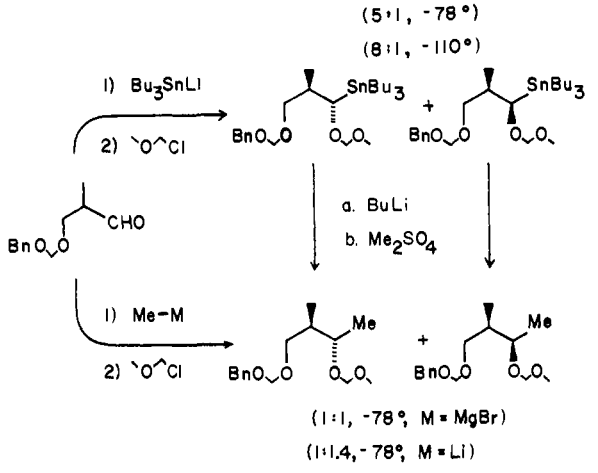
chiral aldehydes. Our results indicate that, for α induction based only on the relative sizes of α-substituents (Cram's rule),[11] the tributylstannyl anion exhibits much the same stereoselectivity as unhindered Grignard reagents. Thus 2,3-dimethylbutanal (THF, −110 °C) gives essentially the same stereochemical product distribution with either tributylstannyllithium (3:1) or methylmagnesium bromide (2.5:1). In the case of the former addition, the product stannylcarbinol mixture was protected ($BnOCH_2Cl$, *i*-Pr_2NEt), lithiated (BuLi, THF, − 78 °C), and methylated (Me_2SO_4) to give the same major methylcarbinol produced by the Grignard addition. This result would seem to indicate that methylation proceeds with retention unless steric α induction with methylmagnesium bromide is opposite that observed with tributylstannyllithium.

Stereoselectivity is somewhat improved with aldehydes substituted at the β position by oxygen. With α-asymmetric aldehydes of this type, the cyclic chelate mechanism[12] would presumably be operative and anti-Cram products would be predicted. When the β-alkoxy aldehyde **7** was treated with



tributylstannyllithium in THF, a 5:1 (−78 °C) or 8:1 (−110 °C) mixture of diastereomeric stannylcarbinols was produced. After protection ($MeOCH_2Cl$, *i*-Pr_2NEt), the major diastereomer was purified by MPLC on silica gel. Lithiation (BuLi, −78 °C, THF) and methylation (Me_2SO_4) then gave the anticipated[13] threo product[14] stereospecifically. For comparison, both methyllithium and methylmagnesium bromide add to **7** (THF, −78 °C) in an essentially stereorandom manner. Although the generality of stereoselection in tin anion additions remains to be established, these preliminary results suggest that tributylstannyllithium may be added to aldehydes with moderate stereoselectivity and that the direction of the addition is that predicted either by Cram's rule or by the cyclic chelation model.[15]

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(5) Other factors which would be expected to raise the barrier to organolithium inversion include intramolecular chelation (which stabilizes the position of lithium) and α-heteroatom substitution [which is known to raise pyramidal inversion barriers for example in the isoelectronic hydroxylamines: reviews by J. B. Lambert, *Top. Stereochem.*, **6**, 19 (1971) and H. A. Bent, *Chem. Rev.*, **61**, 275 (1961); see also H. M. Niemeyer, *Tetrahedron*, **33**, 2267 (1977)].

(6) A 25 × 500 mm LiCroprep Si60 (25–40 μ, E. Merck No. 9390) was used, 15 mL/min: (a) 2% ethyl acetate–petroleum ether; (b) 0.3% ethyl acetate–petroleum ether.

(7) A similar sequence with **2a** at 0 °C gave mainly decomposition of the lithium reagent. The small portion of the reagent which did survive gave a 1:1 mixture of **3a** and **3b** [E = $C(CH_3)_2OH$] on trapping with acetone. It is not clear whether or not the isomerization is due to pyramidal inversion of the anion or due to some other process related to decomposition of the reagent.

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(9) Optical resolution of the tributyltin adduct of propanal could also be effected via formation of a urethane with (−)-α-phenylethylamine [(a) $COCl_2$, *i*-Pr_2NEt; (b) (−)-$PhCH(CH_3)NH_2$]. With this derivative the MPLC separation was more difficult and the *S* urethane analogous to **4b** eluted first. Conversion to the stannyl carbinol was effected without loss of optical activity using $HSiCl_3$–EtY_3N; cf. W. H. Pirkle and J. R. Hauske, *J. Org. Chem.*, **42**, 1939 (1977); W. H. Pirkle and P. L. Rinaldi, *ibid.*, **43**, 3803 (1978).

(10) Although no peaks resulting from the (−)-MTPA ester of the enantiomeric alcohol could be seen, proportions of that material as large as 5% could have escaped detection.

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(13) Assuming retention of stereochemistry during methylation.

(14) Authentic threo material was prepared from tiglic acid as follows: (1) $LiAlH_4$, Et_2O; (2) $BnOCH_2Cl$, *i*-Pr_2NEt; (3) BH_3, THF; NaOH, H_2O_2; (4) $MeOCH_2Cl$, *i*-Pr_2NEt.

(15) This work was supported by NSF Grant CHE 78-01769.

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W. Clark Still,*[16] C. Sreekumar

Department of Chemistry, Columbia University
New York, New York 10027

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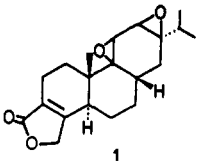
Total Synthesis of Stemolide

Sir:

Falling in the same class as the potent cytotoxic agents triptolide, tripdiolide, and triptonide,[1] the diterpenoid bis-epoxide stemolide (**1**), possessing the novel 18(4→3)*abeo*-abietane skeleton, was recently isolated and described by Manchand and Blount.[2] Herein we report a total synthesis of



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this natural product, the first route to a representative of this structural type.[3]

To prepare for the later incorporation of the bis epoxide moiety, the starting material, methyl dehydroabietate,[4] was first functionalized in the aromatic ring by treatment with acetyl chloride in CS_2 in the presence of Al_2Cl_6, providing methyl 12-acetyldehydroabietate (80%). Baeyer–Villiger oxidation with 3,5-dinitroperbenzoic acid[5]–methanesulfonic acid (CH_2Cl_2, room temperature), saponification, and O-alkylation with MeI–NaH (THF, room temperature) led to methoxy ester **2**,[6] convertible by EtSLi[7] (HMPA–THF, room temperature) into the corresponding acid **3**[6] (76% from **2**). Following the approach of Huffman and and Stockel,[8] the substituted dehydroabietic acid **3** was transformed into the dehydroabietene **7** (mp 75–77 °C) by Curtius degradation to isocyanate **4**, $LiAlH_4$ reduction followed by Eschweiler–Clarke methylation to **5**, N-oxidation to **6**, and Cope elimination (72% from **3**). The α-epoxide resulting from *m*-chloroperbenzoic acid oxidation of **7**, on treatment with Et_2Al–N-*i*-Pr_2[9] (C_6H_6/PE, 50 °C), generated allyl alcohol **8**. After conversion (*n*-Bu_3P/CCl_4, 0 °C) of **8** to halide **9**, displacement by lithium thiophenoxide (THF, room temperature) gave thioether **10** (81% from **7**). The corresponding sulfonium fluoroborate **11** was converted by BuLi (THF, −78 °C) into ylide **12**, which underwent in situ electrocyclic conversion at 0 °C into the

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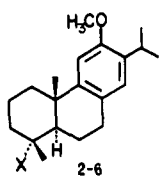
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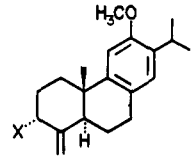
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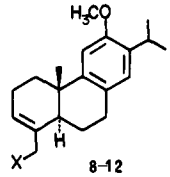
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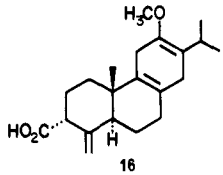
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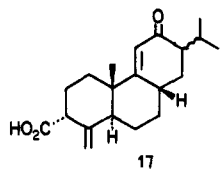
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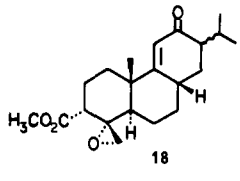
2 X = CO_2CH_3
3 X = CO_2H
4 X = NCO
5 X = $N(CH_3)_2$
6 X = $N(CH_3)_2O$
7 X = H
13 X = $CH_2SC_6H_5$
14 X = CHO
15 X = COOH
8 X = OH
9 X = Cl
10 X = SC_6H_5
11 X = $(CH_3SC_6H_5)^+$, BF_4^-
12 X = $CH_2{=}SC_6H_5$

homologated thioether **13.** Transformation into aldehyde **14** (34% from **10**) was achieved by α-monochlorination of the thioether unit (NCS, CCl_4, room temperature), formation of the monothioacetal by treatment with MeOH (ether, 0 °C), and final treatment with $I_2/NaHCO_3$ (dioxane-H_2O, room temperature). Oxidation of **14** ($NaClO_2/NH_2SO_3H$, THF-H_2O, 0 °C) afforded the unsaturated acid **15** (mp 80–84 °C): NMR (CCl_4) δ 0.98 (s, 3 H, 20-CH_3), 1.16 (d, J = 7.0 Hz, 6 H, 16-CH_3 and 17-CH_3), 3.70 (s, 3 H, 12-OCH_3), 4.77, 4.95 (s, 1 H, 19-CH_2), 6.52 (s, 1 H, 11-CH), 6.67 (s, 1 H, 14-CH).

On subjection to the action of 86 equiv of Li bronze in *t*-BuOH-Et_2O-NH_3 for 4 h, **15** was reduced to the dihydroanisole **16** [NMR (CCl_4) inter alia δ 3.45 (s, 3 H, 12-OCH_3), 4.75, 4.97 (s, 1 H, 19-CH_2)], which was hydrolyzed by 2-h reflux in 6 N $HClO_4$/THF, giving the conjugated ketone **17** [NMR (CCl_4) inter alia δ 4.74, 4.94 (s, 1 H, 19-CH_2), 5.77 (m, 1 H, 11-CH)]. Oxidation of the latter with 3,5-dinitroperbenzoic acid (CH_2Cl_2, room temperature, 13 h), followed by exposure to CH_2N_2/Et_2O at 0 °C, provided (38% from **14**) epoxy ester **18**: NMR (CCl_4) inter alia δ 3.68 (s, 3 H, 18-CO_2CH_3), 5.72 (m, 1 H, 11-CH). Through the action of LiN-*i*-Pr_2/THF (−78 °C), ester **18** presumably suffers elimination to the γ-hydroxy-α,β-unsaturated ester, which spontaneously cyclizes (46%) to the butenolide **19:** NMR (CCl_4) inter alia δ 4.60 (m, 2 H, 19-CH_2), 5.78 (m, 1 H, 11-CH). C-ring reduction of **19** to the conjugated diene level was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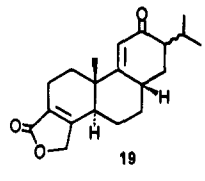
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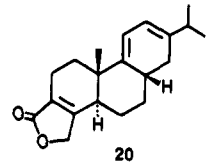
managed by preliminary conversion ($TsNHNH_2$/HCl, MeOH, reflux) into the tosylhydrazone followed by the action of 25 equiv of LiH in refluxing $C_6H_5CH_3$,[10] generating (39%) trienelactone **20:** NMR ($CDCl_3$) δ 0.88 (s, 3 H, 20-CH_3), 1.04 (d, J = 6.8 Hz, 6 H, 16-CH_3 and 17-CH_3), 4.69 (m, 2 H, 19-CH_2), 5.69 (m, 2 H, 11-CH and 12-CH). In keeping with the biosynthetic suggestions of Manchand and Blount,[2] the diene moiety of **20** was subjected to attack by $^1O_2$ (generated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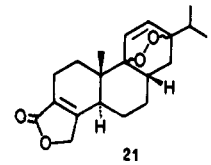
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by irradiation of $^3O_2$ in the presence of methylene blue), giving a stereomeric mixture of peroxides **21** (~2:1 9,13-α:β). After separation of **21** on a silica gel column, the β-peroxide was heated in refluxing xylene for 12 h. The product, formed in nearly quantitative yield and crystallized from ether-ethyl acetate, was found to be identical with natural stemolide, on the basis of IR, NMR, CD ($[\theta]_{223\ nm}$ +15 300, $[\theta]_{246\ nm}$ −4800), mass spectral, as well as melting point (230–232 °C) and mixture melting point (230–232 °C) comparisons.

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E. E. van Tamelen,* E. G. Taylor
Department of Chemistry, Stanford University
Stanford, California 94305
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Spectroscopic Characterization of an Electrophilic Transition-Metal–Methylene Complex, η^5-$C_5H_5[(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2]Fe{=}CH_2^+$

Sir:

The preparation of transition-metal–carbene complexes which lack direct heteroatom stabilization of the electrophilic carbene carbon center is of interest owing to the high reactivity of these species in comparison with that of heteroatom-stabilized systems.[1] To date, Schrock[2] has reported the only successful isolation of an unsubstituted methylene complex, $Cp_2TaCH_3(CH_2)$; however, based on its reactivity, the carbene carbon in this complex is clearly *nucleophilic* in nature. In the electrophilic series, methylene complexes have been frequently postulated as intermediates, but their direct observation has most often been elusive. For example, Pettit and Jolly,[3] Green,[4] and Brookhart[5] have suggested **1a** as a transient species formed on acid treatment of $Cp(CO)_2Fe$-CH_2OCH_3, while Davison[6] and Flood[7] have proposed **1b** as an intermediate formed from $Cp(CO)PPh_3Fe$-CH_2OR in acid-catalyzed methylene transfer to olefins and SO_2 insertion into the C—O bond, respectively. Pettit[8] has recently suggested the formation of the

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