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Three-component hetero-domino cyclization and copper-catalyzed double A^3-coupling reaction of ethane-1,2-diamines, formaldehyde, and alkynes to afford 1,3-dipropargylimidazolidines

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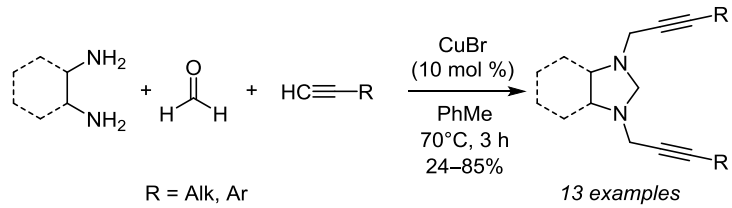


A novel and efficient approach to the synthesis of 1,3-dipropargylimidazolidines *via* a hetero-domino cyclization and copper-catalyzed double A^3-coupling reaction of ethane-1,2-diamines, formaldehyde, and alkynes has been reported. The transformation provides a useful method for the synthesis of imidazolidine derivatives.

Keywords: 1,3-dipropargylimidazolidines, A^3-coupling, copper catalysis, cyclization, hetero-domino reaction, three-component reaction.

Imidazolidines, which are important moieties in many biologically active compounds,[1] have been synthesized and evaluated for their anticonvulsant,[2] antibacterial,[3] antiviral,[4] antitumor,[5] antioxidant,[6] anti-inflammatory and antinociceptive,[7] antiproliferative,[8] antidiabetic,[9] and insecticidal activities.[10] Therefore, the synthesis and application of imidazolidine derivatives have attracted a great deal of attention in synthetic and medicinal chemistry.

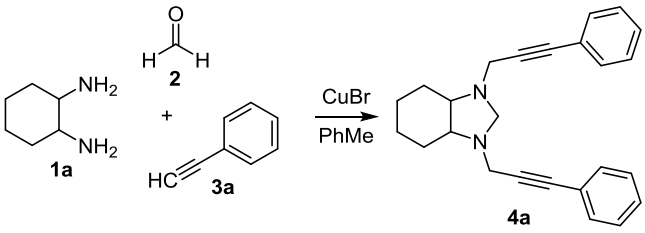
For the synthesis of imidazolidines, various aldehydes,[11] CO_2,[12] and CS_2[13] have been widely utilized to react with 1,2-diamines. Zhao et al. reported a highly diastereoselective synthesis of imidazolidine-dispirooxindoles *via* three-component [3+2] cycloadditions.[14] Recently, Xu et al. also reported a homo-1,3-dipolar [3+2] cycloaddition of azomethine ylides for the enantioselective synthesis of chiral imidazolidine derivatives.[15] Thus, development of novel methodologies for the construction of imidazolidines is still of high interest.

Propargylamines, which can be efficiently synthesized *via* three-component coupling reaction of amine, aldehyde, and alkyne (A^3-coupling),[16] are useful synthetic building blocks and important chemical intermediates for the preparation of many biologically active compounds.[17] As a commonly used and cheap metal, copper is widely exploited in the A^3-coupling.[18] Realizing that both imidazolidines and propargylamines are important moieties in synthetic chemistry and in continuation of the development of novel multicomponent and domino reactions,[19] we reported herein a novel approach to the synthesis of 1,3-dipropargylimidazolidines *via* a hetero-domino cyclization and copper-catalyzed double A^3-coupling reaction of ethane-1,2-diamines, formaldehyde, and alkynes. With a catalyst loading of 10 mol % and under mild conditions, various 1,3-dipropargylimidazolidines were obtained in moderate to high yields.

The optimization of reaction conditions was initially performed on the model reaction of cyclohexane-1,2-diamine (**1a**), formaldehyde (**2**), and ethynylbenzene (**3a**) with a molar ratio of 1:4:2.5 using CuBr (10 mol %) as a catalyst. The highest yield of the desired product 1,3-bis-(3-phenylprop-2-ynyl)octahydro-1*H*-benzimidazole (**4a**) was obtained when the reaction was carried out at 70°C for 3 h (Table 1, entry 2).

We next investigated the catalytic activity of various metal salts including $Ni(OAc)_2$, $PdCl_2$, $Fe(NO_3)_3$, NaCl, AgOAc, $ZnCl_2$, and some copper salts (Table 2). Among the tested metal salts, most of the copper salts were found to be effective for the transformation and possessed

Table 1. Optimization of reaction temperature and time for the synthesis of 1,3-dipropargylimidazolidine **4a***



Entry	Temperature, °C	Time, h	Yield**, %
1	60	3	79
2	70	3	89
3	80	3	75
4	70	0.5	45
5	70	1	57
6	70	2	70
7	70	4	80
8	70	6	78

* Reaction conditions: cyclohexane-1,2-diamine (**1a**) (0.5 mmol), aq formaldehyde (**2**) (40 wt %, 2 mmol), ethynylbenzene (**3a**) (1.25 mmol), CuBr (10 mol %), PhMe (1.0 ml).
** LC yields (biphenyl as an internal standard).

different catalytic activities (Table 2, entries 8–13), while other metal salts were ineffective (entries 1–7). In addition, Cu(I) catalysts showed higher activity than Cu(II) salts. A catalyst loading of 10 mol % CuBr was found to be the most effective (entry 13), while no improvement was observed by increasing or decreasing the amount of CuBr (entries 14–17).

Table 2. Catalytic activity of various metal salts*

Entry	Catalyst	Amount of catalyst, mol %	Yield of product **4a****, %
1	–	–	Trace
2	$Ni(OAc)_2$	10	NR***
3	$PdCl_2$	10	Trace
4	$Fe(NO_3)_3·9H_2O$	10	NR
5	NaCl	10	NR
6	AgOAc	10	Trace
7	$ZnCl_2$	10	Trace
8	$CuFe_2O_4$	10	NR
9	CuI	10	85
10	CuCl	10	76
11	$CuCl_2·2H_2O$	10	54
12	$Cu(acac)_2$	10	Trace
13	CuBr	10	89
14	CuBr	2.5	52
15	CuBr	5	69
16	CuBr	15	84
17	CuBr	20	82

* Reaction conditions: cyclohexane-1,2-diamine (**1a**) (0.5 mmol), aq formaldehyde (**2**) (40 wt %, 2 mmol), ethynylbenzene (**3a**) (1.25 mmol), PhMe (1.0 ml), 70°C, 3 h.
** LC yields (biphenyl as an internal standard).
*** NR – reaction did not proceed.

Table 3. Effects of various solvents on the yield of 1,3-dipropargylimidazolidine **4a***

Entry	Solvent	Yield of product **4a****, %
1	PhMe	89
2	DCE	82
3	1,4-Dioxane	79
4	MeCN	57
5	THF	80
6	EtOH	25
7	H_2O	18
8	DMF	78
9	DMSO	88

* Reaction conditions: cyclohexane-1,2-diamine (**1a**) (0.5 mmol), aq formaldehyde (**2**) (40 wt %, 2 mmol), ethynylbenzene (**3a**) (1.25 mmol), CuBr (10 mol %), solvent (1.0 ml), 70°C, 3 h.
** LC yields (biphenyl as an internal standard).

Furthermore, the effects of various solvents on the yield of 1,3-dipropargylimidazolidine **4a** were screened. As shown in Table 3, PhMe, 1,2-dichloroethane (DCE), 1,4-dioxane, THF, DMF, and DMSO provided reasonable yields of product **4a** (entries 1–3, 5, 8, and 9), while H_2O and EtOH led to significantly declined yields (entries 6 and 7). Accordingly, PhMe was proved to be the most suitable solvent for this reaction system (entry 1).

As shown in Table 4, either increasing or decreasing the molar ratio of formaldehyde (**2**) and ethynylbenzene (**3a**) could not improve the yield of product **4a** (entries 2–5). Thus, the final optimized reaction conditions were determined as follows: a mixture of cyclohexane-1,2-diamine (**1a**) (0.5 mmol), formaldehyde (**2**) (4 equiv), ethynylbenzene (**3a**) (2.5 equiv), CuBr (10 mol %), and PhMe (1 ml) was heated at 70°C for 3 h.

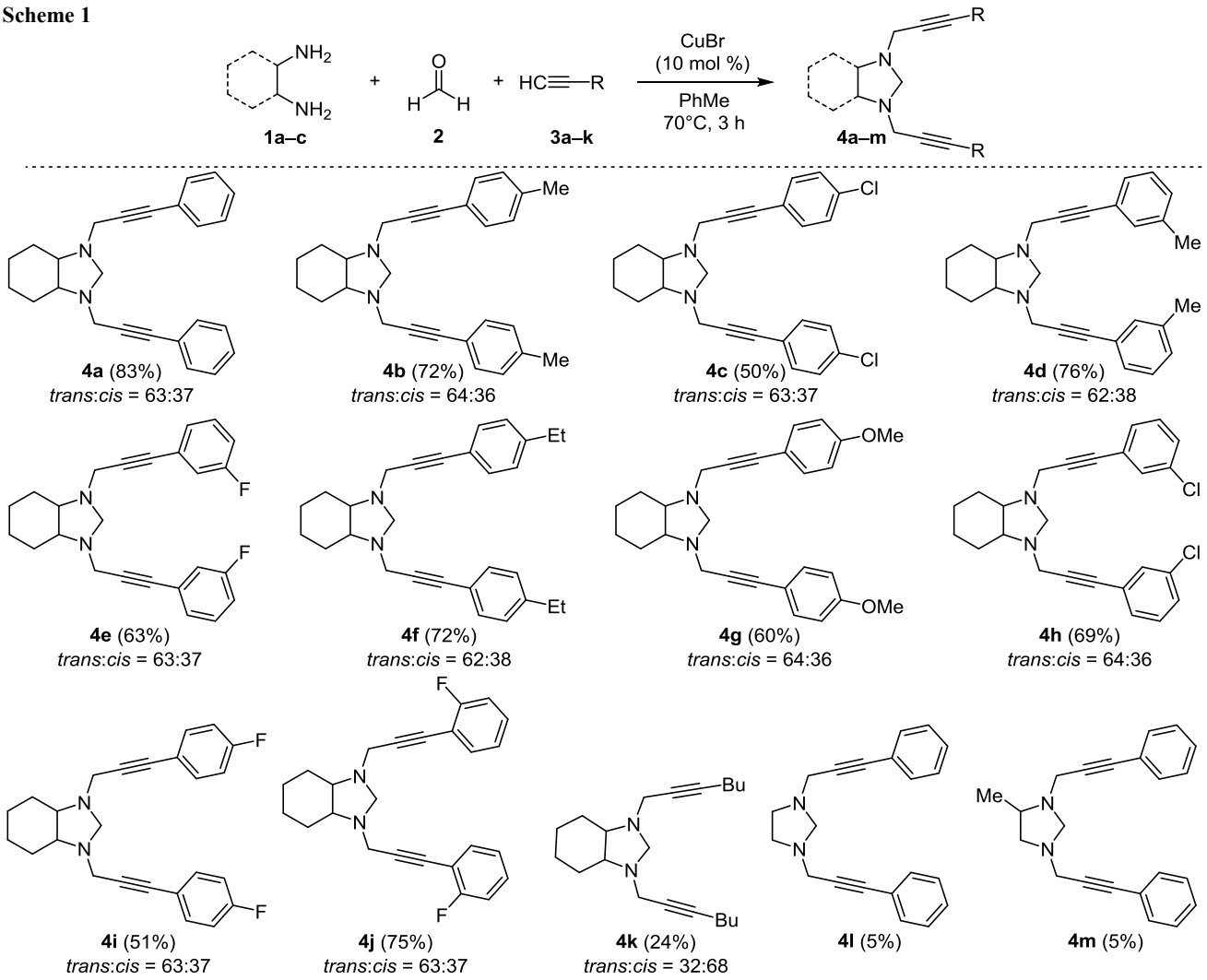
With the optimized conditions in hand, the scope of the hetero-domino cyclization and double A^3-coupling sequence was then explored with various alkynes and 1,2-diamines (Scheme 1). In general, both electron-donating (OMe, Me, and Et) and electron-withdrawing substituents (F and Cl) on the phenyl ring lead to the desired products **4a–j** in moderate to high isolated yields. In addition to phenylacetylenes, 1-hexyne, as an aliphatic

Table 4. Optimization of the molar ratio of formaldehyde (**2**) and ethynylbenzene (**3a**)*

Entry	Compound **2**, equiv	Compound **3a**, equiv	Yield of product **4a****, %
1	4	2.5	89
2	3.5	2.5	78
3	4.5	2.5	75
4	4	2.2	59
5	4	2.8	72

* Reaction conditions: cyclohexane-1,2-diamine (**1a**) (0.5 mmol), aq formaldehyde (**2**) (40 wt %), ethynylbenzene (**3a**), CuBr (10 mol %), PhMe (1.0 ml), 70°C, 3 h.
** LC yields (biphenyl as an internal standard).

Scheme 1

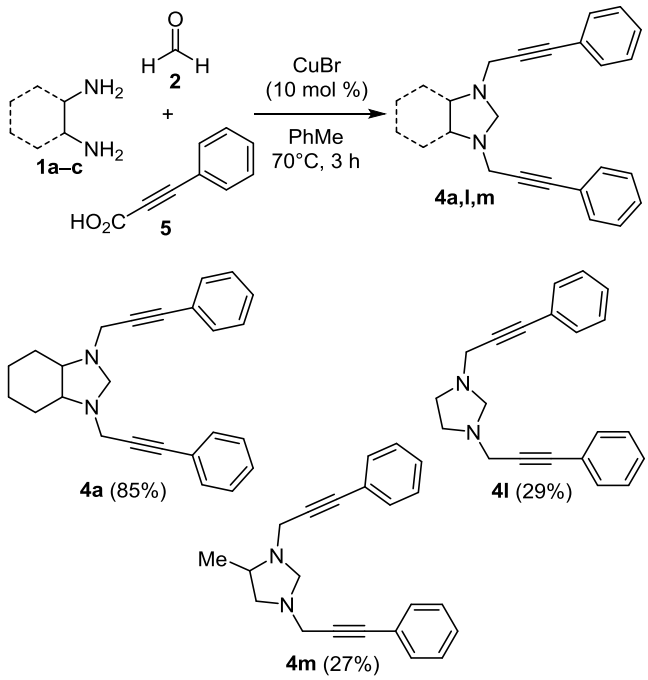


alkyne, was also applicable in this transformation providing 24% yield of product **4k**. Diastereomeric ratios of products **4a**–**k** were determined by ^{1}H NMR. The ^{1}H NMR chemical shift of the representative bridgehead CH group protons in compounds **4a**–**k** appeared at 2.28–2.49 ppm for their *trans*-isomers and 3.00–3.17 ppm for the *cis*-isomers, where the difference between the isomers was in coincidence with *trans*- or *cis*-cyclohexane-1,2-diamine.[20] Interestingly, products **4a**–**j** obtained from phenylacetylenes favored *trans*-isomers, while product **4k** generated from 1-hexyne favored *cis*-isomer. Unfortunately, ethane-1,2-diamine and propane-1,2-diamine provided the corresponding products **4l**,**m** with a low yield of 5%.

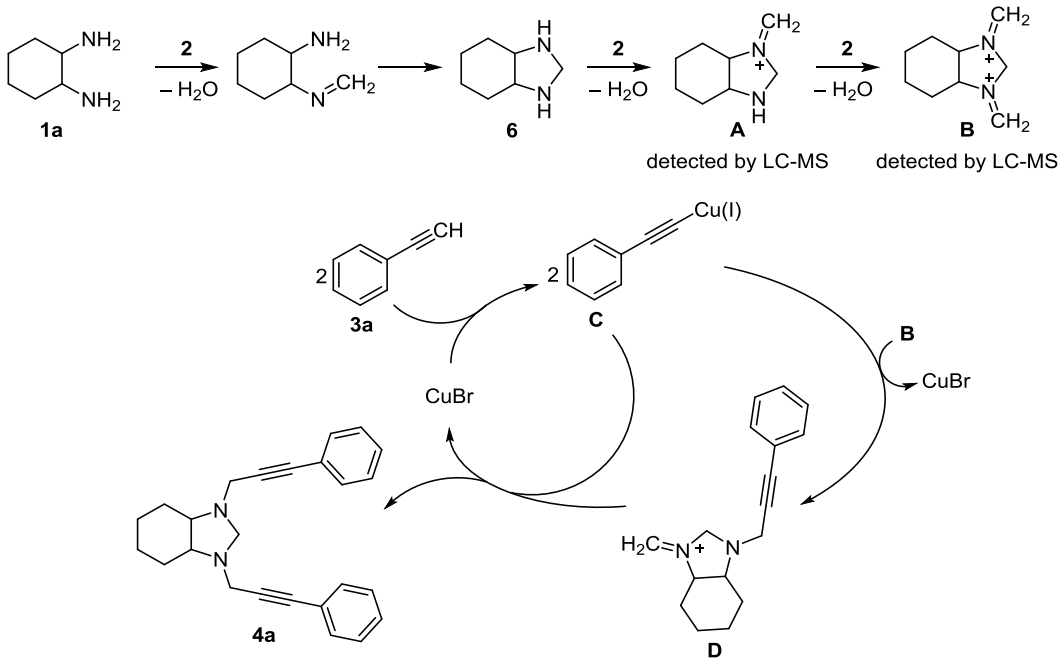
As shown in Scheme 2, the yields of products **4l**,**m** could be greatly improved to 29 and 27%, respectively, when 3-phenylpropiolic acid (**5**) was used instead of ethynylbenzene (**3a**). However, no obvious improvement in the yield of product **4a** was observed.

A tentative mechanism for the three-component reaction of ethane-1,2-diamines **1a–c**, formaldehyde (**2**), and alkynes **3a–k** is proposed in Scheme 3. The reaction of 1,2-diamine **1a** and formaldehyde (**2**) produces octahydro-1*H*-benzimidazole (**6**).[11] Intermediate **6** further reacts with

Scheme 2



Scheme 3



formaldehyde (**2**) to form iminium species **A** and **B** which were detected in the reaction mixture by LC-MS. The copper(I) acetylide intermediate **C**, generated from alkyne **3a** and CuBr, reacts with each of the iminium intermediates **B** and **D** to afford the corresponding product **4a**.[16,17] Thus, the three-component reaction involves a hetero-domino cyclization and copper-catalyzed double A^3-coupling sequence.

In conclusion, we have developed a novel approach to the synthesis of 1,3-dipropargylimidazolidines *via* a hetero-domino cyclization and copper-catalyzed double A^3-coupling reaction of ethane-1,2-diamines, formaldehyde, and alkynes in moderate to high yields. This transformation provides an effective and complementary pathway toward novel imidazolidine derivatives.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III NMR spectrometer (400 and 100 MHz, respectively) using $CDCl_3$ as the solvent and tetramethylsilane as an internal standard. High-resolution mass spectral analyses were performed on a Waters Micromass GCT instrument (EI). Reaction progress was monitored by thin-layer chromatography (TLC) and visualization was performed by UV lamp (254 nm). Preparative TLC was performed on Huanghai® HSGF 254 plates (thickness of coating 0.4–0.5 mm, 20 × 20 cm). All reagents were used as supplied without further purification and drying.

Synthesis of 1,3-dipropargylimidazolidines 4a–m *via* three-component reaction of ethane-1,2-diamines 1a–c, formaldehyde (2), and alkynes 3a–k (General method). A mixture of ethane-1,2-diamine **1a–c** (0.5 mmol), aq formaldehyde (40 wt %, 150 mg, 2 mmol), alkyne **3a–k** (1.25 mmol), CuBr (7.2 mg, 10 mol %), and PhMe (1.0 ml) was placed in a 10-ml glass tube sealed with a cap. The reaction tube was heated at 70°C for 3 h in an oil bath. The resulting suspension was diluted with H_2O (2 ml) and extracted with EtOAc (3 × 6 ml). The combined organic layers were washed with brine, dried over $MgSO_4$, and solvent was then removed under reduced pressure. The resulting crude residue was purified by preparative TLC to give the products (EtOAc–cyclohexane, 1:4, for products **4a–k**, pure EtOAc for products **4l**,**m**).

1,3-Bis(3-phenylprop-2-ynyl)octahydro-1*H*-benzimidazole (4a). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.45–7.41 (4H, m, H Ar); 7.30–7.26 (6H, m, H Ar); 4.00 (2H, s, NCH_2N); 3.73 (2H, d, *J* = 16.9) and 3.57 (2H, d, *J* = 16.9, $NCH_2C{\equiv}$); 2.45–2.43 (2H, m, NCH); 2.07–2.05 (2H, m, CH_2); 1.82–1.81 (2H, m, CH_2); 1.29–1.25 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 131.8 (C Ar); 128.2 (C Ar); 128.1 (C Ar); 123.1 (C Ar); 84.9 ($NCH_2\underline{C}{\equiv}$); 84.5 ($Ar\underline{C}{\equiv}$); 74.0 ($NCH_2N$); 67.2 (NCH); 41.0 ($N\underline{C}H_2C{\equiv}$); 29.0 ($CH_2$); 24.2 ($CH_2$). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.40–7.37 (4H, m, H Ar); 7.30–7.20 (6H, m, H Ar); 4.10 (1H, d, *J* = 5.1) and 3.77 (1H, d, *J* = 5.1, NCH_2N); 3.69 (4H, s, $NCH_2C{\equiv}$); 3.14–3.09 (2H, m, NCH); 1.71–1.66 (4H, m, $2CH_2$); 1.63–1.55 (2H, m, CH_2); 1.34–1.28 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 131.7 (C Ar); 128.2 (C Ar); 128.0 (C Ar); 123.1 (C Ar); 85.2 ($NCH_2\underline{C}{\equiv}$); 84.5 ($Ar\underline{C}{\equiv}$); 72.9 ($NCH_2N$); 59.8 (NCH); 40.8 ($N\underline{C}H_2C{\equiv}$); 26.3 ($CH_2$); 21.4 ($CH_2$). Found, *m*/*z*: 354.2089 $[M]^+$. $C_{25}H_{26}N_2$. Calculated, *m*/*z*: 354.2096.

1,3-Bis[3-(*p*-tolyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4b). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.32 (4H, d, *J* = 8.1, H Ar); 7.09 (4H, d, *J* = 8.0, H Ar); 3.99 (2H, s, NCH_2N); 3.71 (2H, d, *J* = 16.9) and 3.56 (2H, d, *J* = 16.9, $NCH_2C{\equiv}$); 2.44–2.42 (2H, m, NCH); 2.33 (6H, s, CH_3); 2.07–2.05 (2H, m, CH_2); 1.82–1.81 (2H, m, CH_2); 1.29–1.27 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 137.1 (C Ar); 130.7 (C Ar); 127.9 (C Ar); 119.0 (C Ar); 83.5 ($NCH_2\underline{C}{\equiv}$); 83.1

(Ar<u>C</u>≡); 73.0 (NCH_2N); 66.2 (NCH); 40.1 (N<u>C</u>H_2C≡); 27.9 (CH_2); 23.1 (CH_2); 20.4 (CH_3). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.20 (4H, d, *J* = 8.3, H Ar); 6.96 (4H, d, *J* = 7.9, H Ar); 4.03 (1H, d, *J* = 5.1) and 3.68 (1H, d, *J* = 5.1, NCH_2N); 3.69 (4H, s, NCH_2C≡); 3.06–3.01 (2H, m, NCH); 2.25 (6H, s, CH_3); 1.60–1.59 (4H, m, CH_2); 1.55–1.50 (2H, m, CH_2); 1.26–1.22 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 136.9 (C Ar); 130.6 (C Ar); 127.9 (C Ar); 119.0 (C Ar); 83.6 (NCH_2<u>C</u>≡); 83.5 (Ar<u>C</u>≡); 72.0 (NCH_2N); 58.7 (NCH); 39.9 (N<u>C</u>H_2C≡); 25.3 (CH_2); 20.5 (CH_2); 20.4 (CH_3). Found, *m*/*z*: 382.2406 $[M]^+$. $C_{27}H_{30}N_2$. Calculated, *m*/*z*: 382.2409.

1,3-Bis[3-(4-chlorophenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4c). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.30–7.26 (4H, m, H Ar); 7.20–7.17 (4H, m, H Ar); 3.90 (2H, s, NCH_2N); 3.65 (2H, d, *J* = 17.0) and 3.49 (2H, d, *J* = 17.0, NCH_2C≡); 2.37–2.35 (2H, m, NCH); 1.99–1.97 (2H, m, CH_2); 1.76–1.75 (2H, m, CH_2); 1.21–1.20 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 133.1 (C Ar); 132.0 (C Ar); 127.5 (C Ar); 120.5 (C Ar); 84.8 (NCH_2<u>C</u>≡); 82.5 (Ar<u>C</u>≡); 72.9 (NCH_2N); 66.1 (NCH); 39.9 (N<u>C</u>H_2C≡); 27.8 (CH_2); 23.1 (CH_2). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.22–7.19 (4H, m, H Ar); 7.14–7.11 (4H, m, H Ar); 4.01 (1H, d, *J* = 5.0) and 3.68 (1H, d, *J* = 5.0, NCH_2N); 3.60 (4H, s, NCH_2C≡); 3.05–3.00 (2H, m, NCH); 1.61–1.59 (4H, m, CH_2); 1.55–1.48 (2H, m, CH_2); 1.25–1.21 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 133.0 (C Ar); 131.9 (C Ar); 127.5 (C Ar); 120.5 (C Ar); 85.3 (NCH_2<u>C</u>≡); 82.4 (Ar<u>C</u>≡); 71.8 (NCH_2N); 58.7 (NCH); 39.7 (N<u>C</u>H_2C≡); 25.3 (CH_2); 20.4 (CH_2). Found, *m*/*z*: 422.1309 $[M]^+$. $C_{25}H_{24}{}^{35}Cl_2N_2$. Calculated, *m*/*z*: 422.1317. Found, *m*/*z*: 424.1293 $[M]^+$. $C_{25}H_{24}{}^{35}Cl^{37}ClN_2$. Calculated, *m*/*z*: 424.1287. Found, *m*/*z*: 426.1270 $[M]^+$. $C_{25}H_{24}{}^{37}Cl_2N_2$. Calculated, *m*/*z*: 426.1258.

1,3-Bis[3-(*m*-tolyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4d). A faint yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.26–7.23 (4H, m, H Ar); 7.19–7.15 (2H, m, H Ar); 7.11–7.09 (2H, m, H Ar); 4.00 (2H, s, NCH_2N); 3.72 (2H, d, *J* = 16.9) and 3.58 (2H, d, *J* = 16.9, NCH_2C≡); 2.45–2.43 (2H, m, NCH); 2.30 (6H, s, CH_3); 2.07–2.05 (2H, m, CH_2); 1.82–1.81 (2H, m, CH_2); 1.29–1.28 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 137.8 (C Ar); 132.4 (C Ar); 128.9 (C Ar); 128.8 (C Ar); 128.0 (C Ar); 122.9 (C Ar); 84.6 (NCH_2<u>C</u>≡); 84.4 (Ar<u>C</u>≡); 73.8 (NCH_2N); 67.1 (NCH); 41.0 (N<u>C</u>H_2C≡); 28.9 (CH_2); 24.1 (CH_2); 21.1 (CH_3). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.21–7.18 (4H, m, H Ar); 7.13–7.07 (4H, m, H Ar); 4.15 (1H, d, *J* = 4.6) and 3.79 (1H, d, *J* = 5.2, NCH_2N); 3.70 (4H, s, NCH_2C≡); 3.17–3.12 (2H, m, NCH); 2.26 (6H, s, CH_3); 1.70–1.69 (4H, m, CH_2); 1.64–1.59 (2H, m, CH_2); 1.34–1.29 (2H, m, CH_2). Found, *m*/*z*: 382.2407 $[M]^+$. $C_{27}H_{30}N_2$. Calculated, *m*/*z*: 382.2409.

1,3-Bis[3-(3-fluorophenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4e). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.27–7.20 (4H, m, H Ar); 7.14–7.11 (2H, m, H Ar); 7.03–6.97 (2H, m, H Ar); 3.97 (2H, s, NCH_2N); 3.72 (2H, d, *J* = 17.0) and 3.57 (2H, d, *J* = 17.0, NCH_2C≡); 2.43–2.41 (2H, m, NCH); 2.06–2.04 (2H, m, CH_2); 1.83–1.82 (2H, m, CH_2); 1.29–1.26 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 162.3 (d, $^2J_{CF}$ = 246.2, C Ar); 129.7 (d, $^2J_{CF}$ = 8.7, C Ar); 127.7 (d, $^2J_{CF}$ = 3.0, C Ar); 124.9 (d, $^2J_{CF}$ = 9.5, C Ar); 118.6 (d, $^2J_{CF}$ = 22.7, C Ar); 115.5 (d, $^2J_{CF}$ = 21.2, C Ar); 86.0 (NCH_2<u>C</u>≡); 83.4 (d, $^2J_{CF}$ = 3.3, Ar<u>C</u>≡); 74.0 (NCH_2N); 67.2 (NCH); 40.9 (N<u>C</u>H_2C≡); 28.9 (CH_2); 24.1 (CH_2). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.21–7.13 (4H, m, H Ar); 7.08–7.05 (2H, m, H Ar); 7.00–6.95 (2H, m, H Ar); 4.09 (1H, d, *J* = 5.0) and 3.74 (1H, d, *J* = 5.3, NCH_2N); 3.68 (4H, s, NCH_2C≡); 3.13–3.08 (2H, m, NCH); 1.73–1.66 (4H, m, CH_2); 1.63–1.55 (2H, m, CH_2); 1.34–1.28 (2H, m, CH_2). Found, *m*/*z*: 390.1906 $[M]^+$. $C_{25}H_{24}F_2N_2$. Calculated, *m*/*z*: 390.1908.

1,3-Bis[3-(4-ethylphenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4f). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.35 (4H, d, *J* = 8.2, H Ar); 7.11 (4H, d, *J* = 8.3, H Ar); 3.99 (2H, s, NCH_2N); 3.72 (2H, d, *J* = 16.9) and 3.56 (2H, d, *J* = 16.9, NCH_2C≡); 2.63 (4H, q, *J* = 7.6, CCH_2); 2.44–2.42 (2H, m, NCH); 2.07–2.04 (2H, m, CH_2); 1.82–1.80 (2H, m, CH_2); 1.28–1.26 (4H, m, CH_2); 1.21 (6H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 144.4 (C Ar); 131.8 (C Ar); 127.7 (C Ar); 120.3 (C Ar); 84.6 (NCH_2<u>C</u>≡); 84.1 (Ar<u>C</u>≡); 74.0 (NCH_2N); 67.2 (NCH); 41.1 (N<u>C</u>H_2C≡); 29.0 (CH_2); 28.8 (CH_2); 24.2 (CH_2); 15.4 (CH_3). Found, *m*/*z*: 410.2719 $[M]^+$. $C_{29}H_{34}N_2$. Calculated, *m*/*z*: 410.2722.

1,3-Bis[3-(4-methoxyphenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4g). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.38–7.35 (4H, m, H Ar); 6.82–6.78 (4H, m, H Ar); 3.98 (2H, s, NCH_2N); 3.77 (6H, s, OCH_3); 3.70 (2H, d, *J* = 16.8) and 3.54 (2H, d, *J* = 16.8, NCH_2C≡); 2.42–2.40 (2H, m, NCH); 2.06–2.04 (2H, m, CH_2); 1.80–1.79 (2H, m, CH_2); 1.28–1.26 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 159.4 (C Ar); 133.2 (C Ar); 115.3 (C Ar); 113.8 (C Ar); 84.2 (NCH_2<u>C</u>≡); 83.5 (Ar<u>C</u>≡); 74.1 (NCH_2N); 67.2 (NCH); 55.2 (OCH_3); 41.1 (N<u>C</u>H_2C≡); 29.0 (CH_2); 24.2 (CH_2). Found, *m*/*z*: 414.2306 $[M]^+$. $C_{27}H_{30}N_2O_2$. Calculated, *m*/*z*: 414.2307.

1,3-Bis[3-(3-chlorophenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4h). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.42–7.41 (2H, m, H Ar); 7.32–7.25 (4H, m, H Ar); 7.23–7.19 (2H, m, H Ar); 3.96 (2H, s, NCH_2N); 3.72 (2H, d, *J* = 17.0) and 3.57 (2H, d, *J* = 17.0, NCH_2C≡); 2.42–2.40 (2H, m, NCH); 2.05–2.03 (2H, m, CH_2); 1.83–1.81 (2H, m, CH_2); 1.29–1.27 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 134.0 (C Ar); 131.7 (C Ar); 129.9 (C Ar); 129.4 (C Ar); 128.4 (C Ar); 124.8 (C Ar); 86.3 (NCH_2<u>C</u>≡); 83.2 (Ar<u>C</u>≡); 73.9 (NCH_2N); 67.1 (NCH); 40.9 (N<u>C</u>H_2C≡); 28.9 (CH_2); 24.1 (CH_2). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.37–7.36 (2H, m, H Ar); 7.26–7.23 (4H, m, H Ar); 7.17–7.13 (2H, m, H Ar); 4.08 (1H, d, *J* = 5.0) and 3.73 (1H, d, *J* = 5.0, NCH_2N); 3.67 (4H, s, NCH_2C≡); 3.11–3.06 (2H, m, NCH); 1.72–1.66 (4H, m, CH_2); 1.62–1.55 (2H, m, CH_2); 1.32–1.28 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm: 134.0 (C Ar); 131.5 (C Ar); 129.8 (C Ar); 129.4 (C Ar); 128.3 (C Ar); 124.8 (C Ar); 86.8 (NCH_2<u>C</u>≡); 83.1 (Ar<u>C</u>≡); 72.9 (NCH_2N); 59.8 (NCH); 40.7 (N<u>C</u>H_2C≡); 26.3 (CH_2); 21.5 (CH_2). Found, *m*/*z*: 422.1287 $[M]^+$. $C_{25}H_{24}{}^{35}Cl_2N_2$.

Calculated, *m*/*z*: 422.1317. Found, *m*/*z*: 424.1275 $[M]^+$. $C_{25}H_{24}{}^{35}Cl^{37}ClN_2$. Calculated, *m*/*z*: 424.1287. Found, *m*/*z*: 426.1260 $[M]^+$. $C_{25}H_{24}{}^{37}Cl_2N_2$. Calculated, *m*/*z*: 426.1258.

1,3-Bis[3-(4-fluorophenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4i). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.42–7.37 (4H, m, H Ar); 7.00–6.94 (4H, m, H Ar); 3.97 (2H, s, NCH_2N); 3.70 (2H, d, *J* = 16.9) and 3.55 (2H, d, *J* = 16.9, $NCH_2C{\equiv}$); 2.42–2.40 (2H, m, NCH); 2.05–2.04 (2H, m, CH_2); 1.82–1.81 (2H, m, CH_2); 1.28–1.25 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 162.4 (d, $^2J_{CF}$ = 249.1, C Ar); 133.7 (d, $^2J_{CF}$ = 8.3, C Ar); 119.2 (d, $^2J_{CF}$ = 3.5, C Ar); 115.4 (d, $^2J_{CF}$ = 22.0, C Ar); 84.5 ($NCH_2\underline{C}{\equiv}$); 83.4 ($Ar\underline{C}{\equiv}$); 74.0 ($NCH_2N$); 67.2 (NCH); 41.0 ($N\underline{C}H_2C{\equiv}$); 28.9 ($CH_2$); 24.1 ($CH_2$). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.29–7.24 (4H, m, H Ar); 6.88–6.82 (4H, m, H Ar); 4.01 (1H, d, *J* = 5.0) and 3.68 (1H, d, *J* = 5.0, NCH_2N); 3.60 (4H, s, $NCH_2C{\equiv}$); 3.05–3.00 (2H, m, NCH); 1.65–1.59 (4H, m, CH_2); 1.55–1.48 (2H, m, CH_2); 1.27–1.20 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 162.3 (d, $^2J_{CF}$ = 249.1, C Ar); 133.5 (d, $^2J_{CF}$ = 8.3, C Ar); 119.2 (d, $^2J_{CF}$ = 3.5, C Ar); 115.4 (d, $^2J_{CF}$ = 22.0, C Ar); 85.0 ($NCH_2\underline{C}{\equiv}$); 83.4 ($Ar\underline{C}{\equiv}$); 72.9 ($NCH_2N$); 59.7 (NCH); 40.7 ($N\underline{C}H_2C{\equiv}$); 26.3 ($CH_2$); 21.4 ($CH_2$). Found, *m*/*z*: 390.1908 $[M]^+$. $C_{25}H_{24}F_2N_2$. Calculated, *m*/*z*: 390.1908.

1,3-Bis[3-(2-fluorophenyl)prop-2-ynyl]octahydro-1*H*-benzimidazole (4j). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.45–7.41 (2H, m, H Ar); 7.29–7.24 (2H, m, H Ar); 7.08–7.02 (4H, m, H Ar); 4.01 (2H, s, NCH_2N); 3.76 (2H, d, *J* = 17.1) and 3.64 (2H, d, *J* = 17.1, $NCH_2C{\equiv}$); 2.49–2.46 (2H, m, NCH); 2.07–2.04 (2H, m, CH_2); 1.83–1.81 (2H, m, CH_2); 1.32–1.24 (4H, m, CH_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 163.1 (d, $^2J_{CF}$ = 251.2, C Ar); 133.7 (d, $^2J_{CF}$ = 1.3, C Ar); 129.7 (d, $^2J_{CF}$ = 7.9, C Ar); 123.8 (d, $^2J_{CF}$ = 3.8, C Ar); 115.4 (d, $^2J_{CF}$ = 21.0, C Ar); 111.7 (d, $^2J_{CF}$ = 15.7, C Ar); 90.2 (d, $^2J_{CF}$ = 3.3, $NCH_2\underline{C}{\equiv}$); 78.0 ($NCH_2N$); 73.7 ($Ar\underline{C}{\equiv}$); 67.0 (NCH); 40.9 ($N\underline{C}H_2C{\equiv}$); 28.9 ($CH_2$); 24.1 ($CH_2$). ***Cis*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.38–7.34 (2H, m, H Ar); 7.26–7.21 (2H, m, H Ar); 7.02–6.97 (4H, m, H Ar); 4.13 (1H, d, *J* = 5.0) and 3.75 (1H, d, *J* = 5.0, NCH_2N); 3.72 (4H, s, $NCH_2C{\equiv}$); 3.16–3.11 (2H, m, NCH); 1.75–1.67 (4H, m, CH_2); 1.64–1.55 (2H, m, CH_2); 1.34–1.29 (2H, m, CH_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 162.9 (d, $^2J_{CF}$ = 251.1, C Ar); 133.6 (d, $^2J_{CF}$ = 1.2, C Ar); 129.6 (d, $^2J_{CF}$ = 7.9, C Ar); 123.8 (d, $^2J_{CF}$ = 3.8, C Ar); 115.3 (d, $^2J_{CF}$ = 21.0, C Ar); 111.7 (d, $^2J_{CF}$ = 15.7, C Ar); 90.8 (d, $^2J_{CF}$ = 3.3, $NCH_2\underline{C}{\equiv}$); 77.8 ($NCH_2N$); 73.1 ($Ar\underline{C}{\equiv}$); 59.7 (NCH); 40.9 ($N\underline{C}H_2C{\equiv}$); 26.4 ($CH_2$); 21.4 ($CH_2$). Found, *m*/*z*: 390.1905 $[M]^+$. $C_{25}H_{24}F_2N_2$. Calculated, *m*/*z*: 390.1908.

1,3-Di(hept-2-ynyl)octahydro-1*H*-benzimidazole (4k). A faint-yellow liquid. ***Trans*-isomer**: ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.81 (2H, s, NCH_2N); 3.45 (2H, dt, *J* = 16.5, *J* = 2.1) and 3.27 (2H, dt, *J* = 16.5, *J* = 2.2, $NCH_2C{\equiv}$); 2.30–2.28 (2H, m, NCH); 2.19–2.15 (4H, m, CCH_2); 1.97–1.94 (2H, m, CH_2); 1.77–1.76 (2H, m, CH_2); 1.51–1.36 (8H, m, $C\underline{H}_2C\underline{H}_2CH_3$); 1.24–1.16 (4H, m, CH_2); 0.89 (6H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 84.6 ($Ar\underline{C}{\equiv}$); 75.1 ($NCH_2\underline{C}{\equiv}$); 73.9 ($NCH_2N$); 66.9 (NCH); 40.6 ($N\underline{C}H_2C{\equiv}$); 30.9 ($CCH_2\underline{C}H_2$); 28.9 ($CH_2$); 24.1 ($CH_2$); 21.9 ($\underline{C}H_2CH_3$); 18.5 ($C\underline{C}H_2CH_2$); 13.6 ($CH_3$). Found, *m*/*z*: 314.2709 $[M]^+$. $C_{21}H_{34}N_2$. Calculated, *m*/*z*: 314.2722.

1,3-Bis(3-phenylprop-2-ynyl)imidazolidine (4l). A faint-yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.40–7.33 (4H, m, H Ar); 7.24–7.16 (6H, m, H Ar); 3.75 (2H, s) and 3.65 (2H, s, $NCH_2C{\equiv}$); 3.02 (2H, s, NCH_2N); 1.29–1.18 (4H, m, NCH_2CH_2N). ^{13}C NMR spectrum, δ, ppm: 131.7 (C Ar); 128.2 (C Ar); 128.2 (C Ar); 122.9 (C Ar); 84.9 ($Ar\underline{C}{\equiv}$); 84.6 ($NCH_2\underline{C}{\equiv}$); 73.2 ($NCH_2N$); 51.0 ($N\underline{C}H_2\underline{C}H_2N$); 43.0 ($N\underline{C}H_2C{\equiv}$). Found, *m*/*z*: 300.1624 $[M]^+$. $C_{21}H_{20}N_2$. Calculated, *m*/*z*: 300.1626.

4-Methyl-1,3-bis(3-phenylprop-2-ynyl)imidazolidine (4m). A faint-yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.47–7.39 (4H, m, H Ar); 7.30–7.22 (6H, m, H Ar); 3.87 (2H, dd, *J* = 50.4, *J* = 5.4, NCH_2N); 3.77–3.62 (4H, m, $NCH_2C{\equiv}$); 3.23 (1H, dd, *J* = 9.0, *J* = 7.1, $CHC\underline{H}_2N$); 3.17–3.08 (1H, m, $NC\underline{H}CH_3$); 2.62 (1H, dd, *J* = 9.0, *J* = 7.6, $CHC\underline{H}_2N$); 1.20 (3H, d, *J* = 6.1, CH_3). ^{13}C NMR spectrum, δ, ppm: 131.7 (C Ar); 128.2 (C Ar); 128.1 (2C Ar); 123.1 (C Ar); 123.0 (C Ar); 85.1 ($NCH_2\underline{C}{\equiv}$); 84.8 ($Ar\underline{C}{\equiv}$); 84.7 ($NCH_2\underline{C}{\equiv}$); 84.6 ($Ar\underline{C}{\equiv}$); 73.9 ($NCH_2N$); 59.0 ($N\underline{C}HCH_3$); 56.8 ($CH\underline{C}H_2N$); 43.3 ($N\underline{C}H_2C{\equiv}$); 40.8 ($N\underline{C}H_2C{\equiv}$); 18.2 ($CH_3$). Found, *m*/*z*: 314.1780 $[M]^+$. $C_{22}H_{22}N_2$. Calculated, *m*/*z*: 314.1783.

Supplementary information file containing ^{1}H and ^{13}C NMR spectral data of compounds **4a**–**m** is available at the journal website at http://hgs.osi.lv.

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