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Sonochemistry- and mechanochemistry-driven one-pot synthesis of polyfunctionalised 5-iodo-1*H*-1,2,3-triazoles through copper(i)-catalysed click chemistry

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We herein report a dual synthetic approach that integrates sono- and mechanochemical strategies to access a diverse array of 5-iodo-1*H*-1,2,3-triazoles through a copper(i)-catalysed click reaction of aryl/heteroaryl acetylenes with benzyl bromides, sodium azide, and copper iodide (CuI). CuI acts here as both a catalyst and an iodine source. Both synthetic protocols provide a straightforward, efficient, and practical platform for accessing this important class of biologically and synthetically valuable organic compounds. The salient features of the newly developed methods include mild reaction conditions, avoidance of external heating and oxidants, shorter reaction times (in minutes), good to excellent yields with high regioselectivity, broad substrate scope and tolerance toward various functional groups, acceptable *E*-factors in most cases, gram-scale synthetic applicability, and reusability of the solid surface (mechanochemical). Besides, a few selected synthesised 5-iodo-triazoles were converted into a range of biorelevant molecular scaffolds, as part of the synthetic application.

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1. Introduction

The copper-catalysed azide-alkyne cycloaddition (CuAAC) reaction, independently developed by Sharpless^{1a} and Meldal,^{1b} is nowadays a well-established strategy for the synthesis of functionalised 1,2,3-triazoles, due to its operational simplicity and high regioselectivity.² Substituted 1,2,3-triazoles find remarkable applications across diverse fields, including synthetic and medicinal chemistry,³ bioconjugation,⁴ polymer chemistry,⁵ and materials science.⁶ Normal CuAAC reactions produce only 1,4-disubstituted 1,2,3-triazoles, and that is why 5-iodo-1,2,3-triazoles (**4**), a class of 1,4,5-trisubstituted 1,2,3-triazoles, have recently attracted much attention because iodo-derivatives have found wide applications in multicomponent synthesis,⁷ halogen-bonding based anion recognition,⁸ and materials fabrication,⁹ and drug discovery in biomedical research.¹⁰ Also, structurally, they are convenient precursors, readily undergoing diverse post-functionalisation reactions such as Sonogashira alkylation,¹¹ arylation,¹² Heck coupling,¹³ and intramolecular cyclisation.¹⁴

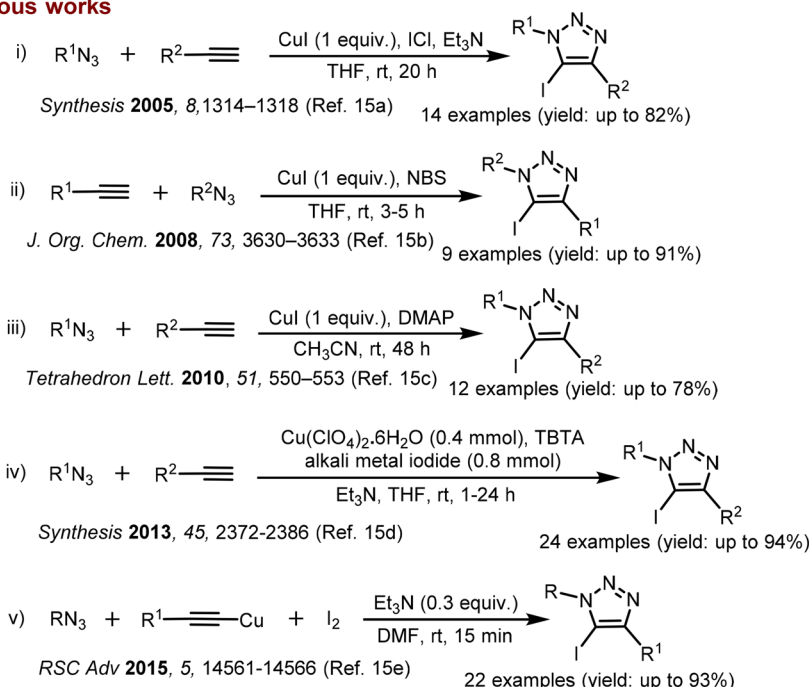
Our comprehensive literature survey disclosed five such previous reports for accessing 5-iodo-1,2,3-triazoles (Scheme 1a(i-v)). In 2005, Chen and co-workers^{15a} synthesised fourteen derivatives of 5-iodotriazoles by stirring a mixture of aryl

acetylenes and alkyl azides in the presence of the CuI catalyst, ICl as an electrophile, and Et₃N as a base in THF solvent at room temperature for 20 h (Scheme 1a(i)). Thereafter, in 2008, Zhang and co-workers^{15b} reported an alternative strategy for the synthesis of these compounds *via* a one-pot reaction between substituted acetylenes and azides in THF, employing CuI as the catalyst and NBS as an oxidant for 3–5 h (Scheme 1a(ii)). Following this, in 2010, the Dzyuba group^{15c} developed a protocol for the synthesis of a limited set of nine 5-iodotriazole derivatives using the CuI catalyst and DMAP base in CH₃CN for 20 h (Scheme 1a(iii)). In 2013, Zhu and co-workers^{15d} disclosed a one-pot protocol for the synthesis of these compounds from acetylenes and azides using Cu(ClO₄)₂·6H₂O as the catalyst in the presence of TBTA as an additive, an alkali metal iodide, Et₃N as the base, and THF as the solvent for 1–24 h (Scheme 1a(iv)). Later, in 2015, the Hu group^{15e} reported a strategy for synthesising 5-iodotriazoles by employing copper acetylides and alkyl azides in the presence of molecular iodine, with Et₃N as the base in DMF for 15 min (Scheme 1a(v)). Despite the inherent synthetic merits of these previous methods, they still bear several limitations, including limited substrate scope, low product yields in most cases, the need for external oxidants, and prolonged reaction times. Hence, the design and development of more facile, eco-friendly, and practical synthetic strategies to functionalise 5-iodotriazoles is highly warranted. As part of our green chemistry-driven organic synthesis,¹⁶ we have successfully explored a dual approach, combining sono-chemical and mechanochemical strategies, to access a wide

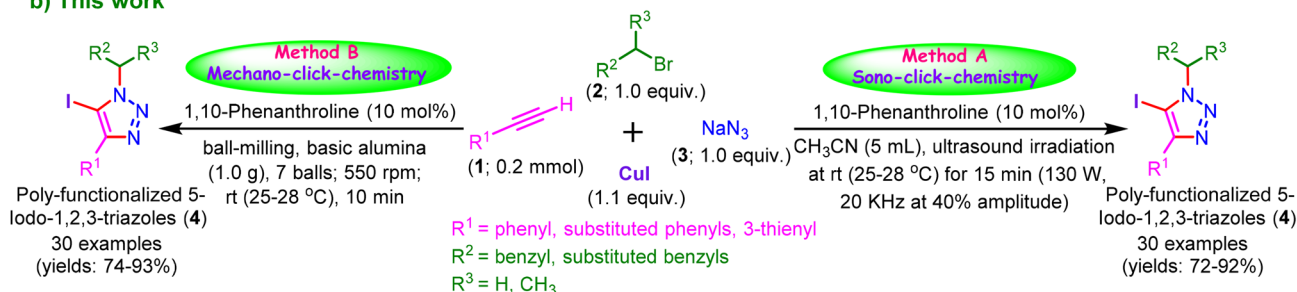
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a) Previous works



b) This work



- ✓ Avoidance of external oxidants
- ✓ Reusability of solid surface (mechanochemical)
- ✓ Good to excellent yields
- ✓ Broad substrate scope
- ✓ Green and eco-friendly
- ✓ Shorter reaction times (in minutes)
- ✓ Gram-scale synthetic applicability
- ✓ Mild and energy efficient processes

Scheme 1 (a) Earlier reports on the synthesis of 5-iodo-1,2,3-triazoles; (b) present work: dual synthetic approaches (sono- and mechanochemical) for diversely substituted 5-iodo-1,2,3-triazoles **4**.

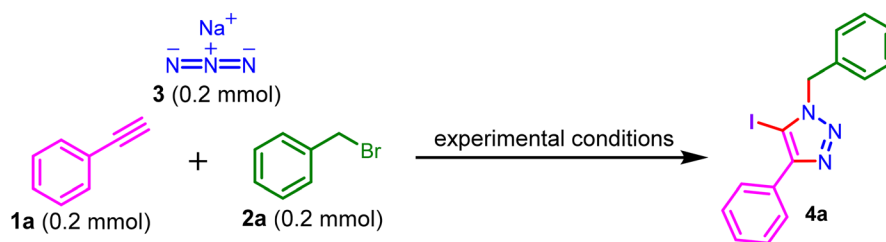
array of diversely substituted 5-iodo-1,2,3-triazoles, as outlined in Scheme 1b. These newly developed methods offer several notable advantages, notably oxidant-free synthesis, short reaction times (in minutes), broad substrate scope, good to excellent yields with high regioselectivity, avoidance of reaction solvents and reusability of the solid surface (in the case of mechanochemistry), acceptable *E*-factors (in most cases), gram-scale synthetic applicability, and eco-friendliness. The applications of sonochemical¹⁷ and mechanochemical¹⁸ strategies are well-established in synthetic organic chemistry.

2. Results and discussion

We initiated our study with the model reaction by stirring the reaction mixture of phenylacetylene (**1a**; 0.2 mmol), benzyl bromide (**2a**; 0.2 mmol), sodium azide (NaN_3 ; **3**; 0.2 mmol), and copper iodide (CuI , 1.1 equiv.) using 1,10-phenanthroline (1,10-

Phen; 10 mol%) as an additive and acetonitrile (CH_3CN ; 5 mL) as a solvent for 12 h under ambient conditions. This afforded the desired product, 1-benzyl-4-phenyl-5-iodo-1*H*-1,2,3-triazole (**4a**), in 52% yield (Table 1, entry 1). With this somewhat encouraging result, we undertook a systematic solvent screening using dimethyl sulfoxide (DMSO), 1,2-dichloromethane (1,2-DCM), *N,N*-dimethylformamide (DMF), 1,4-dioxane, ethanol, and water, keeping all other parameters unchanged; however, none of these solvents outperformed acetonitrile (CH_3CN) except DMF, for which a moderate yield of 47% was obtained (Table 1, entries 2–7). In light of these observations under ambient conditions, we decided to explore the impact of subjecting the reaction mixture to ultrasound irradiation in acetonitrile with a view to accelerating the reaction rate and enhancing the yield. Accordingly, we conducted our model reaction in acetonitrile solvent under ultrasonication (130 W, 20 kHz) at three different amplitudes (*viz.* 30%, 40%,



Table 1 Optimisation of reaction conditions under ultrasonication^{a,b}

Entry	Iodinating agent (equiv.)	Additive (mol%)	Solvent (5 mL)	Conditions (amplitude %)	Time (min)	Yield (%) ^{a,b}
1	CuI (1.1)	1,10-Phen (10)	CH ₃ CN	Stirring at rt	720	52
2	CuI (1.1)	1,10-Phen (10)	DMSO	Stirring at rt	720	28
3	CuI (1.1)	1,10-Phen (10)	DCM	Stirring at rt	720	—
4	CuI (1.1)	1,10-Phen (10)	DMF	Stirring at rt	720	47
5	CuI (1.1)	1,10-Phen (10)	THF	Stirring at rt	720	11
6	CuI (1.1)	1,10-Phen (10)	EtOH	Stirring at rt	720	—
7	CuI (1.1)	1,10-Phen (10)	H ₂ O	Stirring at rt	720	—
8	CuI (1.1)	1,10-Phen (10)	CH ₃ CN	Ultrasound (30%)	20	68
9	CuI (1.1)	1,10-Phen (10)	CH₃CN	Ultrasound (40%)	15	88
10	CuI (1.1)	1,10-Phen (10)	CH ₃ CN	Ultrasound (50%)	15	75
11	CuI (1.1)	—	CH ₃ CN	Ultrasound (40%)	15	—
12	NaI (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	31
13	KI (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	36
14	CaI ₂ (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	—
15	NIS (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	56
16	NH ₄ I (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	15
17	<i>n</i> -Bu ₄ NI (1.0)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	68
18	CuI (0.5)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	56
19	CuI (1.5)	1,10-Phen (10)	CH ₃ CN	Ultrasound (40%)	15	79
20	CuI (1.1)	1,10-Phen (5)	CH ₃ CN	Ultrasound (40%)	15	43
21	CuI (1.1)	1,10-Phen (20)	CH ₃ CN	Ultrasound (40%)	15	75
22	CuI (1.1)	DABCO (10)	CH ₃ CN	Ultrasound (40%)	15	25
23	CuI (1.1)	DBU (10)	CH ₃ CN	Ultrasound (40%)	15	17
24	CuI (1.1)	EN (10)	CH ₃ CN	Ultrasound (40%)	15	—
25	CuI (1.1)	1,10-Phen (10)	DMSO	Ultrasound (40%)	15	36
26	CuI (1.1)	1,10-Phen (10)	DCM	Ultrasound (40%)	15	—
27	CuI (1.1)	1,10-Phen (10)	THF	Ultrasound (40%)	15	29

^a Reaction conditions: a mixture of phenylacetylene (**1a**; 0.2 mmol), benzyl bromide (**2a**; 0.2 mmol) and sodium azide (**3**; 0.2 mmol) was reacted with CuI or other iodinating agents in 5 mL of varying solvent(s) under either room temperature (rt, 25–28 °C) stirring or ultrasound irradiation (US; 130 W, 20 kHz at 30–50% amplitude). ^b Isolated yields.

and 50%). Eventually, we isolated the target compound **4a** with respective yields of 68%, 88% and 75% within 15 min in each case (Table 1, entries 8–10).

Interestingly, the reaction did not occur at all in the absence of 1,10-phenanthroline (Table 1, entry 11), thereby establishing the crucial role of this additive as a ligand in implementing this transformation.

Subsequent trial reactions (Table 1, entries 12–17) revealed that CuI is the best reagent for this transformation when compared with NaI, KI, NIS, NH₄I, and *n*-Bu₄NI. Again, CuI and 1,10-phenanthroline loading variations (Table 1, entries 18–21) revealed that the combination of 1.1 equiv. of CuI and 10 mol% of 1,10-phenanthroline is optimal for the highest yield of the product **4a**. Likewise, lower yields of **4a** were obtained by changing the ligand loading or substituting other nitrogenous additives (DABCO, DBU, and EN (ethylenediamine)) (Table 1,

entries 22–24). Finally, solvent screening under ultrasonic irradiation reaffirmed acetonitrile as the most suitable medium, since DCM was ineffective and DMSO and THF provided only moderate yields (Table 1, entries 25–27). Eventually, we achieved the optimised reaction conditions for our model reaction by irradiating the mixture of phenylacetylene (**1a**), benzyl bromide (**2a**), sodium azide (NaN₃; **3**), and copper iodide (1.1 equiv.) in acetonitrile (5 mL), with ultrasound at 40% amplitude for 15 min to isolate the desired compound **4a** in 88% yield (Table 1, entry 9). Compound **4a** is a known compound, and its physical and spectral properties are well-matched with those reported in the literature.¹⁵ Table 1 explicitly summarises all these experimental outcomes.

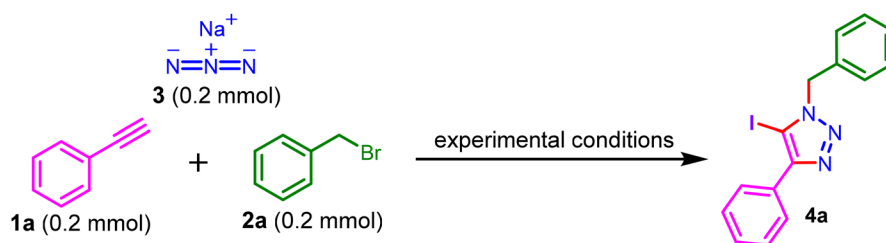
With the optimised sonochemical conditions at hand, we envisioned, based on our research experience and understanding, that the same transformation could be achieved



under mechanochemical conditions in a high-speed ball mill. With this view, we first attempted our model reaction between phenylacetylene (**1a**; 0.2 mmol), benzyl bromide (**2a**; 0.2 mmol), sodium azide (NaN₃; **3**; 0.2 mmol), and copper iodide (CuI; 1.1 equiv.) by grinding the mixture on a basic alumina (1.0 g) surface with seven stainless steel balls at 550 rpm, where no reaction took place even after 1 h. Most strikingly, the conversion improved dramatically when we added 10 mol% of 1,10-phenanthroline (1,10-Phen) as an additive, affording **4a** in 89% yield within just 10 min (rotation in an inverted direction with a 30 s break at a 5 min interval) (Table 2, entry 2). Then, under the same reaction conditions, other iodide reagents were investigated (Table 2, entries 3–8); only NIS and *n*-Bu₄NI produced the product in 56% (Table 2, entry 6) and 75% (Table

2, entry 8) yields, respectively. In contrast, NaI, KI, NH₄I, and CaI₂ were largely ineffective (Table 2, entries 3–5, 7). Variation of CuI loading showed that 1.1 equiv. was optimal, as both lower and higher amounts resulted in lower yields (Table 2, entries 9 and 10). We then performed several other trial reactions with this model entry by varying the equivalents and type of additives, nature of the solid surface, and milling parameters, such as the number of balls, frequency (rpm), and milling time (Table 2, entries 11–22); however, we did not observe any marked improvement. Conventional stirring with varying solvents under ambient conditions was also ineffective (Table 2, entries 24 and 25). We also carried out a control experiment using a tungsten carbide jar and balls to rule out any catalytic intervention by the stainless steel jar and balls (Table 2, entry

Table 2 Optimisation of reaction conditions under ball-milling^{a,b}



Entry	Iodinating agent (equiv.)	Additive (mol%)	Surface (1.0 g)	No. of balls/rpm	Time (min)	% yield ^b 4a
1	CuI (1.1)	—	Basic alumina	7/550	60	—
2	CuI (1.1)	1,10-Phen (10)	Basic alumina	7/550	10	89
3	NaI (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	31
4	KI (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	36
5	CaI ₂ (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	—
6	NIS (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	56
7	NH ₄ I (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	15
8	<i>n</i> -Bu ₄ NI (1.0)	1,10-Phen (10)	Basic alumina	7/550	10	75
9	CuI (0.5)	1,10-Phen (10)	Basic alumina	7/550	10	36
10	CuI (1.5)	1,10-Phen (10)	Basic alumina	7/550	10	78
11	CuI (1.1)	1,10-Phen (5)	Basic alumina	7/550	30	49
12	CuI (1.1)	1,10-Phen (20)	Basic alumina	7/550	10	75
13	CuI (1.1)	1,10-Phen (10)	Acidic alumina	7/550	10	36
14	CuI (1.1)	1,10-Phen (10)	Neutral alumina	7/550	10	15
15	CuI (1.1)	1,10-Phen (10)	SiO ₂ -H ₂ SO ₄	7/550	10	—
16	CuI (1.1)	DABCO (10)	Basic alumina	7/550	10	17
17	CuI (1.1)	DBU (10)	Basic alumina	7/550	10	14
18	CuI (1.1)	EN (10)	Basic alumina	7/550	10	—
19	CuI (1.1)	1,10-Phen (10)	Basic alumina	9/550	10	83
20	CuI (1.1)	1,10-Phen (10)	Basic alumina	5/550	30	59
21	CuI (1.1)	1,10-Phen (10)	Basic alumina	7/600	10	86
22	CuI (1.1)	1,10-Phen (10)	Basic alumina	7/450	30	66
23	CuI (1.1)	1,10-Phen (10)	Basic alumina	—	30	—
24 ^c	CuI (1.1)	1,10-Phen (10)	—	—	720	28
25 ^c	CuI (1.1)	1,10-Phen (10)	—	—	720	43
26 ^d	CuI (1.1)	1,10-Phen (10)	Basic alumina	7/550	10	89

^a Reaction conditions: a mixture of phenylacetylene (**1a**; 0.2 mmol), benzyl bromide (**2a**; 0.2 mmol) and sodium azide (**3**; 0.2 mmol) was ball-milled with CuI or other iodinating agents (using a 25 mL stainless-steel jar and balls of 10 mm diameter and rotation in an inverted direction with a break of 30 s at 5 min intervals) in the presence/absence of catalysts, additives and surface without the aid of any solvent. ^b Isolated yields. ^c Stirring the reaction mixture under ambient conditions (25–28 °C) respectively, in DMSO and CH₃CN. ^d Using a tungsten carbide jar and balls. pH measured (1.0 g of acidic/neutral/basic alumina suspended in 5 mL of distilled water, followed by stirring for 10 min and then leaving undisturbed for 1 h) for acidic alumina was 6.10, for neutral alumina it was 7.07, for basic alumina it was 8.24, and for SiO₂-sulfuric acid it was 1.4. 1,10-Phen = 1,10-phenanthroline; EN = ethylenediamine.



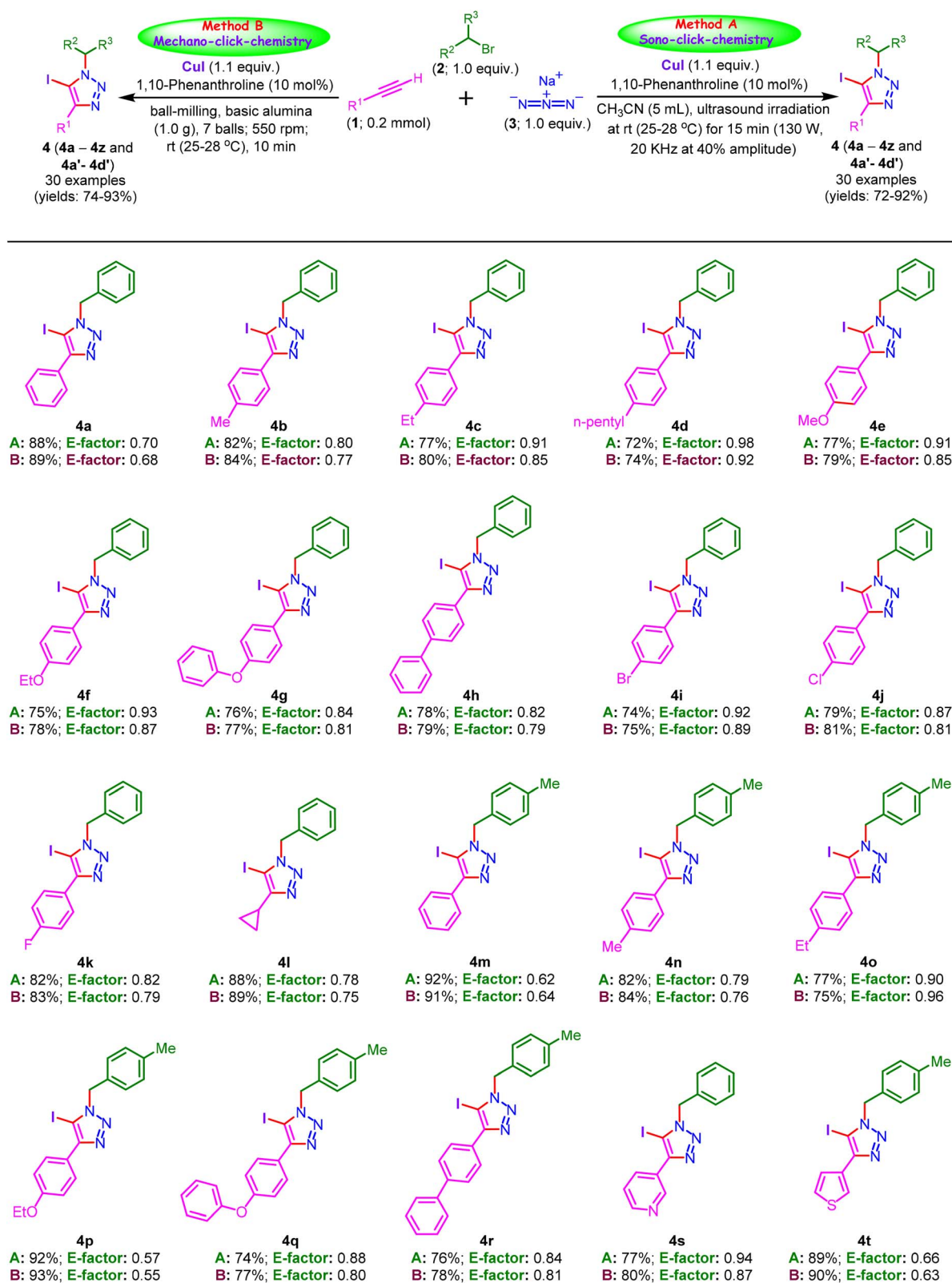
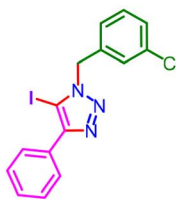
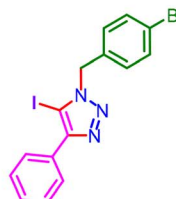
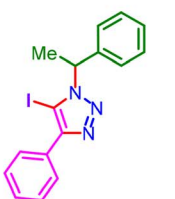
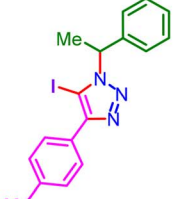
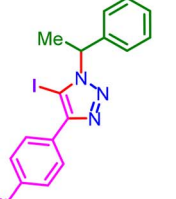
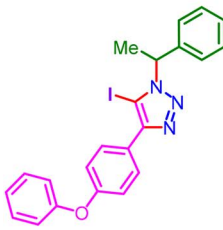
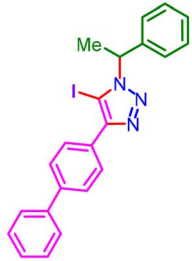
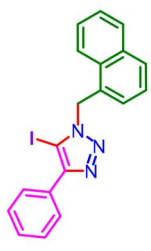
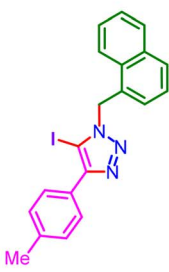
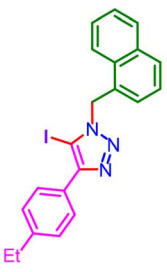
Table 3 Sono- and mechanochemical synthesis of functionalised 5-iodo-1,2,3-triazoles (**4**)^{a,b}

Table 3 (Contd.)

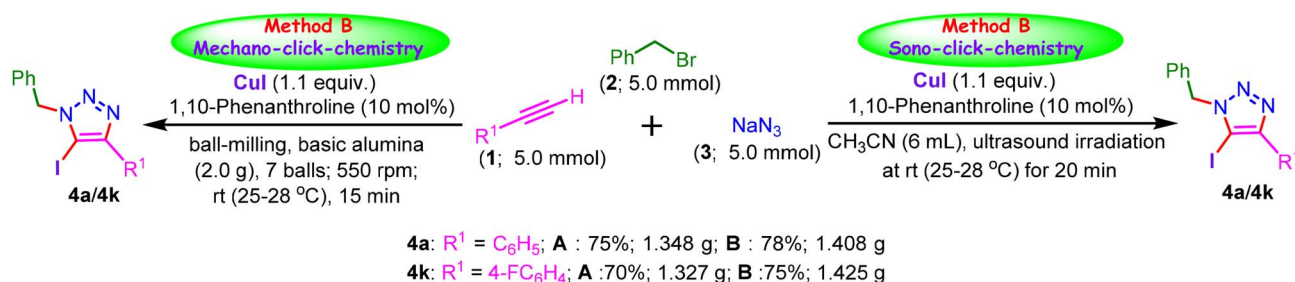
				
A: 76%; E-factor: 0.91 B: 78%; E-factor: 0.85	A: 75%; E-factor: 0.87 B: 78%; E-factor: 0.79	A: 78%; E-factor: 0.89 B: 79%; E-factor: 0.89	A: 76%; E-factor: 0.94 B: 78%; E-factor: 0.88	A: 75%; E-factor: 0.96 B: 78%; E-factor: 0.87
				
A: 83%; E-factor: 0.66 B: 86%; E-factor: 0.62	A: 89%; E-factor: 0.58 B: 91%; E-factor: 0.54	A: 85%; E-factor: 0.70 B: 89%; E-factor: 0.63	A: 90%; E-factor: 0.58 B: 92%; E-factor: 0.56	A: 73%; E-factor: 0.95 B: 75%; E-factor: 0.89

26). Finally, we developed an alternative and efficient protocol for the same transformation to access the desired product **4a** in an excellent yield of 89% (Table 2, entry 2) under ball milling using seven stainless steel balls (10 mm in diameter) milled for 10 min (rotation in an inverted direction with a 30 s break at a 5 min interval) at 550 rpm in the presence of basic alumina (1.0 g) as the surface. Table 2 offers compiled experimental results.

We have thus successfully developed a dual, eco-friendly, and practical synthetic strategy for the synthesis of 5-iodotriazoles using sonochemical (Method A) and mechanochemical (Method B) approaches (Scheme 1b). With the optimised reaction conditions in hand, the substrate scope for both processes was explored using diversely substituted phenylacetylenes **1** and benzyl bromides **2**. Accordingly, we screened a set of ten different phenylacetylenes (**1b–1k**), having substitutions at the *para*-position of the phenyl ring containing both electron-donating and electron-withdrawing groups (such as methyl, ethyl, *n*-pentyl, methoxy, ethoxy, phenyloxy, biphenyl, bromo, chloro, and fluoro), and carried out the click reaction

under the optimised reaction conditions for sonochemical (Method A) and mechanochemical (Method B) processes. To our delight, all of these phenylacetylene derivatives (**1b–1k**) afforded the expected 1-benzyl-4-aryl-5-iodo-1*H*-1,2,3-triazoles (**4b–4k**) upon reacting with benzyl bromide (**2a**), sodium azide (**3**), and CuI under the optimised conditions in excellent yields ranging from 72 to 82% in the sonochemical and 74–84% in the mechanochemical method, within respective reaction times of 15 and 10 min (Table 3, compounds **4b–4k**). Ethynylcyclopropane (**1l**) also underwent conversion to the desired product, 1-benzyl-4-cyclopropyl-5-iodo-1*H*-1,2,3-triazole (**4l**), with excellent yields of 88% and 89% under sono- and mechanochemical conditions, respectively (Table 3, compound **4l**).

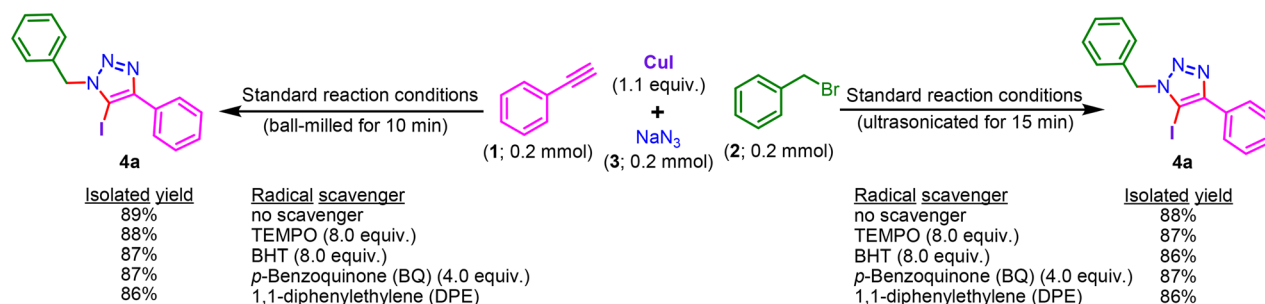
Encouraged by these successful results, we next sought to extend the scope of benzyl bromides. For this purpose, we performed sono- and mechano-click reactions for a set of nine more entries from the reaction between varying aryl/heteroaryl (3-aminophenylacetylene and 3-ethynylthiophene) acetylenes (**1a–1c** and **1f–1h**), 4-methylbenzyl bromide (**2b**)/3-chlorobenzyl bromide (**2c**)/4-bromobenzyl bromide (**2d**), sodium azide (**3**),



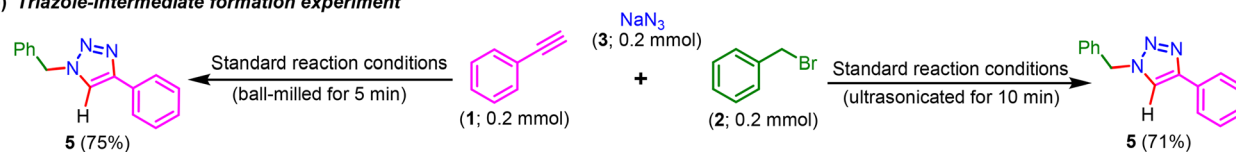
Scheme 2 Gram-scale synthetic applications under both sono- and mechanochemical methods.



a) Radical trapping experiment



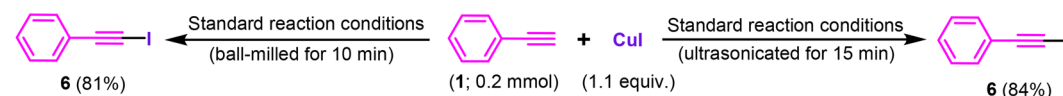
b) Triazole-Intermediate formation experiment



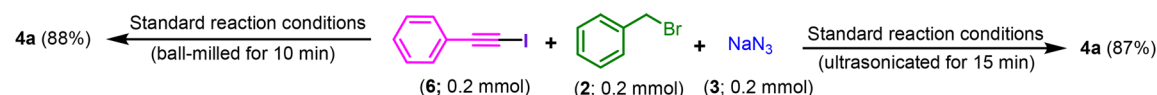
c) Post-synthetic iodination experiment



d) Iodoalkyne formation experiment



e) Iodoalkyne pathway validation experiment



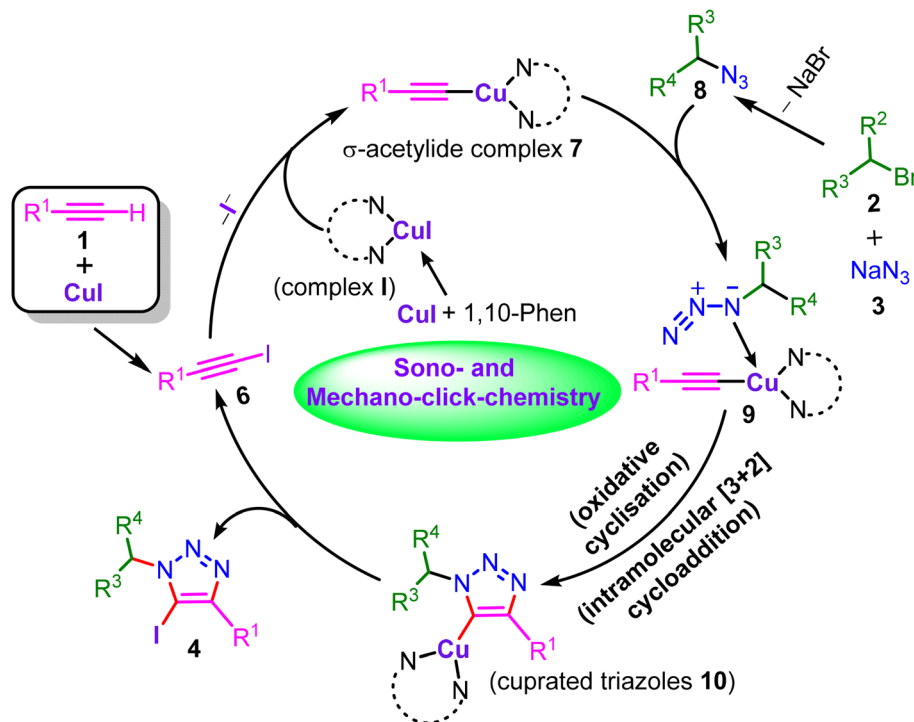
Scheme 3 Control experiments.

and CuI under identical reaction conditions. Gratifyingly, all reactions proceeded smoothly, delivering the corresponding 1-benzyl-4-aryl-5-iodo-1*H*-1,2,3-triazoles (**4m–4v**) in excellent yields ranging from 74% to 92% under sonochemical conditions and 75% to 93% under mechanochemical conditions (Table 3, compounds **4m–4v**). Furthermore, another effective coupling partner was 1-methyl-1-phenyl-methylbromide (**2e**). Under the optimised conditions, five more substrates were successfully converted to the desired 5-iodo-4-aryl-1-(1-phenylethyl)-1*H*-1,2,3-triazoles (**4w–4z** and **4a'**) in remarkably short reaction times of 15 min and 10 min, respectively, in 75–89% yield using ultrasound irradiation and 78–91% yield through ball-milling. Finally, the scope was further extended to 1-naphthylmethyl bromide (**2f**), with which we carried out three more reactions and successfully isolated substituted 1-(naphthalen-1-ylmethyl)-4-phenyl-5-iodo-1*H*-1,2,3-triazole derivatives (**4b'–4d'**) in good yields ranging from 73%–90% in the sonochemical and 75–92% in the ball-milling method (Table 3, compounds **4b'–4d'**). The overall experimental observations are

summarised in Table 3. All isolated products **4**, synthesised using both Method A (sonochemical) and Method B (mechanochemical), were purified by column chromatography (see Experimental). All are new compounds except **4a**, **4b**, **4c**, **4i**, **4j**, **4k**, **4l**, **4n**, **4v**, **4x**, and **4c'**. Each synthesised compound was fully characterised by detailed spectral studies, including ¹H-NMR, ¹³C-NMR, ¹⁹F-NMR (for **4k**), and HRMS (see Experimental).

We herein calculated the individual *E*-factor (g g⁻¹)¹⁹ for each process. The calculated *E*-factors range from 0.98 to 0.57 for the sonochemical method and from 0.96 to 0.54 for the mechanochemical method (see the SI) and are acceptable for most of the reactions, although not for all. Furthermore, to check the efficacy of our method, we performed gram-scale syntheses (5.0 mmol scale; 25-fold enhancement; Scheme 2) for two distinct entries, **4a** and **4k**. Both of these gram-scale reactions proceeded efficiently, yielding 75% and 78% for **4a** and **4k**, respectively, within 20 min under sonochemical conditions (see Experimental). Similarly, the mechanochemical method (Method B) also delivered satisfactory results, affording 70%





Scheme 4 Proposed mechanism.

and 75% yields within just 15 min (see Experimental). The yield and time for each gram-scale synthesis were found to be almost identical to those for the millimolar-scale synthesis (Table 3, compounds **4a** and **4k**).

At this point, our efforts shifted towards uncovering potential mechanistic insights into this sono- and mechanochemically assisted synthetic strategy for a diverse range of iodo-1,2,3-triazoles. With this view, we conducted a set of control experiments with our model reaction in the presence of four different radical scavengers, such as TEMPO, BHT, *p*-benzoquinone (BQ), and 1,1-diphenylethylene (DPE) (Scheme 3). None of the radical scavengers affected the conversion when carried out either sonochemically or mechanochemically, thereby suggesting that the transformation follows an ionic pathway in both cases.

Based on literature reports²⁰ and the results of our control experiments (Scheme 3), a plausible reaction mechanism for the sono- and mechanochemical transformation is herein proposed, as outlined in Scheme 4. At first, the catalytic cycle is initiated by the interaction of the aryl acetylene **1** with the CuI centre, and the resulting coordination leads to the formation of the corresponding (iodoethynyl)benzene intermediate **6**. This species represents an activated alkyne precursor that easily contributes to the subsequent formation of copper-acetylide. An activated *in situ* generated Cu(I)-coordination complex **I** then further coordinates and stabilises intermediate **6** to produce the σ -copper acetylide complex **7**, which serves as the key organo-copper species in the catalytic cycle. In the next step, subsequent coordination of the benzyl azide **8** (formed *in situ* by the reaction between benzyl bromide **2** and sodium azide **3**) with

intermediate **7** through the proximal nitrogen results in the formation of copper-bound azide-alkyne complex **9**, which in turn takes part in an intramolecular [3 + 2] cycloaddition involving oxidative cyclisation, furnishing the cuprated triazole intermediate **10**. In the final step, complex **10** collapses to the desired product **4** via a copper-exchange σ -bond metathesis, containing a 1,2,3-triazole nucleus and an active Cu(I) catalyst that enters the next catalytic cycle.^{15c,21}

Furthermore, the reusability of the solid surface (basic alumina) was investigated using the model reaction on a 0.2 mmol scale to yield 1-benzyl-4-phenyl-5-iodo-1*H*-1,2,3-triazole (**4a**), as illustrated in Fig. 1. Encouragingly, the solid surface displayed excellent reusability, maintaining its catalytic efficiency for six successive cycles without any appreciable loss of its activity. The desired product **4a** was obtained in yields of 89%, 85%, 81%, 75%, 70% and 65% within a uniform reaction time of 10 minutes for each cycle (Fig. 1). Importantly, the recovered solid surface was dried at 70 °C in an oven after isolation during each cycle.

We then planned to extend the synthetic application of the synthesised iodo-triazole derivatives by screening a few representative compounds from this diverse series. As we know, from a medicinal chemistry perspective, installation of an aryl functionality *via* Suzuki coupling is highly valuable, as biaryl motifs frequently enhance binding interactions, lipophilicity, and overall drug-like properties.²² For this purpose, we screened a set of two iodinated triazole substrates **4a** and **4m** and performed the Suzuki–Miyaura cross-coupling reaction with phenylboronic acid under standard reaction conditions²³ using Pd(PPh₃)₄ as the catalyst and K₂CO₃ as the base in a mixed



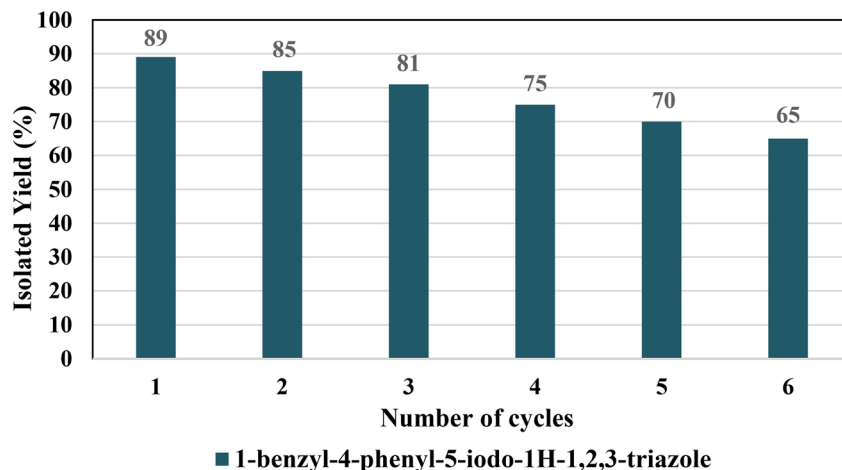
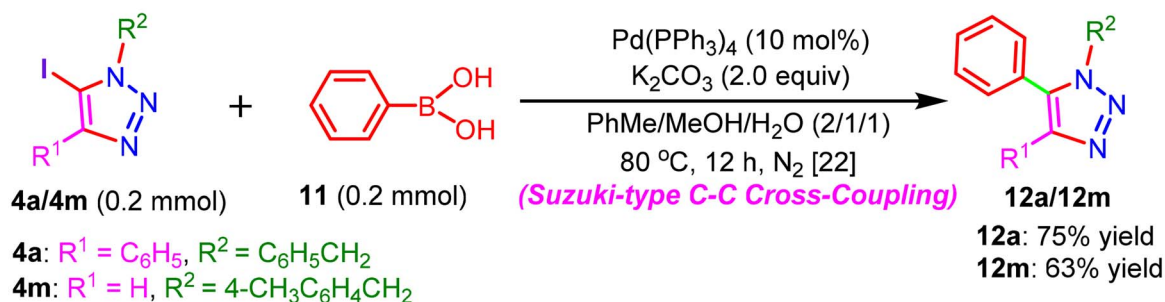


Fig. 1 Reusability of the solid surface (Method B).

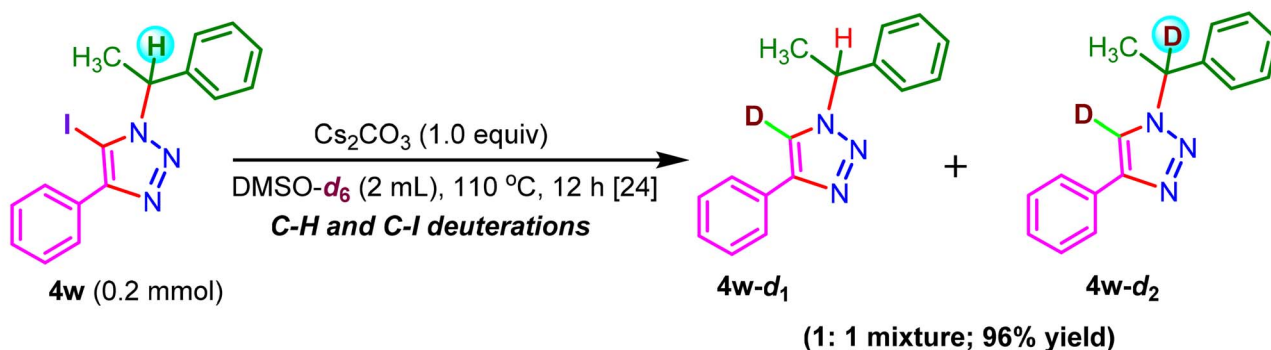
PhMe/MeOH/H₂O solvent system at 80 °C to obtain the desired biaryl products **12a** and **12m** in 75% and 63% isolated yields, respectively (Scheme 5a). In addition, we also targeted the deuterium exchange reaction of one representative compound, 5-iodo-4-phenyl-1-(1-phenylethyl)-1H-1,2,3-triazole (**4w**; 0.2 mmol scale), anticipating deuteration of the iodo and the labile benzylic proton. Deuteration of bioactive organic scaffolds is known to improve medicinal efficacy by enhancing the metabolic stability of drug molecules in the biological system, as a C–D bond being stronger imparts a kinetic isotope effect.²⁴

Accordingly, substrate **4w** (0.2 mmol) dissolved in DMSO-*d*₆ (2 mL), when refluxed at 110 °C for 12 h in the presence of Cs₂CO₃ as the base, afforded an inseparable mixture of mono-deuterated (5-iodo-4-phenyl-1-(1-phenylethyl)-1H-1,2,3-triazole-5-*d*, **4w-d**₁) and bis-deuterated (4-phenyl-1-(1-phenylethyl-1-*d*)-1H-1,2,3-triazole-5-*d*; **4w-d**₂) (Scheme 5b)²⁵ in an almost 1:1 ratio, as evident from the analysis of its ¹H-NMR spectrum. The ¹H-NMR spectrum of the deuterated mixture recorded the benzylic methine proton [–NCH(CH₃)Ph] at δ 5.89–5.85 ppm (see Experimental; Fig. S61) with an integration area of almost

a) Suzuki-type cross-coupling reaction



b) Deuteration reaction



Scheme 5 Synthetic applications of some selected 5-iodotriazole derivatives **4** (**4a**, **4m** and **4w**)^{a,b}.



half compared to that recorded for the same benzylic proton (δ 5.98–5.93 ppm; Fig. S40) of pure substrate compound **4w**. It is worth noting that the benzylic methine proton in **4w-d₁** is relatively more shielded than in **4w**; the $-I$ effect of the iodine atom in **4w** is now absent in **4w-d₁** due to its deuteration. The HRMS spectrum (Fig. S63) of the deuterated mixture also recorded exact masses for both the mono- and bis-deuterated compounds (**4w-d₁**: m/z 251.1413 for $C_{16}H_{15}DN_3$ ($M + H$)⁺; **4w-d₂**: m/z 252.1468 for $C_{16}H_{14}D_2N_3$ ($M + H$)⁺; see Experimental).

3. Conclusions

In conclusion, we have developed dual synthetic approaches, based on sonochemical and mechanochemical strategies, as efficient and straightforward practical alternative synthetic protocols for diversely functionalised 5-iodo-1,2,3-triazoles **4** through a copper(i)-catalysed click reaction between aryl/heteroaryl acetylenes (**1**), benzyl bromides (**2**), sodium azide (**3**), and copper iodide. CuI acts here as both a catalyst and an iodine source. The key advantages of the newly developed methods are mild reaction conditions that use ultrasound and ball-mill as green tools, avoidance of external heating, short reaction time (in minutes), good to excellent yields, high regioselectivity, broad substrate scope and tolerance towards various functional groups, facile gram-scale applications, acceptable *E*-factors (in most cases), and avoidance of reaction solvent and reusability of the solid surface (mechanochemical method). In addition, we have extended the synthetic applications of the synthesised iodo-triazoles, including Suzuki-type C–C cross-coupling and deuteration reactions, thereby providing access to a handful of bio-relevant organic molecules.

4. Experimental section

4.1 General method

All the chemicals and solvents used in this work were purchased from reputable companies. ¹H-, ¹³C-, and ¹⁹F-NMR spectra were collected at 400, 100, and 376 MHz, respectively, on a Bruker DRX spectrometer. A Waters (G2-XS Q-TOF) high-resolution mass spectrometer was utilised to collect HRMS spectra. The melting points were recorded on a Chemiline CL-725 melting point apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed using silica gel 60 F254 (Merck) plates. A Sonics ultrasound probe sonicator (model: VCX 130) with a frequency of 20 kHz and energy of 130 W was used for sonication. A PM 100, Retsch GmbH, Germany, ball-milling apparatus was used for mechanochemical reactions. Safety statement of the procedure: we did not detect/encounter any unexpected, new, or significant hazards or risks associated with the reported work.

4.2 General procedure for the synthesis of functionalised 5-iodo-1,2,3-triazoles (**4**) under the sonochemical method (method A)

A mixture of aryl acetylenes (**1**; 0.2 mmol), benzyl bromides (**2**; 0.2 mmol), sodium azide (**3**; 0.2 mmol), CuI (1.1 equiv.), and

1,10-phenanthroline (10 mol%) was added sequentially to an oven-dried glass vessel (20 mL), followed by the addition of 5 mL of acetonitrile (CH₃CN). The mixture was then irradiated with ultrasound (130 W, 20 kHz at 40% amplitude) for 15 minutes (monitored by TLC). Upon completion of the reaction, the resultant mixture was transferred into a 25 mL separating funnel, followed by the addition of 20 mL of a 3 : 1 (*v/v*) mixture of ethyl acetate and water. The mixture was then shaken well, and the organic layer was separated and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to obtain the crude mass, which was then subjected to column chromatographic purification using EtOAc–hexane mixtures as eluents to isolate the desired products 5-iodo-triazoles **4** (**4a–4z** and **4a'–4d'**). The synthesised compounds were fully characterised by spectroscopic studies, including ¹H-NMR, ¹³C-NMR, ¹⁹F-NMR (for **4k**), and HRMS. The physical and spectral data for known compounds (*viz.* **4a**, **4b**, **4e**, **4i**, **4j**, **4k**, **4l**, **4n**, **4v**, **4x**, and **4c'**) were consistent with previously reported data¹⁵ (see the SI).

4.3 Gram-scale synthesis of two representative compounds **4a** and **4k** under the sonochemical method (Method A)

A mixture of aryl acetylenes (**1**; 5.0 mmol), benzyl bromides (**2**; 5.0 mmol), sodium azide (**3**; 5.0 mmol), CuI (1.1 equiv.), and 1,10-phenanthroline was added sequentially to an oven-dried glass vessel (20 mL), followed by adding 6 mL of acetonitrile. Each reaction mixture was then irradiated with ultrasound (130 W, 20 kHz at 40% amplitude) for 20 minutes (monitored by TLC). Upon completion of each reaction, the resultant reaction mixture was worked up (using a 250 mL separating funnel and adding 60 mL of ethyl acetate–water (3 : 1 *v/v*) mixture for solvent partitioning) and purified following the same procedure (eluents for flash chromatography: hexane/ethyl acetate 96 : 4 *v/v* for **4a** and 95 : 5 *v/v* for **4k**) as mentioned in the general method (Method A) to obtain pure products **4a** and **4k** in 75% (1.348 g) and 70% (1.327 g) yields for 5.0 mmol experiments, respectively.

4.4 General procedure for the synthesis of functionalised 5-iodo-1,2,3-triazoles (**4**) under ball-milling (Method B)

A mixture of aryl acetylenes (**1**; 0.2 mmol), benzyl bromides (**2**; 0.2 mmol), sodium azide (**3**; 0.2 mmol) and CuI (1.1 equiv.) was ball-milled under neat conditions using 7 stainless-steel balls (10 mm in diameter) within a 25 mL stainless-steel jar at 550 rpm for 10 min in the presence of 1,10-phenanthroline (10 mol%) as an additive. The ball-milling operation was performed in an inverted rotation direction, with a 30-second break at 5-minute intervals. On completion of the reaction (confirmed by TLC upon ceasing the grinding operation), 20 mL of ethyl acetate and aqueous solution in a proportion of 3 : 1 (*v/v*) was added to the resulting mixture and shaken well in a separating funnel. The organic layer was separated and dried over anhydrous sodium sulphate. The solvent was then removed under reduced pressure to obtain a white crude mass, which was then subjected to column chromatographic purification using



EtOAc–hexane mixtures as eluents, to obtain pure products of **4** (**4a–4z** and **4a'–4d'**).

4.5 Gram-scale synthesis of two representative compounds **4a** and **4k** under ball-milling (Method B)

A mixture of aryl acetylenes (**1**; 5.0 mmol), benzyl bromides (**2**; 5.0 mmol), sodium azide (**3**; 5.0 mmol) and CuI (1.1 equiv.) was subjected to ball-milling in the presence of basic alumina (2.0 g) as the surface at 550 rpm using a 25 mL stainless steel jar with seven balls (10 mm in diameter) made of the same material for 15 minutes (monitored by TLC). The ball-milling operation was conducted in an inverted rotation direction, with intervals of 7.5 minutes and a break of 30 seconds. Upon completion of each reaction, the resultant reaction mixture was worked up (using a 250 mL separating funnel and adding 60 mL of ethyl acetate–water (3 : 1 v/v) mixture for solvent partitioning) and purified following the same procedure (eluents for flash chromatography: hexane/ethyl acetate 96 : 4 v/v for **4a** and 95 : 5 v/v for **4k**) as mentioned in the general method (Method B) to obtain pure products **4a** and **4k**, in 78% (1.408 g) and 75% (1.425 g) yields for 5.0 mmol experiments, respectively.

4.6 The physical and spectral data of the synthesised 5-iodo-1,2,3-triazoles **4**, **12** and **4w–d₂**

4.6.1 1-Benzyl-5-iodo-4-phenyl-1H-1,2,3-triazole (**4a**).^{15a}

White solid; yield: 88% (64 mg, 0.2 mmol scale, sonochemistry), yield: 89% (65 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 136–138 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.87 (d, 2H, *J* = 7.2 Hz, Ar–H), 7.41–7.37 (m, 2H, Ar–H), 7.34–7.23 (m, 6H, Ar–H), 5.61 (s, 2H, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 150.34 (C), 134.45 (2C), 130.31 (C), 129.05 (CH), 128.74 (2 × CH), 128.67 (2 × CH), 128.63 (CH), 127.94 (2 × CH), 127.56 (2 × CH), 54.53 (–NCH₂Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₅H₁₂IN₃H⁺; 362.0149; found: *m/z* 362.0157.

4.6.2 1-Benzyl-5-iodo-4-(*p*-tolyl)-1H-1,2,3-triazole (**4b**).^{15e}

White solid; yield: 82% (62 mg, 0.2 mmol scale, sonochemistry), yield: 84% (63 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 120–122 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.82 (d, 2H, *J* = 8 Hz, Ar–H), 7.37–7.34 (m, 3H, Ar–H), 7.33–7.29 (m, 3H, Ar–H), 7.27 (s, 1H, Ar–H), 5.67 (s, 2H, –NCH₂Ar), 2.39 (s, 3H, Ar–CH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₆H₁₄IN₃H⁺; 376.0305; found: *m/z* 376.0311.

4.6.3 1-Benzyl-4-(4-ethylphenyl)-5-iodo-1H-1,2,3-triazole (4c**).** White solid; yield: 77% (60 mg, 0.2 mmol scale, sonochemistry), yield: 80% (62 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 120–122 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.86 (d, 2H, *J* = 8.4 Hz, Ar–H), 7.36–7.28 (m, 7H, Ar–H), 5.66 (s, 2H, –NCH₂Ar), 2.69 (q, 2H, *J* = 7.6 Hz, Ar–CH₂CH₃), 1.27 (t, 3H, *J* = 7.6 Hz, Ar–CH₂CH₃) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 150.37 (C), 144.92 (C), 134.48 (C), 131.68 (C), 128.99 (2 × CH), 128.56 (CH), 128.15 (2 × CH), 127.89 (2 × CH), 127.48 (2 × CH), 126.26 (C), 54.45 (–NCH₂Ar), 28.81 (Ar–CH₂CH₃), 15.55 (Ar–

CH₂CH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₇H₁₆IN₃H⁺; 390.0462; found: *m/z* 390.0490.

4.6.4 1-Benzyl-5-iodo-4-(4-pentylphenyl)-1H-1,2,3-triazole (**4d**).

Yellow solid; yield: 72% (62 mg, 0.2 mmol scale, sonochemistry), yield: 74% (64 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 105–107 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.85 (d, 2H, *J* = 8.0 Hz, Ar–H), 7.42–7.28 (m, 7H, Ar–H), 5.67 (s, 2H, –NCH₂Ar), 2.66–2.62 (m, 2H, Ar–CH₂CH₂CH₂CH₂CH₃), 1.61 (d, 2H, *J* = 7.2 Hz, Ar–CH₂CH₂CH₂CH₂CH₃), 1.35–1.31 (m, 4H, Ar–CH₂CH₂CH₂CH₂CH₃), 0.89 (t, 3H, *J* = 6.8 Hz, Ar–CH₂CH₂CH₂CH₂CH₃) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 150.42 (C), 143.70 (C), 134.52 (C), 131.62 (C), 129.02 (2 × CH), 128.71 (2 × CH), 128.58 (CH), 127.90 (2 × CH), 127.40 (2 × CH), 126.21 (C), 54.49 (–NCH₂Ar), 35.87 (Ar–CH₂CH₂CH₂CH₂CH₃), 31.61 (Ar–CH₂CH₂CH₂CH₂CH₃), 31.13 (Ar–CH₂CH₂CH₂CH₂CH₃), 22.66 (Ar–CH₂CH₂CH₂CH₂CH₃), 14.16 (Ar–CH₂CH₂CH₂CH₂CH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₀H₂₂IN₃H⁺; 432.0931; found: *m/z* 432.0940.

4.6.5 1-Benzyl-5-iodo-4-(4-methoxyphenyl)-1H-1,2,3-triazole (4e**).**^{15e} White solid; yield: 77% (60 mg, 0.2 mmol scale, sonochemistry), yield: 79% (62 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 95 : 5, mp = 140–142 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.88–7.86 (m, 2H, Ar–H), 7.39–7.29 (m, 5H, Ar–H), 6.99 (d, 2H, *J* = 8.8 Hz, Ar–H), 5.67 (s, 2H, –NCH₂Ar), 3.85 (s, 3H, Ar–OCH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₆H₁₄ION₃H⁺; 392.0254; found: *m/z* 392.0258.

4.6.6 1-Benzyl-4-(4-ethoxyphenyl)-5-iodo-1H-1,2,3-triazole (4f**).** White solid; yield: 75% (61 mg, 0.2 mmol scale, sonochemistry), yield: 78% (63 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 95 : 5, mp = 152–153 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.85 (d, 2H, *J* = 8.4 Hz, Ar–H), 7.37–7.29 (m, 5H, Ar–H), 6.97 (d, 2H, *J* = 8.4 Hz, Ar–H), 5.65 (s, 2H, –NCH₂Ar), 4.09–4.05 (m, 2H, Ar–OCH₂CH₃), 1.45–1.41 (m, 3H, Ar–OCH₂CH₃) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 159.35 (C), 134.49 (C), 131.05 (C), 128.99 (2 × CH), 128.95 (C), 128.86 (2 × CH), 128.55 (CH), 127.90 (2 × CH), 122.59 (C), 114.55 (2 × CH), 63.59 (Ar–OCH₂CH₃), 54.46 (–NCH₂Ar), 14.93 (Ar–OCH₂CH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₇H₁₆ION₃H⁺; 406.0411; found: *m/z* 406.0402.

4.6.7 1-Benzyl-5-iodo-4-(4-phenoxyphenyl)-1H-1,2,3-triazole (4g**).** Brownish semi-solid; yield: 76% (69 mg, 0.2 mmol scale, sonochemistry), yield: 77% (70 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 195–198 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 7.89 (d, 2H, *J* = 8.4 Hz, Ar–H), 7.41–7.36 (m, 4H, Ar–H), 7.34–7.30 (m, 1H, Ar–H), 7.22 (d, 2H, *J* = 7.2 Hz, Ar–H), 7.19–7.15 (m, 1H, Ar–H), 7.11–7.05 (m, 4H, Ar–H), 5.71 (s, 2H, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆): δ = 157.11 (C), 156.24 (C), 148.74 (C), 135.42 (C), 131.66 (C), 130.32 (2 × CH), 128.96 (2 × CH), 128.87 (2 × CH), 128.23 (CH), 127.50 (2 × CH), 125.62 (C), 124.05 (CH), 119.22 (2 × CH), 118.52 (2 × CH), 53.62 (–NCH₂Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₁H₁₆ION₃H⁺; 454.0411; found: *m/z* 454.0416.

4.6.8 4-([1,1'-Biphenyl]-4-yl)-1-benzyl-5-iodo-1H-1,2,3-triazole (4h**).** Yellow solid; yield: 78% (68 mg, 0.2 mmol scale,



sonochemistry), yield: 79% (69 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 186 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.05 (d, 2H, J = 8.4 Hz, Ar-H), 7.70 (d, 2H, J = 8.4 Hz, Ar-H), 7.66–7.64 (m, 2H, Ar-H), 7.46 (t, 2H, J = 7.6 Hz, Ar-H), 7.39–7.32 (m, 6H, Ar-H), 5.69 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 149.95 (C), 141.40 (C), 140.60 (C), 134.41 (C), 129.22 (C), 129.03 (2 \times CH), 128.96 (2 \times CH), 128.62 (CH), 127.93 (2 \times CH), 127.84 (2 \times CH), 127.66 (CH), 127.47 (C), 127.33 (2 \times CH), 127.19 (2 \times CH), 54.52 ($-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{16}\text{IN}_3\text{H}^+$; 438.0462; found: m/z 438.0465.

4.6.9 1-Benzyl-4-(4-bromophenyl)-5-iodo-1H-1,2,3-triazole (4i).^{15e} White solid; yield: 74% (65 mg, 0.2 mmol scale, sonochemistry), yield: 75% (66 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 120–123 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.01 (d, 1H, J = 8.4 Hz, Ar-H), 7.83 (d, 1H, J = 8.4 Hz, Ar-H), 7.59–7.54 (m, 2H, Ar-H), 7.36–7.30 (m, 5H, Ar-H), 5.66 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{11}\text{IBrN}_3\text{H}^+$; 439.9254; found: m/z 439.9267.

4.6.10 1-Benzyl-4-(4-chlorophenyl)-5-iodo-1H-1,2,3-triazole (4j).^{15e} White solid; yield: 79% (62 mg, 0.2 mmol scale, sonochemistry), yield: 81% (64 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 150–151 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.90–7.88 (m, 1H, Ar-H), 7.44–7.41 (m, 2H, Ar-H), 7.39 (s, 1H, Ar-H), 7.37–7.30 (m, 5H, Ar-H), 5.67 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{11}\text{IClN}_3\text{H}^+$; 395.9759; found: m/z 395.9776.

4.6.11 1-Benzyl-4-(4-fluorophenyl)-5-iodo-1H-1,2,3-triazole (4k).^{15e} White solid; yield: 82% (62 mg, 0.2 mmol scale, sonochemistry), yield: 83% (63 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 135–144 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.15–8.09 (m, 1H, Ar-H), 7.93–87 (m, 1H, Ar-H), 7.48–7.41 (m, 1H, Ar-H), 7.35–7.29 (m, 4H, Ar-H), 7.15–7.09 (m, 2H, Ar-H), 5.64 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. ^{19}F NMR (376 MHz, CDCl_3): δ = -112.51 ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{11}\text{IFN}_3\text{H}^+$; 380.0054; found: m/z 380.0063.

4.6.12 1-Benzyl-4-cyclopropyl-5-iodo-1H-1,2,3-triazole (4l).^{15e} White solid; yield: 88% (57 mg, 0.2 mmol scale, sonochemistry), yield: 89% (58 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 114–116 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.36–7.31 (m, 3H, Ar-H), 7.26 (s, 1H, Ar-H), 7.24 (s, 1H, Ar-H), 5.55 (s, 2H, $-\text{NCH}_2\text{Ar}$) 1.80–1.73 (m, 1H, $-\text{CHCH}_2\text{CH}_2-$), 1.06–1.02 (m, 2H, $-\text{CHCH}_2\text{CH}_2-$), 1.00–0.94 (m, 2H, $-\text{CHCH}_2\text{CH}_2-$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{12}\text{IN}_3\text{H}^+$; 326.0149; found: m/z 326.0160.

4.6.13 5-Iodo-1-(4-methylbenzyl)-4-phenyl-1H-1,2,3-triazole (4m). White solid; yield: 78% (69 mg, 0.2 mmol scale, sonochemistry), yield: 91% (68 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 155–157 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.93 (d, 2H, J = 7.6 Hz, Ar-H), 7.47–7.44 (m, 2H, Ar-H), 7.41–7.37 (m, 1H, Ar-H), 7.22 (d, 2H, J = 8.0 Hz, Ar-H), 7.16 (d, 2H, J = 8.0 Hz, Ar-H), 5.63 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.34 (s, 3H, $-\text{NCH}_2\text{ArCH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$

NMR (100 MHz, CDCl_3): δ = 150.25 (C), 138.47 (2C), 131.41 (C), 130.33 (C), 129.66 (2 \times CH), 128.68 (CH), 128.63 (2 \times CH), 127.94 (2 \times CH), 127.55 (2 \times CH), 54.33 ($-\text{NCH}_2\text{ArCH}_3$), 21.29 ($-\text{NCH}_2\text{ArCH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{14}\text{IN}_3\text{H}^+$; 376.0305; found: m/z 376.0309.

4.6.14 5-Iodo-1-(4-methylbenzyl)-4-(*p*-tolyl)-1H-1,2,3-triazole (4n).^{15e} Light yellow solid; yield: 82% (64 mg, 0.2 mmol scale, sonochemistry), yield: 84% (65 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96.6 : 3.4, mp = 118–121 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.80 (d, 2H, J = 8 Hz, Ar-H), 7.24 (d, 2H, J = 7.2 Hz, Ar-H), 7.21 (d, 2H, J = 8.0 Hz, Ar-H), 7.15 (d, 2H, J = 7.6 Hz, Ar-H), 5.61 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.38 (s, 3H, $-\text{NCH}_2\text{ArCH}_3$), 2.32 (s, 3H, $-\text{ArCH}_2\text{CH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 150.35 (C), 138.60 (2C), 138.44 (C), 131.46 (2C), 129.65 (2 \times CH), 129.33 (2 \times CH), 127.94 (2 \times CH), 127.44 (2 \times CH), 54.30 ($-\text{NCH}_2\text{Ar}$), 21.47 ($-\text{NCH}_2\text{ArCH}_3$), 21.29 (Ar- CH_3) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{16}\text{IN}_3\text{H}^+$; 390.0462; found: m/z 390.0452.

4.6.15 4-(4-Ethylphenyl)-5-iodo-1-(4-methylbenzyl)-1H-1,2,3-triazole (4o). White solid; yield: 77% (62 mg, 0.2 mmol scale, sonochemistry), yield: 75% (60 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 138–139 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.85 (d, 2H, J = 8.0 Hz, Ar-H), 7.30–7.26 (m, 2H, Ar-H), 7.22 (d, 2H, J = 8.4 Hz, Ar-H), 7.16 (d, 1H, J = 8.0 Hz, Ar-H), 5.62 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.69 (q, 2H, J = 7.6 Hz, $-\text{ArCH}_2\text{CH}_3$), 2.34 (s, 3H, $-\text{NCH}_2\text{ArCH}_3$), 1.27 (t, 3H, J = 7.6 Hz, $-\text{ArCH}_2\text{CH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 150.35 (C), 144.90 (2C), 138.44 (C), 131.49 (C), 129.66 (2 \times CH), 128.15 (2 \times CH), 127.94 (2 \times CH), 127.68 (C), 127.50 (2 \times CH), 54.31 ($-\text{NCH}_2\text{Ar}$), 28.82 ($-\text{ArCH}_2\text{CH}_3$), 21.30 ($-\text{NCH}_2\text{ArCH}_3$), 15.56 ($-\text{ArCH}_2\text{CH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{17}\text{IN}_3\text{H}^+$; 404.0618; found: m/z 404.0623.

4.6.16 4-(4-Ethoxyphenyl)-5-iodo-1-(4-methylbenzyl)-1H-1,2,3-triazole (4p). White solid; yield: 92% (77 mg, 0.2 mmol scale, sonochemistry), yield: 93% (78 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 95 : 5, mp = 164–165 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.85 (d, 2H, J = 8.8 Hz, Ar-H), 7.21 (d, 2H, J = 8.0 Hz, Ar-H), 7.15 (d, 2H, J = 8.0 Hz, Ar-H), 6.97 (d, 2H, J = 8.4 Hz, Ar-H), 5.60 (s, 2H, $-\text{NCH}_2\text{ArCH}_3$), 4.09–4.04 (m, 2H, Ar- OCH_2CH_3), 2.33 (s, 3H, Ar- CH_3), 1.45–1.41 (m, 3H, Ar- OCH_2CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 159.31 (C), 150.21 (C), 138.41 (2C), 131.48 (C), 129.63 (2 \times CH), 128.86 (2 \times CH), 127.92 (2 \times CH), 122.66 (C), 114.53 (2 \times CH), 63.58 ($-\text{ArOCH}_2\text{CH}_3$), 54.28 ($-\text{NCH}_2\text{ArCH}_3$), 21.28 ($-\text{NCH}_2\text{ArCH}_3$), 14.93 ($-\text{ArOCH}_2\text{CH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{18}\text{ION}_3\text{H}^+$; 420.0567; found: m/z 420.0561.

4.6.17 5-Iodo-1-(4-methylbenzyl)-4-(4-phenoxyphenyl)-1H-1,2,3-triazole (4q). White solid; yield: 74% (69 mg, 0.2 mmol scale, sonochemistry), yield: 77% (72 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 164–165 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.81 (d, 2H, J = 6.8 Hz, Ar-H), 7.27 (s, 1H, Ar-H), 7.17–7.05 (m, 6H, Ar-H), 6.98 (s, 4H, Ar-H), 5.53 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.25 (s, 3H, $-\text{NCH}_2\text{ArCH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ =



157.87 (C), 156.76 (C), 149.86 (C), 138.48 (2 × C), 131.39 (C), 129.96 (2 × CH), 129.67 (2 × CH), 129.06 (2 × CH), 127.95 (2 × CH), 125.17 (C), 123.78 (CH), 119.44 (2 × CH), 118.60 (2 × CH), 54.35 (–NCH₂Ar), 21.30 (–NCH₂ArCH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₂H₁₈ION₃H⁺; 468.0567; found: *m/z* 468.0578.

4.6.18 4-([1,1'-Biphenyl]-4-yl)-5-iodo-1-(4-methylbenzyl)-1H-1,2,3-triazole (4r). White solid; yield: 76% (69 mg, 0.2 mmol scale, sonochemistry), yield: 78% (70 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 202–204 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.03 (d, 2H, *J* = 7.2 Hz, Ar–H), 7.71–7.64 (m, 4H, Ar–H), 7.46 (s, 2H, Ar–H), 7.38 (d, 1H, *J* = 6.4 Hz, Ar–H), 7.25–7.18 (m, 4H, Ar–H), 5.65 (s, 2H, –NCH₂Ar), 2.35 (s, 3H, –NCH₂ArCH₃) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 149.94 (C), 141.39 (C), 140.64 (C), 138.53 (C), 131.43 (C), 129.71 (2 × CH), 129.30 (C), 128.97 (2 × CH), 127.98 (2 × CH), 127.87 (2 × CH), 127.67 (CH), 127.33 (2 × CH), 127.21 (2 × CH), 114.40 (C), 54.52 (–NCH₂Ar), 21.32 (–NCH₂ArCH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₂₂H₁₈IN₃H⁺; 452.0618; found: *m/z* 452.0624.

4.6.19 3-(1-Benzyl-5-iodo-1H-1,2,3-triazol-4-yl)-pyridine (4s). White solid; yield: 77% (56 mg, 0.2 mmol scale, sonochemistry), yield: 80% (58 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 88 : 12, mp = 165–166 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.21–8.06 (m, 2H, Ar–H), 7.65 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.20–7.12 (m, 3H, Ar–H), 7.08–7.05 (m, 1H, Ar–H), 6.89 (d, 2H, *J* = 7.2 Hz, Ar–H), 5.04 (d, 1H, *J* = 14.8 Hz, –NCH₂Ar), 4.76 (d, 1H, *J* = 14.8 Hz, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 149.77 (C), 149.59 (C), 146.68 (C), 136.60 (CH), 133.71 (CH), 128.77 (2 × CH), 128.73 (CH), 128.53 (2 × CH), 123.36 (C), 122.93 (CH), 121.09 (CH), 52.98 (–NCH₂Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₄H₁₁IN₃H⁺; 363.0101; found: *m/z* 363.0091.

4.6.20 5-Iodo-1-(4-methylbenzyl)-4-(thiophen-3-yl)-1H-1,2,3-triazole (4t). White solid; yield: 89% (68 mg, 0.2 mmol scale, sonochemistry), yield: 90% (69 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 160 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.95 (d, 1H, *J* = 2.0 Hz, Ar–H), 7.76 (d, 2H, *J* = 4.8 Hz, Ar–H), 7.40 (qd, 1H, *J* = 3.2 & 1.6 Hz, Ar–H), 7.17 (qd, 4H, *J* = 8.8 & 8.0 Hz, Ar–H), 5.61 (s, 2H, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 147.22 (C), 138.50 (2C), 131.38 (C), 131.18 (C), 129.68 (2 × CH), 127.88 (2 × CH), 126.73 (CH), 125.97 (CH), 122.75 (CH), 54.27 (–NCH₂Ar), 21.29 (–NCH₂ArCH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₄H₁₂ISN₃H⁺; 381.9869; found: *m/z* 381.9863.

4.6.21 1-(3-Chlorobenzyl)-5-iodo-4-phenyl-1H-1,2,3-triazole (4u). White solid; yield: 76% (60 mg, 0.2 mmol scale, sonochemistry), yield: 78% (62 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 185–188 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.18 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.94 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.51 (br s, 1H, Ar–H), 7.47–7.44 (m, 2H, Ar–H), 7.42–7.40 (m, 1H, Ar–H), 7.32–7.28 (m, 2H, Ar–H), 7.19 (br s, 1H, Ar–H), 5.66 (s, 2H, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 150.47 (C), 148.34 (C), 136.31 (C), 134.99 (C), 131.74 (CH), 130.39 (CH), 128.93 (CH), 128.86 (CH), 128.71 (CH), 128.51 (C), 128.08 (CH), 127.55

(CH), 126.33 (CH), 126.07 (CH), 53.85 (–NCH₂Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₅H₁₁IClN₃H⁺; 395.9759; found: *m/z* 395.9764.

4.6.22 1-(4-Bromobenzyl)-5-iodo-4-phenyl-1H-1,2,3-triazole (4v).²⁶ White solid; yield: 75% (66 mg, 0.2 mmol scale, sonochemistry), yield: 78% (69 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 178–179 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.16 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.94–7.92 (m, 1H, Ar–H), 7.51–7.48 (m, 3H, Ar–H), 7.46–7.44 (m, 2H, Ar–H), 7.42–7.37 (m, 1H, Ar–H), 7.19 (d, 1H, *J* = 8.4 Hz, Ar–H), 5.62 (s, 2H, –NCH₂Ar) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 150.51 (C), 133.79 (C), 133.41 (C), 132.26 (CH), 132.21 (CH), 131.71 (CH), 129.92 (CH), 129.66 (CH), 128.89 (C), 128.86 (CH), 128.72 (CH), 127.56 (CH), 126.34 (CH), 122.83 (C), 53.91 (–NCH₂Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₅H₁₁IBrN₃H⁺; 439.9254; found: *m/z* 439.9273.

4.6.23 5-Iodo-4-phenyl-1-(1-phenylethyl)-1H-1,2,3-triazole (4w). White solid; yield: 78% (59 mg, 0.2 mmol scale, sonochemistry), yield: 79% (59 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 153–156 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 7.88–7.86 (m, 2H, Ar–H), 7.51–7.47 (m, 2H, Ar–H), 7.43–7.36 (m, 3H, Ar–H), 7.32–7.29 (m, 1H, Ar–H), 7.26–7.24 (m, 2H, Ar–H), 5.98–5.93 (m, 1H, –NCH(CH₃)Ar), 1.98 (d, 3H, *J* = 6.8 Hz, –NCH(CH₃)Ar) ppm. ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆): δ = 149.09 (C), 141.23 (C), 130.97 (C), 129.28 (2 × CH), 129.12 (2 × CH), 128.83 (CH), 128.40 (CH), 127.59 (2 × CH), 126.73 (2 × CH), 82.54 (C), 60.84 (–NCH(CH₃)Ar), 22.59 (–NCH(CH₃)Ar) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₆H₁₄IN₃H⁺; 376.0305; found: *m/z* 376.0317.

4.6.24 5-Iodo-1-(1-phenylethyl)-4-(*p*-tolyl)-1H-1,2,3-triazole (4x).^{15c} White solid; yield: 76% (59 mg, 0.2 mmol scale, sonochemistry), yield: 78% (60 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 144–146 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.82 (d, 2H, *J* = 7.6 Hz, Ar–H), 7.41–7.31 (m, 5H, Ar–H), 7.28 (m, 2H, Ar–H), 5.83–5.78 (m, 1H, –CH), 2.41 (s, 3H, Ar–CH₃), 2.13 (d, 3H, *J* = 6.8 Hz, Ar–CH(CH₃)) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₇H₁₆IN₃H⁺; 390.0462; found: *m/z* 390.0473.

4.6.25 4-(4-Ethylphenyl)-5-iodo-1-(1-phenylethyl)-1H-1,2,3-triazole (4y). White solid; yield: 75% (60 mg, 0.2 mmol scale, sonochemistry), yield: 78% (63 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 155–157 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.86 (d, 2H, *J* = 8.0 Hz, Ar–H), 7.37–7.34 (m, 3H, Ar–H), 7.32–7.28 (m, 4H, Ar–H), 5.83–5.78 (m, 1H, –NCH(CH₃)Ar), 2.74–2.68 (m, 2H, –ArCH₂CH₃), 2.14 (d, 3H, *J* = 6.8 Hz, –NCH(CH₃)Ar), 1.29 (d, 3H, *J* = 7.6 Hz, –ArCH₂CH₃) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 149.87 (C), 144.82 (2C), 140.29 (C), 128.96 (C), 128.29 (2 × CH), 128.08 (CH), 127.72 (2 × CH), 127.65 (2 × CH), 126.68 (2 × CH), 61.50 (–NCH(CH₃)Ar), 28.80 (–ArCH₂CH₃), 22.41 (–NCH(CH₃)Ar), 15.54 (–ArCH₂CH₃) ppm. HRMS (ESI-TOF): *m/z* [M + H]⁺ calcd for C₁₈H₁₈IN₃H⁺; 404.0618; found: *m/z* 404.0425.

4.6.26 5-Iodo-4-(4-phenoxyphenyl)-1-(1-phenylethyl)-1H-1,2,3-triazole (4z). Light yellow solid; yield: 83% (78 mg, 0.2 mmol scale, sonochemistry), yield: 86% (80 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was



hexane/EtOAc 96 : 4, mp = 148–150 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.89 (s, 2H, Ar-H), 7.35–7.32 (br s, 7H, Ar-H), 7.13–7.06 (br s, 5H, Ar-H), 5.79 (br s, 1H, $-\text{NCH}(\text{CH}_3)\text{Ar}$), 2.12 (s, 3H, $-\text{NCH}(\text{CH}_3)\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 157.84 (C), 156.81 (C), 149.41 (C), 140.23 (2 \times C), 129.96 (2 \times CH), 129.24 (2 \times CH), 129.01 (2 \times CH), 128.36 (CH), 126.70 (2 \times CH), 125.26 (C), 123.77 (CH), 119.44 (2 \times CH), 118.59 (2 \times CH), 61.59 ($-\text{NCH}(\text{CH}_3)\text{Ar}$), 22.42 ($-\text{NCH}(\text{CH}_3)\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{ION}_3\text{H}^+$; 468.0567; found: m/z 468.0572.

4.6.27 4-([1,1'-Biphenyl]-4-yl)-5-iodo-1-(1-phenylethyl)-1H-1,2,3-triazole (4a'). Light yellow solid; yield: 89% (80 mg, 0.2 mmol scale, sonochemistry), yield: 91% (82 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 96 : 4, mp = 197–200 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.04 (d, 2H, J = 8.4 Hz, Ar-H), 7.70 (d, 2H, J = 8.4 Hz, Ar-H), 7.66–7.64 (m, 2H, Ar-H), 7.47 (t, 2H, J = 7.6 Hz, Ar-H), 7.39–7.29 (m, 6H, Ar-H), 5.85–5.79 (m, 1H, $-\text{NCH}(\text{CH}_3)\text{Ar}$), 2.14 (d, 3H, J = 7.2 Hz, $-\text{NCH}(\text{CH}_3)\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 149.45 (C), 141.32 (C), 140.64 (C), 140.24 (2C), 129.36 (C), 129.03 (2 \times CH), 128.98 (2 \times CH), 128.39 (CH), 128.05 (2 \times CH), 127.67 (CH), 127.31 (2 \times CH), 127.21 (2 \times CH), 126.73 (2 \times CH), 61.61 ($-\text{NCH}(\text{CH}_3)\text{Ar}$), 22.46 ($-\text{NCH}(\text{CH}_3)\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{IN}_3\text{H}^+$; 452.0618; found: m/z 452.0611.

4.6.28 5-Iodo-1-(naphthalen-2-ylmethyl)-4-phenyl-1H-1,2,3-triazole (4b'). White solid; yield: 85% (70 mg, 0.2 mmol scale, sonochemistry), yield: 89% (73 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 215–218 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.21 (d, 1H, J = 8.4 Hz, Ar-H), 7.99–7.97 (m, 2H, Ar-H), 7.92 (d, 1H, J = 8.0 Hz, Ar-H), 7.86 (d, 1H, J = 8.0 Hz, Ar-H), 7.65–7.61 (m, 1H, Ar-H), 7.58–7.55 (m, 1H, Ar-H), 7.49–7.46 (m, 2H, Ar-H), 7.43–7.39 (m, 2H, Ar-H), 7.03 (d, 1H, J = 7.6 Hz, Ar-H), 6.15 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 150.32 (C), 133.82 (C), 130.73 (2C), 130.29 (C), 129.99 (C), 129.29 (CH), 129.14 (CH), 128.79 (CH), 128.69 (2 \times CH), 127.58 (2 \times CH), 127.06 (CH), 126.35 (CH), 125.99 (CH), 125.41 (CH), 122.81 (CH), 52.46 ($-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{14}\text{IN}_3\text{H}^+$; 412.0305; found: m/z 412.0309.

4.6.29 5-Iodo-1-(naphthalen-2-ylmethyl)-4-(*p*-tolyl)-1H-1,2,3-triazole (4c').^{15a} Light yellow solid; yield: 90% (77 mg, 0.2 mmol scale, sonochemistry), yield: 92% (78 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 185–186 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.21 (d, 1H, J = 8.0 Hz, Ar-H), 7.92 (d, 1H, J = 8.0 Hz, Ar-H), 7.86 (t, 3H, J = 8.0 Hz, Ar-H), 7.64–7.60 (m, 1H, Ar-H), 7.58–7.54 (m, 1H, Ar-H), 7.41 (t, 1H, J = 8.0 Hz, Ar-H), 7.28 (d, 2H, J = 8.0 Hz, Ar-H), 7.03 (d, 1H, J = 8.0 Hz, Ar-H) 6.13 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.41 (s, 3H, $-\text{ArCH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 150.41 (C), 138.70 (2C), 133.82 (C), 130.74 (C), 130.05 (C), 129.38 (2 \times CH), 129.25 (CH), 129.11 (CH), 127.48 (2 \times CH), 127.42 (C), 127.03 (CH), 126.33 (CH), 125.98 (CH), 125.41 (CH), 122.83 (CH) 52.41 ($-\text{NCH}_2\text{Ar}$), 21.48 ($-\text{ArCH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{16}\text{IN}_3\text{H}^+$; 426.0462; found: m/z 426.0468.

4.6.30 4-(4-Ethylphenyl)-5-iodo-1-(naphthalen-1-ylmethyl)-1H-1,2,3-triazole (4d'). Light yellow solid; yield: 73% (64 mg, 0.2 mmol scale, sonochemistry), yield: 75% (66 mg, 0.2 mmol scale, mechanochemistry), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 188 °C. ^1H NMR (400 MHz, CDCl_3): δ = 8.21 (d, 1H, J = 8.4 Hz, Ar-H), 7.93–7.89 (m, 3H, Ar-H), 7.85 (d, 1H, J = 8.0 Hz, Ar-H), 7.64–7.60 (m, 1H, Ar-H), 7.58–7.54 (m, 1H, Ar-H), 7.43–7.39 (m, 1H, Ar-H), 7.31 (d, 2H, J = 8.4 Hz, Ar-H), 7.02 (d, 1H, J = 7.2 Hz, Ar-H), 6.14 (s, 2H, $-\text{NCH}_2\text{Ar}$), 2.71 (q, 2H, J = 7.6 Hz, $-\text{ArCH}_2\text{CH}_3$), 1.28 (t, 3H, J = 7.6 Hz, $-\text{ArCH}_2\text{CH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 150.40 (C), 145.01 (2C), 133.82 (C), 130.74 (C), 130.07 (C), 129.25 (CH), 129.12 (CH), 128.20 (2 \times CH), 127.64 (C), 127.53 (2 \times CH), 127.04 (CH), 126.34 (CH), 125.96 (CH), 125.42 (CH), 122.82 (CH), 52.42 ($-\text{NCH}_2\text{Ar}$), 28.84 ($-\text{ArCH}_2\text{CH}_3$), 15.59 ($-\text{ArCH}_2\text{CH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{18}\text{IN}_3\text{H}^+$; 440.0618; found: m/z 440.0628.

4.6.31 1-Benzyl-4-phenyl-1H-1,2,3-triazole (intermediate 5). White solid; yield: 71% (33 mg, 0.2 mmol scale), eluent used for flash column was hexane/EtOAc 93 : 7, mp = 127–128 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.81–7.79 (m, 2H, Ar-H), 7.41–7.35 (m, 5H, Ar-H), 7.33–7.29 (m, 3H, Ar-H), 5.55 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 148.24 (C), 134.74 (C), 130.55 (C), 129.21 (CH), 128.87 (CH), 128.83 (2 \times CH), 128.23 (2 \times CH), 128.11 (2 \times CH), 125.73 (2 \times CH), 119.61 (CH), 54.25 ($-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{H}^+$; 236.1188; found: m/z 236.1199.

4.6.32 1-Benzyl-4,5-diphenyl-1H-1,2,3-triazole (12a). Light yellow solid; yield: 75% (22.5 mg, 0.1 mmol scale), eluent used for flash column was hexane/EtOAc 95 : 5, mp = 112–123 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.55–7.52 (m, 2H, Ar-H), 7.48–7.44 (m, 1H, Ar-H), 7.41–7.37 (m, 2H, Ar-H), 7.25–7.20 (m, 6H, Ar-H), 7.13–7.11 (m, 2H, Ar-H), 7.02–6.99 (m, 2H, Ar-H), 5.39 (s, 2H, $-\text{NCH}_2\text{Ar}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 144.62 (C), 135.43 (C), 134.01 (C), 130.95 (C), 130.19 (2 \times CH), 129.80 (CH), 129.28 (2 \times CH), 128.81 (2 \times CH), 128.56 (2 \times CH), 128.26 (CH), 127.89 (C), 127.82 (CH), 127.59 (2 \times CH), 126.81 (2 \times CH), 52.14 ($-\text{NCH}_2\text{Ar}$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{H}^+$; 312.1495; found: m/z 312.1499.

4.6.33 1-(4-Methylbenzyl)-4,5-diphenyl-1H-1,2,3-triazole (12m). White solid; yield: 63% (19 mg, 0.1 mmol scale), eluent used for flash column was hexane/EtOAc 97 : 3, mp = 132–133 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 7.51 (d, 2H, J = 7.6 Hz, Ar-H), 7.44–7.42 (m, 2H, Ar-H), 7.32–7.27 (m, 5H, Ar-H), 7.07 (d, 2H, J = 8.0 Hz, Ar-H), 6.85 (d, 2H, J = 8.0 Hz, Ar-H), 5.40 (s, 2H, $-\text{NCH}_2\text{ArCH}_3$), 2.22 (s, 3H, $-\text{NCH}_2\text{ArCH}_3$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, $\text{DMSO}-d_6$): δ = 137.31 (C), 134.00 (2C), 132.73 (CH), 130.87 (C), 130.08 (2 \times CH), 129.99 (C), 129.42 (2 \times CH), 129.29 (2 \times CH), 128.74 (2 \times CH), 127.91 (CH), 127.37 (C), 127.31 (2 \times CH), 126.38 (2 \times CH), 51.13 ($-\text{NCH}_2\text{ArCH}_3$), 20.77 ($-\text{NCH}_2\text{ArCH}_3$) ppm. HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{19}\text{N}_3\text{H}^+$; 326.1652; found: m/z 326.1659.

4.6.34 Deuterated mixture of 4-phenyl-1-(1-phenylethyl)-1H-1,2,3-triazole-5-d (4w-d₁) and 4-phenyl-1-(1-phenylethyl-1-d)-1H-1,2,3-triazole-5-d (4w-d₂). White solid; yield: 96% (24 mg, 0.1 mmol scale), eluent used for flash column was hexane/



EtOAc 90 : 10, mp = 116 °C. ^1H NMR (400 MHz, CDCl_3): δ = 7.81–7.79 (m, 2H, Ar–H), 7.41–7.36 (m, 5H, Ar–H), 7.34–7.31 (m, 3H, Ar–H), 5.89–5.85 (m, 0.49 integration area, benzylic proton, $\text{NCH}(\text{CH}_3)\text{Ph}$, of **4w-d₁**), 2.03 (d, 3H, J = 6.8 Hz, $-\text{NCH}(\text{CH}_3)\text{Ph}$) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO-d_6): δ = 147.78 (C), 139.98 (C), 139.91 (C), 130.73 (C), 129.19 (2 × CH), 128.91 (2 × CH), 128.71 (CH), 128.22 (CH), 126.67 (2 × CH), 125.78 (2 × CH), 60.37 ($-\text{NCH}(\text{CH}_3)\text{Ar}$), 21.38 ($-\text{NCH}(\text{CH}_3)\text{Ar}$) ppm. HRMS (ESI-TOF): **4w-d₁**: m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{14}\text{DN}_3\text{H}^+$; 251.1407; found: m/z 251.1413; **4w-d₂**: m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{D}_2\text{N}_3\text{H}^+$; 252.1464; found: m/z 252.1468.

Conflicts of interest

There are no conflicts of interest to declare.

Data availability

The data underlying this study are available in the published article and its supplementary information (SI). Supplementary information: scanned copies of ^1H -NMR, ^{13}C -NMR, and ^{19}F -NMR (for compounds **4k**) for the synthesised compounds **4** (**4a–4z**, and **4a'–4d'**), **12** (**12a** and **12m**), and ^1H -NMR, ^{13}C -NMR, and HRMS of (**4w-d₂** + **4w-d₁**) are supplied (PDF). See DOI: <https://doi.org/10.1039/d6mr00036c>.

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References

- (a) V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596–2599; (b) C. W. Tornøe, C. Christensen and M. Meldal, *J. Org. Chem.*, 2002, **67**, 3057–3062.
- (a) A. Amiri, S. Abedanzadeh, M. H. Khodabandehloo, A. Shaabani and A. A. Moosavi-Movahedi, *Chem. Commun.*, 2025, **61**, 19810–19827; (b) B. Li, C. Xu, X. Zhu, J. Yu, X. Zhang and Y. Fan, *Green Chem.*, 2025, **27**, 6342–6361; (c) Y. Kawasaki, T. Hayashibara, K. Igawa, K. Onizuka, F. Nagatsugi and K. Tomooka, *J. Org. Chem.*, 2025, **90**, 13969–13975; (d) T. A. Pothi and C. V. Ramana, *Org. Lett.*, 2024, **26**, 2233–2237; (e) S. Kumar, B. Lal and R. K. Tittal, *Green Chem.*, 2024, **26**, 1725–1769; (f) H. Tang, H.-N. Zhang, X. Gao, Y. Zou and G.-X. Jin, *J. Am. Chem. Soc.*, 2024, **146**, 16020–16027; (g) Z. Fu, X. Yang and G. C. Tsui, *Org. Lett.*, 2023, **25**, 4945–4949; (h) V. K. Tiwari, B. B. Mishra, K. B. Mishra, N. Mishra, A. S. Singh and X. Chen, *Chem. Rev.*, 2016, **116**, 3086–3240.
- (a) B. L. Wilkinson, L. F. Bornaghi, T. A. Houston and S.-A. Poulsen, in *Drug Design Research Perspectives*, ed. S. P. Kaplan, Nova, Hauppauge, 2007, p. 57; (b) M. Whiting, J. C. Tripp, Y. C. Lin, W. Lindstrom, A. J. Olson, J. H. Elder, K. B. Sharpless and V. V. Fokin, *J. Med. Chem.*, 2006, **49**, 7697–7710; (c) H. C. Kolb and K. B. Sharpless, *Drug Discovery Today*, 2003, **8**, 1128.
- (a) J.-F. Lutz and Z. Zarafshani, *Adv. Drug Delivery Rev.*, 2008, **60**, 958; (b) Q. Wang, T. R. Chan, R. Hilgraf, V. V. Fokin, K. B. Sharpless and M. G. Finn, *J. Am. Chem. Soc.*, 2003, **125**, 3192; (c) A. J. Link and D. A. Tirrell, *J. Am. Chem. Soc.*, 2003, **125**, 11164.
- C. J. Hawker, V. V. Fokin, M. G. Finn and K. B. Sharpless, *Aust. J. Chem.*, 2007, **60**, 381.
- (a) J. A. Johnson, J. T. Koberstein, M. G. Finn and N. J. Turro, *Macromol. Rapid Commun.*, 2008, **29**, 1052; (b) R. A. Evans, *Aust. J. Chem.*, 2007, **60**, 384.
- (a) S. Hassan and T. J. J. Müller, *Adv. Synth. Catal.*, 2015, **357**, 617; (b) A.-C. Bédard and S. K. Collins, *Org. Lett.*, 2014, **16**, 5286; (c) D. Wang, S. Chen and B. Chen, *Tetrahedron Lett.*, 2014, **55**, 7026; (d) Y. Carcenac, F. David-Quillot, M. Abarbri, A. Duchêne and J. Thibonnet, *Synthesis*, 2013, **45**, 633; (e) B. T. Worrell, J. E. Hein and V. V. Fokin, *Angew. Chem., Int. Ed.*, 2012, **51**, 11791; (f) J. C. Morris, J. Chiche, C. Grellier, M. Lopez, L. F. Bornaghi, A. Maresca, C. T. Supuran, J. Pouyssegur and S.-A. Poulsen, *J. Med. Chem.*, 2011, **54**, 6905; (g) A. R. Bogdan and K. James, *Org. Lett.*, 2011, **13**, 4060; (h) E. Schwartz, K. Breitenkamp and V. V. Fokin, *Macromolecules*, 2011, **44**, 4735; (i) J. Deng, Y.-M. Wu and Q.-Y. Chen, *Synthesis*, 2005, **16**, 2730.
- (a) S. W. Robinson, C. L. Mustoe, N. G. White, A. Brown, A. L. Thompson, P. Kennepohl and P. D. Beer, *J. Am. Chem. Soc.*, 2015, **137**, 499; (b) B. R. Mullaney, B. E. Partridge and P. D. Beer, *Chem.–Eur. J.*, 2015, **21**, 1660; (c) B. R. Mullaney, A. L. Thompson and P. D. Beer, *Angew. Chem.*, 2014, **126**, 11642; (d) B. Schulze and U. S. Schubert, *Chem. Soc. Rev.*, 2014, **43**, 2522.
- (a) A.-C. Bedard and S. K. Collins, *Org. Lett.*, 2014, **16**, 5286–5289; (b) E. Schwartz, K. Breitenkamp and V. V. Fokin, *Macromolecules*, 2011, **44**, 4735–4741.
- (a) R. Yan, K. Sander, E. Galante, V. Rajkumar, A. Badar, M. Robson, E. El-Emir, M. F. Lythgoe, R. B. Pedley and E. Årstad, *J. Am. Chem. Soc.*, 2013, **135**, 703; (b) R. Yan, E. El-Emir, V. Rajkumar, M. Robson, A. P. Jathoul, R. B. Pedley and E. Årstad, *Angew. Chem., Int. Ed.*, 2011, **50**, 6793.
- (a) R. Benhida, V. Malnuit, M. Duca, A. Manout and K. Bougrin, *Synlett*, 2009, 2123–2126; (b) J. C. Morris, J. Chiche, C. Grellier, M. Lopez, L. F. Bornaghi, A. Maresca, C. T. Supuran, J. Pouyssegur and S. A. Poulsen, *J. Med. Chem.*, 2011, **54**, 6905–6918.
- J. García-Álvarez, J. Díez, J. Gimeno, F. J. Suárez and C. Vincent, *Eur. J. Inorg. Chem.*, 2012, 5854–5863.
- (a) A. R. Bogdan and K. James, *Org. Lett.*, 2011, **13**, 4060–4063; (b) E. Schwartz, K. Breitenkamp and V. V. Fokin, *Macromolecules*, 2011, **44**, 4735–4741; (c) Q.-Y. Chen, Y.-M. Wu and J. Deng, *Synthesis*, 2005, 2730–2738.



- 14 (a) J. M. Schulman, A. A. Friedman, J. Panteleev and M. Lautens, *Chem. Commun.*, 2012, **48**, 55–57; (b) J. Panteleev, K. Geyer, A. Aguilar-Aguilar, L. Wang and M. Lautens, *Org. Lett.*, 2010, **12**, 5092–5095.
- 15 (a) Y.-M. Wu, J. Deng, Y. Li and Q.-Y. Chen, *Synthesis*, 2005, **8**, 1314–1318; (b) L. Li, G. Zhang, A. Zhu and L. Zhang, *J. Org. Chem.*, 2008, **73**, 3630–3633; (c) N. W. Smith, B. P. Polenz, S. B. Johnson and S. V. Dzyuba, *Tetrahedron Lett.*, 2010, **51**, 550–553; (d) B. Barsoum, C. J. Brassard, J. H. A. Deeb, N. Okashah, K. Sreenath, J. T. Simmons and L. Zhu, *Synthesis*, 2013, **45**, 2372–2386; (e) J. Zhang, W. Chen, B. Wang, Z. Zhao, X. Wang and Y. Hu, *RSC Adv.*, 2015, **5**, 14561–14566.
- 16 (a) P. Karmakar and G. Brahmachari, *Chem.–Eur. J.*, 2025, e01966; (b) D. Mukherjee, I. Karmakar and G. Brahmachari, *Green Chem.*, 2025, **27**, 2565–2577; (c) I. Karmakar and G. Brahmachari, *J. Org. Chem.*, 2024, **89**, 10524–10537; (d) D. Mukherjee, I. Karmakar and G. Brahmachari, *J. Org. Chem.*, 2024, **89**, 12071–12084; (e) P. Karmakar, I. Karmakar, D. Pal, S. Das and G. Brahmachari, *J. Org. Chem.*, 2023, **88**, 1049–1060; (f) A. Bhowmick and G. Brahmachari, *Org. Lett.*, 2023, **25**, 7095–7099; (g) M. Mandal and G. Brahmachari, *J. Org. Chem.*, 2022, **87**, 4777–4787; (h) I. Karmakar and G. Brahmachari, *Green Chem.*, 2022, **24**, 2825–2838; (i) G. Brahmachari, A. Bhowmick and I. Karmakar, *J. Org. Chem.*, 2021, **86**, 9658–9669.
- 17 (a) G. Brahmachari, I. Karmakar, M. Mandal and B. Manda, *Curr. Green Chem.*, 2024, **11**, 210–220; (b) G. Brahmachari, M. Mandal, I. Karmakar, K. Nurjamal and B. Mandal, *ACS Sustain. Chem. Eng.*, 2019, **7**, 6369–6380; (c) G. Brahmachari, I. Karmakar and K. Nurjamal, *ACS Sustain. Chem. Eng.*, 2018, **6**, 11018–11028; (d) G. Brahmachari, *Catalyst-free Organic Synthesis*, Royal Society of Chemistry, Cambridge, U.K., 2018; (e) M. Lupacchini, A. Mascitti, G. Giachi, L. Tonucci, N. d'Alessandro, J. Martinez and E. Colacino, *Tetrahedron*, 2017, **73**, 609–653; (f) B. Banerjee, *Ultrason. Sonochem.*, 2017, **35**, 1–14; (g) R. B. N. Baig and R. S. Varma, *Chem. Soc. Rev.*, 2012, **41**, 1559–1584; (h) R. M. Martín-Aranda, E. Ortega-Cantero, M. L. Rojas-Cervantes, M. A. Vicente-Rodríguez and M. A. Bañares-Muñoz, *J. Chem. Technol. Biotechnol.*, 2005, **80**, 234–238; (i) Y. Penga and G. Song, *Green Chem.*, 2003, **5**, 704–706.
- 18 (a) K. Pal, P. Karmakar and G. Brahmachari, *RSC Mechanochem.*, 2025, **2**, 833–845; (b) P. Karmakar, A. Diger and G. Brahmachari, *Asian J. Org. Chem.*, 2025, e202500428; (c) S. Pan, F. F. Mulks, P. Wu, K. Rissanen and C. Bolm, *Angew. Chem.*, 2024, **136**, e202316702; (d) V. Martinez, T. Stolar, B. Karadeniz, I. Brekalo and K. Užarević, *Nat. Rev. Chem.*, 2023, **7**, 51–65; (e) P. Karmakar, I. Karmakar, D. Mukherjee, A. Bhowmick and G. Brahmachari, *Chem.–Eur. J.*, 2023, **29**, e202302539; (f) V. Martinez, T. Stolar, B. Karadeniz, I. Brekalo and K. Užarević, *Nat. Rev. Chem.*, 2023, **7**, 51–65; (g) G. Brahmachari, I. Karmakar and P. Karmakar, *Green Chem.*, 2021, **23**, 4762–4770; (h) G.-W. Wang, *Chem. Soc. Rev.*, 2013, **42**, 7668–7700; (i) J. Ribas-Arino and D. Marx, *Chem. Rev.*, 2012, **112**, 5412–5487.
- 19 (a) R. A. Sheldon, *ACS Sustainable Chem. Eng.*, 2018, **6**, 32–48; (b) S. Abou-Shehada, P. Mampuy, B. U. W. Maes, J. Clark and H. L. Summerton, *Green Chem.*, 2017, **19**, 249–258; (c) N. J. Willis, C. A. Fisher, C. M. Alder, A. Harsanyi, L. Shukla, J. P. Adams and G. Sandford, *Green Chem.*, 2016, **18**, 1313–1318; (d) F. Roschangar, A. Sheldon and C. H. Senanayake, *Green Chem.*, 2015, **17**, 752–768; (e) C. Jiménez-González, D. J. C. Constable and C. S. Ponder, *Chem. Soc. Rev.*, 2012, **41**, 1485–1498.
- 20 (a) J. L. Arenas and B. Crousse, *Eur. J. Org. Chem.*, 2021, 2665–2679; (b) S. J. Gharpure, S. Naveen, R. S. Chavan and Padmaja, *Eur. J. Org. Chem.*, 2020, **44**, 6870–6886; (c) R. Chung, A. Vo, V. V. Fokin and J. E. Hein, *ACS Catal.*, 2018, **8**, 7889–7897; (d) L. Li, X. Xing, C. Zhang, A. Zhu, X. Fan, C. Chen and G. Zhang, *Tetrahedron Lett.*, 2018, **59**, 3563–3566; (e) P. S. Gribanov, M. A. Topchiy, I. V. Karsakova, G. A. Chesnokov, A. Yu. Smirnov, L. I. Minaeva, A. F. Asachenko and M. S. Nechaev, *Eur. J. Org. Chem.*, 2017, 5225–5230; (f) D. N. Barsoum, N. Okashah, X. Zhang and L. Zhu, *J. Org. Chem.*, 2015, **80**, 9542–9551; (g) J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless and V. V. Fokin, *Angew. Chem., Int. Ed.*, 2009, **48**, 8018–8021.
- 21 (a) Y. Zhu, X. Zhu, X. Pan, L. X. Liu and M. J. Bussemaker, *RSC Mechanochem.*, 2025, **2**, 399–418; (b) A. V. Filgueiras, F. Pena-Pereira, V. Romero, I. Costas-Mora, C. Bendicho and I. Lavilla, *Microchem. J.*, 2017, **133**, 577–582; (c) M. H. Entezari and P. Kruus, *Ultrason. Sonochem.*, 1994, **1**, 75–79.
- 22 (a) A. Uner and L. T. Ball, *Eur. J. Org. Chem.*, 2025, **28**, e202500499; (b) M. J. Buskes and M.-J. Blanco, *Molecules*, 2020, **25**, 3493.
- 23 J. Deng, Y.-M. Wu and Q.-Y. Chen, *Org. Lett.*, 2007, **9**, 2333–2336.
- 24 (a) E. Arutyunova, A. Belovodskiy, P. Chen, M. B. Khan, M. Joyce, H. Saffran, J. Lu, Z. Turner, B. Bai, T. Lamer, H. S. Young, J. C. Vederas, D. L. Tyrrell, M. J. Lemieux and J. A. Nieman, *ACS Bio Med Chem Au*, 2023, **3**, 528–541; (b) T. M. Belete, *Drug Des. Dev. Ther.*, 2022, **16**, 3465–3472.
- 25 D. Wang, S. Chen, J. Wang, D. Astruc and B. Chen, *Tetrahedron*, 2016, **72**, 6375–6379.
- 26 L. Li, X. Xing, C. Zhang, A. Zhu, X. Fan, C. Chen and G. Zhang, *Tetrahedron Lett.*, 2018, **59**, 3563–3566.

