Synthesis of Bicyclic Pyrane Derivatives via Tungsten-Mediated [3 + 3] Cycloaddition of Epoxides with Tethered Alkynes

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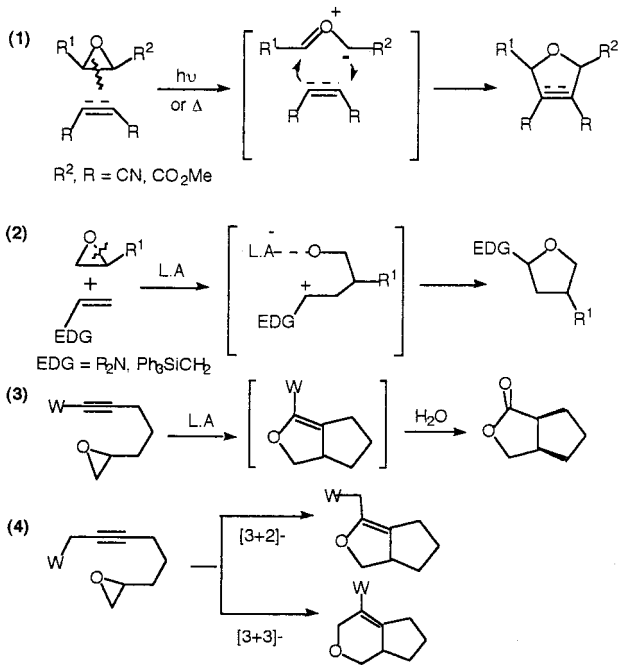
Received July 11, 2001

Propargyltungsten compounds bearing a tethered epoxide were prepared in short steps from readily available materials. In the presence of various Lewis acids, $BF_3{\cdot}Et_2O$ catalysts (25 mol %) most effectively promote the [3 + 3] cycloaddition of the epoxide with its tethered propargyltungsten group, delivering bicyclic pyranyltungsten compounds in reasonable yields. This cyclization proceeds highly diastereoselectively with tolerance of various functional groups. The stereochemical outcome indicates that the cycloaddition is initiated by the ring opening of the epoxides via an exo-attack of the propargyltungsten group. The resulting pyranyltungsten organometallics were demetalated to yield various bicyclic pyranyl derivatives using different oxidants. This new method provides a short enantiospecific synthesis of bicyclic oxygen compounds if chiral epoxide is used in the cyclization. A mechanistic model is presented to rationalize the reaction pathway of this [3 + 3] cycloaddition.

Introduction

The cycloaddition of an epoxide with alkynes and alkenes is a direct and efficient method for the synthesis of oxacyclic compounds.[1,2] Two types of cycloadditions have been reported as shown in Scheme 1. Equation 1 shows [3 + 2] cycloaddition of an epoxide with an electron-deficient alkyne or alkene via cleavage of the C−C bond of the epoxide;[3] this pathway involves a zwitterionic intermediate produced on thermal or photolytic activation.[3] An alternative route entails use of a Lewis acid to effect cycloaddition of an epoxide with an electron-rich alkene;[4] this pathway involves cleavage of the C−O bond of the epoxide to generate the ionic intermediate **B** that leads to a furan framework via a counterattack of its oxygen terminus at the carbonium center. Examples of this cycloaddition are very few and only limited to alkenes of special types.[4] The treatment of epoxides with a mixture of activated alkenes and Lewis acid normally produced addition products.[5,6] The [3 + 2] cycloaddition of epoxide or aziridine with an activated alkyne remained unknown before our study on alkynyl-

Scheme 1



† National Tsing-Hua University.

‡ Yuanpei Institute of Science and Technology.

(1) (a) Gothelf, K. V.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 863. (b) Tufariello, J. J. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A.; Ed.; John Wiley & Sons: Chichester, 1984; Vol. 2, p 83.

(2) (a) Carruthers, W. *Cycloaddition in Organic Synthesis*; Pergamon: Oxford, 1990. (b) Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741. (c) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 497.

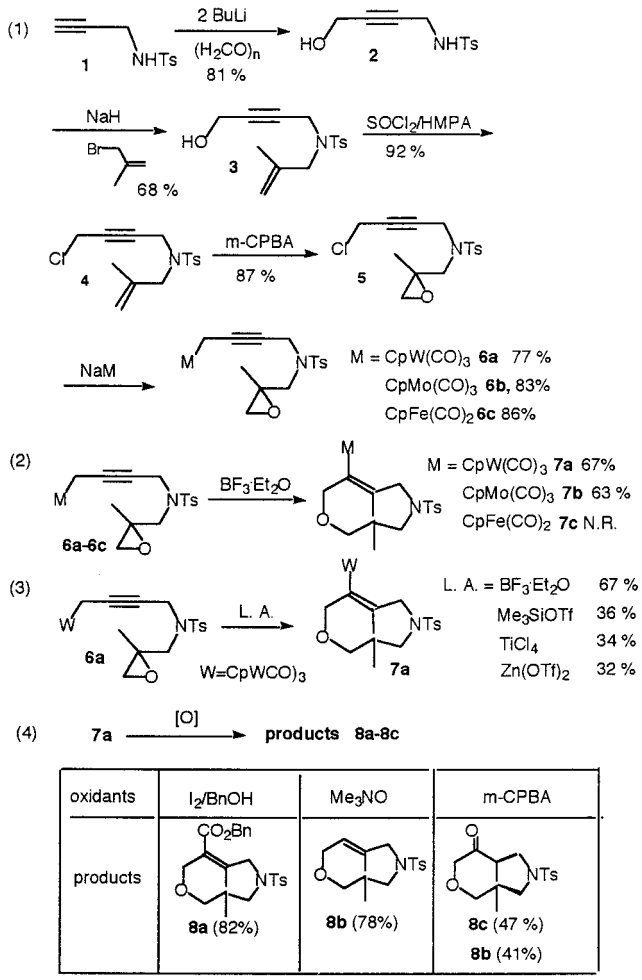
(3) Examples for cycloaddition of epoxide or aziridine with olefin and alkyne ivolving cleavage of the C−C bond: (a) Sisko, J.; Weinreb, S. M. *J. Org. Chem.* **1991**, *56*, 3211. (b) Takano, S.; Iwabuchi, Y.; Ogasawara, K. *J. Am. Chem. Soc.* **1987**, *109*, 5523. (c) DeShong, P.; Kell, D. A.; Sidler, D. R. *J. Org. Chem.* **1985**, *50*, 2309. (d) Metra, P.; Hemelin, J. *J. Chem. Soc., Chem. Commun.* **1980**, 1038. (e) Gaebert, C.; Siegner, C.; Mattay J.; Toubartz, M.; Steenken, S. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2735. (f) Domingo, L. R. *J. Org. Chem.* **1999**, *64*, 3922. (g) Chou, W.-N.; White, J. B. *Tetrahedron Lett.* **1991**, 32, 7637. (h) Gaebert, C.; Mattaay, J. *Tetrahedron* **1997**, *53*, 14297. (i) Palomino, E.; Schaap, A. P.; Heeg, M. J. *Tetrahedron Lett.* **1989**, *30*, 6801.

(4) Cycloaddition of aziridine or epoxide with alkene with cleavage of the C−X bond, see: (a) Bergmeier, S. C.; Fundy, S. L.; Seth, P. P. *Tetrahedron* **1999**, *55*, 8025. (b) Schneider, M. R.; Mann, A.; Taddei, M. *Tetrahedron Lett.* **1996**, *37*, 8493. (c) Sugita, Y.; Kimura, Y.; Yokoe, I. *Tetrahedron Lett.* **1999**, *40*, 5877. (d) Sugita, Y.; Kimura, Y.; Yokoe, I. *Tetrahedron Lett.* **1999**, *40*, 5877. (e) Nakagawa, M.; Kawahara, M. *Org. Lett.* **2000**, *2*, 953.

(5) For review paper, see: (a) Tanner, D. *Angew Chem., Int. Ed. Engl.* **1994**, *33*, 599. (b) Yamamoto, Y.; Asao N. *Chem. Rev.* **2000**, *100*, 2207.

10.1021/jo010698e CCC: $20.00
Published on Web 11/02/2001

Scheme 2



tungsten compounds with the protocol shown in eq 3.[7] This cycloaddition is synthetically useful because it provides a one-pot synthesis of bicyclic lactones via a tungsten enol ether. In the present work, we extend our investigation to propargyltungsten complexes comprising a tethered epoxide. Treatment of these tungsten compounds with Lewis acid leads to [3 + 3] cycloaddition rather than to an expected [3 + 2] pathway as known for special allylsilane derivatives.[4a−d] Most propargyl and allylmetal complexes undergo addition reactions with epoxides in the presence of a Lewis acid.[5,6] We report here the full scope of this cycloaddition.[8]

Results and Discussion

We focus our attention on intramolecular cyclization. Scheme 2 shows an instance for the synthesis of an organic substrate **5** comprising a tethered epoxide. It was conveniently prepared from propargylamino tosylate **1** according to conventional methods; the overall yield of **5** was 45%. Transition-metal carbonyl anions of iron, molybdenum, and tungsten $CpM(CO)_n^-$ (M = Fe, n = 2; M = Mo, W, n = 3) fail to react with epoxide in the absence of Lewis acids. Treatment of this epoxide with these metal anions NaM (M = $CpFe(CO)_2$, $CpMo(CO)_3$, $CpW(CO)_3$) in THF afforded the corresponding propargyltungsten compounds in 77−87% yields. For these three propargylmetal complexes, $BF_3{\cdot}Et_2O$ (25 mol %) effected the cyclization of tungsten and molybdenum complexes **6a** and **6b** in cold CH_2Cl_2 (−40 °C, 6−8 h) to afford the products **7a** and **7b** in 67% and 63% yields, respectively. This reaction failed with the iron species **6c** which was recovered in 66% yield. The failure of iron complex **6c** in cyclization is attributed to its lower reactivity with electrophiles.[9] Bicyclic pyranyl structures were assignable to compounds **7a** and **7b** on the basis of their ^{1}H and ^{13}C NMR spectral data. The ^{13}C NMR of the three W−CO groups of **7a** appeared at δ 228.3 and 221.1 ppm at −45 °C and became broad at 23 °C. The metal fragment of **7a** and **7b** underwent a 1,2-shift to become a vinyltungsten group. We investigate this cycloaddition with other Lewis acids including Me_3SiOTf, $TiCl_4$, and $Zn(OTf)_2$, which were found less reactive as compared to $BF_3{\cdot}Et_2O$. Compound **7a** can produce various bicyclic pyranyl derivatives upon demetalation with various oxidants; a protocol is shown in eq 4. Treatment of this pyranyltungsten complex **7a** with I_2 (1.2 equiv) and BnOH (2.0 equiv) in cold CH_2Cl_2 (−78 °C, 8 h) resulted in carbonylation[10] to afford bicyclic benzyl ester **8a** in 82% yield. Hydrodemetalation[11] of **7a** with Me_3NO (3.0 equiv) in CH_3CN (23 °C, 5 h) gave the protonated product **8b** in 65% yield. Oxidation of **7c** with *m*-chloroperbenzoic acid (*m*-CPBA) in CH_2Cl_2 (23 °C, 8 h) afforded the bicyclic ketone compound **8c** in 47% yield together with the protonated compound **8b** (41%). The cis configuration of the lactone **8c** was determined by ^{1}H−NOE spectra.

We also extended this cyclization on various propargyltungsten compounds containing an epoxide. Compounds **9**−**17** were formed from $NaCpW(CO)_3$ and the corresponding chloropropargyl derivatives; preparation of the latter compounds is described in the Supporting Information. The cyclization followed that of the related alkynyltungsten compound **6a** as described before. In a typical reaction, the alkynyltungsten complex was treated with $BF_3{\cdot}Et_2O$ catalyst (25 mol %) in cold CH_2Cl_2 (−40 °C, 4−10 h) and quenched with a saturated $NaHCO_3$ solution at the end of the reaction. Entries a and b (Table 1) present two instances of formation of pyranyltungsten compounds **18** and **19** fused with a five-membered carbo- and azacyclic ring, respectively. The yields of **18** and **19** were 51% and 61%, respectively. I_2-promoted oxidative carbonylation of **18** and **19** afforded the esters **27** and **28** in 91% and 90% yield, respectively. Entries c−e show [3 + 3] cycloaddition of a tethered cis epoxide comprised in compounds **11**−**13**; bicyclic pyranyl products **20**−**22** were obtained as one diastereomer in good yields (69−72%), with a trans configuration assigned on the basis of their ^{1}H NMR−NOE spectra.[12] This information indicated that a propargyltungsten group effects ring

(6) See the examples: (a) Dubiois, S.; Mehta, A.; Toureet, E.; Dodd, R. H. *J. Org. Chem.* **1994**, *59*, 434. (b) Sato, K.; Kozikowski, A. P. *Tetrahedron Lett.* **1989**, *30*, 4073. (c) Bennani, Y. L.; Zhu, G. D.; Freeman, J. C. *Synlett* **1998**, 754. (d) Marson, C. M.; McGregor, J.; Khan, A. *J. Org. Chem.* **1998**, *63*, 7833.

(7) Madhushaw, R. J.; Li, C.-L.; Shen, K.-H.; Hu, C.-C.; Liu, R.-S. *J. Am. Chem. Soc.* **2001**, *123*, 7427.

(8) Part of this paper has appeared in an earlier communication, see ref 7.

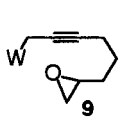
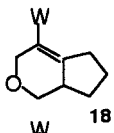
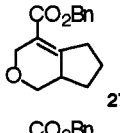
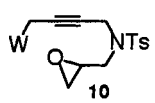
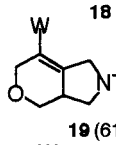
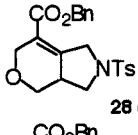
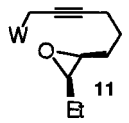
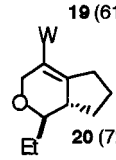
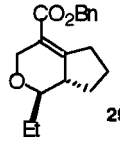
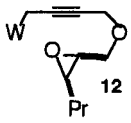
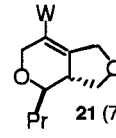
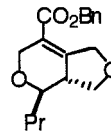
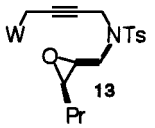
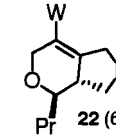
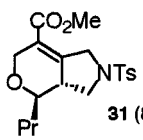
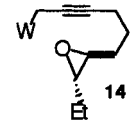
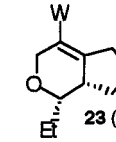
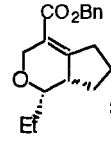
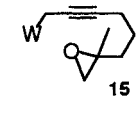
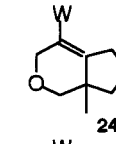
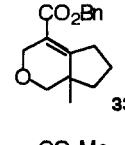
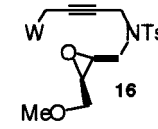
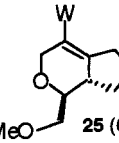
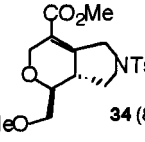
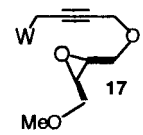
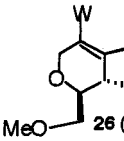
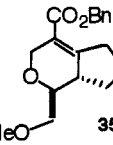
(9) Gilbert, T. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 3502.

(10) Shieh, S.-J.; Tang, T.-C.; Lee, J.-S.; Lee, G.-H.; Peng, S.-M.; Liu, R.-S. *J. Org. Chem.* **1996**, *61*, 3245.

(11) Li, W.-T.; Pan, M.-H.; Wu, Y.-R.; Wang, S.-L.; Liao, F.-L.; Liu, R.-S. *J. Org. Chem.* **2000**, *65*, 3761.

(12) The ^{1}H NMR NOE maps of bicyclic pyranyl compounds **8c**, **21**, and **23** were provided in Supporting Information.

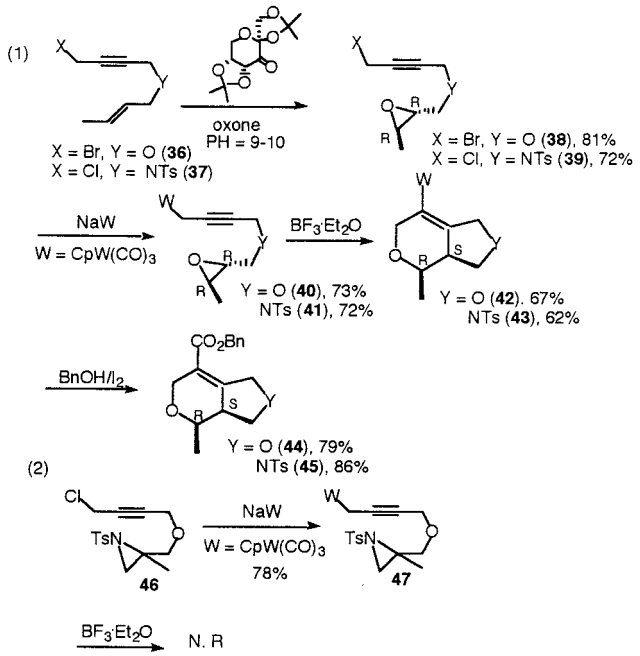
Table 1. [3 + 3] Cycloaddition Reactions and Demetalations (W = CpW(CO)$_3$)

alkynes	products[a,b]	demetal.[c]
(a)  **9**	 **18** (51%)	 **27** (91%)
(b)  **10**	 **19** (61%)	 **28** (90%)
(c)  **11**	 **20** (72%)	 **29** (85%)
(d)  **12**	 **21** (72%)	 **30** (92%)
(e)  **13**	 **22** (69%)	 **31** (81%)
(f)  **14**	 **23** (67%)	 **32** (85%)
(g)  **15**	 **24** (74%)	 **33** (90%)
(h)  **16**	 **25** (68%)	 **34** (82%)
(i)  **17**	 **26** (62%)	 **35** (87%)

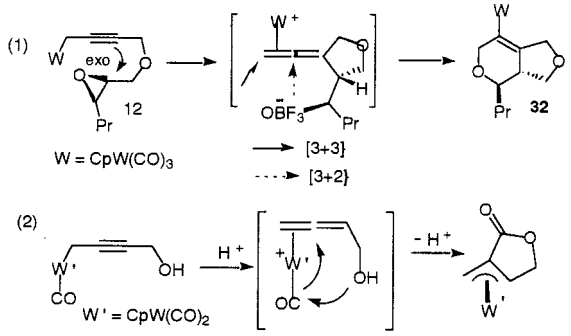
[a] $BF_3{\cdot}Et_2O$ (25 mol %), CH_2Cl_2 (−40 °C). [b] Yields were reported after purification from silica TLC plate. [c] BnOH (2.0 equiv), I_2 (1.1 equiv), CH_2Cl_2 −40 °C.

opening of epoxide via an intramolecular S_N2 attack. Demetalation of these organometallics by I_2/$PhCH_2OH$ in cold CH_2Cl_2 gave the bicyclic esters **29**−**31** in 81−92% yields. In the case of a trans epoxide as in compound **14** (entry f), the BF_3-promoted cyclization afforded a 67% yield of the product **23** that has a cis-substituted configuration according to the ^{1}H−NOE effect. Entry g show an additional example for cyclization of a tethered ternary epoxide **15**, giving the corresponding pyranyltungsten complex **24** in 74% yield. This cycloaddition also works for cis-functionalized epoxides such as compounds **16** and **17** which gave trans-pyranyl products **25** and **26** in 68% and 62% yields, respectively. Pyranyltungsten

Scheme 3



Scheme 4



complexes **23**−**26** were converted smoothly to the corresponding bicyclic benzyl esters **32**−**35** in 82−90% yields. This new method provides a short synthesis of chiral bicyclic pyranyl derivatives. We prepared the chiral epoxides **38** and **39** (Scheme 3) via fructose-based catalytic asymmetric epoxidation of the chloropropargyl alkenes **36** and **37**, developed by Shi et al.[13] The ee values of **38** and **39** were 91% and 93%, respectively, on the basis of HPLC analysis. Cyclization of chiral propargyltungsten epoxides **40** and **41** using the $BF_3{\cdot}Et_2O$ catalyst (25 mol %) in cold CH_2Cl_2 afforded the chiral pyranyltungsten compounds **42** and **43** in 67% and 62% yields, respectively, further leading to the chiral bicyclic esters **44** (79%) and **45** (82%) after I_2-promoted oxidation. The cis configurations of **42** and **43** were confirmed by ^{1}H−NOE spectra. HPLC analyses showed the 90% and 93% ee values for compounds **44** and **45**, respectively. These values were consistent with those of the starting chiral epoxides **38** and **39**. No cycloaddition occurred for a tethered aziridine such as **47**. Treatment of this complex with $BF_3{\cdot}Et_2O$ (25 mol %) in cold diethyl ether failed to yield cycloadducts; instead, the starting aziridine was recovered in 67% yield. Scheme 4 (eq 1) provides a mechanistic model to rationalize a preference for [3 + 3]

(13) Wang, Z.-X.; Yong, T.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224.

cycloaddition rather than an expected [3 + 2] cycloaddition. Special allyl silanes (Scheme 1, eq 2) underwent cyclization with its tethered epoxide to afford the [3 + 2] cycloadduct.[4a−c] In the presence of $BF_3{\cdot}Et_2O$, the propargyltungsten group of compound **12** undergoes an exo-attack at the epoxide to induce ring opening, forming an η^2-tungsten allene cationic intermediate[14] in which the $CpW(CO)_3$ fragment lies opposite to the BF_3O^- terminus. The BF_3O^- terminus of this intermediate attacks the remoted allene carbon rather than the central carbon, in contrast to the case of free allenes comprising a similar alcohol.[15] The central carbon of an η^2-tungsten allene cation is generally more reactive than the terminal carbon, as for the example in cyclocarbonylation (Scheme 4, eq 2). The exact nature of this atypical behavior is unclear at this stage; we propose that it may be due to the coordination of $CpW(CO)_3$ to the external $=C=$C group to make coordination at the carbon nearly tetrahedral. Such an effect disfavors a [3 + 2] cycloaddition pathway corresponding to 5-endo-trig ring closure. In the case of cyclocarbonylation, insertion at the central allene carbon reflects the cis orientation of the tungsten fragment relative to its tethered hydroxy group. Since the ring opening of the epoxide proceeds via an inversion of stereochemistry at the epoxide carbon, the cis epoxide **12** is expected to give the product **32** having a trans configuration.

In summary, we reported a BF_3-catalyzed intramolecular [3 + 3] cycloaddition of propargyltungsten complexes and epoxide. This cycloaddition proceeds with high diastereoselectivity to afford, in reasonable yields, bicyclic pyranyltungsten complexes which can be demetalated to various bicyclic pyranes with diverse oxidants. This new method provides a short enantiospecific synthesis of bicyclic pyrane derivatives.[16] A mechanistic model is presented to rationalize this cycloaddition via altering the coordination of carbon in the allene group.

Experimental Section

Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere in oven-dried glassware using a standard syringe, cannula, and septa apparatus. Benzene, diethyl ether, tetrahydrofuran, and hexane were dried with sodium benzophenone and distilled before use. Dichloromethane was dried over CaH_2 and distilled before use. $W(CO)_6$, $BF_3{\cdot}Et_2O$, dicyclopentadiene, propargyl bromide, benzyl alcohol, I_2, and sodium were obtained commercially and used without purification. Mass data of tungsten compounds were reported according to ^{184}W. $NaCpW(CO)_3$ was prepared by reduction of $[CpW(CO)_3]_2$ with Na/Hg in THF.[17] Spectral data of compounds **6b** and **6c**, **9**−**35**, **37**, **39**, **41**, **43**, **45**−**47** in repetitive experiments are provided in the Supporting Information.

(1) Synthesis of *N*-(4-Hydroxy-but-2-ynyl)-4-methylbenzenesulfonamide (2). To a THF solution (80 mL) of propargylamino tosylate (4.0 g, 19.2 mmol) was added BuLi (16.9 mL, 2.5 M in THF) at −78 °C, and the solution was stirred for 4 h before addition of paraformaldehyde powder (0.69 g, 23.0 mmol). The solution was stirred for 2 h at −78 °C and slowly warmed to 23 °C in a period of 6 h. To this solution was added a saturated NH_4Cl solution (20 mL), and the solution was concentrated to ca. 20 mL. The organic layer was extracted with diethyl ether, concentrated in vacuo, and eluted through a short silica column (diethyl ether/hexane = 1/1) to afford **2** as a colorless solid (3.70 g, 15.6 mmol, 81%). IR (Nujol, cm^{-1}): ν(OH) 3380 (vs, br), ν(C≡C) 2177 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, d, J = 8.0 Hz), 5.78 (1H, br), 4.00 (2H, s), 3.72 (2H, s), 2.36 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 136.2, 129.6, 127.3, 82.8, 78.8, 50.3, 32.9, 21.4. HRMS calcd for $C_{11}H_{14}O_3S$, 226.0663; found, 226.0623.

(2) Synthesis of *N*-(4-Hydroxy-but-2-ynyl)-4-methyl-*N*-(2-methylallyl)-benzenesulfonamide (3). To a THF solution of NaH (0.24 g, 10.1 mmol) was added a THF solution of compound **2** (2.00 g, 8.47 mmol), and the solution was stirred for 4 h before addition of a THF solution of 3-bromo-2-methylpropene (1.21 g, 9.00 mmol). The mixtures were refluxed for 8 h, cooled at 23 °C, and quenched with a NH_4Cl solution (3.0 mL). The solution was concentrated and added with water and diethyl ether. The ether extract was concentrated and eluted through a silica column (diethyl ether/hexane) to afford compound **3** as yellow oil (1.67 g, 5.76 mmol, 68%). IR (Nujol, cm^{-1}): ν(OH) 3380 (vs, br), ν(C≡C) 2177 (m), ν(C=C) 1657 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (2H, d, J = 8.8 Hz), 7.29 (2H, d, J = 8.4 Hz), 4.98 (1H, s), 4.90 (1H, s), 4.03 (2H, t, J = 1.6 Hz), 3.92 (2H, t, J = 1.6 Hz), 3.70 (3H, s), 2.41 (3H, s), 1.74 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 139.1, 136.0, 129.3, 127.8, 115.4, 83.7, 78.2, 52.5, 50.5, 35.7, 21.4, 19.6. HRMS calcd for $C_{15}H_{19}NO_3S$, 293.1085; found, 293.1083.

(3) Synthesis of *N*-(4-Chloro-but-2-ynyl)-4-methyl-*N*-(2-methylallyl)-benzenesulfonamide (4). To a diethyl ether solution (15 mL) of compound **3** (1.20 g, 4.13 mmol) was added HMPA (0.68 mmol, 3.93 mmol), and the mixture was cooled at 0 °C and added with $SOCl_2$ (0.36 mL, 4.96 mmol). The solution was stirred for an additional 5 h and quenched with a saturated $NaHCO_3$ solution. The organic layer was extracted with diethyl ether, concentrated, and eluted through a silica column to afford compound **4** as yellow oil (1.17 g, 3.80 mmol, 92%). IR (Nujol, cm^{-1}): ν(OH) 3380 (vs, br), ν(C≡C) 2167 (m), ν(C=C) 1654 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, J = 8.0 Hz), 7.28 (2H, d, J = 8.0 Hz), 4.93 (1H, s), 4.87 (1H, s), 4.04 (2H, t, J = 1.6 Hz), 3.78 (2H, t, J = 1.6 Hz), 3.67 (2H, s), 2.43 (3H, s), 1.76 (3H, s).^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 139.0, 135.8, 129.4 (CH), 127.7, 115.5, 80.2, 79.2, 52.6, 35.6, 29.7, 21.4, 19.5. HRMS calcd for $C_{15}H_{18}ClNO_2S$, 311.0746; found, 311.0748.

(4) Synthesis of *N*-(4-Chloro-but-2-ynyl)-4-methyl-*N*-(2-methy-oxiranylmethyl)-benzenesulfonamide (5). To a CH_2Cl_2 solution (10 mL) of compound **4** was added *m*-CPBA (0.78 g, 2.10 mmol) at 23 °C, and the mixtures were stirred for 5 h. The solution was concentrated, and the remaining white residues were chromatographed through a short basic alumina column (diethyl ether/hexane = 1/1) to yield the epoxide **5** (0.92 g, 2.82 mmol, 87%). IR (neat, cm^{-1}): ν(C≡C) 2167 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, J = 8.0 Hz), 7.29 (2H, d, J = 8.0 Hz), 4.23 (2H, s), 3.77 (2H, t, J = 1.2 Hz), 3.26 (2H, ABq, J = 14.4 Hz), 2.68 (1H, d, J = 4.4 Hz), 2.61 (1H, d, J = 4.4 Hz), 2.38 (3H, s), 1.36 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 135.7, 129.5, 127.6, 80.3, 79.2, 55.5, 51.3, 51.0, 37.9, 29.7, 21.4, 18.7. HRMS calcd for $C_{15}H_{18}ClNO_3S$, 327.0695; found, 327.0692.

(5) Synthesis of Propargyltungsten Compound 6a. To a THF solution (10 mL) of Na/Hg (10.0 g, 3 wt %) was added $[CpW(CO)_3]_2$ (0.86 g, 1.29 mmol), and the mixtures were stirred for 8 h to yield a light yellow color. This solution was transferred to another flask containing compound **5** (0.60 g, 1.85 mmol), and the mixture was stirred for 6 h to yield a dark yellow solution. The solution was concentrated and chromatographed through a short basic alumina column to yield compound **6a** (0.84 g, 1.35 mmol, 73%). IR (neat, cm^{-1}): ν(CO) 2001 (s), 1903 (s), ν(C≡C) 2167 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (2H, d, J = 8.4 Hz), 7.27 (2H, d, J = 8.4 Hz), 5.33 (5H, s), 4.23 (2H, d, J = 2.2 Hz), 3.32 (2H, ABq, J = 14.4 Hz), 2.65 (1H, ABq, J = 4.8 Hz), 2.38 (1H, d, J = 4.8 Hz), 1.65 (2H, t, J = 2.2 Hz), 1.35 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 228.3, 216.5, 216.4, 143.2, 136.3, 129.4, 127.6, 95.4, 92.3, 71.5,

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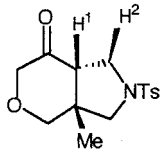
55.5, 51.4, 50.6, 38.5, 21.4, 18.4, −33.3. IR (neat, cm^{-1}): 1719 (s). MS (EI, 75 eV) *m/e* (relative intensities, %): 613 (M^+, 11), 585 (96), 557 (92), 529 (44). Anal. Calcd for $WC_{23}H_{24}NO_6S$: C, 44.08; H, 3.86; N, 2.24. Found: C, 43.78; H, 3.77; N, 2.20.

(6) Cyclization of Propargyltungsten Compound 6a. To a CH_2Cl_2 solution (10 mL) of compound **6a** (0.30 g, 0.48 mmol) was added $BF_3{\cdot}Et_2O$ (0.12 mmol) at −40 °C, and the solution was slowly warmed to 23 °C in a period of 6 h. To this dark yellow suspension was added a saturated $NaHCO_3$ solution, and the organic layer was extracted with diethyl ether, dried over $MgSO_4$, concentrated, and chromatographed through a silica column to afford compound **6a** as a yellow solid **7a** (201 mg, 0.33 mmol, 67%). IR (neat, cm^{-1}): υ(CO) 2001 (s), 1903 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, J = 8.4 Hz), 7.27 (2H, d, J = 8.4 Hz), 5.46 (5H, s), 3.94 (2H, ABq, J = 15.4 Hz), 3.78 (1H, d, J = 14.4 Hz), 3.69 (1H, d, J = 10.4 Hz), 3.49 (1H, d, J = 14.4 Hz), 3.26 (1H, d, J = 8.8 Hz), 3.09 (1H, d, J = 10.4 Hz), 2.56 (1H, d, J = 8.8 Hz), 2.38 (3H, s), 1.08 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1, 143.3, 133.1, 129.6, 127.5, 115.0, 91.2, 77.8, 72.0, 57.2, 54.5, 44.3, 22.4, 21.4. MS (EI, 75 eV) *m/e* (relative intensities, %): 613 (M^+, 13), 585 (86), 557 (92), 529 (26). Anal. Calcd for $WC_{23}H_{25}NO_6S$: C, 44.08; H, 3.86; N, 2.24. Found: C, 43.97; H, 3.97; N, 2.30.

(7) Synthesis of 3a-Methyl-2-(toluene-4-sulfonyl)-1,2,3, 3a,4,6-hexahydropyrano[3,4-c]pyrrole-7-carboxylic Acid Benzyl Ester (8a). To a CH_2Cl_2 solution (2.0 mL) of compound **7a** (0.154 g, 0.24 mmol) was added benzyl alcohol (0.48 mmol) and I_2 (94 mg, 0.38 mmol) at −78 °C, and the mixture was stirred for 30 min and slowly warmed to 23 °C. To this solution was added water (3.5 mL) containing $Na_2S_2O_3$ (50 mg), and the mixture was extracted with CH_2Cl_2, dried over $MgSO_4$, and chromatographed on a small silica column to afford the ester **8a** (88 mg, 0.20 mmol, 82%). IR (neat, cm^{-1}): υ(CO) 1714 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (2H, d, J = 4.0 Hz), 7.29−7.42 (5H, m), 7.29 (2H, d, J = 4.0 Hz), 5.15 (2H, ABq, J = 6.0 Hz), 4.36 (2H, ABq, J = 7.2 Hz), 4.14 (2H, ABq, J = 4.0 Hz), 3.77 (1H, d, J = 10.0 Hz), 3.43 (1H, d, J = 8.8 Hz), 3.07 (1H, d, J = 10.0 Hz), 2.54 (1H, d, J = 8.8 Hz), 2.44 (3H, s), 1.27 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 153.3, 143.7, 135.5, 133.0, 129.8, 128.7, 128.5, 128.4, 127.7, 120.1, 70.7, 66.4, 64.0, 55.8, 51.1, 42.3, 23.1, 21. HRMS calcd for $C_{24}H_{27}NO_5S$, 427.1453; found, 427.1455.

(8) Synthesis of 3a-Methyl-2-(toluene-4-sulfonyl)-1,2,3, 3a,4,6-hexahydropyrano[3,4-c]-pyrrole (8b). To a CH_3CN solution (5 mL) of compound **7a** (200 mg, 0.32 mmol) was added trimethylamine oxide (97 mg, 1.28 mmol) at 0 °C, and the mixtures were stirred for 12 h. To this solution was added water (3 mL), and the CH_2Cl_2 layer was separated, dried over $MgSO_4$, concentrated, and eluted through a silica column to afford compound **8b** as a colorless solid (73 mg, 0.24 mmol, 78%). IR (neat, cm^{-1}): υ(CO) 1704 (s), 1672 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 5.40 (1H, s), 4.11 (1H, m), 4.00 (2H, m), 3.72−3.95 (2H, m), 3.31 (1H, d, J = 9.2 Hz), 3.09 (1H, d, J = 10.4 Hz), 2.73 (1H, d, J = 9.2 Hz), 2.42 (3H, s), 1.06 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 134.7, 133.9, 129.6, 127.5, 118.4, 67.2, 65.4, 55.6, 51.3, 43.7, 23.2, 21.4. HRMS calcd for $C_{15}H_{19}NO_3S$, 293.1085; found, 293.1083.

(9) Synthesis of 3a-Methyl-2-(toluene-4-sulfonyl)-1,2,3, 3a,4,6-hexahydropyrano[3,4-c]-pyrrol-7-one (8c). To a CH_2Cl_2 solution (5.0 mL) of compound **7a** (6 mg, 0.090 mmol) was added *m*-CPBA (71 mg, 0.19 mmol) at −78 °C, and the solution was warmed to 23 °C for 12 h. The solution was filtered over a short basic alumina bed, concentrated, and eluted through a silica column to afford compounds **8b** and **8c** in 47% and 41% yields, respectively. Spectral data for **8c**, IR (neat, cm^{-1}): υ(CO) 1712 (s), 1683 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 3.90 (2H, ABq, J = 9.6 Hz), 3.73 (1H, dd, J = 10.6, 3.9 Hz), 3.58 (2H, ABq, J = 5.6 Hz), 3.47 (1H, dd, J = 10.6, 8.2 Hz), 3.12 (2H, ABq, J = 9.6 Hz), 2.47 (1H, dd, J = 8.2, 3.9 Hz), 2.47 (1H, dd, J = 10.6, 3.9 Hz), 2.42 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2, 143.5, 134.7, 133.2, 129.4, 127.5, 81.0, 77.1, 53.5, 48.9, 36.3, 31.4, 15.1. HRMS calcd for $C_{15}H_{19}NO_4S$, 309.1034; found, 309.1044.

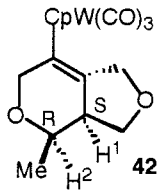


irradiation	increase (%)
H^2 (δ 3.73)	H^1 δ 2.47 (6.2 %)
	Me δ 2.42 (3.0 %)

(10) Synthesis of (2*R*,3*R*)-2-[(4-Bromo-2-butynyl(2*S*,3*R*)-3-methyl-oxiran-2-yl Ether (38). The chiral ketone derived from fructose was prepared according to the method in the literature. A buffer solution (pH 9−10) was prepared from $Na_2B_4O_7{\cdot}10H_2O$ (1.907 g), Na_2EDTA (1 mL, 0.1 M), and water (99 mL). This buffer solution (20 mL) was added with CH_3CN (30 mL), propargyl bromide **36** (0.60 g, 2.96 mmol), chiral fructose-derived ketone (0.46 g, 0.60 mmol), and Bu_4NHSO_4 (0.030 g). To this mixture were added an aqueous K_2CO_3 solution (2.00 g, 13 mL of water) and a Na_2EDTA solution (4×10^{-4} M, 18 mL) of oxone (2.52 g) in a period of 2 h. The mixtures were stirred at 0 °C for an additional 3 h before quenching with pentane (50 mL) and water (30 mL). The organic layer was extracted with pentane, dried over $MgSO_4$, and chromatographed through a Et_3N-pretreated silica column to afford **38** (0.52 g, 2.40 mmol, 81%) as a colorless oil. $[\alpha]_D$ −63.7° (*c* 0.45, $CHCl_3$). IR (Nujol, cm^{-1}): υ(C≡C) 2177 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.23 (2H, m), 3.89 (2H, t, J = 2.0 Hz), 3.68 (1H, dd, J_1 = 11.2, 3.2 Hz), 3.44 (1H, dd, J_1 = 11.2, 5.6 Hz), 2.81−2.89 (2H, m), 1.26 (3H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.4, 81.6, 69.9, 58.5, 57.3, 52.0, 17.1, 14.0. HRMS calcd for $C_8H_{11}BrO_2$, 219.9942; found, 219.9948.

(9) Synthesis of Chiral Propargyltungsten Compound 40. To a THF solution of chiral bromopropargyl epoxide **38** (0.50 g, 2.28 mmol) was added $NaCpW(CO)_3$ (2.30 mmol), and the mixture was stirred for 8 h. The solution was concentrated and eluted through a silica column to afford the chiral propargyltungsten compound **40** as a yellow solid (0.79 g, 1.66 mmol, 73%). $[\alpha]^{25}_D$ −34.2 (*c* 2.5, $CHCl_3$). IR (neat, cm^{-1}): υ(CO) 2001 (s), 1903 (s), 1713 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.42 (5H, s), 4.13 (2H, d, J = 3.0 Hz), 3.68 (1H, dt, J = 11.2, 2.8 Hz), 3.38−3.46 (1H, m), 2.78−2.86 (2H, m), 1.89 (2H, t, J = 3.0 Hz), 1.22 (3H, d, J = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 228.7, 216.5, 96.3, 92.4, 75.3, 69.1, 59.1, 57.4, 51.8, 17.1, −33.1. MS (EI, 75 eV) *m/e* (relative intensities, %): 472 (M^+, 10), 444 (98), 416 (90), 388 (53). Anal. Calcd for $WC_{16}H_{16}O_5$: C, 40.59; H, 3.62. Found: C, 40.77; H, 3.78.

(10) Cyclization of Chiral Propargyltungsten Epoxide 40. Following the preceding procedure, the reaction of $BF_3{\cdot}Et_2O$ (0.16 g, 1.33 mmol) and chiral propargyltungsten epoxide **40** (0.70 g, 1.48 mmol) in CH_2Cl_2 afforded the chiral cycloadduct **42** (0.47 g, 0.99 mmol, 67%). $[\alpha]^{25}_D$ +67.9 (*c* 0.8, $CHCl_3$). IR (neat, cm^{-1}): υ(CO) 2000 (s), 1913 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.54 (5H, s), 3.33 (1H, d, J = 3.6 Hz), 3.96−4.16 (4H, m), 3.15−3.24 (2H, m), 2.59 (1H, dt, J = 12.3, 1.6 Hz), 1.16 (3H, d, J = 2.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 111.9, 91.0, 78.7, 73.7, 72.0, 70.4, 49.8, 20.7. MS (EI, 75 eV) *m/e* (relative intensities, %): 472 (M^+, 10), 444 (91), 416 (88), 388 (66). Anal. Calcd for $WC_{16}H_{16}O_5$: C, 40.62; H, 3.52. Found: C, 40.44; H, 3.77.



42

irradiation	increase (%)
H^1 (δ 2.59)	H^2 δ 3.20 (4.8 %)
	Me δ 1.16 (0 %)

(11) Synthesis of Benzyl(7*R*,7a*S*)-7-methyl-1,3,5,6,7,7a-hexahydro-4-isobenzo-furancarboxylate (44). This compound was prepared similarly from a CH_2Cl_2 solution of I_2 (140 mg, 0.41 mmol), benzyl alcohol (60 mg, 0.55 mmol), and

compound **42** (130 mg, 0.28 mmol). The yield of compound **44** was 79% (61 mg, 0.22 mmol). $[\alpha]^{25}_{D}$ +81.3 (*c* 0.80, $CHCl_3$). IR (neat, cm^{-1}): υ(CO) 1718 (s), υ(C=C) 1621 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.25−7.39 (5H, m), 5.18 (2H, d, J = 1.2 Hz), 4.72 (2H, ABg, J = 2.8 Hz), 4.40 (2H, ABg, J = 8.4 Hz), 4.15 (1H, t, J = 8.0 Hz), 3.18−3.26 (2H, m), 2.63 (1H, bs), 1.28 (3H, d, J = 5.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 154.3, 135.6, 128.6, 128.5, 128.3, 119.0, 71.3, 71.2, 69.1, 66.2, 64.6, 47.3, 20.5. HRMS calcd for $C_{10}H_{18}O_4$, 202.1205; found, 202.1222.

Acknowledgment. The authors wish to thank the National Science Council, Taiwan, for financial support of this work.

Supporting Information Available: Experimental procedures and spectral data of compounds **6b** and **6c**, **9**−**35**, **37**, **39**, **41**, **43**, **45**, **46**, **47** in repetitive experiments; ^1H and ^{13}C NMR of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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