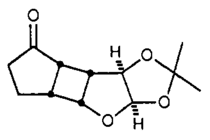
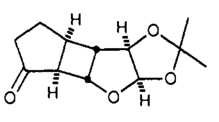


(-)-**12**



(-)-**13**

triflate **14**.[10] Palladium-catalyzed carbomethoxylation was then achieved via the protocol described by Ortar.[6] Finally, oxidation of the dienolate derived from **15**[10] [KN(SiMe$_3$)$_2$, 20% HMPA/THF, −78 °C][19] with the Davis (+)-(camphorsulfonyl)oxaziridine[20] furnished carbinol **16**.[10] The overall yield for the three steps was 55%. Removal of the isopropylidene group (Bio-Rad AG50W-X2 acidic resin, 50% aq CH$_3$CN) then afforded triol **17**.[10a,21]

We next confronted the task of oxidizing the diol unit in **17**. This transformation was best accomplished in a stepwise fashion, first by using the palladium-catalyzed dehydrogenation developed by Tsuji [Pd$_2$(DBA)$_3$·CHCl$_3$ (10 mol %), diallyl carbonate, acetonitrile at 80 °C];[22] the result was hydroxylactone **18**[10a] obtained in 50–55% yield. Subsequent oxidation of **18** with MnO$_2$ provided α-ketolactone **3**,[10a] albeit with variable efficiency. These results, in conjunction with the general instability of **3**, prompted us to explore a useful variation of the oxidation–fragmentation tactic. Thus, ammonolysis of **18** (NH$_4$OH in MeOH)[23] provided cyclobutanol **19**[10a,24] (86%) which in turn was subjected to oxidation.[25] The latter led via fragmentation[7] and recyclization to **20**,[10a] obtained as a 20:1 anomeric mixture.[26] The structure of **20**, and in particular the α-configuration of the anomeric hydroxyl, was secured by preparation of the corresponding acetates (**21**), exploiting the Mitsunobu protocol (DIAD, Ph$_3$P, HOAc in THF).[27] The major acetate was assigned the β-configuration (i.e., **21**β)[10a] on the basis of an observed 6% nuclear Overhauser enhancement between H$_a$ and H$_b$.[28]

The success of the latter transformation suggested that an intramolecular Mitsunobu lactonization would lead to echinosporin (**1**). After considerable experimentation, acid **2**[10a] was prepared by hydrolysis of methyl ester **20** (3.6 N HCl, 2 days), followed by ion-exchange chromatography (DEAE Sephadex) and immediate lyophilization. Without further purification, **2** was subjected to the Mitsunobu reaction,[29] whereupon reverse phase chromatography provided (−)-echinosporin (**1**) in 28–31% yield for the two steps.[30] That indeed synthetic (−)-echinosporin was in hand derived from detailed comparison of synthetic (−)-**1** with natural material (i.e., 500 MHz ^{1}H and 125 MHz ^{13}C NMR, IR, HRMS, and TLC comparison in four solvent systems).[31] The optical rotation of synthetic echinosporin {$[\alpha]^{25}_{D}$ −402° (c 0.08, CH$_3$OH)} was also identical with that of natural (−)-echinosporin {$[\alpha]^{25}_{D}$ −400 °C (c 0.1, CH$_3$OH)}. Thus the absolute configuration of (−)-echinosporin is assigned as 3*R*, 4*R*, 5*S*, and 8*R*.[3b]

In summary, we have completed an enantioselective total synthesis of (−)-echinosporin and thereby have defined the absolute configuration of this potentially important antibiotic–antitumor agent. Progress concerning the preparation of (+)-echinosporin from cycloadduct (−)-**12** as well as further demonstration of the synthetic utility of dihydrofurans (+)- and (−)-**6** will be reported in due course.

Acknowledgment. Support for this work was provided by the National Institutes of Health (National Cancer Institute) through Grant CA-22807.

Supplementary Material Available: Spectral (IR, ^{1}H NMR, and ^{13}C NMR) and analytical (elemental analysis) data for **1**, **2**, **4**, **6**, **12–21**, and i (4 pages). Ordering information is given on any current masthead page.

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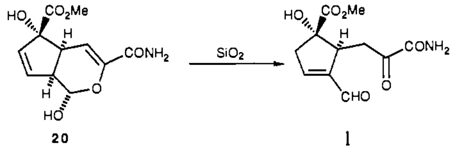

20 **i**

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(28) This assignment was further supported by the chemical shifts and coupling constants of the anomeric hydrogens. The major acetal hydrogen displayed a chemical shift of δ 4.84 and a coupling constant J = 7.88 Hz, while the minor acetal hydrogen appeared at δ 5.25 with a coupling constant J = 3.05 Hz.

(29) The optimal conditions for the desired ring closure entailed preformation of the Mitsunobu complex at −15 °C [Bu$_3$P (2.5 equiv), DEAD (2.5 equiv), THF] followed by addition of the complex to a solution of **2** in THF (4 Å molecular sieves) at −15 °C. Addition of the Mitsunobu complex (2.5 equiv) was repeated after 1 h, and the resultant mixture was then stirred overnight at room temperature.

(30) The low yield obtained in the Mitsunobu ring closure is attributable to the instability of carboxylic acid **2** and the strained character of the lactone. With use of the MNDO method, the strain energy incurred upon lactonization of **2** was calculated to be 17 Kcal/mol.

(31) We thank Dr. Fumio Suzuki of Kyowa Hakko Kogyo Co. for a generous sample of natural echinosporin.

Preparation and Structure of a New Ternary Transition-Metal Zintl Compound Containing High Spin Mn^{III}Bi$_4$ Tetrahedra

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Several rational approaches to solid-state synthesis have been proposed and may lead to a large number of new compounds.[1-3] Such a rational approach is seen in the Zintl concept,[2,4,5] which has been applied to intermetallics,[2,5] ternary main-group compounds,[6,7] ternary transition-metal chalcogenides,[8] and ternary lanthanide transition-metal pnictides.[9] The Zintl concept can

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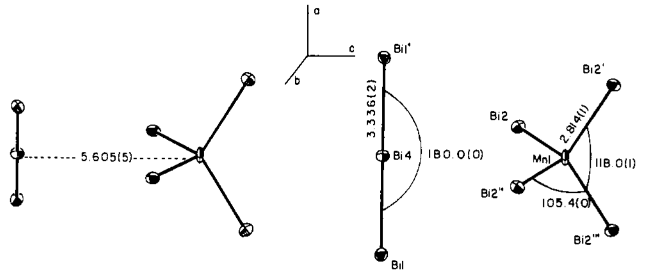

Figure 1. A perspective view 15° off the *b* axis of the polyatomic anions in $Ca_{14}MnBi_{11}$ showing their relative orientation within the unit cell. The thermal ellipsoids are drawn at 70% probability.

be simply stated as the octet rule for all atoms (with the exception of transition metals); electronegative elements gain as many electrons as necessary to complete their octet, and the electropositive metals lose electrons. The variety of structures obtained with ternary main-group Zintl compounds[2,4,6,7] provides inspiration to look for isosteric compounds with transition metals. Although there are examples of discrete transition-metal-containing tellurides,[10,11] there are few examples of discrete transition-metal-containing pnictides.[12] We have prepared a new ternary transition-metal compound, $Ca_{14}MnBi_{11}$, that is isostructural to the Zintl compounds $Ca_{14}AlSb_{11}$[13] and $Ca_{14}GaAs_{11}$.[14] The compound is made up of $Mn^{III}Bi_4{}^{9-}$ tetrahedra, $Bi_3{}^{7-}$ linear chains, and isolated Bi^{3-} and Ca^{2+} ions. This is the first reported example of a Mn^{III} tetrahedron and a $Bi_3{}^{7-}$ linear anion.

The compound, $Ca_{14}MnBi_{11}$, was synthesized from a stoichiometric combination of the elements Ca and Bi with a 4-fold excess of Mn powder. The reactants were sealed in a Ta container under helium and subsequently sealed under argon in a quartz ampoule. The reaction was heated at 1250 °C for 2 h and cooled to room temperature. Nicely formed air-sensitive black cube-shaped crystals were obtained in ≥95% yield. The yield was estimated based on X-ray powder diffraction (Guinier).[15] The products were examined in a nitrogen atmosphere drybox equipped with a microscope and then characterized with single-crystal[16] and Guinier powder diffraction methods, microprobe spectroscopy,[17] and magnetic susceptibility measurements.

$Ca_{14}MnBi_{11}$ crystallizes in the tetragonal space group $I4_1/acd$ with a = 17.002 (6) and c = 22.422 (7) Å (Z = 8). A view of the polyatomic anions in the structure is shown in Figure 1 (important distances and angles are labeled). All the Mn–Bi distances in the $MnBi_4$ tetrahedra are the same, 2.814 (1) Å, and the tetrahedron is distorted with angles 105.4 (1)° and 118.0 (1)°. The Zintl compounds, $Ca_{14}AlSb_{11}$ and $Ca_{14}GaAs_{11}$, have MB_4 (B = As, Sb) tetrahedral units which are also distorted with angles of 107.4° and 114°. In all cases the MB_4 tetrahedra (B = As, Sb, Bi) are separated by a three-atom linear chain that is situated along a plane that bisects the MB_4 tetrahedron. The distance of the central Bi in the linear unit to the Mn is 5.605 (5) Å. All these structures have an unusual three-atom group 15 (V) linear chain, in which the Bi–Bi distance[18] is 3.336 (2) Å compared to 3.196 Å for the Sb chain and 2.967 Å for the As chain. The linear chains are found to be exactly perpendicular to each other and alternate in that respect between $MnBi_4$ tetrahedra. The other Bi–Bi distances are significantly larger than observed in the three-atom chain (>4.50 Å) and are between isolated anions.

Temperature-dependent magnetic susceptibilities for T = 5–300 K were determined by using a Quantum Design SQUID magnetometer. A ferromagnetic transition is observed at 56 K. Above T_c, the magnetic susceptibility obeys Curie–Weiss law, and the data were fit to the relation $\chi_m = C/(T - \theta) + \chi_o$ (C = 2.86 (7), θ = 50 (1), and χ_o = 1.7 (3) × 10^{-3}) over the temperature range 120–300 K. μ_{eff} (4.78 μ_B) was calculated from the Curie constant and is slightly smaller than the expected value for four unpaired spins (4.90 μ_B).

If the Zintl concept is used to rationalize the bonding observed in this compound, the formal oxidation state of the Mn ion can be obtained. An oxidation state of 2+ is assigned to all the Ca atoms, and the isolated Bi atoms are given an oxidation state of 3–, thus satisfying their octet. The charge on the Bi_3 linear unit can be obtained by using the VSEPR model:[19] the central Bi atom has three lone pairs in the equatorial position similar to XeF_2,[20] and the two terminal Bi atoms have complete octets, thus the Bi_3 chain has a formal charge of 7–. Therefore, in one formula unit, there are 14 Ca^{2+} cations, four Bi^{3-} anions, and one $Bi_3{}^{7-}$, leaving a charge of 9– on the tetrahedral $MnBi_4$ unit. The Bi atoms in the tetrahedral unit can be assigned an oxidation state of 3–, thus, Mn is a 3+ ion (d^4). Although the magnetic moment provides evidence that the Zintl concept can be used to obtain the oxidation state on the metal ion within this compound, the low-temperature ferromagnetic behavior indicates that a delocalized electronic description of the solid-state structure may be more appropriate. The slight distortion of the Mn^{III} tetrahedron to D_{2d} symmetry results in a stable high spin d^4 configuration. Although it can be argued that this is a Jahn–Teller effect, this small distortion is also observed in the Al and Ga analogues. This indicates that it may be due to anion–anion repulsion[21] between the central Bi atom in the $Bi_3{}^{7-}$ linear chain and the terminal Bi atoms in the $MnBi_4$ tetrahedron. More sophisticated theoretical calculations are needed to explain the structural details of this compound. Further investigations aimed at understanding the bonding and physical properties of this compound and its structural analogues are underway.

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Supplementary Material Available: Tables of atomic coordinates and anisotropic thermal parameters and selected bond lengths and angles (2 pages). Ordering information is given on any current masthead page.

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(15) Room temperature Guinier powder diffraction data: a = 17.084 (2) Å and c = 22.503 (3) Å.

(16) The space group is tetragonal, $I4_1/acd$, with a = 17.002 (6) Å, and c = 22.422 (7) Å at 130 K, Z = 8, R = 0.054, and R_w = 0.059 for 758 reflections ($2\theta_{max}$ = 50°, Mo Kα radiation) with $I > 2.5\sigma(I)$ and 61 parameters.

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