Pergamon

Tetrahedron 56 (2000) 2203–2209

TETRAHEDRON

A New Procedure for Construction of Oxocane and Oxonane Derivatives Based on Alkyne–$Co_2(CO)_6$ Complexes

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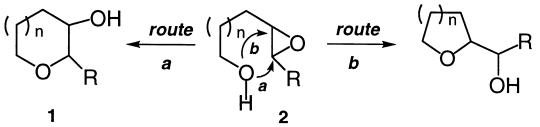
Accepted 7 December 1999

Abstract—Treatment of 2-(3-hydroxy-5-phenylpent-4-yn-1-yl)-2-(trimethylsilylmethyl)tetrahydrofuran (**18**) with $Co_2(CO)_8$ gave the corresponding cobalt complex, which was subsequently exposed to methanesulfonyl chloride and triethylamine in methylene chloride at refluxing temperature to provide the oxocane derivative **20** in 72% yield. This method was found to be applicable for construction of the oxonane framework.

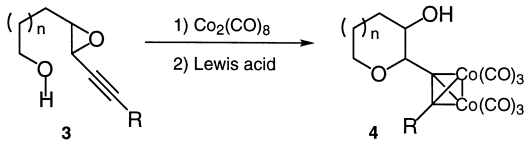
There are many oxygen atom-containing heterocycles such as tetrahydrofuran, tetrahydropyran, oxepane, and oxocane ring systems[1–3] which have frequently been found to be the major component of many biologically important natural products.[4,5] One of the most straightforward processes to build up the substituted oxygen atom-containing heterocycles like the 3-hydroxy-2-substituted derivative **1** would be ring opening of an epoxide by a terminal hydroxy group of the corresponding epoxy-alcohol species **2** via *endo* mode ring closure (Scheme 1, route *a*). According to Baldwin rules,[6] however, the *endo* mode ring closure (route *a*) is generally regarded as an unfavorable pathway and the competing *exo* mode ring closure (route *b*) is often preferred over route *a*. In order to override this disadvantage, several elegant and intriguing methods[7] (e.g. activation of epoxides by an adjacent vinyl moiety or by palladium catalyst) have already been devised.

Alkyne–$Co_2(CO)_6$ complexes, easily derived from the reaction of propynyl alcohol or ethers with dicobaltoctacarbonyl ($Co_2(CO)_8$), have been well known to liberate, upon treatment with a Lewis acid, the corresponding propynyl cation species, which were subsequently captured by various nucleophiles (Nicholas reaction).[8] In the course of our program[9] directed toward the development of highly stereoselective carbon–carbon bond formation reactions mediated by alkyne–$Co_2(CO)_6$ complexes and their application to the total syntheses of bioactive compounds, we paid much attention to the propynyl cation stabilizing ability of the alkyne–$Co_2(CO)_6$ complex for regioselective *endo* mode ring closure. We envisioned that the alkyne–$Co_2(CO)_6$ complex derived from the alkyne–epoxide **3** possessing a terminal hydroxy group would, upon exposure to acidic conditions, regioselectively generate the propynyl cation. The cation stabilized by the cobalt complex moiety might be immediately captured in an *endo* mode fashion by a terminal primary alcohol resulting in exclusive formation of the oxygen atom-containing heterocyclic skeleton **4** (Scheme 2). Thus tetrahydrofuran **4** (n=0) and tetrahydropyran derivatives **4** (n=1)[10,11] had been shown to be formed in a highly stereoselective as well as a stereospecific manner from the corresponding alkyne–epoxide **3** (n=0,1). The oxepane derivatives **4** (n=2)[12] could also be produced by using this *endo* mode cyclization. However, this procedure was found not to be useful for construction of the eight-membered congener **4** (n=3).[13] These results would lead to the conclusion that the newly developed *endo* mode ring closure can be successfully applied for the construction of five-, six- and seven-membered oxygen atom-containing heterocycles, but not for that of medium-sized oxygen atom-containing heterocycles (e.g. oxocane and oxonane species).

In order to overcome the limitation encountered during the transformation of **3** into **4**, an alternative method for the synthesis of eight-membered oxygen atom-containing



Scheme 1.



Scheme 2.

Keywords: oxonane; oxocane; oxepane.

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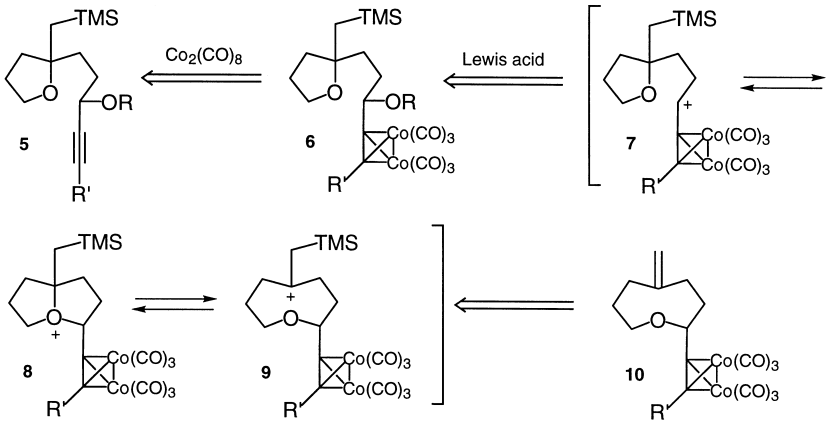
PII: S0040-4020(99)01103-5

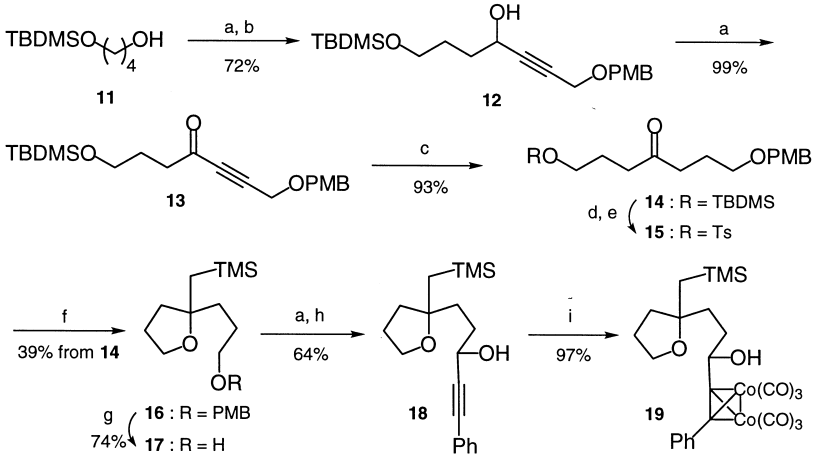


Scheme 3.

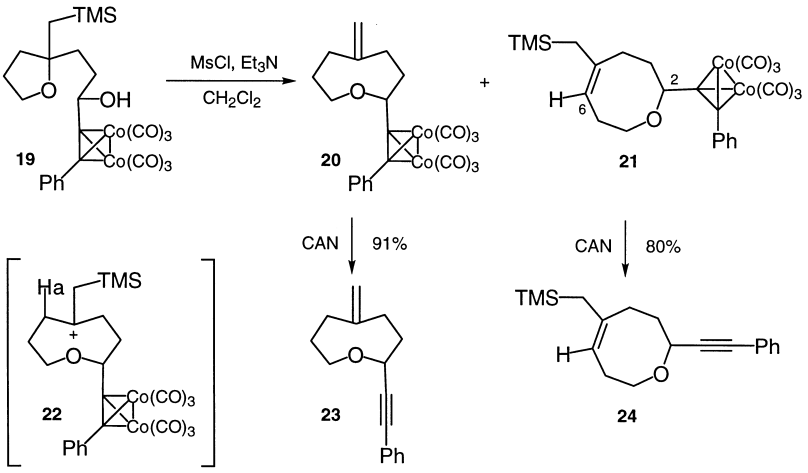
heterocycles based on alkyne–$Co_2(CO)_6$ was developed as in Scheme 3. We envisaged that treatment of the 2-trimethylsilylmethyltetrahydrofuran derivative **5** possessing a propynyl ether portion with $Co_2(CO)_8$ would afford the corresponding cobalt complex **6** as usual. Upon exposure to a Lewis acid, this complex **6** would produce the propynyl cation **7** which might be subsequently captured by an oxygen atom on the tetrahydrofuran ring resulting in the formation of the oxonium intermediate **8**. The β-effect[14] of the trimethylsilylmethyl moiety of **8** would help to generate the eight-membered cation species **9** which is then collapsed to the desired oxocane derivative **10**.[15] On the basis of this consideration, we tried to convert the tetrahydrofuran derivative **5** into the oxocane derivative **10**. This paper describes a new procedure for the preparation of eight-membered and nine-membered oxygen atom-containing heterocycles by taking advantage of the inherent property of the alkyne–$Co_2(CO)_6$ complex.

The required tetrahydrofuran derivative for construction of the oxocane derivative was prepared by conventional means (Scheme 4). Swern oxidation of 4-(*tert*-butyldimethylsiloxy)butan-1-ol (**11**) gave the corresponding aldehyde, which was subsequently treated with the acetylide, derived from 3-(*p*-methoxy-benzyloxy)propyne, at −78°C to afford the propynyl alcohol derivative **12** in 72% yield. The oxidation of **12** under Swern conditions furnished **13** in 99% yield, which was then hydrogenated under hydrogen atmosphere yielding **14** in 93% yield. Adjustment of the protecting group of **14** from TBDMS group to *p*-toluenesulfonyl (Ts) group was realized by successive exposure to tetra-*n*-butylammonium fluoride (TBAF) and Ts chloride producing **15**. Formation of the tetrahydrofuran framework was completed by reaction of **15** with trimethylsilylmethyllithium in THF at −78°C to provide the tetrahydrofuran derivative **16** in 39% overall yield from **14**. The tetrahydrofuran derivative **16** possessing all carbon units required for construction of the oxocane skeleton was thus prepared, although the chemical yield of the conversion of **14** to **16** was unsatisfactory. The next phase in this program was the introduction of the cobalt-complexed propynyl moiety in the tether of **16**. Upon treatment with DDQ, **16** underwent deprotection to easily give the alcohol **17** in 74% yield. Swern oxidation of **17** was followed by the addition of phenylacetylide to afford the adduct **18** as a mixture of diastereoisomers in 64% yield. Cobalt complexation was performed by the reaction of **18** with $Co_2(CO)_8$ in Et_2O at room temperature affording the compound **19** in 97% yield.

With the required tetrahydrofuran derivative **19** having



Scheme 4. Reactions and conditions: (a) Swern oxid.; (b) LiC≡CCH_2OPMB, THF, −78°C; (c) H_2, Pd–C, AcOEt, r.t.; (d) TBAF, THF, r.t.; (e) TsCl, Et_3N, CH_2Cl_2, r.t.; (f) $TMSCH_2Li$, THF, −78°C; (g) DDQ, CH_2Cl_2, H_2O, r.t.; (h) THF, LiC≡CPh, −78°C; (i) $Co_2(CO)_8$, Et_2O, r.t.

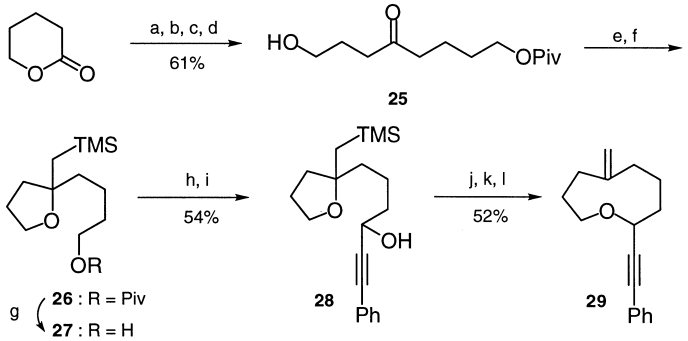


Scheme 5.

the cobalt-complexed propynyl moiety in hand, we next investigated the transformation of **19** into the oxocane derivative **20** (Scheme 5) according to our scenario described in Scheme 3. Treatment of **19** with $BF_3{\cdot}OEt_2$ in methylene chloride, however, only gave an intractable mixture. No desired oxocane derivatives could be obtained when the other Lewis acids[16] were employed. Finally, methanesulfonyl chloride (MsCl) was found to be effective for our purpose. Thus, the cobalt complex **19** was treated with MsCl in methylene chloride in the presence of triethylamine at room temperature to afford the eight-membered *exo*-methylene product **20** in 54% yield along with the *endo*-olefin product **21**[17] in 23% yield. When the reaction was carried out at refluxing temperature in methylene chloride, **20** could be isolated as the sole product in 72% yield. The formation of these two oxocanes, **20** and **21**, can be tentatively rationalized in terms of the intermediacy of the carbocation **22**, stabilized by the β-trimethylsilyl (TMS) group,[14] leading to **20** and **21** through elimination of the β-TMS group[18] and the β-hydrogen (Ha), respectively. Decomplexation of **20** and **21** under standard conditions with cerium ammonium nitrate (CAN) furnished **23** and **24** in 91 and 80% yields, respectively.

A new procedure for construction of the oxocane skeleton was developed based on the chemistry of the alkyne–$Co_2(CO)_6$ complex. The next phase of our study now involved the application of these conditions to prepare other medium sized oxygen atom containing heterocycles. Thus, we chose the oxanone derivative (oxygen atom-containing nine-membered heterocycle) as the second target molecule in this program. The starting δ-valerolactone was successively exposed to the following conditions: addition of the acetylide of 3-(*tert*-butyldimethylsiloxy)propyne, hydrogenation, protection of the resulting hydroxy group with a pivaloyl group, and acid hydrolysis leading to **25** in 61% overall yield. The formation of the tetrahydrofuran framework was realized by the consecutive reaction of **25** with Ts chloride and trimethylsilylmethyllithium to furnish **26**, the pivaloyl protecting group of which was then removed by diisobutylaluminum hydride (DIBAL-H) producing **27** in 26% yield from **25**. Next, the propynyl alcohol derivative **28** was obtained in 54% yield from **27** according to the procedure described for the conversion of **17** to **18**. Treatment of **28** with $Co_2(CO)_8$ provided the corresponding cobalt-complex, which was exposed to the conditions, developed for the conversion of **19** to the oxocane derivative **20** (MsCl, Et_3N, CH_2Cl_2, room temperature), to afford only one product with cobalt complexation. The cobalt complexed **29** was then exposed to CAN in methanol at room temperature to provide the desired oxonane derivative **29** in 52% yield (Scheme 6).

We have developed a new method for the preparation of the



Scheme 6. Reagents and conditions: (a) LiC≡$CCH_2OTBDMS$, THF, −78°C; (b) H_2, Pd–C, AcOEt, r.t.; (c) PivCl, Et_3N, CH_2Cl_2, r.t.; (d) 10% HCl aq., THF, rt; (e) TsCl, DMAP, Et_3N, CH_2Cl_2, rt; (f) $TMSCH_2Li$, THF, −78°C; (g) DIBAL–H, CH_2Cl_2, −78°C (26% from **25**); (h) Swern oxid.; (i) LiC≡CPh, THF, −78°C; (j) $Co_2(CO)_8$, Et_2O, rt; (k) MsCl, Et_3N, CH_2Cl_2, rt; (l) CAN, MeOH, rt.

oxocane as well as the oxonane skeletons by taking advantage of the inherent property of the alkyne–$Co_2(CO)_6$ complex. In combination with the previously reported *endo* mode cyclization procedure of cobalt-complexed epoxy derivatives for construction of tetrahydrofuran and tetrahydropyran frameworks, this method could provide a powerful tool for the preparation of five-membered through medium-sized oxygen atom-containing heterocycles. Further studies in line with this strategy as well as its application to the total synthesis of natural products are now in progress.

Experimental

Infrared spectra were measured with a Shimazu IR-460 spectrometer in $CHCl_3$, mass spectra with a Hitachi M-80 mass spectrometer, ^1H NMR spectra with JEOL JNM-EX270 and JNM-GSX500 spectrometers for samples in $CDCl_3$, using either tetramethylsilane as an internal standard for compounds that have no silyl group or $CHCl_3$ (7.26 ppm) for compounds possessing the silyl group, and ^{13}C NMR spectra with JEOL JNM-EX270 and JNM-GSX500 spectrometers in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal reference. CH_2Cl_2 was freshly distilled from P_2O_5, and THF from sodium diphenylketyl prior to use. Silica gel (Silica gel 60, 230–400 mesh, Merck) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4. All reactions were carried out under nitrogen atmosphere. Reactions involving the complexation with $Co_2(CO)_8$ and decomplexation of the alkyne–$Co_2(CO)_6$ complexes should be carried out under well ventilated conditions since carbon monoxide is produced.

(±)-7-(*tert*-Butyldimethylsiloxy)-1-[(*p*-methoxybenzyl)oxy]-2-heptyn-4-ol (12). A solution of DMSO (1.70 mL, 24.0 mmol) in CH_2Cl_2 (10 mL) was added to a solution of oxalyl chloride (1.05 mL, 12.0 mmol) in CH_2Cl_2 (80 mL) at −78°C over a period of 5 min. After the mixture was stirred for 30 min, a solution of **11** (2.04 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added to the CH_2Cl_2 solution, and the reaction mixture was stirred at the same temperature for 90 min. Et_3N (6.97 mL, 50.0 mmol) was then added to the reaction mixture, which was gradually warmed to room temperature and diluted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane–AcOEt (10:1) to leave the crude aldehyde. To a solution of 3-[(*p*-methoxybenzyl)oxy]prop-1-yne (1.94 g, 11.0 mmol) in THF (90 mL) was added *n*-BuLi in hexane (1.47 M 7.48 mL, 11.0 mmol) at −78°C. After the mixture was stirred for 30 min, a solution of the crude aldehyde in THF (10 mL) was added to the THF solution, and the reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl and extracted with AcOEt which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (6:1) afforded **12** (2.72 g, 72%) as a colorless oil: MS *m/z* (%) 378 (M^+, 0.2), 360 (0.3), 291 (32), 199 (30), 121 (100), 91 (15); IR 3339 (OH) cm^{-1}; ^1H NMR δ 7.28–7.27 (2H, m, aromatic H), 6.89–6.86 (2H, m, aromatic H), 4.52 (2H, s, benzylic H), 4.50 (1H, m, C_4–H), 4.17 (2H, d, J=1.5 Hz, C_1–H), 3.81 (3H, s, OMe), 3.73–3.64 (2H, m, C_7–H), 1.90–1.66 (4H, m, CH_2), 0.90 (9H, s, *t*-Bu–Si), 0.07 (6H, s, Me–Si); ^{13}C NMR δ 59.33, 129.73, 129.47, 113.78, 87.54, 80.48, 71.12, 63.16, 62.10, 57.05, 55.25, 35.34, 28.51, 25.87, 18.27. Anal. Calcd for $C_{21}H_{34}O_4Si$: C, 66.62; H, 9.05. Found: C, 66.24; H, 9.20.

7-(*tert*-Butyldimethylsiloxy)-1-[(*p*-methoxybenzyl)oxy]-2-heptyn-4-one (13). According to the procedure described for Swern oxidation of **11**, **12** (1.50 g, 3.96 mmol) was oxidized with DMSO (0.67 mL, 9.51 mmol), oxalyl chloride (0.42 mL, 4.75 mmol), and Et_3N (2.76 mL, 19.8 mmol) to afford, after chromatography with hexane–AcOEt (10:1), **13** (1.48 g, 99%) as a pale yellow oil: MS *m/z* (%) 376 (M^+, 0.3), 319 (13), 289 (90), 121 (100), 75 (37); IR 1675 (CO) cm^{-1}; ^1H NMR δ 7.29–7.27 (2H, m, aromatic H), 6.9–6.88 (2H, m, aromatic H), 4.55 (2H, s, benzylic H), 4.29 (2H, s, C_1–H), 3.81 (3H, s, OMe), 3.64 (2H, t, J=6.4 Hz, C_7–H), 2.67 (2H, t, J=7.3 Hz, C_5–H), 1.99 (2H, tt, J=7.3, 6.4 Hz, C_6–H), 0.89 (9H, s, *t*-Bu–Si), 0.05 (6H, s, Me–Si); ^{13}C NMR δ 186.48, 158.83, 129.12, 128.01, 113.19, 86.86, 84.66, 76.76, 76.30, 75.81, 70.92, 61.04, 55.80, 54.54, 41.26, 26.17, 25.16, 17.54, −6.12. Anal. Calcd for $C_{21}H_{32}O_4Si$: C, 66.98; H, 8.57. Found: C, 66.66; H, 8.73.

7-(*tert*-Butyldimethylsiloxy)-1-[(*p*-methoxybenzyl)oxy]-heptan-4-one (14). A solution of **13** (387 mg, 1.03 mmol) in AcOEt (10 mL) was hydrogenated in the presence of 5% Pd–C (39.0 mg) under hydrogen atmosphere for 3 h at room temperature. The catalyst was removed by passing through a short pad of Celite and the filtrate was concentrated to dryness. Chromatography of the residue with hexane–AcOEt (10:1) afforded **14** (361 mg, 93%) as a colorless oil: MS *m/z* (%) 380 (M^+, 1.7), 323 (4), 185 (38), 121 (100), 75 (73); IR 1710 (CO) cm^{-1}; ^1H NMR δ 7.25–7.22 (2H, m, aromatic H), 6.89–6.86 (2H, m, aromatic H), 4.41 (2H, s, benzylic H), 3.80 (3H, s, OMe), 3.59 (2H, t, J=6.3 Hz, CH_2), 3.44 (2H, t, J=6.3 Hz, CH_2), 2.52 (2H, t, J=7.3 Hz, CH_2), 2.47 (2H, t, J=7.3 Hz, CH_2), 1.90–1.84 (2H, m, CH_2), 1.79–1.74 (2H, m, CH_2), 0.88 (9H, s, *t*-Bu–Si), 0.03 (6H, Me–Si); ^{13}C NMR δ 210.64, 159.12, 130.48, 129.22, 113.73, 72.47, 69.04, 62.16, 55.22, 39.39, 39.12, 26.79, 25.89, 23.85, 18.27, −5.39; HRMS calcd for $C_{21}H_{36}O_4Si$ 380.2383, found 380.2386. Anal. Calcd for $C_{21}H_{36}O_4Si$: C, 66.27; H, 9.53. Found: C, 65.86; H, 9.61.

(±)-2-[3′-((*p*-Methoxybenzyl)oxy)prop-1′-yl]-2-(trimethylsilylmethyl)tetrahydrofuran (16). To a solution of **14** (2.00 g, 5.25 mmol) in THF (53 mL) was added TBAF in THF (1.0 M, 7.88 mL, 7.88 mmol) at room temperature and the mixture was stirred for 30 min. The reaction mixture was diluted with water and extracted with AcOEt, which was washed with water and brine, dried, and concentrated to dryness. The crude alcohol was dissolved in CH_2Cl_2 (53 mL), to which TsCl (2.00 g, 10.5 mmol) and Et_3N (2.93 mL, 21.0 mmol) was added at room temperature. The reaction mixture was stirred for 10 h at room temperature and washed with water and brine, dried, and concentrated to dryness. Trimethylsilylmethyllithium in pentane (1.0 M 7.88 mL, 7.88 mmol) was added to a solution of the crude tosylate **15** in THF (53 mL) at −78°C. The reaction

mixture was stirred for 30 min, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (10:1) afforded **16** (689 mg, 39% from **14**) as a pale yellow oil: MS *m/z* (%) 336 (M^+, 4), 318 (9), 215 (6), 157 (12), 137 (20), 121 (100), 73 (56); ^{1}H NMR δ 7.23–7.20 (2H, m, aromatic H), 6.85–6.82 (2H, m, aromatic H), 4.43 (2H, s, benzylic H), 3.82–3.72 (2H, m, C_5–H), 3.80 (3H, s, OMe), 3.44 (2H, d, J=6.8 Hz $C_{3'}$–H), 1.95–1.46 (8H, m, CH_2), 1.08, 0.98 (2H, AB-q, J=14.7 Hz, $TMSCH_2$), 0.04 (9H, s, TMS); ^{13}C NMR δ 159.03, 130.76, 129.13, 113.69, 85.05, 72.42, 70.59, 66.54, 55.24, 37.68, 37.38, 28.88, 26.08, 25.00, 0.22; HRMS calcd for $C_{19}H_{32}O_3Si$ 336.2121, found 336.2118.

(±)-2-(3′-Hydroxyprop-1′-yl)-2-(trimethylsilylmethyl)-tetrahydrofuran (17). DDQ (506 mg, 2.23 mmol) was added to a solution of **16** (500 mg, 1.49 mmol) in CH_2Cl_2 and H_2O (15 mL, 20:1). The reaction mixture was stirred at room temperature for 20 min, quenched by addition of saturated aqueous $NaHCO_3$, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (10:1) afforded **17** (236 mg, 74%) as a pale yellow oil; MS *m/z* (%) 199 (M^+-OH, 4), 157 (100), 137 (21), 129 (22), 73 (76); IR 3367 (OH) cm^{-1}; ^{1}H NMR δ 3.81–3.73 (2H, m, C_5–H), 3.63–3.53 (2H, m, $C_{3'}$–H), 2.74 (1H, t, J=4.9 Hz, OH), 1.92–1.86 (4H, m, CH_2), 1.72–1.53 (4H, m, CH_2), 1.12, 0.97 (2H, AB-q, J=14.2 Hz, $TMSCH_2$), 0.04 (9H, s, TMS); ^{13}C δ 85.18, 66.53, 63.49, 38.10, 37.99, 28.57, 27.91, 26.00, 0.20. Anal. Calcd for $C_{11}H_{24}O_2Si$: C, 61.06; H, 11.18. Found: C, 60.76; H, 11.02.

(2*R,3′*R**) and (2*R**,3′*S**)-2-(3′-Hydroxy-5′-phenylpent-4′-yn-1′-yl)-2-(trimethylsilylmethyl)tetrahydrofuran (18).** According to the procedure described for Swern oxidation of **11**, **17** (212 mg, 0.98 mmol) was oxidized with DMSO (0.17 mL, 2.36 mmol), oxalyl chloride (0.10 mL, 1.18 mmol), and Et_3N (0.68 mL, 4.91 mmol) to afford the crude aldehyde after chromatography with hexane–AcOEt (10:1). To a solution of phenylacetylene (0.18 mL, 1.47 mmol) in THF (5.0 mL) was added *n*-BuLi in hexane (1.51 M 0.97 mL, 1.47 mmol) at −78°C. After the mixture was stirred for 30 min, a solution of the crude aldehyde in THF (5.0 mL) was added to the THF solution, and the reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched by addition of water and extracted with AcOEt, which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (15:1) afforded **18** (199 mg, 64%) as a mixture of two diastereoisomers in a ratio of ca. 50–50. Compound **18** was obtained as a pale yellow oil; MS *m/z* (%) 316 (M^+, 1), 298 (1), 229 (7), 185 (4), 157 (100), 127 (19), 102 (35), 73 (79); IR 3218 (OH) cm^{-1}; ^{1}H NMR δ 7.47–7.25 (5H, m, aromatic H), 4.69–4.58 (1H, m, $C_{3'}$–H), 4.18 (1H×50/100, d, J=7.6 Hz, OH), 3.96–3.79 (2H, m, C_5–H), 3.39 (1H×50/100, d, J=5.0 Hz, OH), 2.11–1.58 (8H, m, CH_2), 1.27, 1.05 (2H×50/100, AB-q, J=14.8 Hz, $TMSCH_2$), 1.18, 1.02 (2H×50/100, AB-q, J=14.5 Hz, $TMSCH_2$), 0.06 (9H×50/100, s, TMS), 0.05 (9H×50/100, s, TMS). Anal. Calcd for $C_{19}H_{28}O_2Si$: C, 72.10; H, 8.92. Found: C, 71.85; H, 8.98.

Hexacarbonyl-μ-[η^4-(2*R,3′*R**) and (2*R**,3′*S**)-2-(3′-hydroxy-5′-phenylpent-4′-yn-1′-yl)-2-(trimethylsilylmethyl)tetrahydrofuran]dicobalt](Co–Co) (19).** $Co_2(CO)_8$ (189 mg, 0.55 mmol) was added to a solution of 18 (159 mg, 0.50 mmol) in Et_2O (5.0 mL) at room temperature. After being stirred for 30 min, the Et_2O solution was concentrated to leave the residue, which was chromatographed with hexane–AcOEt (10:1) to afford 19 (294 mg, 97%) as a mixture of two diastereoisomers in a ratio of ca. 50–50. Compound **19** was obtained as a deep brown oil; MS *m/z* (%) 602 (M^+, 0.1), 546 (15), 490 (38), 434 (47), 157 (100), 127 (13), 73 (60); IR 3330 (OH), 2091 (CO), 2054 (CO), 2027 (CO) cm^{-1}; ^{1}H NMR δ 7.65–7.25 (5H, m, aromatic H), 5.10–4.89 (1H, m, $C_{3'}$–H), 4.53 (1H×50/100, d, J=3.0 Hz, OH), 4.01 (1H×50/100, d, J=4.3 Hz, OH), 3.90–3.82 (2H, m, C_5–H), 2.16–1.64 (8H, m, CH_2), 1.23, 1.06 (2H×50/100, AB-q, J=14.5 Hz, $TMSCH_2$), 1.12, 1.03 (2H×50/100, AB-q, J=14.9 Hz, $TMSCH_2$), 0.07 (9H×50/100, s, TMS), 0.04 (9H×50/100, s, TMS). Anal. Calcd for $C_{25}H_{28}Co_2O_8Si$: C, 49.84; H, 4.68. Found: C, 49.99; H, 4.73.

Hexacarbonyl-μ-[η^4-5-methylene-2-(2′-phenylethynyl)-oxocane]dicobalt(Co–Co) (20) and hexacarbonyl-μ-[η^4-5-(trimethylsilylmethyl)-2-(2′-phenylethynyl)-5-oxocene]dicobalt-(Co–Co) (21). MsCl (0.03 mL, 0.35 mmol) was added to a solution of 19 (21.2 mg, 3.5×10^{-2} mmol) in CH_2Cl_2 (0.2 mL) at refluxing temperature. The reaction mixture was stirred for 10 min at the same temperature and diluted with CH_2Cl_2, which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane-AcOEt (100:1) afforded 20 (9.80 mg, 54%) and 21 (4.80 mg, 23%). Compound **20** was obtained as a reddish brown oil; MS *m/z* (%) 512 (M^+, 1.4), 456 (55), 400 (100), 344 (75), 226 (53), 187 (23), 91 (17); IR 2089 (CO), 2053 (CO), 2027 (CO) cm^{-1}; ^{1}H NMR δ 7.56–7.29 (5H, m, aromatic H), 4.90 (1H, s, olefinic H), 4.83 (1H, s, olefinic H), 4.78 (1H, dd, J=10.6, 3.0 Hz, C_2–H), 3.96 (1H, ddd, J=12.5, 6.3, 3.3 Hz, C_8–H), 3.72 (1H, dt, J=12.5, 4.3 Hz, C_8–H), 2.58–1.66 (8H, m, CH_2); ^{13}C NMR δ 190.66, 150.64, 137.90, 129.70, 128.77, 111.36, 79.95, 70.68, 39.30, 34.59, 32.62, 28.97; HRMS calcd for $C_{22}H_{18}Co_2O_7$ 511.9716, found 511.9718. Compound **21** was obtained as a reddish brown oil; MS *m/z* (%) 584 (M^+, 0.9), 528 (47), 472 (38), 416 (73), 386 (20), 298 (37), 115 (22), 73 (100); IR 2090 (CO), 2052 (CO), 2027 (CO) cm^{-1}; ^{1}H NMR δ 7.56–7.28 (5H, m, aromatic H), 5.41 (1H, t, J=7.3 Hz, C_6–H), 4.75 (1H, dd, J=11.2, 3.3 Hz, C_2–H), 4.06 (1H, dt, J=11.9, 3.6 Hz, C_8–H), 3.56–3.43 (1H, m, C_8–H), 2.89–2.75 (1H, m, C_7–H), 2.57 (1H, dddd, J=14.5, 10.9, 7.3, 3.6 Hz, C_7–H), 2.11–1.79 (4H, m, CH_2), 1.60, 1.52 (2H, AB-q, J=13.5 Hz, $TMSCH_2$), 0.04 (9H, s, TMS); ^{13}C NMR δ 199.59, 139.86, 138.01, 129.70, 128.75, 127.60, 120.68, 99.98, 90.60, 80.34, 73.16, 36.39, 30.46, 29.42, 27.03, −1.27; HRMS calcd for $C_{25}H_{26}Co_2O_7Si$ 584.0112, found 584.0106. When MsCl (0.02 mL, 0.21 mmol) was added to a refluxing solution of 19 (12.5 mg, 2.1×10^{-2} mmol) and Et_3N (0.06 mL, 0.42 mmol) in CH_2Cl_2 (0.1 mL) and the reaction mixture

was stirred at the same temperature for 5 min, compound **20** (7.60 mg, 72%) was obtained as a sole product.

5-Methylene-2-(2′-phenylethynyl)oxocane (23). CAN (210 mg, 0.38 mmol) was added to a solution of **20** (49.0 mg, 0.10 mmol) in MeOH (1.0 mL) at 0°C. After being stirred for 30 min, the reaction mixture was concentrated, diluted with water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (40:1) afforded 23 (19.8 mg, 91%) as a colorless oil; MS *m/z* (%) 226 (M^+, 27), 181 (36), 167 (100), 141 (82), 128 (85), 115 (68), 102 (50), 84 (31); ^{1}H NMR δ 7.47–7.27 (5H, m, aromatic H), 4.82 (1H, s, olefinic H), 4.80 (1H, s, olefinic H), 4.52 (1H, dd, J=8.9, 4.3 Hz, C_2–H), 3.89 (1H, ddd, J=12.5, 9.2, 3.6 Hz, C_8–H), 3.70 (1H, dt J=12.5, 4.6 Hz, C_8–H), 2.57–1.69 (8H, m, CH_2); ^{13}C NMR δ 150.66, 131.70, 128.18, 122.86, 110.82, 88.75, 84.44, 69.15, 67.17, 34.29, 32.90, 32.78, 31.13; HRMS calcd for $C_{16}H_{18}O$ 226.1358, found 226.1355.

5-(Trimethylsilylmethyl)-2-(2′-phenylethynyl)-5-oxocene (24). According to the procedure described for preparation of **23** from **20**, **24** (6.80 mg, 80%) was obtained from **21** (16.7 mg, 0.03 mmol) and CAN (62.7 mg, 1.14×10^{-1} mmol). Compound **24** was a colorless oil; MS *m/z* (%) 298 (M^+, 12), 270 (32), 255 (9), 211 (914), 167 (15), 115 (21), 73 (100); ^{1}H NMR δ 7.43–7.21 (5H, m, aromatic H), 5.30 (1H, t, J=7.6 Hz, C_6–H), 4.38 (1H, dd, J=10.9, 3.6 Hz, C_2–H), 3.98 (1H, dt, J=11.9, 3.6 Hz, C_8–H) 3.49 (1H, td, J=11.9, 1.6 Hz, C_8–H), 2.64 (1H, m, C_7–H), 2.43 (1H, dddd, J=14.5, 11.9, 7.6, 3.6 Hz, C_7–H), 2.52–1.80 (4H, m, CH_2), 1.51, 1.45 (2H, AB-q, J=17.5 Hz, $TMSCH_2$), −0.01 (9H, s, TMS); ^{13}C NMR δ 139.46, 131.64, 128.14, 123.04, 120.38, 89.45, 85.00, 72.74, 69.79, 35.74, 30.28, 29.69, 28.63, 27.14, −1.31; HRMS calcd for $C_{19}H_{26}OSi$ 298.1753, found 298.1758.

1-Hydroxy-8-[(pivaloyl)oxy]octan-4-one (25). To a solution of 3-(*tert*-butyldimethylsiloxy). prop-1-yne (5.62 g, 33.0 mmol) in THF (100 mL) was added *n*-BuLi in hexane (1.46 M, 22.6 mL, 33.0 mmol) at −78°C. After the mixture was stirred for 30 min, a solution of δ-valerolactone (3.00 g, 30.0 mmol) in THF (50 mL) was added to the THF solution, and the reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl and extracted with AcOEt, which was washed with water and brine, dried, and concentrated to dryness. A solution of the residue in AcOEt (150 mL) was hydrogenated in the presence of 5% Pd–C (300 mg) under hydrogen atmosphere for 30 min at room temperature. The catalyst was removed by passing through a short pad of Celite and the filtrate was concentrated to leave the residual oil, which was then dissolved in CH_2Cl_2 (150 mL). Et_3N (9.20 mL, 66.0 mmol) and pivaloyl chloride (4.10 mL, 33.0 mmol) were successively added to the CH_2Cl_2 solution and the mixture was allowed to stand at room temperature for 4 h. The reaction mixture was washed with water and brine, dried, and concentrated to dryness. 10% aqueous HCl solution (10.0 mL) was added to a solution of the residue in THF (150 mL) and the reaction mixture was stirred at room temperature for 1 h, diluted with water, and extracted with AcOEt. The extract was washed with saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (1:1) afforded **25** (4.47 g, 61%) as a colorless oil FABMS *m/z* (%) (M^++Na, 12), 227 (100), 154 (20), 125 (32), 97 (29), 57 (90); IR 3467 (OH), 1718 (CO) cm^{-1}; ^{1}H NMR δ 4.06 (2H, t, J=6.9 Hz, C_8–H), 3.65 (2H, t, J=6.4 Hz, C_1–H), 2.56 (2H, t, J=7.4 Hz, CH_2), 2.48 (2H, t, J=6.8 Hz, CH_2), 1.87–1.82 (2H, m, CH_2), 1.70–1.62 (4H, m, CH_2), 1.20 (9H, s, *t*-Bu); ^{13}C NMR δ 211.03, 178.60, 63.81, 61.98, 42.07, 39.37, 38.65, 28.00, 27.08, 26.38, 20.02; HRFABMS calcd for $C_{13}H_{24}O_4Na$ (M^++Na) 267.1572, found 267.1575.

(±)-2-(4′-Hydroxybut-1′-yl)-2-(trimethylsilylmethyl)-tetrahydrofuran (27). According to the procedure described for conversion of **14** into **16**, a solution of **25** (2.00 g, 8.19 mmol) in CH_2Cl_2 (82 mL) was treated with TsCl (2.34 g, 12.3 mmol), 4(-*N*,*N*-dimethylamino)pyridine (100 mg, 8.19×10^{-1} mmol), and Et_3N (3.40 mL, 24.6 mmol) at room temperature for 6 h to provide the crude tosylate. Trimethylsilylmethyllithium in pentane (1.0 M, 16.4 mL, 16.4 mmol) was then added to a solution of the crude tosylate in THF (82 mL) at −78°C. The reaction mixture was stirred for 1 h at the same temperature and work-up gave the crude **26**. To a solution of **26** in CH_2Cl_2 (82 mL) was added DIBAL-H in hexane (0.95 M, 12.9 mL, 12.9 mmol) at −78°C and the reaction mixture was stirred for 30 min at the same temperature and quenched by addition of water. The organic layer was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (3:1) afforded **27** (488 mg, 26%) as a colorless oil; MS *m/z* (%) 230 (M^+, 2.7), 157 (44), 143 (11), 95 (13), 81 (60), 73 (100); IR 3421 (OH) cm^{-1}; ^{1}H NMR δ 3.87–3.73 (2H, m, C_5–H), 3.65 (2H, dt, J=6.4, 5.6 Hz, $C_{4'}$–H), 1.76–1.33 (10H, m, CH_2), 1.09, 0.98 (2H, AB-q, J=14.7 Hz, $TMSCH_2$), 0.04 (9H, s, TMS); ^{13}C NMR δ 85.34, 66.49, 62.70, 40.67, 37.67, 33.12, 28.79, 26.08, 20.63, 0.18; HRMS calcd for $C_{12}H_{26}O_2Si$ 230.1702, found 230.1706.

(2*R,4′*R**) and (2*R**, 4′*S**)-2-(4′-Hydroxy-6′-phenylhex-5′-yn-1′-yl)-2-(trimethylsilylmethyl)tetrahydrofuran (28).** According to the procedure described for conversion of **17** into **18**, **27** (215 mg, 0.93 mmol) was oxidized under Swern conditions oxalyl chloride (0.10 mL, 1.12 mmol), DMSO (0.16 mL, 2.24 mmol), and Et_3N (0.65 mL, 4.67 mmol)] to afford, after chromatography with hexane–AcOEt (10:1), the crude aldehyde. A solution of the crude aldehyde in THF (9.5 mL) was subsequently exposed to lithium phenylacetylide, prepared from phenylacetylene (0.15 mL, 1.40 mmol) and *n*-BuLi in hexane (1.23 M, 1.52 mL, 1.40 mmol) to afford, after chromatography with hexane–AcOEt (10:1), **28** (167 mg, 54%) as a colorless oil MS *m/z* (%) 330 (M^+, 1.2), 271 (5), 243 (7), 157 (100), 141 (10), 115 (9), 73 (35); IR 3389 (OH) cm^{-1}; ^{1}H NMR δ 7.43–7.30 (5H, m, aromatic H), 4.61 91H, t, J=5.9 Hz, C4′–H), 3.84–3.75 (2H, m, C5–H), 2.05–1.48 (10H, m, CH2), 1.11, 1.10 (2H, AB-q, J=14.7 Hz, $TMSCH_2$), 0.04 (9H, s, TMS); HRMS calcd for $C_{20}H_{30}O_2Si$ 330.2015, found 330.2013.

6-Methylene-2-(2′-phenylethynyl)oxonane (29). According to the procedure described for preparation of **19** from

18, **28** (23.8 mg, 0.72×10^{-1} mmol) was treated with $Co_2(CO)_8$ (27.1 mg, 0.79×10^{-1} mmol) to give the cobalt complex. To a solution of the cobalt complex in CH_2Cl_2 (0.7 mL) was added MsCl (0.06 mL, 0.72 mmol) and Et_3N (0.20 mL, 1.44 mmol). The reaction mixture was stirred at room temperature for 10 min, washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (80:1) afforded **29** (9.0 mg, 52%) as a colorless oil; MS *m/z* (%) 240 (M^+, 100), 197 (83), 181 (64), 141 (70), 128 (94), 115 (72), 97 (87), 91 (26); ^{1}H NMR δ 7.43–7.27 (5H, m, aromatic H), 4.99 (1H, d, J=1.5 Hz, olefinic H), 4.87 (1H, d, J=1.5 Hz, olefinic H), 4.45 (1H, t, J=5.8 Hz, C_2–H), 3.81 (1H, ddd, J=10.8, 7.3, 5.4 Hz, C_9–H), 3.57 (1H, dt, J=10.8, 5.4 Hz, C_9–H), 2.29–2.18 (4H, m, CH_2), 1.97–1.71 (6H, m, CH_2); ^{13}C NMR δ 149.22, 131.72, 128.18, 122.93, 112.74, 88.97, 84.30, 68.77, 63.87, 37.76, 31.52, 29.69, 28.83, 21.55; HRMS calcd for $C_{17}H_{20}O$ 240.1514, found 240.1518.

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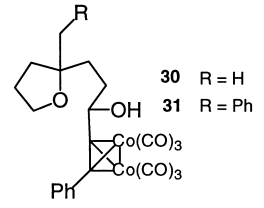
16. Mineral acids and organic acids were also used instead of a Lewis acid. However, the formation of oxocanes could not be detected in the reaction mixture.
17. The structure of **21** was determined by NMR spectral analyses. The decoupling experiments between the C_6-olefinic proton and C_7-methylene protons as well as between C_7- and C_8-protons enabled us to confirm the depicted structure of **21**.
18. When the methyl and benzyl congeners **30** and **31** were independently submitted to the reaction conditions described for the transformation of **19** into **20**, the corresponding oxocane derivatives, **20** and **32**, could not be detected in the reaction mixture. These results can tentatively be interpreted in terms of the lack of a cationic intermediate like **22**. Therefore, it might be concluded that the β-trimethylsilylmethyl group at the C-2 position of the tetrahydrofuran ring is mandatory for conversion of **19** to **20**. The details of these results will be reported in the near future.



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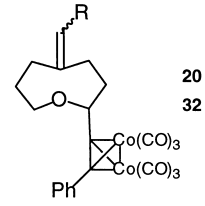

20 R = H
32 R = Ph