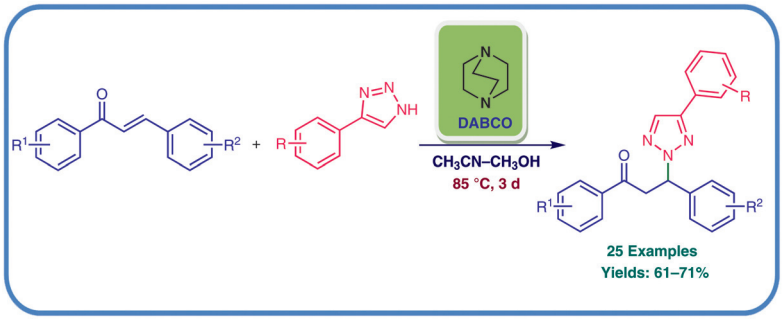
Synlett U. K. Bhagat, R. K. Peddinti Letter

Regiospecific Aza-Michael Addition of 4-Aryl-1*H*-1,2,3-triazoles to Chalcones: Synthesis of 2,4-Disubstituted 1,2,3-Triazoles in Basic Medium

Ujjawal Kumar Bhagat
Rama Krishna Peddinti*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee-247667, Uttarakhand, India
rkpedfcy@iitr.ac.in
ramakpeddinti@gmail.com



Received: 22.07.2017
Accepted after revision: 19.08.2017
Published online: 14.09.2017
DOI: 10.1055/s-0036-1588567; Art ID: st-2017-d0572-l

Abstract A novel metal-free and base-mediated method to display the donor ability of 1,2,3-triazoles for the synthesis of 2,4-disubstituted 1,2,3-triazoles has been developed. A DABCO-promoted aza-Michael addition of 4-aryl NH-1,2,3-triazoles to α,β-unsaturated ketones (chalcones) is presented. The reactions proceeded with complete regiospecificity in a 3:1 mixture of acetonitrile and methanol at 85 °C to provide 2,4-disubstituted 1,2,3-triazoles as Michael adducts, and the addition products 1,3-diaryl-(4-aryl-2*H*-1,2,3-triazol-2-yl)propan-1-ones were isolated in high yields.

Key words triazoles, chalcones, aza-Michael addition, heterocyclic compounds

The 1,2,3-triazole motif belongs to a prominent class of heterocyclic compounds that frequently occur in many natural products, pharmaceutically active compounds, and functional materials.[1] Many compounds bearing the 1,2,3-triazole unit as their core structure exhibit a broad spectrum of biological properties such as anticancer, antituberculosis, antibacterial, and antiviral activities.[2a,b] Disubstituted 1,2,3-triazoles have also been used as chemical sensors, dendrimers, oligomers, linkers, and agrochemicals.[2c–g] Due to the significance of these compounds, the synthesis of 1,2,3-triazole-containing heterocycles has attracted attention from academia and industry.[3]

Among the methods developed for the synthesis of 1,2,3-triazoles, the Huisgen 1,3-dipolar [3+2] cycloaddition of organic azides with alkynes is one of the most popular, efficient, and powerful synthesis routes.[4] The classical Huisgen cycloaddition is a thermally induced reaction that gives a regioisomeric mixture of both 1,4- and 1,5-disubstituted 1,2,3-triazoles.[5] The Cu(I)-catalyzed azide–alkyne 1,3-dipolar cycloaddition (CuAAC) is the most effective strategy for the synthesis of 1,4-disubstituted 1,2,3-triazoles as sole products, as independently exploited by Sharpless, Fokin, and co-workers[6] and by Meldal and co-workers.[7] The CuAAC-catalyzed reaction introduced by Sharpless, referred to as 'click chemistry', has had enormous implications in synthesis.[8] Subsequently, Fokin and Sharpless developed Ru-catalyzed azide–alkyne cycloaddition (RuAAC) processes for the synthesis of 1,5-disubstituted 1,2,3-triazoles with high regioselectivity.[9] Several other metal-catalyzed cycloaddition processes, such as the IrAAC reaction,[10] the AgAAC reaction,[11] and the PdAAC reaction,[12] have been developed for the regioselective synthesis of substituted 1,2,3-triazoles. Recently, a strain-promoted azide–alkyne [3+2] cycloaddition process was developed by Bertozzi and co-workers to furnish 1,4,5-trisubstituted 1,2,3-triazoles as bioorthogonal probes.[13] Ramachary,[14] Wang,[15] Bressy,[16] and their respective co-workers have recently reported new methods for enamine-mediated organocatalytic [3+2] cycloaddition processes to access trisubstituted 1,2,3-triazoles.

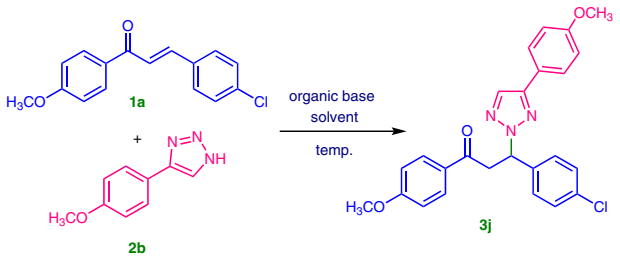
Michael additions and hetero-Michael additions, especially, aza-Michael reactions, are extremely useful transformations in which the formation of C–C and C–N bonds takes place. Such C–N bond-forming reactions are attractive in the context of synthesizing mono-, di-, or trisubstituted 1,2,3-triazoles. The aza-Michael addition reaction of nitrogen-attacking nucleophiles (Michael donors) with α,β-unsaturated electrophiles (Michael acceptors) permits the syntheses of heterocyclic compounds containing a 1,2,3-triazole moiety. However, the nucleophilic reaction of 4-aryl-1*H*-1,2,3-triazoles is underdeveloped, because of the inherent stability of the aromatic 1,2,3-triazole moiety. Recently, Chen and co-workers have reported the selective synthesis of N(2)-substituted 1,2,3-triazoles.[17] Recently, we reported a metal-free, DABCO-mediated, aza-Michael addition of 4-aryl-1*H*-1,2,3-triazoles to cycloalkenones to furnish 2,4-disubstituted 1,2,3-triazoles along with 1,4-disubstituted

1,2,3-triazoles.[18] Under basic conditions, the nucleophilicity of N(2) is enhanced, thereby furnishing 2,4-disubstituted 1,2,3-triazoles as major products. Here, we report a DABCO-mediated aza-Michael addition of 4-aryl-1*H*-1,2,3-triazoles to chalcones under basic conditions to give 2,4-disubstituted 1,2,3-triazole derivatives exclusively.

The required chalcones were synthesized by aldol condensation[19] of aryl aldehydes with acetophenone derivatives in the presence of KOH, and the 4-aryl-1*H*-1,2,3-triazoles were prepared from the corresponding nitrostyrene derivatives.[20] In our initial studies, we examined the reaction of the chalcone **1a** and 4-(4-methoxyphenyl)-1*H*-1,2,3-triazole (**2b**) in acetonitrile at 0 °C in the presence of DABCO (40 mol%). However, no reaction was observed after 10 days (Table 1, entry 1). The reaction was then tried in dichloromethane, 1,2-dichloroethane, and methanol, without any success (entries 2–4). When the reaction was carried out in the presence of DABCO in acetonitrile at room temperature for seven days, the aza-Michael adduct **3j** was isolated in 10% yield (entry 5). The reaction of **1a** and **2b** in the presence of DMAP in acetonitrile or DBU in toluene gave multiple products (entries 6 and 7). The reaction with an increased loading of DABCO in acetonitrile gave slightly improved results on increasing the temperature (entries 8–10). Subsequent reactions were therefore performed with 80 mol% of DABCO in solvents such as acetonitrile–methanol, acetonitrile, methanol, or DCE at 60–80 °C to provide adduct **3j** in moderate yield (entries 11–14). Under these conditions, the use of DMAP did not result in any improvement (entry 15). At this stage, the aza-Michael reaction between **1a** and **2b** was carried out with one equivalent of DABCO in a mixture of acetonitrile and methanol at 85 °C for three days (entries 16–20). We found that an increased amount of methanol resulted in a decreased yield of product **3j**. Thus, screening of various solvents and organic bases at different temperatures, revealed the optimal conditions to be one equivalent of DABCO in a 3:1 mixture of acetonitrile–methanol at 85 °C for three days (entry 16).

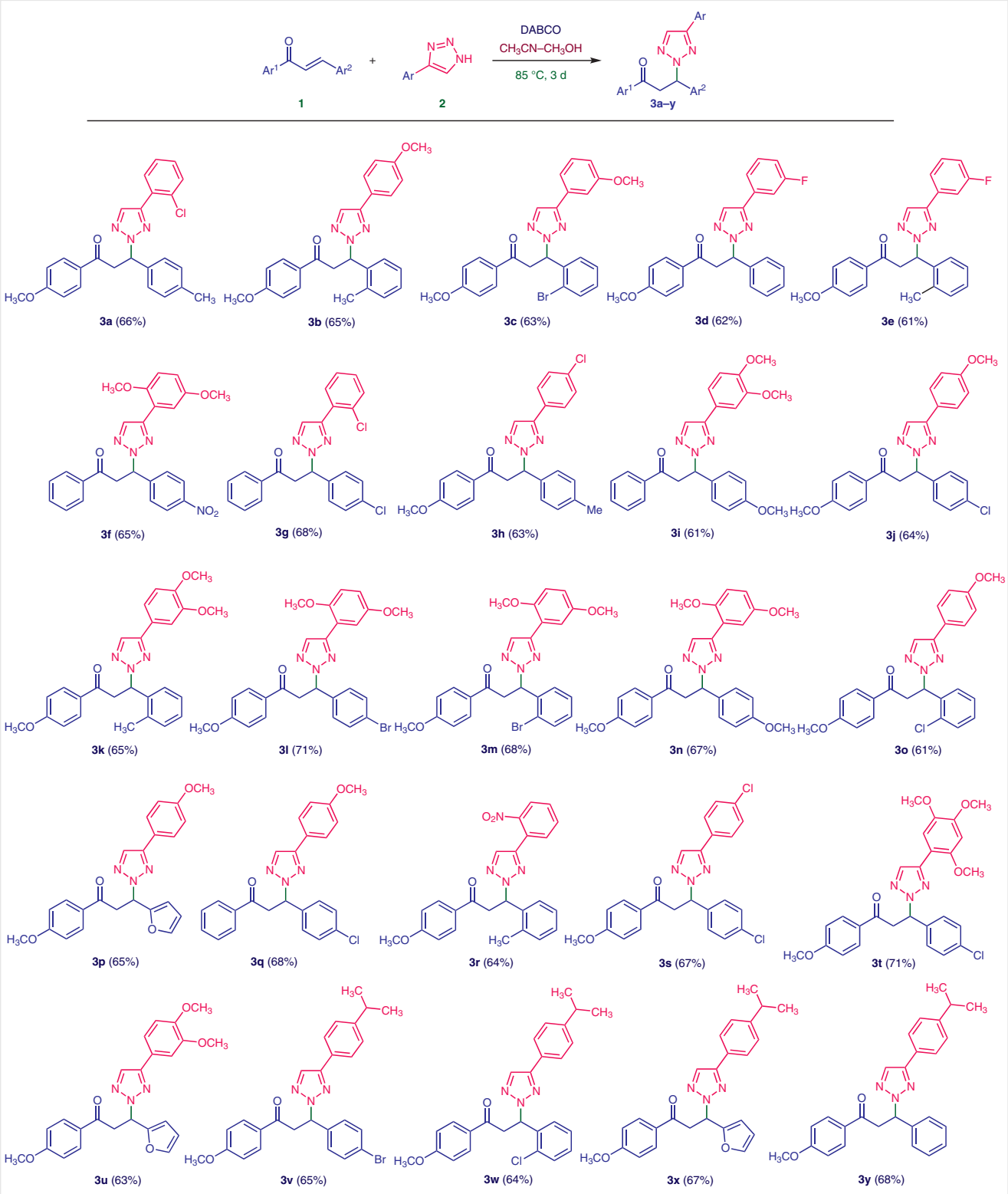
Having the optimized conditions in hand, we then proceeded to investigate the substrate scope for the aza-Michael reaction. As shown in Scheme 1, several substituted chalcones **1a–m** with electron-releasing groups in the aryl ring Ar^1 and electron-releasing or withdrawing groups in the aryl ring Ar^2 of the chalcones were evaluated. Various 4-aryl-1*H*-1,2,3-triazoles bearing electron-releasing and electron-withdrawing groups in the phenyl ring were tested for the aza-Michael reaction. The corresponding aminated products **3a–y** were isolated in yields within the narrow range of 61–71% after three days at 85 °C (Scheme 1). Chalcones bearing electron-releasing groups at the *para*-position of aryl ring Ar^1 and at the *ortho*- or *para*-positions of aryl ring Ar^2 underwent aza-Michael reaction with 4-aryl-1*H*-1,2,3-triazoles bearing aryl electron-releasing groups to give 65–66% yields of Michael adducts **3a**, **3b**, and **3p**. Halogen-substituted 4-(3-fluorophenyl)-1*H*-1,2,3-triazole afforded the adducts **3d** and **3e** in marginally lower yields of 62 and 61%, respectively. The chalcone with a bromo group at the *ortho*-position of aryl ring Ar^2 gave the 3-methoxyphenyltriazole derivative **3c** in 63% yield. 2,5-Dimethoxyphenyl-1,2,3-triazole underwent aza-Michael addition with chalcone derivatives having a *para*-methoxy group on the aryl ring Ar^1 to give the corresponding adducts **3l–n** in 67–

Table 1 Aza-Michael Addition of 4-Methoxyphenyl-1,2,3-triazole **2b** to Chalcone **1a**[a]



Entry	Organic base (mol%)	Solvent (2 mL)	Temp (°C)	Time (d)	Yield[b] (%)
1	DABCO (40)	MeCN	0	10	nr[c]
2	DABCO (40)	CH_2Cl_2	0	10	nr
3	DABCO (40)	DCE	0	10	nr
4	DABCO (40)	MeOH	0	10	nr
5	DABCO (40)	MeCN	r.t.	7	10
6	DMAP (40)	MeCN	r.t.	7	nd[d]
7	DBU (40)	toluene	r.t.	7	nd
8	DABCO (60)	MeCN	r.t.	7	17
9	DABCO (60)	MeCN	60	7	32
10	DABCO (80)	MeCN	60	7	39
11	DABCO (80)	MeCN–MeOH (3:1)	60	7	46
12	DABCO (80)	MeCN	70	4	40
13	DABCO (80)	MeOH	70	4	35
14	DABCO (80)	DCE	80	4	37
15	DMAP (80)	MeCN	80	4	34
16	DABCO (100)	MeCN–MeOH (3:1)	85	3	61
17	DABCO (100)	MeCN–MeOH (1:1)	85	3	50
18	DABCO (100)	MeCN–MeOH (1:3)	85	3	44
19	DABCO (100)	MeCN–MeOH (1:2)	85	3	46
20	DABCO (100)	MeCN–MeOH (2:1)	85	3	55

[a] Reaction conditions: chalcone **1a** (0.2 mmol), 1,2,3-triazole **2b** (0.2 mmol), base, solvent (2 mL).
[b] Isolated yield.
[c] nr = no reaction.
[d] nd = not determined.



Scheme 1 Aza-Michael addition of 4-aryl-1*H*-1,2,3-triazoles **2** to chalcones **1a–m**. *Reaction conditions*: chalcone **1** (0.2 mmol), 4-aryl-1*H*-1,2,3-triazole **2** (0.2 mmol), DABCO (1 equiv), 3:1 MeCN–MeOH (2 mL) at 85 °C, 3 d,[23,24] Yields of the pure and isolated products are reported.

71% yield. 2,5-Dimethoxyphenyl-1,2,3-triazole underwent 1,4-conjugation addition with a chalcone having a *para*-nitro group on Ar^2 to give product **3f** in 65% yield. 4-(2-Chlorophenyl)- and 4-(4-methoxyphenyl)-1*H*-1,2,3-triazoles reacted well with chalcones bearing a *para*-chloro substituent on aryl ring Ar^2 to give the Michael adducts **3g** and **3q**, both in 68% yield. 4-(3,4-Dimethoxyphenyl)-1*H*-1,2,3-triazole also participated in the conjugate addition reaction to give products **3i**, **3k**, and **3u** in 61–65% yield. The enhanced nucleophilicity of 4-(2,4,5-trimethoxyphenyl)-1*H*-1,2,3-triazole was reflected in the reaction in which **3t** was obtained in 71% yield. 4-(4-Isopropylphenyl)-1*H*-1,2,3-triazole also added to chalcones and provided the corresponding disubstituted 1,2,3-triazoles **3v–y** in 64–68% yields. The above results for the formation of 2,4-disubstituted triazoles suggest that electronic and steric factors of substituents on the aryl moieties of both the 1,2,3-triazole and the chalcone have a marginal effects on the outcome of this aza-Michael transformation. The addition of 1,2,3-triazoles to chalcones is regiospecific and furnishes N(2)-adducts exclusively, unlike the addition to cyclohex-2-en-1-ones where N(1)-isomers were also formed;[18] this might be attributed to the lower reactivity of chalcones in comparison with cyclohex-2-en-1-ones. It is worthy of note that N(2)-substituted 1,2,3-triazoles cannot be obtained through click chemistry.

The 2,4-disubstituted 1,2,3-triazoles **3a–y** have a narrow range of chemical shifts (δ = 7.74–8.15 ppm) for the C5-H proton (Table 1, Figure 1-i). These values are comparable with the range of chemical shifts (δ = 7.76–8.14 ppm) for the C5 hydrogen of the aza-Michael adducts derived from 4-aryl-1,2,3-triazoles and cyclic enones [Figure 1(ii)].[18] Similarly, the ^{13}C chemical shifts (δ = 130.3–134.7 ppm) for C5 of the 1,2,3-triazole moiety of **3a–y** [Table 2 and Figures 1(i)] compare closely with those (δ = 130.2–134.4 ppm) of the adducts shown in Figure 1(ii).

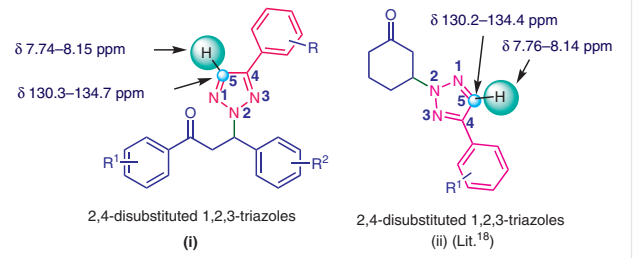


Figure 1 Selected chemical shifts of disubstituted triazoles from aza-Michael addition

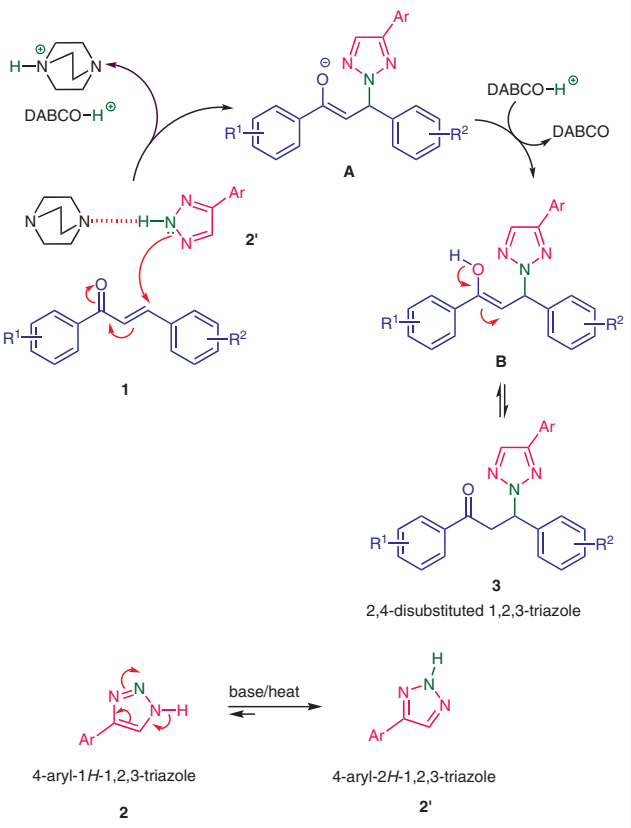
Table 2 Chemical Shifts of C5-H and C5 of 2,4-Disubstituted 1,2,3-Triazoles **3**

Entry	Product	Chemical shift of C5-H (δ, ppm)	Chemical shift of C5 (δ, ppm)
1	**3a**	8.12	130.3
2	**3b**	7.74	130.3
3	**3c**	7.85	130.5
4	**3d**	7.82	131.1
5	**3e**	7.81	131.0
6	**3f**	8.12	133.7
7	**3g**	8.15	134.3
8	**3h**	7.79	130.9
9	**3i**	7.76	130.5
10	**3j**	7.74	130.6
11	**3k**	7.75	130.8
12	**3l**	8.07	134.7
13	**3m**	8.11	134.7
14	**3n**	8.06	134.5
15	**3o**	7.79	130.6
16	**3p**	7.75	130.8
17	**3q**	7.76	130.6
18	**3r**	7.74	130.9
19	**3s**	7.80	131.1
20	**3t**	8.01	134.1
21	**3u**	7.76	130.9
22	**3v**	7.80	131.0
23	**3w**	7.85	130.9
24	**3x**	7.80	–
25	**3y**	7.83	130.8

This trend is in accordance with data reported for 2,4-disubstituted 1,2,3-triazoles derived from the base-mediated reactions of 1,2,3-triazoles.[17,21] In addition, Creary and co-workers recently distinguished between 1,4- and 1,5-disubstituted 1,2,3-triazoles by simple one-dimensional ^{13}C NMR spectroscopy through gated decoupling experiments.[22]

A plausible mechanism for the conjugate addition of 4-aryl-1*H*-1,2,3-triazoles to 2-chalcones **1** is depicted in Scheme 2. The reaction is initiated by the activation of the 4-aryl-1*H*-1,2,3-triazole with DABCO by hydrogen-bonding with the N–H group of the 1,2,3-triazole. In a basic medium and at elevated temperature, the nucleophilicity of the middle nitrogen of 4-aryl-1*H*-1,2,3-triazoles is high.[21b] Subsequently, the activated aryl 1,2,3-triazole attacks the electron-deficient β-carbon of the electrophile. The middle ni-

trogen, having a greater propensity to undergo nucleophilic addition with the β-carbon of the chalcone, generates the enolate intermediate **A**. Proton transfer to intermediate **A** releases the less stable enol form **B**, which in turn undergoes tautomerization to liberate the 2,4-disubstituted 1,2,3-triazole.



Scheme 2 Proposed mechanism for the formation of 2,4-disubstituted 1,2,3-triazoles

In summary, we have illustrated the DABCO-mediated synthesis of 2,4-disubstituted 1,2,3-triazoles by regiospecific aza-Michael addition of 4-aryl-1*H*-1,2,3-triazoles **2** to chalcones **1**. The more-stable aryl-1,2,3-triazoles produced good yields of 2,4-disubstituted 1,2,3-triazoles under metal-free conditions in presence of DABCO at the reflux temperature.

Funding Information

U.K.B. gratefully thanks to Ministry of Human Resource Development, New Delhi, India for providing a fellowship.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1588567.

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(23) **2,4-Disubstituted 1,2,3-Triazoles 3a–y; General Procedure**
DABCO (0.2 mmol) was added to a mixture of the appropriate chalcone **1** (0.2 mmol) and 4-aryl-1*H*-1,2,3-triazole **2** (0.2 mmol) in 3:1 MeCN–MeOH (2 mL) in a 10 mL round-bottomed flask, and the mixture was stirred at 85 °C for 3 d until almost all the reactants were converted (TLC). The product was isolated by subjecting the crude reaction mixture to column chromatography (silica gel, 10–50% EtOAc–hexanes).

(24) **Experimental Data for Selected Compounds3-[4-(2-Chlorophenyl)-2*H*-1,2,3-triazol-2-yl]-1-(4-methoxyphenyl)-3-(4-tolyl)propan-1-one** (**3a**)
Pale-yellow solid; yield: 57.0 mg (66%); mp 117.5–119.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (s, 1 H), 7.99 (d, *J* = 8.8 Hz, 2 H), 7.82 (dd, *J* = 2.4, 7.2 Hz, 1 H), 7.42 (dd, *J* = 2.0, 7.2 Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.29–7.22 (m, 2 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 6.51 (dd, *J* = 8.8, 5.6 Hz, 1 H), 4.49 (dd, *J* = 8.8, 17.6 Hz, 1 H), 3.86 (s, OC*H*$_3$, 3 H), 3.71 (dd, *J* = 5.6, 17.6 Hz, 1 H), 2.32 (s, C*H*$_3$, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.3 (*C*O), 163.7 (C), 144.6 (C), 138.0 (C), 136.4 (C), 134.1 (*C*H), 131.9 (C), 130.5 (2*C*H), 130.3 (*C*H), 130.2 (*C*H), 129.4 (2*C*H), 129.4 (C), 129.2 (C), 129.1 (*C*H), 126.8 (*C*H), 126.6 (2*C*H), 113.7 (2*C*H), 64.2 (*C*H), 55.4 (O*C*H$_3$), 43.6 (*C*H$_2$), 21.1 (*C*H$_3$).
1-(4-Methoxyphenyl)-3-[4-(4-methoxyphenyl)-2*H*-1,2,3-triazol-2-yl]-3-(2-tolyl)propan-1-one (**3b**)
Pale-yellow solid; yield: 55.6 mg (65%); mp 114.0–115.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.8 Hz, 2 H), 7.74 (s, 1 H), 7.65 (d, *J* = 8.8 Hz, 2 H), 7.21–7.12 (m, 4 H), 6.94 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 6.75 (dd, *J* = 4.8, 9.2 Hz, 1 H), 4.49 (dd, *J* = 9.2, 17.6 Hz, 1 H), 3.86 (s, OC*H*$_3$, 3 H), 3.82 (s, OC*H*$_3$, 3 H), 3.57 (dd, *J* = 4.4, 17.6 Hz, 1 H), 2.57 (s, C*H*$_3$, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6 (*C*O), 163.7 (C), 159.6 (C), 147.3 (C), 137.9 (C), 135.2 (C), 130.8 (*C*H), 130.5 (2*C*H), 130.3 (*C*H), 129.5 (C), 128.0 (*C*H), 127.2 (2*C*H), 126.4 (*C*H), 125.9 (*C*H), 123.2 (C), 114.1 (2*C*H), 113.8 (2*C*H), 60.5 (*C*H), 55.5 (O*C*H$_3$), 55.3 (O*C*H$_3$), 42.8 (*C*H$_2$), 19.3 (*C*H$_3$).
3-(2-Bromophenyl)-1-(4-methoxyphenyl)-3-(4-(3-methoxyphenyl)-2*H*-1,2,3-triazol-2-yl)propan-1-one (3c)
Brown viscous liquid; yield: 62.0 mg (63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.8 Hz, 2 H), 7.85 (s, 1 H), 7.61 (d, *J* = 8.0 Hz, 1 H), 7.32–7.26 (m, 3 H), 7.22 (td, *J* = 0.8, 7.6 Hz, 1 H), 7.15 (td, *J* = 1.6, 7.6 Hz, 1 H), 6.95–6.92 (m, 4 H), 6.86 (dt, *J* = 2.4, 7.2 Hz, 1 H), 4.51 (dd, *J* = 10.8, 17.6 Hz, 1 H), 3.86 (s, OC*H*$_3$, 3 H), 3.80 (s, OC*H*$_3$, 3 H), 3.57 (dd, *J* = 3.2, 17.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.9 (*C*O), 163.7 (C), 159.8 (C), 147.6 (C), 139.2 (C), 133.2 (*C*H), 131.5 (C), 131.3 (*C*H), 130.5 (2*C*H), 129.7 (*C*H), 139.5 (*C*H), 129.3 (C), 128.0 (*C*H), 127.4 (*C*H), 122.0 (C), 118.4 (*C*H), 114.2 (*C*H), 113.7 (2*C*H), 111.1 (*C*H), 63.5 (*C*H), 55.4 (O*C*H$_3$), 55.2 (O*C*H$_3$).
3-[4-(3-Fluorophenyl)-2*H*-1,2,3-triazol-2-yl]-1-(4-methoxyphenyl)-3-phenylpropan-1-one (3d)
Pale-yellow solid; yield: 49.8 mg (62%); mp 136.0–137.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.8 Hz, 2 H), 7.82 (s, 1 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.45 (dd, *J* = 2.0, 10.0 Hz, 1 H), 7.39 (d, *J* = 7.6 Hz, 2 H), 7.36–7.27 (m, 4 H), 6.99 (td, *J* = 2.4, 8.4 Hz, 1 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 6.51 (dd, *J* = 4.8, 9.2 Hz, 1 H), 4.51 (dd, *J* = 9.2, 17.6 Hz, 1 H), 3.86 (s, OC*H*$_3$, 3 H), 3.67 (dd, *J* = 5.2, 17.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.2 (*C*O), 163.7 (C), 163.0 (d, *J* = 244.1 Hz, *C*F), 146.4 (C), 139.3 (C), 132.5 (d, *J* = 8.6 Hz, C), 131.1 (*C*H), 130.5 (2*C*H), 130.2 (d, *J* = 7.7 Hz, *C*H) 129.4 (C), 128.8 (2*C*H), 128.3 (*C*H), 126.6 (2*C*H), 121.5 (*C*H), 115.0 (d, *J* = 21.0 Hz, *C*H), 113.8 (2*C*H), 112.8 (d, *J* = 22.9 Hz, *C*H), 64.4 (*C*H), 55.4 (O*C*H$_3$), 43.5 (*C*H$_2$).
3-[4-(3-Fluorophenyl)-2*H*-1,2,3-triazol-2-yl]-1-(4-methoxyphenyl)-3-(2-tolyl)propan-1-one (**3e**)
Pale-yellow solid; yield: 5.7 mg (61%); mp 144.0–145.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.8 Hz, 2 H), 7.81 (s, 1 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.44 (d, *J* = 9.6 Hz, 1 H), 7.33 (q, *J* = 7.6 Hz, 1 H), 7.23–7.14 (m, 4 H), 6.99 (td, *J* = 2.0, 8.4 Hz, 1 H), 6.95 (d, *J* = 8.4 Hz, 2 H), 6.68 (dd, *J* = 4.4, 9.6 Hz, 1 H), 4.52 (dd, *J* = 9.6, 17.6 Hz, 1 H), 3.87 (s, OC*H*$_3$, 3 H), 3.58 (dd, *J* = 4.4, 17.6 Hz, 1 H), 3.59 (s, C*H*$_3$, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.4 (*C*O), 163.8 (C), 163.0 (d, *J* = 244.1 Hz, *C*F), 146.3 (C), 137.7 (C), 135.2 (C), 132.6 (d, *J* = 7.6 Hz, C), 131.0 (*C*H), 130.8 (*C*H), 130.5 (2*C*H), 130.2 (d, *J* = 8.6 Hz, *C*H), 129.4 (C), 128.1 (*C*H), 126.5 (*C*H), 125.8 (*C*H), 121.5 (d, *J* = 2.9 Hz, *C*H), 115.0 (d, *J* = 21.0 Hz, *C*H), 113.8 (2*C*H), 112.8 (d, *J* = 22.9 Hz, *C*H), 60.7 (*C*H), 55.5 (O*C*H$_3$), 42.7 (*C*H$_2$), 19.33 (*C*H$_3$).
3-[4-(2,5-Dimethoxyphenyl)-2*H*-1,2,3-triazol-2-yl]-1-(4-methoxyphenyl)-3-(4-nitrophenyl)propan-1-one (**3f**)
Yellow viscous liquid: yield: 59.6 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.4 Hz, 2 H), 8.12 (s, 1 H), 8.01 (d, *J* = 7.6 Hz, 2 H), 7.59 (t, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.48 (d, *J* = 7.2 Hz, 2 H), 7.47 (t, *J* = 7.6 Hz, 1 H), 6.89 (d, *J* = 8.8 Hz, 1 H), 6.85 (dd, *J* = 3.2, 8.8 Hz, 1 H), 6.62 (dd, *J* = 6.4, 7.6 Hz, 1 H), 4.52 (dd, *J* = 8.0, 17.6 Hz, 1 H), 3.85 (s, OC*H*$_3$, 3 H), 3.83 (dd, *J* = 6.0,

17.6 Hz, 1 H), 3.76 (s, OCH_3, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1 (*C*O), 153.6 (C), 151.0 (C), 147.6 (C), 146.5 (C), 144.6 (C), 136.0 (C), 135.1 (*C*H), 133.7 (*C*H), 128.7 (2*C*H), 128.1 (2*C*H), 127.8 (2*C*H), 124.0 (2*C*H), 119.4 (C), 114.9 (*C*H), 113.1 (*C*H), 112.4 (*C*H), 63.2 (*C*H), 55.9 (O*C*H_3), 55.7 (O*C*H_3), 43.8 (*C*H_2).

3-(4-Chlorophenyl)-3-[4-(2-chlorophenyl)-2*H*-1,2,3-triazol-2-yl]-1-phenylpropan-1-one (**3g**)

Pale-yellow solid; yield: 57.4 mg (68%); mp 84.0–86.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 8.01 (d, *J* = 7.6 Hz, 2 H), 7.81 (dd, *J* = 2.4, 7.6 Hz, 1 H), 7.58 (t, *J* = 7.6 Hz, 1 H), 7.46 (t, *J* = 7.6 Hz, 2 H), 7.44–7.41 (m, 1 H), 7.38 (d, *J* = 8.4 Hz, 2 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.29–7.22 (m, 2 H), 6.53 (dd, *J* = 5.6, 8.4 Hz, 1 H), 4.52 (dd, *J* = 8.4, 18.0 Hz, 1 H), 3.78 (dd, *J* = 5.6, 18.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4 (*C*O), 144.9 (C), 137.6 (C), 136.1 (C), 134.3 (*C*H), 134.2 (C), 133.5 (*C*H), 131.9 (C), 130.3 (2*C*H), 129.3 (*C*H), 128.9 (2*C*H and C), 128.6 (2*C*H), 128.2 (2*C*H), 128.1 (2*C*H), 126.8 (*C*H), 63.5 (*C*H), 43.8 (*C*H_2).

3-[4-(4-Chlorophenyl)-2*H*-1,2,3-triazol-2-yl]-1-(4-methoxyphenyl)-3-(4-tolyl)propan-1-one (**3h**)

White solid; yield: 54.4 mg (63%); mp 125.0–127.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.8 Hz, 2 H), 7.79 (s, 1 H), 7.66 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, 8.0 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 6.46 (dd, *J* = 5.2, 9.2 Hz, 1 H), 4.49 (dd, *J* = 8.8, 17.6 Hz, 1 H), 3.86 (s, OCH_3, 3 H), 3.67 (dd, *J* = 5.2, 17.6 Hz, 1 H), 2.31 (s, CH_3, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.3 (*C*O), 163.7 (C), 146.4 (C), 138.1 (C), 136.4 (C), 133.9 (C), 130.9 (*C*H), 130.5 (2*C*H), 129.4 (2*C*H), 129.4 (C), 129.0 (C), 128.8 (2*C*H), 127.1 (2*C*H), 126.6 (2*C*H), 113.7 (2*C*H), 64.2 (*C*H), 55.4 (O*C*H_3), 43.5 (*C*H_2), 21.1 (*C*H_3).

3-[4-(3,4-Dimethoxyphenyl)-2*H*-1,2,3-triazol-2-yl]-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**3i**)

Yellow viscous liquid: yield: 54.1 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 7.6 Hz, 2 H), 7.76 (s, 1 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.35 (d, 8.8 Hz, 2 H), 7.25 (td, *J* = 1.6, 6.0 Hz, 2 H), 6.87–6.84 (m, 3 H), 6.45 (dd, *J* = 5.2, 8.8 Hz, 1 H), 4.51 (dd, *J* = 8.8, 17.6 Hz, 1 H), 3.86 (s, OCH_3, 3 H), 3.86 (s, OCH_3, 3 H), 3.74 (s, CH_3, 3 H), 3.70 (dd, *J* = 5.2, 17.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.9 (*C*O), 159.3 (C), 149.0 (C), 147.3 (C), 136.3 (C), 133.2 (*C*H), 131.4 (C), 130.5 (*C*H), 128.5 (*C*H), 128.0 (2*C*H), 128.0 (C, merged with two *C*H), 127.8 (2*C*H), 123.2 (C), 118.3 (*C*H), 114.0 (2*C*H), 111.0 (*C*H), 109.0 (2*C*H), 63.6 (*C*H), 55.7 (2O*C*H_3), 55.1 (O*C*H_3) 43.9 (*C*H_2).

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-[4-(4-methoxyphenyl)-2*H*-1,2,3-triazol-2-yl]propan-1-one (**3j**)

White solid; yield: 57.3 mg (64%); mp 120.0–122.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.8 Hz, 2 H), 7.74 (s, 1 H), 7.65 (d, *J* = 8.4 Hz, 2 H), 7.33 (q, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 6.91 (dd, *J* = 6.4, 8.4 Hz, 4 H), 6.45 (dd, *J* = 5.6, 8.4 Hz, 1 H), 4.40 (dd, *J* = 8.4, 17.6 Hz, 1 H), 3.85 (s, OCH_3, 3 H), 3.81 (s, OCH_3, 3 H), 3.70 (dd, *J* = 5.6, 17.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.1 (*C*O), 163.8 (C), 159.7 (C), 147.6 (C), 138.1 (C), 134.0 (C), 130.6 (*C*H), 130.5 (2*C*H), 129.3 (C), 128.9 (2*C*H), 128.2 (2*C*H), 127.2 (2*C*H), 122.9 (C), 114.1 (2*C*H), 113.8 (2*C*H), 63.5 (*C*H), 55.5 (2O*C*H_3), 55.3 (O*C*H_3), 43.5 (*C*H_2).