host and guest, even quite water-soluble guests can experience strong "hydrophobic" binding.

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Total Synthesis of Glycinoeclepin A

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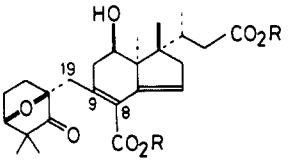
Our recent isolation[1] and structural elucidation[2] of glycinoeclepin A has revealed that this compound possesses an unusual molecular structure (**1**) and shows significant hatch-stimulating activity for the soybean cyst nematode. These characteristics, combined with the lack of a satisfactory natural source, render the title compound an attractive and challenging synthetic target. We describe herein the first total synthesis of **1**.



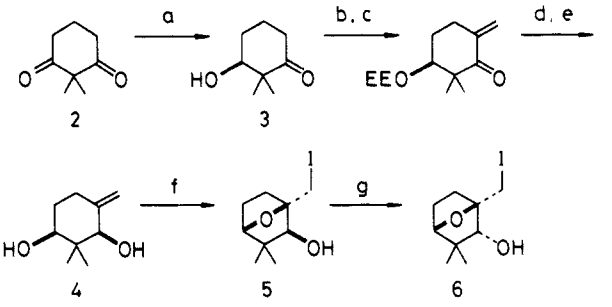
1, R=H
1a, R=$CH_2COC_6H_4Br$

The chiral synthesis of the A-ring of **1** started with enzymatic reduction of 2,2-dimethylcyclohexane-1,3-dione (**2**), which was performed with Baker's yeast, giving (*S*)-2,2-dimethyl-3-hydroxycyclohexan-1-one (**3**)[3] (Scheme I). The keto alcohol **3** (94.3% ee) was converted into an olefinic *cis*-glycol **4** in a five-step process involving formation of an α,β-unsaturated ketone,[4] followed by stereoselective reduction. The compound **4**, when treated with *N*-iodosuccinimide in acetonitrile (MeCN) in the dark, underwent smooth halocyclization to yield (1*R*,2*S*,4*S*)-1-iodomethyl-3,3-dimethyl-7-oxabicyclo[2.2.1]heptan-2-ol (**5**), which on simple recrystallization gave an *optically pure* sample, mp 99–101 °C (100% ee). Jones oxidation and hydride reduction of the pure alcohol (**5**) afforded exclusively the isomeric (2*R*)-alcohol **6**, mp 80–81 °C.

The synthesis of another fragment **7**, corresponding to the C and D ring moiety of **1**, started with (*R*)-(−)-carvone (**8**) and involved stereoselective construction of four successive chiral centers as the key steps (Scheme II). Nucleophilic/electrophilic carba-condensation[5] of **8** proceeded smoothly with high stereoselectivity, giving a dialkylated compound **9**, which underwent annelation[6] to yield an α,β-unsaturated octalone **10**, mp 53–55 °C. Hydrocyanation of **10** under kinetic conditions[7] effected predominant formation (63%) of the desired *cis*-cyano ketone **11**, mp 180–182 °C, accompanied by its trans isomer **11a**, mp 148–149 °C (30%).[8] The configuration of these ketones was confirmed by the X-ray crystallographic analysis of **11**,[9] indicating that stereoselective introduction of the four asymmetric centers has been completed as anticipated. The compound **11** was transformed by a usual several-step sequence into decalone **12**, which was oxidized with peroxytrifluoroacetic acid into ϵ-caprolactone **13** and then submitted to ring opening in a three-step process to give methoxycarbonyl acetate **14**. Cleavage of the two methoxyl groups of **14** was effected according to the Fuji procedure[10] to yield triol monoacetate **15**, which on tritylation and oxidation[11] afforded acetoxycyclohexanone trityl ether **7**.

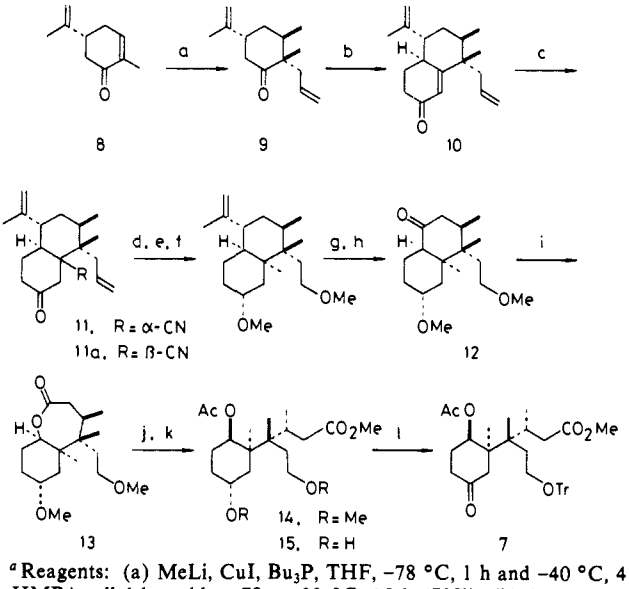
The next phase of synthesis was the combination of the two fragments **6** and **7**, one of the most critical steps of the synthesis.

Scheme I[a]



[a] Reagents: (a) Baker's yeast, D-glucose, KH_2PO_4, $MgSO_4$, DMF–H_2O (1:38), 24 °C (67%); (b) $EtOCH{=}CH_2$, PPTS (97%); (c) DMF–dimethyl acetal, 110 °C, 2 days; DIBAH (63%); (d) $NaBH(OMe)_3$ (87%); (e) HCl (99%); (f) NIS, MeCN, 20 °C, 16 h (79%); (g) Jones oxidation; $NaBH_4$ (92%).

Scheme II[a]



[a] Reagents: (a) MeLi, CuI, Bu_3P, THF, −78 °C, 1 h and −40 °C, 4 h; HMPA, allyl bromide, −78 → 23 °C, 15 h (78%); (b) LDA, MeCOC(TMS)=CH_2; NaOMe (74%); (c) HCN, Et_3Al, THF, 23 °C, 30 h; (d) OsO_4, NMO (80%); (e) $NaIO_4$; $NaBH_4$; MeI, NaH (61%); (f) DIBAH; $NH_2NH_2{\cdot}H_2O$, $NH_2NH_2{\cdot}2HCl$, triethylene glycol, 120 °C, 3.5 h; KOH, 200 °C, 6.5 h (82%); (g) O_3; Me_2S; CF_3CO_3H (55%); (h) $LiAlH_4$; Jones oxidation (93%); (i) CF_3CO_3H (72%); (j) KOH; CH_2N_2; Ac_2O, DMAP, Et_3N (57%); (k) $AlCl_3$, NaI, MeCN, 0 → 20 °C, 6 h; CH_2N_2 (85%); (l) TrCl, DMAP, Et_3N; PDC (91%).

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(9) The intensity measurements were performed by Dr. A. Furusaki, Hokkaido University, at the High Brilliance X-ray Laboratory of Hokkaido University.

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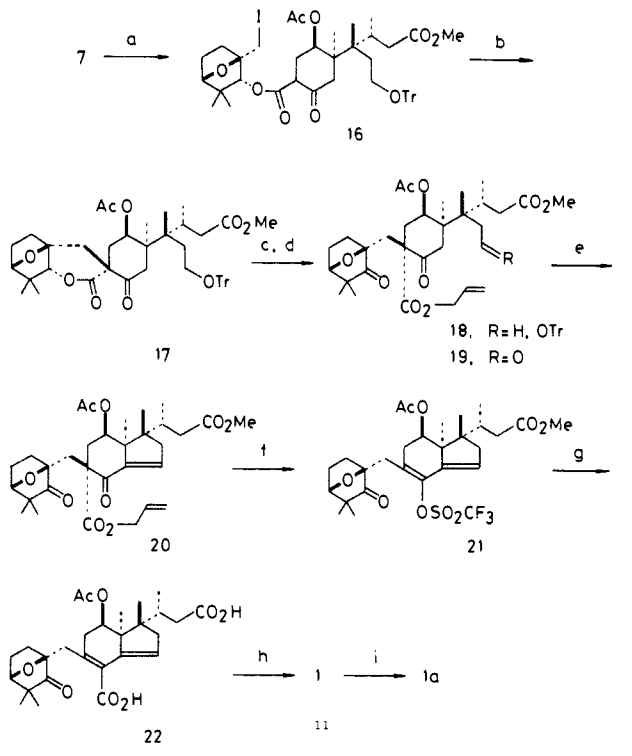
Scheme III[a]



[a] Reagents: (a) bromomagnesium thioureide–CO_2 complex, DMF, 20 °C, 20 h: **6**, DCC, DMAP, CH_2Cl_2, 0 → 20 °C, 20 h (84% "90%"); (b) KF (3 equiv), 18-crown-6-ether (3 equiv), MeCN; 65 °C, 15 h (76% "94%"); (c) sodium allyloxide; Swern oxidation (73% "90%"); (d) PTS; Swern oxidation (91%); (e) *t*-BuOK, DME, −78 °C; 2-FC_5H_4NMe·OTs, Et_3N, CH_2Cl_2 (54%); (f) $Pd(OAc)_2$, $(C_6H_5)_3P$, HCO_2H, Et_3N, THF; $(CF_3SO_2)_2NC_6H_5$, NaH (76%); (g) CO, Bu_3N, $Pd(OAc)_2$, DPPF, aqueous DMF, 95 °C, 3.5 h; (h) NaOMe (66%); (i) *p*-$BrC_6H_4COCH_2Br$, $(i\text{-}Pr)_2NEt$, MeCN (99%).

After many fruitless attempts, we hoped to submit these compounds to an *intramolecular* coupling. Thus, (Scheme III) treatment of the compound **7** with the bromomagnesium thioureide–carbon dioxide complex,[12] resulted in α-carboxylation to yield β-ketocarboxylic acid, which was immediately reacted with **6** in the presence of dicyclohexylcarbodiimide to afford β-keto ester **16**. Further reaction of **16** with potassium fluoride in MeCN in the presence of 18-crown-6 at 65 °C effected the relevant coupling between C(9) and C(19), giving δ-lactone **17** in high yield.[13] The lactone **17**, when treated with sodium allyloxide and then oxidized,[14] was transformed into β-keto ester **18**, which was submitted to detritylation with acid and subsequent oxidation[14] to afford aldehyde ketone **19**. Treatment of **19** with potassium *tert*-butoxide in dimethoxyethane gave rise to the corresponding aldol, which was immediately dehydrated with 2-fluoropyridinium tosylate[15] to afford methoxycarbonyl enone **20**. The allyloxycarbonyl group of **20** was then removed according to the procedure of Tsuji,[16] giving the relevant dienol,[17] which was treated with sodium hydride and phenyl triflimide[18] to yield the corresponding dienyl triflate **21** in a high overall yield.

The stage was now set to introduce the necessary one-carbon unit at the C(8) position of **21**. This was accomplished by a modification of the Ortar method.[19] The compound **21**, when treated with tributylamine, palladium acetate, and 1,1′-bis(diphenylphosphino)ferrocene,[20] in aqueous *N*,*N*-dimethylformamide under a carbon monoxide balloon at 95 °C for 3.5 h, was transformed into acetoxyl dicarboxylic acid **22** in 42% (82% based on the recovered **21**).[21] Compound **22** was smoothly saponified and esterified to give the corresponding bis(*p*-bromophenacyl) ester alcohol. The ester thus obtained was identical in every respect (^1H NMR, IR, MS, CD, HPLC) with **1a**[1,2] derived from the natural sample. The hatch-stimulating activity of the synthetic sample **1** was found to be indistinguishable from that of the natural sample.[22]

Supplementary Material Available: Spectral data and physical properties for compounds **4–7**, **9–12**, **11a**, **14–18**, **20–22**, and an ester of **22** and listings of atomic coordinates and thermal parameters for **11** (8 pages). Ordering information is given on any current masthead page.

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(21) There is no experimental evidence available to detail how the compound **22** was produced under these conditions.
(22) Studies on the biological activity were carried out by Dr. A. Fukuzawa, Hokkaido University.

Heterobimetallic Complexes with (μ-Phenoxo)bis(μ-carboxylato) Cores

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Binuclear metal complexes are important in investigating the magnetic and electronic interactions between metal ions and in probing the structure and function of binuclear metal centers in proteins.[1,2] In studying the coordination chemistry of binucleating ligands such as *N*,*N*′-(2-hydroxy-5-methyl-1,3-xylene)bis(*N*-carboxymethylglycine) (HXTA) and 2,6-bis[(bis(2-pyridylmethyl)amino)methyl)]-4-methylphenol (HBPMP),[4] we have discovered a general synthetic route for preparing heterobimetallic complexes in which one of the metal ions is iron. Herein we report the synthesis and physical properties of the bis(carboxylato) bridged Fe(III)Zn(II), Fe(III)Mn(II), Fe(III)Cu(II), Ga(III)-Fe(II), and Fe(III)Fe(II) complexes of HBPMP.

The Fe(III)Zn(II) complexes were synthesized by treating a methanolic solution of HBPMP with sequential additions of an equivalent of $Fe(NO_3)_3$·$9H_2O$, an equivalent of $ZnBr_2$, and 3 equiv of the appropriate carboxylate salt. The complexes were metathesized with excess $NaBPh_4$ and recrystallized from ace-

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