Pergamon

Tetrahedron 57 (2001) 2729–2738

TETRAHEDRON

Investigation of the synthesis of angular tricyclic compounds by intramolecular Pauson–Khand reaction of *exo*- and *endo*-cyclic enynes

Miyuki Ishizaki,* Kazuhiko Iwahara, Yuka Niimi, Hiroshi Satoh and Osamu Hoshino*

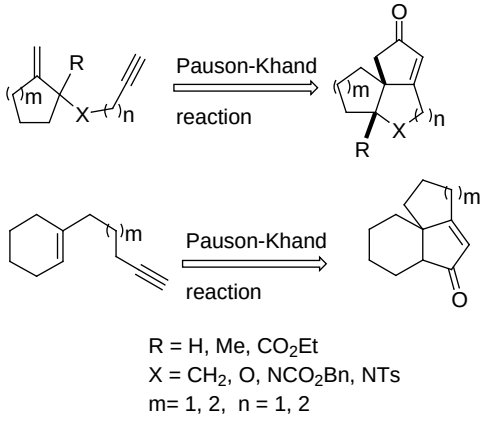
Faculty of Pharmaceutical Sciences, Science University of Tokyo, 12, Ichigaya Funagawara-machi, Shinjuku-ku, Tokyo 162-0826, Japan

Received 11 January 2001; accepted 5 February 2001

Abstract—Intramolecular Pauson–Khand reaction of various alkynyl *exo*-alkylidene-cyclohexanes and -pentane gives angular type 6–5–5 and 5–5–5 tricyclic compounds in good to high yield. The present reaction also offers convenient construction of two contiguous quaternary centers, which could not be synthesized from alkynyl *endo*-cycloolefins. Scope and limitation of the present reaction of various *exo*- and *endo*-cyclic enynes are also described.

1. Introduction

Since the first report[1] of intermolecular Pauson–Khand reaction in 1971, it is well known to be a useful reaction for formation of cyclopentenones from an alkyne–cobalt complex with alkenes by [2+2+1] cycloaddition.[2] In 1981, Schore and co-workers[3] reported the first intramolecular version of the Pauson–Khand reaction and the reaction has been widely applicable protocol for synthesis of natural products.[4] However, for the intramolecular reaction of cyclic olefins, there are many reports on the reaction of *endo*-cyclic cyclopentenes[5] having alkynyl group on olefinic moiety to give angular tricyclic compounds, which constitute the 5–5–5 ring system, so called triquinanes. The similar reaction of *exo*-cyclic enynes is an alternative useful approach to obtain angular tricyclic compounds. However, only a few reports[6] on *exo*-cyclic enynes containing three or four membered ring systems have appeared, despite of the possibility that the latter approach should be superior to the former one; highly hindered tetra-substituted cyclic enynes are required for synthesis of angular tricyclic compounds having continuous quaternary carbon centers[7] by the reaction of *endo*-cyclic enynes.[8] Concurrently, Malacria and co-workers have reported[6d] synthesis of angular triquinane by intramolecular Pauson–Khand reaction of *exo*-cyclic enyne, although the yield was quite moderate (20%). Therefore, the difference of reactivity on intramolecular Pauson–Khand reaction of *exo*- and *endo*-cyclic olefins attracted us to investigate its scope and limitation. Here, we wish to report our results on the reaction of various *exo*- and *endo*-cyclic enynes to form angular type 6–5–5 and 5–5–5 tricyclic compounds (Scheme 1).[9]



Scheme 1.

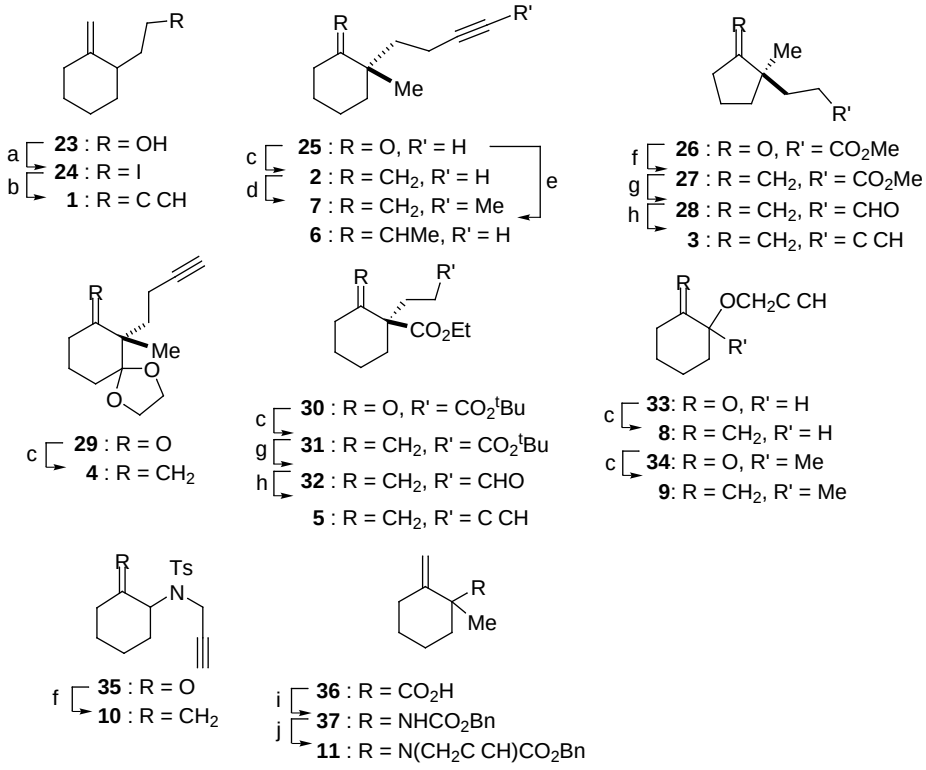
2. Results and discussion

At first, we examined intramolecular Pauson–Khand reactions of various *exo*-cyclic enynes (**1**–**11**), which would lead to 6–5–5 and 5–5–5 angular tricyclic compounds. Synthesis of various *exo*-cyclic enynes (**1**–**11**) was as follows (Scheme 2). Namely, conversion of alcohol (**23**)[10] to iodide (**24**), treatment of which with acetylene–ethylenediamine complex gave an enyne (**1**) in 64% overall yield. Enynes (**2**, **4**, **6**, **8**–**10**) were synthesized in 25–90% yield by Wittig olefination of the corresponding ketones (**25**,[11] **29**,[12] **33**,[13] **34**,[13] **35**[14]). Treatment of **2** with BuLi followed by exposure with MeI afforded **7** in 91% yield. Enynes (**3**, **5**)

Keywords: Pauson–Khand reaction; exocyclic enyne; endocyclic enyne; angular tricyclic compound.

* Corresponding authors. Tel.: +81-3-3260-6725; fax: +81-3-3258-3045; e-mail: ishizaki@ps.kagu.sut.ac.jp; hoshino@ps.kagu.sut.ac.jp

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00151-X



Scheme 2. (a) PPh_3, I_2, Py, CH_2Cl_2; (b) HC≡CLi(en), DMSO–Et_2O; (c) MeBr·PPh_3, *t*-BuOK, THF; (d) BuLi, MeI, THF; (e) EtBr·PPh_3, *t*-BuOK, THF; (f) CH_2Br_2, Zn, $TiCl_4$, CH_2Cl_2; (g) DIBAH, THF; (h) MeCOC(=N_2)P(=O)$(OEt)_2$, K_2CO_3, MeOH; (i) DPPA, Et_3N, BnOH, PhMe; (j) NaH, 3-bromopropyne, THF.

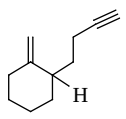
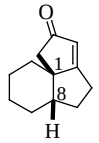
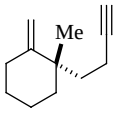
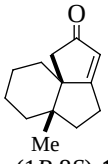
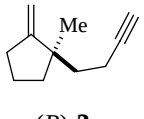
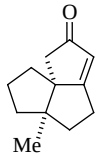
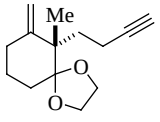
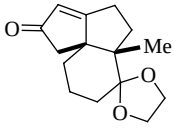
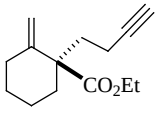
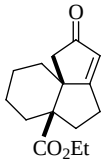
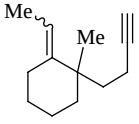
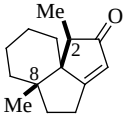
were obtained from **26**[15] and **30**[16] by Wittig olefination, reduction with DIBAH and reaction with diethyl 1-diazo-2-oxopropylphosphonate.[17] A nitrogen atom containing enyne (**11**) was synthesized from **36**[18] by Curtius rearrangement and propargylation.

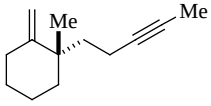
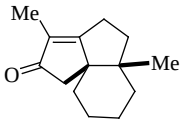
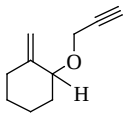
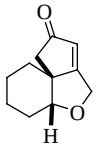
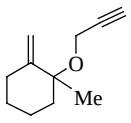
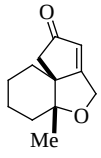
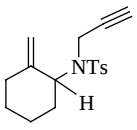
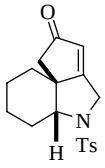
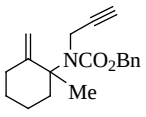
With *exo*-cyclic enynes (**1**–**11**) in hand, intramolecular reaction of an alkyne–cobalt complex bearing *exo*-cyclic olefins (**1**–**11**) was performed by the following methods although there are many methods[19] for the reaction as a convenient treatment; treatment with NMO (*N*-methylmorpholine *N*-oxide)[19a] in CH_2Cl_2 at rt (Method A); refluxing in benzene with TMANO (trimethylamine *N*-oxide)[19b] (Method B); refluxing in benzene (Method C); refluxing in toluene (Method D). The results are shown in Table 1.

At first, we investigated the reaction of 1-(3-butynyl)-2-methylenecyclohexane (**1**). The reaction by Methods A–C smoothly proceeded stereoselectively to give the desired angular tricyclic compound (**12**), which constitutes the 6–5–5 ring system, in 66–81% yield (runs 1–3). To the best of our knowledge, this is the first synthesis of angular type 6–5–5 ring system by intramolecular Pauson–Khand reaction. The reaction of 1-(3-butynyl)-1-methyl-2-methylenecyclohexane (**2**) afforded **13**, which has two continuous quaternary carbon centers, in 57–85% yield (runs 4–6). Stereochemistry of **13** was confirmed by NOE experiment between Me group (δ 0.77) and C_2–H (δ 2.10). Plausible reaction mechanisms on the formation of **13** from **2** are depicted in Scheme 3. The reaction of **2** with $Co_2(CO)_8$ gives a cobalt-complex, the preferable conformation of which would be **2a** by the 1,3-allylic strain. Then, **2a** would produce (1*R*,8*S*)-**13**, stereoselectively. On the basis of the reaction mechanism, stereochemistry of other angular tricyclic products was estimated. Kundensen and Shore have reported[5a,b] that intramolecular Pauson–Khand reaction of *endo*-cyclic tetra-substituted olefin could not give the desired product bearing two continuous quaternary carbon centers, which was attributed to steric hindrance of tetra-substituted olefins. Therefore, the present reaction offers practical method for construction of such product.[8] Similarly, 1-(3-butynyl)-1-methyl-2-methylenecyclopentane (**3**) furnished triquinane (**14**) in 89% yield by Method B (run 7). Functionalized enynes (**4**, **5**) gave the corresponding tricyclic compounds (**15**, **16**) in 50–86% yield (runs 8–10). The reaction of tri-substituted olefin (**6**) afforded **17** as a sole stereochemical product in low yield with amine *N*-oxide (Methods A and B), however, in 49% yield under refluxing in benzene (Method C) and in 53% yield in toluene (Method D) (runs 11–14).[20] Stereochemistry of **17** was determined by NOE experiment between two Me groups attached to C_2 (δ 0.90) and C_8 (δ 1.28). Similarly, the reaction of substituted alkyne (**7**) gave tricyclic compound (**18**) in 32% yield by Method C, and in 63% yield by Method D (runs 17 and 18). This remarkable temperature effect suggested that the transition state in the reaction of hindered enynes (**6**, **7**) would require high activation energy. Synthesis of various angular aza- and oxa-tricyclic compounds (**19**–**22**) from enynes (**8**–**11**) was also successful in good yield (runs 19–29).

We next carried out the reaction of homologues (**40**, **44**) of *exo*-cyclic enynes (**2**, **3**), in order to examine the possibility of formation of 6–6–5 and 5–6–5 tricyclic systems by the

Table 1. Intramolecular Pauson–Khand reaction of various exocyclic olefins bearing alkynyl group

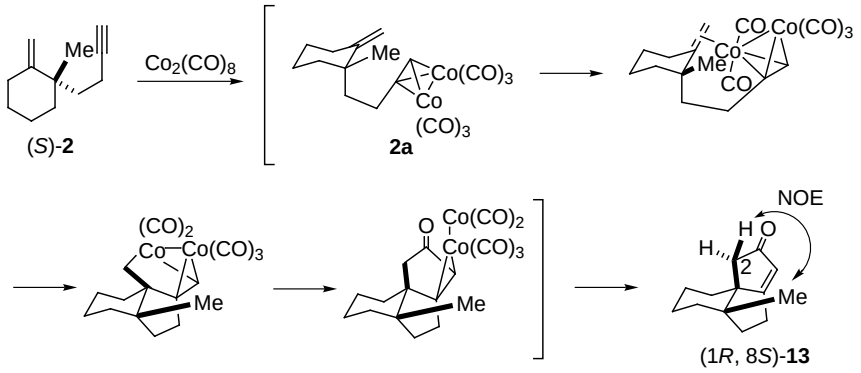
Run	Substrate	Method[a]	Time(h)	Product(%)[b]
1	 (±)-**1**	A	2	 (±)-**12** 71
2		B	3	66
3		C	1	81
4	 (*S*)-**2**	A	3	 (1*R*,8*S*)-**13** 57
5		B	2	85
6		C	2	74
7	 (*R*)-**3**	B	2	 (1*S*,8*R*)-**14** 89
8	 (*S*)-**4**	B	4	 (1*S*,8*S*)-**15** 86
9	 (*S*)-**5**	A	3	 (1*S*,8*R*)-**16** 50
10		C	3	73
11	 (±)-**6**	A	2	 (±)-**17** 22
12	(*E*/*Z* = 18/82)	B	3	25
13		C	2	49
14		D	2	53

Run	Substrate	Method[a]	Time(h)	Product(%)[b]
15	 (±)-**7**	A	13	 (±)-**18** 27
16		B	8	36
17		C	6	32
18		D	6	63
19	 (±)-**8**	A	3	 (±)-**19** 65
20		B	2	67
21		C	3	71
22	 (±)-**9**	A	2	 (±)-**20** 73
23		B	2	43
24		C	3	68
25	 (±)-**10**	A	1	 (±)-**21** 88
26		B	2	48
27		C	2	77
28	 (±)-**11**	A	2	 (±)-**22** 80
29		C	2	80

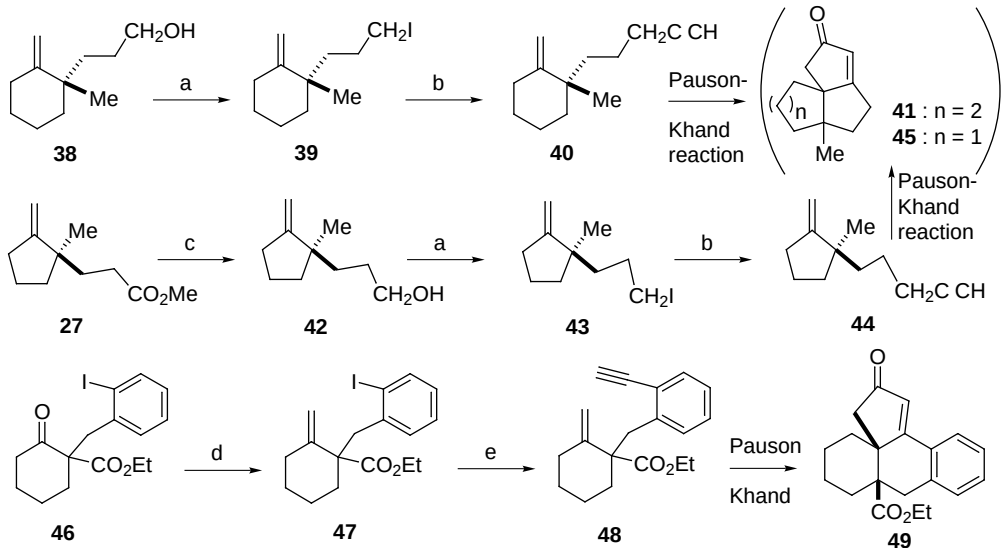
[a] See text.
[b] Isolated yield.

intramolecular Pauson–Khand reaction (Scheme 4). Thus, 1-methyl-2-methylene-1-(4-pentynyl)cyclo-hexane (**40**) and -pentane (**44**) were prepared from alcohol (**38**)[21] and ester (**27**) in several steps. However, the reaction of **40** and **44** by both Methods A and C did not afford the desired tricyclic compounds (**41**, **45**) at all, although formation of alkyne–cobalt complex was detected on TLC. These results mean that a conformation in transition state would play an important role. For confirming the assumption, we also synthesized enyne (**48**) having a rigid conformation due to an aromatic ring by Wittig olefination of **46**[22] followed by Pd-mediated coupling with trimethylsilylacetylene and desilylation.[23] Gratifyingly, the reaction of **48** by Method D gave a new desired angular tetracyclic compound (**49**), although in low yield (11.3%). These results indicated that conformational change of the substrate would be an important factor to occur in the Pauson–Khand reaction of *exo*-cyclic enynes.

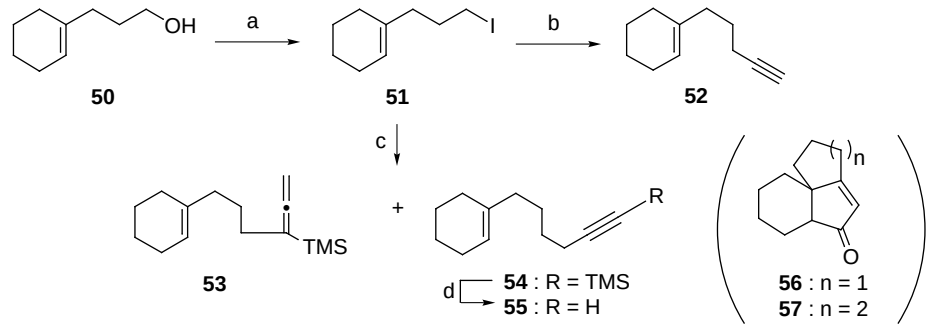
Finally, we examined to synthesize 6–5–5 and 6–5–6 tricyclic compounds by intramolecular Pauson–Khand reaction of *endo*-cyclic enynes (**52**, **55**) (Scheme 5). Thus,



Scheme 3.



Scheme 4. (a) PPh_3, I_2, Py, CH_2Cl_2; (b) HC≡CLi(en), DMSO–Et_2O; (c) $LiAlH_4$, THF; (d) MeBr·PPh_3, *t*-BuOK, THF; (e) TMSC≡CH, $PdCl_2(PPh_3)_2$, CuI, Et_3N, CH_2Cl_2, TBAF, THF.



Scheme 5. (a) PPh_3, I_2, Py, CH_2Cl_2; (b) HC≡CLi(en), DMSO–Et_2O; (c) TMSC≡CCH_3, BuLi, THF; (d) NaOH, MeOH, H_2O.

enyne (**52**) was prepared from **50** in the usual manner as described above. Propargylation[24] of iodide (**51**) with trimethylsilypropynyllithium afforded propadiene (**53**) and enyne (**54**) in 15 and 85% yield, respectively. Desilylation[23] of **54** gave **55** in 94% yield. The reaction of both enynes (**52**, **55**) by Methods A and C did not produce the desired tricyclic compounds (**56**, **57**) at all. At this stage, the reason why desired compounds could not be formed was uncertain.

3. Conclusions

In summary, we have investigated intramolecular Pauson–Khand reaction of *exo*- and *endo*-cyclic enynes. Feature of the present reaction is as follows: (1) 6–5–5 and 5–5–5 type angular tricyclic skeletons including continuous quaternary centers were constructed by the reaction of *exo*-cyclic enynes (**1**–**11**) in good to high yield; (2) cyclization of homologues (**40**, **44**) of enynes (**2**, **3**) did not afford

the desired tricyclic compound, except for the reaction of enyne (**48**) containing an aromatic ring; (3) under conditions similar to those noted for *exo*-cyclic enynes, the reaction of *endo*-cyclic enynes (**52**, **55**) did not give 6–5–5 and 5–6–5 type angular tricyclic compounds at all. Thus, intramolecular Pauson–Khand reaction of *exo*-cyclic enynes offers a convenient preparation of angular type 6–5–5 and 6–6–5 tricyclic compounds, which could not be synthesized from *endo*-cyclic enynes. Furthermore, it is noteworthy that the present reaction is effective for construction of contiguous quaternary centers, which is difficult in the reaction of *endo*-cyclic olefins.[8]

4. Experimental

4.1. General

All melting and boiling points were measured on a Büchi or a Yanagimoto (hot plate) melting point apparatus and by bulb-to-bulb distillation apparatus, and are uncorrected. IR spectra were obtained with a Hitachi 260-10 spectrophotometer or JASCO FT/IR-400. ^{1}H and ^{13}C NMR spectra were taken with a JEOL EX-270 (270 MHz for ^{1}H NMR and 67.5 MHz for ^{13}C NMR) spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi M-80 or a JEOL JMS D-300 spectrometer. Column chromatography was performed over silica gel (Wako gel C-200 or Merck Kiegelsel 60). Preparative TLCs were run on Merck 5744, or Merck 5715 plates. Organic extracts were dried over $MgSO_4$, unless otherwise indicated.

4.2. General procedure for conversion of alcohols (23, 38, 42, 50) to iodides (24, 39, 43, 51)

To a stirred solution of alcohol (1 equiv.), PPh_3 (1.2 equiv.), and pyridine (1.9 equiv.) in CH_2Cl_2 (8 mL per 1 mmol of alcohol) at 0°C was added I_2 (1.2 equiv.) in one portion. After being stirred for 0.5 h, the mixture was washed with 1 M aqueous HCl, 10% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, and brine, in order. The organic layer was dried and evaporated in vacuo to give a residue, which was purified by column chromatography (hexane) to furnish the corresponding iodide.

4.2.1. (±)-1-(2-Iodoethyl)-2-methylenecyclohexane (24). From **23** (3.50 g, 25 mmol), **24** (5.05 g, 80.0%) was obtained as a colorless oil; ^{1}H NMR δ 4.70, 4.61 (each 1H, s), 3.14–3.26 (2H, m), 1.24–2.27 (11H, m); IR 2928, 2854, 1643 cm^{-1}; MS *m/z* 250 (M^+); high-resolution mass *m/z* calcd for $C_9H_{15}I$ (M^+) 250.0219, found: 250.0230.

4.2.2. (*S*)-1-(3-Iodopropyl)-1-methyl-2-methylenecyclohexane (39). From **38** (1.352 g, 8.05 mmol), **39** (2.004 g, 89.6%) was obtained as a colorless oil; $[\alpha]_D^{32}=-57.5°$ (*c* 1.15, $CHCl_3$); ^{1}H NMR δ 4.71, 4.58 (each 1H, s), 3.17 (2H, t, *J*=6.6 Hz, H), 2.10–2.19 (2H, m), 1.41–1.81 (7H, m), 1.20–1.40 (3H, m), 1.02 (3H, s); IR 2925, 2854, 1637 cm^{-1}; MS *m/z* 278 (M^+); high-resolution mass *m/z* calcd for $C_{11}H_{19}I$ (M^+) 278.0531, found: 278.0527.

4.2.3. (*R*)-1-(3-Iodopropyl)-1-methyl-2-methylenecyclopentane (43). From **42** (0.581 g, 3.78 mmol), **43** (0.916 g, 92.0%) was obtained as a colorless oil; $[\alpha]_D^{29}=+42.0°$ (*c* 1.06, $CHCl_3$); ^{1}H NMR δ 4.85, 4.69 (each 1H, s), 3.16 (2H, t, *J*=6.9 Hz), 2.33–2.41 (2H, m), 1.73–1.87 (2H, m), 1.39–1.67 (6H, m), 1.03 (3H, s); IR 1740, 1690, 1680 cm^{-1}; MS *m/z* 264 (M^+); high-resolution mass *m/z* calcd for $C_{10}H_{17}I$ (M^+) 264.0375, found: 264.0380.

4.2.4. 1-(3-Iodopropyl)cyclohexene (51). From **50** (0.420 g, 3.0 mmol), **51** (0.600 g, 80.0%) was obtained as a colorless oil; ^{1}H NMR δ 5.45 (1H, brs), 3.16 (2H, t, *J*=6.8 Hz), 1.86–2.05 (8H, m), 1.49–1.66 (4H, m); IR 2924, 1437 cm^{-1}; EI MS *m/z* 250 (M^+); high-resolution mass *m/z* calcd for $C_9H_{15}I$ (M^+) 250.0219, found: 250.0222.

4.3. General procedure for conversion of iodides (24, 39, 43, 51) to acetylenes (1, 40, 44, 52)

To a stirred suspension of lithium acetylide ethylenediamine complex (1.4 equiv.) in DMSO (1 mL per 1 mmol of iodide) and Et_2O (1 mL per 1 mmol of iodide) at 5°C under argon was added a solution of iodide (1 equiv.) in Et_2O (0.25 mL per 1 mmol of iodide). After being stirred for 0.5 h, the reaction was quenched with water. The mixture was extracted with Et_2O. The organic layer was washed with brine and dried. Usual work-up followed by column chromatography (pentane) afforded the corresponding acetylene.

4.3.1. (±)-1-(3-Butynyl)-2-methylenecyclohexane (1). From **24** (5.05 g, 20 mmol), **1** (2.40 g, 80.3%) was obtained as a colorless oil; bp 140°C/60 mmHg; ^{1}H NMR δ 4.68, 4.59 (each 1H, s), 1.93 (1H, t, *J*=2.6 Hz), 1.27–2.23 (13H, m); IR 3311, 2931, 2856, 2118, 1645, 1446 cm^{-1}; MS *m/z* 148 (M^+); high-resolution mass *m/z* calcd for $C_{11}H_{16}$ (M^+) 148.1252, found: 148.1244.

4.3.2. (*S*)-1-Methyl-2-methylene-1-(4-pentynyl)cyclohexane (40). From **39** (1.974 g, 7.1 mmol), **40** (1.097 g, 87.8%) was obtained as a colorless oil; bp 160°C/15 mmHg; $[\alpha]_D^{27}=-80.0°$ (*c* 1.07, $CHCl_3$); ^{1}H NMR δ 4.70, 4.59 (each 1H, s), 2.11–2.19 (4H, m), 1.94 (1H, t, *J*=2.6 Hz), 1.22–1.85 (10H, m), 1.01 (3H, s); IR 3311, 2933, 2856, 1637, 1450 cm^{-1}; MS *m/z* 176 (M^+); high-resolution mass *m/z* calcd for $C_{13}H_{20}$ (M^+) 176.1565, found: 176.1575.

4.3.3. (*R*)-1-Methyl-2-methylene-1-(4-pentynyl)cyclopentane (44). From **43** (0.863 g, 3.3 mmol), **44** (0.451 g, 85.3%) was obtained as a colorless oil; bp 140°C/16 mmHg; $[\alpha]_D^{29}=+48.4°$ (*c* 1.06, $CHCl_3$); ^{1}H NMR δ 4.85, 4.69 (each 1H, s), 2.34–2.40 (2H, m), 2.16 (2H, dt, *J*=2.6, 6.6 Hz), 1.94 (1H, t, *J*=2.6 Hz), 1.39–1.68 (8H, m), 1.03 (3H, s); IR 3310, 2951, 2118, 1650 cm^{-1}; MS *m/z* 161 (M^+-1); high-resolution mass *m/z* calcd for $C_{12}H_{17}$ (M^+-1) 161.1296, found: 161.1313.

4.3.4. 1-(4-Pentynyl)cyclohexene (52). From **51** (0.500 g, 2.0 mmol), **52** (0.224 g, 75.8%) was obtained as a colorless oil; bp 140°C/60 mmHg; ^{1}H NMR δ 5.42 (1H, s), 2.16 (2H, dt, *J*=2.6, 7.1 Hz), 1.91–2.05 (6H, m), 1.94 (1H, t, *J*=2.6 Hz), 1.52–1.68 (6H, m); IR 3311, 2931, 2119, 1439 cm^{-1}; EI MS *m/z* 148 (M^+); high-resolution mass *m/z* calcd for $C_{11}H_{16}$ (M^+) 148.1255, found: 148.1252.

4.4. General procedure for Wittig reaction of ketones (25, 29, 30, 33, 34, 46)

A suspension of PPh_3·MeBr and *t*-BuOK in THF was stirred for 10 min at rt. To this mixture was added a solution of ketone (1 equiv.) in THF over a period of 3 min. After being stirred, the reaction was quenched with water. The mixture was extracted with Et_2O. The extracts were washed with brine and dried. Usual work-up followed by column chromatography or bulb-to-bulb distillation gave the corresponding *exo*-olefin.

4.4.1. (*S*)-1-(3-Butynyl)-1-methyl-2-methylenecyclohexane (2). PPh_3·MeBr (4.30 g, 12.0 mmol), *t*-BuOK (1.35 g, 12.0 mmol) in THF (40 mL), and **25** (0.984 g, 6.0 mmol) in THF (10 mL) were used (reaction time: 1 h). Column chromatography (hexane) gave **2** (0.877 g, 90.2%) as a colorless oil; $[\alpha]_D^{24}=+116.1°$ (*c* 1.07, $CHCl_3$); ^{1}H NMR δ 4.74, 4.59 (each 1H, s), 1.93 (1H, t, *J*=2.4 Hz), 1.91–2.14 (5H, m), 1.22–1.76 (7H, m), 1.01 (3H, s); ^{13}C NMR δ 153.8, 107.6, 85.5, 67.7, 40.4, 39.2, 36.4, 33.1, 28.4, 25.2, 21.9, 13.5; IR 3311, 2931, 2856, 2119, 1637, 1450 cm^{-1}; MS *m*/*z* 162 (M^+); high-resolution mass *m*/*z* calcd for $C_{12}H_{18}$ (M^+) 162.1407, found: 162.1405.

4.4.2. (*S*)-6-(3-Butynyl)-6-methyl-7-methylene-1,4-dioxaspiro[4.5]decane (4). PPh_3·MeBr (0.380 g, 1.06 mmol), *t*-BuOK (0.119 g, 1.06 mmol) in THF (3 mL), and **29** (0.118 g, 0.53 mmol) in THF (2 mL) were used (reaction time: 24 h). Column chromatography (hexane/AcOEt=20:1) gave **4** (0.048 g, 41.1%) as colorless crystals; mp 80–82°C; $[\alpha]_D^{24}=-57.8°$ (*c* 1.32, $CHCl_3$); ^{1}H NMR δ 4.91 (1H, d, *J*=1 Hz), 4.72 (1H, d, *J*=1.3 Hz), 3.88–4.00 (4H, m), 2.14–2.20 (2H, m), 1.43–2.01 (9H, m), 1.02 (3H, s); ^{13}C NMR δ 150.6, 112.9, 110.7, 85.2, 67.9, 65.2, 65.1, 49.1, 33.6, 31.7, 30.2, 23.4, 15.5, 13.4; MS *m*/*z* 220 (M^+); high-resolution mass *m*/*z* calcd for $C_{14}H_{20}O_2$ (M^+) 220.1463, found: 220.1470.

4.4.3. (*R*)-2-(1-*tert*-Butoxycarbonyl)ethyl-1-ethoxycarbonyl-2-methylenecyclohexane (31). PPh_3·MeBr (10.75 g, 30.1 mmol) and *t*-BuOK (3.36 g, 30.0 mmol) in THF (250 mL), and **30** (5.96 g, 20 mmol) were used (reaction time: 1 h). Column chromatography (hexane/AcOEt=5:1) gave **31** (5.41 g, 91.4%) as a colorless oil; bp 170°C/30 mmHg; $[\alpha]_D^{29}=+43.7°$ (*c* 1.04, $CHCl_3$); ^{1}H NMR δ 4.90, 4.77 (each 1H, s), 4.17 (2H, q, *J*=7.1 Hz), 1.87–2.35 (8H, m), 1.53–1.72 (3H, m), 1.44 (9H, s), 1.36–1.44 (1H, m), 1.26 (3H, t, *J*=7.1 Hz); IR 2980, 2935, 2860, 1728, 1643, 1448 cm^{-1}; MS *m*/*z* 296 (M^+); high-resolution mass *m*/*z* calcd for $C_{17}H_{28}O_4$ (M^+) 296.1988, found: 296.1978.

4.4.4. (±)-2-Methylene-1-propargyloxycyclohexane (8). PPh_3·MeBr (3.929 g, 11.0 mmol), *t*-BuOK (1.209 g, 10.7 mmol) in THF (50 mL), and **33** (0.761 g, 5.0 mmol) in THF (4 mL) were used (reaction time: 1 h); **8** (0.595 g, 79.2%) was obtained as a colorless oil; bp 140°C/14 mmHg; ^{1}H NMR δ 4.87, 4.86 (each 1H, s), 4.17, 4.00 (each 1H, dd, *J*=2.3, 15.6 Hz), 3.98 (1H, t, *J*=3.3 Hz), 2.39 (1H, t, *J*=2.3 Hz), 2.25 (1H, ddd, *J*=4.3, 9.6, 13.3 Hz), 2.06 (1H, dt, *J*=5, 13.3 Hz), 1.58–1.85 (4H, m), 1.39–1.55 (2H, m); IR 2935, 2858, 2118, 1650 cm^{-1}; MS *m*/*z* 150 (M^+); high-resolution mass *m*/*z* calcd for $C_{10}H_{14}O$ (M^+) 150.1044, found: 150.1043.

4.4.5. (±)-1-Methyl-2-methylene-1-propargyloxycyclohexane (9). PPh_3·MeBr (7.86 g, 22.0 mmol), *t*-BuOK (2.40 g, 21.4 mmol) in THF (100 mL), and **34** (1.660 g, 10 mmol) in THF (12 mL) were used (reaction time: 1 h). Column chromatography (hexane then hexane/AcOEt=10:1) gave **9** (1.05 g, 64.0%) as a colorless oil; bp 150°C/15 mmHg; ^{1}H NMR δ 4.95, 4.85 (each 1H, s), 3.95, 3.86 (each 1H, dd, *J*=2.3, 15.2 Hz), 2.37 (1H, t, *J*=2.3 Hz), 2.10–2.28 (2H, m), 1.71–1.95 (3H, m), 1.22–1.57 (3H, m), 1.31 (3H, s); IR 2940, 1643 cm^{-1}; MS *m*/*z* 164 (M^+); high-resolution mass *m*/*z* calcd for $C_{11}H_{16}O$ (M^+) 164.1201, found: 164.1191.

4.4.6. (±)-1-Ethoxycarbonyl-1-(2-iodobenzyl)-2-methylenecyclohexane (47). PPh_3·MeBr (1.68 g, 4.6 mmol), *t*-BuOK (0.505 g, 4.5 mmol) in THF (40 mL), and **46** (1.16 g, 3.0 mmol) were used (reaction time: 3 h). Column chromatography (hexane/AcOEt=30:1) gave **47** (0.985 g, 85.5%) as colorless crystals; mp 85–86°C; ^{1}NMR δ 7.83 (1H, dd, *J*=1.3, 7.9 Hz), 7.20 (1H, dd, *J*=1.3, 7.9 Hz), 7.06 (1H, dd, *J*=1.6, 7.9 Hz), 6.87 (1H, dt, *J*=1.6, 7.9 Hz), 5.00, 4.97 (each 1H, s), 4.15 (2H, q, *J*=7.1 Hz), 3.42, 3.22 (each 1H, d, *J*=14.2 Hz), 2.34–2.41 (1H, m), 2.00–2.12 (2H, m), 1.28–1.77 (5H, m), 1.20 (3H, t, *J*=7.1 Hz); MS *m*/*z* 384 (M^+); high-resolution mass *m*/*z* calcd for $C_{17}H_{21}IO_2$ (M^+) 384.0497, found: 384.5013.

4.4.7. (±)-1-(3-Butynyl)-2-ethylidene-1-methylcyclohexane (6). A suspension of PPh_3·EtBr (2.251 g, 6.06 mmol) and *t*-BuOK (0.676 g, 6.00 mmol) in THF (25 mL) was stirred for 5 min at rt. To this mixture was added a solution of **25** (0.492 g, 3.0 mmol) in THF (7 mL) over a period of 2 min. After being stirred for 24 h, similar work-up as described above gave a residue, which was purified by column chromatography (hexane) to afford **6** (0.321 g, 60.9%) as a colorless oil; bp 170°C/25 mmHg; ^{1}H NMR δ 5.30 (0.82H, q, *J*=7.3 Hz, olefinic H), 5.16 (0.18H, q, *J*=6.7 Hz, olefinic H), 1.71 (2.46H, dd, *J*=1.8, 7.3 Hz, CH*Me*), 1.59 (0.54H, dd, *J*=1.3, 6.7 Hz, CH*Me*), 1.95–2.56 (5H, m), 1.92 (1H, t, *J*=2.5 Hz), 1.25–1.68 (7H, m), 1.23 (3H, s); IR 3311, 2926, 2864, 2119, 1466, 1450 cm^{-1}; MS *m*/*z* 176 (M^+); high-resolution mass *m*/*z* calcd for $C_{13}H_{20}$ (M^+) 176.1564, found: 176.1577.

4.4.8. (±)-1-Methyl-2-methylene-1-(3-pentynyl)cyclohexane (7). To a stirred suspension of **2** (0.324 g, 2.0 mmol) in THF (8 mL) was added at 0°C BuLi (1.8 mL, 2.9 mmol, 1.6 M in hexane). After being stirred for 10 min, MeI (160 μL, 2.6 mmol) was added. The mixture was stirred for 0.5 h. The reaction was quenched with water and extracted with hexane. Usual work-up afforded **7** (0.321 g, 91.2%) as a colorless oil; bp 160°C/40 mmHg; ^{1}H NMR δ 4.71, 4.57 (each 1H, s), 1.84–2.15 (5H, m), 1.76 (3H, t, *J*=2.3 Hz), 1.22–1.73 (7H, m), 0.99 (3H, s); IR 2928, 1637, 1448 cm^{-1}; MS *m*/*z* 176 (M^+); high-resolution mass *m*/*z* calcd for $C_{13}H_{20}$ (M^+) 176.1564, found: 176.1563.

4.4.9. (*R*)-1-(2-Methoxycarbonyl)ethyl-1-methyl-2-methylenecyclopentane (27). To a stirred mixture of Zn (3.704 g,

56.7 mmol) and CH_2Br_2 (3.422 g, 19.1 mmol) in THF (100 mL) at rt under argon was added $TiCl_4$ (13.8 mL, 13.8 mmol, 1 M in CH_2Cl_2). After being stirred for 15 min, the mixture was cooled to 0°C and a solution of **26** (90% ee, 2.35 g, 12.8 mmol) in CH_2Cl_2 (10 mL) was added. After being stirred for 1.5 h, the reaction was diluted with hexane (50 mL). Then, a solution of Na_2CO_3 (24 g) in H_2O (15 mL) was added to the mixture. The precipitate was filtered through Celite 545 short pad. Usual work-up followed by column chromatography (hexane/AcOEt=20:1) gave **27** (1.23 g, 52.7%) as a colorless oil; bp 160–170°C/50 mmHg; $[\alpha]_D^{26}=+38.2°$ (*c* 1.06, $CHCl_3$); ^{1}H NMR δ 4.88, 4.70 (each 1H, s), 3.66 (3H, s), 2.25–2.43 (4H, m), 1.44–1.76 (6H, m), 1.03 (3H, s); IR 2954, 2871, 1743, 1650, 1452, 1434 cm^{-1}; MS *m/z* 182 (M^+); high-resolution mass *m/z* calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found: 182.1300.

4.4.10. (*R*)-1-(2-Formyl)ethyl-1-methyl-2-methylenecyclopentane (28). To a solution of **27** (0.592 g, 3.0 mmol) in toluene (15 mL) was added at −78°C under argon DIBAH (3 mL, 3 mmol, 1 M in toluene). After being stirred for 2 h, the reaction was quenched with 3 M HCl. The mixture was extracted with $CHCl_3$. The extracts were washed with brine and dried. Usual work-up as noted above (hexane/AcOEt=10:1) afforded **27** (0.106 g, 19.4%) and **28** (0.310 g, 68.0%) as a colorless oil; ^{1}H NMR δ 9.77 (1H, t, *J*=1.9 Hz), 4.89 (1H, t, *J*=2 Hz), 4.70 (1H, t, *J*=2.3 Hz), 2.34–2.45 (4H, m), 1.48–1.74 (6H, m), 1.04 (3H, s); IR 2956, 1726, 1650 cm^{-1}; MS *m/z* 152 (M^+); high-resolution mass *m/z* calcd for $C_{10}H_{16}O$ (M^+) 152.1201, found: 152.1200.

4.4.11. (*R*)-1-Methyl-2-methylene-1-propargylclopentane (3). To a stirred suspension of **28** (0.674 g, 3.81 mmol) and K_2CO_3 (1.055 g, 7.64 mmol) in MeOH (50 mL) was added at rt diethyl 1-diazo-2-oxopropylphosphonate (0.861 g, 4.57 mmol) in one portion. After being stirred for 3 h, the reaction was diluted with Et_2O. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, successively. Usual work-up afforded **3** (0.291 g, 51.7%) as a colorless oil; bp 135°C/60 mmHg; ^{1}H NMR δ 4.88, 4.69 (each 1H, s), 1.92 (1H, t, *J*=2.6 Hz), 2.32–2.42 (2H, m), 2.10–2.22 (2H, m), 1.20–1.44 (6H, m), 1.01 (3H, s); MS *m/z* 148 (M^+); high-resolution mass *m/z* calcd for $C_{11}H_{16}$ (M^+) 148.1252, found: 148.1248.

4.4.12. (*R*)-1-Ethoxycarbonyl-1-(2-formyl)ethyl-2-methylenecyclohexane (32). To a solution of **31** (0.592 g, 2.0 mmol) in THF (15 mL) was added at −78°C under argon DIBAH (3 mL, 3 mmol, 1 M in toluene). After being stirred for 2 h, the reaction was quenched with 3 M HCl. The mixture was extracted with $CHCl_3$. Work-up as noted above (hexane/AcOEt=10:1) afforded **32** (0.145 g, 32.4%) and **31** (0.347 g, 58.7%) as a colorless oil; ^{1}H NMR δ 9.78 (1H, t, *J*=1.2 Hz), 5.91, 4.73 (each 1H, s), 4.16 (2H, q, *J*=7 Hz), 1.90–2.65 (8H, m), 1.40–1.79 (4H, m), 1.26 (3H, t, *J*=7 Hz); IR 2930, 1748, 1643 cm^{-1}; MS *m/z* 224 (M^+); high-resolution mass *m/z* calcd for $C_{13}H_{20}O_3$ (M^+) 224.1409, found: 224.1413.

4.4.13. (*R*)-1-(3-Butynyl)-1-ethoxycarbonyl-2-methylenecyclohexane (5). To a stirred suspension of **32** (0.145 g, 0.65 mmol) and K_2CO_3 in MeOH (10 mL) was added at rt diethyl 1-diazo-2-oxopropylphosphonate (0.166 g, 0.75 mmol) in one portion. After being stirred for 2.5 h, the reaction was diluted with Et_2O. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, successively. Usual work-up afforded **5** (0.080 g, 56.3%) as a colorless oil; bp 170°C/20 mmHg; $[\alpha]_D^{26}=+58.8°$ (*c* 1.01, $CHCl_3$); ^{1}H NMR δ 4.91, 4.74 (each 1H, s), 4.17 (2H, q, *J*=7.1 Hz), 1.96 (1H, t, *J*=2.5 Hz), 1.83–2.31 (6H, m), 1.30–1.74 (6H, m), 1.26 (3H, t, *J*=7.1 Hz); IR 3292, 2937, 2858, 2119, 1727, 1643, 1448 cm^{-1}; MS *m/z* 220 (M^+); high-resolution mass *m/z* calcd for $C_{14}H_{20}O_2$ (M^+) 220.1463, found: 220.1463.

4.4.14. (±)-2-Methylene-1-(propargylamino)-*N*-tosylcyclohexane (10). To a stirred mixture of Zn (0.882 g, 13.5 mmol) and CH_2Br_2 (0.791 g, 4.55 mmol) in THF (25 mL) at rt under argon was added $TiCl_4$ (3.3 mL, 3.3 mmol, 1 M in CH_2Cl_2). After being stirred for 15 min, **35** (0.9150 g, 3.0 mmol) was added in one portion and the mixture was stirred for 5 h. The mixture was diluted with Et_2O and washed with 1 M HCl, and brine, successively. Work-up as noted above (hexane/AcOEt=3:1) afforded **10** (0.230 g, 25.3%) as crystals; mp 111–112°C; ^{1}H NMR δ 7.82, 7.27 (each 2H, d, *J*=8.6 Hz), 4.78, 4.63 (each 1H, s), 4.38, 3.87 (each 1H, dd, *J*=2.3, 18.5 Hz), 4.28–4.38 (1H, m), 2.42 (3H, s), 2.11 (1H, t, *J*=2.3 Hz), 1.98–2.08 (1H, m), 1.16–1.90 (7H, m); IR 3307, 2941, 2862, 1650, 1599, 1448 cm^{-1}; MS *m/z* 303 (M^+); high-resolution mass *m/z* calcd for $C_{17}H_{21}NO_2S$ (M^+) 303.1293, found: 303.1290.

4.4.15. (±)-1-Benzyloxycarbonylamino-1-methyl-2-methylenecyclohexane (37). A solution of **36** (1.00 g, 6.5 mmol), DPPA (1.86 g, 6.8 mmol), Et_3N (0.712 g, 7.0 mmol), and benzyl alcohol (0.90 g, 8.3 mmol) in toluene (40 mL) was refluxed for 6 h. After the solvent was removed in vacuo, the residue was purified by column chromatography (hexane/AcOEt=5:1) to afford **37** (0.656 g, 39.0%) as a colorless oil; ^{1}H NMR δ 7.35 (5H, s), 5.08, 5.03 (each 1H, d, *J*=12.9 Hz), 4.87, 4.85 (each 1H, s), 4.76 (1H, brs), 2.04–2.39 (3H, m), 1.49 (3H, s), 1.34–1.72 (5H, m); IR 3350, 2935, 2858, 1724, 1498 cm^{-1}; MS *m/z* 259 (M^+); high-resolution mass *m/z* calcd for $C_{16}H_{21}NO_2$ (M^+) 259.1571, found: 259.1552.

4.4.16. (±)-1-(*N*-Benzyloxycarbonylpropargylamino)-1-methyl-2-methylenecyclohexane (11). To a mixture of NaH (0.060 g, 1.5 mmol) in DMF (3 mL) at 0°C under argon was added a solution of **37** (0.259 g, 1.0 mmol) in DMF (2 mL). After being stirred for 1 h, propargyl bromide (0.104 g, 1.2 mmol) was added and the mixture was stirred for 3 h at rt. Then, the reaction was quenched with water. The mixture was extracted with Et_2O. The extracts were washed with brine and dried (K_2CO_3). Work-up as noted above (hexane/AcOEt=20:1) afforded **11** (0.160 g, 54.0%) as a colorless oil; ^{1}H NMR δ 7.30–7.43 (5H, m, Ph), 5.19, 5.14 (each 1H, d, *J*=13.2 Hz), 4.93, 4.91 (each 1H, s), 4.15, 3.38 (each 1H, dd, *J*=2.3, 17.8 Hz), 3.04–3.10 (1H, m), 2.17 (1H, t, *J*=2.3 Hz), 2.08–2.28 (2H, m), 1.71–1.79 (1H, m), 1.50 (3H, s), 1.15–1.57 (4H, m); IR 3302, 2935, 2858, 1709, 1444 cm^{-1}; MS *m/z* 297 (M^+); high-resolution mass *m/z* calcd for $C_{19}H_{23}NO_2$ (M^+) 297.1728, found: 297.1730.

4.4.17. (*R*)-1-(3-Hydroxypropyl)-1-methyl-2-methylenecyclopentane (42). To a stirred solution of **27** (0.876 g, 4.81 mmol) in THF (15 mL) at 0°C was added $LiAlH_4$ (0.183 g, 4.82 mmol) in small portions. After being stirred for 1 h, the reaction was quenched with saturated aqueous Na_2SO_4. The precipitate was filtered off and the filtrate was dried and evaporated under reduced pressure to give **42** (0.706 g, 95.2%) as a colorless oil; bp 180–190°C/30 mmHg; $[\alpha]_D^{29}$=+42.1° (*c* 1.06, $CHCl_3$); ^{1}H NMR δ 4.85, 4.69 (each 1H, s), 3.62 (2H, t, *J*=6.4 Hz), 2.34–2.42 (2H, m), 1.26–1.64 (8H, m), 1.03 (3H, s); IR 3334, 2952, 2870, 1650, 1456, 1432 cm^{-1}; MS *m/z* 154 (M^+); high-resolution mass *m/z* calcd for $C_{10}H_{18}O$ (M^+) 154.1358, found: 154.1355.

4.4.18. (±)-1-Ethoxycarbonyl-1-(2-ethynylbenzyl)-2-methylenecyclohexane (48). A mixture of **47** (0.768 g, 2.0 mmol), trimethylsilylacetylene (0.34 mL, 2.4 mmol), Et_3N (10 mL), CuI (0.004 g, 0.02 mmol), and $PdCl_2(PPh_3)_2$ (0.028 g, 0.04 mmol) in CH_2Cl_2 (1 mL) was stirred for 1 h at rt. The mixture was washed with saturated aqueous $NaHCO_3$, brine, successively, and dried. Work-up as noted above (AcOEt/hexane=1:30) afforded 1-ethoxycarbonyl-1-(2-trimthylsilylethynylbenzyl)-2-methylenecyclohexane (0.705 g, 99.5%) as colorless crystals; ^{1}H NMR δ 7.39 (1H, dd, *J*=1.7, 7.3 Hz), 7.12–7.30 (2H, m), 6.97 (1H, dd, *J*=1.7, 7.3 Hz), 4.97, 4.95 (each 1H, s), 4.96 (2H, q, *J*=7.1 Hz), 3.40, 3.27 (each 1H, d, *J*=13.2 Hz), 2.30–2.40 (1H, m), 1.91–2.00 (2H, m), 1.28–1.76 (5H, m), 1.17 (3H, t, *J*=7.1 Hz), 0.20 (9H, s). A solution of the 2-(trimethylsilylethynyl)benzyl product (0.531 g, 1.5 mmol) and TBAF (0.45 mL, 0.45 mmol) in THF (3 mL) was stirred for 1 h at rt. After the solvent was removed in vacuo, the residue was purified by column chromatography (hexane/AcOEt=30:1) to afford **48** (0.413 g, 97.5%) as colorless crystals; mp 93–95°C; ^{1}H NMR δ 7.47 (1H, dd, *J*=1.7, 7.3 Hz), 7.16–7.23 (2H, m), 7.04 (1H, dd, *J*=1.7, 7.3 Hz), 5.00, 4.97 (each 1H, s), 4.13 (2H, q, *J*=7.1 Hz), 3.40, 3.30 (each 1H, d, *J*=13.5 Hz), 3.21 (1H, s), 2.34–2.41 (1H, m), 1.97–2.13 (2H, m), 1.32–1.76 (5H, m), 1.19 (3H, t, *J*=7.1 Hz); IR 3248, 2935, 2863, 1716, 1600 cm^{-1}; MS *m/z* 282 (M^+); high-resolution mass *m/z* calcd for $C_{19}H_{22}O_2$ (M^+) 282.1620, found: 282.1639.

4.4.19. 1-[3-(1-Trimethylsilylpropadienyl)propyl]- and 1-(5-pentynyl-6-trimethylsilyl)-cyclohexane (53 and 54). To a stirred solution of 1-trimethylsilylpropyne (225 μL, 1.5 mmol) in THF (4 mL) at 0°C under argon was added BuLi (0.90 mL, 1.39 mmol, 1.54 M in hexane). After being stirred for 30 min, a solution of **51** (0.250 g, 1.0 mmol) in THF (3 mL) was added and stirring was continued for additional 1 h. The reaction was quenched with water. The mixture was extracted with Et_2O. The organic extracts were washed with water, brine, successively, and dried. Work-up as noted above (pentane) to afford **53** (0.035 g, 15.0%) and **54** (0.199 g, 85.0%).

53: Oil; ^{1}H NMR δ 5.38 (1H, brs, olefinic H), 4.31 (2H, t, *J*=3.1 Hz), 1.87–2.00 (8H, m), 1.49–1.65 (6H, m), 0.08 (9H, s); EI MS *m/z* 234 (M^+); high-resolution mass *m/z* calcd for $C_{15}H_{26}Si$ (M^+) 234.1804, found: 234.1803.

54: Oil; ^{1}H NMR δ 5.38 (1H, brs), 2.20 (2H, t, *J*=6.8 Hz), 1.83–2.01 (6H, m), 1.44–1.64 (8H, m), 0.13 (9H, s); EI MS *m/z* 234 (M^+); high-resolution mass *m/z* calcd for $C_{15}H_{26}Si$ (M^+) 234.1804, found: 234.1800.

4.4.20. 1-(4-Pentynyl)cyclohexene (55). A mixture of **54** (0.199 g, 0.85 mmol) and 3 M NaOH (5 mL) in MeOH (5 mL) was stirred for 14 h at rt. The mixture was extracted with Et_2O. The organic extracts were washed with brine and dried. Usual work-up afforded **55** (0.130 g, 94.4%) as a colorless oil; bp 170°C/60 mmHg; ^{1}H NMR δ 5.30 (1H, brs, olefinic H), 2.14–2.23 (2H, m), 1.93 (1H, t, *J*=2.6 Hz), 1.85–2.00 (6H, m), 1.45–1.64 (8H, m); IR 3296, 2940, 2172 cm^{-1}; EI MS *m/z* 162 (M^+); high-resolution mass *m/z* calcd for $C_{12}H_{18}$ (M^+) 162.1409, found: 162.1411.

4.5. General procedures for Pauson–Khand reaction of exocyclic enynes

A mixture of enyne (1 equiv.) and $Co_2(CO)_8$ (1.1 equiv.) in CH_2Cl_2, benzene or toluene was stirred for 1 h at rt. Method A: NMO (3 equiv.) was added to the mixture in three times at intervals of 15 min. 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 Celite 545 short pad. Method B: TMANO (3 equiv.) was added to the mixture and the mixture was refluxed for 2–4 h. Methods C and D: The mixture was refluxed for appropriate time. Purification of the products obtained by Methods A–D was carried out on preparative TLC.

4.5.1. (1*R,8*S**)-Tricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (12).** Oil; ^{1}H NMR δ 5.75 (1H, dd, *J*=1, 2.3 Hz), 2.52–2.82 (2H, m), 2.37, 2.11 (each 1H, d, *J*=17.5 Hz), 2.08–2.20 (1H, m), 1.09–1.95 (10H, m); ^{13}C NMR δ 210.7, 195.6, 123.6, 52.9, 48.7, 41.9, 31.8, 26.8, 24.9, 24.5, 23.4, 19.6; IR 2926, 2858, 1709, 1626, 1456, 1410 cm^{-1}; MS *m/z* 176 (M^+); high-resolution mass *m/z* calcd for $C_{12}H_{16}O$ (M^+) 176.1200, found: 176.1205.

4.5.2. (1*R*,8*S*)-8-Methyltricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (13). Oil; $[\alpha]_D^{24}$=−146.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR δ 5.77 (1H, t, *J*=1.7 Hz), 2.54–2.81 (2H, m), 2.43 (1H, dt, *J*=7.6, 12.2 Hz), 2.29, 2.10 (each 1H, d, *J*=17.8 Hz), 1.22–1.80 (9H, m), 0.77 (3H, s); ^{13}C NMR δ 212.5, 196.5, 124.5, 57.6, 44.8, 41.0, 36.0, 35.6, 34.2, 26.1, 24.9, 24.5, 22.7; IR 2929, 2864, 1705, 1624, 1448, 1412 cm^{-1}; MS *m/z* 190 (M^+); high-resolution mass *m/z* calcd for $C_{13}H_{18}O$ (M^+) 190.1357, found: 190.1358.

4.5.3. (1*S*,8*R*)-8-Methyltricyclo[6.3.0.0^{1,5}]undodec-4-en-3-one (14). Oil; $[\alpha]_D^{27}$=+63.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR δ 5.73 (1H, dd, *J*=1, 2 Hz), 2.53–2.70 (2H, m), 2.48, 2.13 (each 1H, d, *J*=17.7 Hz), 1.61–2.06 (8H, m), 0.96 (3H, s); ^{13}C NMR δ 211.4, 193.1, 122.9, 63.0, 49.4, 46.9, 42.0, 41.0, 40.6, 26.5, 24.5, 24.1; MS *m/z* 176 (M^+); high-resolution mass *m/z* calcd for $C_{12}H_{16}O$ (M^+) 176.1201, found: 176.1205.

4.5.4. (1*S*,8*S*)-9,9-Ethylenedioxy-8-methyltricyclo[6.4.0.0^{1,5}]-dodec-4-en-3-one (15). Oil; $[\alpha]_D^{24}$=−121.7° (*c* 1.03, $CHCl_3$); ^{1}H NMR δ 5.77 (1H, dd, *J*=1.3, 2 Hz, olefinic

H), 3.91–3.99 (4H, m, OCH_2CH_2O), 2.70–2.83 (1H, m), 2.40–2.67 (2H, m), 2.47, 2.15 (each 1H, d, J=18.2 Hz), 1.60–1.82 (6H, m), 1.12–1.17 (1H, m), 0.78 (3H, s, Me); ^{13}C NMR δ 211.9, 193.7, 124.5, 111.6, 65.6, 59.2, 48.5, 45.3, 34.9, 34.5, 30.8, 24.0, 22.2, 16.0; IR 2933, 2870, 1705, 1628 cm^{-1}; MS m/z 248 (M^+); high-resolution mass m/z calcd for $C_{15}H_{20}O_3$ (M^+) 248.1410, found: 248.1411.

4.5.5. (1*S*,8*R*)-8-Ethoxycarbonyltricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (16). Oil; $[\alpha]_D^{26}=-91.2°$ (c 1.04, $CHCl_3$); ^{1}H NMR δ 5.74 (1H, t, J=1.3 Hz), 4.04 (2H, q, J=7.1 Hz), 2.75–2.94 (2H, m), 2.38 (1H, dt, J=9.2, 13.8 Hz), 2.24 (2H, s), 2.17 (1H, ddd, J=4, 7.7, 13.8 Hz), 2.03 (1H, dt, J=4.3, 14 Hz), 1.73–1.80 (3H, m), 1.26–1.62 (4H, m), 1.17 (3H, t, J=7.1 Hz); ^{13}C NMR δ 210.0, 194.4, 175.4, 123.1, 60.6, 55.9, 53.0, 45.6, 36.0, 30.8, 27.1, 25.5, 22.9, 20.9, 14.0; IR 3022, 2935, 1712, 1697, 1628, 1470, 1448, 1417 cm^{-1}; MS m/z 248 (M^+); high-resolution mass m/z calcd for $C_{15}H_{20}O_3$ (M^+) 248.1410, found: 248.1407.

4.5.6. (1*R,2*R**,8*S**)-2,8-Dimethyltricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (17).** Oil; ^{1}H NMR δ 5.82 (1H, s), 2.45–2.77 (3H, m), 2.36 (1H, q, J=7.9 Hz), 1.48–1.75 (7H, m), 1.22–1.34 (1H, m), 1.28 (3H, d, J=7.9 Hz), 1.04–1.12 (1H, m), 0.90 (3H, s); ^{13}C NMR δ 213.8, 194.1, 123.0, 58.9, 53.2, 46.2, 38.4, 36.8, 33.5, 27.0, 23.9, 23.5, 22.0, 15.0; IR 2927, 2868, 1701, 1632, 1458 cm^{-1}; MS m/z 204 (M^+); high-resolution mass m/z calcd for $C_{14}H_{20}O$ (M^+) 204.1513, found: 204.1506.

4.5.7. (1*R,8*S**)-4,8-Dimethyltricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (18).** Mp 87–89°C; ^{1}H NMR δ 2.38–2.68 (3H, m), 2.26, 2.10 (each 1H, d, J=17.8 Hz), 1.06–1.78 (12H, m), 0.71 (3H, s); ^{13}C NMR δ 211.2, 187.7, 130.8, 54.0, 43.3, 40.2, 35.2, 33.6, 25.3, 23.8, 22.9, 22.7, 8.2; IR 2915, 2852, 1700, 1662 cm^{-1}; MS m/z 204 (M^+); high-resolution mass m/z calcd for $C_{14}H_{20}O$ (M^+) 204.1513, found: 204.1518.

4.5.8. (1*S,8*R**)-7-Oxatricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (19).** Oil; ^{1}H NMR δ 5.90 (1H, dd, J=1.1, 1.7 Hz), 4.80 (1H, dd, J=1.7, 16.3 Hz), 4.56 (1H, dd, J=1.1, 16.3 Hz), 3.63 (1H, s), 2.37, 2.13 (each 1H, d, J=17.3 Hz), 2.07–2.17 (1H, m), 1.50–1.79 (5H, m), 1.19–1.32 (2H, m); ^{13}C NMR δ 208.9, 189.1, 122.7, 79.9, 64.8, 51.6, 45.5, 32.2, 26.1, 22.9, 19.3; IR 2933, 2856, 1716, 1643, 1446 cm^{-1}; MS m/z 178 (M^+); high-resolution mass m/z calcd for $C_{11}H_{14}O_2$ (M^+) 178.0994, found: 178.0990.

4.5.9. (1*S,8*R**)-8-Methyl-7-oxatricyclo[6.4.0.0^{1,5}]dodec-4-en-3-one (20).** Mp 57–59°C; ^{1}H NMR δ 5.88 (1H, t, J=1.7 Hz), 4.75, 4.53 (each 1H, dd, J=1.7, 16.8 Hz), 2.29, 2.19 (each 1H, d, J=17.5 Hz), 2.04 (1H, dt, J=3, 14.2 Hz), 1.15–1.77 (7H, m), 1.01 (3H, s); ^{13}C NMR δ 210.0, 190.1, 122.0, 80.6, 63.1, 54.9, 44.7, 35.5, 33.6, 23.3, 22.7, 21.4; IR 2934, 2852, 1702 cm^{-1}; MS m/z 192 (M^+); high-resolution mass m/z calcd for $C_{12}H_{16}O_2$ (M^+) 192.1149, found: 192.1147.

4.5.10. (1*S,8*R**)-7-Aza-8-tosyltricyclo[6.4.0.0^{1,5}]dec-4-en-3-one (21).** Mp 92–93°C; ^{1}H NMR δ 7.67, 7.34 (each 2H, d, J=8.3 Hz), 5.76 (1H, s), 4.53, 4.09 (each 1H, d, J=17.2 Hz), 2.73–2.77 (2H, m), 2.44 (3H, s), 2.23, 2.02 (each 1H, d, J=17.3 Hz), 1.18–1.83 (7H, m); ^{13}C NMR δ 207.0, 180.8, 144.0, 132.6, 129.9, 127.4, 123.8, 63.7, 52.4, 49.0, 46.0, 32.7, 25.7, 23.1, 21.5, 18.9 cm^{-1}; MS m/z 331 (M^+); high-resolution mass m/z calcd for $C_{18}H_{21}NO_3S$ (M^+) 331.1240, found: 331.1231.

4.5.11. (1*S,8*R**)-7-Aza-8-benzyloxycarbonyltricyclo-[6.4.0.0^{1,5}]dec-4-en-3-one (22).** Oil; ^{1}H NMR δ 7.36 (5H, s), 5.90 (1H, s), 5.16, 5.10 (each 1H, d, J=12.9 Hz), 4.62, 4.28 (each 1H, J=18.2 Hz), 3.15, 2.77 (each 1H, d, J=13 Hz), 2.18–2.32 (2H, m), 1.18–1.88 (6H, m), 1.07(3H, s); ^{13}C NMR δ 208.7, 182.9, 154.0, 136.6, 128.5, 128.0, 127.7, 123.1, 66.4, 64.1, 55.8, 46.1, 43.3, 35.7, 32.3, 23.5, 21.6, 21.2; IR 2933, 2860, 1713, 1655, 1448 cm^{-1}; MS m/z 325 (M^+); high-resolution mass m/z calcd for $C_{20}H_{23}NO_3$ (M^+) 325.1676, found: 325.1686.

4.5.12. (1*S,9*S**)-Benzo[*e*]-9-ethoxycarbonyltricyclo-[7.4.0.0^{1,5}]tridec-4-en-3-one (49).** Oil; ^{1}H NMR δ 7.64 (1H, d, J=7.9 Hz), 7.20–7.40 (3H, m), 6.31 (1H, s), 3.93 (2H, q, J=7.1 Hz), 3.55, 2.92 (each 1H, d, J=18.2 Hz), 2.66, 2.53 (each 1H, d, J=18.4 Hz), 1.40–1.95 (6H, m), 1.18–1.31 (2H, m), 0.97 (3H, t, J=7.1 Hz); ^{13}C NMR δ 207.2, 179.1, 174.9, 136.4, 131.1, 129.0, 128.8, 127.0, 126.4, 122.6, 60.7, 48.0, 46.8, 45.0, 34.7, 32.8, 29.7, 22.2, 20.3, 13.8; IR 2935, 2864, 1716, 1647, 1446 cm^{-1}; MS m/z 310 (M^+); high-resolution mass m/z calcd for $C_{20}H_{22}O_3$ (M^+) 310.1567, found: 310.1556.

Acknowledgements

The authors are grateful to Mrs F. Hasegawa of this faculty for her mass spectral measurement.

References

1. Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Chem. Commun.* **1971**, 36.
2. For reviews: (a) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263. (b) Fletcher, A. J.; Christie, S. D. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1657. (c) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297.
3. Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436.
4. (a) Price, M. E.; Schore, N. E. *Tetrahedron Lett.* **1989**, *30*, 5865. (b) Price, M. E.; Schore, N. E. *J. Org. Chem.* **1989**, *54*, 5662. (c) Castro, J.; Sörensen, H.; Riera, A.; Morin, C.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Am. Chem. Soc.* **1990**, *112*, 9388. (d) Bernardes, V.; Kann, N.; Riera, A.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Org. Chem.* **1995**, *60*, 6670. (e) Smit, W. A.; Buhanjuk, S. M.; Simonyan, S. O.; Shashkov, A. S.; Struchkov, Y. T.; Yanovsky, A. I.; Caple, R.; Gybin, A. S.; Anderson, L. G.; Whiteford, J. A. *Tetrahedron Lett.* **1991**, *32*, 2105. (f) Cassayre, J.; Zard, S. Z. *J. Am. Chem. Soc.* **1999**, *121*, 6072. (g) Krafft, M. E.; Wright, C. *Tetrahedron Lett.* **1992**, *33*, 151. (h) Van der Waals, A.; Keese, R. *J. Chem. Soc., Chem. Commun.* **1992**, 570. (i) Takano, S.; Inomata, K.; Ogasawara, K. *Chem. Lett.* **1992**, 443. (j) Takano, S.; Inomata, K.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1992**, 169. (k) Yoo, S.-E.; Lee, S. H.; Jeong, N.; Cho, I. *Tetrahedron Lett.* **1993**, *34*, 3435. (l) Yoo, S.-E.; Lee, S. H. *J. Org. Chem.* **1994**, *59*, 6968. (m) Jeong, N.; Lee, B. Y.; Lee, S. M.; Chung, Y. K.;

Lee, S.-G. *Tetrahedron Lett.* **1993**, *34*, 4023. (n). Johnstone, C.; Kerr, W. J.; Lange, U. *J. Chem. Soc., Chem. Commun.* **1995**, 457. (o). Van Ornum, S. G.; Cook, J. M. *Tetrahedron Lett.* **1996**, *37*, 7185. (p). Van Ornum, S. G.; Bruendl, M. M.; Cook, J. M. *Tetrahedron Lett.* **1998**, *39*, 6649. (q). Thommen, M.; Keese, R. *Synlett* **1997**, 231. (r). Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Screiber, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5505. (s). Brummond, K. M.; Lu, J. *J. Am. Chem. Soc.* **1999**, *121*, 5087.

5. (a) Kundsen, M. J.; Schore, N. E. *J. Org. Chem.* **1984**, *49*, 5025. (b) Schore, N. E.; Kundsen, M. J. *J. Org. Chem.* **1987**, *52*, 569. (c) Schore, N. E.; Rowley, E. G. *J. Am. Chem. Soc.* **1988**, *110*, 5224. (d) Rowley, E. G.; Schore, N. E. *J. Org. Chem.* **1992**, *57*, 6853. (e) Gybin, A. S.; Smit, W. A.; Caple, R.; Veretenov, A. L.; Shashkov, A. S.; Vorontsova, L. G.; Kurella, M. G.; Chertkov, V. S.; Carapetyan, A. A.; Kosnikov, A. Y.; Alexanyan, M. S.; Lindeman, S. V.; Panov, V. N.; Maleev, A. V.; Struchkov, Y. T.; Sharpe, S. M. *J. Am. Chem. Soc.* **1992**, *114*, 5555. (f) Tormo, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 4851. (g) Paquette, L. A.; Borrelly, S. *J. Org. Chem.* **1995**, *60*, 6912. (h) Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4353. (i) Montana, A.-M.; Moyano, A.; Pericàs, M. A.; Serratosa, F. *Tetrahedron* **1985**, *41*, 5995. (j) Van Ornum, S. G.; Cook, J. M. *Tetrahedron Lett.* **1997**, *38*, 3657. (k) Marco-Contelles, J. *J. Org. Chem.* **1996**, *61*, 7666. (l) Almansa, C.; Moyano, A.; Serratosa, F. *Tetrahedron* **1988**, *44*, 2657. (m) Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 3346.
6. Intramolecular reaction: (a) Stolle, A.; Becker, H.; Salaün, J.; de Meijere, A. *Tetrahedron Lett.* **1994**, *35*, 3517. (b) Bräse, S.; Schömenauer, S.; McGaffin, G.; Stolle, A.; de Meijere, A. *Chem. Eur. J.* **1996**, *2*, 545. (c) Corlay, H.; Fouquet, E.; Magnier, E.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1999**, 183. (d) Renaud, J.-L.; Aubert, C.; Malacria, M. *Tetrahedron* **1999**, *55*, 5113. Intermolecular reaction: (e) Smit, W. A.; Kireev, S. L.; Nefedov, O. M.; Tarasov, V. A. *Tetrahedron Lett.* **1989**, *30*, 4021. (f) Corlay, H.; James, I. W.; Fouquet, E.; Schmidt, J.; Motherwell, W. B. *Synlett* **1996**, 990.
7. Reviews for construction of quaternary centers: (a) Martin, S. F. *Tetrahedron* **1980**, *36*, 419. (b) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037.
8. To our knowledge, only one example has been reported on intermolecular Pauson–Khand reaction of tetra-substituted olefin. Thus, the reaction of an ethyne–cobalt complex with tetra-substituted olefin, which was in situ generated by isomerization of trisubstituted olefin, gave angular tricyclic compound in less than 1% yield (6.5% yield when 20 equiv. of olefin was used). Billington, D. C.; Kerr, W. J.; Pauson, P. L.; Farnocchi, C. F.; *J. Organomet. Chem.*, **1998**, *356*, 213. Intramolecular Pauson–Khand reaction of tetra-substituted olefin does not give desired tricyclic product.[5a,b]
9. For a preliminary account of this work: Ishizaki, M.; Iwahara, K.; Kyoumura, K.; Hoshino, O. *Synlett* **1999**, 587.
10. Ikeda, T.; Yue, S.; Hutchinson, C. R. *J. Org. Chem.* **1985**, *50*, 5193.
11. Grattan, T. J.; Whitehurst, J. S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 11.
12. Jung, M. E.; Hatfield, G. L. *Tetrahedron Lett.* **1983**, *24*, 3175.
13. Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1095.
14. Nishida, A.; Takahashi, H.; Takeda, H.; Takada, N.; Yonemitsu, O. *J. Am. Chem. Soc.* **1990**, *112*, 902.
15. Pfau, M.; Revial, G.; Guingant, A.; d'Angelo,, J. *J. Am. Chem. Soc.* **1985**, *107*, 273.
16. Guingant, A.; Hammami, H. *Tetrahedron: Asymmetry* **1991**, *2*, 411.
17. Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.
18. Karpf, M. *Helv. Chim. Acta* **1984**, *67*, 73.
19. (a) NMO: Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (b) TMANO: Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-E. *Synlett* **1991**, 204. (c) BuSMe: Sugihara, T.; Yamada, M.; Yamaguchi, M.; Nishizawa, M. *Synlett* **1999**, 771. (d) primary amines: Sugihara, T.; Yamada, M.; Ban, H.; Yamaguchi, M.; Kaneko, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2801.
20. It is known that Pauson–Khand reaction of tri-substituted olefins furnishes tricyclic products in low yield. Montana, A. M.; Moyano, A.; Pericàs, M. A.; Serratosa, F. *An. Quim. Ser. C* **1988**, *84*, 82.
21. Lee, E.; Lee, Y. R.; Moon, B.; Kwon, O.; Shim, M. S.; Yun, J. S. *J. Org. Chem.* **1994**, *59*, 1444.
22. Mori, M.; Kaneta, N.; Isono, N.; Shibasaki, M. *Tetrahedron Lett.* **1991**, *32*, 6139.
23. The reaction of the trimethylsilylacetylene did not afford the corresponding tetracyclic compound.
24. Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041.