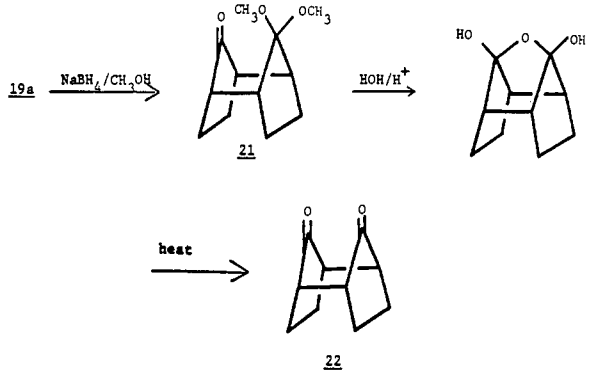
yield as described by J. C. Barborak, L. Watts, and R. Pettit, *J. Am. Chem. Soc.*, **88**, 1328 (1966), and J. C. McKennis, L. Brener, J. S. Ward, and R. Pettit, *ibid.*, **93**, 4957 (1971). Each new compound was characterized appropriately.
(4) The chloro-bridged dimeric structure of these compounds is assumed based on the usual behavior of RhCl–diene complexes. In all probability the bridge is disrupted in Me_2SO.
(5) To our knowledge, this is the first application of this reduction method to rhodium–diene complexes. It proceeds readily in good yield, apparently via σ-bonded intermediates. Saturation of the olefin bonds is intrinsic to the process. The presence of the halogen (and/or the halogen bridge) seems essential, for monomeric acetylacetonate rhodium–diene complexes are reported not to be reduced by sodium borohydride (B. R. G. Johnson, H. V. P. Jones, and J. Lewis, *J. Chem. Soc., Dalton Trans.*, 463 (1972)). We shall consider the mechanism of this reduction in a later paper.
(6) This compound has just recently been prepared by L. A. Paquette and coworkers using a totally different route.[7a]
(7) (a) L. A. Paquette, G. Klein, and C. W. Doecke, *J. Am. Chem. Soc.*, **100**, 1595 (1978); (b) I. A. Akhtar, G. I. Fray, and J. M. Yarrow, *J. Chem. Soc. C*, 812 (1968).
(8) Prepared by stirring $[Rh(NOR)Cl]_2$ with acetylacetone and sodium carbonate in aqueous THF at room temperature, followed by extraction into chloroform and crystallization from methylene chloride; cf. the original, but poorer yield route of F. Bonati and G. Wilkinson, *J. Chem. Soc.*, 3156 (1964). The complexes resulting from reaction of Rh(NOR)acac with **1** and **3** are highly crystalline, mp 142–143 and 90–92 °C, respectively. The NMR spectra closely resemble those of **2** and **4**. The acetonylacetonate complexes (monomeric) are more soluble than the chloro complexes (bridged dimers) and hence better suited for kinetic measurements.
(9) The *endo*-methyl groups are already badly compressed in **6**; $J_{^{13}C-H}$ at the methano bridge is 119 Hz.
(10) The effects of steric compression are clearly evident in the NMR spectra and reactions of the free diene; see C. W. Doecke, G. Klein, and L. A. Paquette, *J. Am. Chem. Soc.*, **100**, 1596 (1978).
(11) An important, related observation has been reported by P. G. Gassman and T. H. Johnson, *J. Am. Chem. Soc.*, **98**, 861 (1976), which see.
(12) P. E. Eaton and C. A. Cerefice, *Chem. Commun.*, 1494 (1970).
(13) Furthermore, sodium borohydride reduction gives the corresponding saturated *syn*-tricyclo[4.2.1.$1^{2,5}$]decane free of rhodium. Thus, for example, **19a** is reduced to **21** (mp 98–99 °C) quantitatively. (Note that the ketone



21 22

group survives; apparently the rhodium black catalyzed reaction of $NaBH_4$ with methanol is much faster than $NaBH_4$ reduction of the ketone.) Hydrolysis of **21** and subsequent desiccation gives dione **22** of C_{2v} symmetry: IR (CCl_4) ν 1770 cm^{-1}; ^1H NMR δ 2.44–2.16 (8 H), 1.89–1.61 ppm (4 H); ^{13}C NMR δ 212.6, 45.7, 18.7 ppm.

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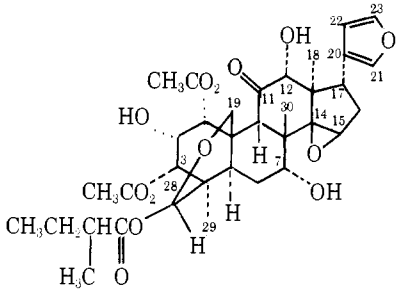
Isolation and Structure of Aphanastatin[1]

Sir:

Certain plants of the order Rutales, especially in the Simaroubaceae family, have a long history of use in primitive medicine for cancer treatment[2] and various amoebic, inflammatory, and malarial problems.[3] In recent years several very promising antineoplastic agents have been isolated from Simaroubaceae species.[3,4] As part of an initial study of the closely related Meliaceae family for potentially useful anticancer constituents we found extracts prepared from seeds of the Eastern Himalayan (India) plant *Aphanamixis grandifolia* Bl.[5] to markedly inhibit growth of the murine lymphocytic leukemia P388.[6] Now we are pleased to report that separation directed by bioassay (P388 cell line) of the *Aphanamixis g.* seed extract (aqueous) led to discovery of a new highly cytotoxic (P388 ED_{50} 0.065 μg/mL) limonoid designated aphanastatin (**1**).[7]



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A chloroform-soluble fraction (P388 ED_{50} 0.33 μg/mL) of the water extract was subjected to successive gradient elution (chloroform–methanol) chromatographic separations on silica gel (E. Merck) to afford aphanastatin (**1**) as crystals (from chloroform–methanol) decomposing at 269–271 °C, $[\alpha]^{22}_D$ −38.9° (*c* 0.46, 1:24 pyridine–methanol), and $CD\Delta^{\epsilon}$ −2.88 (311 nm) in the same solvent, corresponding to molecular formula $C_{35}H_{46}O_{13}$ (mass spectrum *m/e* 674.2907 for M^+).

The mass spectrum of aphanastatin showed significant fragmentation ions at *m/e* 572.2252 ($C_{30}H_{36}O_{11}$), 512.2049 ($C_{28}H_{32}O_9$), and 452.1824 ($C_{26}H_{28}O_7$) corresponding to successive loss from the molecular ion of 1 mol of pentanoic acid and 2 mol of acetic acid. Interpretation of these data and that from the 250-MHz ^1H NMR spectrum[8] (methyl protons at δ 0.81 (s, 3 H), 0.83 (t, 3 H, J = 7.5 Hz), 1.03 (d, 3 H, J = 7.5 Hz), 1.10 (s, 3 H), 1.29 (s, 3 H), acetate methyls at 2.02 and 2.08, and other protons at 3.74 (s, 1 H, H-7), 3.74 (s, 1 H, H-15),[11] 4.10 (s, 1 H, H-9), 4.38 (s, 1 H, H-12), 4.46 (q, 1 H, J = 13.7 Hz, H-19), 4.89 (t, 1 H, J = 5 Hz, H-2), 5.58 (d, 1 H, J = 5 Hz, H-3, 5.82 (1 H, H-28), 5.96 (d, 1 H, J = 5 Hz, H-1), 6.62 (s, 1 H, H-22), 7.25 (s, 1 H, H-21), and 7.52 (s, 1 H, H-23)) suggested compound **1** to be an α-methyl butyrate diacetate derivative of a tetranortriterpene.[9] The ^1H NMR data also indicated the presence of a furan ring and double-resonance experiments suggested presence of the system -CH(OAc)CH(OH)CH(OAc)-.

The structure of aphanastatin (**1**) was completely established by single-crystal x-ray analysis. Orthorhombic crystals of space group $P2_12_12_1$, a = 19.234 (3) Å, b = 14.206 (3) Å, c = 12.363 (5) Å, Z = 4, d_{calcd} = 1.326, were employed. Single-crystal x-ray diffraction data were measured with a Philips PW 1100 diffractometer using the ω–2θ scan technique with graphite monochromated Cu Kα radiation. The structure was solved by direct methods.[10] Full-matrix least-square refinement, with anisotropic temperature factors for the nonhydrogen atoms, resulted in an R factor of 0.050, based on 2060 observed reflexions.

The positions and configuration of substituents are 1α-OAc, 2α-OH, 3α-OAc, 4α-CH_3, 5α-H, 7α-OH, 8β-CH_3, 9α-H, 11-oxo, 12α-OH, 13α-CH_3, 14β,15β-epoxy, and 17α-C_4H_3O (furan ring). Ring C has a twist boat conformation and ring D takes an envelope form with C-17 out of the mean plane through the other four atoms by 0.58 Å. The dihedral angles between H-7 and the two hydrogen atoms bonded to C-6 are +60 and −60° and those between H-15 and the two hydrogen atoms bonded to C-16 are +48° and −72°. The dihedral angle between H-22 and H-23 is −3°.

The quassinoids, limonoids, and meliacins are assumed to have the same biosynthetic precursor.[9] Since the triterpenoid biogenetic origin of the quassinoids has been experimentally

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proven,[3] the absolute configuration of aphanastatin is that shown in **1**. Further evaluation of aphanastatin's antineoplastic properties is in progress.

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Relative Acidity of Superacids: $HF:SbF_5$ Compared with $HSO_3F:SbF_5$

Sir:

Following the pioneering work of Olah and his coworkers from the early sixties up to now, the superacid systems have been used for a variety of applications both in fundamental and applied chemistry.[1] The acidity of a number of superacids has been thoroughly investigated by Gillespie,[2] but the unavailability of weak-enough bases has limited these investigations to HSO_3F containing <11 mol % SbF_5[3] and in HF containing <0.5 mol % SbF_5.[4] With the latter system, a limited number of H_0 measurements showed that HF was weaker than HSO_3F at least in the 0–0.4% SbF_5 region. On the other hand, many experimental results suggested, either on the basis of kinetic measurements[5] or of mechanistic studies,[6,7] that the $HF:SbF_5$ system was by far the strongest and the following classification has been proposed:[5] 1:1 $HF:SbF_5$ > 9:1 $HF:SbF_5$ > 1:1 $HSO_3F:SbF_5$ > 5:1 $HSO_3F:SbF_5$ with the ratio of >500:1: 10^{-1}:10^{-5}. We have shown in a preceding communication[8]

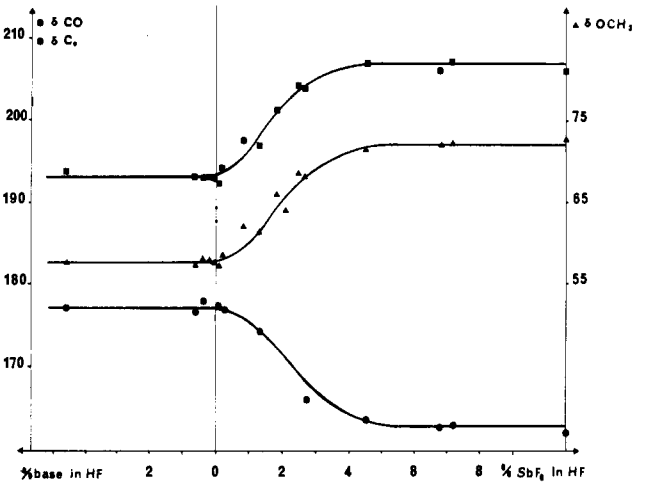
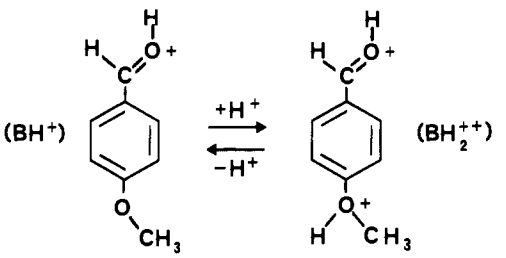


Figure 1. Characteristic chemical shift variation between the BH^+ and BH_2^{2+} forms of the indicator.

how ^1H DNMR and ^1H chemical shift measurements allowed us to evaluate the acidity of HSO_3F containing up to 25 mol % SbF_5, the acidity indicator being monoprotonated *p*-methoxybenzaldehyde ($pK_{BH^{2+}} = -19.5$).

We wish now to report our results on the acidity measurement of the $HF:SbF_5$ system with the same indicator which allows us to compare directly the HF with the HSO_3F solvent system. With increasing acidity, the indicator changes from the BH^+ form (monoprotonated on the carbonyl oxygen) to the BH_2^{2+} form (second proton on the ether oxygen). The use



of ^1H NMR[9] was not convenient with the $HF:SbF_5$ system because (1) the $C{=}OH^+$ chemical shift is too much solvent dependent for a fair interpretation of the titration curve and (2) the HF solvent peak overlaps with the aromatic region in the "low" acidity mixtures (SbF_5 < 3%) preventing DNMR measurements. For this reason, we used FT $^{13}C\{^1H\}$ NMR, with the advantage that three characteristic ^{13}C chemical shifts, could be monitored simultaneously for the neutralization curve with an average chemical shift variation $|\Delta(\delta_{BH_2^{2+}} - \delta_{BH^+})|$ of 14 ppm (Figure 1). In protonated aromatic carbonyl compounds the carbonyl ^{13}C chemical shift is known to be very sensitive to the nature of the para substituent;[10] the 4 carbon bearing either the CH_3O- group or the $CH_3O^+(H)$- group and the methoxy carbon itself are the most sensitive to the second protonation. The 1 carbon is also shifted upfield as it correlates well with the σ^+ value of the para substituent.[11] The chemical shifts of BH^+ and BH_2^{2+} can be taken from the limiting values in "low" and high acidity and compared with those measured in the $HSO_3F:SbF_5$ solvent of known acidity as shown in Table I. One can see directly from Figure 1 that half-protonation, $(BH_2^{2+}/BH^+) = 1$, is achieved with ~2 mol % SbF_5 in HF, whereas >15 mol % were necessary in HSO_3F.[8] By measuring the ionization ratio from the neutralization curve and reporting the values in the Hammett equation $H_0 = pK_{BH_2^{2+}} - \log(BH_2^{2+}/BH^+)$ we can follow the acidity as a function of the SbF_5 content. The result is plotted (○) in Figure 2 and compared with earlier data from the literature. Actually we should not call this function an H_0 function as long as

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