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INTRAMOLECULAR PAUSON-KHAND REACTION OF 3-ALKYNYL-1-ALKYLIDENECYCLES: A CONVENIENT SYNTHESIS OF [5.n.1.0^{1,5}] TRICYCLIC COMPOUNDS

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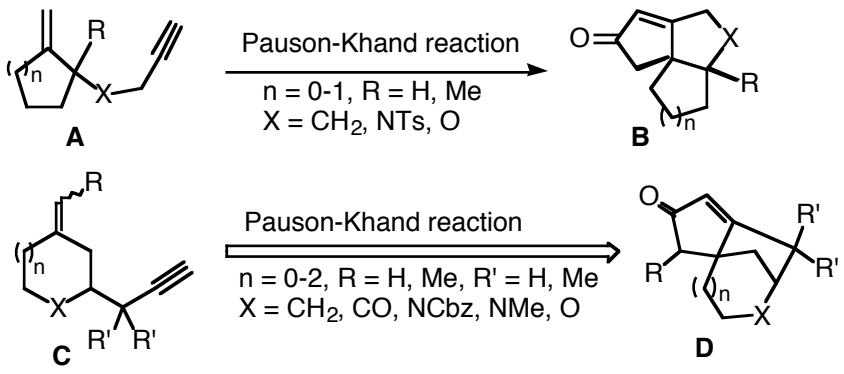
Abstract – An intramolecular Pauson-Khand reaction of various 3-alkynyl-1-alkylidenecyclic compounds was performed to give the corresponding [5.n.1.0^{1,5}] tricyclic compounds (n = 2-4). A facile construction of the core structure in cedrene terpenoids was also investigated in detail and formal total synthesis of α- and β-cedrenes was accomplished.

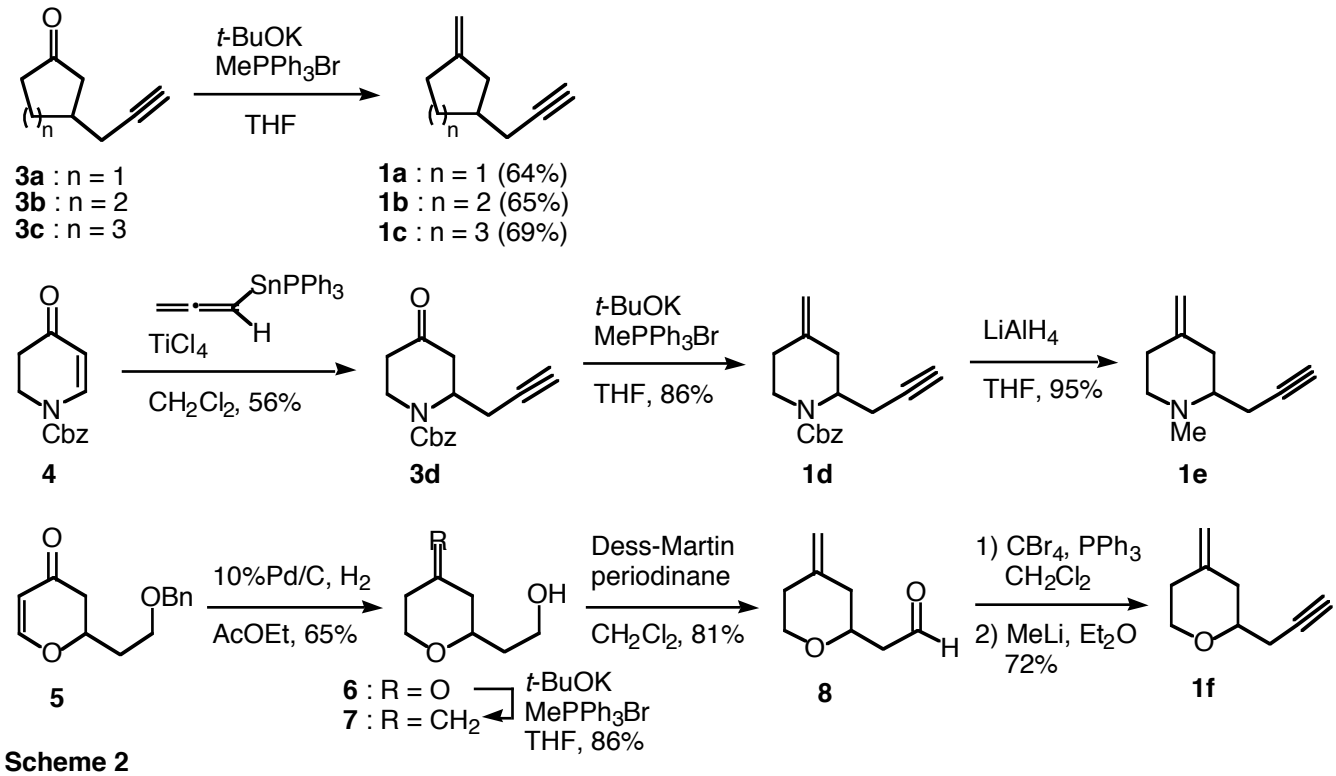
The Pauson-Khand reaction[1] is known as one of the attractive methods for the construction of polycyclic compounds, including cyclopentenone structures. The usefulness of the reaction has been demonstrated in its application to the total synthesis of natural products.[2] Recent work in our laboratory has revealed a facile construction of bi- and tri-cyclic compounds by the Pauson-Khand reaction of *exo*-cyclic enynes.[3] Especially, the intramolecular Pauson-Khand reaction of 2-alkynyl-1-methylenecyclic compounds (**A**) (*exo*-cyclic enynes) formed angular type tricycles (**B**) in good yields (Scheme 1).[3a-e] We envisage that the reaction would be applicable to the synthesis of the [5.3.1.0^{1,5}] tricyclic skeleton (**D**), which is the core structure of the widely known cedrene terpenoids, from 3-propynyl-1-alkylidenecyclic compounds (**C**)



Scheme 1

(*exo*-cyclic enynes). In this paper, we wish to describe our investigation on the generality of the synthesis of [5.n.1.0^{1,5}] tricyclic skeleton (**D**) (n = 2-4) by the intramolecular Pauson-Khand reaction of various 3-alkynyl-1-alkylidenecyclic compounds (**C**) (Scheme 1) and its application to construct various functionalized core structures of cedrene terpenoids.[4,5]

Various Pauson-Khand precursors (**1a**-**f**) bearing the *exo*-methylene group were synthesized as shown in Scheme 2. Thus, Wittig olefination of ketones (**3a**-**c**)[6] afforded enynes (**1a**-**c**) in 64-69% yields. An *N*-Cbz piperidine derivative (**1d**) was obtained by propynylation[6] of the enone (**4**)[7] followed by Wittig olefination. Reduction of **1d** furnished *N*-methyl piperidine (**1e**). A pyrane derivative (**1f**) was synthesized from the enone (**5**)[8] in four steps.



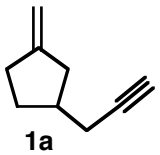
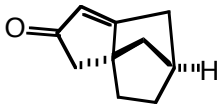
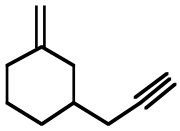
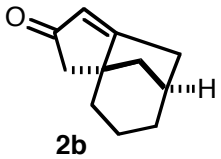
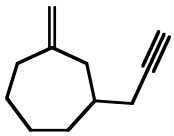
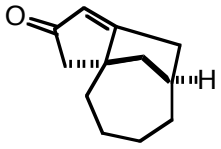
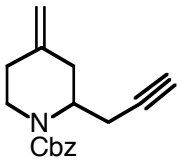
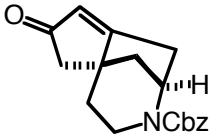
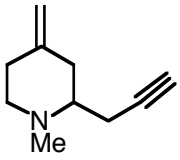
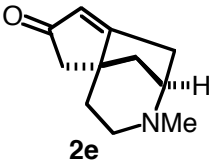
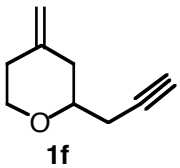
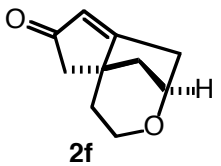
Scheme 2

With enynes in hand, the intramolecular Pauson-Khand reaction of enynes (**1a**-**f**) was examined by the following three procedures: refluxing in toluene (Method A); heating at 83˚C with BuSMe (3.5 eq.)[9a] in $CHCl_2CHCl_2$ (Method B); oxidative treatment with *N*-methylmorpholine *N*-oxide[9b] (9-12 eq.) at room temperature in CH_2Cl_2 (Method C). The results are shown in Table 1. The reaction of methylenecyclohexane (**1b**) gave the corresponding [5.3.1.0^{1,5}] tricyclic compound (**2b**) in moderate to good yields (57-79%) by Methods A-C. A similar reaction of methylenecycloheptane (**1c**) afforded [5.4.1.0^{1,5}] tricycle (**2b**) in moderate yields (55-67%) by Methods A and B, whereas the reaction by Method C furnished **2b** in 21% yield. Unexpectedly, the reaction of methylenecylopentane (**1a**) resulted in the formation of **2a** in low yields despite employment of Methods A-C. The result would be due to a

highly strained tricyclic system in **2a**. In the case of aza and oxa derivatives (**1d-f**), although the reaction of benzyloxy carbamate (**1d**) afforded a tricyclic compound (**2d**) in moderate yields (47-60%), a similar reaction of *N*-methylpiperidine (**1e**) and pyrane (**1f**) formed an intractable mixture and **2e** and **2f** were attained in low yields (8-16%). It was found that generally reactions under thermal conditions (Methods A and B) except for **1a** were superior to an oxidative condition (Method C).

Much attention has been focused on naturally occurring cedrene-type terpenoids, as represented by α- and β-cedrene (**9a**,**b**), because of their intriguing [5.3.1.$0^{1,5}$] tricyclic skeleton and much synthetic work on

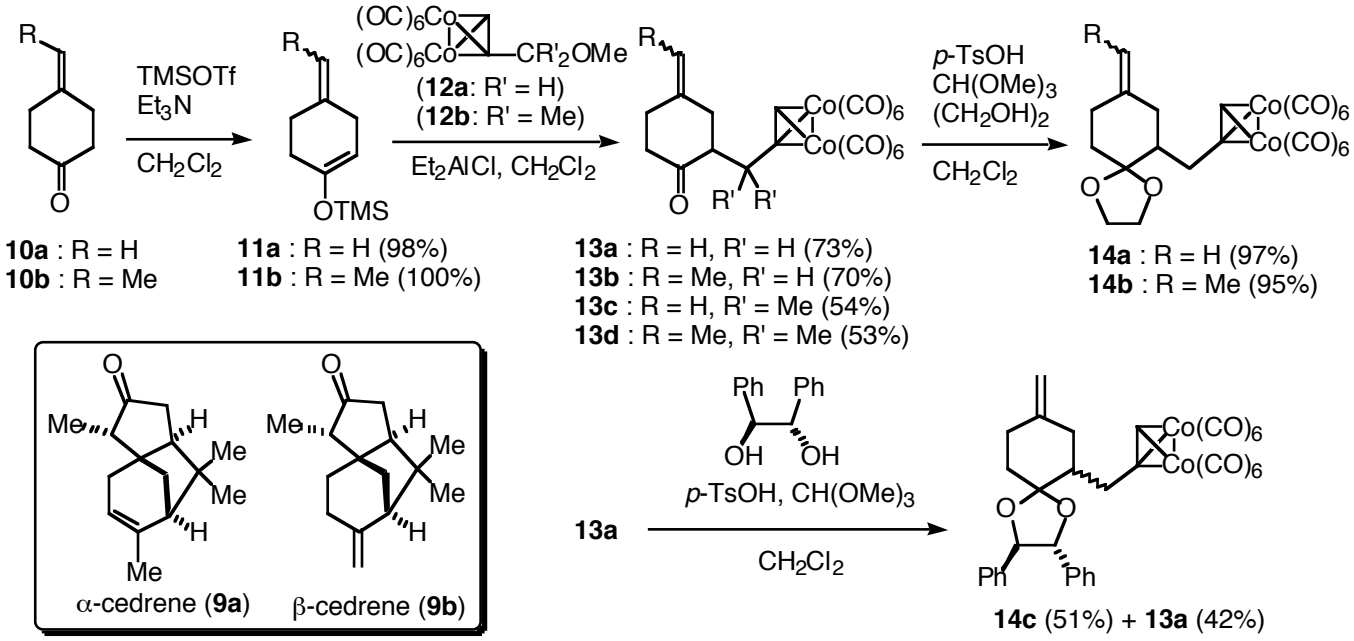
Table 1. Intramolecular Pauson-Khand reaction of various enynes (**1a-f**).

Entry	Substrate	Method[a]	Time (h)	Product	Yield (%)
1	 **1a**	A	4	 **2a**	4
2		B	8		12
3		C	2		13
4	 **1b**	A	4	 **2b**	73
5		B	10		79
6		C	2		57
7	 **1c**	A	4	 **2c**	55
8		B	10		67
9		C	2		21
10	 **1d**	A	4	 **2d**	54
11		B	8		60
12		C	2		47
13	 **1e**	A	4	 **2e**	16
14		B	10		18
15		C	2		8
16	 **1f**	A	4	 **2f**	14
17		B	10		15
18		C	2		10

a) Method A; refluxing in toluene. Method B; heating at 83˚C with BuSMe (3.5 eq.) in $CHCl_2CHCl_2$. Method C; oxidative treatment with *N*-methylmorpholine *N*-oxide (9 eq. for **1a-c, e** and 12 eq. for **1d, f**) at room temperature in CH_2Cl_2.

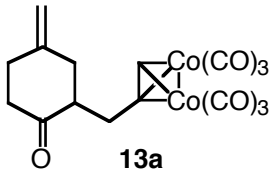
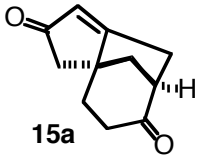
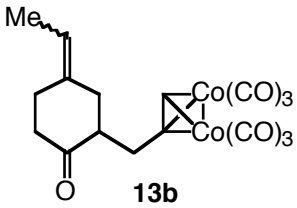
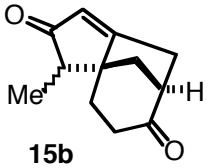
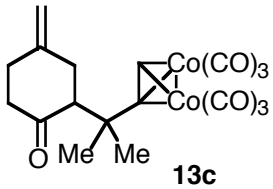
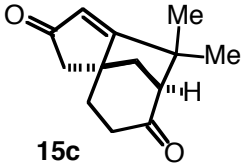
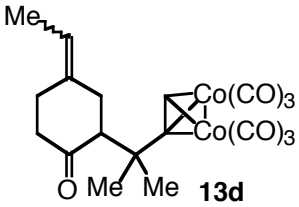
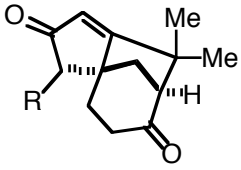
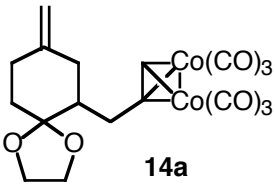
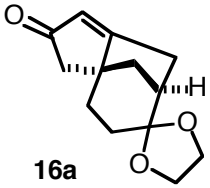
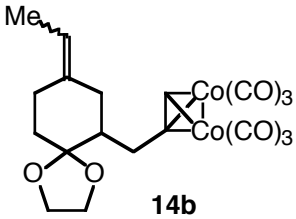
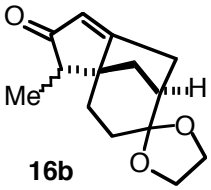
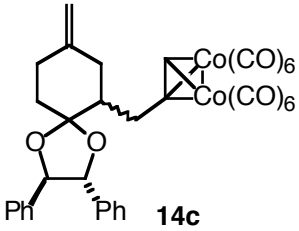
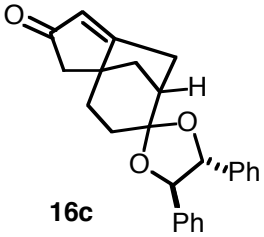
them has been achieved.[5,10] As mentioned above, [5.n.1.0^{1,5}] tricycles could be obtained by the intramolecular Pauson-Khand reaction of 3-alkynyl-1-methylenecycles. Thus, we turned our attention to synthesize functionalized [5.3.1.0^{1,5}] tricyclic compounds by the reaction of 3-alkynyl-1-alkylidenecyclohexanes. For short-step synthesis, we adopted the Nicholas reaction[11] to obtain Pauson-Khand precursors bearing the carbonyl group on a cyclohexane ring (Scheme 3). Thus, 4-alkylidenecyclohexanones (**10a**,**b**)[12] were converted to trimethylsilyl enol ethers (**11a**,**b**), of which the Nicholas reaction reported by Schreiber[13] with the alkyne-cobalt complex (**12a**) afforded the expected Pauson-Khand reaction precursors (**13a,b**) in good yields. Similar reaction of **11a**,**b** with **12b** produced alkyne-cobalt complexes (**13c**,**d**) in moderate yields. Because **11b** was obtained as a mixture of regio-isomers (5 : 4 by ^{1}H-NMR spectrometry), alkyne-cobalt complexes (**13b**,**d**) were also attained as a mixture of diastereomers. The ratio of diastereomers was estimated by ^{1}H-NMR spectroscopic analysis (52 : 48 for **13b** and 59 : 41 for **13d**), although the geometry of the olefinic part could not be determined.

The Pauson-Khand reaction of synthesized alkyne-cobalt complexes bearing alkylidene group was examined. As shown in Table 2, an expected [5.3.1.0^{1,5}] tricyclic compound (**15a**) was obtained by the Pauson-Khand reaction of **13a** in 52-60% yields under thermal conditions (Methods A and B), whereas a low yield was observed under an oxidative condition (Method C). Unfortunately, a similar reaction of **13b** bearing tri-substituted olefinic moiety produced **15b** in low yields despite Methods A-C, which is thought to be attributable to spatially small carbonyl groups in **13a,b**, because Pauson *et al*. have reported that a similar reaction of the acetal substrate gave a tricyclic compound in high yield.[5] Therefore, transformation[14] of ketones (**13a,b**) to acetals (**14a,b**) might cause favorable conformation in a transition state based on a reactive rotamer effect (Scheme 4).[15] As expected, yields of the Pauson-Khand reaction of

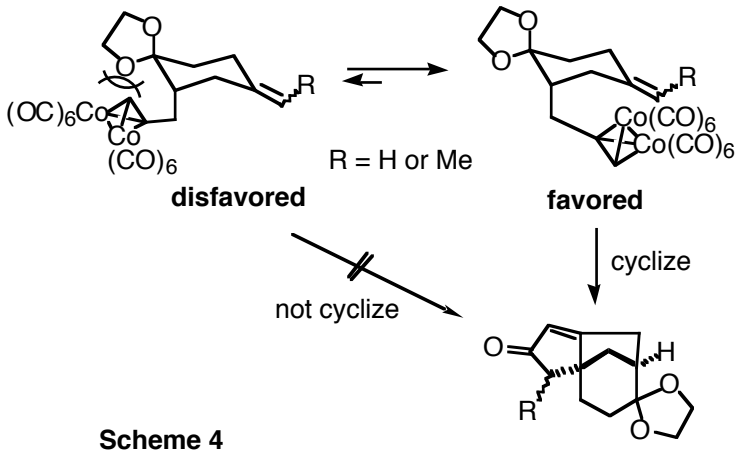


Scheme 2

Table 2. Intramolecular Pauson-Khand reaction of various alkyne-cobalt complexes (**13a-d** and **14a-c**).

Entry	Substrate	Method[a]	Time (h)	Product	Yield (%)
1	 **13a**	A	4	 **15a**	52
2		B	8		60
3		C	2		19
4	 **13b**	A	4	 **15b**	12[b]
5		B	10		30[b]
6		C	2		4[b]
7	 **13c**	A	4	 **15c**	62
8		B	10		72
9		C	2		26
10	 **13d**	A	4	 **15da** : R = α-Me **15db** : R = β-Me	14+16[c]
11		B	10		25+25[c]
12		C	2		3+4[c]
13	 **14a**	A	4	 **16a**	78
14		B	10		85
15		C	2		48
16	 **14b**	A	4	 **16b**	42
17		B	8		60
18		C	2		22
16	 **14c**	A	4	 **16c**	62
17		B	8		80
18		C	2		42

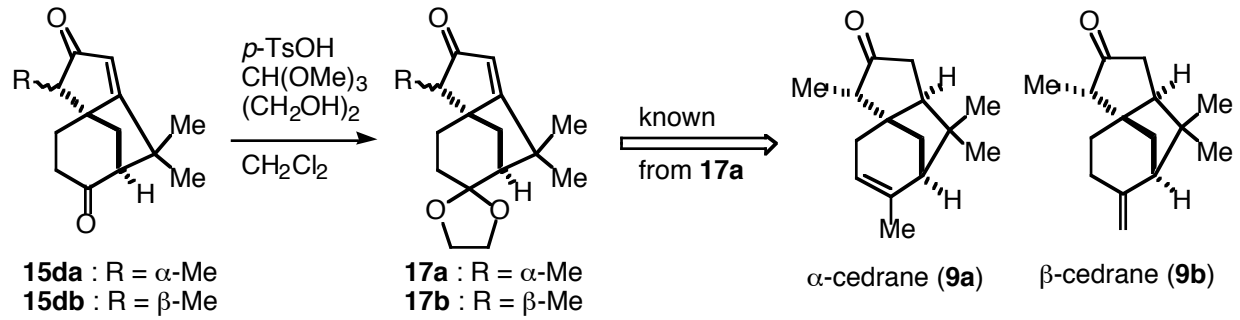
a) Method A; refluxing in toluene. Method B; heating at 83˚C with BuSMe (3.5 eq.) in $CHCl_2CHCl_2$. Method C; oxidative treatment with *N*-methylmorpholine *N*-oxide (12 eq.) at room temperature in CH_2Cl_2. b) Obtained as a mixture of diastereomers. c) Isolated yield of **15da** and **15db**.



Scheme 4

14a,b under thermal conditions remarkably improved to 78-85% for **16a** and 42-60% for **16b**. We also synthesized a chiral acetal (**14c**) from **13a**. However, bulky 1,2-diphenylethanol prevented complete conversion to a chiral acetal (**14c**) and **14c** was obtained as an inseparable 54 : 46 mixture (^{1}H-NMR spectrometry). The Pauson-Khand reaction of **14c** smoothly proceeded by Method B to afford **16c** in 80% yield as a 52 : 48 mixture of diastereomers.

Next, the Pauson-Khand reaction of dimethyl derivatives (**13c,d**) was investigated. Although, unfortunately, acetalization of ketones (**13c**,**d**) did not occur, the reaction of **13c** gave rise to a tricyclic product (**15c**) in moderate to good yields (62-72%) by Methods A and B. A similar reaction of the tri-substituted olefin (**13d**) produced a *ca*. 1 : 1 ratio of desired products (**15da**,**db**) in 50% combined yield by Method B. The results suggested that the bulky dimethyl group in **13c**,**d** would set a favorable conformation in a transition state due to the reactive rotamer effect[15] without acetalization. The stereochemistry of **15da** and **15db** was determined by conversion to known compounds (**17a,b**).[5] Since Pauson *et al*. have reported formal total synthesis of α- and β-cedrenes (**9a**,**b**) from **17a**,[5] we also accomplished formal total synthesis of α- and β-cedrenes (Scheme 5).



15da : R = α-Me
15db : R = β-Me

17a : R = α-Me
17b : R = β-Me

α-cedrane (**9a**)

β-cedrane (**9b**)

Scheme 5

In conclusion, we have investigated the intramolecular Pauson-Khand reaction of various 3-alkynyl-1-alkylidenecyclic derivatives to give corresponding [5.n.1.0^{1,5}] tricyclic compounds (n = 2-4). A

straightforward synthesis of the alkyne-cobalt complex using Schreiber's method (Nicholas reaction), and subsequently the Pauson-Khand reaction, offered short-step access to the functionalized core structure of cedrene terpenoids. The usefulness of this approach was proved by a five-step synthesis of the known precursor (**17a**) for the total synthesis of α- and β-cedrenes.

ACKNOWLEDGEMENTS

The authors are grateful to Mrs. F. Hasegawa of this faculty for her MS spectral measurements.

EXPERIMENTAL

General. All melting points were measured on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were obtained with a JASCO FT/IR-400. ^{1}H and ^{13}C NMR spectra were taken with a JEOL JNM AL-300 (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) spectrometer in a $CDCl_3$ solution with tetramethylsilane as the internal standard. MS spectra were measured on a Hitachi M-80 or a JEOL JMS D-300 spectrometer. Column chromatography was performed over silica gel (Merck Kiegelsel 60). Preparative TLCs were run on a Merck 5744 plate. Organic extracts were dried over $MgSO_4$, unless otherwise noted.

General Procedure for Wittig Reaction of Ketones (3a-d)

To a stirred suspension of methyltriphenylphosphonium bromide (2.5 eq.) and *t*-BuOK (2.4 eq.) in THF was added a solution of ketone (1 eq.) in THF. After being stirred for 2 h, the reaction was quenched with water. The mixture was extracted with Et_2O. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was taken up in pentane. The precipitate was filtered by suction. The filtrate was evaporated under reduced pressure to give an oily residue, which was purified by bulb-to-bulb distillation to afford corresponding olefins (**1a-c**). In the case of **1d**, column purification (AcOEt : hexane = 1 : 10) was performed.

1-Methylene-3-(2-propynyl)cyclopentane (1a); from **3a** (0.381 g, 3.12 mmol), **1a** (0.240 g, 64.0%) was obtained as a colorless oil; bp 100-110°C/70 mmHg; ^{1}H NMR δ 4.83-4.86 (2H, m), 2.03-2.52 (7H, m), 1.94 (1H, t, J = 2.6 Hz), 1.70-1.73 (1H, m), 1.39-1.73 (1H, m); IR 3304, 2942, 2117, 1658, 1431 cm^{-1}; EI MS *m/z* 120 (M^+); HRMS *m/z* calcd for C_9H_{12} (M^+) 120.0939, found: 120.0930.

1-Methylene-3-(2-propynyl)cyclohexane (1b); from **3b** (0.669 g, 4.9 mmol), **1b** (0.461 g, 64.6%) was obtained as a colorless oil; bp 80-100°C/30 mmHg; ^{1}H NMR δ 4.64 (2H, s), 2.13-2.42 (4H, m), 1.98 (1H, t, J = 2.6 Hz), 1.50-1.96 (4H, m), 1.14-1.44 (3H, m); IR 3307, 2929, 2116, 1645 cm^{-1}; EI MS *m/z* 134 (M^+); HRMS *m/z* calcd for $C_{10}H_{14}$ (M^+) 134.1096, found: 134.1097.

1- Methylene-3-(2-propynyl)cycloheptane (1c); from **3c** (0.580 g, 3.87 mmol), **1c** (0.396 g, 69.2%) was obtained as a colorless oil; bp 100-110°C/30 mmHg; ^{1}H NMR δ 4.84 (2H, s), 2.12-2.61 (6H, m), 2.07 (1H,

t, J = 2.6 Hz), 1.75-1.98 (4H, m), 1.34-1.66 (3H, m); IR 3308, 2924, 2853, 2118, 1637, 1445 cm^{-1}; EI MS m/z 147 (M^+-1); HRMS m/z calcd for $C_{11}H_{15}$ (M^+-1) 147.1172, found: 147.1158.

***N*-Benzyloxycarbonyl 4-methylene-2-(2-propynyl)piperidine (1d)**; from **3d** (0.542 g, 2.0 mmol), **1d** (0.460 g, 85.5%) was obtained as a colorless oil; ^1H NMR δ 7.28-7.37 (5H, m), 5.15 (2H, s), 4.89, 4.82 (each 1H, s), 4.57-4.70 (1H, m), 4.18 (1H, br d, J = 11.5 Hz), 2.80-2.95 (1H, m), 2.30-2.46 (4H, m), 2.15-2.29 (2H, m), 1.92 (1H, t, J = 2.6 H); IR 3298, 2118, 1698, 1420 cm^{-1}; EI MS m/z 269 (M^+); HRMS m/z calcd for $C_{17}H_{19}NO_2$ (M^+) 269.1416, found: 269.1427.

***N*-Benzyloxycarbonyl 4-oxo-2-(2-propynyl)piperidine (3d).** To a stirred solution of **4** (2.000 g, 8.66 mmol) and allenyltriphenyltin (6.698 g, 17.2 mmol) in CH_2Cl_2 (50 mL) at –40°C was added a 1M solution of $TiCl_4$ in CH_2Cl_2 (10.4 mL, 10.4 mmol) over a period of 5 min. After being stirred for 4 h, the reaction was quenched with water. The mixture was extracted with $CHCl_3$. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was taken up in Et_2O and treated with 10% aqueous KF for 1 h. The precipitate was filtered by suction. The filtrate was extracted with Et_2O. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 10 then 1 : 2) to afford **3d** (1.322 g, 56.3%) and **4**[7] (0.806 g, 40.3%) as colorless oils; ^1H NMR δ 7.37 (5H, s), 5.18 (2H, s), 4.67-4.76 (1H, m), 4.30-4.45 (1H, m), 4.40-3.55 (1H, m), 2.66 (2H, d, J = 5.6 Hz), 2.36-2.60 (4H, m), 1.99 (1H, t, J = 2.6 H); IR 3288, 2110, 1726, 1697, 1417 cm^{-1}; EI MS m/z 271 (M^+); HRMS m/z calcd for $C_{16}H_{17}NO_3$ (M^+) 271.1208, found: 271.1206.

***N*-Methyl-4-methylene-3-(2-propynyl)piperidine (1e).** To a stirred solution of **3d** (0.269 g, 1.0 mmol) in THF (5 mL) at rt was added $LiAlH_4$ (0.110 g, 2.9 mmol). After being stirred for 0.5 h, the reaction was quenched with saturated an aqueous Na_2SO_4 solution. The precipitates were filtered off and the filtrate was evaporated under reduced pressure to give an oily residue, which was taken up in Et_2O. The ether layer was extracted with 1M HCl. The extracts were washed with Et_2O and made alkaline with 1M NaOH. The aqueous layer was extracted with Et_2O. The organic extracts were dried (K_2CO_3) and evaporated *in vacuo* to afford **1e** (0.141 g, 94.6%) as a colorless oil; ^1H NMR δ 4.71 (2H, s), 2.85 (1H, dt, J = 4.0, 10.1 Hz), 2.14-2.42 (8H, m), 2.34 (3H, s), 2.04 (1H, t, J = 2.6 H); IR 3306, 2941, 2118, 1655 cm^{-1}; EI MS m/z 149 (M^+); HRMS m/z calcd for $C_{10}H_{15}N$ (M^+) 149.1203, found: 149.1201.

2-(2-Hydroxyethyl)tetrahydropyran-4-one (6). A mixture of **5** (2.88 g, 12.4 mmol) and 10% Pd/C (0.8 g) in AcOEt (25 mL) was stirred for 22 h at rt. After the mixture was filtered, the filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 3 then AcOEt) to afford **6** (1.16 g, 64.9%) as a colorless oil; ^1H NMR δ 4.28 (1H, dd, J = 7.6, 11.6 Hz), 3.75-3.86 (3H, m), 3.67 (1H, ddd, J = 3.0, 11.6, 12.2 Hz), 2.57 (1H, ddd, J = 7.6, 12.2, 14.2 Hz), 2.28-2.64 (4H, m), 1.69-1.93 (2H, m); IR 3420, 1715 cm^{-1}; EI MS m/z 144 (M^+); HRMS m/z calcd for

$C_7H_{12}O_3$ (M^+) 144.0786, found: 144.0782.

2-(2-Hydroxyethyl)-4-methylenetetrahydropyran (7). To a stirred suspension of methyltriphenylphosphonium bromide (7.50 g, 21 mmol) and *t*-BuOK (2.22 g, 19.8 mmol) in THF (100 mL) at rt was added a solution of **6** (1.139 g, 7.9 mmol) in THF (20 mL). After being stirred for 1 h, the reaction was quenched with water. The mixture was extracted with Et_2O. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 3 then 1 : 1) to afford **7** (0.960 g, 85.5%) as a colorless oil; ^{1}H NMR δ 4.77, 4.76 (each 1H, d, *J* = 2.0 Hz), 4.11 (1H, ddd, *J* = 1.3, 5.6, 10.9 Hz), 3.82 (2H, t, *J* = 5.4 Hz), 3.38-3.58 (2H, m), 2.07-2.40 (5H, m), 1.71-1.91 (2H, m); IR 3389, 1652 cm^{-1}; EI MS *m/z* 142 (M^+); HRMS *m/z* calcd for $C_8H_{14}O_2$ (M^+) 142.0994, found: 142.0991.

2-Formylmethyl-4-methylenetetrahydropyran (8). To a stirred solution **7** (0.955 g, 6.7 mmol) in CH_2Cl_2 (80 mL) at rt was added Dess-Martin periodinane (3.50 g, 8.2 mmol). After being stirred for 2 h, the reaction was quenched with 10% aqueous $Na_2S_2O_3$. The mixture was extracted with $CHCl_3$. The organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried, and evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 10) to afford **8** (0.765 g, 81.4%) as a colorless oil; ^{1}H NMR δ 9.87 (1H, dd, *J* = 2.0, 2.6 Hz), 4.76 (2H, t, *J* = 1.8 Hz), 4.65 (1H, ddd, *J* = 1.7, 5.3, 10.9 Hz), 3.77-3.86 (1H, m), 3.27 (1H, ddd, *J* = 3.0, 10.9, 13.3 Hz), 2.64 (1H, ddd, *J* = 2.6, 7.9, 16.3 Hz), 2.51 (1H, ddd, *J* = 1.7, 4.6, 16.3 Hz), 2.02-2.36 (4H, m); IR 2941, 2851, 1726, 1654 cm^{-1}; EI MS *m/z* 140 (M^+); HRMS *m/z* calcd for $C_8H_{12}O_2$ (M^+) 140.0837, found: 140.0842.

4-Methylene-2-(2-propynyl)tetrahydropyran (1f). To a stirred suspension of PPh_3 (5.294 g, 20.2 mmol) in CH_2Cl_2 (15 mL) at 0°C was added a solution of CBr_4 (3.349 g, 10 mmol) in CH_2Cl_2 (15 mL). After being stirred for 10 min, a solution of **8** (0.707 g, 5.1 mmol) in CH_2Cl_2 (10 mL) was added. The mixture was further stirred for 2 h at rt and evaporated under reduced pressure to give a residue. Et_2O was added and precipitates were filtered off. The filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 5) to afford 4-methylene-2-(3,3,-dibromo-2-propenyl)tetrahydropyran (1.208 g, 80.8%) as a colorless oil; ^{1}H NMR δ 6.52 (1H, t, *J* = 6.9 Hz), 4.75, 4.74 (each 1H, s), 4.05 (1H, ddd, *J* = 4, 5.6, 9.6 Hz), 3.31-3.42 (2H, m), 1.98-2.34 (6H, m); IR 2896, 2848, 1653 cm^{-1}**.**

To a stirred solution of the dibromide (1.186 g, 4.01 mmol) in Et_2O (10 mL) at 0°C was added 1M MeLi in Et_2O (10 mL, 10 mmol). After being stirred for 1 h, the reaction was quenched with water. The mixture was extracted with Et_2O. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by bulb-to-bulb distillation to afford **1f** (0.487 g, 89.4%) as a colorless oil; bp 130°C/75 mmHg; ^{1}H NMR δ 4.76 (2H, s), 4.10 (1H, ddd, *J* = 1.7, 5.7, 10.9

Hz), 3.36-3.47 (2H, m), 2.28-2.47 (4H, m), 2.10-2.25 (2H, m), 2.04 (1H, t, J = 2.6 Hz); IR 3299, 2942, 2853, 2121, 1654 cm^{-1}; EI MS m/z 136 (M^+); HRMS m/z calcd for $C_9H_{12}O$ (M^+) 136.0888, found: 136.0894.

General Procedures for Pauson-Khand Reaction of *exo*-Cyclic Enynes (1a-f). A mixture of enyne (1 eq.) and $Co_2(CO)_8$ (1.15 eq.) in toluene, CH_2ClCH_2Cl or CH_2Cl_2, was stirred for 1 h at rt. Method A: refluxing in toluene; Method B: heating at 83°C with BuSMe (3.5 eq.) in $CHCl_2CHCl_2$; Method C: oxidative treatment with *N*-methylmorpholine *N*-oxide (9-12 eq.) at rt in CH_2Cl_2. The solvent was removed under reduced pressure to give a residue, which was diluted with Et_2O. The precipitate was removed by suction filtration through a Celite 545 short pad. Purification of the products obtained by Methods A-C was carried out on preparative TLC.

4,5,6,7-Tetrahydro-3a,6-methanoinden-2-one (2a); oil; ^{1}H NMR δ 5.69 (1H, t, J = 1.7 Hz), 2.45, 2.31 (each 1H, d, J = 18.2 Hz), 2.25-2.70 (3H, m), 1.52-1,93 (3H, m), 1.22-1.50 (3H, m); ^{13}C NMR δ 210.4, 194.3, 56.3, 42.5, 38.8, 35.2, 32.0, 30.0, 29.5; IR 2954, 2869, 1711, 1697, 1634 cm^{-1}; EI MS m/z 148 (M^+); HRMS m/z calcd for $C_{10}H_{12}O$ (M^+) 148.0887, found: 148.0882.

5,6,7,8-Tetrahydro-4*H*-3a,7-methanoazulen-2-one (2b); oil; ^{1}H NMR δ 5.81 (1H, s), 2.49-2.64 (3H, m), 2.22 (2H, s), 1.79-1.90 (1H, m), 1.72 (1H, d, J = 12.2 Hz), 1.50-1.66 (5H, m), 1.35-1.41 (1H, m); ^{13}C NMR δ 210.4, 193.8, 123.7, 53.2, 49.9, 42.8, 39.3, 36.2, 31.9, 30.7, 20.0; IR 2931, 2856, 1708, 1692, 1624 cm^{-1}; EI MS m/z 162 (M^+); HRMS m/z calcd for $C_{11}H_{14}O$ (M^+) 162.1044, found: 162.1044.

4,4,6,7,8,9-Hexahydro-3a,8-methanocyclopentacycloocten-2-one (2c); oil; ^{1}H NMR δ 5.79 (1H, t, J = 1.7 Hz), 2.96 (1H, dd, J = 9.2, 19.6 Hz), 2.63-2.78 (1H, m), 2.43 (1H, d, J = 19.6 Hz), 2.39, 2.82 (each 1H, d, J = 16.8 Hz), 2.02 (1H, d, J = 12.5 Hz), 1.23-1.95 (9H, m); ^{13}C NMR δ 210.5, 195.0, 124.1, 55.0, 53.7, 42.5, 38.4, 37.0, 36.8, 33.9, 25.3, 25.0; IR 2920, 2855, 1703, 1624 cm^{-1}; EI MS m/z 176 (M^+); HRMS m/z calcd for $C_{12}H_{16}O$ (M^+) 176.1200, found: 176.1208.

***N*-Benzyloxycarbonyl 3-oxo-8-azatricyclo[5.3.1.0^{1,5}]undec-4-ene (2d)**; oil; ^{1}H NMR δ 7.36 (5H, s), 5.93 (1H, s), 5.15 (2H, s), 4.95-5.20 (1H, m), 4.09 (1H, br s), 2.96-3.15 (1H, m), 2.70-2.87 (2H, m), 2.32 (2H, s), 1.97-2.09 (1H, m), 1.89 (1H, d, J = 11.2 Hz), 1.50-1.65 (1H, m), 1.30-1.45 (1H, m); ^{13}C NMR δ 208.8, 188.4, 136.4, 128.4, 128.2, 128.0, 127.8, 124.9, 67.1, 54.8, 52.2, 48.7, 42.2, 38.8, 36.9, 32.8; IR 2954, 1697, 1624 cm^{-1}; EI MS m/z 297 (M^+); HRMS m/z calcd for $C_{18}H_{19}NO_3$ (M^+) 297.1364, found: 297.1364.

***N*-Methyl-8-azatricyclo[5.3.1.0^{1,5}]undec-4-en-3-one (2e)**; oil; ^{1}H NMR δ 5.85 (1H, s), 3.45 (1H, t, J = 4.8 Hz), 2.89 (1H, d, J = 19.6 Hz), 2.77 (1H, dd, J = 4.8, 11.3 Hz), 2.29 (3H, s), 2.00-2.36 (6H, m), 1.54 (1H, ddd, J = 2.9, 4.4, 13.9 Hz), 1.24-1.33 (1H, m); ^{13}C NMR δ 210.2, 190.7, 124.1, 62.8, 51.8, 48.5, 48.4, 43.1, 43.0, 37.2, 24.5; IR 2986, 2852, 1696, 1624 cm^{-1}; EI MS m/z 177 (M^+); HRMS m/z calcd for $C_{11}H_{15}NO$ (M^+) 177.1152, found: 177.1152.

8-Oxatricyclo[5.3.1.0^{1,5}]undec-4-en-3-one (2f); mp 61-62°C (AcOEt-hexane); ^{1}H NMR δ 5.92 (1H, s), 4.65-4.68 (1H, m), 3.86 (1H, dd, *J* = 6.9, 12.2 Hz), 3.73 (1H, dd, *J* = 4.3, 12.2 Hz), 2.98 (1H, d, *J* = 20.1 Hz), 2.68 (1H, dd, *J* = 4.6, 20.1 Hz), 2.30 (2H, s), 2.18 (1H, dt, *J* = 6.9, 12.5 Hz), 2.06 (1H, dd, *J* = 2.3, 11.5 Hz), 1.43-1.49 (1H, m), 1.25-1.32 (1H, m); ^{13}C NMR δ 209.3, 188.8, 124.6, 76.7, 60.6, 51.9, 48.8, 43.0, 39.0, 32.2; IR 2960, 2857, 1699, 1635 cm^{-1}; EI MS *m/z* 164 (M^+); HRMS *m/z* calcd for $C_{10}H_{12}NO_2$ (M^+) 164.0837, found: 164.0822.

General Procedure for Synthesis of Silyl Enol Ethers (11a,b). To a stirred solution of ketone (**10a** or **10b**) (1 eq.) and Et_3N (1.2 eq.) in CH_2Cl_2 (3 mL per 1 mmol of ketone) at 0°C under argon was added TMSOTf (1.1 eq.). After being stirred for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The organic layer was washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by bulb-to-bulb distillation.

4-Methylene-1-trimethylsilyloxycyclohexene (11a); from **10a** (0.550 g, 5.0 mmol), **11a** (0.890 g, 97.8%) was obtained as a colorless oil; bp 120°C/40 mmHg; ^{1}H NMR δ 4.78-4.81 (1H, m), 4.74, 4.72 (each 1H, s), 2.73-2.80 (2H, m), 2.33 (2H, t, *J* = 6.6 Hz), 2.10-2.15 (2H, m), 0.17 (9H, s); EI MS *m/z* 182 (M^+); HRMS *m/z* calcd for $C_{10}H_{18}OSi$ (M^+) 182.1127, found: 182.1128.

4-Ethylidene-1-trimethylsilyloxycyclohexene (11b); from **10b** (0.992 g, 8.0 mmol), **11b** (1.156 g, 99.9%) was obtained as a colorless oil; bp 140°C/40 mmHg; ^{1}H NMR δ 5.18-5.32 (1H, m), 4.79-4.82 (1H, m), 2.66-2.73 (2H, m), 2.25-2.55 (2H, m), 2.02-2.10 (2H, m), 1.55-1.65 (3H, m), 0.17 (5H, s), 0.16 (4H, s); EI MS *m/z* 196 (M^+); HRMS *m/z* calcd for $C_{11}H_{20}OSi$ (M^+) 196.1283, found: 196.1281.

General Procedure for Synthesis of Pauson-Khand Precursors (13a-d). To a stirred solution of the silyl enol ether (**11a** or **11b**) (5.0 mmol) and the cobalt complex (**12a** or **12b**) (6.0 mmol) in CH_2Cl_2 (60 mL) at –78°C under argon was added a 0.95M hexane solution of Et_2AlCl (5.9 mmol). The mixture was warmed up to 0°C for 24 h. After the reaction was quenched with water, the mixture was extracted with $CHCl_3$. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by column chromatography (benzene : hexane = 1 : 2 then 1 : 1) to afford the corresponding alkyne-cobalt complex (**13a-d**).

13a; from **12a**, **13a** (1.584 g, 72.9%) was obtained as black mass solid; ^{1}H NMR δ 6.09 (1H, s), 5.00 (2H, s), 3.54 (1H, d, *J* = 15.3 Hz), 2.25-3.05 (8H, m); IR 2090, 2050, 1993, 1704 cm^{-1}; EI MS *m/z* 406 (M^+-CO); HRMS *m/z* calcd for $C_{15}H_{12}O_6Co_2$ (M^+-CO) 406.9298, found: 406.9296.

13b; from **12b**, **13b** (1.576 g, 70.4%) was obtained as a mixture of regio-isomers as a black tar; ^{1}H NMR δ 6.06 (0.52H, s), 6.02 (0.48H, s), 5.30-5.50 (1H, m), 3.38-3.54 (1H, m), 1.99-3.08 (8H, m), 1.66 (3H, d, *J* = 6.3 Hz); IR 2091, 2050, 1998, 1714 cm^{-1}; EI MS *m/z* 420 (M^+-CO); HRMS *m/z* calcd for $C_{16}H_{14}O_6Co_2$ (M^+-CO) 419.9454, found: 419.9450.

13c; from **12a**, **13c** (1.255 g, 54.4%) was obtained as a black mass solid; ^{1}H NMR δ 6.02 (0.52H, s), 6.00

(0.48H, s), 5.44 (1H, br s), 3.40-3.53 (1H, m), 1.90-3.10 (8H, m), 1.66 (3H, d, J = 6.7 Hz); EI MS m/z 433 (M^+-C_2H_4); HRMS m/z calcd for $C_{16}H_{12}O_7Co_2$ (M^+-C_2H_4) 433.9247, found: 433.9250.

13d; from **12b**, **13d** (1.238 g, 52.9%) was obtained as a mixture of regio-isomers as a black tar; ^{1}H NMR δ 6.13 (1H, s), 5.39 (1H, br s), 2.10-3.20 (6H, m), 1.50-2.67 (4H, m), 1.41 (1.23H, s), 1.44 (1.77H, s), 1.34 (1.23H, s), 1.31 (1.77H, s); IR 2974 cm^{-1}; EI MS m/z 448 (M^+- C_2H_4); HRMS m/z calcd for $C_{17}H_{14}O_7Co_2$ (M^+-C_2H_4) 447.9408, found: 447.9404.

Convesion of Ketones (13a,b) to Acetals (14a,b). A solution of the ketone (**13a** or **13b**) (1 eq.), trimethyl orthoformate (2 eq.), ethylene glycol (10 eq.), and p-TsOH•H_2O (0.4 eq.) in CH_2Cl_2 (10 mL per 1 mmol of **13a,b**) at rt was stirred for 22 h. The mixture was washed with water and brine, successively. The organic layer was dried and evaporated under reduced pressure to give the corresponding acetal (**14a** or **14b**).

(14a); from **13a** (0.679 g, 1.57 mmol), **14a** (0.724 g, 96.7%) was obtained as a black oil; ^{1}H NMR δ 6.06 (1H, s), 4.73 (1H, s), 4.69 (1H, s), 3.99 (4H, br s), 3.18 (1H, d, J = 15.3 Hz), 2.71 (1H, dd, J = 10.0, 15.3 Hz), 2.55 (1H, dd, J = 4.5, 13.3 Hz), 2.19-2.30 (3H, m), 1.77-1.86 (2H, m), 150-1.59 (1H, m); IR 2091, 2050, 2016 cm^{-1}; EI MS m/z 450 (M^+-CO); HRMS m/z calcd for $C_{17}H_{16}O_7Co_2$ (M^+-CO) 449.9560, found: 449.9559.

(14b); from **13b** (0.538 g, 1.20 mmol), **14b** (0.558 g, 94.5%) was obtained as a mixture of regio-isomers as a black oil; ^{1}H NMR δ 6.09 (0.53H, s), 6.06 (0.47H, s), 5.20-5.30 (1H, m), 3.99 (4H, br s), 3.12-3.22 (1H, m), 2.10-2.73 (5H, m), 1.41-1.89 (6H, m); IR 2090, 2050, 2015, 1736 cm^{-1}; EI MS m/z 464 (M^+-CO); HRMS m/z calcd for $C_{18}H_{18}O_7Co_2$ (M^+-CO) 463.9717, found: 463.9733.

Convesion of Ketone (13a) to Acetal (14c). A solution of **13a** (0.100 g, 0.23 mmol), trimethyl orthoformate (30 μL, 0.27 mmol), (1*S*,2*S*)-hydrobenzoin (0.060 g, 0.28 mmol), and p-TsOH•H_2O (0.018 g, 0.09 mmol) in CH_2Cl_2 (2 mL) at rt was stirred for 22 h. The mixture was washed with water and brine, successively. The organic layer was dried and evaporated under reduced pressure to give a residue, which was purified by TLC (hexane : AcOEt = 8 : 1) to afford **14c** (0.073 g, 50.4%) as a mixture of regio-isomers as a black oil and **13a** (0.042 g, 42.2%). ^{1}H NMR δ 7.18-7.31 (10H, m), 6.10 (0.54H, s), 6.09 (0.46H, s), 4.65-4.88 (4H, m), 3.57 (0.54H, d, J = 14.8 Hz), 3.46 (0.46H, d, J = 14.5 Hz), 3.01 (0.54H, dd, J = 10.2, 14.8 Hz), 2.87 (0.46H, dd, J = 10.7, 14.5 Hz), 2.55-2.74 (1H, m), 2.30-2.50 (3H, m), 1.80-2.20 (3H, m); IR 2090, 2053, 2018 cm^{-1}; EI MS m/z 602 (M^+-CO); HRMS m/z calcd for $C_{29}H_{24}O_7Co_2$ (M^+-CO) 602.0816, found: 602.0811.

General Procedures for Pauson-Khand Reaction of *exo*-Cyclic Enynes (13a-d, 14a-c). The reaction of enyne (1 eq.) in toluene, CH_2ClCH_2Cl or CH_2Cl_2, was performed. Method A: refluxing in toluene; Method B: heating at 83°C with BuSMe (3.5 eq.) in $CHCl_2CHCl_2$; Method C: oxidative treatment with *N*-methylmorpholine *N*-oxide (12 eq.) at rt in CH_2Cl_2. The solvent was removed under reduced pressure to give a residue, which was diluted with Et_2O. The precipitate was removed by suction filtration through a

Celite 545 short pad. Purification of the products obtained by Methods A-C was carried out on preparative TLC.

4,5,7,8-Tetrahydro-3a,7-methanoazulene-2,6-dione (15a); mp 73-74˚C (AcOEt-hexane); ^{1}H NMR δ 6.00 (1H, t, *J* = 1.6 Hz), 3.04 (1H, t, *J* = 5.4 Hz), 2.86-2.90 (2H, m), 2.33-2.59 (2H, m), 2.43 (2H, s), 2.21, 2.13 (each 1H, d, *J* = 11.4 Hz), 1.88-2.04 (1H, m), 1.68-1.78 (1H, m); ^{13}C NMR δ 210.2, 208.8, 188.6, 125.7, 52.3, 51.2, 48.4, 40.5, 36.7, 34.7, 31.5; IR 2960, 2869, 1716, 1691, 1624 cm^{-1}; EI MS *m/z* 176 (M^+); HRMS *m/z* calcd for $C_{11}H_{12}O_2$ (M^+) 176.0837, found: 176.0847.

4,5,7,8-Tetrahydro-3-methyl-3a,7-methanoazulene-2,6-dione (15b); oil; ^{1}H NMR δ 6.04 (0.25H, t, *J* = 1.7 Hz, olefinic H), 5.93 (0.75H, t, *J* = 1.7 Hz, olefinic H), 2.75-3.10 (3H, m), 2.30-2.60 (3H, m), 1.41-2.23 (4H, m), 1.16 (0.75H, d, *J* = 7.3 Hz), 1.09 (2.25H, d, *J* = 7.6 Hz); ^{13}C NMR δ 212.8, 210.7, 187.3, 124.6, 123.4, 56.1, 53.1, 51.6, 50.9, 50.8, 40.9, 38.1, 35.9, 35.0, 34.6, 33.3, 31.8, 31.7, 29.7, 14.3, 9.3; IR 2964, 2932, 2872, 1707, 1696, 1633 cm^{-1}; EI MS *m/z* 190 (M^+); HRMS *m/z* calcd for $C_{12}H_{14}O_2$ (M^+) 190.0994, found: 190.0991.

4,5,7,8-Tetrahydro-8,8-dimethyl-3a,7-methanoazulene-2,6-dione (15c); mp 134-135˚C (AcOEt-hexane); ^{1}H NMR δ 5.92 (1H, s), 2.61 (1H, d, *J* = 3.6 Hz), 2.53, 2.40 (each 1H, d, *J* = 17 Hz), 1.95-2.45 (5H, m), 1.60-1.73 (1H, m), 1.33, 1.29 (each 3H, s); ^{13}C NMR δ 210.4, 208.5, 198.9, 123.1, 63.7, 52.8, 50.4, 42.4, 36.9, 35.8, 35.6, 31.3, 22.5; IR 2969, 2872, 1700, 1620 cm^{-1}; EI MS *m/z* 204 (M^+); HRMS *m/z* calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found: 204.1142.

4,5,7,8-Tetrahydro-3,8,8-trimethyl-3a,7-methanoazulene-2,6-dione (15da); mp 167-168˚C (AcOEt-hexane); ^{1}H NMR δ 5.96 (1H, s), 2.63 (1H, d, *J* = 3.9 Hz), 2.56 (1H, dd, *J* = 9.0, 18.6 Hz), 2.54 (1H, q, *J* = 7.2 Hz), 2.36 (1H, dt, *J* = 9.8, 18.6 Hz), 2.10, 2.03 (each 1H, d, *J* = 10.8 Hz), 2.05-2.12 (1H, m), 1.43 (1H, t, *J* = 11.4 Hz), 1.34, 1.27 (each 3H, s), 1.15 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ 210.4, 197.2, 172.8, 122.3, 64.2, 56.4, 54.9, 42.7, 37.5, 35.7, 32.8, 31.2, 22.2, 9.3; IR 2967, 2932, 2871, 1700, 1621 cm^{-1}; EI MS *m/z* 218 (M^+); HRMS *m/z* calcd for $C_{14}H_{18}O_2$ (M^+) 218.1305, found: 218.1303.

4,5,7,8-Tetrahydro-3,8,8-trimethyl-3a,7-methanoazulene-2,6-dione (15db); mp 156-157˚C (AcOEt-hexane); ^{1}H NMR δ 5.84 (1H, s), 2.61 (1H, d, *J* = 4.9 Hz), 2.54 (1H, dd, *J* = 9.0, 18.6 Hz), 2.36 (1H, q, *J* = 7.6 Hz), 2.33-2.43 (1H, m), 2.16-2.24 (2H, m), 1.83 (1H, d, *J* = 12.4 Hz), 1.63-1.70 (1H, m), 1.33, 1.26 (each 3H, s), 1.11 (3H, d, *J* = 7.6 Hz); ^{13}C NMR δ 212.7, 210.6, 197.8, 120.9, 63.4, 56.8, 52.8, 42.7, 37.8, 36.0, 32.4, 30.8, 22.3, 14.8; IR 2973, 2956, 2937, 2868, 1701, 1621 cm^{-1}; EI MS *m/z* 218 (M^+); HRMS *m/z* calcd for $C_{14}H_{18}O_2$ (M^+) 218.1305, found: 218.1312.

6,6-Ethylenedioxy-4,5,7,8-tetrahydro-3a,7-methanoazulene-2-one (16a); mp 113-114˚C (AcOEt-hexane); ^{1}H NMR δ 5.87 (1H, s), 3.85-4.08 (4H, m), 2.76 (1H, d, *J* = 19.8 Hz), 2.65 (1H, dd, *J* = 1.0, 18.1 Hz), 2.44 (1H, t, *J* = 5.8 Hz), 2.28 (2H, s), 2.21 (1H, dd, *J* = 1.7, 5.8 Hz), 1.91-2.02 (1H, m), 1.66-1.72 (2H, m), 1.50 (1H, ddd, *J* = 3.0, 5.6, 11.6 Hz), 1.31-1.39 (1H, m); ^{13}C NMR δ 209.9, 191.7, 124.7, 109.6,

64.7, 64.1, 52.0, 48.7, 44.9, 38.7, 35.7, 30.7, 30.2; IR 1696, 1621 cm^{-1}; EI MS *m/z* 220 (M^+); HRMS *m/z* calcd for $C_{13}H_{16}O_3$ (M^+) 220.1097, found: 220.1097.

6,6-Ethylenedioxy-4,5,7,8-tetrahydro-3-methyl-3a,7-methanoazulene-2-dione (16b); mp 113-118°C; ^1H NMR δ 5.90 (0.26H, s), 5.80 (0.74H, s), 3.85-4.08 (4H, m), 2.79 (0.26H, s), 2.72 (0.74H, s), 2.42-2.63 (2H, m), 2.17-2.28 (1H, m), 1.26-1.84 (6H, m), 1.10 (0.78H, d, *J* = 7.3 Hz), 1.02 (2.22H, d, *J* = 7.6 Hz); ^{13}C NMR δ 213.9, 190.4, 189.7, 123.5, 122.5, 110.1, 109.9, 64.8, 64.2, 55.8, 55.3, 53.3, 51.1, 45.2, 44.5, 39.0, 37.2, 34.0, 31.9, 31.0, 30.9, 30.4, 29.9, 29.6, 14.1; IR 1691, 1627 cm^{-1}; EI MS *m/z* 234 (M^+); HRMS *m/z* calcd for $C_{14}H_{18}O_3$ (M^+) 234.1255, found: 234.1264.

6,6-(1,2-Diphenylethylenedioxy)-4,5,7,8-tetrahydro-3a,7-methanoazulen-2-one (16c); amorphous solid; ^1H NMR δ 7.15-7.43 (10H, m), 5.93 (0.52H, s), 5.92 (0.48H, s), 4.67-4.84 (2H, m), 2.61-3.04 (3H, m), 1.90-2.52 (6H, m), 1.40-1.75 (2H, m); ^{13}C NMR δ 209.9, 191.6, 191.5, 137.0, 136.8, 136.4, 136.1, 128.5, 128.4, 128.3, 126.8, 126.7, 126.6, 126.5, 125.0, 124.9, 110.6, 110.2, 85.7, 84.8, 52.4, 52.0, 48.8, 48.7, 46.4, 39.1, 38.4, 35.8, 35.6, 32.1, 31.4, 30.9, 30.6; IR 1696, 1626 cm^{-1}; EI MS *m/z* 372 (M^+); HRMS *m/z* calcd for $C_{25}H_{24}O_3$ (M^+) 372.1725, found: 372.1720.

6,6-Ethylenedioxy-4,5,7,8-tetrahydro-3,8,8-trimethyl-3a,7-methanoazulene-2,6-dione (17a); mp 86°C (hexane); ^1H NMR δ 5.83 (1H, s), 3.80-4.06 (4H, m), 2.30 (1H, q, *J* = 7.2 Hz), 2.23 (1H, dd, *J* = 11.7 Hz), 1.98 (1H, d, *J* = 5.1 Hz), 1.69-1.87 (4H, m), 1.48, 1.20 (each 3H, s), 1.14-1.25 (1H, m), 1.09 (3H, d, *J* = 7.2 Hz); ^{13}C NMR δ 211.5, 200.3, 120.9, 110.0, 64.8, 63.5, 56.5, 56.3, 55.0, 42.3, 37.8, 33.7, 32.8, 30.9, 22.6, 8.8; IR 2969, 2932, 2883, 1706, 1623 cm^{-1}; EI MS *m/z* 262 (M^+); HRMS *m/z* calcd for $C_{16}H_{22}O_3$ (M^+) 262.1569, found: 262.1570.

6,6-Ethylenedioxy-4,5,7,8-tetrahydro-3,8,8-trimethyl-3a,7-methanoazulene-2,6-dione (17b); mp 84°C (hexane); ^1H NMR δ 5.77 (1H, s), 3.79-4.05 (4H, m), 2.24 (1H, q, *J* = 7.5 Hz), 1.90-2.03 (3H, m), 1.69-1.79 (3H, m), 1.48, 1.19 (each 3H, s), 1.22-1.34 (1H, m), 1.01 (3H, d, *J* = 7.5 Hz); ^{13}C NMR δ 213.8, 201.2, 119.6, 110.1, 64.8, 63.5, 57.0, 55.6, 52.5, 42.3, 39.1, 32.7, 32.5, 31.6, 22.6, 14.8; IR 2968, 2926, 2876, 1699, 1623 cm^{-1}; EI MS *m/z* 262 (M^+); HRMS *m/z* calcd for $C_{16}H_{22}O_3$ (M^+) 262.1569, found: 262.1574.

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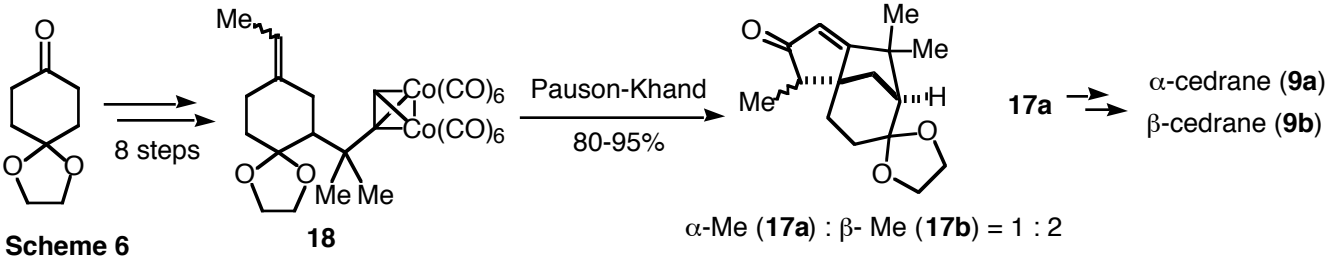

Scheme 6 **18**

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