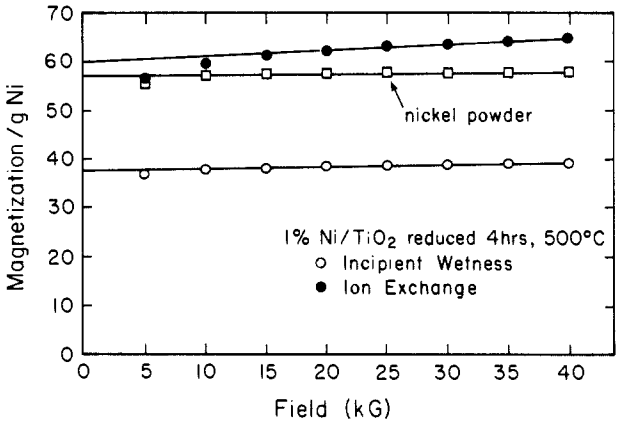

Figure 2. Magnetization per gram of Ni vs. the applied magnetic field measured at 5 K for (A) 1.0% Ni/TiO_2 prepared by incipient wetness (open circles) and (B) 1.0% Ni/TiO_2 prepared by ion exchange (closed circles). Both samples were reduced at 773 K for 4 h. The magnetization of a sample of pure nickel powder is included for comparison.

a SHE SQUID magnetometer. Figure 2 shows the magnetization per gram of Ni for samples A and B reduced at 773 K for 4 h. Data for a sample of nickel powder (Puratronic, 99.999% pure, 100 mesh) are shown for comparison. Extrapolation of the data for fields greater than 25 kG to zero gives the saturation magnetization M_s(A) = 37 per g of Ni for sample A and M_s(B) = 60 per g of Ni for sample B. If all the nickel were present as pure nickel metal, a value of 57.5 per g of Ni is expected, as observed for the sample of nickel powder. The small value of M_s observed for sample A indicates that 36% of the nickel has reacted with the TiO_2 support. In contrast, the sample prepared by ion exchange showed no strong interaction between the nickel and the TiO_2; no loss of ferromagnetic nickel was detected. Since one difference between the two samples is that the composite prepared by ion exchange has less hydroxyl groups on the TiO_2 surface, it is proposed that the surface hydroxyl groups are important in the initial steps in the reaction between nickel and TiO_2. Another possibility which cannot be excluded is that the nitrate groups in the incipient wetness sample produce a reactive intermediate which is not formed in the sample prepared by ion exchange.

The hydrogen chemisorption and magnetism results show that the method used to prepare Ni/TiO_2 composites can be used to manipulate the extent to which the two materials react. We feel that the key difference between the two samples studied here is the number of hydroxyl groups present on the TiO_2 surface. The TiO_2 surface in sample B, prepared by ion-exchange, has very few hydroxyl groups compared with sample A prepared by incipient wetness. In fact, for a 1.0% by weight loading of nickel ion exchanged onto the low surface area TiO_2 used in this study, the entire surface of the TiO_2 is coated with Ni^{+2} and no surface hydroxyl groups should remain. Various studies have shown that at elevated temperatures hydroxyl groups are removed from the surface of the TiO_2 as water, thereby generating Ti^{4+} ions which are coordinatively unsaturated.[4] These unsaturated Ti^{4+} sites are reduced by hydrogen spillover[5] from the metal to form reduced TiO_x ($x < 2$) moieties[6] which diffuse onto and into the metal particles.[7] This reaction of TiO_x with the nickel particles is thought to cause the change in surface chemistry observed for the Ni/TiO_2 composite prepared by incipient wetness. We propose that for the ion-exchanged sample, the reduction of TiO_2 is kinetically slow because the initial concentration of surface hydroxyl groups is too low; for this sample, a strong interaction between the metal and the support is not induced after reduction at 773 K for 4 h.

In summary, we have shown that it is possible to turn off the interaction between nickel and TiO_2 (Cerac, 5.1 m^2/g) if ion-exchange methods are used to disperse the metal onto a low surface area TiO_2 support. For the sample prepared by ion exchange, the chemisorption of hydrogen is not suppressed and the saturation magnetization indicates that the nickel is present as the pure metal. We conclude that the removal of surface hydroxyl groups is important for the facile reduction of the TiO_2 surface at 773 K; if the number of surface hydroxyl groups is too low, the metal–support interaction is suppressed. Since the number of hydroxyl groups initially present on the surface depends also on the preparation and thermal history of the TiO_2, we postulate that the chemistry of metal–TiO_2 composites can be manipulated by controlling the surface properties of the TiO_2 used as the support.

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Total Synthesis of (+)-Aplasmomycin[1]

James D. White,* Thalathani R. Vedananda, Myung-chol Kang, and Satish C. Choudhry

Department of Chemistry, Oregon State University Corvallis, Oregon 97331

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Aplasmomycin (**1**)[2] and its congeners **2** and **3**[3] are metabolites of *Streptomyces griseus*[4] that, along with the closely related boromycin (**4**),[5] represent a unique family of ionophoric antibiotics. The elaborate architecture of these natural cryptands, as revealed by X-ray crystallographic studies,[6,7] is centered around a borate core that serves as the anionic companion of the transported alkali-metal cation. Complete elucidation of the stereochemical features of **1** and **4**, including their conformation with and without the borate nucleus,[8] has enabled rational synthetic routes to be designed which have already resulted in syntheses of **1**,[9] the

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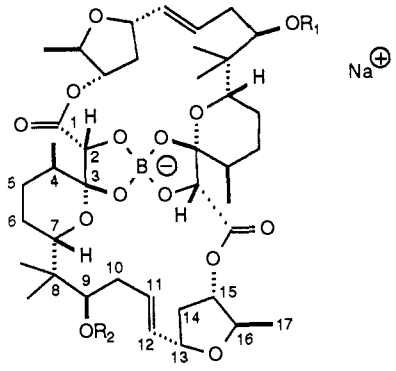

1 $R_1 = R_2 = H$
2 $R_1 = Ac, R_2 = H$
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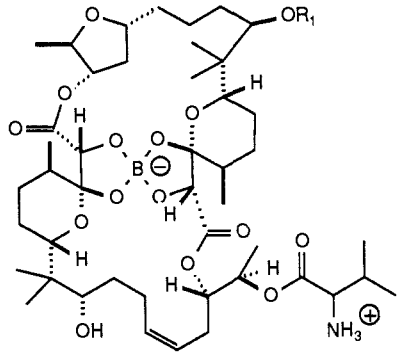
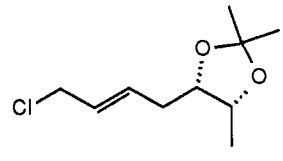


4

half-structures of **4**,[10,11] and abbreviated segments of these macrodiolides.[12] We now report a synthesis of aplasmomycin (**1**) in which the 28-membered cycle is generated via a novel ring *contraction* that utilizes a rearrangement of α-(acyloxy)acetates first demonstrated by Chan.[13]

Following a published route,[11] **5** and **6**[14] were taken to ketone **7**, which was reduced in a highly stereoselective process to the *R* alcohol **8**.[15] The derived acetate **9** was subjected to acidic



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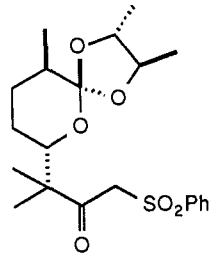
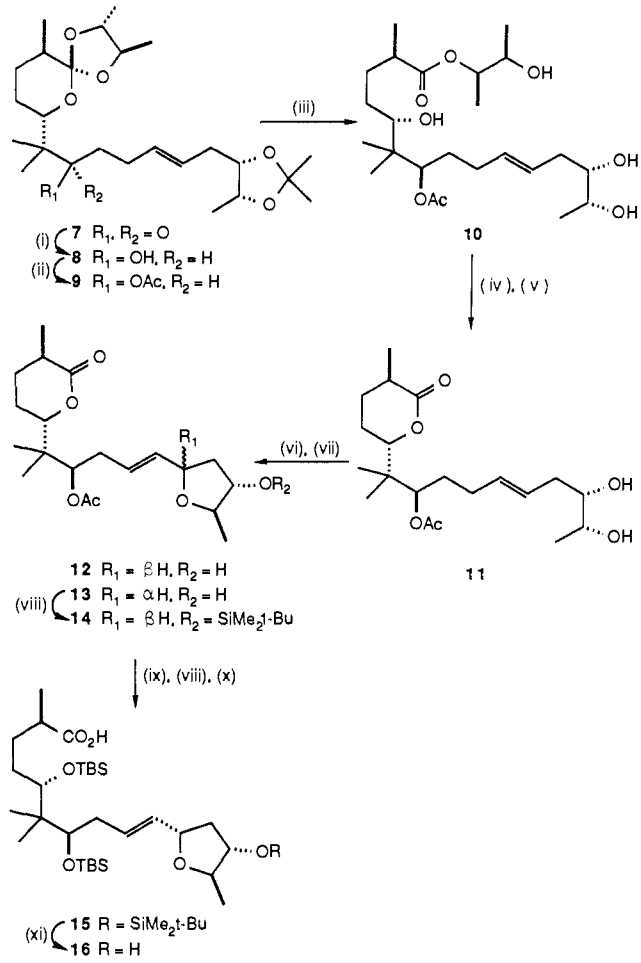


6

hydrolysis and the ester **10** was carefully saponified to give an acid which lactonized readily in the presence of HCl to **11**. Previous studies on a close relative of **11** suggested that intramolecular oxyselenation of the olefin–diol moiety could be expected to lead, after oxidative elimination of the selenide, to the trans-$\Delta^{11,12}$ tetrahydrofuran substructure present in the upper left and lower right quadrants of **1**.[11] In fact, exposure of **11** to phenylselenyl chloride at 70 °C and then hydrogen peroxide furnished

Scheme I[a]



[a] (i) $LiAlH_4$, ether, −110 °C; (ii) Ac_2O, DMAP, (78% from **7**); (iii) *p*-TsOH, THF–H_2O, 24 h; (iv) aqueous NaOH; (v) 5% HCl THF (74% from **9**); (vi) PhSeCl, CCl_4, 70 °C (94%, **12**:**13** ~ 1:1); (vii) 30% H_2O_2, 0–25 °C, 7.5 h (91%); (viii) *t*-$BuMe_2SiOTf$, 2,6-lutidine, CH_2Cl_2, −20 °C (90%); (ix) NaOH, MeOH–H_2O, 25 °C; (x) K_2CO_3, MeOH–THF–H_2O (92% from **14**); (xi) *n*-BuNF, THF, 25 °C, 8 h (90%).

12 accompanied by its epimer **13**. These were easily separated via their *tert*-butyldimethylsilyl ethers and the pure lactone **14** was manipulated into a form suitable for its induction into the macrostructure of **1** by vigorous saponification, followed by silylation of the intermediate dihydroxyacid, yielding **15**. The tetrahydrofuryl silyl ether of **15** was then selectively cleaved with fluoride to give hydroxy acid **16** representing C(3)–C(17) of the aplasmomycin half-structure (Scheme I).

Several gambits were explored for attaching the α-hydroxy β-ketal acid segment at the carboxyl terminus of **15** through acylation of various glycolate equivalents but, for the most part, they foundered on the retro-aldol cleavage to which these adducts are prone. However, although the C(1)–C(3) array is fickle in the half-structures of **1** and **4**, it is quite stable in the intact macrocycles, as demonstrated by the inertness of the deboro versions of **1** and **4** to both acidic and basic reagents. Elaboration of this substructure in an already assembled macrocycle could take advantage of this stabilization and, fortunately, a means was at hand for reducing this idea to practice.

Reaction of the potassium salt of **16** with 2-(trimethylsilyl)ethyl α-bromoacetate[16] yielded **17** which was esterified with α-bromoacetyl chloride to give **18**. The latter was linked to **16** to produce **19**, and after removing the protective ester, lactonization of the resulting hydroxy acid was effected by the Mukaiyama protocol[17] to furnish **20** in excellent yield. The C_2 symmetry of

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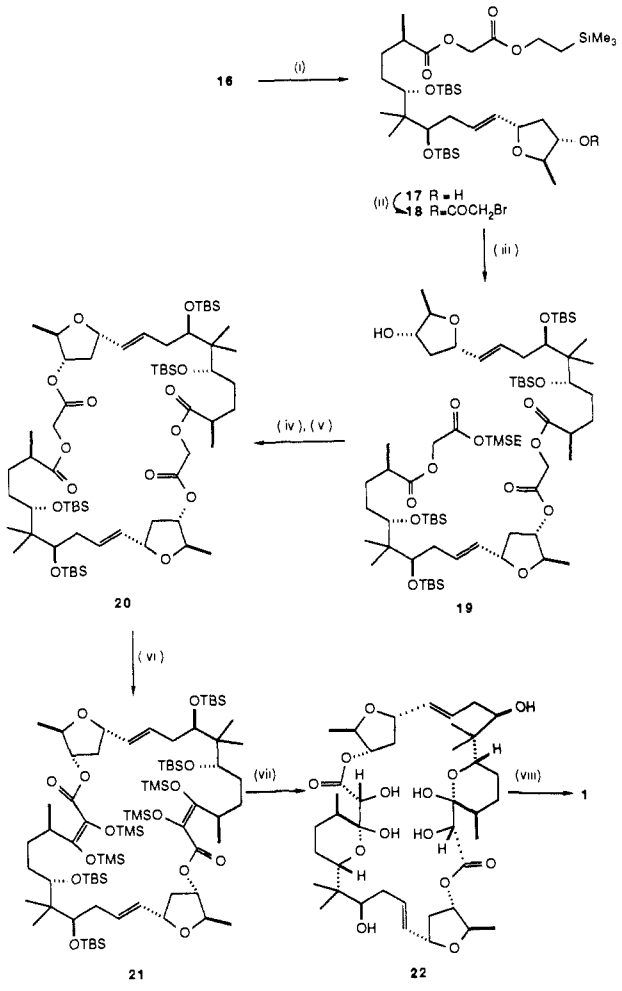
(14) An improved, enantiospecific synthesis of (+)-**6** from (*R*)-(+)-pulegone will be disclosed in due course.
(15) The *R*:*S* alcohol ratio was 22:1 at −110 °C, a result that can be rationalized in terms of selective hydride delivery to the *si* face of a carbonyl chelated with the pyran oxygen.
(16) Prepared from α-bromoacetyl chloride and 2-(trimethylsilyl)ethanol.

Scheme II[a]



[a] (i) $BrCH_2CO_2(CH_2)_2SiMe_3$, K_2CO_3, acetone, reflux (93%); (ii) $BrCH_2COCl$, DMAP, Py, CH_2Cl_2, 0 °C (92%); (iii) **16**, K_2CO_3, acetone, reflux (88%); (iv) *n*-Bu_4NF, THF, 0 °C; (v) 2-chloropyridinium methiodide, Et_3N, CH_2Cl_2 (86%); (vi) LDA, THF, 0 °C, then −78 °C, Me_3SiOTf; (vii) 5% HF, CH_3CN, 3.5 h, 25 °C; (viii) $(MeO)_3B$, MeOH, heat.

this macrocycle is evident from its ^1H and ^{13}C NMR spectra and, upon treatment with lithium diisopropylamide followed by trimethylsilyl triflate, a "double-Chan" reaction[13] of **20** afforded **21** in good yield. Simultaneous removal of all silyl protecting groups was accomplished with HF, which also catalyzed intramolecular hemiketalization, to give deboroaplasmomycin **22**, corresponding to material obtained from natural **1** with citric acid. Finally, **22** was treated with anhydrous trimethyl borate[9,18] furnishing aplasmomycin that was identical by comparison of chromatographic properties, infrared and ^1H NMR spectra, and optical rotation with the natural substance (Scheme II).

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Supplementary Material Available: Spectral data for **5–7**, **9**, **11**, **14–20**, **22**, **23**, **25–29**, and **31** and synthetic scheme for **6** (8 pages). Ordering information is given on any current masthead page.

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Benzoannelated Centropolyquinanes. 2.[1] *all-cis*-Tetrabenzotetracyclo[5.5.1.$0^{4,13}$.$0^{10,13}$]tridecane, "Fenestrindan"

Dietmar Kuck* and Hartmut Bögge

Fakultät für Chemie, Universität Bielefeld
D-4800 Bielefeld, West Germany

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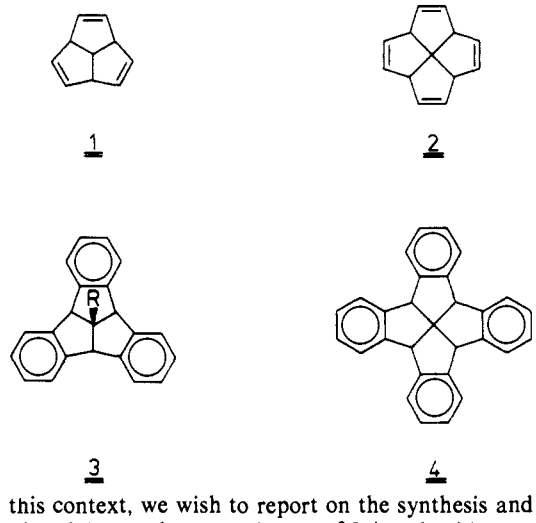
The carbon skeletons of tricyclo[5.2.1.$0^{4,10}$]deca-2,5,8-triene (triquinacene) (**1**)[2] and tetracyclo[5.5.1.$0^{4,13}$.$0^{10,13}$]trideca-2,5,8,11-tetraene (**2**)[3] have attracted considerable interest in recent years.[4,5] Both structures offer or promise an access to more highly unsaturated, strained polyquinanes,[6] or, more stricty, *centro*polyquinanes,[7] as well as to related carbanions,[5a] carbocations, and transition-metal complexes.[5e] In particular, centrotetracyclic species like **2** have been investigated by several groups as potential precursors to compounds containing a planar or planarizable carbon atom.[8] In contrast to polyquinenes, benzoannelated polyquinanes have been studied scarcely,[1,8b,c,9] though, in general, strained polycycles gain stability by fusion to aromatic rings.



In this context, we wish to report on the synthesis and some properties of the tetrabenzo analogoue of **2**, i.e., the title compound

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