Electronic Supplementary Material (ESI) for Catalysis Science & Technology

Electronic Supplementary Information ESI for:

Zinc-Catalyzed Meinwald Rearrangement of Tetrasubstituted 1-Alkynyloxiranes to Tertiary α-Alkynylketones

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General remarks.

All reactions were carried out under nitrogen using standard Schlenk techniques. Dichloromethane and 1,2-dichloroethane were distilled from CaH_2 under nitrogen atmosphere. Solvents for column chromatography were obtained from commercial suppliers and used without further purification. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator. Flash column chromatography was carried out on silica gel (230-240 mesh). ^{1}H-NMR (300, 400 MHz) and ^{13}C-NMR (75.5 and 100 MHz) spectra were recorded at ambient temperature in $CDCl_3$ on a Bruker DPX-300, or Bruker AVANCE-300 MHz and 400 MHz instruments. Chemical shifts (δ) are given in ppm relative to TMS (^{1}H, 0.0 ppm) or $CDCl_3$ (^{13}C, 77.0 ppm). Carbon multiplicities were assigned by DEPT experiments. High-resolution mass spectra were recorded in an Agilent 6520Q-TOF and a Finnigan Mat95 spectrometers.

The preparation of starting 1-alkynyloxiranes **1** was accomplished following previously reported procedures.[1] All catalysts were purchased from commercial suppliers of the best commercial grade available, used without further purification and stored under inert atmosphere at 0–4 ºC.

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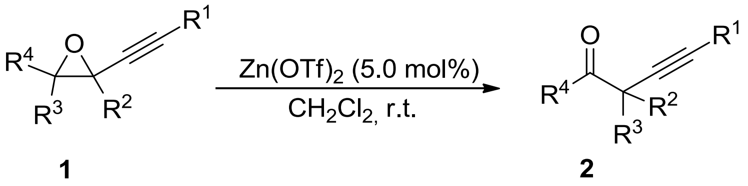
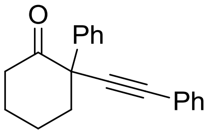
[1] M. J. González, J. González and R. Vicente, *Eur. J. Org. Chem.* 2012, 6140.

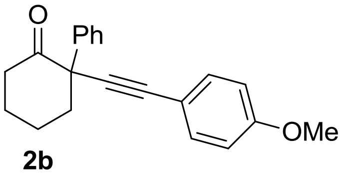
Representative procedure for $Zn(OTf)_2$-catalyzed rearrangement of 1-alkynyloxiranes 1 to *α*-alkynylketones 2.





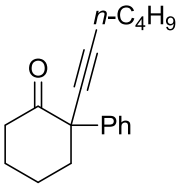
2a

2-Phenyl-2-(phenylethynyl)cyclohexanone (2a): To a stirred solution of $Zn(OTf)_2$ (9.0 mg, 5.0 mol%) in CH_2Cl_2 (ca. 0.1 M) at 20 ºC, the corresponding alkynyl epoxide **1a** (137 mg, 0.5 mmol) was added in one portion. The resulting mixture was stirred at this temperature until the consumption of **1a** (checked by TLC analysis). Then, the solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) to yield **2a** (125 mg, 91%) as a white solid. M. p. = 81-83 ºC. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.57-7.52 (m, 4H), 7.44-7.35 (m, 6H), 3.23 (dt, *J* = 13.5, 5.9 Hz, 1H), 2.51 (ddd, *J* = 14.4, 12.6, 3.5 Hz, 1H), 2.44-2.30 (m, 3H), 2.26-2.13 (m, 1H), 2.00-1.81 (m, 2H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 206.8 (C), 139.8 (C), 132.1 (2 x CH), 128.9 (CH), 128.8 (2 x CH), 128.6 (2 x CH), 128.3 (2 x CH), 127.8 (CH), 123.3 (C), 89.8 (C), 89.3 (C), 56.9 (C), 42.0 (CH_2), 39.7 (CH_2), 28.1 (CH_2), 23.1 (CH_2). **HR-MS** (IE) calc. for $[C_{20}H_{18}O]^+$ 274.1358, found 274.1361. The spectroscopic data are in accordance with those previously reported.[1]



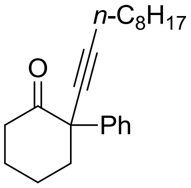
2b

2-((4-Methoxyphenyl)ethynyl)-2-phenylcyclohexanone (2b): The representative procedure was followed using epoxide **1b** (152 mg, 0.5 mmol). After 2 h, purification by flash column chromatography (hexanes/ethyl acetate = 3:1, SiO_2) afforded **2b** (135 mg, 89%) as a white solid (M. p. = 98-100 ºC). **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.54-7.50 (m, 2H), 7.46 (d, *J* = 8.9 Hz, 2H), 7.44-7.38 (m, 2H), 7.35-7.30 (m, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.85 (s, 3H), 3.22 (ddd, *J* = 13.9, 13.0, 6.1 Hz, 1H), 2.50 (dddd, *J* = 13.9, 4.5, 3.4, 1.3 Hz, 1H), 2.14-2.29 (m, 3H), 2.25-2.13 (m, 1H), 1.99-1.79 (m, 2H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 206.7 (C), 159.7 (C), 139.6 (C), 133.1 (2 x CH), 128.1 (2 x CH), 127.9 (2 x CH), 127.3 (CH), 115.0 (C), 114.0 (2 x CH), 88.8 (C), 87.8 (C), 56.5 (C), 55.3 (CH_3), 41.7 (CH_2), 39.2 (CH_2), 27.7 (CH_2), 22.7 (CH_2). **HR-MS** (IE) calc. for $[C_{21}H_{20}O_2]^+$ 304.1463, found 304.1467. The spectroscopic data are in accordance with those previously reported.[1]



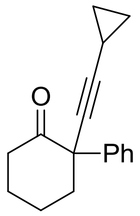
2c

2-(Hex-1-yn-1-yl)-2-phenylcyclohexanone (2c): The representative procedure was followed using epoxide **1c** (127 mg, 0.5 mmol). After 6 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2c** (100 mg, 79%) as a colorless oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.46 (d_{ap}, J = 8.1 Hz, 2H), 7.39 (dd, J = 8.1, 7.1 Hz, 2H), 7.33-7.28 (m, 1H), 3.15 (ddd, J = 13.4, 12.5, 6.0 Hz, 1H), 2.44 (ddd, J = 12.5, 4.6, 1.4 Hz, 1H), 2.36 (t, J = 7.0 Hz, 2H), 2.29-2.12 (m, 4H), 1.97-1.73 (m, 2H), 1.60 (quint, J = 7.3 Hz, 2H), 1.50 (quint, J = 7.7 Hz, 2H), 0.97 (t, J = 7.2 Hz, 3H) (*subindex ap denotes apparent*). **^{13}C-NMR** (75 MHz, $CDCl_3$): 207.3 (C), 140.1 (C), 128.0 (2 x CH), 127.9 (2 x CH), 127.1 (CH), 89.5 (C), 80.0 (C), 56.0 (C), 41.8 (CH_2), 39.0 (CH_2), 30.9 (CH_2), 27.6 (CH_2), 22.6 (CH_2), 22.1 (CH_2), 18.7 (CH_2), 13.6 (CH_3). **HR-MS** (IE) calc. for $[C_{18}H_{22}O]^+$ 254.1671, found 254.1672. The spectroscopic data are in accordance with those previously reported.[1]



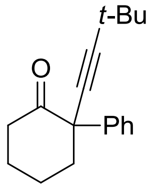
2d

2-(Dec-1-yn-1-yl)-2-phenylcyclohexanone (2d): The representative procedure was followed using epoxide **1d** (155 mg, 0.5 mmol). After 8 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2d** (102 mg, 66%) as a yellow oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.48-7.44 (m, 2H), 7.40-7.36 (m, 2H), 7.32-7.27 (m, 1H), 3.15 (ddd, J = 14.0, 13.0, 6.0 Hz, 1H), 2.43 (dddd, J = 14.0, 4.6, 3.4, 1.6 Hz, 1H), 2.35 (t, J = 6.9 Hz, 2H), 2.30-2.11 (m, 4H), 1.91-1.74 (m, 2H), 1.60 (quint, J = 6.9 Hz, 2H), 1.41-1.39 (m, 2H), 1.39-1.25 (m, 8H), 0.91 (t, J = 7.0 Hz, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 207.3 (C), 140.1 (C), 128.0 (2 x CH), 127.9 (2 x CH), 127.2 (CH), 89.6 (C), 80.1 (C), 56.0 (C), 41.8 (CH_2), 39.0 (CH_2), 31.8 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 27.6 (CH_2), 22.7 (CH_2), 22.6 (CH_2), 19.0 (CH_2), 14.1 (CH_3). **HR-MS** (IE) calc. for $[C_{22}H_{30}O]^+$ 310.2297, found 310.2300. The spectroscopic data are in accordance with those previously reported.[1]



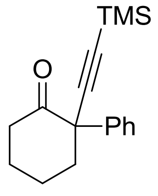
2e

2-(Cyclopropylethynyl)-2-phenylcyclohexanone (2e): The representative procedure was followed using epoxide **1e** (119 mg, 0.5 mmol). After 2 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2e** (64 mg, 54%) as a colorless oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.46-7.35 (m, 4H), 7.33-7.27 (m, 1H), 3.11 (ddd, J = 13.8, 12.5, 6.0 Hz, 1H), 2.42 (dddd, J = 13.8, 5.1, 3.4, 1.4 Hz, 1H), 2.30-2.11 (m, 4H), 1.94-1.73 (m, 2H), 1.40 (tt, J = 8.3, 5.1 Hz, 1H), 0.88-0.81 (m, 2H), 0.80-0.74 (m, 2H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 207.1 (C), 140.0 (C), 128.0 (2 x CH), 127.8 (2 x CH), 127.1 (CH), 92.5 (C), 75.2 (C), 55.9 (C), 41.7 (CH_2), 39.0 (CH_2), 27.6 (CH_2), 22.6 (CH_2), 8.4 (CH_2), 8.3 (CH_2), -0.2 (CH). **HR-MS** (IE) calc. for $[C_{17}H_{18}O]^+$ 238.1358, found 238.1554. The spectroscopic data are in accordance with those previously reported.[1]



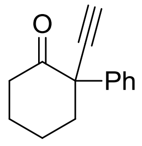
2f

2-(3,3-Dimethylbut-1-yn-1-yl)-2-phenylcyclohexanone (2f): The representative procedure was followed using epoxide **1f** (127 mg, 0.5 mmol). After 16 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2f** (120 mg, 94%) as a white solid (M. p. = 87-89 ºC). **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.49-7.45 (m, 2H), 7.42-7.36 (m, 2H), 7.34-7.28 (m, 1H), 3.20 (ddd, J = 13.8, 12.6, 6.1 Hz, 1H), 2.43 (dd, J = 13.8, 1.6 Hz, 1H), 2.15-1.91 (m, 4H), 1.91-1.73 (m, 2H), 1.34 (s, 9H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 207.3 (C), 140.1 (C), 127.9 (4 x CH), 127.1 (CH), 98.2 (C), 78.6 (C), 55.9 (C), 42.1 (CH_2), 39.0 (CH_2), 31.0 (3 x CH_3), 27.8 (C), 27.6 (CH_2), 22.7 (CH_2). **HR-MS** (IE) calc. for $[C_{18}H_{22}O]^+$ 254.1671, found 254.1676. The spectroscopic data are in accordance with those previously reported.[1]



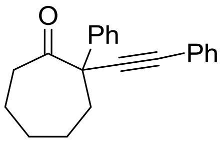
2g

2-Phenyl-2-((trimethylsilyl)ethynyl)cyclohexanone (2g): The representative procedure was followed using epoxide **1g** (135 mg, 0.5 mmol). After 5 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2g** (104 mg, 77%) as a white solid (M. p. = 85-87 ºC). **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.48-7.44 (m, 2H), 7.42-7.36 (m, 2H), 7.34-7.29 (m, 1H), 3.19 (ddd, *J* = 13.6, 12.5, 6.2 Hz, 1H), 2.45 (dddd, *J* = 13.6, 4.3, 3.1, 1.6 Hz, 1H), 2.36-2.15 (m, 4H), 1.94-1.75 (m, 2H), 0.26 (s, 9H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 206.4 (C), 139.1 (C), 128.0 (2 x CH), 127.9 (2 x CH), 127.3 (CH), 105.6 (C), 93.9 (C), 57.1 (C), 41.7 (CH_2), 39.0 (CH_2), 27.6 (CH_2), 22.6 (CH_2), -0.1 (3 x CH_3). **HR-MS** (IE) calc. for $[C_{17}H_{22}OSi]^+$ 270.1440, found 270.1442. The spectroscopic data are in accordance with those previously reported.[1]



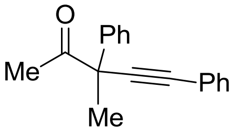
2h

2-Ethynyl-2-phenylcyclohexanone (2h): The representative procedure was followed using epoxide **1h** (99 mg, 0.5 mmol). After 8 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2h** (82 mg, 83%) as a pale yellow oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.48-7.30 (m, 5H), 3.09 (ddd, *J* = 13.7, 11.7, 5.9 Hz, 1H), 2.71 (s, 1H), 2.51-2.08 (m, 5H), 1.95-1.78 (m, 2H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 206.3 (C), 138.7 (C), 128.3 (2 x CH), 127.6 (2 x CH), 127.5 (CH), 84.2 (C), 76.5 (CH), 55.7 (C), 40.9 (CH_2), 39.0 (CH_2), 27.7 (CH_2), 22.3 (CH_2). **HR-MS** (IE) calc. for $[C_{14}H_{14}O]^+$ 198.1045, found 198.1042. The spectroscopic data are in accordance with those previously reported.[1]



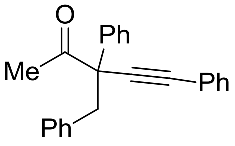
2i

2-Phenyl-2-(phenylethynyl)cycloheptanone (2i): The representative procedure was followed using epoxide **1i** (144 mg, 0.5 mmol) in 1,2-dichloroethane. After 14 h at 70 ºC, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2i** (95 mg, 66%) as a pale yellow oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.60-7.56 (m, 2H), 7.54-7.48 (m, 2H), 7.52-7.28 (m, 6H), 2.86-2.71 (m, 2H), 2.42 (dd, *J* = 5.5, 5.3 Hz, 2H), 2.07-1.82 (m, 5H), 1.64-1.51 (m, 1H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 208.8 (C), 141.1 (C), 131.8 (2 x CH), 128.5 (2 x CH), 128.2 (2 x CH), 128.1 (CH), 127.4 (CH), 127.1 (2 x CH), 123.2 (C), 90.9 (C), 86.0 (C), 58.4 (C), 41.8 (CH_2), 38.5 (CH_2), 29.9 (CH_2), 25.9 (CH_2), 25.6 (CH_2). **HR-MS** (IE) calc. for $[C_{21}H_{20}O]^+$ 288.1514, found 288.1513. The spectroscopic data are in accordance with those previously reported.[1]



2j

3-Methyl-3,5-diphenylpent-4-yn-2-one (2j): The representative procedure was followed using epoxide **1j** (124 mg, 0.5 mmol) in 1,2-dichloroethane. After 15 h at 70 ºC, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2j** (78 mg, 63%) was obtained as a yellow oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.62-7.51 (m, 4H), 7.46-7.32 (m, 6H), 2.25 (s, 3H), 1.78 (s, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 204.2 (C), 140.3 (C), 131.7 (2 x CH), 128.9 (2 x CH), 128.5 (CH), 128.4 (2 x CH), 127.6 (CH), 126.4 (2 x CH), 122.9 (C), 89.7 (C), 87.3 (C), 54.3 (C), 26.1 (CH_3), 26.0 (CH_3). **HR-MS** (IE) calc. for $[C_{18}H_{16}O]^+$ 248.1201, found 248.1200. The spectroscopic data are in accordance with those previously reported.[1]

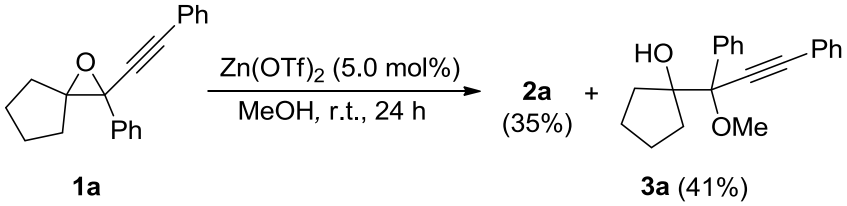


2k

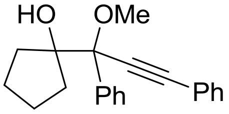
3-Benzyl-3,5-diphenylpent-4-yn-2-one (2k): The representative procedure was followed using epoxide **1k** (162 mg, 0.5 mmol). After 14 h, purification by flash column chromatography (hexanes/ethyl acetate = 5:1, SiO_2) afforded **2k** (134 mg, 83%) as a yellow oil. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.48-7.43 (m, 4H), 7.40-7.32 (m, 6H), 7.18-7.12 (m, 3H), 7.02-6.97 (m, 2H), 3.57 (d, *J* = 13.3 Hz, 1H), 3.28 (d, *J* = 13.3 Hz, 1H), 2.27 (s, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 204.0 (C), 138.1 (C), 137.0 (C), 131.5 (2 x CH), 130.8 (2 x CH), 128.7 (2 x CH), 128.5 (CH), 128.4 (2 x CH), 127.8 (CH), 127.4 (2 x CH), 127.3 (2 x CH), 126.4 (CH), 122.8 (C), 90.2 (C), 88.0 (C), 60.4 (C), 44.2 (CH_2), 27.0 (CH_3). **HR-MS** (IE) calc. for $[C_{24}H_{20}O]^+$ 324.1514, found 324.1514. The spectroscopic data are in accordance with those previously reported.[1]

Mechanistic experiments.

Scheme 5, a



To a stirred solution of $Zn(OTf)_2$ (9.0 mg, 5.0 mol%) in methanol (ca. 0.1 M) at 20 ºC, the corresponding alkynyl epoxide **1** (137 mg., 0.5 mmol) was added in one portion. The resulting mixture was stirred at this temperature until the consumption of compound **1** (checked by TLC analysis). Then, the solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (hexanes/ethyl acetate = 5:1 to 3:1, SiO_2) to afford **2a** (48 mg, 35%) and **3a** (63 mg, 41%).



3a

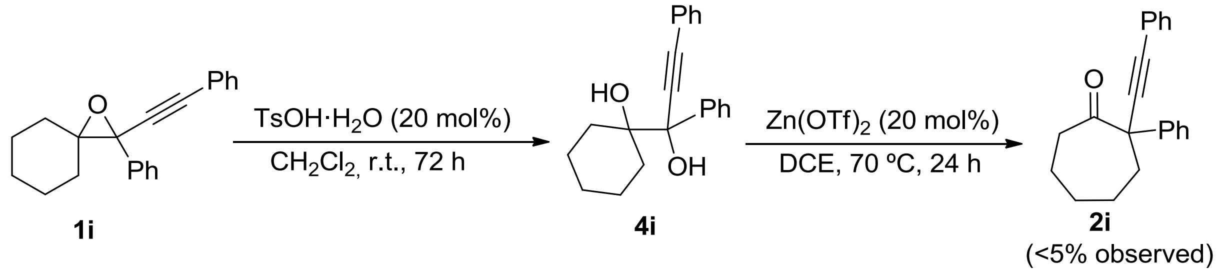
1-(1-Methoxy-1,3-diphenylprop-2-yn-1-yl)cyclopentanol (3a): Obtained as a white solid. M. p. = 107-109 ºC. ^{1}**H-NMR** (300 MHz, $CDCl_3$): 7.71-7.67 (m, 2H), 7.59-7.53 (m, 2H), 7.44-7.33 (m, 6H), 3.41 (s, 3H), 2.38-2.28 (m, 1H), 2.15 (s, 1H), 2.09-2.00 (m, 1H), 1.90-1.75 (m, 2H), 1.73-1.58 (m, 3H), 1.35-1.27 (m, 1H). ^{13}**C-NMR** (75 MHz, $CDCl_3$): 138.0 (C), 131.8 (2 x CH), 128.6 (CH), 128.33 (2 x CH), 128.25 (2 x CH), 127.8 (CH), 127.6 (2 x CH), 122.5 (C), 88.6 (C), 88.0 (C), 87.4 (C), 85.2 (C), 53.0 (CH_3), 36.8 (CH_2), 36.1 (CH_2), 24.5 (CH_2), 24.2 (CH_2). **HR-MS** (IE) calc. for $[C_{21}H_{22}O_2]^+$ 306.1620, found 306.1624. The spectroscopic data of both **2a** and **3a** are in accordance with those previously reported.[1]

Scheme 5, b

$$\mathbf{3a} \xrightarrow[CH_2Cl_2,\ r.t.,\ 24\ h]{Zn(OTf)_2\ (X\ mol\%)} \mathbf{2a} \quad \begin{array}{l} X = 5.0,\ \mathbf{2a}\ \text{(not observed)} \\ X = 20.0,\ \mathbf{2a}\ (12\%) \end{array}$$

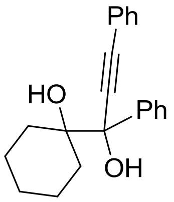
To a stirred solution of $Zn(OTf)_2$ (18 mg, 20 mol%) in CH_2Cl_2 (ca. 0.1 M) at 20 ºC, the corresponding alkynol **3a** (77 mg., 0.25 mmol) was added in one portion. The resulting mixture was stirred at this temperature for 24 h. Then, the solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (hexanes/ethyl acetate = 5:1 to 3:1, SiO_2) to afford **2a** (8 mg, 12%) and part of **3a** was recovered (63 mg, 47%). The spectroscopic data of both **2a** and **3a** are in accordance with those previously reported.[1]

Scheme 5, c



Synthesis of 4i:

To a stirred solution of $TsOH\cdot H_2O$ (19 mg, 20 mol%) in CH_2Cl_2 (ca. 0.1 M) at 20 ºC, the alkynyl epoxide **1i** (144 mg., 0.5 mmol) was added in one portion. The resulting mixture was stirred at this temperature for 72 h. Then, the solvent was removed under vacuum and the resulting residue was purified by flash column chromatography (hexanes/ethyl acetate = 3:1, SiO_2) to afford **4i** (101 mg, 66%) as a white solid.

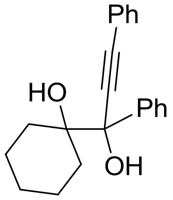


4i

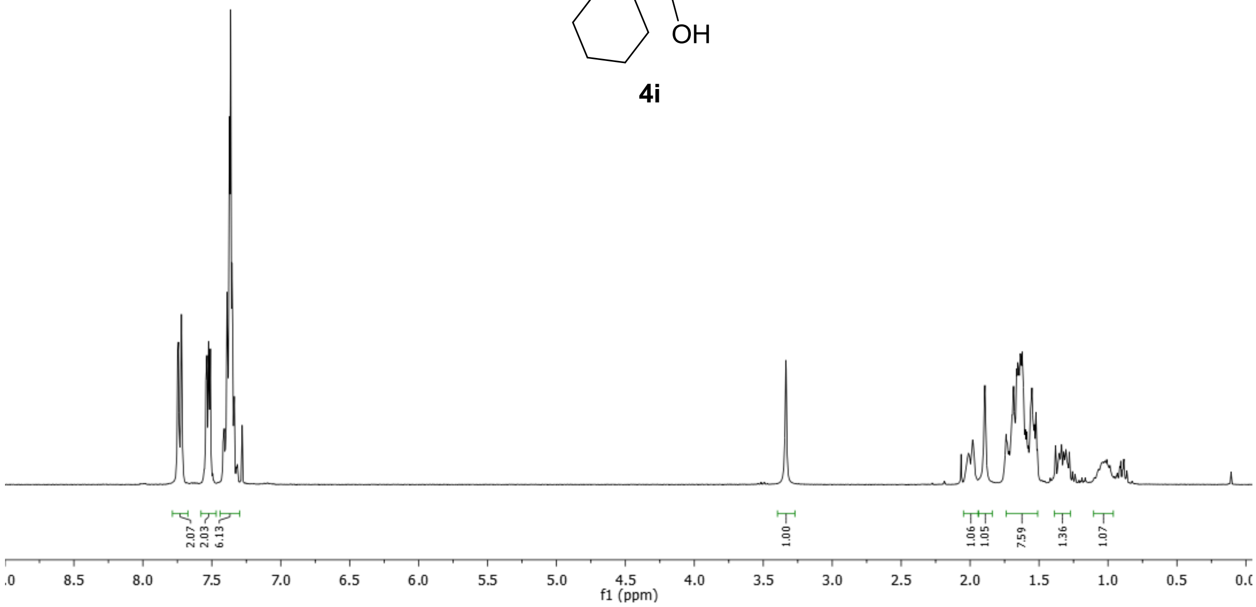
1-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)cyclohexanol (4i): M. p. = 138-140 ºC. **^{1}H-NMR** (300 MHz, $CDCl_3$): 7.75-7.72 (m, 2H), 7.54-7.51 (m, 2H), 7.42-7.31 (m, 6H), 3.34 (s, 1H), 2.05-1.96 (m, 1H), 1.89 (s, 1H), 1.74-1.51 (m, 7H), 1.38-1.28 (m, 1H), 1.07-0.97 (m, 1H). **^{13}C-NMR** (75 MHz, $CDCl_3$): 13C NMR (75 MHz, CDCl3) δ = 140.7 (C), 132.2 (2 x CH), 129.0 (CH), 128.8 (2 x CH), 128.2 (CH), 128.0 (2 x CH), 127.9 (2 x CH), 122.8 (C), 91.3 (C), 87.0 (C), 80.3 (C), 77.3 (C), 32.8 (CH_2), 30.8 (CH_2), 26.0 (CH_2), 22.1 (CH_2), 21.9 (CH_2). **HR-MS** (IE) calc. for $[C_{21}H_{22}O_2]^+$ 306.1620, found 306.1616.

Reaction of 4i in the presence of $Zn(OTf)_2$

To a stirred solution of $Zn(OTf)_2$ (7.3 mg, 20 mol%) in 1,2-dichloroethane (ca. 0.1 M) at 20 ºC, alkynol **4i** (30 mg, 0.10 mmol) was added in one portion. The resulting mixture was stirred at 70 ºC for 24 h. Then, the solvent was removed under vacuum and the resulting residue was analysed by ^{1}H-NMR, where the ketone **2i** was observed in trace amounts (<5%, measured using 1,2-dichloroethane as internal standard).


Ph
HO
Ph
OH

4i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1.00
1.06
1.05
7.59
1.36
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9.0
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8.0
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7.0
6.5
6.0
5.5
5.0
4.5
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3.5
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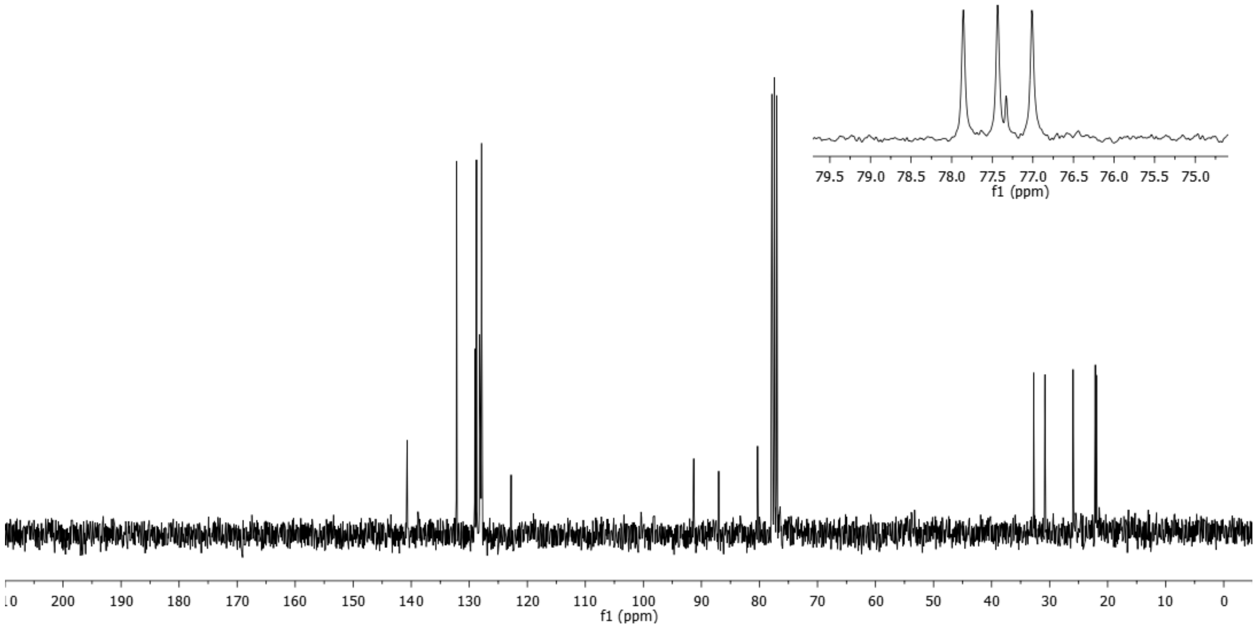
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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76.0
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75.0
f1 (ppm)
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180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)