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ARTICLE

Manganese(II) chloride catalyzed highly efficient one pot synthesis of propargylamines and fused triazoles *via* three component coupling reaction under solvent free condition†

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A one-pot green and highly efficient method for synthesis of propargylamines and diastereoselective synthesis of fused triazoles via three component coupling in the presence of manganese(II) chloride as catalyst followed by catalyst free 1,3-dipolar cycloaddition reaction respectively, without using co-catalyst or activator is reported. This methodology is efficient, eco-friendly, operationally simple and effective for reactions involving aromatic, aliphatic, and heterocyclic aldehydes and provides an easy access to propargylamines in excellent yields and fused triazoles in good yield and excellent diastereoselectivities.

Introduction

Development of environmentally benign methods by avoiding toxic reagents and solvent has become increasingly important for industrial applications.[1] Multicomponent coupling reaction[2, 3] (MCR) is potential interest as it enables the coupling of aldehyde, amine and alkyne resulting in propargylamine with new C–C bond.[2, 3] Solvent-free reaction[4] is an important synthetic boon from the view point of green and sustainable chemistry. Over the last few years, solvent-free heterocyclic synthesis[5] has rapidly increased. This paved the way for the development of greener synthesis.[6] Synthesis of propargylamine is an intense research area in organic synthesis because propargylamine is versatile building block in natural product synthesis[7] and acts as precursors in the synthesis of nitrogen containing heterocyclic compound.[8a-8f, 9] Moreover, propargylamines are frequent skeletons[10a] and synthetically versatile key intermediate[11] for the synthesis of biologically active compounds such as β-lactams, oxotremorine analogues, conformationally restricted peptides, isosteres and therapeutic drug molecules.[10b,12] Traditionally, propargylamines are synthesized by nucleophilic attack of lithium acetylides or Grignard reagents to imines or their derivatives.[13] However, these reagents are stoichiometric, highly moisture sensitive and require strictly controlled reaction condition.

In recent years to overcome such problems, tremendous progress has made to develop an alternative atom-economical approach to their synthesis and perform this type of reaction by catalytic coupling of three components (A^3 coupling) by C–H activation, where water is only theoretical by-product.[3] There are various transition metal catalysts for C–H bond activation of terminal alkyne, such as, Cu^I salts,[14] Cu^{II} derivatives,[15a] Cu/Ru^{II} bimetallic systems,[15b] Ir^I complexes,[16] Au^I/Au^{III} salts,[17] Au^{III} salen complexes,[18] Ag^I salts,[19] In^{III} salts,[20] Ni^{II} salts,[21] and Fe^{III} salts[22] have been used for this reaction under homogeneous reaction condition. Recently, Ag(I)[23a] and Cu(I)[23b] in ionic liquids, Zn dust,[24] supported Au(III),[25a] Ag(I),[25b-25d] or Cu(I),[26c-26h] Fe_3O_4 nanoparticles,[27] and nano indium oxide[26] were successfully used to catalyze A^3 coupling reaction under heterogeneous reaction condition with recyclability and reusability of the transition metal catalyst.[25h, 28]

Huisgen 1,3-dipolar cycloaddition is the reaction of a dipolarophile (alkyne) with a 1,3-dipolar (azide) compound that leads to 1,2,3-triazole (5-membered ring) have attracted significant attention as one of the most important heterocycles.[29] Within the past few years, applications of this building block have been extended widely into various research fields,[30] such as chemical biology, material science, and medicinal chemistry. 1,2,3-Triazole moiety is present in many compounds exhibiting different biological properties such as antibacterial[31] (cefmatilen), anti-HIV,[32] antiallergic,[33] and inhibitory (tazobactam) activities. Triazolobenzodiazepines[34] have shown high affinity toward benzodiazepine receptors. Triazole chemistry was revisited and has seen exponential growth over the years and enormous gain in popularity in areas of chemistry such as dyes, photostabilizers, agrochemicals[35] and in the designining of new drugs.[36] Among the

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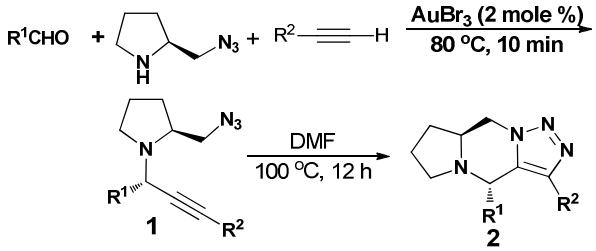
nitrogen heterocycles, tetrahydropyrazine represents important class of organic molecules that attracts the interest of both synthetic and medicinal chemists due to their significant biological activities.[37]

Recently, we have described a practical and efficient two step protocol for the synthesis of 4,6,7,8,8*a*,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines,[38] (Scheme 1) the first step involved $AuBr_3$ catalyzed three component coupling of aldehyde, amine and alkyne to form propargylamines and in second step propargylamine undergos intramolecular 1,3-dipolar cycloaddition using DMF as solvent. Considering briefly importance of propargylamine, 1,2,3-triazole moiety, tetrahydropyrazine and eco-friendly reaction condition, in this paper we like to present the use for the first time Mn(II) chloride as an efficient catalyst for the synthesis of propargylamine via three componant coupling and one pot diastereoselective synthesis of 4,6,7,8,8*a*,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines via three component coupling followed by Huisgen intramolecular 1,3-dipolar cycloaddition reaction at solvent free condition. To the best of our knowledge, the utilization of manganese chloride for three component coupling of aldehyde, amine and alkyne has never been reported. Manganese chloride has received a great deal of interest because, it is inexpensive, easily available, easy to handle and relatively insensitive to air and moisture and have been used for cross-coupling reactions between aryl Grignard reagents and simple alkenyl halides.[39]



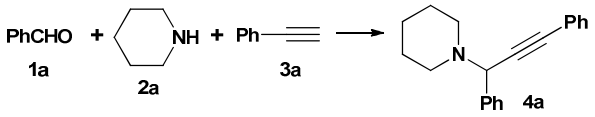
Scheme 1. Diastereoselective synthesis of propargylamines and 4,6,7,8,8*a*,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines.

Results and Discussion

Manganese(II) chloride catalyzed three component coupling reaction

We focused our initial investigation on the effect of various types of solvents and catalyst loading on the reaction of benzaldehyde, piperidine and phenylacetylene at different temperatures (Table 1). The results indicates that reaction temperature, solvent and catalyst loading influence the product yield in the A^3 coupling reaction. After several screening experiments, the best condition proved to be, a mixture of benzaldehyde (1 mmol), piperidine (1.2 mmol), phenyl acetylene (1.5 mmol), $MnCl_2$ (10 mol%) was stirred at 90 °C without solvent for 12 h (Table 1, entry 9). we started to screen solvents first with water but there was no formation of desired product (Table 1, entry 1). Then we screened various organic solvents on A^3 coupling of model substrates by using 10 mol% of $MnCl_2$ as catalyst such as DMF, DMSO, dioxane, and DCM, at 100 °C, 80 °C, 101 °C, and 35 °C, respectively, generated the corresponding products in very few amount (Table 1, entries 2, 3, 5, 7). Using ethanol and acetonitrile as solvent afforded the desired products in 45% and 61% yield respectively at 80 °C (Table 1, entries 5, 6) , whereas, toluene was inferior and generated corresponding product in moderate yield (88%) at 120 °C (Table 1, entry 8). To further investigate the reaction condition, the same reaction with 10 mol% of $MnCl_2$ was carried out at solvent free condition at 90 °C which afforded the desired product in 98% yield (Table 1, entry 9). In order to seek the most effective catalyst for the coupling of aldehyde, amine and alkyne, we used 10 mol% of Mn powder, MnO_2, and $Mn(OAc)_2{\cdot}4H_2O$ to catalyze the reaction at solvent free condition at 90 °C with conversion 51, 20, and 62% respectively (Table 1, entries 10–12). We next performed the reaction with 2 mol % $MnCl_2$ and 5 mol % $MnCl_2$ which generated desired product in 69% and 82% yield (Table 1, entries 13, 14), and we observed that higher catalyst loading increased the yield of desired product and decreased reaction time, therefore, using $MnCl_2$ (10 mol%), 90 °C and solvent free (Table 1, entry 9) was selected as the best condition for A^3 coupling reaction of aldehyde, amine and alkyne.

Table 1. Optimization studies for the $MnCl_2$ catalyzed multicomponent synthesis of propargylamine **4a**[a]



Entry	Mn source (mol%)	Solvent	Temp (°C)	Time (h)	**4a** (%)
1	$MnCl_2$ (10)	H_2O	100	24	0
2	$MnCl_2$ (10)	DMF	100	24	traces
3	$MnCl_2$ (10)	DMSO	80	24	traces
4	$MnCl_2$ (10)	ethanol	80	24	45
5	$MnCl_2$ (10)	dioxane	101	24	traces
6	$MnCl_2$ (10)	CH_3CN	80	24	61
7	$MnCl_2$ (10)	CH_2Cl_2	35	72	traces
8	$MnCl_2$ (10)	toluene	120	14	88
9	$MnCl_2$ (10)	-	90	12	98
10	Mn (10)	-	90	18	51
11	MnO_2 (10)	-	90	12	20
12	$Mn(OAc)_2{\cdot}4H_2O$ (10)	-	90	16	62
13	$MnCl_2$ (2)	-	90	15	69
14	$MnCl_2$ (5)	-	90	14	82

Reaction conditions: **1a** - aldehyde (1 mmol), **2a** - amine (1.2 mmol), **3a** - alkyne (1.5 mmol), with 10 mol% manganese source heated with solvents and without solvent at different temperature.

Having optimized the conditions in hand the catalysis was then applied to various aldehydes, alkynes and amines as summarized in Table 2. Initially we performed coupling of benzaldehyde and phenylacetylene with cyclic amines such as piperidine and morpholine leading to products **1a** and **1b** with yields of 98 and 90% respectively (Table 1, entries 1, 2). Considering high reactivity of benzaldehyde with morpholine and phenylacetylene in A^3 coupling reaction, we also studied reactivity of aliphatic and heterocyclic aldehyde such as isobutyraldehyde and 3-thienyl carbaldehyde with morpholine and phenylacetylene under optimized reaction condition.

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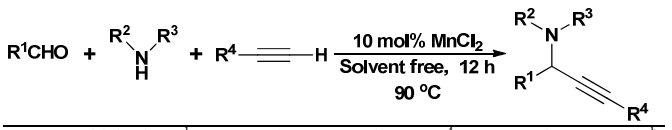
Surprisingly both generated desired products **1c** and **1d** with excellent yields of 96 and 93% (Table 1, entries 3, 4). In case of diisopropylamine and aniline formation of desired products **1e** and **1f** with 65 and 69 % yield (Table 2, entries 5, 6). We also tried various aliphatic primary amines in A^3 coupling reaction, but there was no formation of desired product. Benzaldehyde bearing electron-donating and electron-withdrawing groups at *o*-, *m*-, and *p*-position such as alkyl, chloro, and fluoro were able to undergo three-component coupling and generated the corresponding products, **1g**–**1m**, in excellent yields (91–97%) respectively (Table 2, entries 7–13). The electronic properties of the substituents on the phenyl ring did not have an obvious effect on the yields of corresponding product. 1-Napthaldehyde and biphenyl-2-carbaldehyde reacted well under optimized condition even though they are bulky and furnished desired products **1n** and **1o** with 96 and 94 % yields respectively (Table 2, entries 14, 15**)**. Aliphatic alkynes such as trimethylsilyl acetelyne worked effectively and furnished product **1p** in good yield 89%, (Table 2, entry 16). Whereas aromatic alkyne bearing electron donating group (methoxy) shown good reactivity in A^3 coupling reaction under optimized condition and generated desired product **1q** in very high yield 97% (Table 2, entry 17). Due to excellent yield in case of benzaldehyde, we also studied reactivity of *p*-methoxyphenyl acetylene with substituted-benzaldehyde bearing electron donating and electron withdrawing group in A^3 coupling reaction such as *p*-tolualdehyde, *m*-chlorobenzaldehyde and also with aliphatic aldehyde such as trimethylacetaldehyde in A^3 coupling reaction generated desired products **1r, 1s** and **1t** with excellent yields 96, 94 and 98% respectively (Table 2, entries 18–20). Aliphatic aldehydes displayed high reactivity under the optimized reaction condition generated desired products **1u–1ad** in excellent yields (95–98%) (Table 2, entries 21–30). Trimerization in case of aliphatic aldehydes was never observed, even though it has been major limitation of the A^3 coupling reaction.[14, 17] heterocyclic aldehyde such as 2-thienyl carbaldehyde and 3-thienyl carbaldehyde reacted smoothly under optimized reaction condition to give **1ae** and **1af** in 91 and 97% yields (Table 2, entries 31, 32). The structure of the **1a** in $CDCl_3$ methine proton (N-CH–) at ***δ* = 4.79** ppm was observed as a characteristic singlet and in the ^{13}C NMR spectrum, two peaks at ***δ* = 85.97** and **87.80** ppm corresponded to the two acetylenic carbons were observed, these observation supported to formation of propargylamine (**1a**).

Table 2. $MnCl_2$ catalyzed one pot synthesis of propargylamines **1a–1af**[a]



Entry	Aldehyde (R^1)	Amine (R^2, R^3)	Alkyne (R^4)	Product	Yield[b] (%)
1	ph	piperidine	ph	**1a**	98
2	ph	morpholine	ph	**1b**	90
3	isopropyl	morpholine	ph	**1c**	96
4	3-thienyl	morpholine	ph	**1d**	93
5	ph	diisopropyl amine	ph	**1e**	65
6	ph	Aniline	ph	**1f**	69
7	*o*-$CH_3C_6H_4$	piperidine	ph	**1g**	91
8	*m*-$CH_3C_6H_4$	piperidine	ph	**1h**	95
9	*p*-$CH_3C_6H_4$	piperidine	ph	**1i**	97
10	*o*-ClC_6H_4	piperidine	ph	**1j**	93
11	*m*-ClC_6H_4	piperidine	ph	**1k**	92
12	*p*-ClC_6H_4	piperidine	ph	**1l**	96
13	*p*-FC_6H_4	piperidine	ph	**1m**	94
14	1-napthyl	piperidine	ph	**1n**	96
15	2-(1,1'-biphenyl)	piperidine	ph	**1o**	94
16	ph	piperidine	$(CH_3)_3Si$	**1p**	89
17	ph	piperidine	*p*-$CH_3OC_6H_4$	**1q**	97
18	*p*-$CH_3C_6H_4$	piperidine	*p*-$CH_3OC_6H_4$	**1r**	96
19	*m*-ClC_6H_4	piperidine	*p*-$CH_3OC_6H_4$	**1s**	94
20	*tert*-butyl	piperidine	*p*-$CH_3OC_6H_4$	**1t**	98
21	cyclohexyl	piperidine	ph	**1u**	95
22	*tert*-butyl	piperidine	ph	**1v**	97
23	ethyl	piperidine	ph	**1w**	96
24	propyl	piperidine	ph	**1x**	95
25	pentyl	piperidine	ph	**1y**	97
26	hexyl	piperidine	ph	**1z**	96
27	heptyl	piperidine	ph	**1aa**	97
28	octyl	piperidine	ph	**1ab**	98
29	nonyl	piperidine	ph	**1ac**	96
30	Ph-$(CH_2)_2$-	piperidine	ph	**1ad**	97
31	2-thienyl	piperidine	ph	**1ae**	91
32	3-thienyl	piperidine	ph	**1af**	97

[a] Reaction conditions: aldehyde (1.0 mmol), amine and (1 mmol), phenylacetylene (1 mmol), $MnCl_2$ (10 mol %) heated at solvent free condition at 90 °C, in sealed tube. [b] Isolated yields after flash chromatography.

Manganese(II) chloride catalyzed three component coupling followed by catalyst free 1,3-dipolar cycloaddition

With this simple and effective method in hand, our next step was to develop one pot synthesis of 4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines via three component coupling of aldehyde, amine and alkyne followed by 1,3-dipolar cycloaddition. During our investigation, it was observed that $MnCl_2$ could provide 4,6,7,8,8a,9-hexahydropyrrolo[1,2-a][1,2,3]triazolo[1,5-d]pyrazines in good yield and excellent diastereoselectivity without solvent in one pot operation. Encouraged by this result we started our methodology by preparing (*S*)-azidomethylpyrrolidine from commercially available L-proline by using reported procedure.[40]

Having established optimal reaction condition in case of the synthesis of propargylamine via three component coupling of benzaldehyde, piperidine and phenyl acetylene, we tested scope of three components such as benzaldehyde, (*S*)-azidomethylpyrrolidine and phenyl acetylene at above optimized condition and fortunately found that both reactions, coupling and intramolecular Huisgen [3 + 2] dipolar cycloaddition were going well in one pot operation and furnished desired product **2a** with 84% yield and excellent diastereoselectivity (Table 3, entry 1). Next we tested DMF, toluene as solvent for the synthesis of 4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*] via three component coupling followed by 1,3-dipolar cycloaddition, these solvents also generated desired product in good yield but considering toxicity of these solvents we

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decided to carry out further reactions with different substrate at solvent free condition. This method applicable for aromatic, aliphatic, heterocyclic aldehydes and also for aliphatic and aromatic alkynes and avoids isolation, purification and characterization of coupling product (**1**). Aromatic aldehydes formed the desired products **2b–2l** in good yield (75–83%) and excellent diastereoselectivities, via three component coupling followed by 1,3-dipolar cycloaddition reaction (Table 3, entries 2–12). 1-Napthaldehyde also worked well under optimized condition and furnished desired product **2m** in 81% yield and excellent diastereoselectivity. Also alkyne such as *p*-methoxyphenyl acetylene and 1-hexyne reacted well under optimized reaction condition and generated desired products **2n** and **2o** in 83 and 74% yields and excellent diastereoselectivities respectively (Table 3, entries 14, 15). Aliphatic aldehydes such as 3-phenylpropanal, isovaleraldehyde and butanal displayed good reactivity under optimized reaction condition, this time we also screened various kind of heterocyclic aldehydes but only 3-thienyl carbaldehyde and 2-thienyl carbaldehyde were shown good reactivity under optimized reaction condition and generated desired products **2s** and **2t** in 82 and 78 % yield, and excellent diastereoselectivities respectively (Table 3, entries 19, 20). The structure of the fused tricyclic compound **2a** was confirmed by ^{1}H NMR, ^{13}C NMR, IR and mass spectrometry. In ^{1}H NMR spectrum of compound **2a** in $CDCl_3$ methine proton (N–CH–) at δ = **5.52** ppm was observed as a characteristic singlet and in the ^{13}C NMR spectrum, two peaks at δ = **128.9** and **141.6** ppm corresponded to olefinic carbon atoms of triazole ring, these observation supported to confirm formation of desired product **2a**. The absolute configuration of (4*S*,8a*S*)-3-phenyl-4-(thien-3-yl)-4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines was confirmed by X ray diffraction analysis of monocrystals which clarified that new formed stereocenter had **(*S*)** configuration. The configuration of other products were assigned **(*S*)** by analogy.

Table 3. One pot diastereoselective synthesis of 4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines **2a**–**2t** at solvent free condition.[a]

Entry	R_1	R_2	Product	Yield[c] (%)	Time (h)
1	Ph	Ph	**2a**	84	12
2	4-MeC_6H_4	Ph	**2b**	83	12
3	3-MeC_6H_4	Ph	**2c**	81	12
4	2-MeC_6H_4	Ph	**2d**	79	12
5	4-MeOC_6H_4	ph	**2e**	76	12
6	3-BrC6H_4	Ph	**2f**	77	12
7	4-FC_6H_4	Ph	**2g**	79	12
8	3-FC_6H_4	Ph	**2h**	77	12
9	3-CNC_6H_4	Ph	**2i**	75	12.5
10	4-ClC_6H_4	Ph	**2j**	82	12
11	3-ClC_6H_4	Ph	**2k**	79	12
12	2-ClC_6H_4	Ph	**2l**	76	12
13	1-napthyl	ph	**2m**	81	13
14	ph	*p*-$CH_3OC_6H_4$	**2n**	83	13.5
15	Ph	1-hexyne	**2o**	74	12.5
16	Ph$(CH_2)_2$	ph	**2p**	77	12
17	isobutyl	ph	**2q**	76	12
18	propyl	ph	**2r**	75	12
19	3-thienyl	ph	**2s**	82	14
20	2-thienyl	ph	**2t**	78	14

[a] Reaction condition: aldehyde (1.0 mmol.), (*S*)-azidomethylpyrrolidine (1.2 mmol), phenylacetylene (1.5 mmol.), $MnCl_2$ (10 mol %), heated at solvent free condition at 90 °C in sealed tube. [b] Diastereomeric ratio was determined by ^{1}H NMR spectroscopy. [c] Isolated yields after flash chromatography.

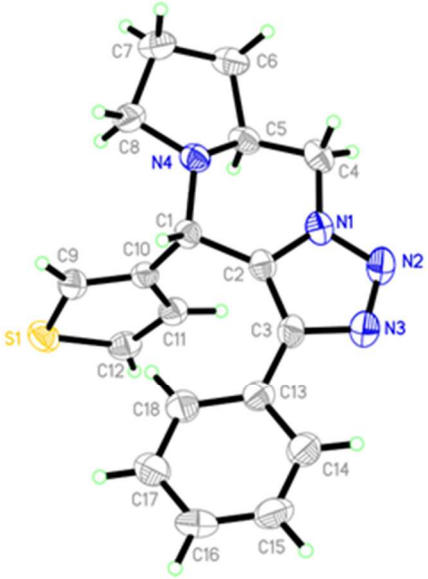
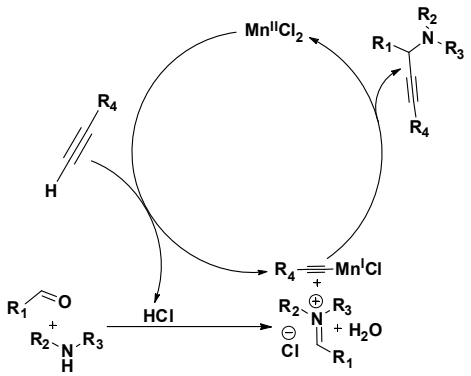


Figure 1. Crystal structure of (4*S*,8a*S*)-3-phenyl-4-(thien-3-yl)-4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazine (**2s**) (**CCDC-956372**).

The possible mechanism was involved, manganese(II) chloride was reacted with alkyne, manganese acetylide intermediate and hydrochloric acid thus generated. We predicted formed HCl accelerate the formation of immonium ion generated in situ from aldehydes and secondary amine.[41a, 41b], resulting manganese acetylide subsequently reacted with immonium salt formed in situ to form propargylamine and regenerate the Mn(II) catalyst for further reactions.



Scheme 3. Possible mechanism for manganese(II) chloride catalyzed three component coupling reaction of aldehyde, amine and alkyne.

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In one pot synthesis of fused triazoles there is in situ formation of propargylamine **(1)**, using Mn(II) chloride, mechanistic path way for formation of **(1)** is same as drawn in scheme 3. Further propargylamines undergo catalyst free intramolecular 1,3-dipolar cycloaddition by heating.[38, 42]

Conclusion

We have successfully developed a novel, efficient, operationally simple economically and enviornmental friendly, $MnCl_2$ catalyzed one pot synthesis of propargylamines *via* three component coupling. Meanwhile, one pot diastereoselective synthesis of 4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-d]pyrazines *via* three component coupling followed by catalyst free 1,3-dipolar cycloaddition reaction at solvent free condition. The process requires manganese chloride as an inexpensive catalyst and generated diverse range of propargylamine and interesting fused heterocycle, 4,6,7,8,8a,9 hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazines. Manganese catalysis is an interesting field of investigation for sustainable development. The synthetic application of A^3 coupling reaction and 1,3-dipolar cycloaddition are currently under investigation.

Experimental section

General experimental procedure for manganese(II) chloride catalyzed three component coupling reaction

A mixture of aldehyde (1.0 mmol), amine (1.2 mmol), alkyne (1.5 mmol) and $MnCl_2$ (10 mol%) in sealed tube was stirred without solvent for 12 h at 90 °C. The progress of reaction was monitored by TLC. After completion of reaction, the product was purified by column chromatography using *n*-hexane/EtOAc as eluent to give the desired product. The products were identified by **FT-IR, ^{1}H** and **^{13}C NMR** spectroscopy, **LRMS** and **HRMS**.

1-(1,3-Diphenylprop-2-yn-1-yl)piperidine 1a. R_f = 0.44 (EtOAc/hexane 1:9), Yield: 98%, Pale yellow solid; mp: 66–67 °C. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm δ): 7.64–7.62 (d, J = 6.0 Hz, 2H), 7.53–7.50 (m, 2H), 7.38–7.28 (m, 6H), 4.79 (s, 1H), 2.57–2.54 (m, 4H), 1.61–1.56 (m, 4H), 1.47–1.42 (m, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$, δ): 138.52, 131.69, 128.38, 128.15, 127.93, 127.34, 123.27, 87.80, 85.97, 62.29, 50.61, 26.10, 24.36; **IR** (KBr, thin film, cm^{-1}): 3049, 2923, 2802 1596, 1486, 1445, 1270, 1152, 1094, 758, 691; **LRMS-EI** (*m*/*z*): 275 (12), 246 (3), 232 (4), 198 (50), 191 (100), 165 (7), 139 (2), 115 (9), 86 (5), 56 (6); **HRMS-EI** (m/z): M^+ calcd for $C_{20}H_{21}N$, 275.1674; found: 275.1669.

General experimental procedure for manganese(II) chloride catalyzed three component coupling followed by catalyst free 1,3-dipolar cycloaddition reaction.

A mixture of aldehyde (1.0 mmol), (*S*)-azidomethylpyrrolidine (1.2 mmol), alkyne (1.5 mmol) and $MnCl_2$ (10 mol%) in sealed tube was stirred without solvent for 12–14 h at 90 °C. The progress of reaction was monitored by TLC. After completion of reaction, the product was purified by column chromatography using *n*-hexane/EtOAc as eluent to give the desired product. The products were identified by **FT-IR**, **^{1}H** and **^{13}C NMR** spectroscopy, **LRMS** and **HRMS**.

4*S*,8a*S*)-3,4-diphenyl-4,6,7,8,8a,9-hexahydropyrrolo[1,2-*a*][1,2,3]triazolo[1,5-*d*]pyrazine 2a: R_f = 0.31 (EtOAc/hexane 3:7), Yield:84%. **Diastereomeric ratio: >99**, **$[\alpha]^{25}_D$** –79.2° (*c* 1.0, $CHCl_3$), brown solid, mp: 198–199 °C. **^{1}H NMR** (300 MHz, $CDCl_3$, ppm, δ): 7.49–7.47 (d, J = 6.0 Hz, 2H), 7.32–7.30 (d, J = 6.0 Hz, 3H), 7.25–7.17 (m, 3H), 7.10–7.01 (m, 2H), 5.56 (s, 1H), 4.83–4.77 (m, 1H), 4.12–4.04 (t, J = 12.0 Hz, 1H), 3.25–3.22 (m, 1H), 2.96–2.92 (m, 1H), 2.38–2.25 (q, J = 9.0 Hz, 1H), 1.99–1.90 (m, 2H), 1.76–1.72 (m, 1H), 1.60–1.50 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm, δ): 141.92, 134.71, 130.83, 130.74, 129.23, 128.87, 128.33, 128.16, 127.99, 127.92, 127.41, 127.33, 126.20, 58.02, 51.67, 49.97, 48.63, 27.69, 21.92; **IR** (KBr, thin film, cm^{-1}): 3056, 3027, 2950, 2876, 2808, 1493, 1448, 1127, 1007, 722, 696; **LRMS-EI** (*m*/*z*): 317 (80), 287 (20), 277 (23), 191 (22), 138 (69), 106 (100), 65 (39); **HRMS-EI** (m/z) M^+ calcd for $C_{20}H_{20}N_4$, 316.1688; found 316.1681.

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