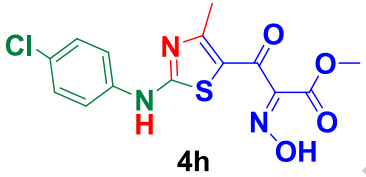
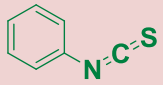
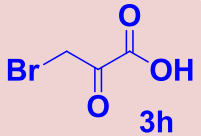
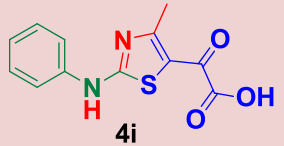
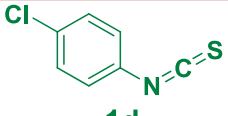
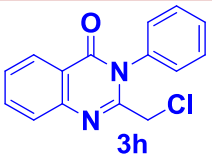
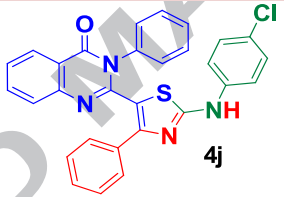
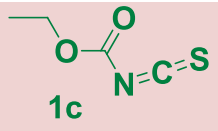
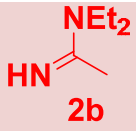
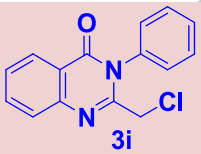
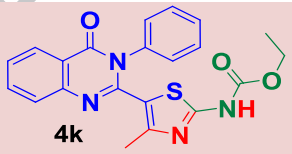
References and Notes

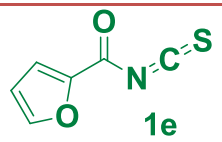
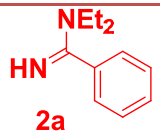
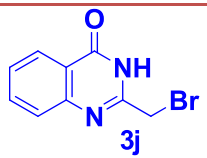
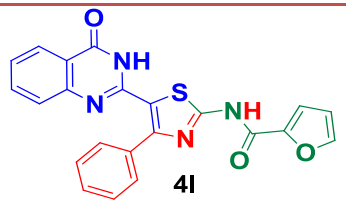
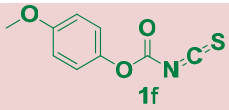
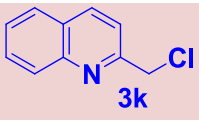
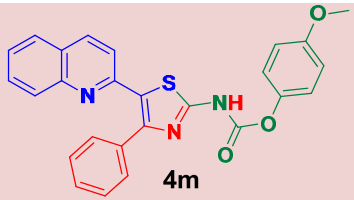
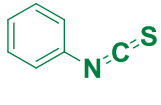
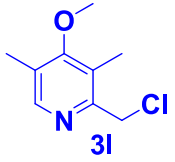
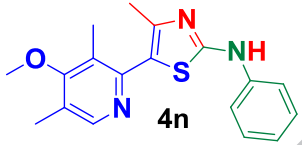
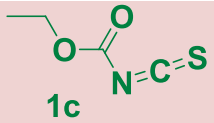
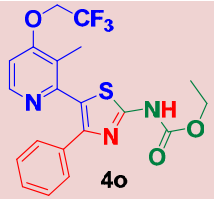
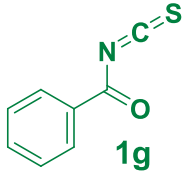
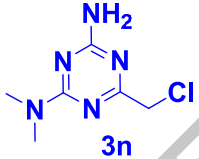
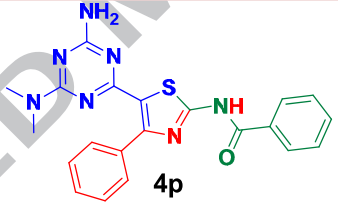
1. Smith, B.; Chang, H-H.; Medda F.; Gokhale, V.; Dietrich, J.; Davis, A.; Meuillet, E.; Hulme, C. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3567.
2. (a) Liu, C.; Phadke, A.; Wang, X.; Zhang, S. PCT Int. Appl., WO 2009149436 A1 20091210, 2009.; (b) Liebig, H.; Pfetzing, H.; Grafe, A. *Arzneimittel-Forschung* **1974**, *24*, 887.
3. (a) Thomas, K. K.; Reshmy, R. *Asian J. Chem.* **2008**, *20*, 1457; (b) More, P. G.; Bhalvankar, R. B. *J. Indian Chem. Soc.* **2006**, *83*, 113; (c) Ming, Z.; Zhen-Feng, C.; Hong, L.; Shao-Ming, S. *Guangxi Shifan Daxue Xuebao, Ziran Kexueban* **2002**, *20*, 42.
4. Ghaemmaghami, S.; May, B. C. H.; Renslo, A. R.; Prusiner, S. B. *J. Virol.* **2010**, *84*, 3408.
5. Zablotskaya, A.; Segal, I.; Germane, S.; Shestakova, I.; Domracheva, I.; Nesterova, A.; Geronikaki, A.; Lukevies, E. *Chem. Heterocycl. Compd.* **2002**, *38*, 859 (New York, USA). 6. (a) Xavier, F. P., Pillai, A. D., Rathod, P. D., Yerande, S. G., Nivsarkar, M., Padh, H., Sudarsanam, V., Vasu, K. K., *Eur. J. Med. Chem.,* **2008**, *43*, 129; (b) Inamdar, G. S.; Pandya, A. N.; Thakar, H. M.; Sudarsanam, V.; Kachler, S.; Sabbadin, D.; Moro, S.; Klotz, K-N.; Vasu, K. K. *Eur. J. Med. Chem.,* **2013**, *63*, 924-934.
7. Scheiff, A. B., Yerande, S. G., El-Tayeb, A., Li, W., Inamdar, G. S., Vasu, K. K., Sudarsanam, V., Muller, C. E, *Bioorg. Med. Chem.* **2010**, *18*, 2195.
8. Zhang, A.; Xiong, W.; Hilbert, J. E.; DeVita, E. K.; Bidlack, J. M.; Neumeyer, J. L. *J. Med. Chem.* **2004**, *47*, 1886.
9. Erion, M. D.; van Poelje, P. D.; Dang, Q.; Kasibhatla, S. R.; Potter, S. C.; Reddy, M. R.; Reddy, K. R.; Jiang, T.; Lipscomb, W. N. *Proc. Natl. Acad. Sci.* **2005**, *102*, 7970.
10. (a) Al-Balas, Q.; Anthony, N. G.; Al-Jaidi, B.; Alnimr, A.; Abbott, G. *PLoS ONE* **2009**, *4*, 5617; (b) Roy, K. K.; Singh, S.; Sharma, S. K.; Srivastava, R.; Chaturvedi, V.; Saxena, A. K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5589.
11. (a) Hantzsch, A. R.; Weber, J. H. *Ber.* **1887**, *20*, 3118; (b) Garcia-Egido, E.; Wong, S. Y. F.; Warrington, B. H. *Lab Chip* **2002**, *2*, 31; (c) Lin, P. Y.; Hou, R. S.; Wang, H.M.; Kang, I. J.; Chen, L. C. *J. Chin. Chem. Soc.* **2009**, *56*, 455; (d) Arutyunyan, S.; Nefzi, A. *J. Comb. Chem.* **2010**, *12*, 315; (e) Kumar, D.; Kumar, N. M.; Patel, G.; Gupta, S.; Varma, R. S. *Tetrahedron Lett.* **2011**, *52,* 1983.
12. (a) Baily, N.; Dean, A. W.; Judd, D. B.; Middlemiss, D.; Storer, R.; Watson, S. P. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1409; (b) Kearney, P. C.; Fernandez, M. *J. Org. Chem.* **1998**, *63*, 196; (c) Rudolp, J. *Tetrahedron* **2000**, *56*, 3161; (d) Schantl, J. G.; Lagoja, I. M. *Synth. Commun.* **1998**, *28*, 1451; (d) Aoyama, T.; Murata, S.; Arai, I.; Araki, N.; Takido, T.; Suzuki, Y.; Kodomari, M. *Tetrahedron* **2006**, *62*, 3201.
13. Dahiya, R.; Pujari, H. K. *Indian J. Chem.* **1986**, *25B*, 966.

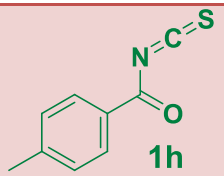
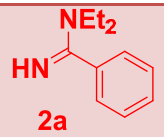
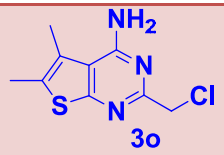
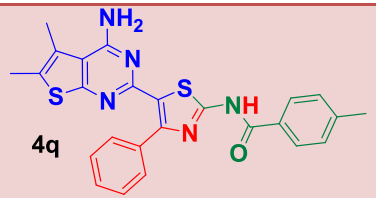
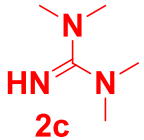
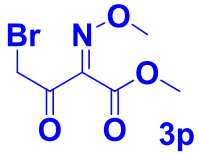
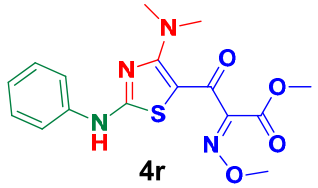
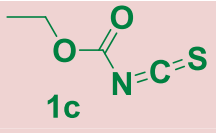
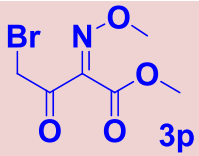
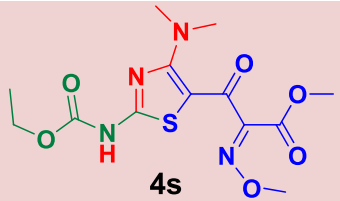
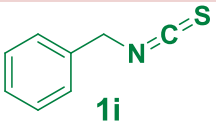
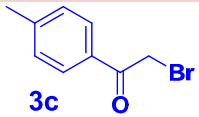
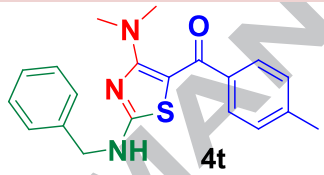
14. Cruzer, F. *J. Chem. Soc.* **1956**, 2345.
15. Rajappa, S.; Advani, B. G. *Indian J. Chem.* **1970**, *8*, 1145.
16. (a) Franklin, P. X.; Pillai, A. D.; Rathod, P. D.; Yerande, S.; Nivsarkar, M.; Padh, H.; Vasu, K. K.; Sudarsanam, V. *Eur. J. Med. Chem.* **2008**, *43*, 129. (b) Sudarsanam, V.; Giordano, A.; Vasu, K. K.; Thakar, H. M.; Giri, R. S.; Yerande, S.; Inamdar, G. S. WO 2006148113, **2007**; *Chem. Abstr.* **2007**, *147*, 469324 (c) Giordano, A.; Vasu, K. K.; Thakar, H. M.; Giri, R. S.; Yerande, S.; Inamdar, G. S.; Sudarsanam, V. US 20090306073, **2009**.
17. (a) Kaila, J. C.; Baraiya, A. B.; Pandya, A. N.; Jalani, H. B.; Vasu, K. K.; Sudarsanam, V. *Tetrahedron Lett.* **2009**, *50*, 3955. (b) Kaila, J. C.; Baraiya, A. B.; Vasu, K. K.; Sudarsanam, V. *Tetrahedron Lett.* **2008**, *49*, 7220.
18. Kaila, J. C.; Baraiya, A. B.; Pandya, A. N.; Jalani, H. B.; Vasu, K. K.; Sudarsanam, V. *Tetrahedron Lett.* **2010**, *51*,1486.
19. Kaila, J. C. *Ph.D. Thesis*; Bhavnagar University: Gujarat, India, **2009**.
20. Jalani, H. B.; Sudarsanam, V., Vasu, K. K.; *Synthesis,* **2012**, *44*, 3378.
21. Giri, R. S., Thaker, H. M., Giordano, T., Chen, B., Nuthalapaty, S., Vasu, K. K., Sudarsanam, V. *Eur. J. Med. Chem.* **2010**, *45*, 3558.
22. (a) Nefzi, A.; Arutyunyan, S. *Tetrahedron Lett.* **2010**, *51*, 4797; (b) Potewar, T. M.; Ingale, S. A.; Srinivasa, K. V. *Tetrahedron* **2008**, *64*, 5019.
23. *General experimental procedure for the preparation of 2-aminothiazoles:* To a hot air dried round bottom flask, containing solution of isothiocyanate (2.0 mmol) and DMF (5 mL), amidine/guanidine (2.0 mmol) was added at 20-25 ^{0}C temperature and the solution was stirred for 2-3 h. To the above solution, halomethylene compound (2.0 mmol) in DMF (5 mL) was added at ambient temperature and it was further maintained for 8-24 h with stirring. (in the case of chloro compounds, reaction was warmed to 40-45 ^{0}C). Progress of the reaction was monitored by TLC using ethyl acetate/hexane (2:8). After the completion of reaction, the reaction mixture was poured into ice. Upon stirring, precipitate was observed (in the case of no precipitation, reaction mass was extracted with either dichloromethane or ethyl acetate) which were collected through Buchner funnel. These precipitates were then dissolved in either dichloromethane or ethyl acetate and dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residues were further subjected to purification either by chromatography or by treating with hexane and/or ether to give the pure compounds (**4a-t**).

Table-1: One-pot synthesis of 2-aminothiazoles from isothiocyanates, amidines/guanidines and halomethylenes

Entry	Isothiocyanate (1)	Amidine/ Guanidine(2)	Halomethylene (3)	2-aminothiazole (4)	Yield (%)[a] & Melting range (^{o}C)	^{1}H-NMR & LC-MS Spectrum data[b]
1	 1a	 2a	 3a	 4a	68 (192-194)	**^{1}H NMR ($CDCl_3$)** = 6.91-6.93 (d, 2H), 6.99-7.10 (m, 3H), 7.15-7.17 (d, 2H), 7.20-7.29 (m, 3H), 7.34-7.36 (d, 2H), 7.39-7.48 (m, 3H), 8.69 (s, 1H). Mol. Wt. = 356.44, Found = 357.0.
2	 1b	 2a	 3b	 4b	89 (187-189)	**^{1}H NMR ($CDCl_3$)** 3.81 (s, 3H), 6.81-6.86 (d, 4H), 7.02-7.11 (m, 3H), 7.14-7.16 (d, 2H), 7.26-7.28 (d, 2H), 7.36-7.38 (d, 2H), 8.96 (s, 1H). Mol. Wt. = 420.91, Found = 422.0.
3	 1b	 2a	 3c	 4c	79 (154-157)	**^{1}H NMR ($CDCl_3$)** = 2.24 (s, 3H,), 3.81 (s, 3H), 6.85-6.91 (d, 4H), 7.04-7.14 (m, 3H), 7.18-7.20 (d, 2H), 7.31-7.33 (d, 2H), 7.39-7.41 (d, 2H), 8.49 (s, 1H). Mol. Wt. = 400.49, Found = 401.0.
4	 1a	 2a	 3d	 4d	76 (214-216)	**^{1}H NMR ($CDCl_3$)** = 3.10 (s, 3H,), 7.02-7.11 (m, 3H), 7.20-7.30 (m, 3H), 7.40-7.44 (m, 2H), 7.51-7.60 (m, 6H), 11.06 (s, 1H). Mol. Wt. = 434.53, Found = 436.0.
5	 1c	 2b	 3e	 4e	68 (224-226)	**^{1}H NMR ($CDCl_3$)** = 1.22-1.28 (t, 3H,), 1.84 (s, 3H), 4.21-4.32 (q, 2H), 7.39-7.56 (m, 5H), 11.81 (s, 1H), 11.83 (s, 1H). Mol. Wt. = 305.35, Found = 357.40.

6	 1c	 2b	 3f	 4f	71 (153-156)	**^{1}H NMR ($CDCl_3$)** = 1.32-1.46 (m, 9H,), 2.73 (s, 3H), 4.30-4.49 (m, 6H), 10.90 (s, 1H). Mol. Wt. = 357.38, Found = 358.0.
7	 1d	 2b	 3f	 4g	70 (249-251)	**^{1}H NMR (DMS0-d_6)** = 1.23-1.27 (t, 3H,), 1.31-1.36 (t, 3H), 2.59 (s, 3H), 4.26-4.38 (m, 4H), 7.38-7.40 (d, 2H), 7.61-7.63 (d, 2H), 11.09 (s, 1H). Mol. Wt. = 395.86, Found = 396.0.
8	 1d	 2b	 3g	 4h	70 (>270°C)	**^{1}H NMR ($CDCl_3$)** = 2.47 (s, 3H,), 2.50 (s, 3H), 7.43-7.45 (d, 2H), 7.65-7.67 (d, 2H), 11.20 (s, 1H), 11.81 (s, 1H). Mol. Wt. = 353.78, Found = 354.50.
9	 1a	 2b	 3h	 4i	78 (249-251)	**^{1}H NMR (DMS0-d_6)** = 2.14 (s, 3H,), 7.21-7.27 (m, 1H), 7.39-7.41 (d, 2H), 7.49-7.51 (d, 2H), 11.46 (s, 1H), 12.48 (s, 1H). Mol. Wt. = 262.28, Found = 263.0.
10	 1d	 2a	 3h	 4j	61 (>270°C)	**^{1}H NMR (DMS0-d_6)** = 6.59-6.61 (d, 2H), 7.07-7.84 (m, 15H), 8.33-8.35 (d, 1H), 9.39 (s, 1H). Mol. Wt. = 507.00, Found = 507.0.
11	 1c	 2b	 3i	 4k	59 (249-252)	**^{1}H NMR (DMS0-d_6)** = 1.25-1.32 (t, 3H), 2.36 (s, 3H,), 4.21-4.29 (q, 2H), 7.22-7.84 (m, 8H), 8.33-8.35 (d, 1H), 10.75 (s, 1H). Mol. Wt. = 406.45, Found = 407.0.

12	 1e	 2a	 3j	 4l	76 (>270°C)	**^{1}H NMR (DMS0-d_6)** = 6.76-6.78 (d, 1H), 7.34-7.62 (m, 6H), 7.69-8.10 (m, 5H), 12.19 (s, 1H), 13.09 (s, 1H). Mol. Wt. = 414.43, Found = 415.0.
13	 1f	 2a	 3k	 4m	72 (179-182)	**^{1}H NMR (DMS0-d_6)** = 3.90 (s, 3H), 6.79 (s, 1H), 6.90-6.92 (d, 2H), 7.10-7.13 (d, 2H), 7.25-8.11 (m, 9H). Mol. Wt. = 453.51, Found = 454.0.
14	 1a	 2b	 3l	 4n	64 (178-181)	**^{1}H NMR (CDCl$_3$)** = 2.20 (s, 3H,), 2.40 (s, 3H,), 2.45 (s, 3H,), 3.90 (s, 3H), 7.30-7.50 (m, 6H), 8.30 (s, 1H). Mol. Wt. = 325.42, Found = 326.0.
15	 1c	 2a	 3m	 4o	73 (169-171)	**^{1}H NMR (CDCl$_3$)** = 1.15-1.20 (t, 3H,), 1.82 (s, 3H), 4.12-4.18 (q, 2H), 4.38-4.46 (q, 2H), 6.73-6.75, (d, 1H,), 7.22-7.28 (m, 3H), 7.37-7.42 (m, 2H), 8.50-8.52 (d, 1H), 9.58 (s, 1H). Mol. Wt. = 437.43, Found = 338.0.
16	 1g	 2a	 3n	 4p	69 (>270°C)	**^{1}H NMR (CDCl$_3$)** = 2.60 & 2.93 (s, 6H,), 6.94 (s, 2H), 7.31-8.13 (m, 10H), 9.50 (s, 1H). Mol. Wt. = 417.48, Found = 418.0.

17	 1h	 2a	 3o	 4q	62 (>270°C)	**^{1}H NMR ($CDCl_3$)** = 2.42 (s, 3H,), 2.46 (s, 3H,), 2.52 (s, 3H,), 6.85 (s, 2H), 7.33-7.87 (m, 9H), 9.62 (s, 1H). Mol. Wt. = 371.59, Found = 472.0.
18	 1a	 2c	 3p	 4r	68 (180-182)	**^{1}H NMR ($CDCl_3$)** = 3.07 (s, 6H), 3.88 (s, 3H), 4.04 (s, 3H), 7.13-7.51 (m, 5H), 7.88 (s, 1H). Mol. Wt. = 362.40, Found = 363.00.
19	 1c	 2c	 3p	 4s	65 (158-160)	**^{1}H NMR ($CDCl_3$)** = 1.25-1.37 (t, 3H,), 3.13 (s, 6H), 3.88 (s, 3H), 4.12 (s, 3H), 4.28-4.35 (q, 2H), 8.49 (s, 1H). Mol. Wt. = 358.37, Found = 358.40.
20	 1i	 2c	 3c	 4t	76 (164-167)	**^{1}H NMR ($CDCl_3$)** = 2.39 (s, 3H), 3.09 (s, 6H), 4.40-4.41 (d, 2H), 5.86-5.88 (t, 1H), 7.18-7.20 (d, 2H), 7.31-7.35 (m, 5H), 7.63-7.65 (d, 2H). Mol. Wt. = 351.46, Found = 352.50.

[a] Yields refer to isolated products. Melting points are uncorrected. [b] LC-MS analysis M^{+1} at m/z.

An efficient one-pot synthesis of functionally diverse 2-aminothiazoles from isothiocyanates, amidines/guanidines and halomethylenes

Hitesh B. Jalani, Amit N. Pandya, Dhaivat H. Pandya, Jayesh A. Sharma, V. Sudarsanam and Kamala K. Vasu*