Journal of the Iranian Chemical Society
https://doi.org/10.1007/s13738-018-1410-3

ORIGINAL PAPER

Friedlander synthesis of highly functionalized isoxazolyl quinoline libraries via addition of C(sp3)–H bond to aldehydes

Ramakrishna Saini[1] · **Nagaraju Dharawath**[2]

Received: 1 March 2018 / Accepted: 21 May 2018

Abstract
A novel protocol for ionic liquid (IL)-mediated C(sp^3)–H bond functionalization of 3,5-dimethyl-4-nitroisoxazoles **4** to substituted *o*-amino benzaldehydes **5** was developed in excellent yields. Isoxazolyl aryl ethanones **7** have been synthesized from isoxazolyl aryl ethanol synthon **6**. Furthermore, utilizing the later as synthons for IL promoted Friedlander synthesis of highly functionalized isoxazole substituted quinoline libraries **9**. The merit of this synthesis is easily available and economical starting materials, effective utilization of all the reactants, and simple workup procedure. It is noteworthy that ionic liquid used in C(sp^3)–H bond functionalization and Friedlander synthesis reactions can be recycled and reused five times without significant decrease in activity.

Keywords Ionic liquid · C(sp^3)–H bond functionalization · Friedlander synthesis · Isoxazolyl quinolines

Introduction

It is well known that heterocyclic compounds play an important role in developing a new class of structural entities for pharmaceutical applications. Isoxazoles functionalized with an additional nitrogen-containing group have had applications in medicinal chemistry [1–14]. They possess interesting medicinal or crop protection properties as well as other industrial utility. They are important constituents of various drugs such as COX-2 selective inhibitor Valdecoxib (**I**) [15], anti-rheumatic Leflunomide (**II**) [16], β-lactamase-resistant Cloxacillin (**III**) [17] (Fig. 1). The immense bioactivity of isoxazole ring may be attributed to the facile cleavage of N–O bond, which leads to the formation of other more reactive species. Because of their versatility towards chemical transformations to useful intermediates involved in various natural product synthesis, substituted isoxazoles are considered as one of the important synthons [18–20].

Among the heterocyclic compounds quinoline and its derivatives are pharmacologically important because of their wide spectrum of biological activities [21]. One of the quinoline derivatives, Quinine (**IV**) shows antimalarial, antipyretic, anti-inflammatory and analgesic properties. Quinoline based compound Mefloquine (**V**) is known for potent anti-tubercular activity [22–25] have exhibited moderate to sub micromolar anti-TB activity [26, 27]. Tibotec Medicinal Compound TMC207 (**VI**) (Fig. 1) has emerged as a lead molecule in the development of new anti-TB agent and currently this compound is approved by US-FDA on 28th December 2012. It is also known as Bedaquiline (**VI**). It is first new drug for TB in more than forty years. It is on World health organization's list of essential medicines [28, 29].

For decades, it had been generally believed that the cleavage of a C–H bond via oxidative addition was a difficult process because of its strong bond strength. Consequently, the majority of studies focused on the cleavage of C–H bonds via the use of stoichiometric amounts of transition metal complexes. At present, it has been accepted that the cleavage of C–H bonds is not always a difficult process, and that the cleavage of a C–H bond is often not the rate determining step [30]. On the basis of a recent literature survey, C(sp^3)–H bonds which are adjacent to a heteroatom are, however, more reactive than those surrounded by carbon atoms.

The development of new strategies for the direct functionalization of C(sp^3)–H bonds of methyl azaarenes has become a major topic of research [31]. The C(sp^3)–H bond activation [32] adjacent to nitrogen followed by C-C bond

✉ Ramakrishna Saini
chemistram@gmail.com

[1] Department of Chemistry, Kakatiya University, Warangal, TS 506 009, India

[2] Department of Chemistry, Telangana University, Nizamabad, TS 503 322, India

Published online: 28 May 2018

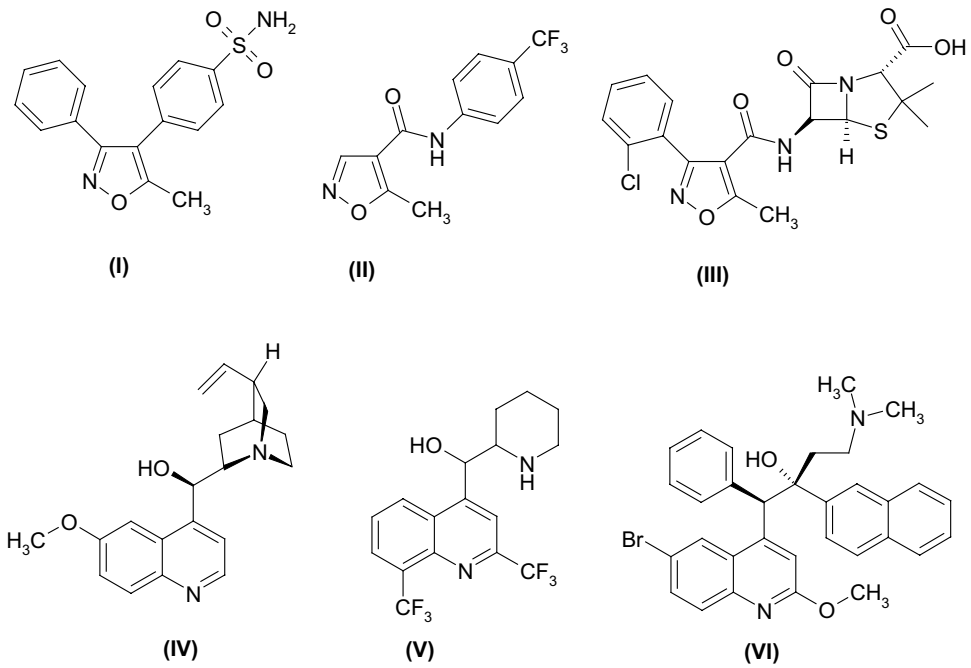


Fig. 1 Clinically used drugs containing isoxazole and quinoline motif

forming reactions of azaarenes provide [33] straightforward access to useful building blocks for the design and synthesis of biologically active compounds. In view of significance of isoxazole and bioactive quinoline skeletons and as our continuous efforts on the synthesis of heterocycles with potential bioactivities [34–40], herein we report ionic liquid mediated C(sp^3)–H bond functionalization of 3,5-dimethyl-4-nitroisoxazole to substituted *o*-amino benzaldehydes, and furthermore, utilizing the later as synthons for the Friedlander synthesis of highly functionalized isoxazole substituted quinoline libraries.

Experimental

General procedure for the addition of 3,5-dimethyl-4-nitroisoxazole-C(sp^3)–H bond to substituted *o*-amino benzaldehydes (**6a–k**).

A mixture of 3,5-dimethyl-4-nitroisoxazole **4** (1 mmol) and substituted *o*-amino benzaldehyde **5** (1 mmol) were taken in triethyl amino acetic acid (TEAA) ionic liquid (5 mL) and the reaction mixture was stirred at 60 °C. After the completion of the reaction (monitored by TLC), the reaction mixture was extracted with diethyl ether. The combined layers were separated and dried over anhyd. Na_2SO_4, and evaporated under reduced pressure to afford the crude products (**6a–k**). The ionic liquid left over in the reaction was washed with ethyl acetate and dried over 80 °C under vacuum and was reused for 5 consecutive runs. The procedure was followed for all the reactions, as listed in Table 2.

General procedure for the synthesis of 2-(3-methyl-4-nitro-5-isoxazolyl)-1-aryl-1-ethanones (**7a–k**).

A mixture of 2-(3-methyl-4-nitro-5-isoxazolyl)-1-aryl-1-ethanols **5** (1 mmol) and *o*-iodoxybenzoic acid (IBX) (1 mmol) in EtOAc (10 mL) was refluxed at 80 °C for 4 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and filtered. The separated solid was washed with water and recrystallized from ethanol.

General procedure for Friedlander synthesis of highly functionalized isoxazole substituted quinoline libraries (**9a–q**).

A mixture of 2-(3-methyl-4-nitro-5-isoxazolyl)-1-aryl-1-ethanones **7** (1 mmol) and α-methylene carbonyls **8** (1 mmol) were taken in triethyl amino acetic acid (TEAA) ionic liquid (5 mL) and the reaction mixture was stirred at 60 °C. After the completion of the reaction (monitored by TLC), the reaction mixture was extracted with diethyl ether. The combined layers were separated and dried over anhyd. Na_2SO_4, and evaporated under reduced pressure to afford the crude products (**9a–q**). The ionic liquid left over in the reaction was washed with ethyl acetate and dried over 80 °C under vacuum and was reused for 5 consecutive runs.

Results and discussion

Until today most, of the methods for obtaining pyridine and quinoline derivatives is the direct C(sp^3)–H functionalization of alkyl substituted azaarenes [41–43]. Zhang and coworkers reported the ionic liquid (IL) promoted addition of

C(sp^3)–H bond to aldehydes [44]. Here in we considered the oxa-azaarene *viz*., 3,5-dimethyl-4-nitro isoxazole **4** [45, 46] in the place of oxa-azaarenes *viz*., pyridine and quinoline derivatives for direct C(sp^3)–H functionalization of alkyl substituted oxa-azaarenes. Considering the similarity between compounds **1**, and **4**, we posed the question of whether the later could be employed in addition of C(sp^3)–H bond to aldehyde (Scheme 1). Resulting oxa-azaarene substituted aryl ethanols contain several chemo-differentiable functionalities and could be subsequently employed to generate chemical diversity.

Table 1 Optimization of reaction conditions for the synthesis of 6a

Entry	Ionic liquid	Solvent	Condition	Time (min)	Yield[a] (%)
1	TEEA	None	CH[b]	25	96
2	[bmIm]BF_4	None	CH[b]	40	25
3	[bmIm]OH	None	CH[b]	35	41
4	[bmIm]Br	None	CH[b]	85	36
5	[HmIm]BF_4	None	CH[b]	40	32
6	[HmIm][HSO_4]	None	CH[b]	60	65
7	[Hnhm][HSO_4]	None	CH[b]	75	25
8	TEEA	None	MW[c]	15	61
9	[bmIm]BF_4	None	MW[c]	20	41
10	[bmIm]OH	None	MW[c]	10	29
11	[bmIm]Br	None	MW[c]	10	45
12	[HmIm]BF_4	None	MW[c]	25	38
13	[HmIm][HSO_4]	None	MW[c]	20	41
14	[Hnhm][HSO_4]	None	MW[d]	15	30
15	TEEA	H_2O	MW[c]	20	38
16	[bmIm]BF_4	H_2O	MW[c]	40	11
17	[bmIm]OH	H_2O	MW[c]	35	22
18	[bmIm]Br	H_2O	MW[c]	40	12
19	[HmIm]BF_4	H_2O	MW[c]	25	16
20	[HmIm][HSO_4]	H_2O	MW[c]	50	20
21	[Hnhm][HSO_4]	H_2O	MW[c]	60	19
22	None	H_2O	MW[c]	100	trace

Reaction conditions: 3,5-Dimethyl-4-nitro isoxazole **4** (1 mmol), *o*-amino benzaldehyde **5a** (1 mmol) and IL (5 mL)

[a]Isolated and unoptimized yields

[b]Conventional Heating

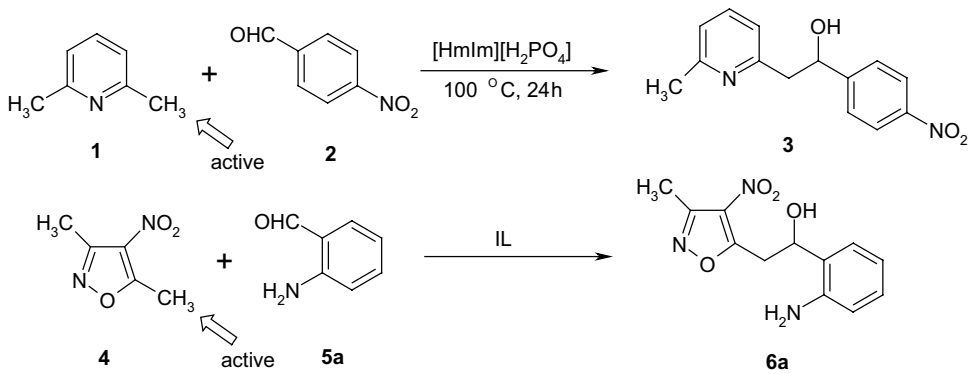
[c]Microwave Condition. Irradiation Power: 850 W; Ramp time: 1 min. 70 °C; holding temp: 100 °C

To establish the feasibility of the strategy, and optimize the reaction conditions, the reaction was initially carried out in the presence of different ILs (Scheme 2). Among the ILs employed triethylamino acetic acid (TEAA) [47, 48] proved to be the most effective in terms of yields, reaction time and more recyclability. Utilization of other ILs was found to be quite unsatisfactory (Table 1). For comparison purpose, we attempted addition of isoxazole C(sp^3)–H bond to aldehyde under microwave irradiation using different ILs. As can be seen from Table 1, a moderate yield (61%) of desired product was isolated when ionic liquid TEAA was used (Table 1, Entry 8). We further investigated the reactions with ILs in presence of H_2O. When H_2O was employed as a solvent with ILs, lower yields were obtained (Table 1, Entries 15–21). The reason that the lower yields of this reaction may be somewhat be attributed to the low solubility of reactants in H_2O.

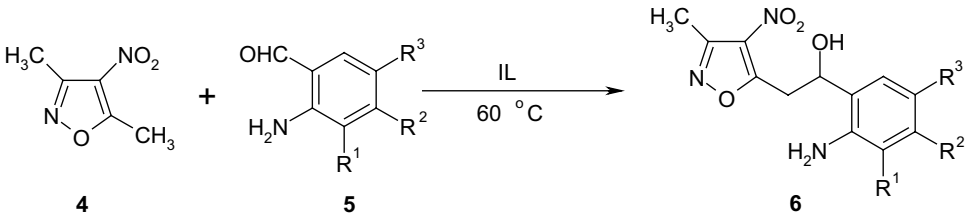
We presume the mechanism of this reaction may be shown in scheme 3. Only 5-methyl group of 3,5-dimethyl-4-nitro isoxazole is activated by the nitro group, which is in agreement with literature observation [49]. The nucleophilic addition of intermediate **A** to aromatic aldehyde which was activated by TEAA would occur to afford the desired adduct.

To investigate the scope of TEAA IL in the addition of isoxazole C(sp^3)–H bond to aldehyde (Scheme 2), several substituted *o*-amino benzaldehydes are examined and the result are summarized in Table 2. As shown in Table 2, substituted *o*-amino benzaldehydes with electron with drawing groups attached to benzene ring, such as chloro, bromo could react with 3,5-dimethyl-4-nitro isoxazole smoothly to generate the corresponding products in excellent yields (Entry 2,3, and 5). When electron-donating groups attached to benzene ring such as methoxy and methyl were subjected to this reaction, slightly, lower yields were realized. There

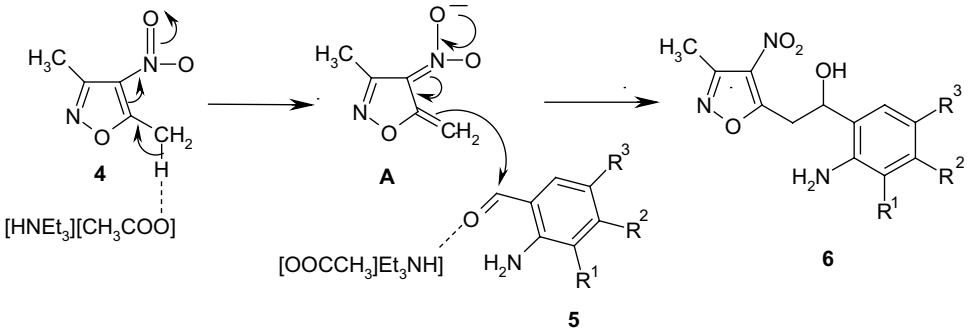
Scheme 1 Addition of C(sp^3)–H bond to aldehydes



Scheme 2 Addition of 3,5-dimethyl-4-nitroisoxazole-C(sp^3)–H bond to aldehydes



Scheme 3 Proposed mechanism of addition of isoxazole C(sp^3)–H bond to aldehyde



is no considerable hindrance of amino group on yields of the reaction. In all the cases, the products were obtained in good to excellent yields.

All the reactions were carried out with **4** (1 mmol), **5** (1 mmol) and TEAA (5 mL) at 60 °C. Isolated and unoptimized yields.

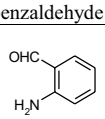
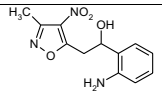
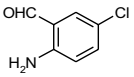
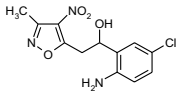
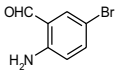
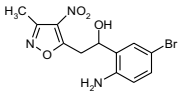
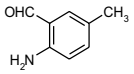
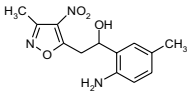
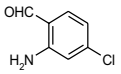
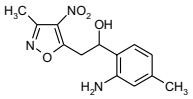
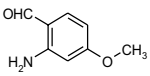
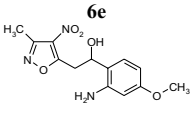
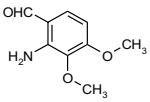
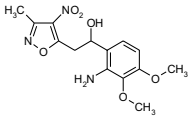
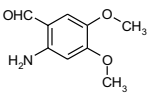
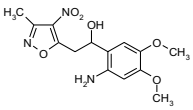
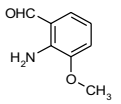
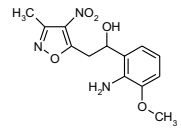
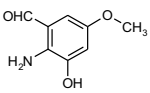
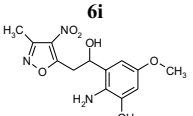
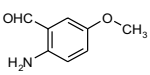
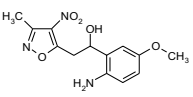
With the findings of addition of 3,5-dimethyl-4-nitroisoxazole **4** C(sp^3)–H bond to aldehyde **5**, we utilize these synthons *viz*., isoxazolyl aryl ethanols **6** as building blocks for the synthesis of novel highly functionalized isoxazolyl quinolines. The initial reaction was explored by refluxing 1-(2-aminophenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethanol **6a** with *o*-iodoxy benzoic acid (IBX) in DMF at 80 °C to afford the 1-(2-aminophenyl)-2-(3-methyl-4-nitroisoxazol-5-yl)ethanone **7a** in excellent yields [36] (Table 3). The reaction was carried out with different isoxazolyl aryl ethanols **6a-k**, and in each case the reaction proceeded smoothly and products are obtained in excellent yields (Scheme 4).

Heterogenous catalysis has also been employed in Friedlander synthesis by Das and co-workers [26]. Vittal Rao et al., have observed in Friedlander synthesis of quinolines, catalysed by BDMS, heterocyclic aldehydes/ketones gave low yields, and aliphatic and aromatic aldehydes were not good substrates and reaction did not progress [51]. To establish the TEAA IL promoted Friedlander synthesis of isoxazolyl quinolines, we started our investigation by reacting, 1-(2-aminophenyl)-2-(3-methyl-4-nitroisoxazol-5-yl) ethanone **7a** and α-methylene carbonyl **8a** [36] in TEAA IL (5 mL) as a model reaction. To our surprise the reaction resulted in the formation of isoxazolyl substituted quinoline *viz*., 3-methyl-5-((3-(3-methyl-4-nitroisoxazol-5-yl)-2-phenylquinolin-4-yl)methyl)-4-nitroisoxazole **9a** in excellent yield (90%) (Scheme 5). The generality of the reaction was investigated by employing heterocyclic ketones, cyclic ketones, 1,3-diketones and so forth, and results are presented in Table 4. Both electron-rich and electron deficient isoxazolyl aryl amines **7** provided excellent yields. Electron deficient α-methylene carbonyls **8** reacted with isoxazolyl aryl amines **7** very effectively in excellent yields, but some electron-rich α-methylene carbonyls took more time comparatively. This set of experiments set a proof of principle for the desired isoxazolyl quinolines and this method is general and tolerate to substitutions as well as changes in carbonyls.

The Friedlander synthesis proceeds *via*., aldol condensation **8** and imine formation **9**. A rate limiting aldol reaction, followed by elimination of water and imine formation with further loss of water leads to quinoline **9** (Scheme 6). Alternatively, Schiff's base formation followed by aldol reaction and water elimination also leads to the formation of quinoline **9**. However, in this case aldol reaction is the first step, because reaction does not proceed at low temperature. Since aldol condensation, being an equilibration reaction, which can be propelled only by heating. TEAA plays active role in enolization as well as Schiff's base formation and cyclization.

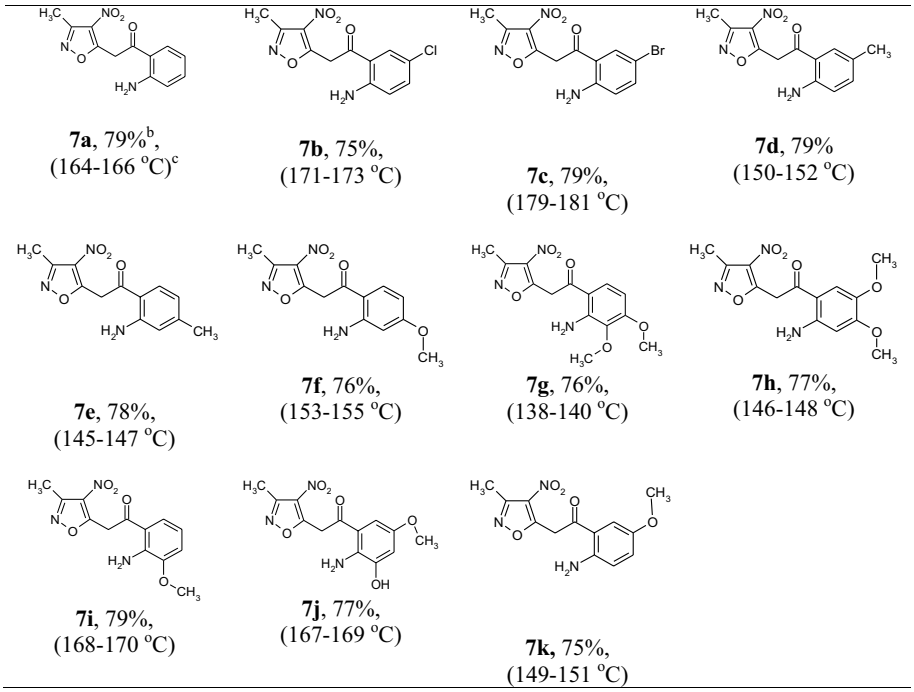
The assigned structures of new products (**6a–k, 7a–k** and **9a–q**) were established from their spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR). IR spectra of **6a-k** showed absorption bands around 3440–3478 cm^{-1} for hydroxyl group. Similarly, IR spectra of compounds **7a-k** have showed absence of absorption band around 3440–3478 cm^{-1} for hydroxy group and exhibited new absorption band around 1641–1684 cm^{-1} for the formation of carbonyl group. The IR spectra of **9a-q** have exhibited

Table 2 Substrate scope of the 3,5-dimethyl-4-nitroisoxazole, substituted *o*-amino benzaldehyde

Entry	3,5-dimethyl-4-nitro isoxazole **4**	substituted *o*-amino benzaldehyde **5**	Product **6**	Time (min)	Yield (%)	M.P. (°C)
1	**4**	 **5a**	 **6a**	25	90	126-128
2	**4**	 **5b**	 **6b**	30	96	137-139
3	**4**	 **5c**	 **6c**	35	95	135-137
4	**4**	 **5d**	 **6d**	25	90	109-111
5	**4**	 **5e**	 **6e**	30	96	103-105
6	**4**	 **5f**	 **6f**	35	92	131-333
7	**4**	 **5g**	 **6g**	25	91	128-130
8	**4**	 **5h**	 **6h**	35	89	121-123
9	**4**	 **5i**	 **6i**	30	89	119-121
10	**4**	 **5j**	 **6j**	30	90	116-118
11	**4**	 **5k**	 **6k**	25	90	140-142

[c]All the reactions were carried out with 4 (1 mmol), 5 (1 mmol) and TEAA (5 mL) at 60 °C. Isolated and unoptimized yields

Table 3 Substrate scope of isoxazolyl aryl ethanols

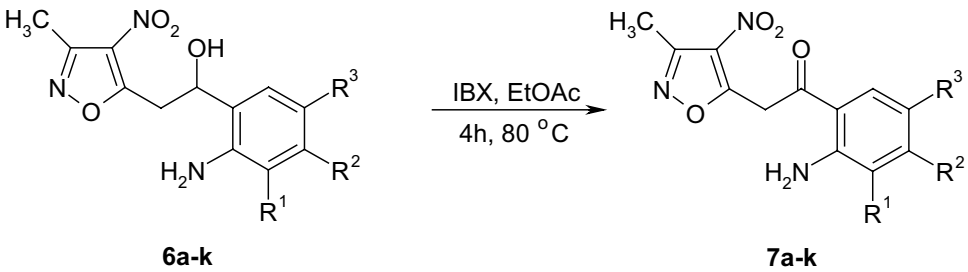


All reaction were carried out with **6** (1 mmol) and *o*-iodoxybenzoic acid (IBX) (1 mmol) in EtOAc (10 mL) was refluxed at 80 °C for 4 h

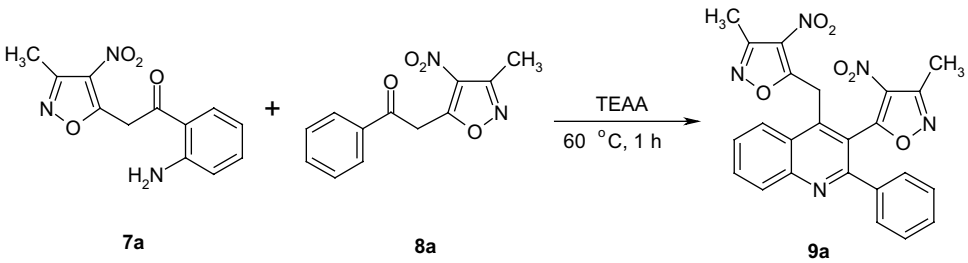
[a]Isolated yields

[b]Melting Point found reported

Scheme 4 Synthesis of isoxazolyl aryl ethanones

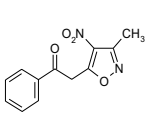
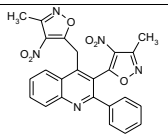
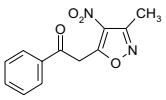
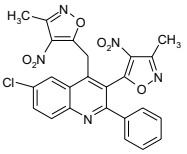
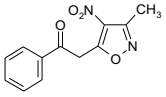
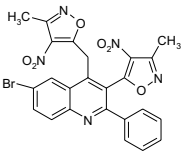
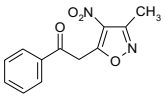
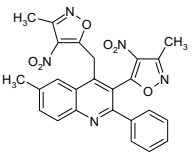
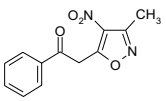
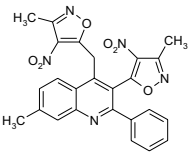
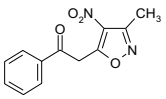
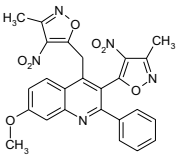
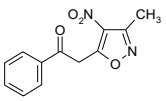
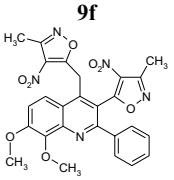
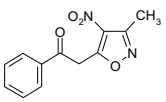
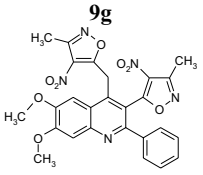


Scheme 5 Friedlander synthesis of highly functionalized isoxazole substituted quinolines



a sharp band at 1650–1654 cm^{-1} due to C=N stretching vibration confirming cyclization. In particular, it must be pointed out that ^{1}H NMR of compounds **6a–k** showed two doublet of doublets at δ 3.18 and 3.29 due to methylene protons and triplet at δ 4.81 asymmetric CH proton. A characteristic peak as broad singlet at δ 4.39 confirm the formation of hydroxy group. In ^{1}H NMR spectra of compounds, **7a–k** absence of triplet at δ 4.81 confirms the formation of carbonyl group. In ^{1}H NMR spectra of **9a–q** exhibited singlet at δ 4.21 due to methylene protons and absence of broad singlet at δ 8.66 in the reactant **7** due to amino group confirm the cyclization product **9**. The ^{13}C

Table 4 Friedlander synthesis of highly functionalized isoxazole substituted quinolines

Entry	Amino isoxazolyl aryl ethanones **7**	α-methylene carbonyls **8**	Product **9**	Yield[b] (%)	Time (min)	M.P. (°C)
1	**7a**	 **8a**	 **9a**	90	50	208-210
2	**7b**	 **8a**	 **9b**	88	55	242-244
3	**7c**	 **8a**	 **9c**	87	60	283-285
4	**7d**	 **8a**	 **9d**	91	50	239-241
5	**7e**	 **8a**	 **9e**	91	60	246-248
6	**7f**	 **8a**	 **9f**	88	55	233-235
7	**7g**	 **8a**	 **9g**	89	60	257-259
8	**7h**	 **8a**		88	60	263-265

NMR spectra of **6a–k** exhibited a prominent peak at δ 160.87 assignable to hydroxyl carbon. The ^{13}C NMR spectra of **7a–k** exhibited signal at δ 191.83 assignable to carbonyl carbon. The formation of isoxazolyl quinolines **9a–q** was supported by ^{13}C NMR spectra of the compounds, which shown a peak at δ 157.10 due to CN carbon, with the disappearance of carbonyl carbon peak at δ 191.83 present in **7a–k**.

Table 4 (continued)

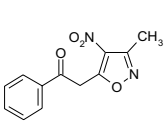
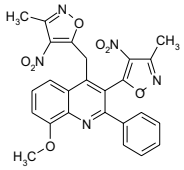
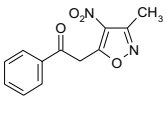
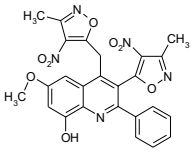
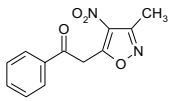
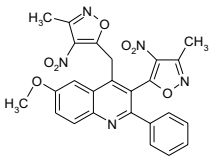
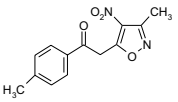
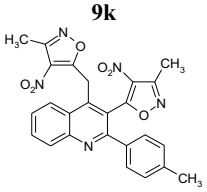
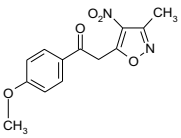
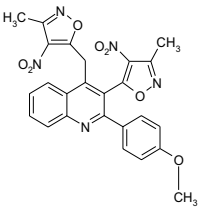
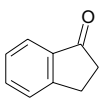
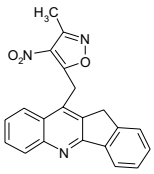
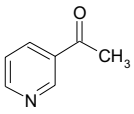
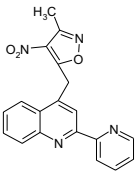
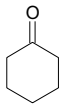
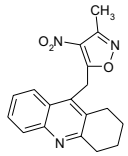
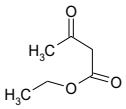
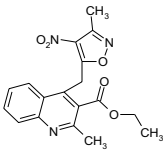
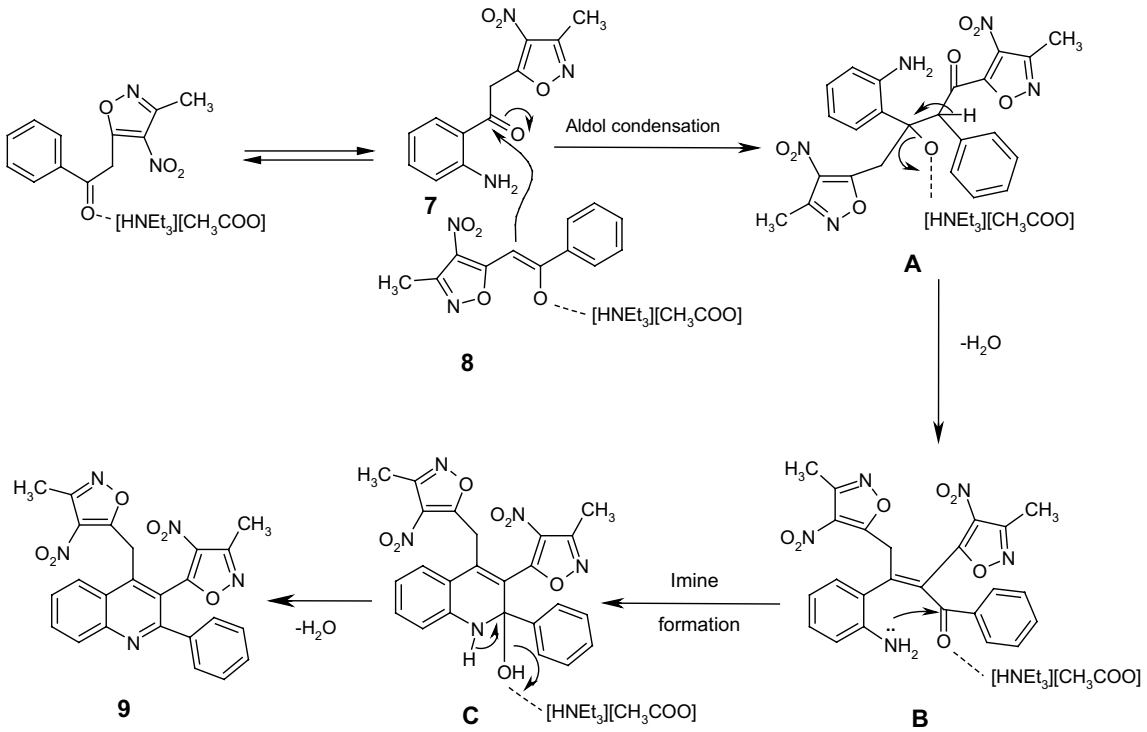
Entry	Amino isoxazolyl aryl ethanones **7**	α-methylene carbonyls **8**	Product **9**	Yield[b] (%)	Time (min)	M.P. (°C)
9	**7i**	 **8a**	 **9i**	87	55	241-243
10	**7j**	 **8a**	 **9j**	89	60	264-266
11	**7k**	 **8a**	 **9k**	88	55	256-258
12	**7a**	 **8b**	 **9l**	89	85	231-233
13	**7a**	 **8c**	 **9m**	87	55	253-255
14	**7a**	 **8d**	 **9n**	86	80	291-293
15	**7a**	 **8e**	 **9o**	86	75	285-287

Table 4 (continued)

Entry	Amino isoxazolyl aryl ethanones **7**	α-methylene carbonyls **8**	Product **9**	Yield[b] (%)	Time (min)	M.P. (°C)
16	**7a**	 **8f**	 **9p**	83	85	274-276
17	**7a**	 **8g**	 **9q**	80	75	250-252

All the reactions were carried out with **7** (1 mmol), **8** (1 mmol) and TEAA (5 mL) at 60 °C

[a]Isolated and unoptimized yields



Scheme 6 Putative pathway for the TEAA IL promoted Friedlander synthesis of isoxazolyl quinolines

Conclusions

In summary, we have developed an efficient ionic liquid promoted addition of 3,5-dimethyl-4-nitroisoxazole to aldehydes through C(sp^3)–H bond functionalization in excellent yields. Further investigation is applied utilizing these synthons *viz.*, isoxazolyl aryl ethanols as building blocks for the Friedlander synthesis of novel highly functionalized isoxazolyl quinolines.

Acknowledgements The authors are thankful to the Head, Department of Chemistry, Telangana University, Nizamabad for providing

the facilities, the Director, Indian Institute of Chemical Technology, Hyderabad for recording ^{1}H NMR, ^{13}C NMR and Mass Spectral data.

References

1. S.A. Lang, Y.-I. Lin, In: *Comprehensive heterocyclic chemistry*, ed. by K.T. Potts ed. (Pergamon Press, New York, 1984)
2. N.K. Kochetkov, S.D. Sokolov, In Advances in heterocyclic chemistry, ed. by A.R. Katritzky ed. (Academic Press, New York, 1963)
3. B.J. Wakefield, D.J. Wright, Adv. Heterocycl. Chem. **25**, 147 (1979)
4. P. Krogsgaard-Larsen, G.A.R. Johnston, D.R. Curtis, C.J.S. Game, R.M. Mc Gulloch, J. Neurochem. **25**, 803 (1975)
5. S.R. Naik, A. Guidotti, E. Costa, Neuropharmacol. **15**, 479 (1976)
6. P. Grünanger, P. Vita-Finzi, in: in: The chemistry of the heterocyclic compounds, ed. by E.C. Taylor ed. (John Wiley & Sons, New York, 1991)
7. R.E. Sammelson, R.B. Miller, M.J. Kurth, J. Org. Chem. **65**, 2225 (2000)
8. Y.R. Mirzaei, B.M. Simpson, D.J. Triggle, N.R. Natale, J. Org. Chem. **57**, 6271 (1992)
9. Y.R. Mirzaei, T.N. Balasubramaniam, B.J. Lefler, N.R. Natale, J. Heterocycl. Chem. **27** 2001 (1990)
10. T.N. Balasubramaniam, Y.R. Mirzaei, N.R. Natale, Synthesis **11**, 1076 (1990)
11. Y.R. Mirzaei, N.R. Natale, Org. Prep. Proced. Int. **25**, 515 (1993)
12. Y.R. Mirzaei, S.B. Tabrizi, M.H. Gohareh, H.Z. Neirizi, L. Edjlali, Org. Prep. Proced. Int. **35**, 207 (2003)
13. L. Edjlali, S.M. Golabi, Y.R. Mirzaei, Bull. Electrochem. **16**, 354 (2000)
14. H. Theobald, Ger. Offen: 2754832 (C1. C07C135100). Chem. Abstr. **91**, (1979) P 140372b (1979)
15. A. Balsamo, I. Coletta, A. Guglielmotti, C. Landolfi, F. Mancini, A. Martinelli, C. Milanese, F. Minutolo, S. Nencetti, E. Orlandini, M. Pinza, S. Rapposelli, A. Rossello, Eur. J. Org. Chem. **38**, 157 (2003)
16. M.L. Herrmann, R. Schleyerbach, B.J. Kirschbaum, Immunopharmacology, 47 (2000) 273
17. D.M. Livermore, Clin. Microbiol. Rev. **8**, 557 (1995)
18. S. Batra, T. Srinivasan, S.K. Rastogi, B. Kundu, A. Patra, A.P. Bhaduri, M. Dixit, Bioorg. Med. Chem. Lett. **12** 1905 (2002)
19. P.G. Baraldi, A. Basco, S. Benetti, G.P. Pollini, D. Simoni, Synthesis. 857 (1987)
20. A.P. Kozikowski, Acc. Chem. Res. **17**, 410 (1984)
21. T.A.K. Prescott, I.H. Sadler, R. Kiapranis, S.K. Maciver, J. Ethnopharmacol. **109**, 289 (2007)
22. S. Jayaprakash, Y. Iso, B. Wan, S.G. Franzblau, A.P. Kozikowski, ChemMed Chem **1**, 593 (2006)
23. L.E. Bermudez, P. Kolonoski, M. Petrofsky, M. Wu, C.B. Inderlied, L.S. Young, J. Infect. Dis. **187** 1977 (2003)
24. L.E. Bermudez, P. Kolonoski, L.E. Seitz, M. Petrofsky, R. Reynolds, M. Wu, Antimicrob. Agents Chemother. **48**, 3556 (2004)
25. L.E. Bermudez, P. Kolonoski, M. Wu, P.A. Aralar, C.B. Inderlied, L.S. Young, Antimicrob. Agents Chemother. **43**, 1870 (1999)
26. K. Andries, P. Verhasselt, J. Guillemont, H.W.H. Goehlmann, J.M. Neefs, H. Winkler, Science **307**, 223 (2005)
27. J. Mao, Y. Wang, B. Wan, A.P. Kozikowski, S.G. Franzblau, Chem. Med. Chem. **2**, 1624 (2007)
28. A. Koul, N. Dendouga, K. Vergauwen, B. Molenberghs, L. Vranckx, R. Willebrords, Nat. Chem. Biol. **3**, 323 (2007)
29. R. Rustomjee, A.H. Diacon, J. Allen, A. Venter, C. Reddy, R.F. Patientia, Antimicrob. Agents Chemother. **52**, 2831 (2008)
30. T. Matsubara, N. Kaga, D.G. Masaev, K. Morokuma, Organometallics **19**, 2318 (2000)
31. V. Ritleng, C. Sirlin, M. Pfeffer, Chem. Rev. **102**, 1731 (2002)
32. M. Tobisu, N. Chatami, Angew. Chem. Int. Ed. **45**, 1683 (2006)
33. M. Rueping, N. Tolstoluzhsky, Org. Lett. **13**, 1095 (2011)
34. E. Rajanarendar, S. Ramakrishna, S. Raju, J. Iranian. Chem. Soc. **10**, 653 (2013)
35. E. Rajanarendar, S. Ramakrishna, K. Govardhan Reddy, D. Nagaraju, Y.N. Reddy, Bioorg. Med. Chem. Lett. **23**, 3954 (2013)
36. E. Rajanarendar, S. Ramakrishna, D. Nagaraju, K. Govardhan Reddy, B. Kishore, Y.N. Reddy, Bioorg. Med. Chem. Lett. **25**, 1630 (2015)
37. E. Rajanarendar, M. Nagi Reddy, S. Ramakrishna, K. Govardhan Reddy, Y.N. Reddy, M.V. Rajam, Eu. J. Med. Chem. **50**, 344 (2012)
38. E. Rajanarendar, S. Raju, M. Nagi Reddy, S. Ramakrishna, L. Hari kiran, A. Ram Narasimha Reddy, Y.N. Reddy, Eu. J. Med. Chem. **50** 274 (2012)
39. E. Rajanarendar, K. Govardhan Reddy, S. Ramakrishna, M. Nagi Reddy, B. Shireesha, G. Durgaiah, Y.N. Reddy, Bioorg. Med. Chem. Lett. **22**, 6677 (2012)
40. E. Rajanarendar, K. Govardhan Reddy, S. Ramakrishna, B. Shireesha, Y.N. Reddy, M.V. Rajam, Med. Chem. Res. **22**, 143 (2013)
41. V.N.V. Srinivasn, Y.R. Lee, Tetrahedron. **68**, 8286 (2012)
42. J.-J. Jin, D.-C. Wang, H.-Y. Niu, S.B. Wu, G.-R. Qu, Z.-B. Zhang, H.-M. Guo, Tetrahedron. **60**, 6579 (2012)
43. R. Niu, J. Xiao, T. Liang, X. Li, Org. Lett. **14**, 676 (2012)
44. X.-Y. Zhang, D.-Q. Dong, T. Yuen, S.-H. Hao, Z.-L. Wang, Tetrahedron Lett. **55**, 5462 (2014)
45. G.T. Morgan, H.B.J. Burgess, Chem. Soc. 699 (1921)
46. A.K. Murthy, N.V.S. K.S.R.K.M. Rao, Rao, J. Indian Chem. Soc. **53**, 1047 (1976)
47. A. Pankaj, M. Pal, Green Chem. Lett. Rev. **3**, 249 (2010)
48. E. Rajanarendar, K. Thirupathaiah, S. Ramakrishna, B. Kishore, Green Sustain. Chem. **3**, 9 (2013)
49. C. Kashima, Y. Yamamoto, Y. Tsuda, Heterocycles. **6**, 805 (1977)
50. B. Das, K. Damodar, N. Chowdhury, R. Aravind Kumar, J. Mol. Catal. A: Chem. **274**, 148 (2007)
51. R. Venkatesham, A. Manjula, B. Vittal Rao, J. Heterocyclic. Chem. **49**, 833 (2012)