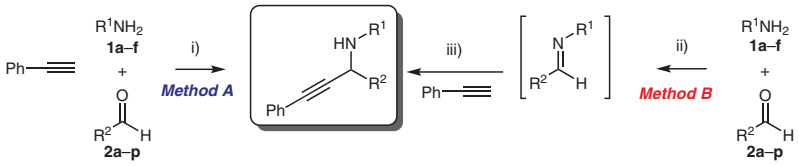
Synthesis C. Cimarelli et al. Paper

Activation of Primary Amines by Copper(I)-Based Lewis Acid Promoters in the Solventless Synthesis of Secondary Propargylamines

Cristina Cimarelli[*a]
Federica Navazio[a]
Federico V. Rossi[a]
Fabio Del Bello[b]
Enrico Marcantoni[a]

[a] School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino 1, 62032 Camerino, Italy
cristina.cimarelli@unicam.it
[b] School of Pharmacy, Medicinal Chemistry Unit, University of Camerino, Via S. Agostino 1, 62032 Camerino, Italy



Method A: *9 examples up to 62% yield*
i) $CuSO_4$ (30 mol%)/NaI (60 mol%), PhCOOH (5 mol%), solventless, N_2, 80 °C

Method B: *20 examples up to 95% yield*
ii) $MgSO_4$, $CeCl_3$•$7H_2O$ (30 mol%), solventless, N_2, r.t., 0.25 h
iii) CuI (30 mol%), solventless, N_2, 40 °C

Received: 12.11.2018
Accepted after revision: 24.01.2019
Published online: 11.03.2019
DOI: 10.1055/s-0037-1612253; Art ID: ss-2018-t0759-op

Abstract Primary amines are activated by copper(I)-based Lewis acid promoters in an A^3-coupling one-pot solventless reaction with aldehydes and phenylacetylene for the synthesis of secondary propargylamines. The reaction is promoted by a $CuSO_4$/NaI system, a practical precursor of the *in situ* generated effective CuI/I_2 system, that worked well, but only in a restricted number of examples. Substitution of I_2 with $CeCl_3$·$7H_2O$ in a one-pot two-step reaction provided good yields and a wider applicability, with the added value given by a safer procedure.

Key words propargylamines, A^3 coupling, primary amines, copper, cerium trichloride, Lewis acids

Propargylamines are a class of building blocks involved in the synthesis of several important heterocyclic scaffolds, as direct precursors or as starting materials for the preparation of key intermediates. These compounds are susceptible to many different chemical transformations because of their characteristic structure that encompasses an amine group suitable for nucleophilic reactions, placed at the β-position to an alkyne moiety that in turn can act both as an electrophile and as a source of electrons in nucleophilic reactions.

Many synthetic methods have been developed for the synthesis of different classes of heterocycles[1–10] starting from propargylamines. At the same time, propargylamines are direct precursors of propargylureas that can undergo silver- or gold-catalyzed cycloisomerization to produce a series of other nitrogen-containing heterocyclic compounds.[11–15] Furthermore, the synthesis of oxazolidinones[16–23] and oxazolones[24] through carboxylative cyclization of propargylic amines with CO_2 is a clean and atom-economic reaction for CO_2 fixation in the field of green chemistry.

Since the pioneering work of Li and Wei[25] the issue of the synthesis of propargylamines by direct addition of terminal alkynes to imines, defined in short as A^3 coupling, has been addressed in different ways, under solvent or solventless conditions, by metal catalysis or organocatalysis, and also in an enantioselective manner.[26–29]

Our goal was the development of a green and simple Lewis acid catalyzed or promoted A^3 reaction with aldehydes and alkynes for the activation of primary amines that are, in general, less applied in such reactions due to their lower reactivity. In particular, many synthetic methods based on Lewis acid catalysis have been developed, and copper(I) or copper(II) revealed as the most useful and frequently applied metal in A^3 reactions. In general, the coordination of Lewis acids with the final propargylamine is stronger than with the intermediate imine, so a catalytic amount of Lewis acid may not be enough for the reaction. A second Lewis acid may offset this unfavorable factor.

With this aim, we explored the effect of the use of iodine, because it possesses a strong C–C multiple bond coordination ability and may be both a σ- and a π-electrophilic Lewis acid. Reactions catalyzed by this element are very similar to ones catalyzed by transition metals, but it is cheaper than, for example, Pt, Pd and Os, and more environmentally friendly.[30] Iodides of cations at high charge are unstable, due to the propensity of iodine to lose an electron to transform into its stable form, I_2, that in turn tends to break down heterolytically to form iodide in the presence of strong organic nucleophiles, such as amines.[31] Furthermore, iodine has been used as a mild Lewis acid to activate imines in the synthesis of quinolines via a three-component reaction of amines, aldehydes and alkynes.[32] At the same time, molecular iodine is corrosive and toxic, so attempts to generate it *in situ* in copper-catalyzed reactions have been

made, with the CuI/I_2 system obtained by direct reaction of copper(II) perchlorate[33] or sulfate[34] with NaI, in the last case according to Equation 1.

$$2\ CuSO_4 + 4\ NaI \rightarrow 2\ CuI + I_2 + 2\ Na_2SO_4 \quad (1)$$

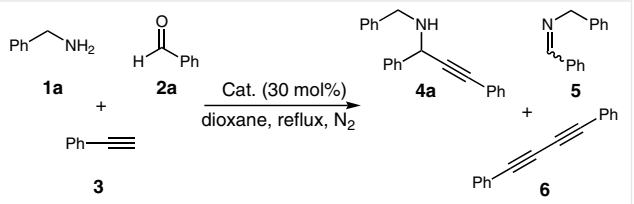
Equation 1

On the basis of these considerations, we studied the application of the CuI/I_2-promoting system in the A^3 reaction of primary amines, aldehydes and phenylacetylene, and also the *in situ* formation of the promoting system by using a $CuSO_4$/NaI couple that avoids the direct manipulation of iodine. Unfortunately, the reactions promoted by the $CuSO_4$/NaI system gave good results only in a limited number of examples. A partial result obtained in a preliminary catalyst screening when using a $CeCl_3{\cdot}7H_2O$/CuI-promoting system prompted us to also explore the A^3 coupling with this Lewis acid, under the same conditions developed for the $CuSO_4$/NaI system.

Lanthanides have played an important role in the search for affordable and environmentally benign synthetic methodologies. In particular, numerous reactions and synthetic procedures have been developed based on cerium(III) as key component, through its more available source $CeCl_3{\cdot}7H_2O$. The salt is interesting because of its high efficiency, and low toxicity and cost, and for the ease of application also under non-anhydrous conditions.[35] While $CeCl_3{\cdot}7H_2O$ has been used as a catalyst in multicomponent reactions,[36] to generate new products in a single step and to avoid large amounts of solvents and expensive purification techniques, to the best of our knowledge there are no reports on its use in the synthesis of propargylamines.

Often reactions catalyzed by $CeCl_3{\cdot}7H_2O$ require a stoichiometric amount of catalyst and long reaction times. A more reactive Lewis acid is represented by the mixture $CeCl_3{\cdot}7H_2O$/metal iodides in a 1:1 ratio,[37] also in supported form,[38] and with copper being the transition metal of choice for A^3 reactions, CuI was chosen also to widen the application of a promoting system used experimentally before only in the synthesis of 2-substituted benzimidazoles.[39]

To find the best conditions for the synthesis of secondary propargylamines, we began by screening a series of Lewis acids, performing the pilot reaction of benzylamine



Scheme 1 Catalyst screening in the pilot A^3-coupling reaction

(**1a**), benzaldehyde (**2a**) and phenylacetylene (**3**) in dioxane at reflux and under nitrogen atmosphere, as depicted in Scheme 1. The results obtained are reported in Table 1.

It is clear that the CuI/I_2-promoting system is active in the reaction and that its action results from the synergy of both copper(I) and iodine, as shown by the very poor results obtained when one or the other of the two components was used independently (Table 1, entries 1–3). On the other hand, also $CeCl_3{\cdot}7H_2O$, alone or in combination with other Lewis acids, proved to be a good promoter for the synthesis of imine **5**, as previously known,[40] but in solution it did not afford the product, except with CuI, with comparable results (Table 1, entries 5–10). Copper(I) gave a much better performance than copper(II) (Table 1, entries 1, 11). The $CuSO_4$/NaI couple has been revealed as a good way to generate the actual promoting system CuI/I_2 *in situ* by direct mixing, through a quick, quantitative and spontaneous reaction. The lower cost, the major commercial availability and the ease of use of $CuSO_4$ and NaI make them an interesting alternative. *In situ* generated CuI/I_2 was more reactive than the catalyst obtained by direct mixing of CuI and I_2 in the same ratio in the synthesis of 5-iodotriazoles.[33]

Solvent screening (Table 2) showed that propargylamine **4a** is obtained in water and also in water/ethanol mixtures in higher yields (11–43%) than in dioxane (see Table 1), but with a consistent parallel dimerization of phenylacetylene (10–40%). We found also that a higher yield of **4a** was obtained under solventless conditions, where the formation of dimer was reduced.

Table 1 Catalyst Screening for the Synthesis of Secondary Propargylamines[a]

Entry	Catalyst	Yield (%)	
		4a	**5**
1[b]	CuI/I_2	27	29
2	CuI	2	92
3[c]	I_2	–	70
4	NaI	–	94
5	$CeCl_3{\cdot}7H_2O$/NaI	–	>99
6	$CeCl_3{\cdot}7H_2O$/CuI	28	20
7	$CeCl_3{\cdot}7H_2O$	–	43
8	dry $CeCl_3$	–	30
9[d]	$CeCl_3{\cdot}7H_2O$/NaI/I_2	–	25
10	$CeCl_3{\cdot}7H_2O$/CuI/I_2	–	41
11	$CuSO_4$/I_2	<2	22

[a] Reaction conditions: **1a** (1 mmol), **2a** (1 mmol) and **3** (1 mmol) were mixed together with the Lewis acid (0.30 mmol), in dioxane (5 mL) under N_2 atmosphere, and left at reflux until a constant composition of the mixture was reached. Chromatographic yields.
[b] 4% diiodostyrene was formed.
[c] 23% diiodostyrene was formed.
[d] 44% diiodostyrene was formed.

Table 2 Solvent Screening for the Synthesis of Secondary Propargylamines[a]

Entry	Solvent	Catalyst	Yield (%)		
			4a	**5**	**6**
1	CH_3CN	CuI/I_2	29	45	13
2	EtOAc	CuI/I_2	–	49	–
3	*i*-PrOH	CuI/I_2	1	53	–
4	anhydrous EtOH	CuI/I_2	–	81	–
5	MeOH	CuI/I_2	–	90	10
6	EtOH	CuI/I_2	–	80	8
7	H_2O	CuI/I_2	33	6	40
8	EtOH/H_2O[b]	CuI/I_2	11	62	25
9	EtOH/H_2O[c]	CuI/I_2	–	77	22
10	EtOH/H_2O[d]	CuI/I_2	43	30	26

[a] Reaction conditions: **1a** (1 mmol), **2a** (1 mmol) and **3** (1 mmol) were mixed together in solvent (5 mL) at 80 °C, with catalyst (0.30 mmol, 1:1 molar ratio) under N_2 atmosphere, until a constant composition of the mixture was reached. Chromatographic yields.
[b] EtOH/H_2O, 50:50 v/v.
[c] EtOH/H_2O, 75:25 v/v.
[d] EtOH/H_2O, 25:75 v/v.

Table 3 summarizes the temperature effect on the CuI/I_2-promoted reaction, the comparison with *in situ* prepared promoter from $CuSO_4$ and NaI, and the optimization of the $CuSO_4$/NaI ratio under solventless conditions.

At room temperature the reaction did not take place (Table 3, entry 1), and a temperature increase from 80 °C to 100 °C had no effect on the reaction (Table 3, entries 2, 3).

Table 3 Catalyst Composition and Temperature Screening for the Solventless Synthesis of Secondary Propargylamines[a]

Entry	Promoter (mol%)	Yield (%)		
		4a	**5**	**6**
1[b]	CuI (30)/I_2 (30)	–	87	–
2	CuI (30)/I_2 (30)	40	50	1
3[c]	CuI (30)/I_2 (30)	39	56	1
4	CuI (30)/NaI (30)	60	33	0
5	$CuSO_4 \cdot 5H_2O$ (30)/NaI (30)	10	78	11
6	$CuSO_4$ (30)/NaI (30)	39	41	15
7	$CuSO_4$ (30)/NaI (60)	69	15	4
8	$CuSO_4$ (30)/NaI (90)	55	29	4
9[d]	I_2 (30)/NaI (30)	–	73	–

[a] Reaction conditions: **1a** (1 mmol), **2a** (1 mmol) and **3** (1 mmol) were mixed together with the promoter, at 80 °C unless differently reported, under N_2 atmosphere, until a constant composition of the mixture was reached. Chromatographic yields.
[b] At r.t.
[c] At 100 °C.
[d] 18% diiodostyrene was formed.

The best results were obtained under solventless conditions, at 80 °C, using a mixture of dry $CuSO_4$ and NaI to prepare the CuI/I_2 system *in situ* and with the formation of a reduced amount of phenylacetylene dimer **6** (Table 3, entry 7).

Beyond Equation 1, the reactions of Cu^{2+} and I_2/I^- may produce different ions, depending also on their relative amounts, as depicted in Equations 2 and 3.

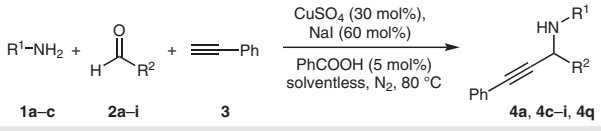
$$CuI + I^- \rightarrow [CuI_2]^- \quad (2)$$

$$I_2 + I^- \rightarrow [I_3]^- \quad (3)$$

Equations 2 and 3

The reaction outlined in Scheme 1 was then performed under conditions that allow the formation of $[I_3]^-$ only or of $[CuI_2]^-$ and CuI/I_2. The results clearly indicate that $[I_3]^-$ acts only as an iodinating agent of phenylacetylene, as expected (Table 3, entry 9). The addition of an equimolecular amount of NaI to CuI improved the yield more than the same amount of iodine (Table 3, entries 2, 4). The $CuSO_4$/NaI system worked as a good precursor of the CuI/I_2 promoter (Table 3, entries 2, 7). An increase in the NaI/$CuSO_4$ ratio to 3:1 did not improve the yield of **4a** (Table 3, entry 8). In particular, a lack of NaI with respect to the stoichiometric 1:2 ratio of Equation 1 afforded a lower yield (Table 3, entry 6), showing that the effective promoting agent is the CuI/I_2 system, formed as per Equation 1. In almost all the reactions we found an amount of 1,4-diphenylbuta-1,3-diyne (**6**) ranging from 4% to 15%, formed from phenylacetylene (**3**) through Glaser coupling.[41] This side reaction diverts reagent **3** towards an undesired product, decreasing the final yield of the propargylamine, and can be suppressed by the addition of a small percentage of benzoic acid.[42]

The reaction was then explored with different amines and aldehydes. Aldehydes **2a–i** and phenylacetylene (**3**) were mixed in the reaction vessel under inert atmosphere, then NaI and $CuSO_4$ were added. As the two salts get mixed, a deep brown color develops, indicating that the reaction in Equation 1 has gone to completion, then amines **1a–c** were added. The mixture was stirred at 80 °C until a constant composition was reached (2–5 h); the final propargylamines **4a**, **4c–i**, **4q** were obtained in yields from acceptable to good, with slightly better results starting from aliphatic aldehydes (Scheme 2 and Table 4).



Scheme 2 $CuSO_4$/NaI-promoted synthesis of secondary propargylamines

Table 4 $CuSO_4$/NaI-Promoted Synthesis of Secondary Propargylamines

Entry	1	R^1	2	R^2	4	Yield[a] (%)
1	**1a**	Bn	**2a**	Ph	**4a**	39
2	**1a**	Bn	**2b**	4-*t*-BuC_6H_4	**4b**	n.r.
3	**1a**	Bn	**2c**	4-ClC_6H_4	**4c**	30
4	**1a**	Bn	**2d**	4-MeOC_6H_4	**4d**	37
5	**1a**	Bn	**2e**	Pr	**4e**	42
6	**1a**	Bn	**2f**	*i*-Pr	**4f**	40
7	**1a**	Bn	**2g**	*t*-Bu	**4g**	11
8	**1a**	Bn	**2h**	cyclohexyl	**4h**	50
9	**1a**	Bn	**2i**	2-butyl	**4i**	62[b]
10	**1b**	*i*-Pr	**2a**	Ph	**4q**	53
11	**1c**	1-phenylethyl	**2a**	Ph	**4r**	n.r.

[a] Isolated yields.
[b] d.r. 21:79.

Table 5 Optimization of the Catalyst Amount and Temperature in the $CeCl_3{\cdot}7H_2O$/CuI-Promoted Synthesis of Secondary Propargylamines[a]

Entry	Promoter[b]	Conditions		
		25 °C[c]	40 °C[d]	80 °C[e]
		Yield (%) of **4a**		
1	10 mol%	70	80	49
2	30 mol%	87	**85**	70
3	60 mol%	60	78	65
4	100 mol%	55	60	62

[a] Reaction conditions: benzylamine (**1a**, 1 mmol) and benzaldehyde (**2a**, 1 mmol) were stirred in the presence of $CeCl_3{\cdot}7H_2O$ and $MgSO_4$ and then, after formation of the imine, phenylacetylene (**3**, 1.6 mmol) and CuI were added. The reactions were stopped when a constant composition of the mixture was reached. Isolated yields.
[b] mol% of each Lewis acid.
[c] Constant composition reached in 24 h.
[d] Constant composition reached in 15 h.
[e] Constant composition reached in 5 h.

In the second stage of this study, the application of $CeCl_3{\cdot}7H_2O$ instead of iodine was examined, in order to obtain better yields and a more general applicability of the reaction, with the added value which would be given by a safer procedure.

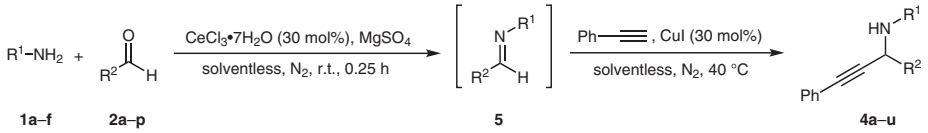
The conditions for the $CeCl_3{\cdot}7H_2O$/CuI-promoted reaction were optimized with respect to temperature and amount of promoting system (Table 5), with the finding that the reaction already had a good performance at room temperature, comparable with the results obtained at 40 °C, that are reached in shorter reaction times. At 80 °C, decreased yields were observed, although the reaction is completed in a much shorter time. So, the best results were found at 40 °C, in 15 hours, with 30 mol% of the promoting system.

The reactions with $CeCl_3{\cdot}7H_2O$ were performed by also pre-forming the imine: the formation of imines **5** catalyzed

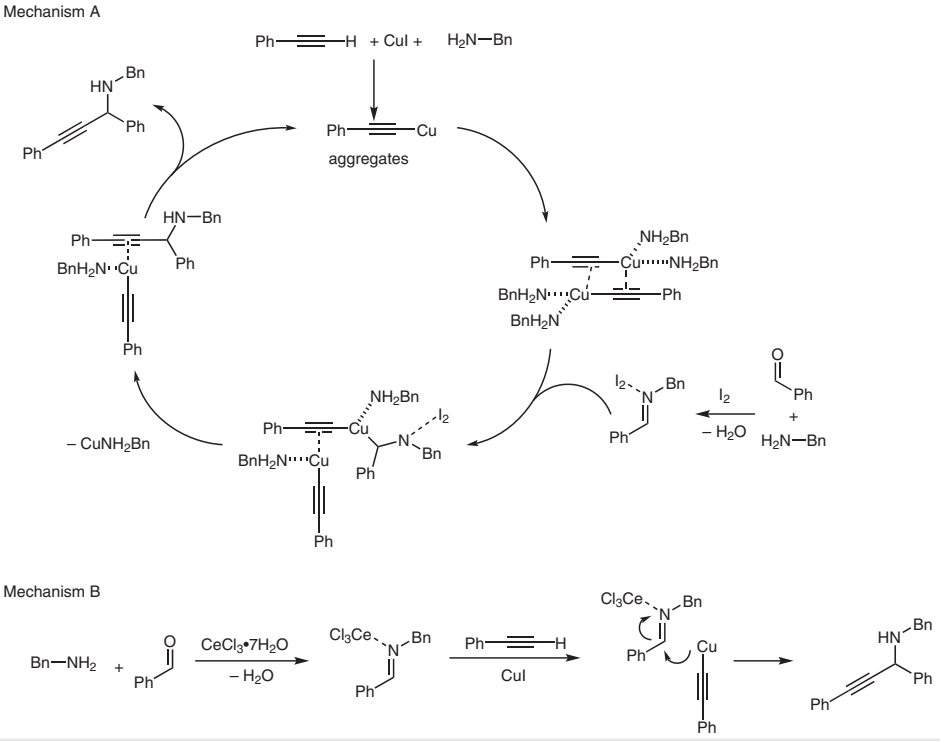
Table 6 $CeCl_3{\cdot}7H_2O$/CuI-Promoted Synthesis of Secondary Propargylamines

Entry	1	R^1	2	R^2	4	Yield[a] (%)
1	**1a**	Bn	**2a**	Ph	**4a**	85
2	**1a**	Bn	**2b**	4-*t*-BuC_6H_4	**4b**	81
3	**1a**	Bn	**2c**	4-ClC_6H_4[b]	**4c**	67
4	**1a**	Bn	**2d**	4-MeOC_6H_4	**4d**	50
5	**1a**	Bn	**2e**	Pr	**4e**	52
6	**1a**	Bn	**2f**	*i*-Pr	**4f**	76
7	**1a**	Bn	**2g**	*t*-Bu	**4g**	50
8	**1a**	Bn	**2h**	cyclohexyl	**4h**	75
9	**1a**	Bn	**2i**	2-butyl	**4i**	95[c]
10	**1a**	Bn	**2j**	4-MeC_6H_4	**4j**	57
11	**1a**	Bn	**2k**	4-*n*-PrC_6H_4	**4k**	78
12	**1a**	Bn	**2l**	4-*i*-PrC_6H_4	**4l**	60
13	**1a**	Bn	**2m**	4-FC_6H_4	**4m**	54
14	**1a**	Bn	**2n**	4-BrC_6H_4[b]	**4n**	55
15	**1a**	Bn	**2o**	3-formylphenyl	**4o**	70
16	**1a**	Bn	**2p**	2-furyl	**4p**	45
17	**1b**	*i*-Pr	**2a**	Ph	**4q**	72
18	**1c**	1-phenylethyl	**2a**	Ph	**4r**	64[d]
19	**1d**	*i*-Bu	**2a**	Ph	**4s**	71
20	**1e**	4-MeO$C_6H_4CH_2$	**2d**	4-MeOC_6H_4	**4t**	62
21	**1f**	2-furylmethyl	**2p**	2-furyl	**4u**	47

[a] Isolated yields.
[b] Solid imines. The reaction was performed in CH_3CN (2 mL).
[c] d.r. 68:32.
[d] d.r. 72:28.



Scheme 3 $CeCl_3{\cdot}7H_2O$/CuI-promoted synthesis of secondary propargylamines



Scheme 4 Mechanism hypotheses for the copper-based Lewis acid promoted synthesis of secondary propargylamines. Mechanism A: $CuSO_4$/NaI-promoted A^3 coupling. Mechanism B: $CeCl_3 \cdot 7H_2O$/CuI-promoted synthesis.

by the first Lewis acid was monitored by GC-MS or ^1H NMR spectroscopy in some cases, then phenylacetylene (**3**) and the second Lewis acid were added. After the reaction time, the final propargylamine **4** was isolated. When the reaction of **1a**, **2a** and **3** was performed by mixing together all the reagents and catalysts, only a 50% yield of product **4a** was obtained vs the 85% yield observed with imine pre-formation.

The order of addition of the two Lewis acids was investigated and the results are very similar one another either when we change the order of addition of the two acids: 90% yield of **4a** after 24 hours starting from CuI and 85% starting from $CeCl_3 \cdot 7H_2O$. In any case, the reaction mixtures obtained using CuI first and then $CeCl_3 \cdot 7H_2O$ resulted in more viscous mixtures and were therefore difficult to work up, so the procedure that uses $CeCl_3 \cdot 7H_2O$ in the first step and CuI in the subsequent step was chosen to prepare a series of secondary propargylamines.

Amines **1a–f** and aldehydes **2a–p** were mixed in the presence of $CeCl_3 \cdot 7H_2O$ and $MgSO_4$ at room temperature under inert atmosphere, and the formation of the corresponding imines, monitored by GC and NMR spectroscopy in some cases, took place generally in 85–90% yield after 15 minutes. Then, phenylacetylene (**3**) and CuI were added, and the reaction mixture was warmed and left at 40 °C until a constant composition was reached (12–15 h), then worked up. The final propargylamines **4a–u** were isolated in good yields (Scheme 3 and Table 6).

Generally, the $CuSO_4$/NaI-promoted reactions are faster and better yields were obtained with aliphatic aldehydes than with aromatic aldehydes. The reactions promoted by the $CuSO_4$/NaI system gave good results only in a limited number of examples and the yields were generally lower than the corresponding reactions promoted by $CeCl_3 \cdot 7H_2O$/CuI. Using the latter promoting system, the reaction showed wider applicability and resulted in better yields both with aliphatic and aromatic aldehydes; Glaser coupling was not observed. The reaction was also applied to chiral starting materials and, interestingly, the diastereomeric ratio of product **4i** from the reaction of chiral aldehyde **2i** promoted by $CuSO_4$/NaI was reversed with respect to the same reaction promoted by $CeCl_3 \cdot 7H_2O$/CuI (Tables 4 and 6).

Some facts allow us to hypothesize that the $CuSO_4$/NaI-promoted reaction proceeds according to a different mechanism than the one promoted by the $CeCl_3 \cdot 7H_2O$/CuI system. First of all, the noted change in the stereochemistry of the reaction suggests the said difference. The reaction promoted by $CuSO_4$/NaI clearly takes place under oxidative coupling conditions (Scheme 4, Mechanism A), as demonstrated by the dimerization of phenylacetylene (**3**) and by the presence of small percentages of derivatives obtained

by oxidative coupling of the starting amine. Such products are absent in the reaction promoted by $CeCl_3·7H_2O$/CuI, that instead gives better results upon pre-forming the imine, in a two-step one-pot reaction. This fact prompts us to think that in these reactions the promoter activates the imine towards attack by the copper acetylide (Scheme 4, Mechanism B). In Scheme 4, both mechanistic hypotheses are depicted. Further studies on this aspect are underway.

In summary, two different Lewis acid based promoting systems, CuI/I_2 and $CeCl_3·7H_2O$/CuI, were applied for the synthesis of secondary propargylamines by A^3 reaction of less studied primary amines, aldehydes and phenylacetylene, both systems characterized by ease of use, low toxicity and cost. The $CuSO_4$/NaI couple revealed itself as a good and practical precursor for the *in situ* generation of CuI and I_2. The $CeCl_3·7H_2O$/CuI promoter represents an improvement with respect to $CuSO_4$/NaI due to the increased performance of the reaction in terms of yields, although at the expense of longer reaction times, and with the added value of a lower toxicity of the promoting system itself, that avoids the use of toxic and corrosive molecular iodine. The desired propargylamines were obtained in yields ranging from moderate to good and in some cases unprecedented products were synthesized.

All reagents and solvents were purchased from commercial suppliers and used without further purification, unless mentioned otherwise. Dry $CuSO_4$ was freshly prepared by heating $CuSO_4·5H_2O$ in an oven at 200 °C for 3 h, until the blue powder became white. Chiral reagents were used as racemates. All reactions were monitored by TLC using EMD/Merck silica gel 60 pre-coated plates (0.25 mm), and the compounds were visualized by using UV light (254 nm) or iodine vapors as developing agent. Purification of the reaction products was carried out by column flash chromatography using silica gel (0.25 mm). IR specra were recorded on a Perkin Elmer UATR two instrument. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 spectrometer (400 MHz and 100 MHz, respectively). Chemical shifts are given in ppm with reference to residual H in deuterated solvents as the internal standard. Coupling constants *J* are reported in Hz. Diastereomeric ratios were determined by integration of the respective ^{1}H NMR signals of the diastereomers isolated as a mixture by column chromatography. Mass spectra were obtained using an Agilent 6850 gas chromatograph equipped with a HP5MS column (0.25 mm diameter) and an Agilent 5973N mass selective detector. Microanalyses were performed with an EA1108 CHNS D Fisons instrument.

$CuSO_4$/NaI-Promoted Synthesis of Propargylamines 4; Method A General Procedure

Aldehyde **2a–i** (1 mmol), phenylacetylene (**3**; 0.306 g, 3 mmol), NaI (0.090 g, 0.6 mmol), dry $CuSO_4$ (0.048 g, 0.3 mmol), $MgSO_4$ (0.050 g), benzoic acid (0.006 g, 0.05 mmol) and amine **1a–c** (1 mmol) were put in this order, under an inert atmosphere, in a three-necked flask equipped with magnetic stirring. The mixture was heated at 80 °C and the reaction monitored by TLC and GC-MS until a constant composition was reached (2–5 h). The mixture was then diluted with CH_2Cl_2 and washed with 0.5 M ammonia/ammonium chloride buffer. The organic phase was separated and dried over Na_2SO_4, then filtered, and the solvent was evaporated under reduced pressure. The crude was purified by flash chromatography (hexane/EtOAc, 9:1) to afford the desired propargylamine **4a**, **4c–i**, **4q**.

$CeCl_3·7H_2O$/CuI-Promoted Synthesis of Propargylamines 4; Method B General Procedure

Aldehyde **2a–p** (1 mmol) and amine **1a–f** (1 mmol) were put in a three-necked flask equipped with magnetic stirring and under N_2 atmosphere. $MgSO_4$ (0.050 g) and $CeCl_3·7H_2O$ (0.112 g, 0.3 mmol) were added and the mixture was stirred at r.t. for 15 min, checking for the complete formation of the corresponding imine by TLC and GC-MS. Phenylacetylene (**3**; 0.163 g, 1.6 mmol) and CuI (0.057 g, 0.3 mmol) were added and the mixture was heated at 40 °C under N_2 atmosphere for 15 h. Then, the mixture was diluted with CH_2Cl_2 and washed with 0.5 M ammonia/ammonium chloride buffer solution. The organic layer was separated and dried over Na_2SO_4, then the solvent was evaporated under reduced pressure. The crude was purified by flash chromatography (hexane/EtOAc, 9:1) to afford the desired propargylamine **4a–u**.

N-Benzyl-1,3-diphenylprop-2-yn-1-amine (4a)

Method A: yield: 0.116 g (39%); Method B: yield: 0.253 g (85%); oil. Spectroscopic data in agreement with literature.[43]

IR: 3065, 3024, 1595, 1492, 1448, 1065, 1028, 755, 689 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.5 Hz, 2 H), 7.55–7.50 (m, 2 H), 7.47–7.29 (m, 11 H), 4.84 (s, 1 H), 4.03 (s, 2 H), 1.71 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.2, 139.6, 132.0, 129.09, 128.8, 128.7, 128.5, 128.4, 128.1, 128.0, 127.4, 123.3, 89.1, 86.0, 53.8, 51.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 297 (M^+, 19), 296 (39), 220 (52), 191 (100), 91 (66).

Anal. Calcd for $C_{22}H_{19}N$: C, 88.85; H, 6.44; N, 4.71. Found: C, 89.15; H, 6.24; N, 5.01.

N-Benzyl-1-(4-*tert*-butylphenyl)-3-phenylprop-2-yn-1-amine (4b)

Method B: yield: 0.286 g (81%); oil.

IR: 3028, 2958, 2869, 1492, 1455, 1274, 1109, 829, 752, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8 Hz, 2 H), 7.58–7.56 (m, 2 H), 7.48 (t, *J* = 8 Hz, 4 H), 7.43–7.37 (m, 5 H), 7.33 (d, *J* = 7.4 Hz, 1 H), 4.86 (s, 1 H), 4.11 (d, *J* = 13.0 Hz, 1 H), 4.07 (d, *J* = 13.0 Hz, 1 H), 2.05 (br s, 1 H), 1.40 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.0, 140.1, 137.6, 132.1, 128.8, 128.7, 128.6, 128.4, 127.6, 127.4, 125.8, 123.5, 89.7, 85.9, 53.6, 51.5, 34.8, 31.7.

GC-MS (EI, 70 eV): *m*/*z* (%) = 353 (M^+, 63), 352 (76), 296 (78), 247 (100), 217 (62), 91 (78).

Anal. Calcd for $C_{26}H_{27}N$: C, 88.34; H, 7.70; N, 3.96. Found: C, 88.17; H, 7.57; N, 4.32.

N-Benzyl-1-(4-chlorophenyl)-3-phenylprop-2-yn-1-amine (4c)

Method A: yield: 0.100 g (30%); Method B: yield: 0.222 g (67%); oil.

IR: 3027, 2843, 1488, 1444, 1090, 1013, 829, 752, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68–7.26 (m, 14 H), 4.82 (s, 1 H), 4.02 (s, 2 H), 1.94 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.8, 139.1, 132.0, 129.4, 128.9, 128.8, 128.7, 128.6, 128.5, 128.0, 127.5, 123.1, 88.8, 86.4, 53.2, 51.3.

GC-MS (EI, 70 eV): *m*/*z* (%) = 331 (M^+, 25), 330 (45), 254 (25), 225 (100), 189 (41), 128 (11), 91 (70).

Anal. Calcd for $C_{22}H_{18}ClN$: C, 79.63; H, 5.47; Cl, 10.68; N, 4.22. Found: C, 79.57; H, 5.39; Cl, 10.91; N, 4.36.

***N*-Benzyl-1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-amine (4d)**

Method A: yield: 0.121 g (37%); Method B: yield: 0.164 g (50%); oil.

IR: 2895, 2832, 1610, 1506, 1241, 1171, 1035, 821, 759, 693 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 8.6 Hz, 2 H), 7.54–7.52 (m, 2 H), 7.47 (d, *J* = 7.4 Hz, 2 H), 7.38–7.28 (m, 6 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 4.80 (s, 1 H), 4.01 (s, 2 H), 3.82 (s, 3 H), 2.08 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 131.8, 129.4, 129.1, 128.8, 128.5, 128.3, 127.4, 126.6, 122.9, 114.15, 113.9, 88.4, 86.3, 55.3, 52.8, 50.6.

GC-MS (EI, 70 eV): *m*/*z* (%) = 327 (M^+, 17), 326 (25), 236 (41), 221 (100), 178 (21), 91 (44).

Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28. Found: C, 84.78; H, 6.74; N, 4.12.

***N*-Benzyl-1-phenylhex-1-yn-3-amine (4e)**

Method A: yield: 0.110 g (42%); Method B: yield: 0.137 g (52%); oil. Spectroscopic data in agreement with literature.[14]

IR: 2059, 1597, 1491, 1458, 1325, 1031, 755, 736, 589 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.23 (m, 10 H), 4.11 (d, *J* = 13.0 Hz, 1 H), 3.92 (d, *J* = 13.0 Hz, 1 H), 3.62 (dd, *J* = 6.3, 7.4 Hz, 1 H), 1.90 (br s, 1 H), 1.80–1.65 (m, 2 H), 1.64–1.50 (m, 2 H), 0.97 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1, 131.9, 128.7, 128.6, 128.5, 128.2, 127.3, 123.6, 91.1, 84.3, 51.7, 50.0, 38.4, 19.7, 14.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 263 (M^+, 1), 262 (2), 220 (100), 115 (10), 91 (44).

Anal. Calcd for $C_{19}H_{21}N$: C, 86.64; H, 8.04; N, 5.32. Found: C, 86.48; H, 7.88; N, 5.44.

***N*-Benzyl-4-methyl-1-phenylpent-1-yn-3-amine (4f)**

Method A: yield: 0.105 g (40%); Method B: yield: 0.200 g (76%); oil. Spectroscopic data in agreement with literature.[44]

IR: 2926, 2852, 1487, 1443, 1068, 1027, 755, 683 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.26 (m, 10 H), 4.17 (d, *J* = 13.0 Hz, 1 H), 3.95 (d, *J* = 13.0 Hz, 1 H), 3.46 (d, *J* = 5.4 Hz, 1 H), 2.01 (d hept, *J* = 6.5, 6.5 Hz, 1 H), 1.59 (br s, 1 H), 1.13 (d, *J* = 6.7 Hz, 3 H), 1.12 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.3, 131.8, 128.5, 128.4, 128.3, 127.9, 127.0, 123.6, 89.9, 84.8, 56.3, 51.9, 33.0, 19.9, 18.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 263 (M^+, 69), 262 (23), 248 (15), 220 (91), 162 (16), 91 (100).

Anal. Calcd for $C_{19}H_{21}N$: C, 86.64; H, 8.04; N, 5.32. Found: C, 86.57; H, 8.29; N, 5.47.

***N*-Benzyl-4,4-dimethyl-1-phenylpent-1-yn-3-amine (4g)**

Method A: yield: 0.030 g (11%); Method B: yield: 0.138 g (50%); oil. Spectroscopic data in agreement with literature.[44]

IR: 2955, 2863, 1480, 1439, 1097, 1031, 755, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.44 (m, 4 H), 7.37–7.26 (m, 6 H), 4.19 (d, *J* = 13.3 Hz, 1 H), 3.92 (d, *J* = 13.3 Hz, 1 H), 3.19 (s, 1 H), 1.45 (br s, 1 H), 1.10 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.6, 131.9, 128.6, 128.5, 128.4, 128.0, 127.2, 127.1, 90.5, 84.8, 60.3, 52.5, 35.4, 26.9.

GC-MS (EI, 70 eV): *m*/*z* (%) = 277 (M^+, 66), 276 (17), 262 (19), 220 (100), 173 (16), 144 (42), 117 (87), 91 (86).

Anal. Calcd for $C_{20}H_{23}N$: C, 86.59; H, 8.36; N, 5.05. Found: C, 86.47; H, 8.21; N, 5.23.

***N*-Benzyl-1-cyclohexyl-3-phenylprop-2-yn-1-amine (4h)**

Method A: yield: 0.152 g (50%); Method B: yield: 0.227 g (75%); oil. Spectroscopic data in agreement with literature.[45]

IR: 2924, 2845, 1492, 1451, 1070, 752, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.26 (m, 10 H), 4.14 (d, *J* = 13.4 Hz, 1 H), 3.93 (d, *J* = 13.4 Hz, 1 H), 3.43 (d, *J* = 5.8 Hz, 1 H), 2.00–1.60 (m, 7 H), 1.35–1.19 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.4, 132.0, 128.7, 128.6, 128.5, 128.1, 127.2, 123.8, 90.4, 85.0, 55.7, 52.0, 42.9, 30.5, 29.1, 26.8, 26.5, 26.4.

GC-MS (EI, 70 eV): *m*/*z* (%) = 303 (M^+, 1), 302 (1), 220 (100), 91 (35).

Anal. Calcd for $C_{22}H_{25}N$: C, 87.08; H, 8.30; N, 4.62. Found: C, 87.23; H, 8.22; N, 4.46.

***N*-Benzyl-4-methyl-1-phenylhex-1-yn-3-amine (4i)**

Method A: yield: 0.173 g (62%); d.r. 21:79; Method B: yield: 0.264 g (95%); d.r. 68:32; oil.

IR: 3027, 2961, 1735, 1584, 1488, 1451, 1381, 1028, 748, 685, 527 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.23 (m, 20 H), 4.14 (d, *J* = 13.0 Hz, 2 H), 3.92 (d, *J* = 13.0 Hz, 2 H), 3.56 (d, *J* = 5.0 Hz, 1 H), 3.49 (d, *J* = 5.0 Hz, 1 H), 1.81–1.59 (m, 6 H), 1.43–1.29 (m, 2 H), 1.08 (d, *J* = 6.6 Hz, 6 H), 0.95 (t, *J* = 7.4 Hz, 3 H), 0.94 (t, *J* = 7.2 Hz, 3 H). Diastereomers isolated as a mixture; the d.r. was determined by comparing the relative areas of the proton signals at δ 3.56 and 3.49.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1, 131.9, 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 127.3, 123.7, 89.6, 85.1, 55.1, 54.9, 53.9, 52.0, 51.4, 39.9, 39.7, 29.9, 27.1, 25.5, 16.1, 15.1, 11.9.

GC-MS (EI, 70 eV): *m*/*z* (%) = 277 (M^+, 71), 262 (22), 249 (60), 220 (65), 200 (25), 186 (29), 144 (38), 117 (47), 91 (100).

Anal. Calcd for $C_{20}H_{23}N$: C, 86.59; H, 8.36; N, 5.05. Found: C, 86.84; H, 8.23; N, 4.77.

***N*-Benzyl-3-phenyl-1-(*p*-tolyl)prop-2-yn-1-amine (4j)**

Method B: yield: 0.177 g (57%); oil. Spectroscopic data in agreement with literature.[45]

IR: 3024, 2921, 1488, 1444, 1025, 814, 755, 685 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.21 (m, 14 H), 4.82 (s, 1 H), 4.03 (s, 2 H), 2.39 (s, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.6, 131.8, 129.2, 128.6, 128.5, 128.3, 128.2, 127.7, 127.6, 127.2, 123.2, 89.0, 85.8, 53.3, 51.0, 21.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 311 (M^+, 30), 310 (49), 220 (62), 205 (100), 91 (52).

Anal. Calcd for $C_{23}H_{21}N$: C, 88.71; H, 6.80; N, 4.50. Found: C, 88.97; H, 6.98; N, 4.33.

***N*-Benzyl-3-phenyl-1-(4-propylphenyl)prop-2-yn-1-amine (4k)**

Method B: yield: 0.265 g (78%); oil.

IR: 2961, 2924, 2862, 1488, 1448, 1090, 755, 685 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.5 Hz, 2 H), 7.57–7.25 (m, 10 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 4.82 (s, 1 H), 4.07 (d, *J* = 12.0 Hz, 1 H), 4.03 (d, *J* = 12.0 Hz, 1 H), 2.63 (t, *J* = 7.6 Hz, 2 H), 2.03 (br s, 1 H), 1.68 (sext, *J* = 7.5 Hz, 2 H), 0.99 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 140.0, 137.8, 132.0, 128.9, 128.8, 128.7, 128.6, 128.4, 127.8, 127.4, 123.5, 89.7, 85.9, 53.6, 51.4, 38.0, 24.9, 14.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 339 (M^+, 48), 338 (64), 296 (39), 262 (25), 248 (49), 233 (100), 204 (58), 91 (63).

Anal. Calcd for $C_{25}H_{25}N$: C, 88.45; H, 7.42; N, 4.13. Found: C, 88.39; H, 7.47; N, 4.06.

N-Benzyl-1-(4-isopropylphenyl)-3-phenylprop-2-yn-1-amine (4l)

Method B: yield: 0.203 g (60%); oil.

IR: 2960, 1697, 1489, 1215, 830, 754, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.25 (m, 14 H), 4.83 (s, 1 H), 4.08 (d, *J* = 13.1 Hz, 1 H), 4.03 (d, *J* = 13.1 Hz, 1 H), 2.96 (sept, *J* = 6.9 Hz, 1 H), 1.94 (br s, 1 H), 1.30 (d, *J* = 6.9 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.7, 140.0, 137.9, 132.0, 128.8, 128.7, 128.6, 128.4, 127.9, 127.4, 126.9, 123.5, 89.7, 85.8, 53.6, 51.4, 34.1, 24.3.

GC-MS (EI, 70 eV): *m*/*z* (%) = 339 (M^+, 38), 338 (52), 296 (48), 250 (40), 233 (100), 218 (48), 91 (95).

Anal. Calcd for $C_{25}H_{25}N$: C, 88.45; H, 7.42; N, 4.13. Found: C, 88.33; H, 7.49; N, 4.02.

N-Benzyl-1-(4-fluorophenyl)-3-phenylprop-2-yn-1-amine (4m)

Method B: yield: 0.170 g (54%); oil.

IR: 3027, 2847, 1602, 1506, 1219, 1153, 832, 759, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.60 (m, 2 H), 7.53–7.51 (m, 2 H), 7.48–7.26 (m, 8 H), 7.11–7.05 (m, 2 H), 4.81 (s, 1 H), 4.01 (s, 2 H), 1.97 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.6 (d, $^1J_{C-F}$ = 248.6 Hz), 139.8, 136.2, 132.0, 129.6 (d, $^3J_{C-F}$ = 8.2 Hz), 128.7 (d, $^4J_{C-F}$ = 2.2 Hz), 128.6, 128.5, 128.0, 127.4, 123.2, 115.5 (d, $^2J_{C-F}$ = 22.4 Hz), 89.0, 86.3, 53.1, 51.3.

GC-MS (EI, 70 eV): *m*/*z* (%) = 315 (M^+, 20), 314 (34), 238 (21), 224 (54), 209 (100), 91 (40).

Anal. Calcd for $C_{22}H_{18}FN$: C, 83.78; H, 5.75; F, 6.02; N, 4.44. Found: C, 84.11; H, 6.03; F, 5.87; N, 4.77.

N-Benzyl-1-(4-bromophenyl)-3-phenylprop-2-yn-1-amine (4n)

Method B: yield: 0.206 g (55%); oil.

IR: 3061, 3028, 2843, 1484, 1455, 1072, 1009, 821, 755, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.48 (m, 6 H), 7.43–7.26 (m, 8 H), 4.78 (s, 1 H), 3.99 (s, 2 H), 2.11 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.5, 139.4, 132.0, 131.8, 129.7, 128.8, 128.7, 128.6, 128.5, 127.5, 123.0, 122.0, 88.6, 86.4, 53.2, 51.2.

GC-MS (EI, 70 eV): *m*/*z* (%) = 376 ([M + 1]$^+$, 31), 374 (M^+, 30), 286 (33), 284 (34), 271 (75), 269 (74), 220 (32), 189 (78), 91 (100).

Anal. Calcd for $C_{22}H_{18}BrN$: C, 70.22; H, 4.82; Br, 21.23; N, 3.72. Found: C, 70.11; H, 4.93; Br, 21.31; N, 3.56.

3-[1-(Benzylamino)-3-phenylprop-2-yn-1-yl]benzaldehyde (4o)

Method B: yield: 0.228 g (70%); oil.

IR: 3024, 2836, 2729, 1694, 1595, 1488, 1440, 1138, 755, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.06 (s, 1 H), 8.17 (s, 1 H), 7.95 (d, *J* = 7.6 Hz, 1 H), 7.85 (d, *J* = 6.6 Hz, 1 H), 7.57–7.10 (m, 11 H), 4.90 (s, 1 H), 4.03 (s, 2 H), 2.15 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.5, 141.6, 139.5, 136.9, 134.2, 132.3, 132.1, 129.5, 129.4, 129.3, 128.8, 128.7, 128.6, 127.6, 123.0, 88.3, 86.8, 53.4, 51.4.

GC-MS (EI, 70 eV): *m*/*z* (%) = 325 (M^+, 44), 324 (55), 298 (15), 248 (43), 234 (51), 219 (100), 218 (74), 189 (43), 91 (69).

Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30. Found: C, 84.76; H, 5.94; N, 4.22.

N-Benzyl-1-(furan-2-yl)-3-phenylprop-2-yn-1-amine (4p)

Method B: yield: 0.130 g (45%); oil. Spectroscopic data in agreement with literature.[46]

IR: 3061, 3026, 2843, 1489, 1144, 1073, 1007, 754, 728, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.25 (m, 11 H), 6.48–6.44 (m, 1 H), 6.38–6.35 (m, 1 H), 4.93 (s, 1 H), 4.02 (d, *J* = 13.0 Hz, 1 H), 3.98 (d, *J* = 13.0 Hz, 1 H), 2.61 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 142.8, 139.2, 132.1, 128.8, 128.7, 128.6, 128.5, 127.5, 122.9, 110.5, 108.0, 86.5, 85.2, 50.8, 47.9.

GC-MS (EI, 70 eV): *m*/*z* (%) = 287 (M^+, 12), 286 (20), 258 (11), 196 (49), 181 (100), 152 (50), 91 (42).

Anal. Calcd for $C_{20}H_{17}NO$: C, 83.59; H, 5.96; N, 4.87. Found: C, 83.72; H, 5.83; N, 4.63.

N-Isopropyl-1,3-diphenylprop-2-yn-1-amine (4q)

Method A: yield: 0.132 g (53%); Method B: yield: 0.180 g (72%); oil.

IR: 2959, 1594, 1491, 1167, 753, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.32 (m, 10 H), 4.88 (s, 1 H), 3.28 (hept, *J* = 6.2 Hz, 1 H), 1.60 (br s, 1 H), 1.19 (d, *J* = 6.2 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.2, 132.0, 128.9, 128.7, 128.4, 128.0, 127.8, 123.5, 89.9, 85.4, 52.5, 46.6, 23.9, 22.4.

GC-MS (EI, 70 eV): *m*/*z* (%) = 249 (M^+, 7), 248 (9), 234 (16), 206 (11), 191 (100), 172 (13), 130 (9), 128 (9), 77 (10).

Anal. Calcd for $C_{18}H_{19}N$: C, 86.70; H, 7.68; N, 5.62. Found: C, 86.91; H, 7.47; N, 5.68.

1,3-Diphenyl-*N*-(1-phenylethyl)prop-2-yn-1-amine (4r)

Method B: yield: 0.200 g (64%); d.r. 72:28; oil.

IR: 3054, 3028, 2970, 2863, 2250, 1491, 1443, 1104, 1031, 751, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.25 (m, 30 H), 4.72 (s, 1 H), 4.51 (s, 1 H), 4.42 (q, *J* = 6.5 Hz, 1 H), 3.96 (q, *J* = 6.5 Hz, 1 H), 1.75 (br s, 2 H), 1.46 (d, *J* = 6.5 Hz, 3 H), 1.43 (d, *J* = 6.5 Hz, 3 H). Diastereomers isolated as a mixture; the d.r. was determined by comparing the relative areas of the proton signals at δ 4.72 and 4.51. Data in agreement with literature.[47]

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.9, 141.0, 132.0, 128.9, 128.7, 128.5, 128.4, 128.0, 127.8, 127.5, 127.2, 123.5, 56.4, 55.5, 52.4, 25.3, 23.8.

GC-MS (EI, 70 eV): *m*/*z* (%) = 311 (M^+, 8), 310 (7), 296 (32), 234 (12), 206 (24), 191 (100), 105 (13), 77 (6).

Anal. Calcd for $C_{23}H_{21}N$: C, 88.71; H, 6.80; N, 4.50. Found: C, 88.54; H, 6.97; N, 4.31.

N-(2-Methylpropyl)-1,3-diphenylprop-2-yn-1-amine (4s)

Method B: yield: 0.187 g (71%); oil.

IR: 2961, 1492, 1448, 1098, 755, 685 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.6 Hz, 2 H), 7.51–7.25 (m, 8 H), 4.84 (s, 1 H), 2.65 (dd, *J* = 11.4, 7.0 Hz, 1 H), 2.58 (dd, *J* = 11.4, 6.5 Hz, 1 H), 2.02 (br s, 1 H), 1.83 (hept, *J* = 6.5 Hz, 1 H), 0.98 (dd, *J* = 3.5, 6.6 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1, 131.7, 128.5, 128.3, 128.1, 127.8, 127.7, 123.2, 89.2, 85.5, 55.1, 54.7, 28.3, 20.9, 20.7.

GC-MS (EI, 70 eV): *m*/*z* (%) = 263 (M^+, 4), 262 (3), 220 (24), 191 (100), 165 (7).

Anal. Calcd for $C_{19}H_{21}N$: C, 86.64; H, 8.04; N, 5.32. Found: C, 86.43; H, 7.85; N, 5.39.

N-(4-Methoxybenzyl)-1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-amine (4t)

Method B: yield: 0.221 g (62%); oil.

IR: 2833, 1608, 1505, 1244, 1027, 828, 751, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.53 (m, 4 H), 7.36–7.33 (m, 5 H), 6.93–6.89 (m, 4 H), 4.76 (s, 1 H), 3.94 (s, 2 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 2.14 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 159.0, 132.6, 132.0, 130.0, 129.1, 128.5, 128.4, 123.4, 114.3, 114.1, 114.0, 89.6, 85.9, 55.6, 55.5, 53.1, 50.6.

GC-MS (EI, 70 eV): *m*/*z* (%) = 357 (M^+, 22), 356 (19), 280 (22), 250 (17), 236 (34), 221 (100), 178 (20), 121 (55).

Anal. Calcd for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 80.51; H, 6.67; N, 3.78.

1-(Furan-2-yl)-N-(furan-2-ylmethyl)-3-phenylprop-2-yn-1-amine (4u)

Method B: yield: 0.130 g (47%); oil.

IR: 3014, 1664, 1597, 1487, 1439, 1222, 1009, 747, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.26 (m, 7 H), 6.49–6.47 (m, 1 H), 6.37–6.28 (m, 3 H), 4.97 (s, 1 H), 4.03 (d, *J* = 14.2 Hz, 1 H), 4.00 (d, 14.2 Hz, 1 H), 2.70 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 152.0, 142.9, 142.4, 132.1, 128.7, 128.5, 122.8, 110.6, 110.5, 108.3, 108.1, 85.9, 85.4, 47.7, 43.3.

GC-MS (EI, 70 eV): *m*/*z* (%) = 277 (M^+, 6), 276 (21), 260 (11), 248 (26), 200 (32), 181 (100), 152 (51), 109 (63), 81 (34).

Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.21; H, 5.37; N, 5.31.

Funding Information

This work was carried out under the framework of the University Research Project 'Chemical Swiss tools to treat tumors, metastases and infections' supported by the University of Camerino (FAR 2014-2015).

Acknowledgment

We thank Pfizer Global Supply – Ascoli Piceno Site for granting doctoral fellowships to F.N. and F.V.R.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1612253.

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