Supplementary Material

Synthesis of N-unsubstituted 1,2,3-triazoles via a cascade including propargyl azides, allenyl azides, and triazafulvenes

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Warning: All propargyl azides are known to be potentially explosive.[S-1] These compounds should be handled only in small quantities or in solution. Elemental analyses of azides could not be performed because of instability and explosive decomposition.

Synthesis of 5-azidopent-1-en-3-yne (2v)

Pent-4-en-2-ynyl methanesulfonate[57] (1.00 g, 6.24 mmol) was added to a solution of sodium azide (0.81 g, 12.5 mmol) in dimethyl sulfoxide (50 mL) and stirred at ambient temperature for 12 h. The mixture was diluted with water, extracted with diethyl ether, washed with water, and dried over magnesium sulfate. The diethyl ether was removed under reduced pressure by cooling the flask to afford the crude products **2v**, which was directly used for the synthesis of NH-1,2,3-triazoles.

5-Azidopent-1-en-3-yne (2v)

Light-yellow liquid, yield (63%). IR ($CDCl_3$): $\tilde{\nu}$ = 2236 (C≡C), 2108 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.98 (s, 2H, CH_2N_3), 5.50 (d, $^3J_{cis}$ = 11.0 Hz, 1H, CH=CH_2), 5.64 (d, $^3J_{trans}$ = 17.0 Hz, 1H, CH=CH_2), 5.76 (ddt, $^3J_{trans}$ = 17.0 Hz, $^3J_{cis}$ = 11.0 Hz, ^5J = 2.0 Hz, 1H, CH=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 40.79 (t, CH$_2$N$_3$), 81.48 (s, C), 85.61 (s, C), 115.80 (t, CH=CH$_2$), 126.20 (d, CH=CH$_2$).

Synthesis of 6-azidohexa-1,2-dien-4-yne (2x)

As similarly described in literature,[S-2] hexa-4,5-dien-2-yn-1-ol[58] (2.00 g, 21.25 mmol) was reacted with pyridine (137 mg, 140 µL, 1.73 mmol) and phosphorous tribromide (0.72 mL, 7.6 mmol). The pure product was obtained after workup and directly utilized for the next step.

6-Bromohexa-1,2-dien-4-yne

Colorless liquid, yield (64%). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 4.04 (s, 2H, CH_2Br), 5.03 (d, ^4J = 7.0 Hz, 2H, C=CH_2), 5.41 (tm, ^4J = 7.0 Hz, 1H, C=CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 15.35 (t, CH$_2$Br), 74.71 (d, C=CH), 77.46 (t, C=CH$_2$), 79.11 (s, C), 85.62 (s, C), 216.81 (s, C=CH$_2$). GC-MS [*IP* 70 eV; *m/z* (% rel. int.)]: 156 (14, M^+). Anal. calcd. for C_6H_5Br: C, 45.90; H, 3.21. Found: C, 45.13; H, 3.24.

6-Bromohexa-1,2-dien-4-yne (2.16 g, 13.7 mmol) was dissolved in methanol (20 mL) and was added to a solution of sodium azide (1.78 g, 27.4 mmol) and water (20 mL). The mixture was stirred at room temperature for 12 h. The workup was carried out as described at the workup of **2v**, and the product was directly used for the synthesis of NH-1,2,3-triazoles.

6-Azidohexa-1,2-dien-4-yne (2x)

Yellow liquid, yield (56%). IR ($CDCl_3$): $\tilde{\nu}$ = 2108 (N_3), 1939 (C=C=C) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.98 (s, 2H, CH_2N_3), 5.06 (dm, ^4J = 7.0 Hz, 2H, C=CH_2), 5.44 (tt, ^4J = 7.0 Hz, ^5J = 2.0 Hz, 1H, C=CH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 40.48 (t, CH$_2$N$_3$), 74.29 (d, C=CH), 77.30 (t, C=CH$_2$), 79.35 (s, C), 82.52 (s, C), 216.60 (s, C=CH$_2$).

Synthesis of (4-azidobut-2-ynyl)amine (2y)

(4-Chlorobut-2-ynyl)amine hydrochloride[60] (10.0 g, 71.4 mmol) in water (50 mL) was added to a solution of sodium azide (13.8 g, 212 mmol) and water (100 mL) and stirred overnight at room temperature. The mixture was extracted with methyl *tert*-butyl ether at pH 12, and the organic layer dried over magnesium sulfate. The solvent was removed under reduced pressure and the product (4.80 g, 61%) was isolated by recondensation at 10^{-3} Torr. This product included a small amount (ca. 11%) of (2-azidobuta-2,3-dienyl)amine after storage at room temperature.

(4-Azidobut-2-ynyl)amine (2y)

Colorless liquid; yield (61%). IR ($CDCl_3$): $\tilde{\nu}$ = 3388 (NH_2), 2107 (N_3), 1589 (NH_2), 1247 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.70 (s, 2H, N*H*$_2$), 3.45 (s, 2H, C*H*$_2$NH$_2$), 3.88 (s, 2H, C*H*$_2$N$_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 31.27 (t, *C*H$_2$NH$_2$), 39.91 (t, *C*H$_2$N$_3$), 74.09 (s, *C*), 88.25 (s, *C*).

Synthesis of 2z and 2aa

1,4-Dichlorobut-2-yne (10.1 g, 0.18 mol) was added dropwise to ethylene glycol (99.2 g, 1.60 mol) or alternatively to a solution of benzene-1,2-diol (176 g, 1.60 mol) in dimethyl sulfoxide (100 mL). The reaction mixture was charged with fine machine powdered potassium hydroxide (10.1 g, 0.18 mol) in portions and heated at 70–80 °C for 3 h. In the case of the reaction with benzene-1,2-diol, the solution was stirred for further 12 h at room temperature. Ice water was added to the reaction mixture, which was extracted with diethyl ether, washed with sodium bicarbonate and water, and dried over magnesium sulfate. Diethyl ether was evaporated to afford the crude products. In the case of the reaction with benzene-1,2-diol, the black solid was suspended in *n*-hexane, and the insoluble benzene-1,2-diol was filtered off. Remaining 1,4-dichlorobut-2-yne was evaporated under reduced pressure (40 °C, $5 \cdot 10^{-3}$ mbar) to afford the crude products, which were directly utilized for the next step.

2-((4-Chlorobut-2-yn-1-yl)oxy)ethanol

Brown oil; yield (7%). IR ($CDCl_3$): $\tilde{\nu}$ = 2605 (OH), 2245 (C≡C) cm^{-1}. ^1H NMR (400 MHz, d_6-DMSO): δ (ppm) = 2.48 (s, 1H, O*H*), 3.44 (m, 2H, OC*H*$_2$), 3.51 (m, 2H, OC*H*$_2$), 4.22 (t, 2H, ^5J = 2.0 Hz, C*H*$_2$), 4.49 (t, ^5J = 2.0 Hz, 2H, C*H*$_2$). ^{13}C NMR (100.6 MHz, d_6-DMSO): δ (ppm) = 29.89 (t, *C*H$_2$Cl), 56.59 (t, *C*H$_2$), 58.97 (t, *C*H$_2$), 70.26 (t, *C*H$_2$), 80.37 (s, *C*), 82.15 (s, *C*).

2-((4-Chlorobut-2-yn-1-yl)oxy)phenol

Brown oil; yield (8%). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 4.17 (t, ^5J = 2.0 Hz, 2H, C*H*$_2$Cl), 4.80 (t, ^5J = 2.0 Hz, 2H, OC*H*$_2$), 5.81 (s, 1H, O*H*). 6.80–7.12 (m, 4H, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 30.41 (t, *C*H$_2$Cl), 57.10 (t, O*C*H$_2$), 80.95 (s, *C*), 82.70 (s, *C*), 112.70 (d, *C*H, Ar), 115.20 (d, *C*H, Ar), 120.10 (d, *C*H, Ar), 122.60 (d, *C*H, Ar), 144.53 (s, *C*, Ar), 145.93 (s, *C*, Ar).

2-(4-Chlorobut-2-ynyloxy)ethanol (0.93 g, 6.3 mmol) or 2-(4-Chlorobut-2-ynyloxy)phenol (2.40 g, 12.2 mmol) was dissolved in dimethyl sulfoxide. Sodium azide (5 eq) was added (in case of synthesis of **2aa**, diluted in water) and the solution was stirred at ambient temperature for 12 h. The workup was carried out as described at the workup of **2v**. The azides were directly used for the synthesis of NH-1,2,3-triazoles.

2-((4-Azidobut-2-yn-1-yl)oxy)ethanol (2z)

Yellow liquid; yield (70%). IR ($CDCl_3$): $\tilde{\nu}$ = 3634 (OH), 2107 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.14 (s, 1H, O*H*), 3.65 (t, ^3J = 4.0 Hz, 2H, OCH_2), 3.78 (t, ^3J = 4.0 Hz, 2H, OCH_2), 3.97 (s, 2H, CH_2N_3), 4.29 (t, ^5J = 1.7 Hz, 2H, CCH_2O). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 39.08 (t, CH_2N_3), 567.59 (t, OCH_2), 60.82 (t, OCH_2), 70.26 (t, OCH_2), 77.81 (s, *C*), 82.20 (s, *C*).

2-((4-Azidobut-2-yn-1-yl)oxy)phenol (2aa)

Yellow oil; yield (79%). IR ($CDCl_3$): $\tilde{\nu}$ = 3549 (OH), 2133 (N_3), 2109 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.96 (s, 2H, CH_2N_3), 4.83 (s, 2H, OCH_2), 5.79 (s, 1H, O*H*), 6.92 (m, 4H, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 39.94 (t, CH_2N_3), 56.96 (t, OCH_2), 80.23 (s, *C*), 81.84 (s, *C*), 112.70 (d, *C*H, Ar), 115.20 (d, *C*H, Ar), 120.10 (d, *C*H, Ar), 122.80 (d, *C*H, Ar), 144.32 (s, *C*, Ar), 145.90 (s, *C*, Ar).

Synthesis of 3,4-diazido-1,4-diphenylbut-1-yne (2cc)

A solution of ethyl bromide (3.55 g, 32.5 mmol) in dry THF (50 mL) was added under inert conditions to magnesium turnings (0.75 g, 31.2 mmol), and the mixture was stirred for additional 15 min. In a second flask, phenylacetylene was continuously dissolved in dry THF (30 mL) and cooled to 0 °C before the solution of ethylmagnesium bromide was carefully added. After stirring for 30 min, 2-bromo-2-phenylethanal[61,62] (5.97 g, 30.0 mmol) in dry THF (20 mL) was poured into the reaction mixture at 0 °C. The suspension was warmed to ambient temperature, stirred for additional 2 h, and hydrolyzed with saturated aqueous ammonium chloride at 0 °C. The aqueous layer was extracted with diethyl ether, the combined organic extracts were washed with water and dried over magnesium sulfate. The volatiles were removed under reduced pressure ($5 \cdot 10^{-3}$ mbar) to afford the bromohydrin, which was directly utilized for the next step.

1-Bromo-1,4-diphenylbut-3-yn-2-ol (two diastereomers)

Orange oil; yield (81%). IR ($CDCl_3$): $\tilde{\nu}$ = 3565 (OH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.37 (s, 1H, O*H*), 3.46 (s, 1H, O*H*), 4.91 (d, ^3J = 5.0 Hz, 1H, C*H*), 4.98 (d, ^3J = 7.0 Hz, 1H, C*H*), 5.13 (d, ^3J = 7.0 Hz, 1H, C*H*), 5.19 (d, ^3J = 5.0 Hz, 1H, C*H*), 7.11–7.65 (m, 20 H, C*H*, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 58.56 (d, *C*H), 58.67 (d, *C*H), 67.29 (d, *C*H), 67.42 (d, *C*H), 85.97 (s, *C*≡*C*), 86.40 (s, *C*≡*C*), 87.16 (s, *C*≡*C*), 87.18 (s, *C*≡*C*), 121.69 (s, *C*), 121.82 (s, *C*), 128.09 (d, *C*H, Ar), 128.14 (d, *C*H, Ar), 128.17 (d, *C*H, Ar), 128.31 (d, *C*H, Ar), 128.33 (d, *C*H, Ar), 128.59 (d, *C*H, Ar), 128.63 (d, *C*H, Ar), 128.66 (d,

*C*H, Ar), 131.47 (d, *C*H, Ar), 131.59 (d, *C*H, Ar), 136.82 (s, *C*), 137.47 (s, *C*) (two signals of phenyl *C*H are not separated from other signals).

The synthesized 1-bromo-1,4-diphenylbut-3-yn-2-ol (6.0 g, 20.0 mmol) was dissolved in dimethyl sulfoxide (30 mL) and added to a solution of sodium azide (2.6 g, 40 mmol) in dimethyl sulfoxide (10 mL). The mixture was stirred overnight at room temperature, diluted with water, and extracted with diethyl ether. The organic layer was washed with water and dried over magnesium sulfate. The diethyl ether was removed under reduced pressure at low temperature to afford the azidohydrin, which was directly used for the next step.

1-Azido-1,4-diphenylbut-3-yn-2-ol (both stereoisomers)

Orange-brown oil; yield (90%). IR ($CDCl_3$): $\tilde{\nu}$ = 3585 (OH), 2109 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.78 (s, 1H, O*H*), 2.88 (s, 1H, O*H*), 4.74–4.80 (m, 3H, C*H*), 4.81 (d, ^3J = 5.0 Hz, 1H, C*H*), 7.14–7.88 (m, 20H, C*H*, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 66.79 (d, *C*H), 66.84 (d, *C*H), 69.82 (d, *C*H), 70.43 (d, *C*H), 85.85 (s, *C*≡*C*), 86.06 (s, *C*≡*C*), 87.39 (s, *C*≡*C*), 87.54 (s, *C*≡*C*), 121.77 (s, *C*), 121.84 (s, *C*), 127.75 (d, *C*H, Ar), 127.81 (d, *C*H, Ar), 128.15 (d, *C*H, Ar), 128.19 (d, *C*H, Ar), 128.48 (d, *C*H, Ar), 128.53 (d, *C*H, Ar), 128.63 (d, *C*H, Ar), 128.67 (d, *C*H, Ar), 128.76 (d, *C*H, Ar), 128.79 (d, *C*H, Ar), 131.49 (d, *C*H, Ar), 131.60 (d, *C*H, Ar), 135.06 (s, *C*), 135.40 (s, *C*).

To a solution of 1-azido-1,4-diphenylbut-3-yn-2-ol (7.00 g, 37.4 mmol) and dry dichloromethane (40 mL) was added triethylamine (2.28 g, 22.6 mmol). The mixture was charged with methanesulfonyl chloride (1.95 g, 17.0 mmol) at 0 °C and stirred at ambient temperature for 30 h. After adding water, it was extracted with chloroform, the organic layer washed with hydrochloric acid, aqueous sodium bicarbonate and water, and dried over magnesium sulfate. The volatiles were removed under reduced pressure, and the crude product was purified by flash chromatography (diethyl ether/*n*-hexane 1:4) to afford 1-azido-1,4-diphenylbut-3-yn-2-yl methanesulfonate (1.93 g, 50%, 1:1.2 ratio of diastereomers). With the help of HPLC (diethyl ether/*n*-hexane 1:4), separation of the *syn*- and *anti*-products (this order of elution) was possible.

anti-1-Azido-1,4-diphenylbut-3-yn-2-yl methanesulfonate

Yellow oil; yield (11% after HPLC). IR ($CDCl_3$): $\tilde{\nu}$ = 2111 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.15 (s, 3H, CH_3), 4.90 (d, ^3J = 7.5 Hz, 1H, C*H*N_3), 5.49 (d, ^3J = 7.5 Hz, 1H, OC*H*), 7.19–7.49 (m, 10H, C*H*, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 39.31 (q, *C*H_3), 67.95 (d, *C*H), 73.91 (d, *C*H), 81.31 (s, *C*≡*C*), 90.94 (s, *C*≡*C*), 120.64 (s, *C*), 127.99 (d, *C*H, Ar), 128.36 (d, *C*H, Ar), 128.73 (d, *C*H, Ar), 129.37 (d, *C*H, Ar), 129.49 (d, *C*H, Ar), 131.67 (d, *C*H, Ar), 134.00 (s, *C*).

syn-1-Azido-1,4-diphenylbut-3-yn-2-yl methanesulfonate

Yellow oil; yield (10% after HPLC). IR ($CDCl_3$): $\tilde{\nu}$ = 2111 (N_3) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.04 (s, 3H, CH_3), 5.00 (d, ^3J = 5.0 Hz, 1H, C*H*N_3), 5.54 (d, ^3J = 5.0 Hz,

1H, OC*H*), 7.26–7.51 (m, 10H, C*H*, Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 39.18 (q, *C*H_3), 67.72 (d, *C*H), 73.94 (d, *C*H), 80.93 (s, *C*≡*C*), 90.81 (s, *C*≡*C*), 120.72 (s, *C*), 127.82 (d, *C*H, Ar), 128.41 (d, *C*H, Ar), 128.74 (d, *C*H, Ar), 129.28 (d, *C*H, Ar), 129.56 (d, *C*H, Ar), 131.86 (d, *C*H, Ar), 133.89 (s, *C*).

1-Azido-1,4-diphenylbut-3-yn-2-yl methanesulfonate (76 mg, 0.22 mmol) was dissolved in dimethyl sulfoxide (1 mL), charged with sodium azide (30 mg, 0.46 mmol) and stirred at 30 °C for 22.5 h. The workup of **2cc** was carried out as described at the workup of the azidohydrin. It turned out that *syn*-methanesulfonate led to *anti*-**2cc** and the *anti*-substrate yielded *syn*-**2cc**. The diazides were directly utilized for the synthesis of NH-1,2,3-triazoles.

anti-3,4-Diazido-1,4-diphenylbut-1-yne (anti-2cc)

Light-yellow oil; yield (70%). IR ($CDCl_3$): $\tilde{\nu}$ = 2107 (N_3) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 4.51 (d, ^3J = 5.3 Hz, 1H, C*H*), 4.76 (d, ^3J = 5.3 Hz, 1H, C*H*), 7.04–7.69 (m, 10H, C*H*, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 58.09 (d, C≡C*C*H), 68.51 (d, *C*HPh), 80.48 (s, *C*≡*C*), 90.08 (s, *C*≡*C*), 121.35 (s, *C*), 127.61 (d, *C*H), 128.36 (d, *C*H), 128.72 (d, *C*H), 129.13 (d, 2 x *C*H), 131.96 (d, *C*H), 135.12 (s, *C*).

syn-3,4-Diazido-1,4-diphenylbut-1-yne (syn-2cc)

Light-yellow oil; yield (67%). IR ($CDCl_3$): $\tilde{\nu}$ = 2108 (N_3) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 4.52 (d, ^3J = 6.7 Hz, 1H, C*H*), 4.76 (d, ^3J = 6.7 Hz, 1H, C*H*), 7.17–7.70 (m, 10H, C*H*, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 58.05 (d, C≡C*C*H), 68.57 (d, *C*HPh), 80.98 (s, *C*≡*C*), 89.86 (s, *C*≡*C*), 121.22 (s, *C*), 127.74 (d, *C*H), 128.30 (d, *C*H), 128.60 (d, *C*H), 129.07 (d, *C*H), 129.10 (d, *C*H), 131.79 (d, *C*H), 135.18 (s, *C*).

References

S-1. For potential hazards in handling hydrazoic acid and organic azides, see: Keicher, T.; Löbbecke, S. In *Organic Azides: Syntheses and Applications*, Bräse, S.; Banert, K. (Eds.); Wiley: Chichester, UK, 2010, pp. 3–27.

S-2. Brandsma, L. Preparative Acetylenic Chemistry, sec. ed.; Elsevier: Amsterdam, 1988, pp. 247–248.

