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Zinc-Catalyzed Meinwald Rearrangement of Tetrasubstituted 1-Alkynyloxiranes to Tertiary $\alpha$-Alkynylketones

María J. González, Jesús González, Carmela Pérez-Calleja, Luis A. López,* and Rubén Vicente*

Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo
c/ Julián Clavería 8, 33006-Oviedo, Spain.
Fax: +34985103450; Tel:+34985106223;
e-mail: lalg@uniovi.es; vicenteruben@uniovi.es
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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 CaH₂ 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 F₂₅₄ indicator. Flash column chromatography was carried out on silica gel (230-240 mesh). ¹H-NMR (300, 400 MHz) and ¹³C-NMR (75.5 and 100 MHz) spectra were recorded at ambient temperature in CDCl₃ on a Bruker DPX-300, or Bruker AVANCE-300 MHz and 400 MHz instruments. Chemical shifts (δ) are given in ppm relative to TMS (¹H, 0.0 ppm) or CDCl₃ (¹³C, 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 °C.

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

$$\begin{align*}
\text{R}^4 & \quad \text{O} & \quad \text{R}^1 \\
\text{R}^3 & \quad \text{C} & \quad \text{R}^2
\end{align*}$$

2-Phenyl-2-(phenylethynyl)cyclohexanone (2a): To a stirred solution of Zn(OTf)$_2$ (9.0 mg, 5.0 mol%) in CH$_2$Cl$_2$ (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$_3$), 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.$^1$

$$\begin{align*}
\text{R}^4 & \quad \text{O} & \quad \text{Ph} & \quad \text{R}^1 \\
\text{R}^3 & \quad \text{C} & \quad \text{Ph}
\end{align*}$$

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), S-3
114.0 (2 x CH), 88.8 (C), 87.8 (C), 56.5 (CH₃), 41.7 (CH₂), 39.2 (CH₃), 27.7 (CH₂), 22.7 (CH₂).

HR-MS (IE) calc. for [C₂₁H₂₉O₂]⁺ 304.1463, found 304.1467. The spectroscopic data are in accordance with those previously reported.¹

**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, SiO₂) afforded 2c (100 mg, 79%) as a colorless oil. ¹H-NMR (300 MHz, CDCl₃): 7.46 (d, 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). ¹³C-NMR (75 MHz, CDCl₃): 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 (CH₂), 39.0 (CH₃), 30.9 (CH₃), 27.6 (CH₂), 22.6 (CH₂), 22.1 (CH₂), 18.7 (CH₂), 13.6 (CH₃). HR-MS (IE) calc. for [C₁₈H₂₉O]⁺ 254.1671, found 254.1672. The spectroscopic data are in accordance with those previously reported.¹

**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, SiO₂) afforded 2d (102 mg, 66%) as a yellow oil. ¹H-NMR (300 MHz, CDCl₃): 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 (ddd, 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). ¹³C-NMR (75 MHz, CDCl₃): 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 (CH₂), 39.0 (CH₂), 31.8 (CH₃), 29.2 (CH₂), 29.1 (CH₂), 29.0 (CH₂), 28.8 (CH₂), 27.6 (CH₃), 22.7 (CH₂), 22.6 (CH₂),
19.0 (CH₂), 14.1 (CH₃). **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

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, SiO₂) afforded 2e (64 mg, 54%) as a colorless oil. **¹H-NMR** (300 MHz, CDCl₃): 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 (ddd, 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). **¹³C-NMR** (75 MHz, CDCl₃): 207.1 (C), 140.0 (C), 128.0 (2 x CH), 127.1 (CH), 92.5 (C), 75.2 (C), 55.9 (C), 41.7 (CH₂), 39.0 (CH₂), 27.6 (CH₂), 22.6 (CH₂), 8.4 (CH₂), 8.3 (CH₂), -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

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, SiO₂) afforded 2f (120 mg, 94%) as a white solid (M. p. = 87–89 ºC). **¹H-NMR** (300 MHz, CDCl₃): 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). **¹³C-NMR** (75 MHz, CDCl₃): 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 (CH₂), 39.0 (CH₂), 31.0 (3 x CH₃), 27.8 (C), 27.6 (CH₂), 22.7 (CH₂). **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
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\textsubscript{2}) afforded 2g (104 mg, 77%) as a white solid (M. p. = 85-87 °C). \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{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 (ddddd, 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). \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{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\textsubscript{2}), 39.0 (CH\textsubscript{2}), 27.6 (CH\textsubscript{2}), 22.6 (CH\textsubscript{2}), -0.1 (3 x CH\textsubscript{3}). HR-MS (IE) calc. for [C\textsubscript{17}H\textsubscript{22}OSi]\textsuperscript{+} 270.1440, found 270.1442. The spectroscopic data are in accordance with those previously reported.\textsuperscript{1}

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\textsubscript{2}) afforded 2h (82 mg, 83%) as a pale yellow oil. \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{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). \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{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\textsubscript{2}), 39.0 (CH\textsubscript{2}), 27.7 (CH\textsubscript{2}), 22.3 (CH\textsubscript{2}). HR-MS (IE) calc. for [C\textsubscript{14}H\textsubscript{14}O]\textsuperscript{+} 198.1045, found 198.1042. The spectroscopic data are in accordance with those previously reported.\textsuperscript{1}

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 °C, 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.$^1$

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 °C, 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.$^1$

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%).

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$_3$), 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

To a stirred solution of Zn(OTf)$_2$ (18 mg, 20 mol%) in CH$_2$Cl$_2$ (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

![Scheme 5, c](image)

**Synthesis of 4i:**

To a stirred solution of TsOH·H₂O (19 mg, 20 mol%) in CH₂Cl₂ (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, SiO₂) to afford 4i (101 mg, 66%) as a white solid.

**1-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)cyclohexanol (4i):** M. p. = 138-140 ºC. ¹H-NMR (300 MHz, CDCl₃): 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). ¹³C-NMR (75 MHz, CDCl₃): 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 (CH₂), 30.8 (CH₃), 26.0 (CH₃), 22.1 (CH₂), 21.9 (CH₂). HR-MS (IE) calc. for [C₂₁H₂₂O₂]^+ 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 ¹H-NMR, where the ketone 2i was observed in trace amounts (<5%, measured using 1,2-dichloroethane as internal standard).