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Synthesis of biologically as well as industrially important 1,4,5-trisubstituted-1,2,3-triazoles using a highly efficient, green and recyclable DBU–H_2O catalytic system†

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Substituted 1,2,3-triazoles are important heterocyclic molecules with applications in diverse research areas. 1,3-Dipolar cycloaddition reaction of azides and enolizable compounds is an important method of generating substituted 1,2,3-triazoles. However, the reported methods in the literature for 1,3-cycloaddition of aryl azides involve long reaction time, use of hazardous/volatile reagents, and toxic organic solvents. In this paper we have reported the novel environment friendly protocols for the synthesis of 1,4,5-trisubstituted-1,2,3-triazoles by reaction of various aryl azides with active methylene compounds in a DBU–water system under conventional heating, ultrasonic and microwave irradiation. The methodologies defined herein showed synthetic advantages in terms of high atom economy, low environmental impact, mild reaction conditions and good yields in shorter reaction time and recyclability of the reaction medium.

Introduction

1,2,3-Triazoles are important heterocycles with diverse applications such as antiviral,[1] antimicrobial,[2] anti-HIV[3] activity, anticonvulsants,[4] anti-allergic,[5] dyes, corrosion inhibitors, sensors and photo-stabilizers.[6] Copper catalyzed 1,3-dipolar cycloaddition reaction of various azides and alkynes or enolizable compounds is an important method of generating substituted 1,2,3-triazoles. Copper-catalyzed 1,3-dipolar cycloaddition of azides and alkynes is often used to prepare substituted 1,2,3-triazoles as it provides a product in good yields and in shorter reaction time. However, there are certain disadvantages associated with this method like the presence of copper ions which may induce degradation of viruses or oligonucleotide strands in biological systems as copper ions are also potentially cytotoxic for living organisms. Therefore, this method is not suitable for used in living systems/cells.[7] Further due to limited availability of structurally diverse alkynes, metal free base catalyzed reactions of various aryl azides with active methylene compounds represent a powerful approach to a synthesis of variety of 1,2,3-triazole derivatives with different substitution patterns in positions 4 and 5 of the ring. However most of the reported methods for base catalyzed 1,3-cycloaddition of aryl azides to active methylene compounds involves the disadvantages like long reaction time, lower yield of products, use of hazardous/volatile reagents, use of limited active methylene compounds/azides and toxic organic solvents.[8] In the view of these limitations, we decided to explore the novel protocols of 1,3-cycloaddition reaction of various azides with active methylene compounds to overcome the above disadvantages.

In view of the environmental concerns, industries have started implementing green chemistry practices such as using new catalysts and the use of less toxic solvents. Disposal of organic solvents is still a problem in chemical industries which accounts around 80% of their waste. In this context, use of water as the reaction medium offers several advantages[9–11] such as inexpensive, nonflammable, nontoxic, easy isolation of water insoluble products. There are undoubtedly concerns regarding isolation of water soluble products from water as medium. However in reactions which involve the formation of water insoluble products, the products can be easily separated from the reaction medium water by simple filtration.[12] 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), regarded as a non-nucleophilic, strong tertiary amine base has been widely used as an effective corrosion free catalyst in many organic transformations in recent years.[13] Interestingly, it has also been observed that the catalytic activity of DBU improved considerably in the presence of water.[14] Use of ultrasonic irradiation and microwave irradiation as alternative sources of energy has proved to be one of the stepping stone towards the green

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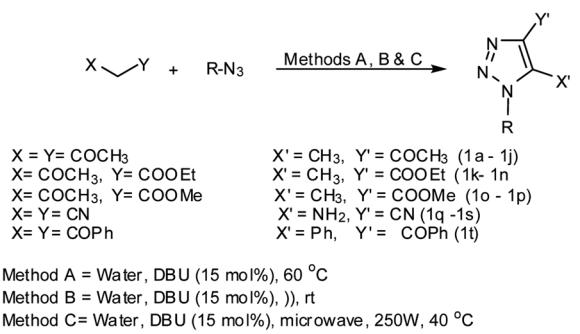
syntheses as it offers advantage of enhanced reactivity, shorter reaction times and higher yields of pure products compared to the traditional heating methods.[15,16] Inspired by importance of water as a reaction medium and in view of limitations of existing methods for synthesis of 1,2,3-triazoles, we wish to report the new protocol for synthesis of 1,4,5-trisubstituted-1,2,3-triazoles in water using DBU as a catalyst under conventional heating, ultrasonic and microwave irradiation.

Result and discussion

We report herein an efficient and environmental friendly methodologies for the synthesis of 1,4,5-trisubstituted-1,2,3-triazoles by 1,3-dipolar cycloaddition reaction of various aryl azides with active methylene compounds in water in presence of DBU as catalyst under conventional heating, ultrasonic and microwave irradiation (Scheme 1).

The optimum reaction conditions were investigated by the initial reaction of 4-bromophenyl azide (1 mmol) and acetylacetone (1 mmol) as model substrates in water using different base catalysts as shown in Table 1.

The best result was obtained when the reaction was carried out in water in presence of a catalytic amount of DBU (15 mol%) at 60 °C. The reaction underwent completion in 10 min yielding 95% of 1-(1-(4-bromophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-ethanone (**1a**) after a simple workup (Table 1). Reaction using piperidine (10 mol%) as a catalyst at 80 °C resulted in a incomplete reaction with inferior yield (72%) of **1a**. Reaction in presence of KOH (10 mol%) as a catalyst resulted in incomplete reaction yielding 75% of **1a**. Similarly reaction using K_2CO_3, Et_3N, imidazole, morpholine, DABCO and pyridine (10 mol%) resulted in longer reaction times and inferior yields. There was no reaction in the absence of any catalyst even after 240 min. While reaction using 10 mol% of DBU also gave slightly inferior yield and longer reaction time, reaction using 20 mol% of DBU did not affect the reaction time and yield significantly. Thus application of catalytic DBU (15 mol%) in water at 60 °C was selected as the optimum system for this protocol. No significant relation between base basicity and reactivity was found. However DBU gives better reactivity because of its ability to form a complex with water which increases its catalytic activity. The subsequent reactions of variously substituted aromatic azides with acetylacetone were carried out under these conditions. The



Scheme 1 Synthesis of 1,4,5-trisubstituted-1,2,3-triazoles.

Table 1 Optimization of reaction conditions

Entry	Base	Temperature	Time (min)	Yield (%)
1	Piperidine (10 mol%)	80 °C	70	72[a]
2	KOH (10 mol%)	80 °C	50	75[a]
3	K_2CO_3 (10 mol%)	80 °C	120	80
4	DBU (10 mol%)	80 °C	15	89
5	Et_3N (10 mol%)	80 °C	45	82
6	—	80 °C	240	—[b]
7	Imidazole (10 mol%)	80 °C	60	71[a]
8	Morpholine (10 mol%)	80 °C	60	70[a]
9	DABCO (10 mol%)	80 °C	40	85
10	Pyridine (10 mol%)	80 °C	50	83
11	DBU (15 mol%)	80 °C	10	94
12	DBU (20 mol%)	80 °C	10	92
13	DBU (15 mol%)	100 °C	10	92
14	DBU (15 mol%)	60 °C	10	95
15	DBU (15 mol%)	RT	120	80[a]
16	DBU (15 mol%)	RT	15	92[c]
17	DBU (15 mol%)	RT	120 s	94[d]

[a] Incomplete reaction. [b] No reaction. [c] Reaction under ultrasonic irradiation. [d] Reaction under microwave irradiation (250 W).

reactions proceeded smoothly for different aryl azides with both electron releasing and electron withdrawing groups and also with butyl azide to afford corresponding 1,4,5-trisubstituted-1,2,3-triazoles in excellent yields. The results have been summarized in Table 2 (entries 1–10).

The protocol was further extended by exploring 1,3-dipolar cycloaddition of various aryl azides, alkyl azides and also with other active methylene compounds such as ethyl acetoacetate, methyl acetoacetate, 1,3-diphenylpropane-1,3-dione and malononitrile. The reaction of 4-bromophenyl azide (1 mmol) with ethyl acetoacetate (1 mmol) in water using DBU (15 mol%) as a catalyst under similar conditions yielded 92% of ethyl 1-(4-bromophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate **1k** in 15 min. Similarly reaction of 4-bromophenyl azide (1 mmol) with methyl acetoacetate (1 mmol) and malononitrile (1 mmol) in water using DBU (15 mol%) as a catalyst under similar conditions yielded 80% and 92% of methyl 1-(4-bromophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate **1o** and 5-amino-1-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carbonitrile **1q**, respectively. Other substituted aryl azides also underwent successful 1,3-dipolar addition reaction with ethyl acetoacetate, methyl acetoacetate and malononitrile, giving high yields of corresponding 1,2,3-triazole derivatives (Table 2, entries 11–20).

We decided to explore these reactions using DBU as catalyst under ultrasonic irradiation. The control reaction of 4-bromophenyl azide (1 mmol) with acetylacetone (1 mmol) was attempted in water in presence of DBU (15 mol%) under ultrasonic irradiation at ambient temperature. To our delight, the reaction was complete in 15 min and yielded **1a** in 92% yield after workup (Table 1, entry 10). The reaction of other substituted aryl azides and butyl azide with acetylacetone under similar conditions also yielded corresponding triazoles in good yield (Table 3, entries 2–10). Similarly reactions of different substituted aryl azides with different active methylene compounds such as ethyl acetoacetate, methyl acetoacetate,

Table 2 Synthesis of various 1,4,5-trisubstituted-1,2,3-triazoles under heating at 60 °C (method A)

Entry	R	X	Y	X′	Y′	Product	Time (min)	Yield (%)
1	4-BrC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1a**	10	95
2	4-MeC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1b**	25	90
3	4-$(NO_2)C_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1c**	10	94
4	4-ClC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1d**	20	79
5	4-$MeOC_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1e**	30	87
6	C_6H_5	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1f**	15	81
7	4-FC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1g**	20	79
8	4-F,3-ClC_6H_3	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1h**	25	82
9	*n*-Butyl	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1i**	45	89
10	$CH_2C_6H_5$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1j**	60	85
11	4-BrC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1k**	15	92
12	4-ClC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1l**	45	78
13	4-$(NO_2)C_6H_4$	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1m**	10	93
14	4-F,3-ClC_6H_3	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1n**	35	82
15	4-BrC_6H_4	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1o**	35	80
16	4-$(NO_2)C_6H_4$	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1p**	25	85
17	4-BrC_6H_4	CN	CN	NH_2	CN	**1q**	05	92
18	4-$(NO_2)C_6H_4$	CN	CN	NH_2	CN	**1r**	05	94
19	4-F,3-ClC_6H_3	CN	CN	NH_2	CN	**1s**	15	93
20	4-$(NO_2)C_6H_4$	COPh	COPh	Ph	COPh	**1t**	80	79

1,3-diphenylpropane-1,3-dione and malononitrile in presence of DBU under ultrasonic irradiation yielded the corresponding 1,4,5-trisubstituted-1,2,3-triazoles products in good to excellent yields as reported in Table 3, entries 11–20.

We also examined the scope of this protocol under microwave irradiation. Reaction of 4-bromophenyl azide (1 mmol) and acetylacetone (1 mmol) was attempted in DBU (15 mol%)–water system under microwave irradiation at 40 °C and 250 W. The reaction was complete in 120 s and yield **1a** in 94% yield. The reaction of other substituted aryl azides and butyl azide with acetylacetone under similar conditions also yielded corresponding triazoles in good yield (Table 4, entries 2–10). Similarly reactions of different substituted aryl azides with different active methylene compounds such as ethyl acetoacetate, methyl acetoacetate, 1,3-diphenylpropane-1,3-dione and malononitrile in presence of DBU (15 mol%) under microwave irradiation yielded the corresponding 1,4,5-trisubstituted-1,2,3-triazoles products in excellent yields and shorter reaction time as reported in Table 4, entries 11–20.

We observed that reactions by both methods took place with 100% regioselectivity and only one product was obtained in case of unsymmetrical active methylene compounds. Structure of compound **1o** was further confirmed single crystal X-ray diffraction study (Fig. 1). Further reactions by both methods

Table 3 Synthesis of various 1,4,5-trisubstituted-1,2,3-triazoles under ultrasonic irradiation at room temperature (method B)

Entry	R	X	Y	X′	Y′	Product	Time (min)	Yield (%)
1	4-BrC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1a**	15	92
2	4-MeC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1b**	30	89
3	4-$(NO_2)C_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1c**	10	93
4	4-ClC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1d**	35	79
5	4-$MeOC_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1e**	40	91
6	C_6H_5	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1f**	20	85
7	4-FC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1g**	25	80
8	4-F,3-ClC_6H_3	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1h**	25	81
9	*n*-Butyl	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1i**	55	93
10	$CH_2C_6H_5$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1j**	50	81
11	4-BrC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1k**	20	93
12	4-ClC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1l**	40	75
13	4-$(NO_2)C_6H_4$	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1m**	15	90
14	4-F,3-ClC_6H_3	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1n**	40	85
15	4-BrC_6H_4	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1o**	20	81
16	4$(NO_2)C_6H_4$	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1p**	40	80
17	4-BrC_6H_4	CN	CN	NH_2	CN	**1q**	10	91
18	4-$(NO_2)C_6H_4$	CN	CN	NH_2	CN	**1r**	5	92
19	4-F,3-ClC_6H_3	CN	CN	NH_2	CN	**1s**	15	90
20	4-$(NO_2)C_6H_4$	COPh	COPh	Ph	COPh	**1t**	70	87

Table 4 Synthesis of various 1,4,5-trisubstituted-1,2,3-triazoles under microwave irradiation at room temperature (method C)

Entry	R	X	Y	X′	Y′	Product	Time (s)	Yield (%)
1	4-BrC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1a**	120	94
2	4-MeC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1b**	110	82
3	4-$(NO_2)C_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1c**	90	90
4	4-ClC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1d**	100	80
5	4-$MeOC_6H_4$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1e**	180	92
6	C_6H_5	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1f**	140	82
7	4-FC_6H_4	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1g**	120	82
8	4-F,3-ClC_6H_3	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1h**	110	84
9	*n*-Butyl	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1i**	280	90
10	$CH_2C_6H_5$	$COCH_3$	$COCH_3$	CH_3	$COCH_3$	**1j**	320	84
11	4-BrC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1k**	120	90
12	4-ClC_6H_4	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1l**	110	72
13	4-$(NO_2)C_6H_4$	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1m**	80	88
14	4-F,3-ClC_6H_3	$COCH_3$	$COOCH_2CH_3$	CH_3	$COOCH_2CH_3$	**1n**	100	86
15	4-BrC_6H_4	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1o**	180	82
16	4$(NO_2)C_6H_4$	$COCH_3$	$COOCH_3$	CH_3	$COOCH_3$	**1p**	90	83
17	4-BrC_6H_4	CN	CN	NH_2	CN	**1q**	80	94
18	4-$(NO_2)C_6H_4$	CN	CN	NH_2	CN	**1r**	60	90
19	4-F,3-ClC_6H_3	CN	CN	NH_2	CN	**1s**	70	92
20	4-$(NO_2)C_6H_4$	COPh	COPh	Ph	COPh	**1t**	360	84

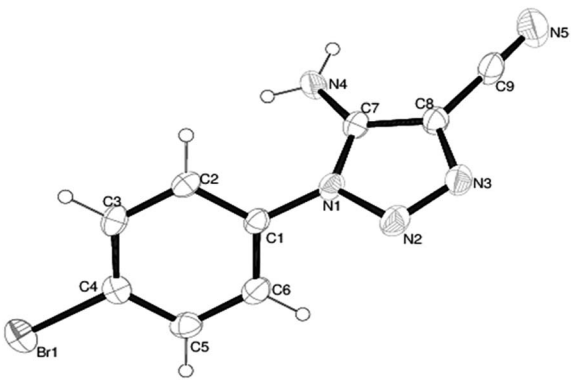


Fig. 1 Ortep diagram of compound **1o** drawn with 30% ellipsoid probability.

Table 5 Recycling of DBU–H_2O system for synthesis of compound **1a, 1i, 1o** under ultrasonic irradiation

Run	Yield (%)	Product
1	92	**1a**
2	90	**1i**
3	91	**1o**
4	88	**1a**
5	84	**1i**
6	85	**1o**

proceed fast and gave better yields with aryl azides having electron withdrawing groups compared to azides with electron donating groups.

We also examined the recyclability of the catalyst and solvent by using reactions for the synthesis of **1a, 1i, 1o** under ultrasonic irradiation. The recyclability of DBU–water system was tested by six run recycling experiment by changing substrates from one cycle to another cycle. The product was separated from the reaction mixture by simple filtration. This allows quick recovery of catalyst and solvent for reuse in the next run. The results of recycling experiment are shown in Table 5. All reactions were complete in 15–25 min and afforded the products in 92–85% yield. The catalyst showed no substantial reduction in activity therefore this system can act as a excellent recyclable reaction medium for synthesis of trisubstituted triazoles in good yield.

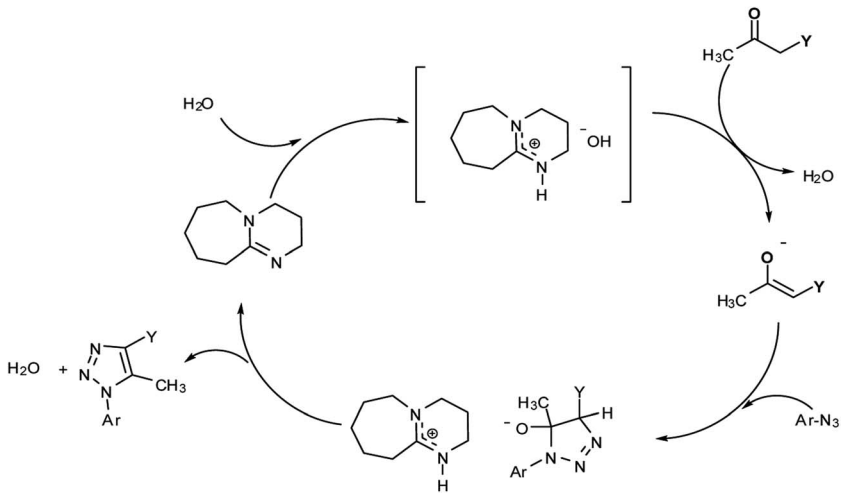
The plausible mechanism of 1,3-dipolar addition reaction of aryl azides with active methylene compounds is shown in Scheme 2. Firstly, DBU reacts with water and changes to DBU–H_2O complex with Brønsted basic properties. Reaction of this complex with active methylene compound resulted in formation of enolate, which on subsequent 1,3-dipolar cycloaddition of aryl azide, followed by elimination of water gave the desired substituted 1,2,3-triazoles with regeneration of catalyst.

Conclusion

We have reported efficient and environmentally benign methodologies for the synthesis of 1,4,5-trisubstituted-1,2,3-triazoles by reaction of various aryl/alkyl azides with active methylene compounds using catalytic DBU in water at 60 °C, ultrasonic and microwave irradiation at room temperature. These protocols offer several advantages in terms of operational simplicity, tolerance of variety of alkyl/aryl azides, active methylene compounds, recyclability of both catalyst and solvent, easy workup, short reaction time, and good yields of product.

Experimental

Structures of all the compounds were identified by their spectral data. Silica gel 60 F_{254} (precoated aluminium plates) from Merck were used to monitor reaction progress. Melting points were determined on a melting point apparatus and are



Scheme 2 Plausible mechanism for synthesis of 1,4,5-trisubstituted-1,2,3-triazoles catalyzed by DBU–H_2O system.

uncorrected. IR (KBr) spectra were recorded on Perkin Elmer FTIR spectrophotometer and the values are expressed as ν_{max} cm^{-1}. Mass spectral data were recorded on a Waters micromass Spectrometer running under Mass Lynex version 4.0 software and equipped with an ESI source. The NMR (^1H and ^{13}C) spectra were recorded on Jeol JNM ECX-400P at 400 MHz and 100 MHz respectively. The chemical shift values are recorded on δ scale and the coupling constants (J) are in Hz. Ultrasonic bath (54 kHz, 300 W, 3 L, capacity) of Throughclean ultrasonic Pvt. Ltd. (India) was used for reactions under ultrasonic irradiation. CEM discover microwave reactor was used for reactions. Different aryl azides were prepared from corresponding aryl amines by reported procedure.[17]

Procedure for preparation of compounds 1a–t under conventional heating conditions

A mixture of aryl/alkyl azide (1.0 mmol), active methylene compound (1.0 mmol), DBU (15 mol%) and water (5 mL) was placed in a 50 mL round-bottomed flask. The mixture was stirred at 60 °C for appropriate time as mentioned in Table 2. After completion of reaction as monitored by TLC using ethyl acetate: petroleum ether (40 : 60, v/v) as eluent, the reaction mixture was allowed to cool to room temperature. The precipitate formed was collected by filtration at pump, washed firstly with water, then with cold ethanol and dried to yield pure 1,4,5-trisubstituted-1,2,3-triazoles in high yields.

Procedure for preparation of compounds 1a–t under ultrasonic irradiation

A mixture of aryl/alkyl azide (1.0 mmol), active methylene compound (1.0 mmol), DBU (15 mol%) and water (5 mL) was placed in a 50 mL round-bottomed flask. The reaction mixture was sonicated at room temperature for appropriate time as mentioned in Table 3. After completion of reaction as monitored by TLC using ethyl acetate : petroleum ether (40 : 60, v/v) as eluent, the precipitate formed was collected by filtration at pump, washed with water followed by cold ethanol. The product was dried to yield pure 1,4,5-trisubstituted-1,2,3-triazoles in high yields.

Procedure for preparation of compounds 1a–t under microwave irradiation

A mixture of aryl/azide (1.0 mmol), active methylene compound (1.0 mmol), DBU (15 mol%) and water (2 mL) was placed in sealed vial and placed in a CEM Discover microwave reactor. The vial was subjected to microwave irradiation, programmed at 40 °C and 250 W for appropriate time as mentioned in Table 4. After completion of the reaction as indicated as monitored by TLC using ethyl acetate : petroleum ether (40 : 60, v/v) as eluent, the precipitate formed was collected by filtration at pump, washed firstly with water, then with cold ethanol and dried to yield pure 1,4,5-trisubstituted-1,2,3-triazoles in high yields.

Characterization data

1-(1-(4-Bromophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1a).[18] White solid; mp 120–122 °C (ethanol); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.45 (d, 2H, J = 8.8 Hz, Ar-H), 7.23 (d, 2H, J = 8.8 Hz, Ar-H), 2.62 (s, 3H, $COCH_3$), 2.47 (s, 3H, CH_3).

1-(5-Methyl-1-*p*-tolyl-1*H*-1,2,3-triazol-4-yl)ethanone (1b).[18] White solid; mp 117–119 °C (ethanol); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.50–7.42 (m, 4H, Ar-H), 2.76 (s, 3H, $COCH_3$), 2.42 (s, 3H, CH_3), 2.25 (s, 3H, CH_3).

1-(5-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)ethanone (1c).[18] White solid; mp 145–146 °C (ethanol); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.44 (d, 2H, J = 9.16 Hz, Ar-H), 7.70 (d, 2H, J = 9.16 Hz Ar-H), 2.74 (s, 3H, $COCH_3$), 2.66 (s, 3H, CH_3).

1-(1-(4-Chlorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1d).[18] White solid; mp 115–116 °C (ethanol); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.59–7.41 (m, 4H, Ar-H), 2.74 (s, 3H, $COCH_3$), 2.43 (s, 3H, CH_3).

1-(1-(4-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1e).[18] White solid; mp 120–122 °C (ethanol); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.30 (d, 2H, J = 8.8 Hz, Ar-H), 7.01 (d, 2H, J = 8.8 Hz Ar-H), 3.84 (s, 3H, OCH_3), 2.70 (s, 3H, $COCH_3$), 2.50 (s, 3H, CH_3).

1-(5-Methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)ethanone (1f).[18] White solid; mp 118–120 °C (ethanol); 7.55–7.53 (m, 3H, Ar-H), 7.51–7.43 (m, 2H, Ar-H), 2.72 (s, 3H, $COCH_3$), 2.56 (s, 3H, CH_3).

1-(1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1g).[19] White solid; mp 80–83 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.57–7.40 (m, 4H, Ar-H), 2.73 (s, 3H, $COCH_3$), 2.40 (s, 3H, CH_3).

1-(1-(3-Chloro-4-fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl) ethanone (1h).[19] White solid; mp 95–96 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.44–7.24 (m, 3H, Ar-H), 2.62 (s, 3H, $COCH_3$), 2.47 (s, 3H, CH_3).

1-(1-Butyl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1i).[18] Brown liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.33–4.30 (t, 2H, J = 6.6 Hz, CH_2), 2.55 (s, 3H, $COCH_3$), 2.19 (s, 3H, CH_3), 1.88–1.84 (m, 2H, CH_2), 1.36–1.32 (m, 2H, CH_2), 0.96–0.91 (t, 2H, J = 6.2 Hz, CH_2).

1-(1-Benzyl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone (1j).[18] Brown liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.32–7.26 (m, 5H, Ar-H), 5.44 (s, 2H, CH_2), 2.61 (s, 3H, $COCH_3$), 2.38 (s, 3H, CH_3).

Ethyl 1-(4-bromophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (1k).[19] White solid; mp 164–166 °C (ethanol); ^{1}H NMR (400 MHz, DMSO) δ_H: 7.85 (d, 2H, J = 8.8 Hz, Ar-H), 7.60 (d, J = 8.76 Hz, 2H, Ar-H), 4.31–4.36 (q, J = 7.32 Hz, 2H, OCH_2), 2.50 (s, 3H, CH_3), 1.29–1.33 (t, J = 7.36 Hz, 3H, CH_2 CH_3).

Ethyl 1-(4-chlorophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (1l).[19] White solid; mp 90–92 °C (ethanol); 7.56–7.36 (m, 4H, Ar-H), 4.43–4.37 (q, J = 7.32 Hz, 2H, OCH_2), 2.39 (s, 3H, CH_3), 1.40–1.36 (t, J = 7.32 Hz, 3H, CH_2 CH_3).

Ethyl 5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylate (1m).[19] White solid; mp 123–124 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.44 (d, 2H, J = 8.76 Hz, Ar-H), 7.71 (d, J = 8.8 Hz, 2H, Ar-H), 4.45–4.42 (q, J = 7.32 Hz, 2H, OCH_2), 2.66 (s, 3H, CH_3), 1.44–1.40 (t, J = 7.32 Hz, 3H, CH_2 CH_3).

Ethyl 1-(3-chloro-4-fluorophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylate (1n).[19] White solid; mp 55–57 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.55 (d, 1H, J = 6.6 Hz, Ar-H), 7.33 (d, 2H, J = 6.6 Hz Ar-H), 4.41–4.46 (q, J = 7.32 Hz, 2H, OCH_2), 2.57 (s, 3H, CH_3), 1.40–1.43 (t, J = 7.32 Hz, 3H, CH_2 CH_3).

Methyl 5-methyl-1-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (1o).[20] White solid; mp 204–206 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.56 (d, 2H, J = 6.68 Hz, Ar-H), 7.35 (d, 2H, J = 6.4 Hz Ar-H), 4.50 (s, 3H, OCH_3), 2.58 (s, 3H, CH_3).

Methyl 5-methyl-1-(4-nitophenyl)-1*H*-1,2,3-triazole-4-carboxylate (1p).[20] White solid; mp 155–157 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.68 (d, 2H, J = 8.04 Hz, Ar-H), 7.31 (d, 2H, J = 7.76 Hz Ar-H), 4.53 (s, 3H, OCH_3), 2.54 (s, 3H, CH_3).

5-Amino-1-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carbonitrile (1q). White solid; mp 240–242 °C (ethanol); IR (KBr, cm^{-1}): ν_{max} = 3338, 3327, 3249, 3204, 2247, 1653, 1506; ^{1}H NMR (400 MHz, DMSO) δ_H: 7.77 (d, 2H, J = 8.8 Hz, Ar-H), 7.49 (d, 2H, J = 8.8 Hz, Ar-H), 7.17 (bs, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO) δ 147.98, 133.23, 132.80, 127.18, 122.70, 113.34, 101.39; LCMS (ESI): m/z = 264. 3532 [M^+ + 2].

5-Amino-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carbonitrile (1r).[20] White solid; mp 205–207 °C (ethanol); ^{1}H NMR (400 MHz, DMSO) δ_H: 8.41 (d, 2H, J = 8.8 Hz, Ar-H), 7.92 (d, 2H, J = 8.8 Hz, Ar-H), 7.21 (bs, 2H, NH_2).

5-Amino-1-(3-chloro-4-fluorophenyl)-1*H*-1,2,3-triazole-4-carbonitrile (1s). White solid; mp 260–262 °C (ethanol); IR (KBr, cm^{-1}): ν_{max} = 3492, 3387, 3354, 3212, 2211, 1683, 1587, 1507; ^{1}H NMR (400 MHz, DMSO) δ_H: 8.37–8.35 (m, 1H, Ar-H), 8.35–8.33 (m, 1H, Ar-H), 8.10–8.07 (m, 1H, Ar-H), 7.65–7.60 (m, 1H, Ar-H), 6.97 (bs, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO) δ 151.21, 147.30, 122.96, 122.69, 121.79, 121.71, 117.82, 117.60, 115.93; LCMS (ESI): m/z = 237.3848 [M^+].

(1-(4-Nitrophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)(phenyl) methanone (1t).[20] White solid; mp 172–175 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.21 (d, 2H, J = 9.6 Hz, Ar-H), 7.86–7.63 (m, 5H, Ar-H), 7.51–7. 29 (m, 5H, Ar-H), 7.12 (d, 2H, J = 8.8 Hz, Ar-H).

Single crystal X-ray structure determination of 5-Amino-1-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carbonitrile. See ESI.†

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