(5) Professor R. M. Coates and his co-workers have independently synthesized gymnomitrol, and their findings are described in the accompanying communication. We thank Professor Coates for a friendly exchange of information, and for having agreed to simultaneous publication.
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A Stereoselective Total Synthesis of (±)-Gymnomitrol

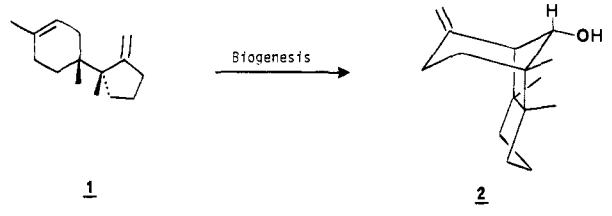
Sir:

The tricyclic sesquiterpenoid gymnomitrol (**2**) was isolated as a major metabolite from liverwort *Gymnomitrion obtusum* (Lindb.) Pears.[1] The corresponding hydrocarbon, gymnomitrene (previously known as β-barbatene[2] or β-pompene[3]), also occurs with **2**. The structure and stereochemistry of **2** were determined by degradation and spectroscopy in conjunction with biogenetic considerations.[1] The unique carbon framework of this cyclotrichothecane is thought to arise, biogenetically, from bazzanene (**1**, Scheme I).[1,4] We report in this communication an efficient and stereoselective total synthesis of (±)-gymnomitrol (**2**).[5,26]

The starting material chosen for the synthesis of **2** is 2-methylcyclopentanone (**3**). Normally, cyclopentanones are difficult to alkylate because of the relative ease of enolization, aldol condensation, and polyalkylation.[6] A number of methods for the regioselective synthesis of unsymmetrical ketones such as **3** have been developed.[7-9] In practice, however, we found that generation of the enolate anion of **3** with 0.95 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C, equilibration to the thermodynamically more stable enolate anion[10] at room temperature for 4–5 h, and then quenching with 2,3-dibromopropene at 0 °C afford after chromatography on silica gel ketone **4** in 79% yield (Scheme II). Hydrolysis of vinyl bromide **4** with 90% sulfuric acid at 0 °C proceeds smoothly in 91% yield on small scale (200 mg) to give diketone **5**; however, the yields decrease dramatically in larger scale runs. To circumvent this troublesome step an alternative method was selected. Vinyl bromide **4** is conveniently hydrolyzed to diketone **5** in 91% yield using mercury(II) acetate in 88% formic acid at room temperature.[11] Cyclization of diketone **5** to bicyclic enone **6**[12] is accomplished in 84% yield with potassium hydroxide in ethanol at reflux.

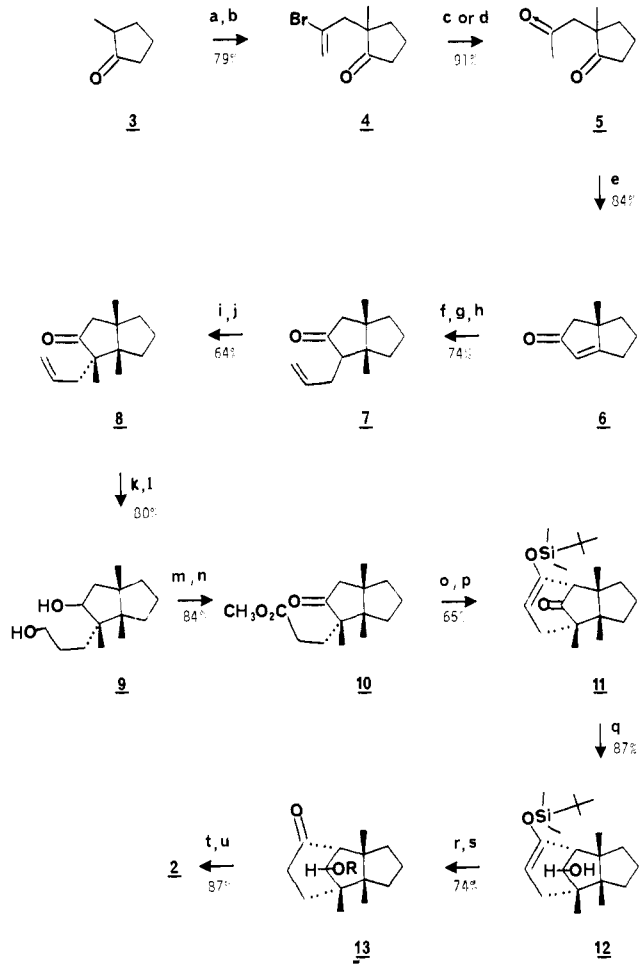
Addition of enone **6** to a solution of lithium dimethylcopper in THF at −78 °C, followed by quenching with allyl chloride in hexamethylphosphoric triamide (HMPT) at room temperature and an aqueous hydrochloric acid workup, affords bicyclic ketone **7** in 74% yield as a 60:40 ratio of diastereomers.[13] Alkylation of ketone **6** using sodium hydride in 1,2-dimethoxyethane (DME), followed by addition of methyl iodide, produces ketone **8** in 64% yield as a single diastereomer.[14,15] This alkylation takes place with the alkylating agent, methyl iodide, approaching the less hindered convex side of the thermodynamically more stable enolate anion. The stereochemical assignment of this methylation product **8** is confirmed by analysis of the europium-induced NMR shifts[16] for the three quarternary methyl groups in the two isomeric alcohols formed by reduction of ketone **8** with sodium borohydride in 100% ethanol. This reduction affords a 79:21 ratio of diastereomeric alcohols which are separated by chromatography on silica gel. The magnitudes for the europium-induced NMR shifts for the methyl groups in these two isomers are quite different. In the major isomer (β-OH) the C-1 methyl group moves at a faster rate than the two bridge methyl groups; however, in the minor isomer (α-OH) all three methyl groups move at similar rates upon increasing the concentration of $Eu(DPM)_3$. The europium-induced NMR shifts of these isomers are in agreement with those shifts observed by Connolly

Scheme I



1 2

Scheme II[a]



[a] (a) 0.95 × LDA, THF, −78 °C to room temperature, 4–5 h; (b) CH_2=$CBrCH_2Br$; (c) 90% H_2SO_4, 0 °C; (d) $Hg(OAc)_2$, 88% HCO_2H; (e) KOH, EtOH, heat; (f) $LiMe_2Cu$, THF; (g) CH_2=$CHCH_2Cl$, HMPT; (h) H_3O^+; (i) NaH, DME; (j) CH_3I; (k) Sia_2BH, THF; (l) H_2O_2, NaOH, H_2O; (m) CrO_3, H_2SO_4, H_2O, acetone; (n) CH_2N_2, Et_2O (small scale) or CH_3I, K_2CO_3, acetone (large scale); (o) 2.0 × $LiN(SiMe_3)_2$, THF, reflux, 2 h and 35 min; (p) HMPT, *t*-$BuMe_2$-SiCl, 0 °C; (q) $NaBH_4$, 100% ethanol, 0 °C to room temperature, 6 h; (r) CH_2=$C(OCH_3)CH_3$, $POCl_3$ catalyst (R = $-C(CH_3)_2OCH_3$; (s) *n*-Bu_4F, THF; (t) $(C_6H_5)_3P$=CH_2, Me_2SO, 75 °C, 16 h; (u) MeOH, 5% HCl catalyst, room temperature, 0.5 h.

0002-7863/79/1501-6768$01.00/0

and co-workers for gymnomitrol (**2**)[1] as well as those shifts observed by Coates and co-workers for the two alcohols produced upon reduction of the diastereomer of ketone **8**.[17]

Hydroboration of alkene **8** with excess disiamylborane in THF, followed by oxidation with basic hydrogen peroxide, gives diol **9** in 80% yield.[18] Oxidation of diol **9** with Jones reagent[19] and esterification of the resultant keto acid afford keto ester **10** in 84% yield. The tricyclic structure of **2** now requires a Claisen condensation on keto ester **10.** The rationale for performing a modified Claisen condensation on keto ester **10** is as follows: (1) differentiation between the two potential carbonyl moieties, (2) selective and stereoselective reduction of the cyclopentanone carbonyl, and (3) ease of protection of the resultant cyclopentanol and unmasking of the silylated cyclohexanone. Addition of keto ester **10** to a solution of 2.0 equiv of lithium bis(trimethylsilyl)amide[20] in anhydrous THF–hexane (95:5) at reflux over a period of 20 min, followed by continued heating at reflux for 2.25 h, cooling to 0 °C, addition of HMPT, and enolate anion trapping with *tert*-butyldimethylsilyl chloride,[21,22] affords tricyclic ketone **11** in 65% yield. Stereoselective reduction of ketone **11** with sodium borohydride in 100% ethanol at 0 °C to room temperature for 6 h gives alcohol **12** in 87% yield containing a small amount of the diastereomeric alcohol.[21,23]

Sequential treatment of silyl enol ether alcohol **12** with 2-methoxypropene in the presence of a catalytic amount of phosphorus oxychloride[24] at room temperature for 16 h, followed by the addition of tetra-*n*-butylammonium fluoride[21] in THF and stirring at room temperature for an additional 10 h, produces keto ketal **13** (R = $-C(CH_3)_2OCH_3$) in 74% yield along with the isomeric keto ketal in 5% yield.[23] Finally, a Wittig reaction on keto ketal **13** with methylenetriphenylphosphorane[25] in anhydrous dimethyl sulfoxide at 75 °C for 16 h and methanolysis in the presence of a catalytic amount of 5% hydrochloric acid solution at room temperature for 0.5 h afford (±)-gymnomitrol (**2**) in 87% yield. Synthetic **2** was found to be identical with a sample of the natural substance with respect to NMR, IR, GLC, and TLC data.

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(26) Professors R. M. Coates (University of Illinois) and G. Büchi (Massachusetts Institute of Technology) and their respective co-workers have recently synthesized (±)-gymnomitrol by independent routes. We congratulate them on their synthetic achievements. See the two accompanying communications in this issue.
(27) After submission of this manuscript we learned that Professor L. A. Paquette and co-worker also have synthesized (±)-gymnomitrol. See Paquette, L. A.; Han, Y.-K., *J. Org. Chem.*, in press. We congratulate them on their successful synthesis.

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Photoactivation of Cobalt Carbonyl Catalysts: Generation of Reactive Mononuclear Fragments from Dinuclear, Metal–Metal Bonded Complexes

Sir:

Metal–metal bonded complexes are generally photosensitive with respect to cleavage of the metal–metal bond,[1] and certain dicobalt complexes are known[2] to be hydroformylation catalyst precursors under thermal conditions. We report herein our preliminary results concerning the photogeneration of catalytically active mononuclear cobalt carbonyl fragments from dinuclear, metal–metal bonded complexes. The results illustrate the potential utility of photoinduced metal–metal bond cleavage in probing catalytic mechanisms and in initiating catalytic chemistry under thermal conditions where there would be no reaction without light activation. The complexes studied thus far are $[Co_2(CO)_6L_2]$ (L = P(*n*-Bu)$_3$, P(OPh)$_3$) and $[Fe(\eta^5\text{-}C_5H_5)(CO)_2Co(CO)_3(P(OPh)_3)]$,[3] and the catalytic probe chemistry has been reaction of 1-pentene–$HSiEt_3$ mixtures. The cobalt systems have been chosen for study be-

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