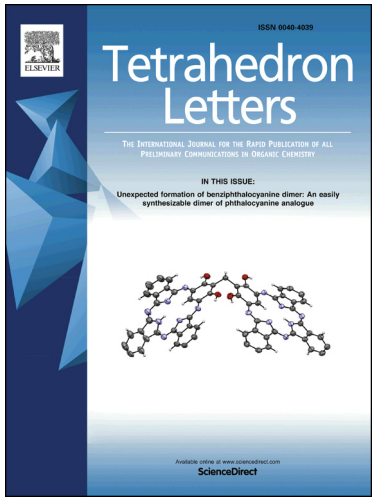


Cyanuric chloride catalyzed metal-free mild protocol for the synthesis of highly functionalized tetrahydropyridines

Rathinam Ramesh, Subramani Maheswari, Mani Arivazhagan, Jan Grzegorz Malecki, Appaswami Lalitha

PII: S0040-4039(17)31096-1
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.08.074
Reference: TETL 49264

To appear in: *Tetrahedron Letters*

Received Date: 13 July 2017
Revised Date: 26 August 2017
Accepted Date: 29 August 2017

Please cite this article as: Ramesh, R., Maheswari, S., Arivazhagan, M., Malecki, J.G., Lalitha, A., Cyanuric chloride catalyzed metal-free mild protocol for the synthesis of highly functionalized tetrahydropyridines, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.08.074

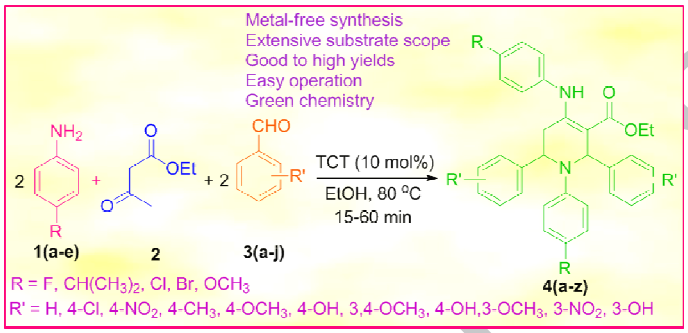
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Cyanuric chloride catalyzed metal-free mild protocol for the synthesis of highly functionalized tetrahydropyridines

Leave this area blank for abstract info.

Rathinam Ramesh, Subramani Maheswari, Mani Arivazhagan, Jan Grzegorz Malecki, Appaswami Lalitha*



ELSEVIER

Tetrahedron Letters
journal homepage: www.elsevier.com

Cyanuric chloride catalyzed metal-free mild protocol for the synthesis of highly functionalized tetrahydropyridines

Rathinam Ramesh[a], Subramani Maheswari[a], Mani Arivazhagan[a], Jan Grzegorz Malecki[b] and Appaswami Lalitha[a,]*

[a]*Department of Chemistry, Periyar University, Periyar Palkalai Nagar, Salem-636011, Tamil Nadu, India*
[b]*Department of Crystallography, University of Silesia, Szkolna 9, 40-006 Katowice, Poland*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Cyanuric chloride
Pseudo five-component reaction
Tetrahydropyridines
Green synthesis

ABSTRACT

An environmentally benign, facile and elegant synthetic approach for the convenient access of a series of diverse 2,6-diaryl-tetrahydropyridine-3-carboxylates *via* a one-pot, pseudo five-component condensation of ethyl acetoacetate, anilines and aromatic aldehydes under mild reaction conditions has been described. This domino strategy allows rapid cyclization in the presence of 10 mol% of cyanuric chloride as a source of hydrochloric acid to afford the desired target skeletons in excellent yields. The present protocol offers prominent advantages of simple operational procedure, metal-free organocatalyst, practically robust and extensive substrate scope.

In recent years, the chemical industry and academia have been functioning together in order to facilitate the newer as well as environmentally benign catalysts and solvents.[1,2] The ultimate intend is to diminish significantly the hazards associated with metal salts and traditional solvents and replacing them with efficient non-toxic alternatives. The explorations of economically viable and readily existing catalysts that create organic transformations in facile route are constantly an attractive approach in modern organic and medicinal chemistry. In this regard, cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) has been accounted as an inexpensive, frequently accessible, low toxic and less corrosive reactants than other similar ones. Owing to their valuable specifics, quite numbers of researchers have been deliberated well with TCT as an efficient catalyst.[3-8]

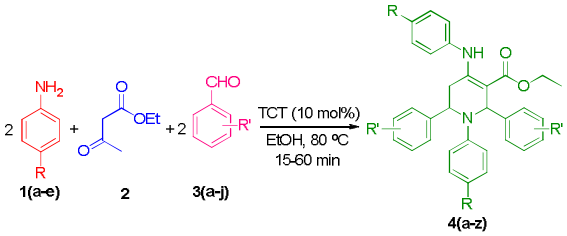
Tetrahydropyridine like compounds are extensively emerging as potent building blocks for numerous natural as well as medicinally privileged synthetic scaffolds.[9-11] Fascinatingly, some of the synthetic methods have been documented in literature for the access of THPs with diverse statics due to their pronounced pharmaceutical usage as, anti-HIV,[12] anticancer,[13] antihistamic,[14] antimicrobial,[15] antimalarial,[16] antiinflammatory[17] and anti-insecticidal[18] agents. In addition, a few of these derivatives have been emerged as potent inhibitors of farnesyl transferase,[19] dihydroorotate dehydrogenase[20] and MAO-based mechanism in Parkinson's diseases.[21,22]

Multicomponent reactions (MCRs) are powerful and highly valuable synthetic tool for the construction of complex and novel organic skeletons with the limited synthetic steps. Simplicity fused with operational procedure, low costs, minimization of chemical wastes and time, high degrees of atom economy and environmental friendliness are the immense advantages over conventional step by step synthetic strategies.[23,24] Following our continuous efforts devoted to the synthesis of diverse heterocyclic compounds with the abets of green solvents or catalysts,[25-31] herein we described an efficient protocol for the convenient access of some novel 2,6-diaryl-tetrahydropyridine-3-carboxylates *via* a one-pot, pseudo five-component reaction using cyanuric chloride (TCT) as a catalyst under mild reaction conditions.

To begin with, stoichiometric amounts of 4-fluoroaniline (**1a**), ethyl acetoacetate (**2**) and 4-chlorobenzaldehyde (**3b**) were taken as model substrates in ethanol for optimization studies. Initially, the reaction was performed without any catalyst at reflux temperature for about 3 h. Where, no tetrahydropyridine derivative (**4b**) was produced. Next, the model reaction was conducted in the presence of sulfamic acid (20 mol%) under identical reaction conditions. In this case, the desired THP derivative was produced in poor yield (47%) after 2 h. In order to get the better outcome of the reaction various catalysts were screened such as, trifluororacetic acid, *p*-toluenesulfonic acid and cyanuric chloride (20 mol% each) and the results are summarized in Table 1. Among the catalysts tested, it was clear that TCT in

* Corresponding author. Tel.: +91-427-234-5271; fax: +91-427-234-5124; e-mail: lalitha2531@yahoo.co.in

ethanol under reflux condition provided the best results (96% yield in 15 min).



Scheme 1. Synthesis of 2,6-diaryl-tetrahydropyridine-3-carboxylate derivatives

Encouraged by this observation, we next examined the reaction with the use of a variety of polar protic and aprotic solvents such as, methanol, acetonitrile, 2-propanol and tetrahydrofuran as reaction medium. The results furnished in Table 1 revealed that, ethanol would be the more desirable solvent for the better outcome of this multicomponent reaction. We have checked the feasibility of our methodology with different percentage of TCT (5, 10, 15 and 20 mol%) as catalyst in ethanol at reflux temperature (Table 1, entries 4, 5, 6 and 7). The reaction proceeded smoothly in the presence of 10 mol% of TCT and offered the desired 2,6-diaryl-tetrahydropyridine-3-carboxylate (**4b**) in excellent yield (Table 1, entry 6). In our quest to fix the optimal temperature for the best results, the model reaction was carried out at ambient conditions and it was found that the reaction was sluggish and provided poor yield of **4b** (29%) even after 8 h. With these findings, we have selected 10 mol% of TCT in ethanol at reflux temperature as a suitable strategy for the preparation of tetrahydropyridine derivatives in an attractive manner.

Table 1. Effect of catalyst and solvent on the synthesis of compound **4b**[a]

Entry	Catalyst	Solvent	Time (min)	Yield[b] (%)
1	NH_2-SO_3H (20 mol%)	EtOH	120	47
2	CF_3COOH (20 mol%)	EtOH	90	69
3	*p*-TSA (20 mol%)	EtOH	120	54
4	TCT (20 mol%)	EtOH	15	96
5	TCT (15 mol%)	EtOH	15	95
6	**TCT (10 mol%)**	**EtOH**	**15**	**95**
7	TCT (5 mol%)	EtOH	45	82
8	TCT (10 mol%)	MeOH	30	87
9	TCT (10 mol%)	CH_3CN	60	81
10	TCT (10 mol%)	$(CH_3)_2CHOH$	60	74
11	TCT (10 mol%)	THF	120	58
12	-	EtOH	180	No Reaction

[a]Reaction conditions: ethyl acetoacetate (2.0 mmol), 4-fluoroaniline (4.0 mmol), 4-chlorobenzaldehyde (4.0 mmol) and catalyst in different solvent (10 ml) stirred at reflux temperature.

[b]Isolated yields.

Next, we turned our interest to explore the generality and scope of the present pseudo five-component reaction with the optimized conditions by using diverse aryl aldehydes (**3a-j**) bearing different functional groups. The unsubstituted benzaldehyde (**3a**) underwent the reaction efficiently and gave the desired product **4a** in 90% yield (Table 2, entry 1). The results depicted in Table 2 revealed that the aldehydes possessing electron-withdrawing (Table 2, entries 2, 3 and 9) or electron-donating substituents (Table 2, entries 4, 5, 6, 7, 8 and 10) in various positions reacted smoothly to afford the corresponding 2,6-diaryl-tetrahydropyridine-3-carboxylates (**4b-j**) in good to excellent yields (89-96%, Table 2, entries 2-10). Finally, the synthesized polyfunctionalized tetrahydropyridine derivatives were confirmed by their melting points, ^1H and ^{13}C NMR spectral analyses.

Table 2. Cyanuric chloride catalyzed pseudo five-component synthesis of 2,6-diaryl-tetrahydropyridine-3-carboxylates[a]

Entry	R	R'	Product	Time (min)	Yield[b] (%)
1	4-F	H	**4a**	20	90
2	4-F	4-Cl	**4b**	15	95
3	4-F	4-NO_2	**4c**	15	96
4	4-F	4-CH_3	**4d**	12	91
5	4-F	4-OCH_3	**4e**	35	93
6	4-F	4-OH	**4f**	45	89
7	4-F	3,4-OCH_3	**4g**	60	91
8	4-F	4-OH,3-OCH_3	**4h**	60	90
9	4-F	3-NO_2	**4i**	20	93
10	4-F	3-OH	**4j**	40	89
11	4-$CH(CH_3)_2$	H	**4k**	30	89
12	4-$CH(CH_3)_2$	4-Cl	**4l**	20	92
13	4-$CH(CH_3)_2$	4-NO_2	**4m**	20	94
14	4-$CH(CH_3)_2$	4-CH_3	**4n**	40	88
15	4-$CH(CH_3)_2$	4-OCH_3	**4o**	45	90
16	4-$CH(CH_3)_2$	4-OH	**4p**	60	87
17	4-$CH(CH_3)_2$	3,4-OCH_3	**4q**	55	90
18	4-$CH(CH_3)_2$	4-OH,3-OCH_3	**4r**	60	88
19	4-$CH(CH_3)_2$	3-NO_2	**4s**	25	91
20	4-$CH(CH_3)_2$	3-OH	**4t**	60	88
21	4-Cl	4-Cl	**4u**	20	93
22	4-Br	4-Cl	**4v**	20	95
23	4-OCH_3	4-Cl	**4w**	35	89
24	4-F	2-NO_2	**4x**	30	91
25	4-F	2-Cl	**4y**	30	88
26	4-F	2-OH	**4z**	60	85

[a]Reaction conditions: ethyl acetoacetate (2.0 mmol), 4-substituted aniline (4.0 mmol), aromatic aldehyde (4.0 mmol) and cyanuric chloride (10 mol%) in ethanol (10 ml) stirred at 80 °C.

[b]Isolated yields.

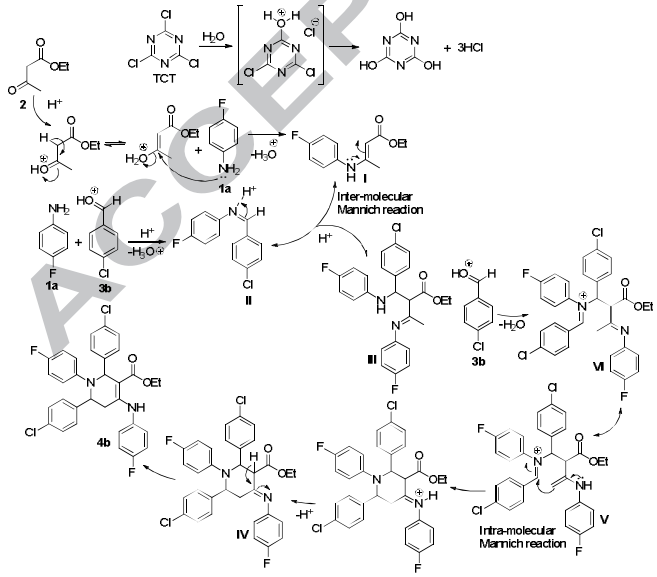
In the ^1H NMR spectrum of compound **4b** as a representative example, the ethoxy (-OCH_2CH_3) protons appeared as a triplet at δ 1.35 ppm (J = 7.2 Hz) and two multiplets at δ 4.23-4.38 ppm (J = 7.2 Hz). A couple of doublets observed at δ 2.66 ppm (J = 14.8 Hz) and δ 2.92ppm (J = 15.2 Hz) corresponds to the methylene (CH_2) protons of the THP ring. One of the benzylic methine (-CH) proton of the THP ring showed a singlet at δ 5.33 ppm and another methine proton (-CH) showed a singlet at δ 6.17 ppm respectively. The aromatic protons were observed as multiplets in the range at δ 6.32-7.39 ppm. The NH proton was observed as a singlet at δ 10.15 ppm clearly indicating that it was connected to

the vicinal carbonyl group (-C=O) *via* a intramolecular H-bond formation. In the ^{13}C NMR spectrum, the carbonyl carbon (-C=O) showed a peak at δ 165.3 ppm and the aromatic carbons were observed in the range at δ 114.8-148.8 ppm respectively. In addition, the methylene and methine carbons showed signals at δ 52.0-62.6 ppm. Specifically, the mono crystal structure of compound **4d** was further confirmed by X-ray diffraction analysis (Figure 1). With these spectral evidences we unambiguously confirmed the structure of the synthesized compounds.

The efficacy of TCT is compared with the earlier reported catalytic methods by the chemical yield, catalyst quantity and reaction time. Besides, this protocol works adequately on gram scale (50 mmol) for the preparation of compound **4b** (25.62g, 88%) as representative reaction. The results revealed (Table 3, Entry 10), that 10 mol% cyanuric chloride is most effective for the better outcome of the present synthetic approach and this may opened a new avenue for the efficient access of polyfunctionalized THPs in gram scale production.

Table 3. Comparison of efficacy of TCT with reported catalytic methods

Entry	Catalyst	Conditions	Time (min)	Yield (%)
1	Graphene oxide	CH_3CN, Reflux	210	91[32]
2	CAN (15 mol%)	CH_3CN, RT	2100	68[33]
3	[Dsbim]Cl (10 mol%)	Solvent-free, 80 °C	30	96[34]
4	Fe@Si-Gu-Prs	Solvent-free, RT	25	91[35]
5	ZnO NPs	Solvent-free, RT	180	89[36]
6	2,6-PDCA (10 mol%)	MeOH, RT	480	80[37]
7	NFS-PWA	Solvent-free, RT	30	91[38]
8	[Bmim-G-$(SO_3H)_4$]$^+$[HSO_4]$^-$	EtOH, 40 °C	600	83[39]
9	$CoFe_2O_4$ MNPs (8 mol%)	H_2O:EtOH, 120 °C	60	94[40]
10	TCT (10 mol%)	EtOH, Reflux	15	95[This work]



Scheme 2. Plausible mechanistic steps in the formation of compound **4b**

The possible mechanism that suits for the synthesis of tetrahydropyridines has been outlined in Scheme 2. Initially, the cyanuric chloride reacts with atmospheric moisture to give three molecules of HCl with cyanuric acid as a by-product. The starting substrates 4-fluoroaniline (**1a**) and ethyl acetoacetate (**2**) reacted together to afford the β-enaminone intermediate (**I**) which was assisted by the HCl generated from TCT. In the next step, the 4-chlorobenzaldehyde (**3b**) condensed with another molecule of 4-fluoroaniline (**1a**) gives the desired Schiff's base (**II**). Then the enaminone (**I**) and the Schiff's base (**II**) undergo intermolecular Mannich reaction in the presence of H^+ to afford the intermediate **III**. Here, one more molecule of activated aldehyde (**3b**) reacted with **III** to offer the intermediate **IV** by the removal of water molecule. Then, the intermediate **IV** undergoes tautomerization to generate the more reactive intermediate **V**, which subsequently undergoes intramolecular Mannich reaction to give the functionalized piperidine (**VI**) skeleton. Finally, the intermediate **VI** tautomerizes under acidic condition to afford the polyfunctionalized tetrahydropyridine (**4b**) as a sole product.

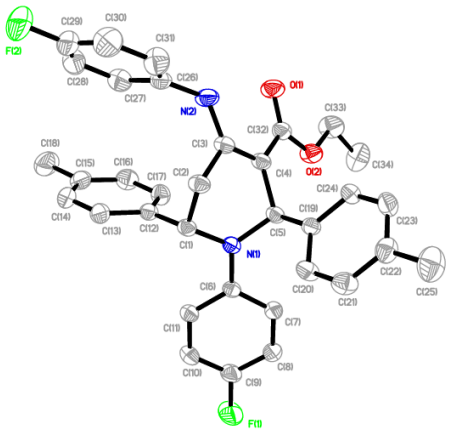


Figure 1. ORTEP of compound **4d** (CCDC 1561955)

After the execution of our strategy in a successive manner, we further enlarging the versatility of this pseudo multi-component approach by using 4-isopropylaniline (**1b**) as an alternative for 4-fluoroaniline (**1a**) under the optimal reaction conditions. The results are also furnished in Table 2 (Entries 11-20). The model experiment by the employment of benzaldehyde (**3a**) was also found to be appropriate for the pseudo-reaction and provided the corresponding product (**4k**) in 89% yield (Table 2, entry 11). It is more clear from the results outlined in Table 2 that, all the studied reactions proceeded very smoothly and aldehydes bearing substituents in different positions were also well tolerated to provide the corresponding targets **4(l-t)** in moderate to good yields (87-94%). In addition, the scope of this methodology was further explored to the other aryl amines **1(c-d)** and *ortho*-substituted benzaldehydes (*nitro, chloro* and *hydroxy*) proved to be fine substrates. Pleasingly, the reactions were accomplished effectively under similar reaction conditions affording the desired products **4u-4z** in good yields (Table 2, entries 21-26). The structural skeleton of the synthesized tetrahydropyridine derivatives were in fine concurrence with the spectral data.

Furthermore, the employment of TCT as a catalyst with the production of cyanuric acid as by-product reveals the lack of ability in catalytic recycle and it can be removed by washing with water. In order to find the catalytic activity of *in-situ* cyanuric acid, we have conducted the reaction between 4-fluoroaniline (**1a**), ethyl acetoacetate (**2**) and 4-chlorobenzaldehyde (**3b**) with 10 mol % of cyanuric acid as a catalyst and observed that the reaction could not be completed even after 8 h.

The utilization of this protocol for the preparation of tetrahydropyridines catalyzed by TCT was exemplified as a newer approach for the efficient access of pyridine bearing candidates corroborating as natural and drug like molecules. It is the more practical and shortest route for the syntheses of THPs amid the reported avenue till date.

In conclusion, we have introduced the cyanuric chloride catalyzed, an efficient, green and practical approach for the preparation of 2,6-diaryl-tetrahydropyridine-3-carboxylates through the pseudo five-component reaction of ethyl acetoacetate, anilines and aryl aldehydes under mild reaction conditions. Owing to the exemplary synthetic versatility, this protocol offers some other advantages such as, use of organocatalyst, simple starting substrates, shorter reaction times and good chemical yields. The proficient catalytic activity of the TCT in this cyclocondensation reaction will definitely accumulate to the already existing synthetic methodologies for gram scale productions which make the present domino process more convenient and eco-friendly.

Acknowledgments

R. Ramesh gratefully thank DST-Inspire Fellowship, New Delhi, India (No: DST/INSPIRE Fellowship/2012/690) for financial assistance.

References and notes

1. Shekouhya, M.; Nezhad, A. K. *Green Chem*. **2015**, *17*, 4815-4829.
2. Safaei, H. R.; Shekouhy, M.; Rahmanpur, S.; Shirinfeshan, A. *Green Chem.* **2012**, *14*, 1696-1704.
3. Bigdeli, M. A.; Heravi, M. M.; Mahdavinia, G. H. *Catal. Commun*. **2007**, *8*, 1595-1598.
4. Luca, L. D.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272-6274.
5. Sharma, G. V. M.; Reddy, J. J.; Lakshmi, P. S. *Tetrahedron Lett*. **2004**, *45*, 7729-7732.
6. Sharma, G. V. M.; Reddy, K. L.; Lakshmi, P. S.; Radhakrishna, S. *Synthesis* **2006**, *1*, 55-58.
7. Sivaguru, P.; Theerthagiri, P.; Lalitha, A. *Tetrahedron Lett*. **2015**, *56*, 2203-2206.
8. Sharma, M.; Pandey, S.; Chauhan, K.; Sharma, D.; Kumar, B.; Chauhan, P. M. S. *J. Org. Chem.* **2012**, *77*, 929-937.
9. Tawara, J. N.; Lorenz, P.; Stermitz. F. R. *J. Nat. Prod*. **1999**, *62*, 321-323.
10. Lebold, T. B.; Leduc, A. B.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 3770-3772.
11. Watson, P. S.; Jiang, B.; Scott, B. A. *Org. Lett*. **2000**, *2*, 3679-3681.
12. Imamura, S.; Nishikawa, Y.; Ichikawa, T.; Hattori, T.; Matsushita, Y.; Hashiguchi, S.; Kanzaki, N.; Iizawa, Y.; Baba, M.; Sugihara, Y. *Bioorg. Med. Chem.* **2005**, *13*, 397-416.
13. Srinivas, C.; Kumar, C. N.; Raju, B. C.; Rao, V. J.; Naidu, V. G. M.; Ramakrishna, S.; Diwan, P. V. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 5915-5918.
14. Saxena, M.; Gaur, S.; Prathipati, P.; Saxena, A. K. *Bioorg. Med. Chem.* **2006**, *14*, 8249-8258.
15. Umamatheswari, S.; Balaji, B.; Ramanathan, M.; Kabilan, S. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 6909-6914.
16. Misra, M.; Pandey, S. K.; Pandey, V. P.; Pandey, J.; Tripathi, R.; Tripathi, R. P. *Bioorg. Med. Chem.* **2009**, *17*, 625-633.
17. Khanum, S. A.; Girish, V.; Suparshwa, S. S.; Khanum, N. F. *Bioorg. Med. Chem. Lett*. **2009**, *19*, 1887-1891.
18. Bandaraa, K. A. N.; Kumara, V.; Jacobsson, U.; Molleyresc, L. P. *Phytochemistry* **2000**, *54*, 29-32.
19. Gwaltney, S. L.; Connor, S. J. O.; Nelson, L. T. J.; Sullivan, G. M.; Imade, H.; Wang, W.; Hasvold, L.; Li, Q.; Cohen, J.; Gu, W. Z.; Tahir, S. K.; Bauch, J.; Marsh, K.; Ng, S. C.; Frost, D. J.; Zhang, H.; Muchmore, S.; Jakob, C. G.; Stoll, V.; Hutchins, C. *Bioorg. Med. Chem. Lett*. **2003**, *13*, 1363-1366.
20. Nallan, L.; Bauer, K. D.; Bendale, P.; Rivas, K.; Yokoyama, K.; Horney, C. P.; Pendyala, P. R.; Floyd, D.; Lombardo, L. J.; Williams, D. K.; Hamilton, A.; Sebti, S.; Windsor, W. T.; Weber, P. C.; Buckner, F. S.; Chakrabarti, D.; Gelb, M. H.; Van Voorhis, W. C. *J. Med. Chem.* **2005**, *48*, 3704-3713.
21. Beeler, A. B.; Gadepalli, R. S. V.; Steyn, S.; Castagnoli, N.; Rimoldi, J. M. *Bioorg. Med. Chem*. **2003**, *11*, 5229-5234.
22. Deskus, J. A.; Epperson, J. R.; Charles, P. S.; Joseph, A. C.; Dextraze, P.; Cutrone, J. Q.; Gao, Q.; Ma, B.; Beno, B. R.; Mattson, G. K.; Molski, T. F.; Krause, R. G.; Taber, M. T.; Lodge, M. J.; Mattson, R. J. *Bioorg. Med. Chem. Lett*. **2007**, *17*, 3099-3104.
23. Dömling, A.; Wang, W.; Wang, K. *Chem. Rev*. **2012**, *112*, 3083-3135.
24. Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K. *Chem. Rev*. **2014**, *114*, 8323-8359.
25. Ramesh, R.; Lalitha, A. *RSC Adv*. **2015**, *5*, 51188-51192.
26. Ramesh, R.; Lalitha, A. *Res. Chem. Intermed*. **2015**, *41*, 8009-8017.
27. Ramesh, R.; Maheswari, S.; Murugesan, S.; Sandhiya, R.; Lalitha, A. *Res. Chem. Intermed*. **2015**, *41*, 8233-8243.
28. Ramesh, R.; Vadivel, P.; Maheswari, S.; Lalitha, A. *Res. Chem. Intermed*. **2016**, *42*, 7625-7636.
29. Ramesh, R.; Lalitha, A. *ChemistrySelect* **2016**, *1*, 2085-2089.
30. Ramesh, R.; Madhesh, R.; Malecki, J. G.; Lalitha, A. *ChemistrySelect* **2016**, *1*, 5196-5200.
31. Ramesh, R.; Nagasundaram, N.; Meignanasundar, D.; Lalitha, A. *Res. Chem. Intermed*. **2017**, *43*, 1767-1782.
32. Gupta, A.; Kaur, R.; Singh, D.; Kapoor, K. K. *Tetrahedron Lett*. **2017**, *58*, 2583-2587.
33. Wang, H. J.; Mo, L. P.; Zhang, Z. H. *ACS Comb. Sci*. **2011**, *13*, 181-185.
34. Abbasi, M. *RSC Adv*. **2015**, *5*, 67405-67411.
35. Eshghi, H.; Khojastehnezhad, A.; Moeinpour, F.; Rezaeian, S.; Bakavoli, M.; Teymouri, M.; Rostami, A.; Haghbeen, K. *Tetrahedron* **2015**, *71*, 436-444.
36. Kataria, M.; Pramanik, S.; Kumar, M.; Bhalla, V. *Chem. Commun*. **2015**, *51*, 1483-1486.
37. Khan, M.; Khan, S.; Iqbal, S.; Saigal.; Yousuf, R. *New J. Chem.* **2016**, *40*, 7504-7512.
38. Eshghi, H.; Khojastehnezhad, A.; Moeinpour, F.; Bakavoli, M.; Seyedi, S. M.; Abbasi, M. *RSC Adv*. **2014**, *4*, 39782-39789.
39. Zhou, Q.; Wan, Y.; Zhang, X.; Zhang, L.; Zou, H.; Cui, H.; Zhou, S.; Wang, H.; Wu, H. *Tetrahedron* **2015**, *71*, 7070-7072.
40. Remaily, M. A. A.; Dief, A. M. A.; Khatib, R. M. *Appl. Organometal. Chem.* **2016**, *30*, 1022-1029.

Supplementary Material

A detailed experimental procedure, spectral data, copy of ^{1}H and ^{13}C NMR and X-ray crystallographic data were attached.

Click here to remove instruction text...

- Cyanuric chloride (TCT) is a stable, inexpensive and easily accessible reagent
- High-yielding multicomponent reaction under mild conditions
- Easier work-up method that is environmentally benign and can be readily scaled-up
- Structures were also confirmed by single crystal X-ray diffraction