Stereochemical Course in Tungsten-Promoted Cyclocarbonylation Reactions To Form Five-, Six-, and Seven-Membered Lactone Rings

Chi-Chung Chen,† Jang-Shyang Fan,† Gene-Hsian Lee,† Shie-Ming Peng,‡ Sue-Lang Wang,† and Rai-Shung Liu*,†

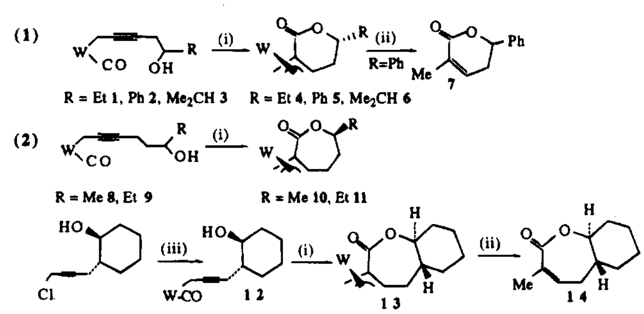
Departments of Chemistry
National Tsing Hua University
Hsinchu 30043, Taiwan, Republic of China
National Taiwan University
Taipei 10764, Taiwan, Republic of China

Received November 14, 1994

Metal-mediated cyclocarbonylation[1-3] is an important reaction in organic synthesis. This reaction is more useful and economical if performed catalytically[1-2] rather than stoichiometrically. Nevertheless, stoichiometric cyclocarbonylation[3] may be accessible to more complex molecules if metal-controlled stereoselective functionalization can be implemented sequentially. Toward this direction, we report stereocontrolled synthesis of tungsten η^3-γ-, -δ-, and -ϵ-lactones derived from intramolecular alkoxycarbonylation[4,5] of η^1-propargyl compounds. These reactions are very useful because lactone is an important structure in natural products.

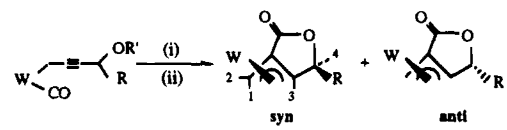
Compounds **1–3** were easily prepared[4] from $CpW(CO)_3Na$ and the corresponding propargyl halides (yields > 90%). Further treatment of **1–3** with CF_3SO_3H (0.25 equiv) in cold CH_2Cl_2 (−40 °C) provided η^3-δ-lactones **4–6** in high yields (>90%). No second diastereomer was detected in ^1H NMR spectra. The molecular structures[6,7] of **4** and **5** reveal that the compounds have *anti* configurations, i.e., the ethyl and phenyl groups lie away from the metal fragment. Further treatment of **5** with CF_3CO_2H in $CHCl_3$ (23 °C, 48 h) liberated the unsaturated lactone **7** in 85% isolated yield.

Scheme 1[a]



[a] W = $CpW(CO)_2$; (i) CF_3SO_3H (0.25 equiv, CH_2Cl_2 −40 °C, 1 h), (ii) CF_3CO_2H (1.0 equiv, 23 °C, 48 h), $CHCl_3$, (iii) $CpW(CO)_3Na$ (THF, 23 °C, 4 h).

Scheme 2[a]



η^1-propargyl	lactone(syn/anti)	yields
R' = H		
R = Et **15**	**22** (71/29)	87%
i-Bu **16**	**23** (62/38)	88%
i-Py **17**	**24** (49/51)	87%
R' = $SiMe_2$(t-Bu)		
R = Me **18**	**25**-syn	90%
Et **19**	**22**-syn	91%
i-Bu **20**	**23**-syn	88%
i-py **21**	**24**-syn	88%

[a] W = $CpW(CO)_2$, (i) CF_3SO_3H (0.25 equiv, −40 °C, 1 h), (ii) CF_3CO_2H (1.0 equiv, 23 °C, 48 h), (iii) $CpW(CO)_3Na$ (1.0 equiv, 23 °C, 4 h).

Scheme 1 (eq 2) shows the formation of η^3-ϵ-lactones derived from **8–9** under the same conditions; the yields exceeded 80% after workup. Because of *exo*/*endo* isomerization,[8] the ^1H NMR spectra of **10**/**11** were broad at 23 °C but became well defined at −40 °C to show the presence of only one diastereomer with conformational ratios *endo*/*exo* = 1/2–2/5. The X-ray structure[9] of **10** indicated a surprising *syn* configuration, i.e., the R substituent lies on the metal face. To apply this cyclization to a more complex molecule, we prepared the η^1-propargyl **12**, and further converted it to bicyclic η^3-ϵ-lactone **13** as a single diastereomer (84%) which likewise adopts a *syn* configuration according to the ORTEP drawing.[10] Demetalation of **13** with CF_3CO_2H in $CHCl_3$ (23 °C, 48 h) provided lactone **14** in 85% yield.

CF_3SO_3H-promoted cyclization of **15–17** gave η^3-butyrolactones **22–24** composed of *syn* and *anti* diastereomers which were not separable either on column chromatography or by fractional crystallization. The *syn*/*anti* ratios and combined yields are given in Scheme 2. The two diastereomers are distinguishable by ^1H NMR spectra that show coupling constant J_{34} = 0 Hz for the *anti* isomer and J_{34} = 3–4 Hz for the *syn* isomer. In Scheme 2, that the *syn*/*anti* ratios decrease with larger size R is reasonable, as the *syn* substituent exerts an additional steric hindrance with the metal fragment.

To circumvent the stereochemical problem of η^3-γ-lactone, we found that acidification of silylated compounds **18–21** in the presence of H_2O (1 equiv) gave only the *syn* diastereomers of **22–25** even for bulky Me_2CH; the yields were excellent

† National Tsing Hua University.
‡ National Taiwan University.

(1) (a) Heck, R. F.; Wu, G.; Tao, W.; Rheingold, A. L. In *Catalysis of Organic Reactions;* Blackburn, D. W., Ed.; Marcel Decker Inc.: New York, 1990; p 169. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Application of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 12, p 619. (c) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, 1994; Chapter 4, p 103.

(2) For representative examples of catalytic cyclocarbonylation, see: (a) Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4107. (b) Semmelhack, M. F.; Brickner, S. J. *J Am. Chem. Soc.* **1981**, *103*, 3945. (c) Matsuda, I.; Ogiso, A.; Sato, S. *J. Am. Chem. Soc.* **1990**, *112*, 6120. (d) Negishi, E. I.; Sawada, H.; Tour, J. M.; Wei, Y. *J. Org. Chem.* **1988**, *53*, 913. (e) Tsuji, Y.; Kondo, T.; Watanabe, Y. *J. Mol. Catal.* **1987**, *40*, 295.

(3) For examples of stoichiometric cyclocarbonylation, see: (a) Schrieber, S. L.; Semmekia, T.; Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *108*, 3128. (b) Billington, D. C.; Pauson, P. L. *Organometallics* **1982**, *1*, 1560. (c) Magnus, P.; Principe, M. J.; Slater, J. *J. Org. Chem.* **1987**, *52*, 1483. (d) Berk, S. C.; Grossman, S. L.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912. (e) Frank-Neuman, M.; Michelotti, E. L.; Simler, R.; Vernier, J. M. *Tetrahedron Lett.* **1992**, *33*, 7361.

(4) For alkoxylcarbonylation of metal η^1-propargyl compounds, see: (a) Charrier, C.; Collin, J.; Merour, J. Y.; Roustan, J. L. *J Organomet. Chem.* **1978**, *162*, 57. (b) Cheng, M.-H.; Ho, Y. H.; Chen, C. H.; Lee, G. H.; Peng, S. M.; Chu, S. Y.; Liu, R. S. *Organometallics* **1994**, *13*, 4082. (c) Tseung, T. W.; Wu, I. Y.; Lin, Y. C.; Cheng, M. C.; Tsai, Y. J.; Chen, M. C.; Wang, Y. *Organometallics* **1991**, *10*, 43.

(5) There was one report regarding intramolecular alkoxylcarbonylation of molybdenum η^1-propargyls to form δ-lactonyl allyls, but no stereochemistry was reported. We first applied the cyclization method of this report to δ and ϵ η^3-lactonyl formation, but we obtained complicated mixtures of organometallic and organic products. See Benaim, J.; Giulieri, F. *J Organomet. Chem.* **1979**, *165*, C 28.

(6) Crystal data for **4**: monoclinic, space group $P2_1/n$, a = 7.6459(12) Å, b = 16.614(3) Å, c = 11.3874(4) Å, β = 90.191(13)°, V = 1446.5(6) Å^3, Z = 4; final R = 0.039 and R_w = 0.037.

(7) Crystal data for **5**: monoclinic, space group, $P2_1/c$, a = 7.9199(13) Å, b = 10.337(3) Å, c = 20.759(4) Å, β = 100.90(3)°, V = 1668.8(8) Å^3, Z = 4; final R = 0.063 and R_w = 0.080.

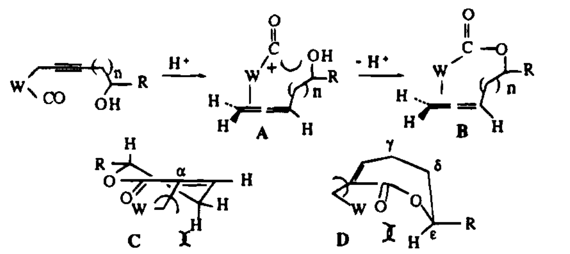
(8) Faller, J. W.; Chen, C. C.; Mattina, M. J.; Jakubowski, A. *J Organomet. Chem.* **1973**, *52*, 361.

(9) Crystal data for **10**: monoclinic, space group, $P2_1/c$, a = 7.780(2) Å, b = 10.761(2) Å, c = 17.042(4) Å, β = 92.87(2)°, V = 1425.1(6) Å, Z = 4; final R = 0.0361 and R_w = 0.0386.

(10) Crystal data for **13**: triclinic, space group, $P\bar{1}$, a = 7.675(2) Å, b = 10.435(3) Å, c = 10.880(3) Å, α = 102.38(2)°, β = 94.45(2)°, γ = 102.88(2)°, V = 821.4(11) Å^3, Z = 2; final R = 0.0367 and R_w = 0.0385.

0002-7863/95/1517-2933$09.00/0

Scheme 3



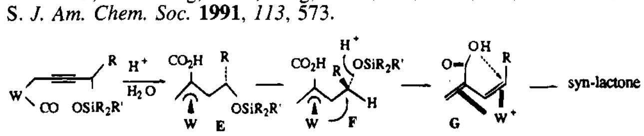
W=CpW(CO)$_2$, n = 1, 2

(>88%). The *syn* configuration of **23** was confirmed by X-ray diffraction study.[11] We performed a reaction involving **18**, CF_3SO_3H, and $H_2{}^{18}O$ (95% purity); the isotopic ^{18}O content of the resulting lactone **5** was ca. 65−70%. This implies that **18−21** reacted first with a proton, then with H_2O to give a 2-carboxylated allyl intermediate that subsequently underwent proton-promoted cleavage of the C−OSi bond to give the syn isomers.[12]

To account for the stereochemical formation of δ- and ϵ-lactones, we propose that the initial step involves intramolecular hydroxyl attack on η^2-W−allene cationic intermediate **A** to form a species represented by **B** (Scheme 3). In accordance with this concept, the two key transition states **C** and **D** determine the stereochemistry of δ- and ϵ-lactones when the conformation is further considered. State **C** has a chairlike conformation with R in a pseudoequatorial position, and the W−CH_2 σ bond parallels the C_α−CO single bond to show the *cis* insertion. A preferable *anti* configuration is generated by rotating the WCH_2−C_α σ bond to bring $CpW(CO)_2$ away from the axial H hydrogen. State **D** represents a twisted boat conformation according to X-ray structures of **10** and **13**; this form is the most stable conformation because the $C\gamma$−C_δ and C_δ−C_ϵ units are staggered to each other and the R substituent is in the less hindered equatorial position. Rotation of the WC−C_α σ bond to form a π-allyl complex preferably proceeds in a way such that $CpW(CO)_2$ turns away from the proximal axial C_ϵH hydrogen to give the *syn* isomer.

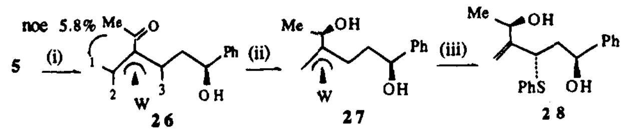
(11) Crystal data for **23** (*syn* isomer): triclinic, space group, $P\bar{1}$, a = 7.9642(17) Å, b = 8.6516(22) Å, c = 12.207(3) Å, α = 70.023(21)°, β = 87.345(20)°, γ = 81.480(20)°, V = 781.8(3) Å^3, Z = 2; final R = 0.021 and R_w = 0.023.

(12) We propose that the *syn* formation of **22−25** first involves an allyl intermediate **E**. The most stable configuration of **E** has its most bulky group $OSiMe_2(t\text{-}Bu)$ and allyl carbons arranged in a zigzag conformation with the medium-size R opposite the metal, as represented by **E**. Further ionization of **E** in an intramolecular S_N2 mechanism generates *cis*-η^4-*s-trans*-diene **G**. Intramolecular CO_2H attack on the =CR carbon of **G** is expected to give the *syn*-lactone. For the chemistry related to the ionization of **E** to **G**, see: Vong, W. J.; Peng, S. M.; Lin, S. H.; Lin, W. J.; Liu, R. S. *J. Am. Chem. Soc.* **1991**, *113*, 573.



W=CpW(CO)$_2$, OSiR$_2$R'= OSiMe$_2$(t-Bu)

Scheme 4[a]



[a] W = $CpW(CO)_2$, (i) MeLi (1.2 equiv), −78 °C, (ii) DIBAL-H (2.2 equiv), (iii) $NOBF_4$ (1.1 equiv, CH_3CN, 2 h, −40 °C), PhSNa (1.5 equiv; −40 °C), $(NH_4)_2Ce(NO_3)_6$ (1.5 equiv).

The η^3-lactones can be also applied to synthesis of acyclic diols, as depicted in Scheme 4. Addition of MeLi to **5** led to ring opening to give **26** (88%). The methyl group of **26** is on the same side as the allyl CH_2 fragment according to proton NOE spectra. With $CpW(CO)_2$ as a stereotemplate, reduction of **26** with DIBAL-H produced the diol **27** as a single diastereomer (79%). Further treatment of **27** with $NOBF_4$ generated an allyl cation[13] that reacted with PhSNa, and then on Ce(IV) oxidation gave the diol **28** in 44% yield. Here, the stereochemistry of **28** is given on the basis of a well-established *trans* attack of PhS^- at the allyl CH^3 carbon.[14]

In summary, we have elucidated the stereochemistry in a tungsten-promoted alkoxycarbonylation cyclization. Application of the resulting lactones to synthesis of complex oxygenated compounds is in progress.

Acknowledgment. We thank the National Science Council, R.O.C., for financial support of this work.

Supplementary Material Available: Listing of sample preparation and characterization of all new compounds; tables of crystal data, structural parameters, and ORTEP drawings of **4**, **5**, **10**, **13**, and **23** (41 pages); listing of observed and calculated structure factors for **4**, **5**, **10**, **13** and **23** (48 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA943699F

(13) (a) Adams, R. D.; Chodosh, D. F.; Faller, J. W.; Rosan, A. M. *J. Am. Chem. Soc.* **1979**, *101*, 2570. (b) Cosford, N. D. P.; Liebeskind, L. S. *Organometallics* **1994**, *13*, 1498.

(14) Faller, J. W.; Chao, K. H. *J. Am. Chem. Soc.* **1983**, *105*, 3893. (d) Pearson A. J.; Mallik, S.; Pinkerton, A.; Adams, J. P.; Zheng, S. *J. Org. Chem.* **1992**, *57*, 2910.