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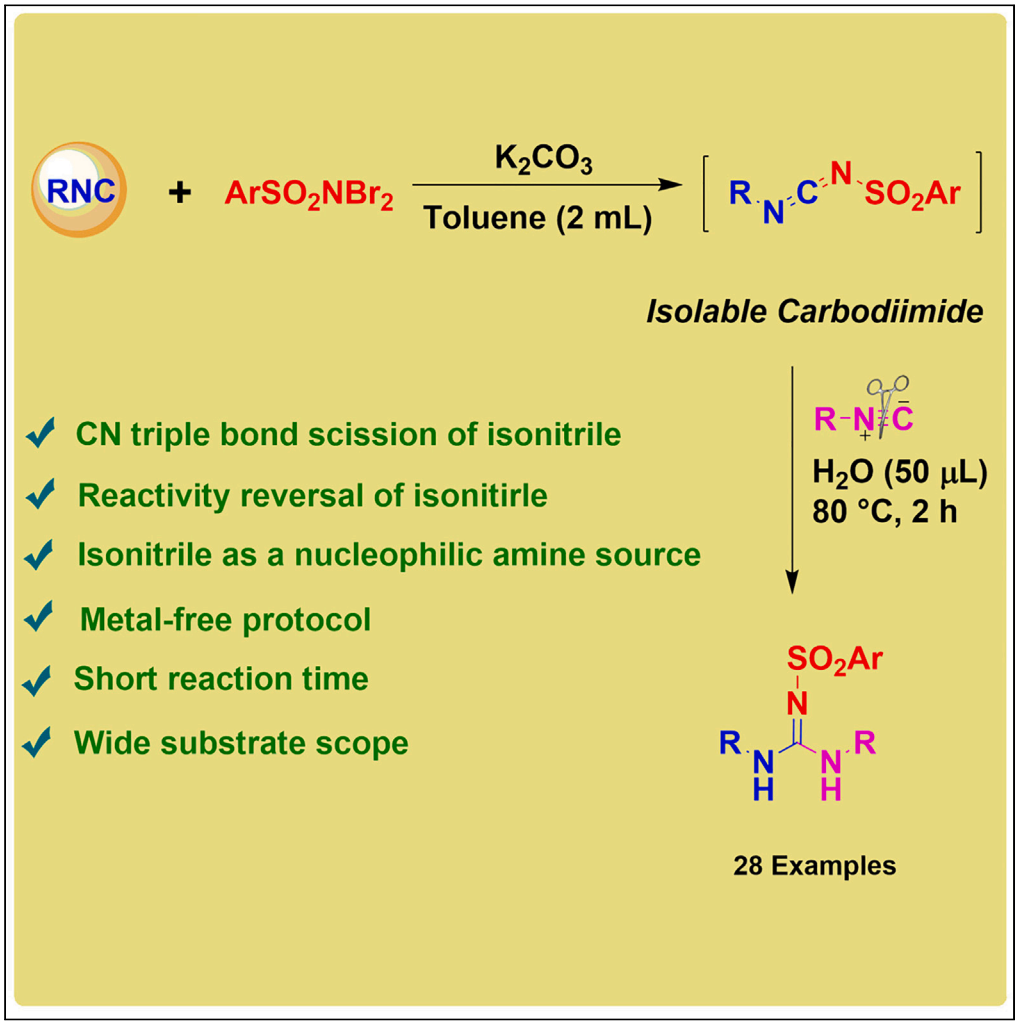

Debashish Mishra, Sagarika Rajkhowa, Prodeep Phukan

pphukan@gauhati.ac.in

Highlights

Metal-free protocol for synthesis of symmetrical sulfonyl guanidine

Reactivity reversal of isonitrile & use of isonitrile as amine source

Cleavage of C≡N bond of isonitrile

The *in-situ* generated isolable carbodiimide intermediate

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Unanticipated switch of reactivity of isonitrile via N≡C bond scission: Cascade formation of symmetrical sulfonyl guanidine

Debashish Mishra,[1] Sagarika Rajkhowa,[1] and Prodeep Phukan[1,2,*]

SUMMARY

Unanticipated formation of symmetrical sulfonyl guanidine was observed while treating isonitriles with *N,N*-dibromoarylsulfonamides in absence of an external amine source. Interesting feature of this work is that one molecule of isonitrile initially reacts with dibromoarylsulfonamide via the C-end to produce the intermediate carbodiimide while the other molecule undergoes C≡N triple bond cleavage to react as amine source with the intermediate. This switch of reactivity from C-center to N-center of the isonitrile generated symmetrical guanidine.

INTRODUCTION

The Guanidine derivatives have received momentous attention over the past decades due to their immense medicinal and therapeutic applicability.[1–4] Presence of guanidine moiety in arginine containing compound and many other biologically active substances makes them attractive for synthetic as well as medicinal chemists. Relenza, Famotidine, Clonidine etc. are extensively used as antiviral, antiulcer, and anesthetic drugs, respectively.[5,6] In addition, guanidine derivatives also act as catalysts, organoligands, superbases, and superpotent sweeteners.[7–9] In view of their importance and usefulness, the development of an efficient pathway for the synthesis of symmetrical tri-substituted guanidine has attracted great interest from organic as well as medicinal chemists.

Due to their diverse applicability, chemists have already developed a number of methods for the synthesis of substituted guanidines. Classical approach for the synthesis of guanidine involves a reaction of amine with guanylating agents such as thiourea, isothiourea, amidine, cyanamide, and carbodiimide.[2,3,10] Among the existing methods for the synthesis of substituted guanidine, the guanylation of amines with electrophilic carbodiimides attract most.[11–24] However, carbodiimide synthesis requires tedious and strict conditions along with a transition metal catalyst.[25–32] Recently, a few approaches were developed for the synthesis of sulfonyl guanidines (Scheme 1). In most cases, the involvement of a transition metal catalyst is necessary for the generation of carbodiimide intermediate which on further treatment with an amine result in the formation of sulfonyl guanidine (Scheme 1A).[33–35] A cobalt catalyzed oxidative isocyanide insertion reaction of amines was also developed by Ji et al. for the same purpose (Scheme 1B).[36]

In 2019, Ji's group also reported a cobalt-catalyzed cascade reaction of sulfonyl azides with *o*-diisocyanoarenes and anilines for the synthesis of sulfonyl guanidines. In this case, *o*-diisocyanoarenes act as a source for C1-fragment of the guanidine product (Scheme 1C).[37] Although various methods have been developed, most of the reported methods for the synthesis of sulfonyl guanidine via carbodiimide intermediate require a transition metal catalyst system or oxidative reaction conditions and extra amine as a nucleophilic source. Moreover, there are only a few methods for the synthesis of symmetrical guanidine. Therefore, development of an efficient metal-free protocol for the synthesis of symmetrical sulfonyl guanidine is highly desirable in the context of synthetic chemistry.

The cleavage of C≡N bond is a challenging task as it is regarded as one of the strongest chemical bonds. The metalloenzyme molybdenum nitrogenase was found to catalyze reductive cleavage of the C≡N bond of nitrile.[38] During the last several decades, carbon-nitrogen bond cleavage of nitrile has been demonstrated by using different transition metal reagents and catalysts.[39–43] However, similar breakthrough was not achieved for C≡N bond of isonitrile until Yamashita reported the use of a diborane reagent in the year 2014. They established that the use of an unsymmetrical diborane reagent facilitates the cleavage of isonitrile carbon-nitrogen triple bond (Scheme 1D).[44] Besides this report there is no method in the

[1]Department of Chemistry, Gauhati University, Guwahati, Assam 781014, India

[2]Lead contact

*Correspondence: pphukan@gauhati.ac.in

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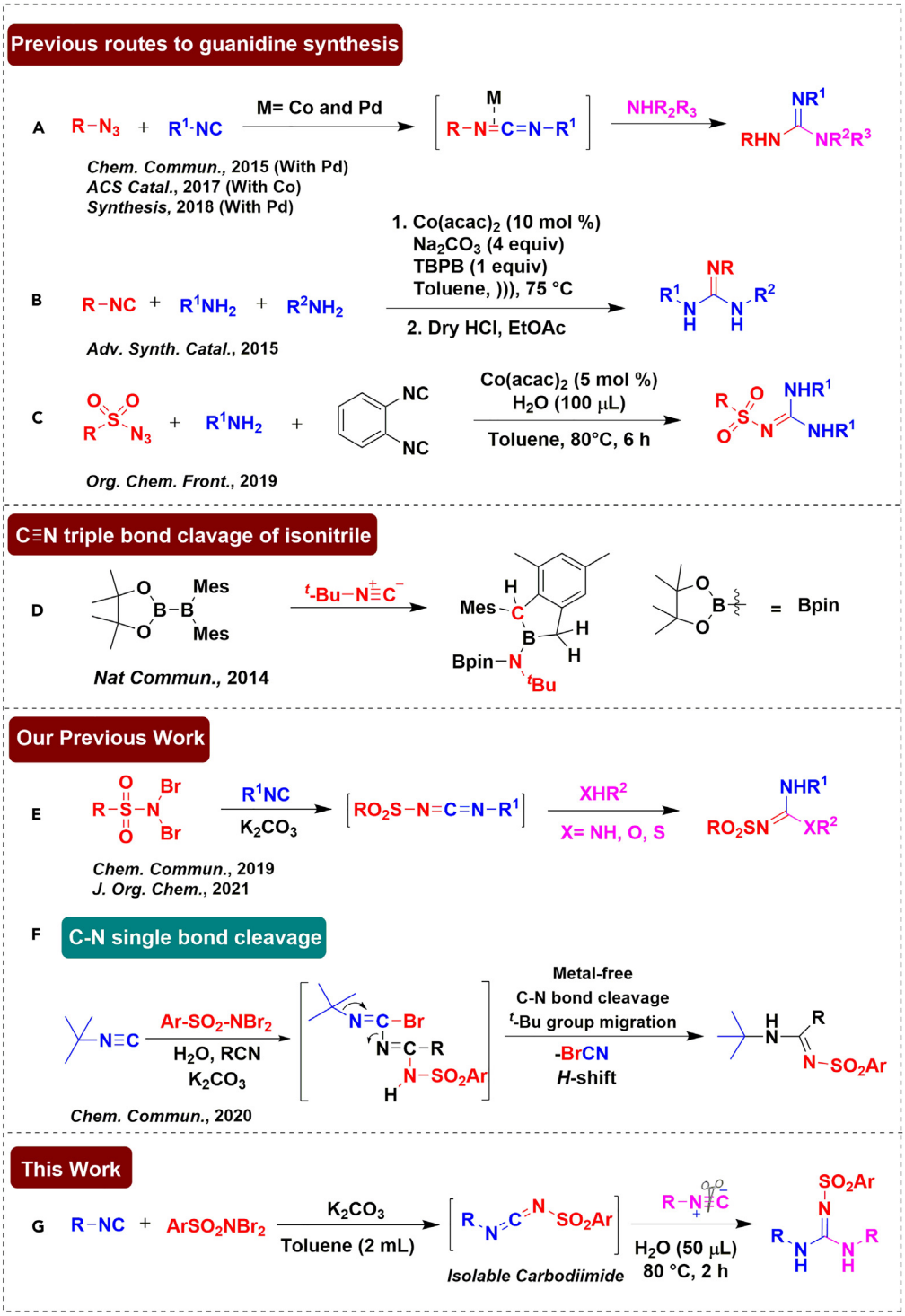


Scheme 1. Synthesis of sulfonyl guanidine and N≡C bond scission

literature for the N≡C bond scission of isonitrile. Recently, we have developed few metal-free protocols where *in-situ* generated carbodiimides were used as an intermediate for generation of organo-nitrogen compounds such as guanidine, isourea and isothiourea (Scheme 1E), and amidine.[45,46] In one instance, we observed simultaneous cleavage of the C–N single bond of isonitrile and 1,3-migration of the *tert*-butyl counterpart to the adjacent nitrogen atom (Scheme 1F).[47]

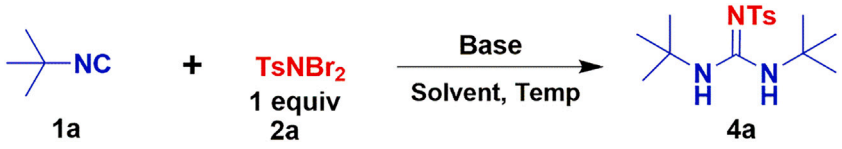
N,N-Dibromoarylsulfonamides are an important class of organic reagents used in various organic transformations.[48–60] In continuation of our effort in the development of synthetic methods with such reagents, herein, we disclose a new pathway for complete cleavage of C-N triple bond of isonitrile which leads to the formation of symmetrical guanidines. Interesting feature of this reaction is that in the initial phase, isonitrile works as a source of carbodiimide reacting via C-end of the isonitrile where no cleavage of C≡N bond occurs. However, in the second phase of the reaction, the same isonitrile molecule behaves as a nitrogen source via C≡N bond scission for final formation of symmetrical guanidine.

RESULTS AND DISCUSSION

In order to appraise the optimum conditions, the reaction of *tert*-butyl isocyanide and $TsNBr_2$ was explored by employing various bases and solvents at different temperatures (Table 1).

Initially, the reaction of *tert*-butyl isocyanide (1 equiv) and $TsNBr_2$ (1 equiv) in DCE (2 mL) was carried out in presence of K_2CO_3 (2 equiv). However, the desired product was not obtained after 12 h of reaction at room temperature (Table 1, entry 1). Interestingly, when the same reaction was carried out at 70°C within 6 h, the corresponding symmetrical guanidine was obtained in 40% yield (Table 1, entry 2). A minor increase in reaction yield was observed, when the temperature changes from 70ºC to 80ºC (Table 1, entry 3). When the reaction was carried out in toluene, 46% of the desired product was obtained within 2 h (Table 1, entry 4). To our satisfaction, the addition of a minute amount of water into the reaction system (50 μL), marginally increased the product yield up to 49% within 2 h of reaction at 80°C (Table 1, entry 5). A notable change in the product yield was observed when the reaction was carried out using 1.2 equivalent of *tert*-butyl isocyanide (Table 1, entry 6). Further optimization experiments with varying amounts of *tert*-butyl isocyanide under previous conditions revealed that the use of 2.2 equivalent of *tert*-butyl isocyanide produced the best result with 81% of the desired product (Table 1, entry 9). On lowering the base equivalence, the product yield was found to be diminished (Table 1, entries 11–12). We also screened the reaction with various bases (Table 1, entries 13–15) but the results were found to be inferior.

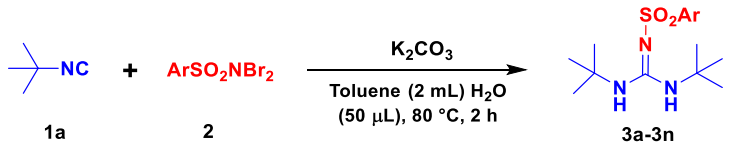
Table 1. Optimization of reaction conditions

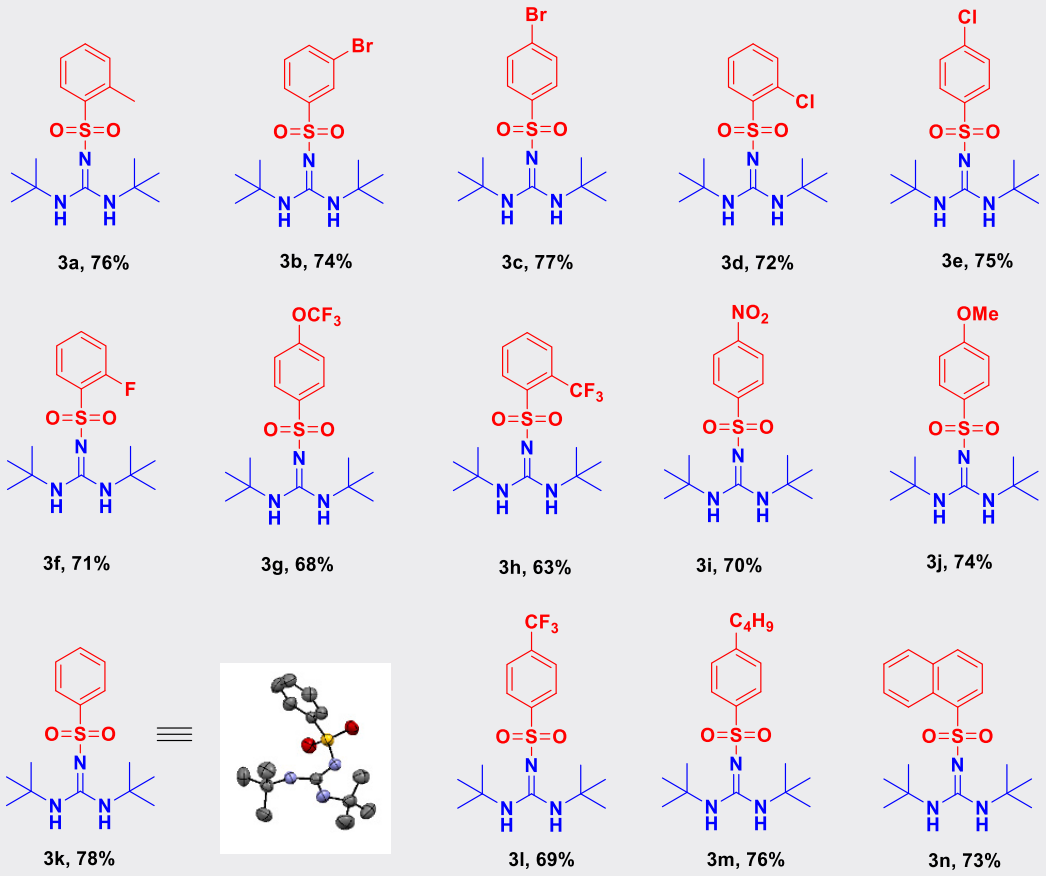


Entry[a]	^{t}BuNC (equiv)	Solvent	Base (equiv)	Time (h)	Temp (ºC)	Yield (%)[b]
1	1	DCE (2 mL)	K_2CO_3 (2)	12 h	RT	–
2	1	DCE (2 mL)	K_2CO_3 (2)	6 h	70	40
3	1	DCE (2 mL)	K_2CO_3 (2)	6 h	80	43
4	1	Toluene (2 mL)	K_2CO_3 (2)	2 h	80	46
5	1	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (2)	2 h	80	49
6	1.2	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (2)	2 h	80	56
7	1.5	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (2)	2 h	80	67
8	2	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (2)	2 h	80	76
9	**2.2**	**Toluene (2 mL) + H_2O (50 μL)**	**K_2CO_3 (2)**	**2 h**	**80**	**81**
10	2.5	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (2)	2 h	80	83
11	2.2	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (1.5)	2 h	80	73
12	2.2	Toluene (2 mL) + H_2O (50 μL)	K_2CO_3 (1)	2 h	80	68
13	2.2	Toluene (2 mL) + H_2O (50 μL)	KF (2)	2 h	80	61
14	2.2	Toluene (2 mL) + H_2O (50 μL)	$KHCO_3$ (2)	2 h	80	56
15	2.2	Toluene (2 mL) + H_2O (50 μL)	Cs_2CO_3 (2)	2 h	80	49

[a]Reaction conditions: **1a** (1.1 mmol), **2a** (0.5 mmol), K_2CO_3 (1 mmol) at 80°C for 2 h.
[b]Isolated yields.

Table 2. Substrate scope of sulfonamides



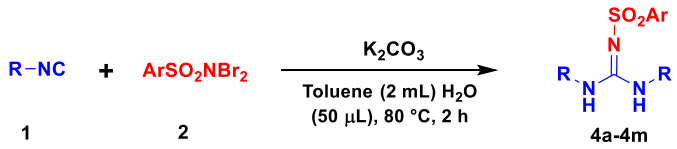


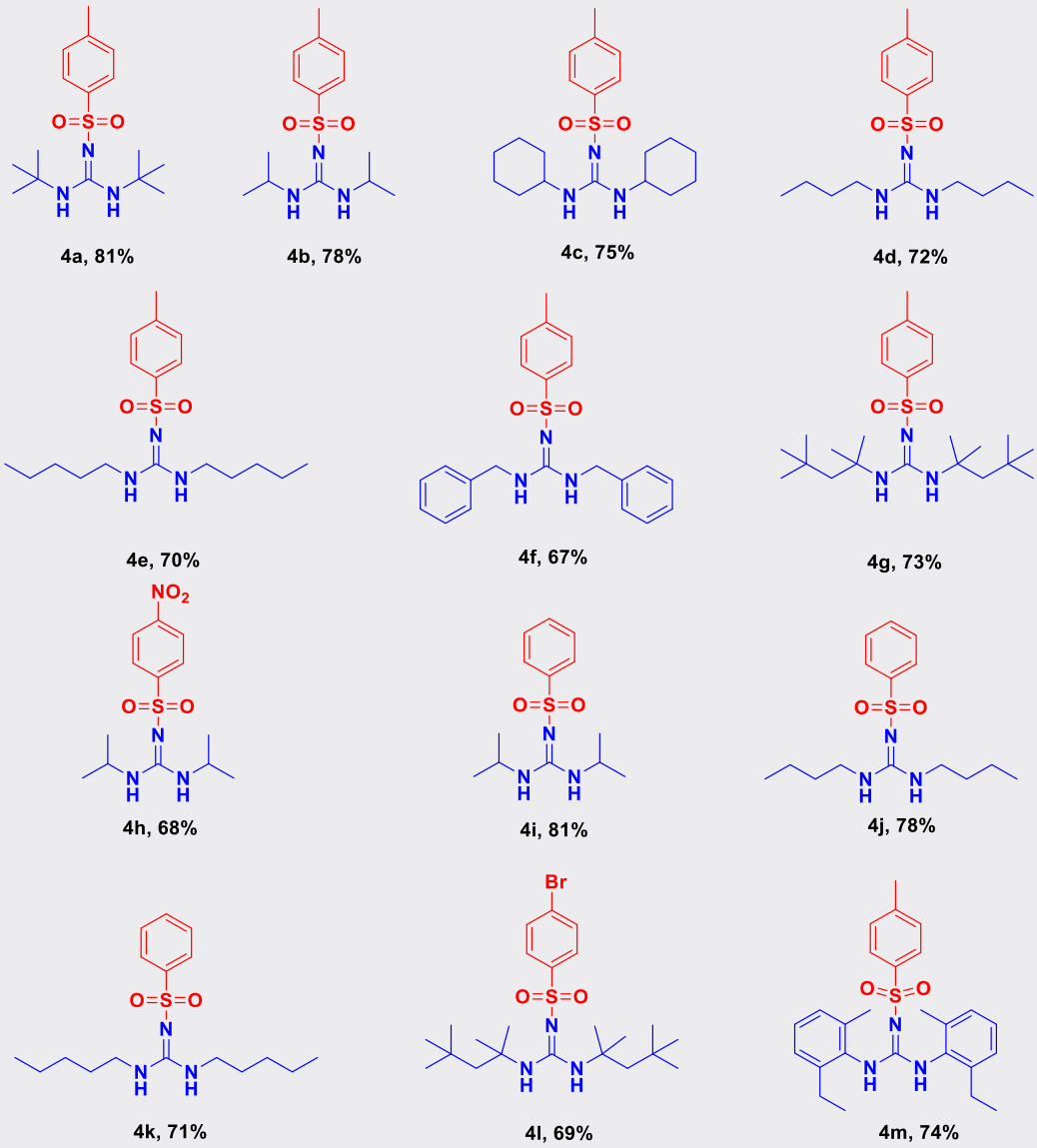
Reaction conditions: 1 (1.1 mmol), 2 (0.5 mmol), K_2CO_3(1 mmol), 80°C, 2 h. Isolated yields.

With the optimized reaction condition in hand, initially, the scope of the reaction was investigated with various substituted sulfonamides. A wide variety of *N,N*-dibromoarylsulfonamides could be transformed using *tert*-butyl isocyanide to the corresponding *N,N´,N´´*-sulfonyl guanidines in moderate to high yields irrespective of the electronic nature and position of the substituents on the aromatic ring of the dibromoarylsulfonamides. From Table 2, a marginal increase in product yield was observed with sulfonamide having electron donating substituent on the benzene ring. The halo functionalities are also well tolerated (F, Cl, and Br) and exhibited high reactivity.

To further explore the diversity of the products, we next investigated the scope of isocyanides under the optimal conditions. Various acyclic and cyclic isocyanides are worked well to furnish the substituted *N,N´,N´´*-sulfonyl guanidine products (Table 3, 4a-4g) in high yields. We have also extended our investigations to check the compatibility of various dibromoarylsulfonamides with different isonitriles. These experiments generated a library of *N,N´,N´´*-sulfonyl guanidines (Table 3, 4h–4L). We have also tested the reaction with an aromatic isocyanide such as 1-ethyl-2-isocyano-4-methylbenzene and interestingly isolated the desired product in high yield (4m, 74%). The structure of **3k** was ascertained by single-crystal X-ray crystallogaphy (see Figure S66 and Table S1). To demonstrate the practical utility of this method as a synthetic

Table 3. Substrate scope of isocyanide and compatibility

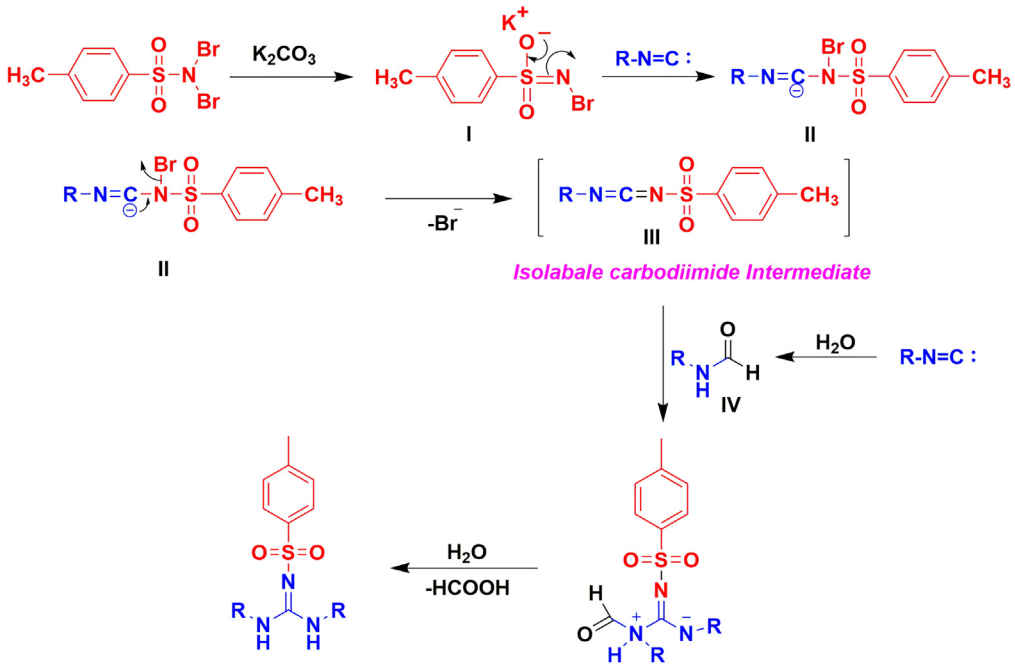




Reaction conditions: 1a (1.1 mmol), 2 (0.5 mmol), K_2CO_3 (1 mmol) at 80°C for 2 h. Isolated yields.

tool, an experiment was carried out by employing 1 g of $TsNBr_2$ for the synthesis of symmetrical guanidine on a larger scale. The reaction in the presence of a corresponding mole equivalent of *tert*-butyl-isonitrile produced the symmetrical guanidine 4a in 76%.

Based on our previous work along with literature reports,[45,46,61] a plausible mechanism for the formation of sulfonyl guanidine was proposed in Scheme 2. Initially, in presence of base, $TsNBr_2$ eliminates a

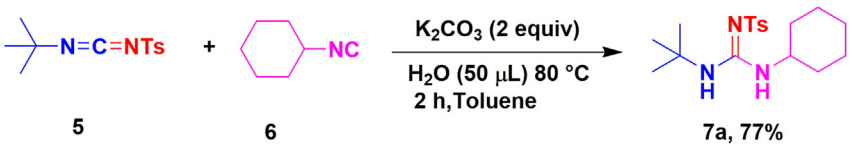


Scheme 2. Plausible reaction mechanism

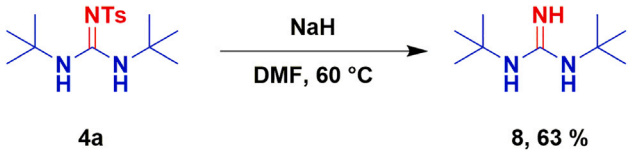
bromonium ion and produces an intermediate **I**, which subsequently react with isonitrile to generate the carbodiimide intermediate **III**. The reaction proceeds via the formation of a formamide **IV** from another molecule of isocyanide in the presence of H_2O. GC-MS analysis of the reaction mixture indicates the presence of formamide species in the reaction (see Figure S1). Finally, the *in-situ* generated formamide (**IV**) reacts with carbodiimide (**III**) to produce the corresponding sulfonyl guanidine via the loss of formic acid which was also detected using GC-MS (see Figure S2).

To explore the possibility of the formation of unsymmetrical guanidine, we have added a different isocyanide, such as cyclohexyl isocyanide, after the formation of carbodiimide in a one-pot reaction. However, a mixture of symmetrical and unsymmetrical guanidine was observed. For the exclusive synthesis of unsymmetrical guanidine, a reaction was planned between an isolated carbodiimide intermediate and another isonitrile. Accordingly, the carbodiimide intermediate was synthesized by reacting with $TsNBr_2$ and *tert*-butyl isonitrile at room temperature. When the isolated carbodiimide was treated with cyclohexyl isocyanide in the presence of 50 μL of water under the same optimized conditions, we could gratifyingly isolate the desired guanidine product in high yield. This reaction opens a new pathway for the synthesis of tri-substituted unsymmetrical guanidine using isonitrile as a nucleophilic source (Scheme 3).

After successfully establishing a convenient procedure for the synthesis of sulfonyl guanidine, we further focused on their synthetic utility to derive *N,N´*-disubstituted symmetrical guanidine derivatives via the detosylation of sulfonyl guanidine. Thus, when the derivative 4a was treated with NaH in DMF at 60°C, corresponding 1,3-di-*tert*-butylguanidine, (8) was isolated in 63% yield (Scheme 4).[62]



Scheme 3. Synthesis of unsymmetrical guanidine



Scheme 4. Synthetic modification of guanidine

Conclusion

In conclusion, we have developed a metal-free protocol for the synthesis of symmetrical *N,N′,N′′*-substituted sulfonyl guanidines by treating *N,N*-dibromoarylsulfonamides with isonitriles using K_2CO_3 as a base without the aid of an extra amine source. The cascade reaction proceeds via an isolable carbodiimide intermediate to give the corresponding guanidine product within a very short reaction time. The wide substrate scope, good to high yields and good functional group tolerance are the remarkable achievements of the present protocol. Further, tri-substituted guanidine was transformed into di-substituted symmetrical guanidine.

Limitations of the study

This work reports a highly efficient metal-free protocol for the synthesis of symmetrical guanidine by treating *N,N*-dibromoarylsulfonamides and isonitriles without the use of an external amine source. Although a good substrate scope of *N,N*-dibromoarylsulfonamides and isonitriles have been demonstrated. However, this method has limitation on the use of *N,N*-dibromo(methanesulfonamide) due to difficulty in isolation of pure *N,N*-dibromo derivative of methanesulfonamide via bromination reaction.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2023.107258.

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AUTHOR CONTRIBUTIONS

P.P. and D.M. conceived the idea of this work, investigated the problem and wrote the manuscript. D.M. and S.R. carried out the experiments for synthesis.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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REFERENCES

1. Santos, M.F.C., Harper, P.M., Williams, D.E., Mesquita, J.T., Pinto, É.G., da Costa-Silva, T.A., Hajdu, E., Ferreira, A.G., Santos, R.A., Murphy, P.J., et al. (2015). Anti-parasitic guanidine and pyrimidine alkaloids from the marine sponge monanchora arbuscula. J. Nat. Prod. *78*, 1101–1112. https://doi.org/10.1021/acs.jnatprod.5b00070.

2. Alonso-Moreno, C., Antiñolo, A., Carrillo-Hermosilla, F., and Otero, A. (2014). Guanidines: from classical approaches to efficient catalytic syntheses. Chem. Soc. Rev. *43*, 3406–3425. https://doi.org/10.1039/c4cs00013g.

3. Zhang, W.-X., Xu, L., and Xi, Z. (2015). Recent development of synthetic preparation methods for guanidines via transition metal catalysis. Chem. Commun. *51*, 254–265. https://doi.org/10.1039/c4cc05291a.

4. Berlinck, R.G.S., Burtoloso, A.C.B., Trindade-Silva, A.E., Romminger, S., Morais, R.P., Bandeira, K., and Mizuno, C.M. (2010). The chemistry and biology of organic guanidine derivatives. Nat. Prod. Rep. *27*, 1871–1907. https://doi.org/10.1039/c0np00016g.

5. Kim, S.-H., Semenya, D., and Castagnolo, D. (2021). Antimicrobial drugs bearing guanidine moieties: A review. Eur. J. Med. Chem. *216*, 113293. https://doi.org/10.1016/j.ejmech.2021.113293.

6. Greenhill, J.V., and Lue, P. (1993). 5 Amidines and guanidines in medicinal chemistry. In In Progress in Medicinal Chemistry, G.P. Ellis and D.K. Luscombe, eds. (Elsevier), pp. 203–326. https://doi.org/10.1016/S0079-6468(08)70378-3.

7. Dong, S., Feng, X., and Liu, X. (2018). Chiral guanidines and their derivatives in asymmetric synthesis. Chem. Soc. Rev. *47*, 8525–8540. https://doi.org/10.1039/c7cs00792b.

8. Castagnolo, D., Schenone, S., and Botta, M. (2011). Guanylated diamines, triamines, and polyamines: chemistry and biological properties. Chem. Rev. *111*, 5247–5300. https://doi.org/10.1021/cr100423x.

9. Ishikawa, T., Araki, Y., Kumamoto, T., Isobe, T., Seki, H., and Fukuda, K. (2001). Modified guanidines as chiral superbases: application to asymmetric Michael reaction of glycine imine with acrylate or its related compounds. Chem. Commun. 245–246. https://doi.org/10.1039/B009193F.

10. Manimala, J., and Anslyn, E. (2002). Solid-phase synthesis of guanidinium derivatives from thiourea and isothiourea functionalities. Eur. J. Org Chem. *2002*, 3909–3922. https://doi.org/10.1002/1099-0690(200212)2002:23<3909:aid-ejoc3909>3.0.co;2-j.

11. Ong, T.-G., Yap, G.P.A., and Richeson, D.S. (2003). Catalytic construction and reconstruction of guanidines: Ti-mediated guanylation of amines and transamination of guanidines. J. Am. Chem. Soc. *125*, 8100–8101. https://doi.org/10.1021/ja035716j.

12. Powell, D.A., Ramsden, P.D., and Batey, R.A. (2003). Phase-transfer-catalyzed alkylation of guanidines by alkyl halides under biphasic conditions: a convenient protocol for the synthesis of highly functionalized guanidines. J. Org. Chem. *68*, 2300–2309. https://doi.org/10.1021/jo0265535.

13. Hou, Z., Zhang, W.-X., and Nishiura, M. (2006). Catalytic addition of secondary amines to carbodiimides by a half-sandwich yttrium complex: An efficient route to *N,N′,N″,N‴*-tetrasubstituted guanidines. Synlett *2006*, 1213–1216. https://doi.org/10.1055/s-2006-939081.

14. Shen, H., Chan, H.-S., and Xie, Z. (2006). Guanylation of amines catalyzed by a half-sandwich titanacarborane amide complex. Organometallics *25*, 5515–5517. https://doi.org/10.1021/om060811x.

15. Ong, T.-G., O'Brien, J.S., Korobkov, I., and Richeson, D.S. (2006). Facile and atom-efficient amidolithium-catalyzed C−C and C−N formation for the construction of substituted guanidines and propiolamidines. Organometallics *25*, 4728–4730. https://doi.org/10.1021/om060539r.

16. Li, Q., Wang, S., Zhou, S., Yang, G., Zhu, X., and Liu, Y. (2007). Highly atom efficient guanylation of both aromatic and secondary amines catalyzed by simple lanthanide amides. J. Org. Chem. *72*, 6763–6767. https://doi.org/10.1021/jo0709089.

17. Zhang, W.-X., Nishiura, M., and Hou, Z. (2007). Catalytic addition of amine N-H bonds to carbodiimides by half-sandwich rare-earth metal complexes: efficient synthesis of substituted guanidines through amine protonolysis of rare-earth metal guanidinates. Chemistry *13*, 4037–4051. https://doi.org/10.1002/chem.200601383.

18. Zhang, W.-X., Li, D., Wang, Z., and Xi, Z. (2009). Alkyl aluminum-catalyzed addition of amines to carbodiimides: A highly efficient route to substituted guanidines. Organometallics *28*, 882–887. https://doi.org/10.1021/om801035t.

19. Zhu, X., Du, Z., Xu, F., and Shen, Q. (2009). Ytterbium triflate: a highly active catalyst for addition of amines to carbodiimides to *N,N′,N″*-trisubstituted guanidines. J. Org. Chem. *74*, 6347–6349. https://doi.org/10.1021/jo900903t.

20. Alonso-Moreno, C., Carrillo-Hermosilla, F., Garcés, A., Otero, A., López-Solera, I., Rodríguez, A.M., and Antiñolo, A. (2010). Simple, versatile, and efficient catalysts for guanylation of amines. Organometallics *29*, 2789–2795. https://doi.org/10.1021/om1003122.

21. Looper, R.E., Haussener, T.J., and Mack, J.B.C. (2011). Chlorotrimethylsilane activation of acylcyanamides for the synthesis of mono-N-acylguanidines. J. Org. Chem. *76*, 6967–6971. https://doi.org/10.1021/jo201264j.

22. Pottabathula, S., and Royo, B. (2012). First iron-catalyzed guanylation of amines: a simple and highly efficient protocol to guanidines. Tetrahedron Lett. *53*, 5156–5158. https://doi.org/10.1016/j.tetlet.2012.07.065.

23. Tan, D., Mottillo, C., Katsenis, A.D., Štrukil, V., and Friščić, T. (2014). Development of C-N coupling using mechanochemistry: catalytic coupling of arylsulfonamides and carbodiimides. Angew Chem. Int. Ed. Engl. *53*, 9321–9324. https://doi.org/10.1002/anie.201404120.

24. Xu, L., Dai Perrard, X., Perrard, J.L., Yang, D., Xiao, X., Teng, B.B., Simon, S.I., Ballantyne, C.M., and Wu, H. (2015). Mechanistic considerations of the catalytic guanylation reaction of amines with carbodiimides for guanidine synthesis. Organometallics *35*, 1787–1797. https://doi.org/10.1021/acs.organomet.5b00251.

25. Wang, Y., Zhang, W.-X., and Xi, Z. (2020). Carbodiimide-based synthesis of *N*-heterocycles: moving from two classical reactive sites to chemical bond breaking/forming reaction. Chem. Soc. Rev. *49*, 5810–5849. https://doi.org/10.1039/c9cs00478e.

26. Stevens, C.L., Singhal, G.H., and Ash, A.B. (1967). Carbodiimides. Dehydration of ureas. J. Org. Chem. *32*, 2895. https://doi.org/10.1021/jo01284a056.

27. Saegusa, T., Ito, Y., and Shimizu, T. (1970). Synthetic reactions by complex catalysts. XVIII. Reaction of an azide with isocyanide using an iron carbonyl catalyst. New route to carbodiimide. J. Org. Chem. *35*, 3995–3996. https://doi.org/10.1021/jo00836a105.

28. Cowley, R.E., Eckert, N.A., Elhaïk, J., and Holland, P.L. (2009). Catalytic nitrene transfer from an imidoiron(III) complex to form carbodiimides and isocyanates. Chem. Commun. 1760–1762. https://doi.org/10.1039/b820620a.

29. Cowley, R.E., and Holland, P.L. (2012). Ligand effects on hydrogen atom transfer from hydrocarbons to three-coordinate iron

imides. Inorg. Chem. *51*, 8352–8361. https://doi.org/10.1021/ic300870y.

30. Kogut, E., Wiencko, H.L., Zhang, L., Cordeau, D.E., and Warren, T.H. (2005). A terminal Ni(III)-imide with diverse reactivity pathways. J. Am. Chem. Soc. *127*, 11248–11249. https://doi.org/10.1021/ja0533186.

31. Laskowski, C.A., and Hillhouse, G.L. (2009). Group-transfer reactions of Ni(II)−Ni(II) bridging imido complexes. Catalytic formation of carbodiimides and isocyanates via nitrene transfer from organoazides. Organometallics *28*, 6114–6120. https://doi.org/10.1021/om900783u.

32. Badiei, Y.M., Krishnaswamy, A., Melzer, M.M., and Warren, T.H. (2006). Transient terminal Cu-nitrene intermediates from discrete dicopper nitrenes. J. Am. Chem. Soc. *128*, 15056–15057. https://doi.org/10.1021/ja065299l.

33. Zhang, Z., Li, Z., Fu, B., and Zhang, Z. (2015). Palladium-catalyzed cross-coupling reaction of azides with isocyanides. Chem. Commun. *51*, 16312–16315. https://doi.org/10.1039/c5cc05981j.

34. Gu, Z.-Y., Liu, Y., Wang, F., Bao, X., Wang, S.-Y., and Ji, S.-J. (2017). Cobalt(II)-catalyzed synthesis of sulfonyl guanidines via nitrene radical coupling with isonitriles: A combined experimental and computational study. ACS Catal. *7*, 3893–3899. https://doi.org/10.1021/acscatal.7b00798.

35. Zhang, Z., Qiao, G., Zhang, Z., Huang, B., Zhu, L., and Xiao, F. (2018). Palladium-catalyzed one-pot synthesis of *N*-sulfonyl, *N*-phosphoryl, and *N*-acyl guanidines. Synthesis *50*, 330–340. https://doi.org/10.1055/s-0036-1588576.

36. Zhu, T.-H., Wang, S.-Y., Wei, T.-Q., and Ji, S.-J. (2015). Cobalt-catalyzed intermolecular oxidative isocyanide insertion with two amines: An approach to guanidines. Adv. Synth. Catal. *357*, 823–828. https://doi.org/10.1002/adsc.201400911.

37. Fang, Y., Yang, J.-M., Zhang, R., Wang, S.-Y., and Ji, S.-J. (2019). Cobalt-catalyzed condensation of sulfonyl azides with *o*-diisocyanoarenes and anilines: a new approach to N-sulfonyl guanidines. Org. Chem. Front. *6*, 3383–3386. https://doi.org/10.1039/C9QO00815B.

38. Burgess, B.K., and Lowe, D.J. (1996). Mechanism of molybdenum nitrogenase. Chem. Rev. *96*, 2983–3012. https://doi.org/10.1021/cr950055x.

39. Tanabe, Y., Seino, H., Ishii, Y., and Hidai, M. (2000). Reaction mechanism of the C≡N triple bond cleavage of β-ketonitriles on a molybdenum(0) Ccenter1. J. Am. Chem. Soc. *122*, 1690–1699. https://doi.org/10.1021/ja9921928.

40. Kawashima, T., Takao, T., and Suzuki, H. (2006). Cleavage of the C≡N bond on a triruthenium cluster: Synthesis and structure of a triruthenium complex containing a μ_3-nitrido ligand. Angew Chem. Int. Ed. Engl. *118*, 499–502. https://doi.org/10.1002/ange.200503267.

41. Thompson, R.R., Rotella, M.E., Zhou, X., Fronczek, F.R., Gutierrez, O., and Lee, S. (2021). Impact of ligands and metals on the formation of metallacyclic intermediates and a nontraditional mechanism for group VI alkyne metathesis catalysts. J. Am. Chem. Soc. *143*, 9026–9039. https://doi.org/10.1021/jacs.1c01843.

42. Boyd, J., Schlangen, M., Grohmann, A., and Schwarz, H. (2008). Room-temperature alkyne-nitrile metathesis and unambiguous proof for the existence of a high-Valent iron-nitrido dication in the gas phase. Short communication. Helv. Chim. Acta *91*, 1430–1434. https://doi.org/10.1002/hlca.200890155.

43. Wiedner, E.S., Gallagher, K.J., Johnson, M.J.A., and Kampf, J.W. (2011). Synthesis of molybdenum nitrido complexes for triple-bond metathesis of alkynes and nitriles. Inorg. Chem. *50*, 5936–5945. https://doi.org/10.1021/ic1024247.

44. Asakawa, H., Lee, K.-H., Lin, Z., and Yamashita, M. (2014). Facile scission of isonitrile carbon-nitrogen triple bond using a diborane(4) reagent. Nat. Commun. *5*, 4245. https://doi.org/10.1038/ncomms5245.

45. Hazarika, D., Borah, A.J., and Phukan, P. (2019). Facile, catalyst-free cascade synthesis of sulfonyl guanidines via carbodiimide coupling with amines. Chem. Commun. *55*, 1418–1421. https://doi.org/10.1039/c8cc08564a.

46. Mishra, D., and Phukan, P. (2021). A unified approach for the synthesis of isourea and isothiourea from isonitrile and *N,N*-dibromoarylsulfonamides. J. Org. Chem. *86*, 17581–17593. https://doi.org/10.1021/acs.joc.1c01578.

47. Mishra, D., Borah, A.J., Phukan, P., Hazarika, D., and Phukan, P. (2020). Unprecedented 1,3-*tert*-butyl migration via the C-N single bond scission of isonitrile: an expedient metal-free route to *N*-sulfonyl amidines. Chem. Commun. *56*, 8408–8411. https://doi.org/10.1039/d0cc02430a.

48. Saikia, I., Borah, A.J., and Phukan, P. (2016). Use of bromine and bromo-organic compounds in organic synthesis. Chem. Rev. *116*, 6837–7042. https://doi.org/10.1021/acs.chemrev.5b00400.

49. Phukan, P., Rajbongshi, K., and Borah, A. (2016). *N,N*-Dibromo-*p*-toluenesulfonamide ($TsNBr_2$): A promising alternative bromo-organic reagent. Synlett *27*, 1618–1634. https://doi.org/10.1055/s-0035-1562024.

50. Phukan, P., Chakraborty, P., and Kataki, D. (2006). A simple and efficient method for regioselective and stereoselective synthesis of vicinal bromohydrins and alkoxybromides from an olefin. J. Org. Chem. *71*, 7533–7537. https://doi.org/10.1021/jo0600611.

51. Saikia, I., and Phukan, P. (2009). Facile generation of vicinal bromoazides from olefins using $TMSN_3$ and $TsNBr_2$ without any catalyst. Tetrahedron Lett. *50*, 5083–5087. https://doi.org/10.1016/j.tetlet.2009.06.059.

52. Saikia, I., Kashyap, B., and Phukan, P. (2011). A facile noncatalytic pathway for the nitrene transfer process: expeditious access to aziridines. Chem. Commun. *47*, 2967–2969. https://doi.org/10.1039/c0cc05387b.

53. Borah, A.J., and Phukan, P. (2012). A highly efficient catalyst-free protocol for C-H bond activation: sulfamidation of alkyl aromatics and aldehydes. Chem. Commun. *48*, 5491–5493. https://doi.org/10.1039/c2cc31258a.

54. Rajbongshi, K.K., Saikia, I., Chanu, L.D., Roy, S., and Phukan, P. (2016). A Metal-Free Protocol for aminofunctionalization of olefins using $TsNBr_2$. J. Org. Chem. *81*, 5423–5432. https://doi.org/10.1021/acs.joc.6b00785.

55. Rajbongshi, K.K., Hazarika, D., and Phukan, P. (2016). $TsNBr_2$ mediated oxidative functionalization of alkynes. Tetrahedron *72*, 4151–4158. https://doi.org/10.1016/j.tet.2016.05.017.

56. Hazarika, D., and Phukan, P. (2017). Metal free synthesis of quinoxalines from alkynes via a cascade process using $TsNBr_2$. Tetrahedron *73*, 1374–1379. https://doi.org/10.1016/j.tet.2017.01.056.

57. Loukrakpam, D.C., and Phukan, P. (2019). $TsNBr_2$ mediated synthesis of 2-acylbenzothiazoles and quinoxalines from aryl methyl ketones under metal free condition. ChemistrySelect *4*, 3180–3184. https://doi.org/10.1002/slct.201900713.

58. Loukrakpam, D.C., and Phukan, P. (2019). Metal-free one-pot conversion of olefins and alkynes to amides using $TsNBr_2$, I_2 and aqueous NH_3 at room temperature. ChemistrySelect *4*, 8978–8982. https://doi.org/10.1002/slct.201901530.

59. Mishra, D., Loukrakpam, D.C., Neog, S.R., Hazarika, D., and Phukan, P. (2022). A switchable protocol for selective synthesis of gem -dibromo compounds and amides from ketoximes using TsNBr 2. ChemistrySelect *7*. https://doi.org/10.1002/slct.202203449.

60. Goswami, D., Mishra, D., and Phukan, P. (2022). Silver acetate-catalyzed synthesis of cyclic sulfonyl guanidine with exocyclic double bond. Mol. Divers. https://doi.org/10.1007/s11030-022-10568-5.

61. Bianchini, G., La Sorella, G., Canever, N., Scarso, A., and Strukul, G. (2013). Efficient isonitrile hydration through encapsulation within a hexameric self-assembled capsule and selective inhibition by a photo-controllable competitive guest. Chem. Commun. *49*, 5322–5324. https://doi.org/10.1039/c3cc42233j.

62. Sun, W., Chen, X., Hu, Y., Geng, H., Jiang, Y., Zhou, Y., Zhu, W., Hu, M., Hu, H., Wang, X., et al. (2020). A NaH-promoted *N*-detosylation reaction of diverse *p*-toluenesulfonamides. Tetrahedron Lett. *61*, 152442. https://doi.org/10.1016/j.tetlet.2020.152442.

63. Tajbakhsh, M., Khazaei, A., Mahalli, M.S., and Vaghi, R.G. (2004). *N,N*-Dibromobenzenesulfonamide: A useful regenerable reagent for bromination of various carbanionic substrates. Phosphorus Sulfur Silicon Relat. Elem *179*, 1159–1163. https://doi.org/10.1080/10426500490459768.

64. Khazaei, A., Rostami, A., Tanbakouchian, Z., and Zinati, Z. (2006). *N,N*-Dibromo-4-methylbenzenesulphonimide as economical reagent for facile and selective catalyzed acetylation of alcohols under mild conditions. Catal. Commun. *7*, 214–217. https://doi.org/10.1016/j.catcom.2005.11.010.

STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Other		
DCE	FINAR	CAS No. 107-06-2
Toluene	FINAR	CAS No. 108-88-3
DMF	FINAR	CAS No. 68-12-2
K_2CO_3	Merck	CAS No. 584-08-7
KF	Merck	CAS No. 7789-23-3
$KHCO_3$	Merck	CAS No. 298-14-6
$CsCO_3$	Merck	CAS No. 534-17-8
NaH	Merck	CAS No. 7646-69-7
t-butyl isocyanide	TCI	CAS No. 7188-38-7
Cyclohexyl isocyanide	TCI	CAS No. 931-53-3
n-butyl isocyanide	Merck	CAS No. 2769-64-4
n-pentyl isocyanide	Merck	CAS No. 18971-59-0
Benzyl isocyanide	TCI	CAS No. 10340-91-7
1,1,3,3-tetramethyl butyl isocyanide	Merck	CAS No. 14542-93-9
Isopropyl isocyanide	Merck	CAS No. 598-45-8
2-methyl benzene sulfonamide	Merck	CAS No. 88-19-7
3-bromo benzene sulfonamide	TCI	CAS No. 89599-01-9
4-bromo benzene sulfonamide	Merck	CAS No. 701-34-8
2-chloro benzene sulfonamide	Merck	CAS No. 6961-82-6
4-chloro benzene sulfonamide	Merck	CAS No. 98-64-6
2-flouro benzene sulfonamide	TCI	CAS No. 30058-40-3
4- triflouromethoxy benzene sulfonamide	TCI	CAS No. 1513-45-7
2-triflouro methyl benzene sulfonamide	TCI	CAS No. 1869-24-5
4-nitro benzene sulfonamide	TCI	CAS No. 6325-93-5
4-methoxy benzene sulfonamide	Merck	CAS No. 1129-26-6
4-triflouro methyl benzene sulfonamide	TCI	CAS No. 830-43-3
4-*n*-butyl benzene sulfonamide	TCI	CAS No. 1135-00-8
Naphthalene-2- sulfonamide	Merck	CAS No. 1576-47-2
2-ethyl-6-methylaniline	TCI	CAS No. 24549-06-2
Silica gel (230–400 mesh)	SRL	
TLC Silica gel plates	Merck	
IR	SHIMADZU	https://www.ssi.shimadzu.com/
NMR 400 MHz	JEOL	https://www.jeolusa.com/
NMR 500 MHz	Bruker	https://www.bruker.com/
NMR 600 MHz	Bruker	https://www.bruker.com/
X-ray diffraction	Bruker	https://www.bruker.com/
HRMS	Water	https://www.waters.com/
Deposited data		
CIF of 3k	CCDC 2205824	https://www.ccdc.cam.ac.uk/structures/

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Prodeep Phukan (pphukan@yahoo.com; pphukan@gauhat.ac.in).

Materials availability

All other data supporting the findings of this study are available within the article and the supplemental information or from the lead contact upon reasonable request.

Data and code availability

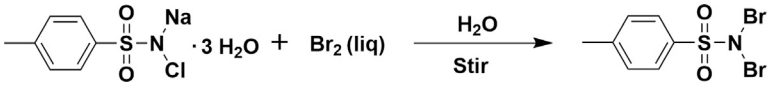
Crystallographic data for the structures reported in this article have been deposited at the Cambridge Crystallographic Data Centre (CCDC) under accession numbers CCDC 2205824 (3k). Copies of the data can be obtained free of charge from https://www.ccdc.cam.ac.uk/structures/. All other data are available from the lead contact upon reasonable request.

METHOD DETAILS

Preparation of substrates

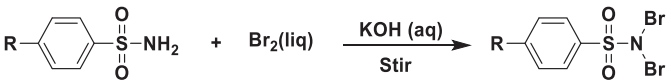
General procedure for the synthesis of *N,N*-dibromoarylsulfonamides[63,64]

Procedure A: From chloramine-T trihydrate



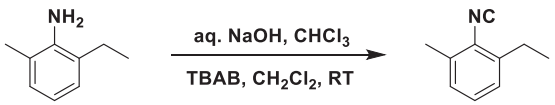
Liquid bromine (2 mL) was added dropwise to a solution of chloramine-T (10 g) in water (200 mL) with vigorous stirring at ambient temperature. The golden yellow precipitated of *N,N*-dibromo-*p*-tolunesulfonamide was washed thoroughly with water, filtered under suction and dried under desiccator for 24 hours.

Procedure B: From Aryl sulfonamide.



Arylsulfonamide (5 g) in aqueous potassium hydroxide (3.6 g) solution in water (25 mL) was placed to a 250 mL three necked flask. Then with vigorous stirring 10 g of bromine was added slowly with the help of a burette. The golden yellow of *N,N*-dibromo-arylsulfonamide precipitated out from the solution was filtered, washed with water. After workup, the isolated compound was kept under suction for 1h and dried in a desiccator for 24 hours.

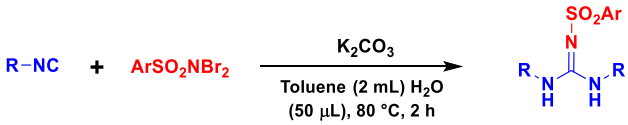
Synthesis of 2-ethyl-6-methyl isocyanobenzene[45]



To a solution of 2-ethyl-6-methyl aniline (22 mmol, 1 equiv) in CH_2Cl_2 (100 mL), 50 wt % of aqueous NaOH (50 mL), TBAB (1 mol %) and $CHCl_3$ (33 mmol, 1.5 equiv) was added and stirred at room temperature for 6 h. After completion of the reaction, the mixture was diluted with 200 mL of water and the organic layer was separated. The organic layer was further washed twice with 100 mL of water and once with 100 mL saturated NaCl solution. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography using petroleum etherdichloromethane (4:1) as eluent to afford 2-ethyl-6-methyl isocyanobenzene as pale yellow liquid.

Preparation of products

General procedure for the synthesis of sulfonyl guanidine

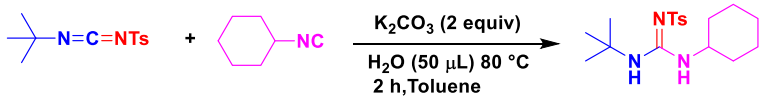


To a solution of isocyanide (1.1 mmol, 2.2 equiv) in toluene (2 mL), *N,N*-dibromoarylsulfonamide (0.5 mmol, 1.0 equiv) and K_2CO_3 (2 equiv) was added followed by 50 μL of H_2O and stirred at 80°C for 2 h. After completion of the reaction as monitored by TLC, the reaction mixture was passed through a short pad of celite and washed with ethyl acetate. The solvent was concentrated under reduced pressure and the crude was purified by flash column chromatography using petroleum ether-ethyl acetate as eluent.

*Gram scale synthesis of N-(bis(tert -butylamino)methylene)-4-*Methylbenzenesulfonamide (4a)

To an ice cooled solution of *tert*-butyl isocyanide (6.69 mmol, 2.2 equiv) in toluene (6 mL), K_2CO_3 (6.08 mmol, 2 equiv) and *N,N*-dibromo-*p*-toluenesulfonamide (3.04 mmol, 1g, 1 equiv) was added in portion followed by 304 μL of H_2O and stirred at 80°C for 2 h. After completion of the reaction as monitored by TLC, the reaction mixture was passed through a short pad of Celite and washed with ethyl acetate. The solvent was concentrated under reduced pressure and the crude was Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 8:2). Colorless solid (76%, 751 mg).

Synthesis of N-((tert-butylamino)(cyclohexylamino)methylene)-4-methylbenzenesulfonamide (7a)

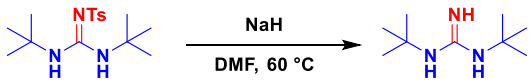


5 6 7a, 77%

To a stirred solution of *N*-(*tert*-butyliminomethylene)-4-methylbenzenesulfonamide (0.5 mmol, 1.0 equiv) in toluene (2 mL), cyclohexyl isocyanide (0.5 mmol, 1.0 equiv) and K_2CO_3 (1 mmol, 2.0 equiv) was added followed by 50 μL of H_2O and stirred at 80°C for 2 h. After completion of the reaction, the reaction mixture was passed through a celite pad and washed with ethyl acetate. The filtrate was concentrated under reduced pressure. Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 9:1). Colorless liquid (77%, 135 mg).

Transformations of products

Synthesis of 1,3-di-tert-butylguanidine (8)[62]

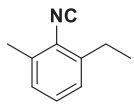


4a 8, 63 %

To a solution of NaH (0.4 mmol, 2 equiv) in dry DMF (1 mL) under N_2 atmosphere, 1,3-di-*tert*-butyl-2-tosylguanidine (0.2 mmol, 1.0 equiv) was added and heat the reaction mixture at 60°C for 2 h. After completion of the reaction as monitored by TLC, the reaction mixture was passed through a Celite pad and washed with ethyl acetate. The filtrate was concentrated under reduced pressure. Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 8:2). Semi solid (63%, 21 mg).

Characterization of substrates

2-Ethyl-6-methyl isocyanobenzene

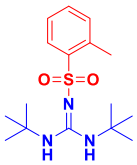


^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27–7.21 (m, 1H), 7.11 (d, *J* = 7.5 Hz, 2H), 2.79 (q, *J* = 7.5 Hz, 2H), 2.43 (s, 3H), 1.28 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.5, 140.5, 134.9, 128.8, 127.7, 126.1, 25.6, 18.9, 13.8.

Characterization of products 3a-3n

N-(bis(tert-butylamino)methylene)-2-methylbenzenesulfonamide (3a)



3a

Following the general procedure, compound **3a** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-2-methylbenzenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (76%, 123 mg); mp 58°C–60°C.

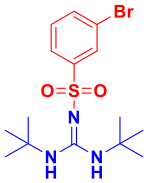
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.98 (d, J = 7.8 Hz, 1H), 7.36 (t, J = 7.2 Hz, 1H), 7.28–7.24 (m, 3H), 4.41 (br, 1H), 2.72 (s, 3H), 1.36 (s, 18H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.8, 142.0, 136.8, 131.9, 131.1, 127.2, 125.3, 52.4, 29.7, 20.4.

IR (KBr, cm^{-1}): ν 3402, 3352, 2960, 1597, 1481.

HRMS m/z (ESI) calculated for $C_{16}H_{28}N_3O_2S$ $(M + H)^+$ 326.1897, found 326.1899.

N-(bis(tert -butylamino)methylene)-3-bromobenzenesulfonamide (3b)



3b

Following the general procedure, compound **3b** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-3-bromobenzenesulfonamide (197 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (74%, 144 mg).

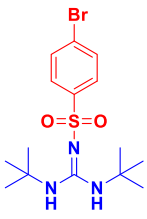
^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.01 (s, 1H), 7.79 (d, J = 6.5 Hz, 1H), 7.58 (d, J = 6.5 Hz, 1H), 7.31 (t, J = 6.5 Hz, 1H), 7.15 (br, 1H), 4.47 (br, 1H), 1.33 (s, 18H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.9, 145.8, 134.0, 130.0, 128.9, 124.5, 122.2, 60.3, 29.7.

IR (KBr, cm^{-1}): ν 3351, 2930, 1547, 1486, 670.

HRMS m/z (ESI) calculated for $C_{15}H_{25}BrN_3O_2S$ $(M + H)^+$ 390.0845, found 390.0840.

N-(bis(tert -butylamino)methylene)-4-bromobenzenesulfonamide (3c)



3c

Following the general procedure, compound **3c** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-bromobenzenesulfonamide (197 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg).

Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (77%, 150 mg); mp 72°C–74°C.

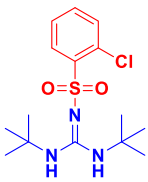
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.74 (d, J = 7 Hz, 2H), 7.57 (d, J = 7 Hz, 2H), 7.17 (br, 1H), 4.46 (br, 1H), 1.34 (s, 18H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.9, 143.2, 131.6, 127.5, 125.6, 53.7, 29.7.

IR (KBr, cm^{-1}): ν 3391, 2950, 1597, 1471, 678.

HRMS m/z (ESI) calculated for $C_{15}H_{25}BrN_3O_2S$ $(M + H)^+$ 390.0845, found 390.0843.

N-(bis(tert -butylamino)methylene)-2-chlorobenzenesulfonamide (3 days)



3d

Following the general procedure, compound **3d**ays was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-2-chlorobenzenesulfonamide (174 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (72%, 124 mg).

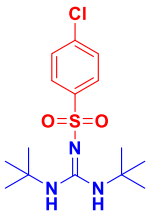
^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.14 (d, J = 7.5 Hz, 1H), 7.44–7.32 (m, 4H), 4.45 (br, 1H), 1.33 (s, 18H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.9, 141.3, 131.9, 131.7, 131.1, 129.3, 126.4, 53.7, 29.6.

IR (KBr, cm^{-1}): ν 3357, 2897, 1638, 1479, 832.

HRMS m/z (ESI) calculated for $C_{15}H_{25}ClN_3O_2S$ $(M + H)^+$ 346.1351, found 346.1357.

*N-(bis(tert -butylamino)*methylene)-4-chlorobenzenesulfonamide (3e)



3e

Following the general procedure, compound **3e** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-chlorobenzenesulfonamide (174 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (75%, 129 mg); mp 66°C–68°C.

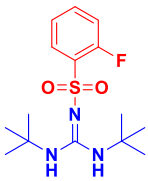
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.82 (d, J = 9 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.18 (br, 1H), 4.45 (br, 1H), 1.34 (s, 18H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.8, 142.7, 137.3, 128.6, 127.4, 60.4, 29.7.

IR (KBr, cm^{-1}): ν 3341, 2956, 1597, 1481, 702.

HRMS m/z (ESI) calculated for $C_{15}H_{25}ClN_3O_2S$ $(M + H)^+$ 346.1351, found 346.1361.

N-(bis(tert -butylamino)methylene)-2-fluorobenzenesulfonamide (3f)



3f

Following the general procedure, compound **3f** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-2-fluorobenzenesulfonamide (166 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (71%, 116 mg).

^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.97 (d, J = 6.6 Hz, 1H), 7.45 (d, J = 6 Hz, 2H), 7.20 (t, J = 7.8 Hz, 1H), 7.11 (t, J = 9 Hz, 1H), 4.48 (br, 1H), 1.35 (s, 18H).

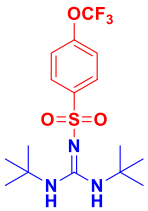
^{13}C NMR ($CDCl_3$, 150 MHz): δ 158.9 (J_{CF} = 251.5 Hz), 153.9, 133.1 (J_{CF} = 8.8 Hz), 131.9 (J_{CF} = 15.4 Hz), 128.9, 123.7 (J_{CF} = 4.3 Hz), 116.4 (J_{CF} = 22.0 Hz), 60.4, 29.6.

^{19}F NMR ($CDCl_3$, 564 MHz): δ −110.54.

IR (KBr, cm^{-1}): ν 3289, 2887, 1595, 1484, 997.

HRMS m/z (ESI) calculated for $C_{15}H_{25}FN_3O_2S$ $(M + H)^+$ 330.1646, found 330.1643.

N-(bis(tert -butylamino)methylene)-4-(trifluoromethoxy)benzenesulfonamide (3g)



3g

Following the general procedure, compound **3g** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-trifluoromethoxybenzenesulfonamide (199 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (68%, 134 mg).

^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.93 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.15 (br, 1H), 4.50 (br, 1H), 1.34 (s, 18H).

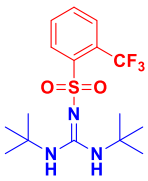
^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 151.5 (J_{CF} = 157.2 Hz), 142.4, 137.5 (J_{CF} = 575.8 Hz), 128.4 (J_{CF} = 170.2 Hz), 120.6 (J_{CF} = 18.6 Hz), 53.8, 29.6.

^{19}F NMR ($CDCl_3$, 564 MHz): δ −57.78.

IR (KBr, cm^{-1}): ν 3349, 3311, 2928, 1575, 1434, 977.

HRMS m/z (ESI) calculated for $C_{16}H_{25}F_3N_3O_3S$ $(M + H)^+$ 396.1563, found 396.1566.

N-(bis(tert -butylamino)methylene)-2-(trifluoromethyl)benzenesulfonamide (3h)



3h

Following the general procedure, compound **3h** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-2-trifluoromethylbenzenesulfonamide (191 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (63%, 118 mg).

^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.27 (s, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7. 28 (br, 1H), 4.44 (br, 1H), 1.31 (s, 18H).

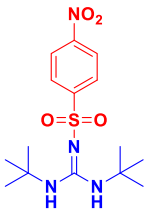
^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.3, 142.9, 131.4 (J_{CF} = 117.4 Hz), 129.9, 127.5 (J_{CF} = 6.6 Hz), 122.9 (J_{CF} = 272.5 Hz), 52.5, 29.6.

^{19}F NMR ($CDCl_3$, 564 MHz): δ −57.44.

IR (KBr, cm^{-1}): ν 3389, 2932, 1595, 1424, 983.

HRMS m/z (ESI) calculated for $C_{16}H_{25}F_3N_3O_2S$ $(M + H)^+$ 380.1614, found 380.1609.

N-(bis(tert -butylamino)methylene)-4-nitrobenzenesulfonamide (3i)



3i

Following the general procedure, compound **3i** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-nitrobenzenesulfonamide (179 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (70%, 124 mg).

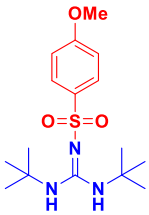
^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.29 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 9 Hz, 2H), 7. 23 (br, 1H), 4. 53 (br, 1H), 1.35 (s, 18H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.8, 149.9, 149.1, 127.0, 123.8, 53.2, 29.7.

IR (KBr, cm^{-1}): ν 3389, 2927, 1574, 1503, 1468.

HRMS m/z (ESI) calculated for $C_{15}H_{25}N_4O_4S$ $(M + H)^+$ 357.1591, found 357.1593.

N-(bis(tert -butylamino)methylene)-4-methoxybenzenesulfonamide (3j)



3j

Following the general procedure, compound **3j** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-methoxybenzenesulfonamide (172 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (74%, 126 mg); mp 112°C–114°C.

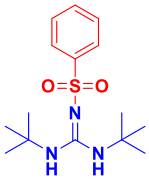
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.81 (d, *J* = 10.2 Hz, 2H), 7.16 (br, 1H), 6.91 (d, *J* = 10.8 Hz, 2H), 4.39 (br, 1H), 3.84 (s, 3H), 1.33 (s, 18H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.6, 153.9, 136.4, 127.8, 113.5, 56.4, 55.4, 29.8.

IR (KBr, cm^{-1}): ν 3343, 3312, 2910, 1587, 1474.

HRMS m/z (ESI) calculated for $C_{16}H_{28}N_3O_3S$ $(M + H)^+$ 342.1846, found 342.1846.

N-(bis(tert -butylamino)methylene)benzenesulfonamide (3k)



3k

Following the general procedure, compound **3k** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromobenzenesulfonamide (157 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (78%, 121 mg); mp 78°C–80°C.

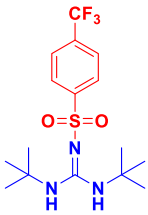
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.89 (d, *J* = 7.8 Hz, 2H), 7.47–7.43 (m, 3H), 7.18 (br, 1H), 4.42 (br, 1H), 1.34 (s, 18H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 141.4, 141.3, 128.9, 125.9, 52.6, 29.8.

IR (KBr, cm^{-1}): ν 3452, 3364, 2970, 1590, 1560, 1416, 1363.

HRMS m/z (ESI) calculated for $C_{15}H_{26}N_3O_2S$ $(M + H)^+$ 312.1740, found 312.1739.

N-(bis(tert -butylamino)methylene)-4-(trifluoromethyl)benzenesulfonamide (3l)



3l

Following the general procedure, compound **3L** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-trifluoromethylbenzenesulfonamide (191 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (69%, 125 mg).

^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.0 (d, *J* = 9 Hz, 2H), 7.71 (d, *J* = 9.6 Hz, 2H), 7.22 (br, 1H), 4.49 (br, 1H), 1.35 (s, 18H).

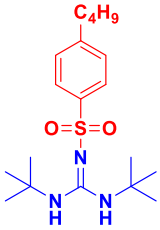
^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 147.6, 132.9 (J_{CF} = 38.4 Hz), 126.4, 125.6 (J_{CF} = 4.3 Hz), 123.6 (J_{CF} = 324.6 Hz), 52.7, 29.7.

^{19}F NMR ($CDCl_3$, 564 MHz): δ −62.89.

IR (KBr, cm^{-1}): ν 3389, 3336, 2957, 1567, 1443, 978.

HRMS m/z (ESI) calculated for $C_{16}H_{25}F_3N_3O_2S$ $(M + H)^+$ 380.1614, found 380.1603.

N-(bis(tert -butylamino)methylene)-4-butylbenzenesulfonamide (3m)



3m

Following the general procedure, compound **3m** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-4-butylbenzenesulfonamide (186 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (76%, 139 mg).

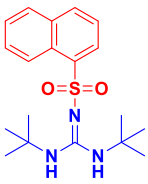
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.77 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.11 (br, 1H), 4.39 (br, 1H), 2.64 (t, J = 7.8 Hz, 2H), 1.62–1.57 (m, 2H), 1.34–1.26 (s, 20H), 0.92 (t, J = 7.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 146.4, 141.3, 128.3, 125.9, 60.3, 35.4, 33.2, 29.6, 22.1, 13.8.

IR (KBr, cm^{-1}): ν 3316, 2937, 1577, 1453.

HRMS m/z (ESI) calculated for $C_{19}H_{34}N_3O_2S$ $(M + H)^+$ 368.2366, found 368.2369.

N-(bis(tert -butylamino)methylene)naphthalene-1-sulfonamide (3n)



3n

Following the general procedure, compound **3n** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-2-naphthalenesulfonamide (183 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (73%, 131 mg).

^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.43 (s, 1H), 7.95–7.88 (m, 4H), 7.61–7.56 (m, 2H), 7.28 (br, 1H), 4.45 (br, 1H), 1.35 (s, 18H).

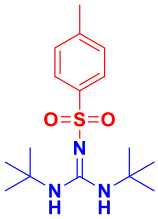
^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 140.9, 134.2, 132.1, 129.0, 128.6, 127.8, 127.7, 126.9, 126.0, 122.6, 53.6, 29.6.

IR (KBr, cm^{-1}): ν 3423, 3356, 2945, 1596, 1456.

HRMS m/z (ESI) calculated for $C_{19}H_{28}N_3O_2S$ $(M + H)^+$ 362.1897, found 362.1903.

Characterization of products 4a-4m

N-(bis(tert -butylamino)methylene)-4-methylbenzenesulfonamide (4a)



4a

Following the general procedure, compound **4a** was prepared from *tert*- butyl isocyanide (125 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (81%, 130 mg); mp 94°C–96°C.

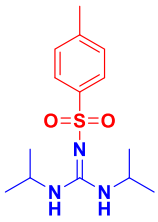
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 7.18 (br, 1H), 4.40 (br, 1H), 2.38 (s, 3H), 1.33 (s, 18H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.9, 141.5, 141.2, 128.9, 128.8, 125.9, 50.9, 29.8, 21.4.

IR (KBr, cm^{-1}): ν 3321, 2940, 1587, 1483.

HRMS m/z (ESI) calculated for $C_{16}H_{28}N_3O_2S$ $(M + H)^+$ 326.1897, found 326.1896.

N-(bis(isopropylamino)methylene)-4-methylbenzenesulfonamide (4b)



4b

Following the general procedure, compound **4b** was prepared from isopropyl isocyanide (105 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (78%, 115 mg); mp 96°C–98°C.

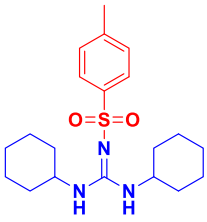
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.77 (d, J = 8 Hz, 2H), 7.23 (d, J = 7.5 Hz, 2H), 3.89–3.62 (m, 2H), 2.39 (s, 3H), 1.16 (d, J = 6.5 Hz, 12H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.6, 141.5, 141.3, 128.9, 125.9, 43.4, 22.9, 21.4.

IR (KBr, cm^{-1}): ν 3340, 2980, 1576, 1470.

HRMS m/z (ESI) calculated for $C_{14}H_{24}N_3O_2S$ $(M + H)^+$ 298.1584, found 298.1581.

N-(bis(cyclohexylamino)methylene)-4-methylbenzenesulfonamide (4c)



4c

Following the general procedure, compound **4c** was prepared from cyclohexyl isocyanide (135 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (75%, 141 mg); mp 110°C–112°C.

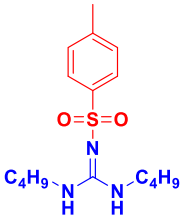
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J* = 8 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 2.39 (s, 3H), 1.87–1.85 (m, 4H), 1.70–1.68 (m, 4H), 1.61–1.58 (m, 5H), 1.36–1.33 (m, 4H), 1.21–1.19 (m, 5H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.5, 141.5, 141.4, 128.9, 125.9, 50.0, 33.0, 25.3, 24.3, 21.4.

IR (KBr, cm^{-1}): ν 3337, 2957, 1567, 1457.

HRMS m/z (ESI) calculated for $C_{20}H_{32}N_3O_2S$ $(M + H)^+$ 378.2210, found 378.2208.

N-(bis(butylamino)methylene)-4-methylbenzenesulfonamide (4days)



4d

Following the general procedure, compound **4d** was prepared from butyl isocyanide (116 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (72%, 116 mg); mp 68°C–70°C.

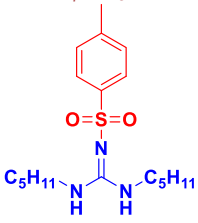
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 9 Hz, 2H), 3.15 (br, 2H), 2.38 (s, 3H), 1.48 (s, 4H), 1.29–1.25 (m, 6H), 0.87 (q, *J* = 7.2 Hz, 6H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.3, 141.5, 141.2, 128.9, 125.8, 41.2, 29.6, 21.3, 19.8, 13.6.

IR (KBr, cm^{-1}): ν 3353, 2948, 1581, 1451.

HRMS m/z (ESI) calculated for $C_{16}H_{28}N_3O_2S$ $(M + H)^+$ 326.1897, found 326.1907.

N-(bis(pentylamino)methylene)-4-methylbenzenesulfonamide (4e)



4e

Following the general procedure, compound **4e** was prepared from pentyl isocyanide (168 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (70%, 123 mg); mp 56°C–58°C.

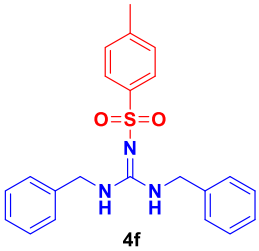
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 3.14 (br, 4H), 2.38 (s, 3H), 1.68 (br, 1H), 1.51 (s, 4H), 1.29–1.26 (m, 9H), 0.87 (t, *J* = 6.6 Hz, 6H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.2, 141.6, 141.3, 128.9, 125.9, 41.5, 29.7, 28.8, 22.2, 21.4, 13.9.

IR (KBr, cm^{-1}): ν 3373, 2948, 1576, 1463.

HRMS m/z (ESI) calculated for $C_{18}H_{32}N_3O_2S$ $(M + H)^+$ 354.2210, found 354.2229.

N-(bis(benzylamino)methylene)-4-methylbenzenesulfonamide (4f)



4f

Following the general procedure, compound **4f** was prepared from benzyl isocyanide (133 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (67%, 131 mg); mp 72°C–74°C.

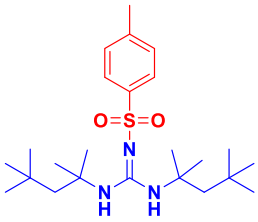
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.57 (d, J = 9.6 Hz, 2H), 7.21–7.15 (m, 10H), 7.09 (d, J = 9 Hz, 2H), 4.25–4.24 (m, 6H), 2.32 (s, 3H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.3, 141.8, 140.8, 139.2, 129.0, 128.5, 127.3, 127.1, 126.0, 45.4, 44.4, 21.4.

IR (KBr, cm^{-1}): ν 3411, 2897, 1603, 1487.

HRMS m/z (ESI) calculated for $C_{22}H_{24}N_3O_2S$ $(M + H)^+$ 394.1584, found 394.1582.

N-(bis((2,4,4-trimethylpentan-2-yl)amino)methylene)-4-methylbenzenesulfonamide (4g)



4g

Following the general procedure, compound **4g** was prepared from 1,1,3,3-tetramethylbutyl isocyanide (190 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (73%, 159 mg); mp 82°C–84°C.

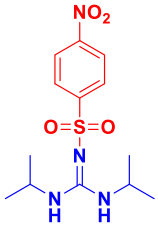
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.77 (d, J = 8.4 Hz, 2H), 7.28 (br, 1H), 7.21 (d, J = 8.4 Hz, 2H), 4.32 (br, 1H), 2.37 (s, 3H), 1.79 (s, 2H), 1.56 (s, 2H), 1.39–1.38 (m, 12H), 1.0 (s, 9H), 0.91 (s, 9H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.1, 141.6, 141.3, 128.8, 125.9, 56.5, 54.6, 52.9, 51.2, 31.4, 21.3.

IR (KBr, cm^{-1}): ν 3351, 2977, 1583, 1441.

HRMS m/z (ESI) calculated for $C_{24}H_{44}N_3O_2S$ $(M + H)^+$ 438.3149, found 438.3147.

N-(bis(isopropylamino)methylene)-4-nitrobenzenesulfonamide (4h)



4h

Following the general procedure, compound **4h** was prepared from isopropyl isocyanide (105 μL), *N,N*-dibromo-4-nitrobenzenesulfonamide (174 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (68%, 111 mg).

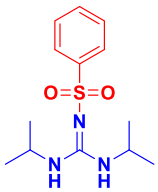
^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.29 (d, J = 9 Hz, 2H), 8.06 (d, J = 9 Hz, 2H), 4.06–3.84 (m, 2H), 1.19 (d, J = 5.4 Hz, 12H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.5, 149.8, 149.2, 127.1, 123.8, 43.6, 22.9.

IR (KBr, cm^{-1}): ν 3337, 2953, 1547, 1519, 1428.

HRMS m/z (ESI) calculated for $C_{13}H_{21}N_4O_4S$ $(M + H)^+$ 329.1278, found 329.1279.

N-(bis(isopropylamino)methylene)benzenesulfonamide (4i)



4i

Following the general procedure, compound **4i** was prepared from isopropyl isocyanide (105 μL), *N,N*-dibromobenzenesulfonamide (157 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (81%, 115 mg); mp 56°C–58°C.

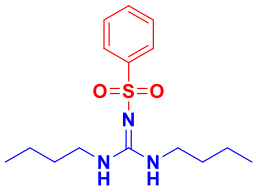
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.88 (d, J = 8.4 Hz, 2H), 7.47–7.41 (m, 3H), 3.93–3.68 (m, 2H), 1.15 (d, J = 7.8 Hz, 12H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.7, 144.1, 131.1, 128.4, 125.9, 43.4, 22.8.

IR (KBr, cm^{-1}): ν 3331, 2959, 1577, 1452.

HRMS m/z (ESI) calculated for $C_{13}H_{22}N_3O_2S$ $(M + H)^+$ 284.1427, found 284.1435.

N-(bis(butylamino)methylene)benzenesulfonamide (4j)



4j

Following the general procedure, compound **4j** was prepared from butyl isocyanide (115 μL), *N,N*-dibromobenzenesulfonamide (164 mg) in presence of water (105 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (78%, 121 mg).

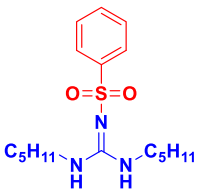
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.90 (d, J = 7.2 Hz, 2H), 7.49–7.43 (m, 3H), 3.18 (br, 2H), 1.59 (s, 2H), 1.52 (s, 2H), 1.35–1.26 (m, 6H), 0.91 (t, J = 7.2 Hz, 6H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.3, 144.0, 131.1, 128.4, 125.8, 41.2, 29.6, 19.8, 13.6.

IR (KBr, cm^{-1}): ν 3335, 2963, 1558, 1487.

HRMS m/z (ESI) calculated for $C_{15}H_{26}N_3O_2S$ $(M + H)^+$ 312.1740, found 312.1747.

N-(bis(pentylamino)methylene)benzenesulfonamide (4k)



4k

Following the general procedure, compound **4k** was prepared from pentyl isocyanide (168 μL), *N,N*-dibromobenzenesulfonamide (157 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless solid (71%, 120 mg); mp 52°C–54°C.

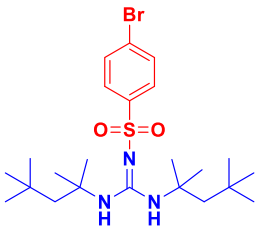
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.86 (d, J = 7.2 Hz, 2H), 7.47–7.40 (m, 3H), 3.15 (br, 4H), 1.49 (s, 4H), 1.28–1.23 (s, 8H), 0.85 (t, J = 6.6 Hz, 6H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.3, 144.0, 131.1, 128.4, 125.8, 41.5, 29.6, 28.7, 22.2, 13.8.

IR (KBr, cm^{-1}): ν 3357, 2945, 1538, 1451.

HRMS m/z (ESI) calculated for $C_{17}H_{30}N_3O_2S$ $(M + H)^+$ 340.2053, found 340.2057.

N-(bis((2,4,4-trimethylpentan-2-yl)amino)methylene)-4-bromobenzenesulfonamide (4L)



4l

Following the general procedure, compound **4L** was prepared from 1,1,3,3-tetramethylbutyl isocyanide (190 μL), *N,N*-dibromo-4-bromobenzenesulfonamide (197 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Colorless liquid (69%, 173 mg).

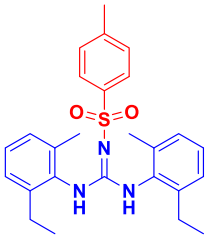
^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.77 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.28 (br, 1H), 4.39 (br, 1H), 1.79 (s, 2H), 1.71 (s, 2H), 1.40 (s, 12H), 1.01 (s, 9H), 0.92 (s, 9H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.1, 143.5, 131.5, 127.6, 125.5, 56.6, 54.8, 52.8, 51.3, 31.4.

IR (KBr, cm^{-1}): ν 3339, 2986, 1547, 1465, 702.

HRMS m/z (ESI) calculated for $C_{23}H_{41}BrN_3O_2S$ $(M + H)^+$ 502.2097, found 502.2086.

N-(bis((2-ethyl-6-methylphenyl)amino)methylene)-4-methylbenzenesulfonamide (4m)



4m

Following the general procedure, compound **3o** was prepared from 1-ethyl-2-isocyano-3-methylbenzene (159 μL), *N,N*-dibromo-*p*-toluenesulfonamide (164 mg) in presence of water (50 μL) and K_2CO_3 (2 equiv, 138 mg). Purified by column chromatography on silica gel (Petroleum ether: EtOAc = 7:2). Brown color solid (74%, 165 mg); mp 128°C–130°C.

^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.95 (br, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.31–7.29 (m, 1H), 7.26–7.21 (m, 4H), 7.15–7.12 (m, 1H), 7.03–7.01 (m, 2H), 5.45 (br, 1H), 2.80–2.74 (m, 1H), 2.63–2.57 (m, 1H), 2.43 (s, 3H), 2.40–2.39 (m, 1H), 2.37 (s, 3H), 2.07 (s, 3H), 1.71 (br, 1H), 1.26 (t, *J* = 7.8 Hz, 3H), 1.0 (t, *J* = 7.8 Hz, 3H).

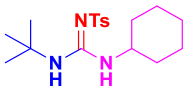
^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.9, 143.1, 141.9, 141.5, 140.8, 137.3, 136.5, 132.3, 131.5, 129.4, 129.2, 128.9, 128.2, 128.1, 127.4, 126.3, 126.2, 60.3, 24.8, 24.4, 21.4, 18.5, 18.0, 14.7, 14.4.

IR (KBr, cm^{-1}): ν 3327, 2937, 1567, 1463.

HRMS m/z (ESI) calculated for $C_{26}H_{32}N_3O_2S$ $(M + H)^+$ 450.2210, found 450.2213.

Characterization of product 7a

N-((*tert*-butylamino)(cyclohexylamino)methylene)-4-methylbenzenesulfonamide (*7a*)



7a

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.75 (d, *J* = 8 Hz, 2H), 7.22 (d, *J* = 8 Hz, 2H), 7.17 (br, 1H), 4.23 (br, 1H), 2.38 (s, 3H), 1.86–1.84 (m, 2H), 1.72–1.69 (s, 3H), 1.68–1.67 (m, 1H), 1.58–1.33 (m, 15H).

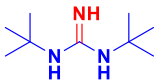
^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.9, 141.4, 141.3, 128.9, 125.9, 125.8, 50.2, 33.9, 29.6, 29.5, 25.3, 24.2, 21.4.

IR (KBr, cm^{-1}): ν 3341, 2984, 1551, 1455.

HRMS m/z (ESI) calculated for $C_{18}H_{30}N_3O_2S$ $(M + H)^+$ 352.2053, found 352.2043.

Characterization of product 8

1,3-di-tert-butylguanidine (8).



8

^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.94 (br, 3H), 2.89 (s, 9H), 2.81 (s, 9H).

^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.4, 61.4, 36.3, 31.2.

IR (KBr, cm^{-1}): ν 3342, 3321, 2947.

HRMS m/z (ESI) calculated for $C_9H_{21}N_3Na$ $(M + Na)^+$ 194.1628, found 194.1620.