This constitutes the first report of stereoselective formation and ring closure of acyclic selenyl diols to highly substituted tetrahydrofurans. The synthetic potential of the selenium residue[15] retained on the ring should be emphasized. In addition to reductive removal, other synthetic transformations such as oxidative elimination to dihydrofurans and radical coupling processes are areas we are actively pursuing. Previous reports of similar cyclizations involving sulfur species[16] appear more limited in this regard.

Application of our method to a variety of important targets is indicated. The structural motif in **15** has been sought in ionophore synthesis[17] as have 2,5-cis-disubstituted tetrahydrofurans represented by **6**, **7**, and **18**. Further work in this and related areas will be reported in due course.

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Total Synthesis of Glycinoeclepin A

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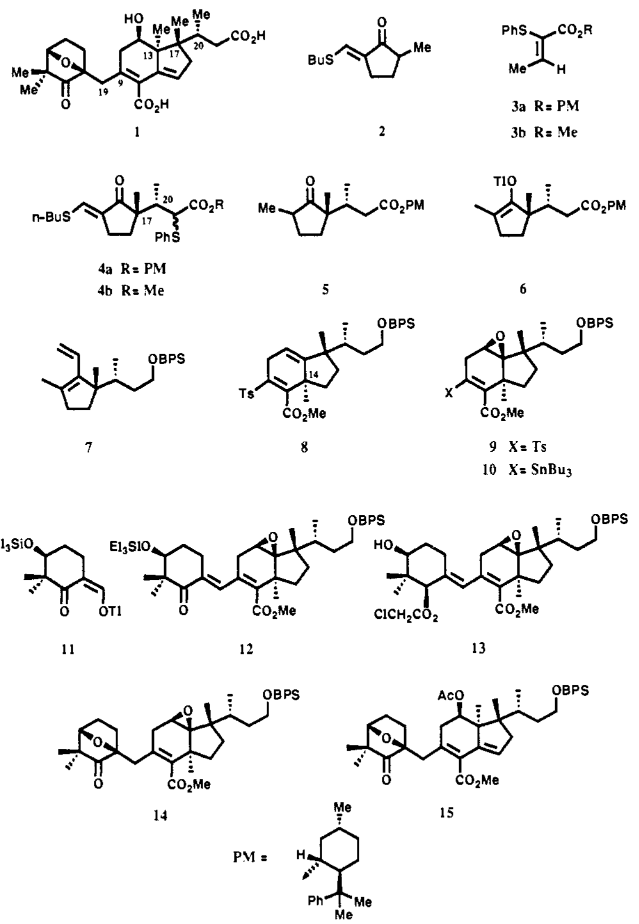
It is remarkable that glycinoeclepin A (**1**),[1] a product of the soybean plant (and various other beans) for which it may be a biochemical regulator, stimulates hatching (at 10^{-12} g/mL) of dormant eggs of the predatory nematode *Heterodera glycines*. In this paper we describe a total synthesis of glycinoeclepin A[2] which is direct and enantiocontrolled, and which depends on a number of unusual steps.

The construction of **1** (steroid numbering), which involved a coupling of mono and bicarbocyclic moieties at the C(9)–C(19) linkage, commenced with the enantioselective establishment of the C(17)–C(20) stereocenters as follows. Cyclopentanone **2**[3] was converted to the potassium enolate ($KN(SiMe_3)_2$ in 5:1 THF–toluene) which was allowed to react at −100 °C for 3 h with the ester (**3a**) of (*Z*)-2-(phenylthio)crotonic acid[4] and (−)-8-phenylmenthol[5,6] (PM) to give as the major product the adduct **4a** with 95:5 enantioselectivity and 5:1 C(17)–C(20) diastereoselectivity (89% total yield).[7] The corresponding reaction of the potassium enolate of **2** with methyl ester **3b** (THF, 15 min at −78 °C) gave (±)-**4b** (82%) with 97:3 C(17)–C(20) diastereoselectivity.[8,9] Chiral adduct **4a** was separated from the minor C(17)–C(20) diastereomer by silica gel chromatography (sgc) with use of 3:1 hexane–ether and converted by Raney nickel in ethanol at 23 °C for 1 h to keto ester **5** (85%) and thence sequentially with $KN(SiMe_3)_2$ and *N*-phenylbistrifluoromethanesulfonamide in THF at −78 °C to enol triflate **6** (oil), $[\alpha]^{26}_D$ +41.3° (*c* = 1.3, $CHCl_3$), which was obtained in pure form (84%) after sgc (13:1 hexane–ether). Vinylation[10] of **6** with vinyltributyltin–LiCl in the presence of 0.07 equiv of $(Ph_3P)_4Pd$ at 65 °C for 12 h afforded the desired diene ester (87%) which was reduced (i-Bu_2AlH, 0 °C, THF)[11] and protected (*tert*-butyldiphenylsilyl chloride (BPSCl)–imidazole–DMF, 25 °C, 15 min) to give diene **7** (oil,

Chart I



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(2) Two syntheses of **1** have been reported previously. (a) Murai, A.; Tanimoto, N.; Sakamoto, N.; Masamune, T. *J. Am. Chem. Soc.* **1988**, *110*, 1985–1986. (b) Mori, K.; Watanabe, H. *Pure Appl. Chem.* **1989**, *61*, 543–546.

(3) Prepared from 2-methylcyclopentanone by the method of: Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615–1629.

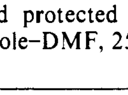
(4) Prepared from methyl 2-bromopropionate by the following sequence: (1) displacement with 1.1 equiv of thiophenol and 1.2 equiv of 1,8-diazabicyclo[5.4.0]undec-7-ene at 23 °C for 20 min to form methyl 2-(phenylthio)propionate (98%); (2) sequential treatment with 1.2 equiv of SO_2Cl_2 in CH_2Cl_2 at −10 °C for 10 min and Al_2O_3 in toluene at 75 °C for 12 h to form methyl (*Z*)-2-(phenylthio)crotonate (60%) (Cf. Trost, B. M.; Salzmann, T. M.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887–4902); and (3) saponification with 3 equiv of LiOH in 2:1 H_2O–dimethoxyethane at 23 °C for 16 h.

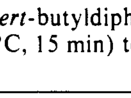
(5) Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 6908–6909. (−)-8-Phenylmenthol was conveniently purified by recrystallization of the chloroacetate ester after synthesis from (*R*)-(+)-pulegone.

(6) Ester **3a** was produced by reaction of (*Z*)-2-(phenylthio)crotonic acid and (−)-8-phenylmenthol with dicyclohexylcarbodiimide and 4-(dimethylamino)pyridine in THF at 26 °C for 6 h.

(7) Because of the additional complication of diastereomers α to the ester carbonyl, analysis was performed after conversion (Ni) to keto ester **5** (gas chromatography) or to **6** (HPLC).

(8) The opposite C(17)–C(20) diastereopreference was observed for the reaction of 1-((triethylsilyl)oxy)-2-methylcyclopentene with *N*-(*E*)-crotonylbenzoxazolidinone and ethylaluminum dichloride at −78 °C in CH_2Cl_2. Stereochemical assignments were made in the 2-methylcyclopentanone series by rigorous chemical correlation with diastereomeric enones *i* and *ii* (cf.: Scanio, C. J. V.; Starrett, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 1539–1540).


i


ii

(9) (a) For precedent and mechanistic rational for the stereoselective formation of adducts **4a** and **4b** see: Corey, E. J.; Peterson, R. T. *Tetrahedron Lett.* **1985**, *26*, 5025–5028. (b) For the use of methyl α-methylthioacrylate as a Michael acceptor, see: Cregge, R. J.; Herrmann, J. L.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2603–2606.

(10) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033–3040.

(11) 8-Phenylmenthol was recovered efficiently after sgc.

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91% over two steps), $[\alpha]^{26}_{D}$ +47.0° (c = 0.7, $CHCl_3$).

The Diels–Alder reaction of diene **7** with 3-(p-toluenesulfonyl)propiolic acid[12] (3 equiv) proceeded with position specificity at 23 °C for 24 h to give an excellent yield (>95%) of adduct **8** and the C(14) diastereomer in a ratio of 3:1. After epoxidation of the mixture (anhydrous CF_3CO_3H in CH_2Cl_2 containing Na_2HPO_4 at −25 °C for 24 h) and sgc with 2:1 hexane–ether the pure epoxide **9** was obtained in 61–65% yield overall from diene **7**.[13] The p-toluenesulfonyl group of **9** was replaced by tributylstannyl by heating with 3 equiv of tri-n-butyltin hydride with a catalytic amount of azoisobutyronitrile as a free radical initiator in toluene at 95 °C for 12 h to give vinylstannane **10** (84%). Coupling of **10** with vinyl triflate **11**[14] was accomplished by heating with 0.07 equiv of $Pd(OAc)_2$ (but not Pd(0) reagents) and 0.14 equiv of PPh_3 in THF at 70 °C for 15 min to provide **12** in 66% yield. Carbonyl reduction ($NaHB(OMe)_3$, −20 °C, THF, 8 h), chloroacetylation (chloroacetic anhydride and pyridine in CH_2Cl_2 at 23 °C for 30 min), and desilylation (1 equiv of Cl_3CCOOH in 10:1 THF–H_2O at 23 °C for 5 h) transformed **12** into hydroxy diene **13** (82% overall). Reaction of **13** with mercuric trifluoroacetate–HgO in CH_3CN at 23 °C for 24 h followed by treatment with Et_4NCl and sgc effected internal oxymercuration to give a single bridged ether chloromercurial (78%) which underwent the required demercuration reaction with Bu_2SnH_2 (but not Bu_3SnH) in toluene at −78 to 0 °C (81%); chloroacetate cleavage with K_2CO_3–methanol at 23 °C for 10 min and oxidation (pyridinium dichromate in DMF at 23 °C for 30 min) provided keto ether **14** (92%, oil), $[\alpha]^{23}_{D}$ =24.5° (c = 0.1, $CHCl_3$). Reaction of **14** in 10:1 Ac_2O–CH_2Cl_2 with 1.1 equiv of anhydrous $FeCl_3$ in Ac_2O at −78 °C for 12 h gave after sgc purification the rearranged acetate **15** (83%, oil), $[\alpha]^{23}_{D}$ −20.5° (c = 1.6, $CHCl_3$).[16] Transformation of **15** to glycinoeclepin was effected by the following sequence: (1) desilylation with HF in CH_3CN buffered with excess pyridine for 45 min at 23 °C, (2) oxidation of primary hydroxyl to formyl with pyridinium chlorochromate–Al_2O_3 in CH_2Cl_2 at 23 °C for 12 h, and (3) oxidation of formyl to carboxyl with sodium chlorite–NaH_2PO_4 in t-BuOH–H_2O at 23 °C for 30 min in the presence of 2-methyl-2-butene (as chlorine scavenger) to give after reaction with CH_2N_2 acetyl glycinoeclepin dimethyl ester (oil, 63% overall), $[\alpha]^{23}_{D}$ −41.1° (c = 0.36, $CHCl_3$). Saponification of acetyl glycinoeclepin mono- or dimethyl ester with 1:1 dimethoxyethane–1 M aqueous lithium hydroxide at 46 °C for 36 h afforded glycinoeclepin A (**1**) (68%). Synthetic **1** was converted to the p-bromophenacyl ester for comparison with an authentic sample.[17] The synthetic and authentic samples were identical by HPLC, MS, IR, 500-MHz ^1H NMR, and optical rotation measurements.

The synthesis reported herein is considerably shorter and simpler than those previously reported and has the potential to provide adequate amounts of **1** for further research. Noteworthy steps in the synthesis include the enantioselective Michael reaction of **2** and **3a** and the conversions **7** → **8**, **8** → **9**, and **14** → **15**. In addition, it should be noted that the coupling reaction, **10** + **11** → **12**, which did not occur with Stille's conditions (Pd(0) reagents), is unusual and probably occurs by replacement of Bu_3Sn in **10** by XPd and a subsequent Heck-type reaction.[18]

Supplementary Material Available: Full spectral data on compounds **1** and **4–15** as well as other synthetic intermediates (13 pages). Ordering information is given on any current masthead page.

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(12) Corey, E. J.; Jardine, P. D. S.; Rohloff, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 3672–3673.

(13) The stereochemistry of the epoxidation reaction was established by chemical studies involving lactonization of the carboxylic acid corresponding to the BPS ether **9** as well as by the successful conversion to **1**.

(14) Vinyl triflate **11** was prepared enantioselectively and in excellent yields from 2,2-dimethylcyclohexane-1,3-dione by the following sequence: (1) reduction with Baker's yeast[2a,b] or reduction at −78 °C in toluene with catechol borane in the presence of a catalytic amount of the oxazaborolidine from (R)-2-(diphenylhydroxymethyl)pyrrolidine and n-butylboronic acid;[15] (2) silylation with triethylsilyl chloride (TESCl)–imidazole in DMF at 23 °C; (3) formylation (HCOOEt, NaH, THF); and (4) reaction with NaH–THF at 23 °C, cooling to −40 °C, and triflate formation with Tf_2NPh.

(15) Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611-614.

(16) Lewis acids such as $EtAlCl_2$, Et_2AlCl, $BF_3{\cdot}Et_2O$, or $FeCl_3$ in ether converted **14** to the isomeric ketone by rearrangement of hydrogen instead of carbon. The successful rearrangement of **14** to **15** is probably initiated by transfer of CH_3CO^+ to the epoxide oxygen of **14**.

(17) Generously provided by Profs. A. Murai and T. Masamune, Hokkaido University, to whom we express our warmest gratitude.

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The Large Range of Cr–Cr Quadruple Bond Distances: Structural and Theoretical Analysis

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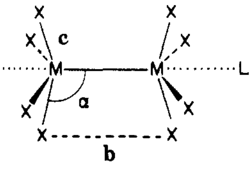
Two aspects of the beautiful conceptual structure of metal–metal multiple bonding[1] remain puzzling; the large variability of the supershort Cr(II)–Cr(II) quadruple bonds, and their response to axial ligation. We present a simple explanation of both phenomena here.

The essential geometrical features of the LX_4MMX_4L system are defined in **1**. We focus on five geometrical parameters: the M–M, M–L, and M–X distances; the "pyramidality" of the MX_4 group, defined by the M–M–X angle α; and the nonbonded X···X distance, which we will call b. In many of the known compounds the latter is fixed as part of a bidentate ligand.



1

Previous efforts to understand the bond-length variations in the system have focused on the distance to the axial ligands L. But look at Figure 1, a plot of the Cr–Cr separation as a function of the pyramidality angle α, for 40 quadruply bonded systems with two, one, or no axial ligands.[2,3] The straight line through these

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(1) Cotton, F. A.; Walton, R. A. *Multiple Bonds Between Metal Atoms*; J. Wiley: New York, 1982. Cotton, F. A.; Walton, R. A. *Struct. Bonding (Berlin)* **1985**, *62*, 1 and references within.

(2) The literature references for the compounds plotted are given in the supplementary material.

(3) A few Cr(II) complexes were not included in this analysis: (a) those with a noneclipsed configuration;[4] (b) those having Li^+ ions relatively close to the Cr–Cr bond;[5] and (c) organometallic complexes.[5a,b,6] For a carboxylato compound,[7] the average α is too large because one of the angles is very different from the rest (111° as compared to an average of 99.2°); if this angle is disregarded, the Cr–Cr distance calculated with our least-squares equation is 1.898 Å (experimental value, 1.870 Å).

(4) Cotton, F. A.; Rice, G. W.; Sekutowski, J. C. *Inorg. Chem.* **1979**, *18*, 1143.

(5) (a) Krause, J.; Schödl, G. *J. Organomet. Chem.* **1971**, *27*, 59. (b) Krause, J.; Marx, G.; Schödl, G. *J. Organomet. Chem.* **1970**, *21*, 159. (c) Cotton, F. A.; Koch, S. *Inorg. Chem.* **1978**, *17*, 2021.

(6) Aoki, T.; Furusaki, A.; Tomiie, Y.; Ono, K.; Tanaka, K. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 545.

(7) Cotton, F. A.; Mott, G. N. *Organometallics* **1982**, *1*, 302.

(8) On the same experimental plot of Figure 1, with no adjustment whatsoever, are superimposed some theoretical points from recent GVB calculations by Davy and Hall: Davy, R. D.; Hall, M. B. *J. Am. Chem. Soc.* **1989**, *111*, 1268. It becomes evident that the difficulties encountered in reproducing theoretically the supershort Cr–Cr bond distances are tied to the small value of α obtained from calculations.

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