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Novel Syntheses of Eight-Membered−Five-Membered Fused-Ring Compounds from Zirconacyclopentadienes

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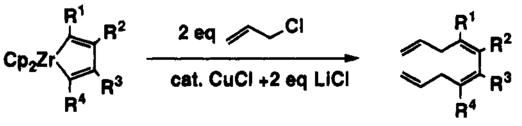
Summary: Zirconacyclopentadienes reacted with 2 equiv of allyl chloride in the presence of either a catalytic or a stoichiometric amount of CuCl and LiCl salts (2 equiv) to give stereodefined 1,4,6,9-decatetraenes in 66−96% yields. Reaction of 1,4,6,9-decatetraenes obtained here such as 4,5,6,7-tetraethyldeca-1,4,6,9-tetraene with 1 equiv of Negishi reagent (Cp_2ZrCl_2 + 2 n-BuLi) in THF at room temperature for 3 h and subsequent carbonylation at 0 °C gave eight-membered−five-membered fused-ring ketones such as 3,4,5,6-tetraethylbicyclo[6.3.0]-undeca-3,5-dien-10-one in 76% yield.

The eight-membered−five-membered (8−5) fused-ring system is an attractive synthetic target,[2] since some natural products such as cyclooctanoid terpenes contain this system.[3] One of the most exciting approaches for the fused-ring system is the intramolecular direct bicyclization of dienes, enynes, or diynes using transition metals followed by carbonylation or related reactions.[4] However, this type of direct cyclization reaction has a critical limitation for the ring size.[4a,5] In this paper we report the novel copper-catalyzed diallylation reaction of zirconacyclopentadienes to give the tetraenes and novel 8−5 fused-ring formation from the tetraenes using zirconium.

Zirconacyclopentadienes can be readily prepared in high yields by the reaction of two alkynes or diynes with reduced zirconium species.[5b,6,7] Although many reactions with electrophiles have been reported,[7] the further C−C bond formation reaction of zirconacyclopentadiene is very rare.[8] Recently we have reported the Cu-catalyzed allylation reaction of (trisubstituted alkenyl)-zirconocenes.[9] This reaction could be applied for zirconacyclopentadienes. Zirconacyclopentadienes **1** reacted with 2 equiv of allyl chloride in the presence of either a catalytic or a stoichiometric amount of CuCl and LiCl (or Mg) salts to give diallylation products **2** in high yields. Results of the diallylation of zirconacyclopentadienes are shown in Table 1. The diallylation reaction proceeded for various substituents such as alkyl, aryl, and trimethylsilyl groups. Yields were high in all cases. Simple distillation gave pure products. The zirconaindene compound **1g**[10] could be used for diallylation.[11]



1 **2** (1)

A convenient zirconium-mediated preparation of 5−5 or 6−5 fused-ring compounds from nonconjugated dienes and enynes has been reported.[12] However, 1,2-bis(3-butenyl)cyclohexane (**6**) did not give eight-membered-

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[1] JSPS fellow (1993, Institute for Molecular Science).

[2] For eight-membered-ring and 8−5 fused-ring systems, see a review: Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757−5821 and references therein. For recent work, see: (a) Lottaz, P.-A.; Edwards, T. R. G.; Mentha, Y. G.; Burger, U. *Tetrahedron Lett.* **1993**, *34*, 639−642. (b) Wagner, P. J.; Cheng, K.-L. *Tetrahedron Lett.* **1993**, *34*, 907−910. (c) Paquette, L. A.; Wang, T.-Z.; Vo, N. H. *J. Am. Chem. Soc.* **1993**, *115*, 1676−1683. (d) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 4895−4896. (e) Myers, A. G.; Condroski, K. R. *J. Am. Chem. Soc.* **1993**, *115*, 7926−7927. (f) Funk, R. L.; Stallman, J. B.; Wos, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 8847−8848. (g) Funk, R. L.; Fitzgerald, J. F.; Olmstead, T. A.; Para, K. S.; Wos, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 8849−8850. (h) Boussie, T. R.; Streitwieser, A. *J. Org. Chem.* **1993**, *58*, 2377−2380. (i) Wang, Z.; Wander, S. E.; Perrier, H.; Grimm, E. L.; Bernstein, M. A. *J. Org. Chem.* **1993**, *58*, 2931−2932.

[3] Glasby, J. S. *Encyclopedia of Terpenoids*; Wiley: New York, 1982.

[4] For Zr: (a) Negishi, E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1163−1184, and references therein. (b) Agnel, G.; Owczarczyk, Z.; Negishi, E. *Tetrahedron Lett.* **1992**, *33*, 1543−1546. (c) Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 7424−7426. (d) Davis, J. M.; Whitby, R. J.; Jaxa-Chamiec, A. *Tetrahedron Lett.* **1992**, *33*, 5655−5658. (e) Davis, J. M.; Whitby, R. J.; Jaxa-Chamiec, A. *Tetrahedron Lett.* **1994**, *35*, 1445−1448. For Co: (f) Schore, N. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1053−1064, and references therein. For Ti: (g) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 5803−5805. (h) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912−4913. For other metals: (i) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 1129−1162, and references therein. (j) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154−1156. (k) Pearson, A. J.; Dubbert, R. A. *J. Chem. Soc., Chem. Commun.* **1991**, 202−203.

[5] (a) Maye, J. P.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 3359−3362. (b) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788−2796.

[6] (a) Takahashi, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* **1987**, 623−626. (b) Skibbe, V.; Erker, G. *J. Organomet. Chem.* **1983**, *241*, 15−26. (c) Rausch, M. D.; Boon, W. H.; Alt, H. G. *J. Organomet. Chem.* **1977**, *141*, 299−312. (d) Alt, H.; Rausch, M. D. *J. Am. Chem. Soc.* **1974**, *96*, 5936−5937. (e) Watt, G. W.; Drummond, F. O., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 826−828. (f) Lau, C. P.; Chang, B. H.; Grubbs, R. H.; Brubaker, C. H. *J. Organomet. Chem.* **1981**, *214*, 325−337. (g) Thanedar, D.; Farona, M. F. *J. Organomet. Chem.* **1982**, *235*, 65−68. (h) Yoshifuji, M.; Gell, K. I.; Schwartz, J. *J. Organomet. Chem.* **1978**, *153*, C15−C18. (i) Parshall, G. W.; Nugent, W. A.; Chan, D. M. T.; Tam, W. *Pure Appl. Chem.* **1985**, *57*, 1809−1818. (j) Reference 12f.

[7] (a) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 2544−2546. (b) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310−2312. (c) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870−2874. (d) Fagan, P. J.; Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1994**, *116*, 1880−1889.

[8] Alkyne insertion of zirconacyclopentadienes has been reported; see: (a) Famili, A.; Farona, M. F.; Thanedar, S. *J. Chem. Soc., Chem. Commun.* **1983**, 435−436. It was reported that the reaction of $Cp_2Zr(CO)_2$ with an excess of diphenylacetylene gave cyclopentadienone as a minor product. See: (b) Sikora, D. J.; Rausch, M. P. *J. Organomet. Chem.* **1984**, *276*, 21−37.

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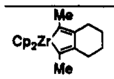
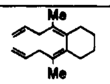
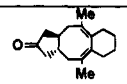
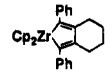
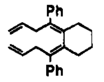
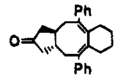
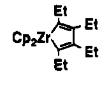
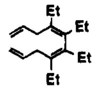
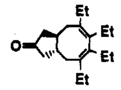
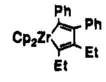
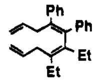
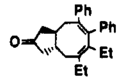
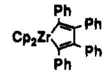
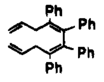
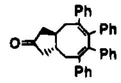
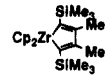
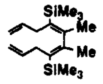
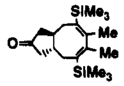
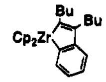
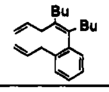
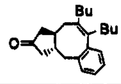
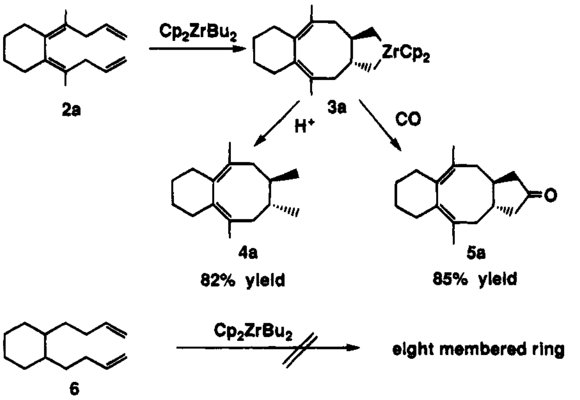
Table 1. Diallylation of Zirconacyclopentadienes and Formation of 8−5 Fused-Ring Compounds

Zirconacyclopentadienes		Diallylation^a Temp /°C	Time /h	Tetraenes		Yield /%^{b}	Cyclization product^c		Yield /%^{b,d}	Trans/Cis
	1a	25	1		2a	82		5a	85 (69)	trans only
	1b	25^e	1		2b	(66)		5b	(47)	3:1
	1c	25	1		2c	96		5c	76 (55)	trans only
	1d	50	1		2d	73		5d	(50)	2.1:1
	1e	25^e	1		2e	(88)		5e	(52)	3:1
	1f	25	1		2f	76		5f	(74)	10:1
	1g	50	1		2g	72		5g	69 (52)	2.8:1

^{a}Diallylation was carried out using 10 mol % of CuCl as a catalyst and 2 eq of allyl chloride unless otherwise stated. ^{b}GC yield. Isolated yields were given in parentheses. ^{c}Cyclization was carried out at 0°C for 6h. Major isomer is shown. ^{d}Combined yields of cis and trans isomers. ^{e}2 equiv CuCl was used.

ring compounds when it was treated with Negishi reagent (Cp_2ZrCl_2/2 *n*-BuLi).[12d]

We found, surprisingly, that the reaction of tetraenes (**2a**) obtained here with 1 equiv of Negishi reagent in THF at room temperature for 3 h gave 2,4,5,7-tetramethylbicyclo[6.4.0]dodeca-1,7-diene (**4a**)[13] in 82% yield after hydrolysis. Carbonylation of the zirconium-containing compound at 0 °C instead of hydrolysis gave the 6−8−5 fused-ring ketone **5a**[14] in 85% yield. The structure of **5a** was determined by X-ray analysis[15] and is shown in Figure 1. Only the trans isomer was obtained in both cases for **4a** and **5a**, as judged by a combination of ^1H and ^{13}C NMR, GLC, and X-ray analysis.



(2)

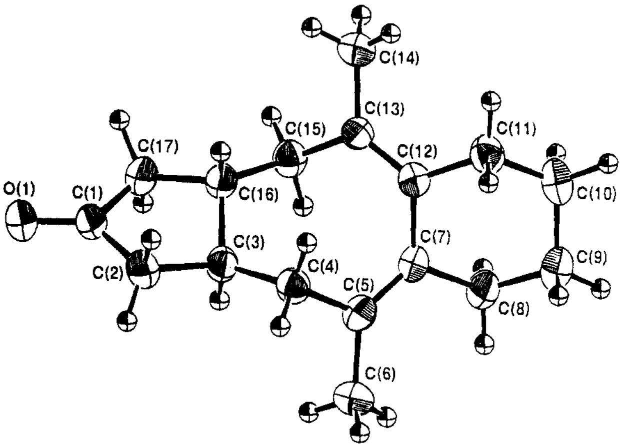


Figure 1. Perspective view of **5a**.

Eight-membered-ring formation of 1,9-dienes[5a] or 1,9-diynes[5b] was not favorable. Probably, the side reaction

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(9) (a) Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Tetrahedron Lett.* **1994**, *35*, 5685−5688. The copper-catalyzed conjugated addition reaction of alkenylzirconocene to α,β-unsaturated carbonyl compounds has been reported; see: (b) Lipshutz, B. H.; Wood, M. R. *J. Am. Chem. Soc.* **1993**, *115*, 12625−12626. For the stoichiometric reaction dimerization of alkenylzirconocene, see: (c) Yoshifuji, M.; Loots, M. J.; Schwartz, J. *Tetrahedron Lett.* **1977**, 1303−1306. For addition of alkenylzirconocene to α,β-unsaturated carbonyl, see: (d) Lipshutz, B. H.; Ellsworth, E. *J. Am. Chem. Soc.* **1990**, *112*, 7440−7441. (e) Babiak, K. A.; Behling, J. R.; Dygos, J. H.; McLanghlin, K. T.; Ng, J. S.; Kalish, V. J.; Kramer, S. W.; Shone, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 7441−7442. (f) Lipshutz, N. H.; Hato, K. *Tetrahedron Lett.* **1991**, *32*, 5647−5650. (g) Lipshutz, B. H.; Fatheree, P.; Hagan, W.; Stevens, K. L. *Tetrahedron Lett.* **1992**, *33*, 1041−1044. (h) Lipshutz, B. H.; Keil, R. *J. Am. Chem. Soc.* **1992**, *114*, 7919−7920. However, there is no Cu-catalyzed or -mediated C−C bond formation reaction for zirconacycles such as zirconacyclopentadiene.

(10) Buchwald, S. L.; Watson, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 7411−7413.

(11) The Zr−Ph bond was also reactive for the copper-catalyzed allylation reaction. For example, diphenylzirconocene (Cp_2ZrPh_2) reacted with allyl chloride in the presence of 10 mol % of CuCl and 2 equiv of LiCl to afford allylbenzene in 97% yield.

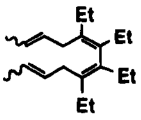
(12) (a) Reference 4a−e. (b) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568−2569. (c) Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65−72. (d) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829−2832. (e) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917−920. (f) Negishi, E.; Holmes, S. J.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336−3346. For zirconium-mediated or -catalyzed cyclization of dienes, see also: (g) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* **1989**, *30*, 5105−5108. (h) Rajan Babu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 7128−7135. (i) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 6435−6437. (j) Knight, K. S.; Waymouth, R. M. *J. Am. Chem. Soc.* **1991**, *113*, 6268−6270. (k) Wischmeyer, U.; Knight, K. S.; Waymouth, R. M. *Tetrahedron Lett.* **1992**, *33*, 7735−7738. (l) Knight, K. S.; Wang, D.; Waymouth, R. M.; Ziller, J. *J. Am. Chem. Soc.* **1994**, *116*, 1845−1854.

(13) **4a**: 85% GC yield (69% isolated); ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90−0.92 (m, 2H), 0.94 (s, 6H), 1.38−1.46 (m, 2H), 1.57 (d, J = 13 Hz, 2H), 1.69 (s, 6H), 1.72−1.80 (m, 4H), 2.09−2.17 (m, 2H), 2.53−2.59 (m, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.01, 23.45, 27.44, 30.04, 36.23, 43.70, 127.69, 133.65; IR (Nujol) 1235 (m), 1136 (m), 1111 (m), 1034 (m), 943 (m), 905 (m) cm^{-1}; HRMS calcd for $C_{16}H_{26}$ 218.2034, found 218.2043.

(14) **5a**: 85% yield (49% isolated); ^1H NMR ($CDCl_3$, Me_4Si) δ 1.42−1.54 (m, 4H), 1.75 (s, 6H), 1.77−1.81 (m, 4H), 1.88−1.94 (m, 4H), 2.18 (dd, J = 12, 9 Hz, 2H), 2.35 (dd, J = 16, 6 Hz, 2H), 2.60−2.66 (m, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.94, 28.00, 31.36, 38.08, 42.73, 47.35, 125.60, 134.98, 217.66; IR (Nujol) 1749 (w), 1738 (w) cm^{-1}; HRMS calcd for $C_{17}H_{24}O$ 244.1827, found 244.1820.

(15) Crystallographic data: space group *Cc*, $Z = 4$; $a = 9.792(1)$ Å, $\beta = 115.02(1)°$, $V = 1411(4)$ Å^3. Diffraction data were collected (θ−2θ scans) using graphite-monochromated Cu Kα radiation ($\lambda = 1.5418$ Å) for the range $2 < 2\theta < 140°$ on an Enraf-Nonius CAD-4 diffractometer. Lattice parameters were determined from 25 reflections (30° < 2θ). Three standard reflections were measured every 2 h, and there was no significant decrease in intensities. The intensities were corrected for Lorentz and polarization effects. A total of 2951 reflections were measured, of which 1276 reflections with $|F_o| > 3\sigma(|F_o|)$ were used in the calculations. The structures were solved by direct methods using SHELXS86 and Fourier methods. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included in the refinements with isotropic temperature factors. The calculations were carried out on a HITAC M-680H computer at the Computer Center of the Institute for Molecular Science using the Universal Crystallographic Computation Program System UNICS-III. The final *R* factor converged to 0.049 (R_w = 0.074).

proceeds before two double or triple bonds coordinate to zirconium to make a new C—C bond.[5a] On the other hand, in the case of tetraenes **2**, six carbons associated with the conjugated diene system are fairly fixed. Two double bonds, therefore, come closer to each other, and when **2** is treated with Negishi reagent, those two terminal double bonds easily coordinate to zirconocene. Sequential cyclization results in the formation of the desired eight-membered ring. Results on the formation of 8–5 fused ketones from several tetraenes are shown in Table 1. The products were isolated in good yields (47–74%) with high purities after column separation. The trans configuration was favorable. The cis:trans ratio was dependent on the substituents, although the factor determining the cis:trans ratio has not yet been elucidated. When the substituents were alkyl groups, only trans isomers were formed. Tetraenes with two terminal double bonds gave eight-membered-ring compounds. Tetraene **7** without two terminal double bonds afforded only the olefin positional isomerization product **8** in 64% yield. No eight-membered-ring compounds were obtained.



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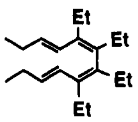

8

A combination of the formation of zirconacyclopentadienes, tetraene formation by diallylation of zirconacyclopentadienes, direct eight-membered-ring formation, and its carbonylation led to a convenient one-pot reaction from alkynes to 8–5 fused-ring compounds such as **5c** (65% yield).

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Supplementary Material Available: Text giving experimental procedures and analytical data and tables of positional and thermal parameters and selected bond distances and bond angles for **5a** (16 pages). Ordering information is given on any current masthead page.

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