Rhodium(I)-Catalyzed Intramolecular Pauson–Khand-Type [2 + 2 + 1] Cycloaddition of Allenenes
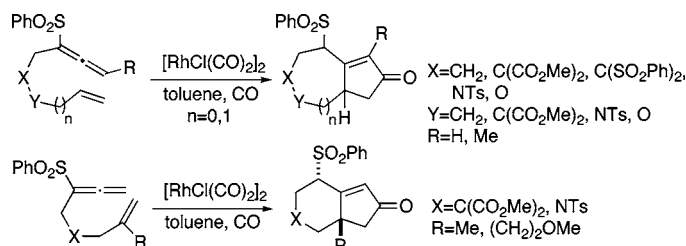
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Received January 13, 2006

ABSTRACT

The novel [RhCl(CO)$_2$]$_2$-catalyzed [2 + 2 + 1] cycloaddition of allenenes leading to the bicyclo[4.3.0]non-1(9)-en-8-one as well as the bicyclo-[5.3.0]dec-1(10)-en-9-one skeletons has been developed. This method also provides a new procedure for the construction of the bicyclo[4.3.0]-non-1(9)-en-8-one skeleton having an alkyl appendage at the ring juncture, which was hardly attained in a satisfactory yield by the Pauson–Khand reaction of the corresponding enynes.

The intramolecular Pauson–Khand reaction[1] is a formal metal-mediated (or -catalyzed) [2 + 2 + 1] cycloaddition of the alkyne π-bond, the alkene π-bond, and carbon monoxide (CO) and provides the straightforward as well as powerful methodology for the construction of the cyclopentenone-fused frameworks. This ring-closing reaction has been almost exclusively limited to the use of the alkyne π-bond as one of the two carbon–carbon π-bond components, although the stepwise stoichiometric conversion[2] of 1-phen-ylhepta-1,6-diene (bis-alkene derivatives) into the carbonylative bicyclo[3.3.0] compounds via the zirconacyclopentane has been reported. Wender[3] very recently reported the first example of the [RhCl(CO)$_2$]$_2$-catalyzed [2 + 2 + 1] cycloaddition of 1,3-dienes, alkenes, and CO, in which the 1,3-diene moiety served as the alkene π-bond[4] instead of the alkyne π-component. On the other hand, Itoh[5] reported an example of the [RhCl(CO)$_2$]$_2$-catalyzed intramolecular [2 + 2 + 1] cycloaddition between the proximal double bond of the allenyl moiety and a vinylsilane of (8E)-6,6-bis-(methoxycarbonyl)-2-methyl-9-trimethylsilylnona-2,3,8-tri-ene under 3 atm of CO resulting in the formation of 2-isopropylidenebicyclo[3.3.0]octan-3-ones. When allenenes without a silyl group on the olefin moiety were exposed to

(1) For leading reviews, see: (a) Pauson, P. L. In *Organometallics in Organic Synthesis. Aspects of a Modern Interdisciplinary Field*; de Meijere, A., tom Dieck, H., Eds.; Springer: Berlin, 1988; pp 233–246. (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081–1119. (c) Schore, N. E. *Org. React.* **1991**, *40*, 1–90. (d) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, pp 1037–1064. (e) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: New York, 1995; Vol. 12, pp 703–739. (f) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523–596. (g) Jeong, N. In *Transition Metals in Organic Synthesis*; Beller, H., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 1, pp 560–577. (h) Geis, O.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **1998**, *37*, 911–914. (i) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297–341. (j) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263–3283. (k) Boñaga, L. V. R.; Krafft, M. E. *Tetrahedron* **2004**, *60*, 9795–9833.

(2) Negishi, E.; Choueiry, D.; Nguyen, T. B.; Swanson, D. R.; Suzuki, N.; Takahashi, T. *J. Am. Chem. Soc.* **1994**, *116*, 9751–9752.
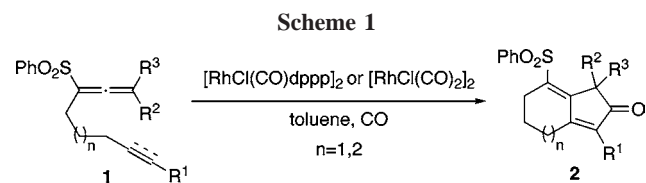
(3) Wender, P. A.; Croatt, M. P.; Deschamps, N. M. *J. Am. Chem. Soc.* **2004**, *126*, 5948–5949.

(4) Wender reported that several bis-enes failed to give the [2 + 2 + 1] products under the optimized [RhCl(CO)$_2$]$_2$-catalyzed conditions.[3]

(5) (a) Makino, T.; Itoh, K. *Tetrahedron Lett.* **2003**, *44*, 6335–6338. (b) Makino, T.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 395–405.

the Rh(I) catalyst, however, the ring-closing reaction proceeded in a different way to produce the seven-membered monocyclic products instead of the Pauson−Khand-type products.

Our recent interest[6] in the development of the [RhCl(CO)$_2$]$_2$- or [RhCl(CO)dppp]$_2$-catalyzed intramolecular Pauson−Khand-type reaction[7] between the alkyne π-bond and the allenyl π-bond of the phenylsulfonylallenynes 1 (allenynes) in the presence of CO led to the easy preparation of the bicyclo[4.3.0]nonadienone ($n = 1$) as well as the bicyclo[5.3.0]decadienone ($n = 2$) frameworks 2 (Scheme 1). These observations prompted us to investigate the [RhCl(CO)$_2$]$_2$- or [RhCl(CO)dppp]$_2$-catalyzed cyclocarbonylation between the alkene π-bond and the allenyl π-bond of 1 (allenenes). We report herein the preliminary results of the Rh(I)-catalyzed [2 + 2 + 1] cycloaddition of the alkene π-bond, the distal π-bond of the allenyl moiety, and CO resulting in the preparation of the bicyclo[4.3.0]nonenone and bicyclo[5.3.0]decenone skeletons.

Our initial evaluation for the Rh(I)-catalyzed cyclocarbonylation of a phenylsulfonylallenene was carried out using compounds 3a[8] and 3b[9] (Table 1). According to the previously reported conditions[6] for the Pauson−Khand-type reaction of substrates 1 (allenynes), a solution of 3a in toluene was refluxed for 20 h in the presence of 2.5 mol % of [RhCl(CO)dppp]$_2$ under an atmosphere of CO to afford the desired 2-phenylsulfonylbicyclo[4.3.0]nonenone 4a in 64% yield as a mixture of the cis-4a and trans-4a[10] in a ratio of 21:79 (entry 1).[11]

An alternative catalyst, [RhCl(CO)$_2$]$_2$, gave the ring-closed products 4a in a rather lower yield (entry 2). A significant

(6) (a) Mukai, C.; Nomura, I.; Yamanishi, K.; Hanaoka, M. *Org. Lett.* **2002**, *4*, 1755−1758. (b) Mukai, C.; Nomura, I.; Kitagaki, S. *J. Org. Chem.* **2003**, *68*, 1376−1385. (c) Mukai, C.; Inagaki, F.; Yoshida, T.; Kitagaki, S. *Tetrahedron Lett.* **2004**, *45*, 4117−4121. (d) Mukai, C.; Inagaki, F.; Yoshida, T.; Yoshitani, K.; Hara, Y.; Kitagaki, S. *J. Org. Chem.* **2005**, *70*, 7159−7171. (e) Mukai, C.; Hirose, T.; Teramoto, S.; Kitagaki, S. *Tetrahedron* **2005**, *61*, 10983−10994.

(7) Brummond independently developed the [RhCl(CO)$_2$]$_2$-catalyzed Pauson−Khand-type [2 + 2 + 1] cycloaddition of allenynes. See: (a) Brummond, K. M.; Chen, H.; Fisher, K. D.; Kerekes, A. D.; Rickards, B.; Sill, P. C.; Geib, S. J. *Org. Lett.* **2002**, *4*, 1931−1934. (b) Brummond, K. M.; Gao, D. *Org. Lett.* **2003**, *5*, 3491−3494. (c) Brummond, K. M.; Mitasev, B. *Org. Lett.* **2004**, *6*, 2245−2248. (d) Brummond, K. M.; Curran, D. P.; Mitasev, B.; Fischer, S. *J. Org. Chem.* **2005**, *70*, 1745−1753.

(8) Padwa, A.; Filipkowski, M. A.; Meske, M.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1993**, *115*, 3776−3777.

(9) The preparation and characterization of the unknown allenenes are described in SI.

(10) The relative stereochemistry was determined by ¹H NMR spectral considerations, in particular, by an NOE analysis.

(11) The ring-closing reaction of allenenes, having the other substituent instead of a phenylsulfonyl group on the allenyl moiety, has not been examined yet. The effect of a phenylsulfonyl group in this reaction will be investigated in due course.

Table 1. Rhodium(l)-Catalyzed [2 + 2 + 1] Cycloaddition of 3a,b

a: Z=CO$_2$Me, b: Z=H A: [RhCl(CO)dppp]$_2$, B: [RhCl(CO)$_2$]$_2$
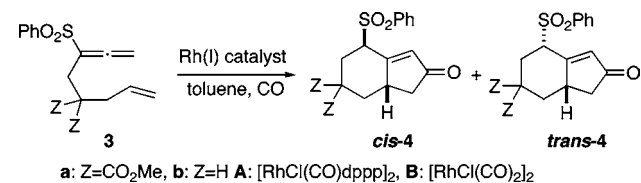
entry	allenene	Rh(l)	mol %	CO (atm)	T (°C)	t (h)	product (%)	cis:trans[a]
1	3a	A	2.5	1	reflux	20	4a (64)[b]	21:79
2	3a	B	2.5	1	reflux	10	4a (22)	21:79
3	3a	A	2.5	5	120	2	4a (53)	21:79
4	3a	B	2.5	5	120	12	4a (96)	21:79
5	3b	A	2.5	5	120	3	4b (74)	62:38
6	3b	A	5	5	120	3	4b (77)	62:38

[a] Ratio was determined by ¹H NMR. [b] The starting material 3a was recovered in 30% yield.
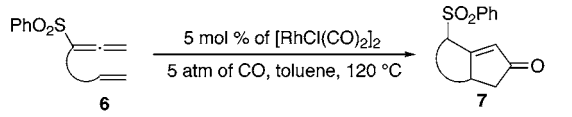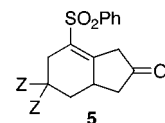

improvement (4a, 96%) was observed when the ring-closing reaction of 3a was carried out in the presence of [RhCl(CO)$_2$]$_2$ under 5 atm of CO at 120 °C (entry 4). [RhCl(CO)dppp]$_2$ furnished 4a in 53% yield under 5 atm of CO (entry 3).[12] The ring-closing reaction of 3b under 5 atm of CO with a catalytic amount of [RhCl(CO)$_2$]$_2$ also proceeded as expected to produce 4b in 74% yield (entry 5). Increase of the loading amounts of [RhCl(CO)$_2$]$_2$ from 2.5 to 5 mol % provided 4b in a similar yield (entry 6). The formation of 4 can be rationalized in terms of the intermediacy of the initially formed 2-phenylsulfonylbicyclo[4.3.0]non-1-en-8-one derivative 5, which should immediately isomerize to the α,β-unsaturated ketones.

We next investigated the scope of the [RhCl(CO)$_2$]$_2$-catalyzed ring-closing reaction under 5 atm of CO using several 1,2,7-octatrienes 6. These results are summarized in Table 2. The allenenes 6a,b, having a heteroatom on the alkyl tether, consistently produced the corresponding bicyclic compounds 7a,b in good yields (entries 1 and 2). The 6-alkylbicyclo[4.3.0]nonenone frameworks 7c−e could be constructed from the 1,1-dialkylalkene derivatives 6c−e in acceptable yields (entries 3−5), respectively. Similarly, compound 6g with a trisubstituted allenyl moiety produced 7g in 51% yield along with its double bond isomer 9 (36%) (entry 7). Whereas the Pauson−Khand reaction of the 2-alkyl (or phenyl)-1-hepten-6-ynes are well-known to efficiently afford the 5-alkyl (or phenyl) bicyclo[3.3.0]oct-1-en-3-
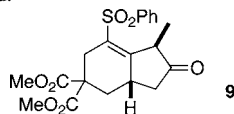
(12) During our investigations[6] of the intramolecular Pauson−Khand-type [2 + 2 + 1] cycloaddition of allenynes under an atmosphere of CO, we found that [RhCl(CO)dppp]$_2$ generally more efficiently catalyzed the ring-closing reaction than [RhCl(CO)$_2$]$_2$, whereas the latter is much a more effective catalyst compared to the former when the reaction was carried out under CO pressure (5−10 atm). A similar behavior was observed in the ring-closing reaction of 3.

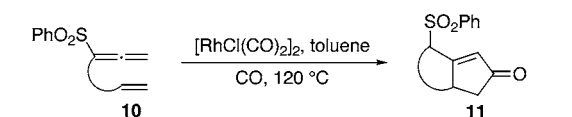**Table 2.** [RhCl(CO)$_2$]$_2$-Catalyzed [2 + 2 + 1] Cycloaddition of 1,2,7-Trienes

entry	allenene	product	yield (%)	cis:trans[a]
1	6a	7a	89	71:29
2	6b	7b	63	82:18
3	6c	7c	85	0:100[b]
4	6d	7d	69	0:100[b]
5	6e	7e	58	0:100[b]
6	6f	8	68	—
7	6g	7g	51[c]	33:67
8	6h		0[d]	—

[a] Ratio was determined by ^{1}H NMR. [b] Isolated as a single isomer. [c] Compound 9 was also obtained in 36% yield. [d] Starting material 6h was recovered in 50% yield.

Table 3. [RhCl(CO)$_2$]$_2$-Catalyzed [2 + 2 + 1] Cycloaddition of 1,2,8-Trienes

entry	allenene	Rh (mol %)	CO (atm)	product	yield (%)	cis:trans[a]
1	10a Z=CO$_2$Me	2.5	5	11a	49	15:85
2	10a	5	10	11a	73	25:75
3	10a	10	10	11a	82	35:65
4	10b Z=SO$_2$Ph	5	10	11b	36	60:40
5	10b	10	10	11b	47	60:40
6	10c	10	10	11c	33	93:7
7	10d	10	10	11d	73	80:20
8	10e	10	10	11e	30	100:0[b]
9	10f Z=CO$_2$Me	5	5	12	68	—

[a] Ratio was determined by ^{1}H NMR. [b] Isolated as a single isomer.

tion of allenenes, the formation of 8[17] would be interpreted by the thermal [2 + 2] cycloaddition between the proximal π-bond of the allenyl moiety and the terminal olefin. In fact,

ones,[1,13] there are only two examples[14] that described the low yield formation of the one-carbon-homologated bicyclo-[4.3.0] skeletons, possessing an alkyl appendage at the ring juncture, from the acyclic enynes.[15] Thus, the newly developed Pauson–Khand-type [2 + 2 + 1] cycloaddition of allenenes would provide an efficient and general way for preparing the bicyclo[4.3.0] skeletons, possessing an alkyl group at the ring juncture. In sharp contrast to the alkyl derivatives 6c–e, the phenyl congener 6f was transformed into a different product, the bicyclo[3.2.0]heptane derivative 8, in 68% yield (entry 6). Based on Padwa's extensive studies[8,16] on the thermal intramolecular [2 + 2] cycloaddi-

(13) For selected references, see: (a) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159–3160. (b) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285–2286. (c) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249–250. (d) Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **1998**, *120*, 10782–10783. (e) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 5881–5898. (f) Krafft, M. E. Bonaga, L. V. R.; Hirosawa, C. *Tetrahedron Lett.* **1999**, *40*, 9171–9175. (g) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Asymmetry* **2000**, *11*, 797–808. (h) Fletcher, A. J.; Christie, S. D. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1657–1668. (i) Krafft, M. E.; Wright, J. A.; Boñaga, L. V. R. *Synlett* **2005**, 71–74. (j) Tang, Y.; Deng, L.; Zhang, Y.; Dong, G.; Chen, J.; Yang, Z. *Org. Lett.* **2005**, *7*, 593–595.

(14) Bolton obtained the azabicyclo[4.3.0]nonenone derivative, having a methyl group at the ring juncture, in a less than 5% yield, whereas Ishizaki and Hoshino prepared the bicyclo[4.3.0]nonenone derivative, having a methyl group at the ring juncture, in 28% yield. See: (a) Bolton, G. L.; Hodges, J. C.; Rubin, J. R. *Tetrahedron* **1997**, *53*, 6611–6634. (b) Ishizaki, M.; Satoh, H.; Hoshino, O. *Chem. Lett.* **2002**, 1040–1041. (c) Ishizaki, M.; Satoh, H.; Hoshino, O.; Nishitani, K.; Hara, H. *Heterocycles* **2004**, *63*, 827–844.

compound **8** was obtained by simply heating in toluene at 120 °C without the Rh(I)-catalyst. The tetrasubstituted allene derivative **6h** was found to be an inadequate substrate for this ring-closing reaction, and the starting material was recovered in 50% yield (entry 8).

The application of the newly developed [RhCl(CO)$_2$]$_2$-catalyzed Pauson–Khand-type [2 + 2 + 1] cycloaddition of allenenes for the synthesis of the bicyclo[5.3.0]decenones was the next subject. Exposure of the 1,2,8-nonatriene **10a** to the standard ring-closing conditions (2.5 mol % of [RhCl-(CO)$_2$]$_2$, 5 atm of CO, 120 °C in toluene) afforded the bicyclo[5.3.0]decenone derivative **11a** in 49% yield as a mixture[10] of the *cis*- and *trans*-isomers in the ratio 15:85 (Table 3, entry 1). Increasing both the loading amounts of the Rh(I) catalyst (5 mol %) and CO pressure (10 atm) produced an improvement in the chemical yield (73%) (entry 2). Furthermore, 10 mol % of the Rh(I) catalyst under 10 atm of CO provided **11a** in 82% yield (entry 3). Compound **10b** also furnished the ring-closed product **11b** in moderate yields (entries 4 and 5). However, the simpler 3-phenylsulfonylnona-1,2,8-triene (**10c**) gave the ring-closed product **11c** in a rather low yield (entry 6). The nitrogen atom containing substrate **10d** afforded the corresponding azabicyclo[5.3.0]-decenone **11d** in 73% yield (entry 7), while the oxabicyclo congener **11e** was formed in a low yield (entry 8). The low yields for compounds **10c**,**e** might be attributable to the loss of the Thorpe–Ingold-type effects[18] compared to those of other substrates. The 1,1-dialkylalkene derivative **10f** unexpectedly produced the bicyclo[4.2.0]nonene framework **12**[19]

instead of the carbonylative 7-methylbicyclo[5.3.0]decenone derivative (entry 9). Interestingly, compound **12** was not obtained when **10f** was heated for a prolonged time without the Rh(I) catalyst. Thus, the formation of **12** would tentatively be rationalized by the first isomerization of the double bond of **10f**, followed by the thermal [2 + 2] cycloaddition.[16] Coordination of the Rh(I) catalyst with the olefin moiety would accelerate the conversion of the terminal olefin into the internal one.

In summary, we have described the novel [RhCl(CO)$_2$]$_2$-catalyzed intramolecular [2 + 2 + 1] cycloaddition of 3-phenylsulfonyl-1,2,7-octatrienes leading to the formation of the bicyclo[4.3.0]non-1(9)-en-8-one, in which the distal double-bond of the allenyl moiety exclusively served as a π-component. This method not only was shown to be applicable to the construction of the one-carbon homologated bicyclo[5.3.0]dec-1(10)-en-9-one skeleton but also provided a new entry for the construction of the bicyclo[4.3.0]non-1(9)-en-8-one skeleton having an alkyl appendage at the ring juncture, which was hardly attained in a satisfactory yield by the Pauson–Khand reaction of the corresponding enynes. Determining the scope and limitations of this method as well as application to the synthesis of natural products are now in progress.

Supporting Information Available: General procedures for the [2 + 2 + 1] cycloaddtion and preparation of sulfonylallenenes, characterization data for all new compounds, and ^{1}H and ^{13}C NMR spectra for compounds **6d,e, 7b,d,e,g, 10c,e,f**, and **11e**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0600990

(15) A few precedents dealing with the construction of the more complexed ring-fused cyclic compounds (including a bicyclo[4.3.0]nonenone framework) from enynes are available. See: (a) Corlay, H.; Fouquet, E.; Magnier, E.; Motherwell, W. B. *Chem. Commun.* **1999**, 183–184. (b) Ishizaki, M.; Iwahara, K.; Niimi, Y.; Satoh, H.; Hoshino, O. *Tetrahedron* **2001**, *57*, 2729–2738. (c) Magnus, P.; Fielding, M. R.; Wells, C.; Lynch, V. *Tetrahedron Lett.* **2002**, *43*, 947–950.

(16) (a) Padwa, A.; Meske, M.; Murphree, S.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1995**, *117*, 7071–7080. (b) Padwa, A.; Lipka, H.; Watterson, S. H.; Murphee, S. S. *J. Org. Chem.* **2003**, *68*, 6238–6250.

(17) No bicyclo[3.2.0] compounds, such as compound **8**, could be detected except during the reaction of **6f**.

(18) For a recent review, see: Jung, M. E.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735–1766.

(19) Padwa[16a] reported that the thermolysis of 5,5-bis(methoxycarbonyl)-3-phenylsulfonylnona-1,2,8-triene and 3,5,5-tris(phenylsulfonyl)nona-1,2,8-triene in refluxing xylene afforded the monocyclic eight-membered products in high yields instead of the bicyclo[5.2.0]nonenes.