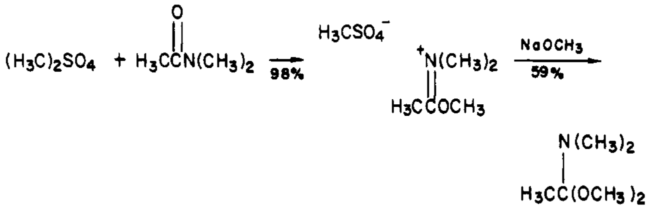
dialkyl sulfates are more readily available (less expensive) and easier to handle than the oxonium salts.

O-Methylation of *N,N*-dimethylacetamide with dimethyl sulfate proceeds readily at 70–80 °C in a few hours to afford an oily salt in excellent yield. Reaction of the latter with sodium methoxide provides the target acetal in 58% overall yield from *N,N*-dimethylacetamide.



Experimental Section

Eastman dimethyl sulfate was used as received. Eastman *N,N*-dimethylacetamide was purified by stirring with barium oxide for 3 days followed by distillation of the supernatant under water aspirator vacuum and was stored over 4-Å molecular sieves. Fisher ACS Certified benzene was freshly distilled from potassium benzophenone ketyl. Ether was freshly distilled from $LiAlH_4$. Methanol was freshly distilled from sodium methoxide prepared by addition of metallic sodium to Fisher ACS Certified anhydrous methanol.

***N,N*-Dimethylacetamide–Dimethyl Sulfate Complex.** In a 2-L three-necked, round-bottom flask with a magnetic stirrer, thermometer, and dry nitrogen inlet were placed 630 g (473 mL, 5 mol) of dimethyl sulfate and 435 g (464 mL, 5 mol) of *N,N*-dimethylacetamide. The mixture was heated at 70–80 °C with a heating mantle for 3 h with magnetic stirring. After cooling with an ice–water bath, the reaction mixture was then washed successively with 350 mL of dry benzene and twice with 250 mL of dry ether. The washings were conveniently removed from the reaction vessel with a large hypodermic syringe. The last traces of wash solvents were removed from the product by evaporation under reduced pressure, first with a water aspirator vacuum and then with a mechanical pump. The complex was obtained as a colorless viscous oil: 1042 g (98% yield); $n^{20}{}_D$ 1.4700; ^1H NMR ($CDCl_3$) δ 2.68 (3 H, s), 3.35 (3 H, s), 3.52 (3 H, s), 3.67 (3 H, s), 4.33 (3 H, s).

***N,N*-Dimethylacetamide Dimethyl Acetal.**[4] In a 5-L three-necked, round-bottom flask with a mechanical stirrer, 1-L pressure-equalizing addition funnel, and condenser topped with a gas inlet for maintaining an atmosphere of dry nitrogen were placed 1585 mL of anhydrous methanol. Then 112.5 g (4.9 mol) of sodium was added in small pieces (3–5 g each) gradually. After all of the sodium had reacted, the resulting sodium methoxide solution was cooled to 1–4 °C with an ice–salt–water bath, and 1042 g of *N,N*-dimethylacetamide–dimethyl sulfate complex was added dropwise with vigorous stirring over 3 h. The reaction mixture was stirred at room temperature for 20 h and then allowed to stand for an additional 20 h.[7] The addition funnel was then replaced with a stopper and the reflux condenser was set for distillation. The reaction mixture was heated with a mantle and methanol was distilled from the reaction mixture at atmospheric pressure. Methanol containing some *N,N*-dimethylacetamide dimethyl acetal was collected with a boiling range of 60° to 78 °C. After most of the methanol had been distilled, the receiver was changed. A second fraction was collected into a receiver which was cooled in an ice-salt-water bath, and the pressure was gradually reduced with a water aspirator while the temperature of the mantle[8] was gradually increased to 160–170 °C. The first fraction was then carefully fractionated by distillation through a 17 mm × 40 cm column packed with glass helices and surrounded by a 5 cm × 40 cm glass insulating jacket which can be heated by a nichrome wire helix with approximately 1 turn per cm. The product boiling in the range 100–118 °C was collected as *N,N*-dimethylacetamide dimethyl acetal. During the redistillation of the first fraction, methanol distilled first. Then the fractionating column was gradually and gently heated as needed to allow distillation of the desired *N,N*-dimethylacetamide dimethyl acetal. This product, 162 g, shows $n^{20}{}_D$ 1.4158. The ^1H NMR spectrum of this product in $CDCl_3$ shows resonances associated with the desired *N,N*-dimethylacetamide dimethyl acetal at δ 1.2 (3 H, s), 2.27 (6 H, s), 3.2 (6 H, s). In addition, a few very small resonances appear at δ 1.43, 2.57, 3.27, and 3.6 owing to minor impurities. The second fraction, collected under aspirator vacuum, was also carefully fractionated by distillation at atmospheric pressure through the glass helices-packed column. The product boiling in the range 110–118 °C was collected as *N,N*-dimethylacetamide dimethyl acetal: 221 g; $n^{20}{}_D$ 1.4118. This light yellow oil shows ^1H NMR resonances in $CDCl_3$ at δ 1.2, 2.27, 3.2 only (vide supra). The total yield, 383 g, is 59%.

Acknowledgment. We thank the National Science Foundation for generous financial support.

Registry No. Me_2SO_4, 77-78-1; $CH_3C(O)NMe_2$, 127-19-5; $CH_3C(O)NMe_2$–Me_2SO_4, 920-98-9; MeONa, 124-41-4; $CH_3C(OMe)_2NMe_2$, 18871-66-4.

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(6) A similar synthesis is suggested in footnote 3 of ref 1a.

[7] The precipitate of NaO_3SOCH_3 became too heavy to stir.

[8] Measured with an iron–constantan thermocouple.

Communications

Structure of Aphanamol I and II

Summary: Unique sesquiterpenoids, named aphanamol I and II, have been obtained from a Meliaceous plant *Aphanamixis grandifolia* as minor toxic principles. Structures **1** and **2** were established by spectral study, in which the two-dimensional NMR pulse sequence COSY/COSY-45 takes an essential role.

Sir: In a series of investigation of Indonesian tropical plant constituents showing interesting biological properties, much interest has been focused on toxic principles of various Meliaceous plants which have traditionally been employed as fish or dart arrow poisons.[1,2] *Aphanamixis grandifolia* is a timber tree of *Meliaceous* family occuring in Java, Indonesia, and produces poisonous fruits. Extraction of this fruit peel afforded three kinds of active constituents. The major toxic component was a known triterpenoid, aphanamixin, which was already reported as a constituent of a related species, *A. polystachya*.[3] The minor toxic compounds were found to be new hydroazulene-type sesquiterpenoids with a unique carbon

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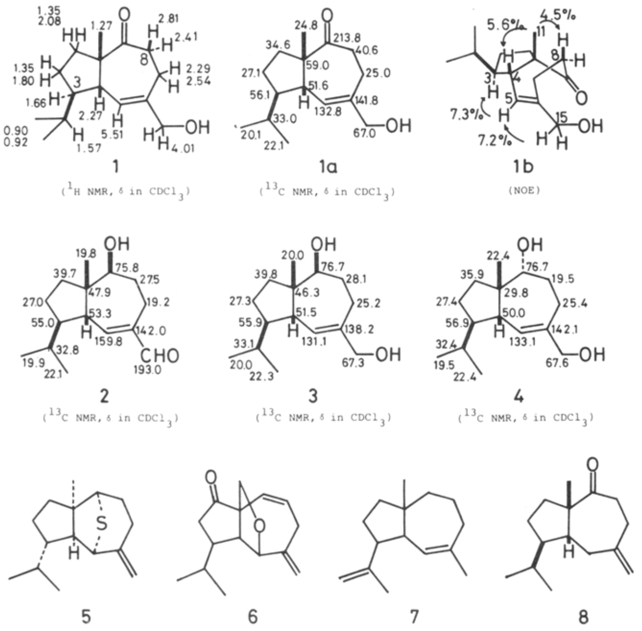
[1] Nishizawa, M.; Nishide, H.; Hayashi, Y.; Kosela, S. *Tetrahedron Lett.* **1982**, *23*, 1349; *J. Org. Chem.* **1983**, *48*, 4462.

[2] Nishizawa, M.; Inoue, A.; Sastrapradja, S.; Hayashi, Y. *Phytochemistry* **1983**, *22*, 2083.

[3] Chatterjee, A.; Kundu, A. B. *Tetrahedron Lett.* **1967**, 1471.

0022-3263/84/1949-3660$01.50/0

Chart I



skeleton. Herein described are the isolation and structure determination of two new sesquiterpenoids named aphanamols I and II.

Dried peel (1.15 kg) of *A. grandifolia* was crushed and extracted with hexane in a Soxhlet apparatus for 48 h to give a crude extract (136 g). Fractionation was always monitored by toxicity against fish, *Oryzias latipes*. The major constituent aphanamixin, showing a toxicity of LC$_{50}$ 0.06 ppm (48 h), was easily isolated by silica gel column chromatography followed by recrystallization in ca. 1.1% yield. The minor toxic components, aphanamols I and II, were isolated after consecutive purification by normal phase (silica gel, hexane–ethyl acetate) and reverse phase (Fuji-Devison Micro Beads Silica Gel 5D-ODS, 100–200 mesh, acetonitrile–water) column chromatography and finally by HPLC (Nomura Chemicals Develosil ODS-5 column, Altex RI detector, acetonitrile–water).

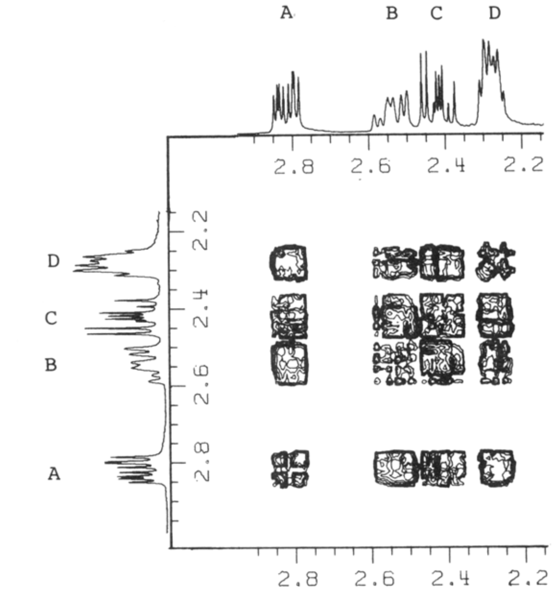


Figure 1. COSY NMR.

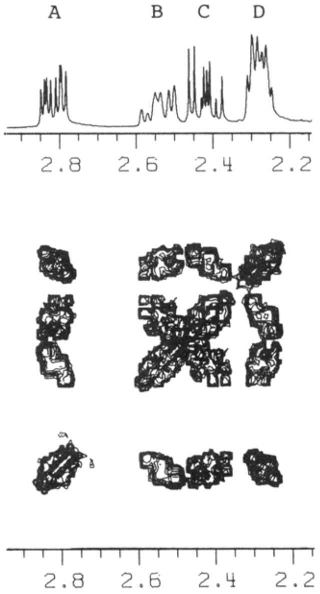


Figure 2. COSY-45 NMR.

Table I. Relative Sign of Coupling Constants[a]

J(A,B) and J(A,C)	opposite signs
J(A,B) and J(A,D)	like signs
J(A,B) and J(B,C)	like signs
J(A,B) and J(B,D)	opposite signs
J(A,C) and J(A,D)	opposite signs
J(A,C) and J(B,C)	opposite signs
J(A,C) and J(C,D)	opposite signs
J(A,D) and J(B,D)	opposite signs
J(A,D) and J(C,D)	like signs
J(B,C) and J(B,D)	opposite signs
J(B,C) and J(C,D)	like signs
J(B,D) and J(C,D)	opposite signs

[a] A–D indicate the proton signals at C-7 and C-8. See also the spectra of Figures 1 and 2.

Aphanamol I (1) (Chart I), obtained as colorless oil [0.015% yield; LC$_{50}$ 28 ppm (48 h); $C_{15}H_{24}O_2$; $[\alpha]^{18}_D$ +13.8° (c 0.29, CHCl$_3$)] showed hydroxyl (3400 cm^{-1}) and carbonyl (1690 cm^{-1}) absorption in the IR spectrum. The ^{13}C NMR spectrum (CDCl$_3$) revealed the presence of three methyls (δ 19.9, 22.1, and 24.7), five methylenes (δ 25.0, 27.1, 34.6, 40.0, and 67.0), three methines (δ 33.0, 51.5, and 56.1), and a quaternary carbon (δ 59.0). A pair of sp^2 carbon signals (δ 132.7 and 141.8) is attributed to a trisubstituted double bond. A signal due to the carbonyl carbon at δ 213.8 is characteristic to a saturated ketone. Two of the methyl groups correspond to an isopropyl group since a pair of doublets appears in the ^{1}H NMR spectrum (δ 0.90 and 0.91, J = 7 Hz). The other methyl group gives a sharp signal (δ 1.22), connecting to the sole sp^3 quaternary carbon. The assignment of all protons as shown in formula 1 was achieved by two-dimensional homonuclear J-correlated spectroscopy, COSY and COSY-45. The latter, a relatively new NMR pulse sequence, is particularly useful in order to assign a complicated pattern of ^{1}H NMR signals such as a pair of methylene groups.[4] The proton signals due to H-7 and H-8 were observed in the region δ 2.25–2.85, which revealed the typical pattern of a four-spin system in the COSY (90°–t_1–90°–t_2) spectrum (A–D in Figure 1). Two pairs of the signals, (A, C) and (B, D), were assigned to H-7 and H-8, respectively, by determining the relative sign of the coupling constants (Table I) in the COSY-45 (90°–t_1–45°–t_2) spectrum[4] (Figure 2) and proton NOE. On the basis of the assignment of all proton signals, carbon signals were also assigned by chemical shift correlated

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[4] Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542.

spectroscopy (CSCM)[5] as shown in formula **1a**. Thus, the presence of two CH_2CH_2 groups in a bicyclic system along with a carbonyl, a trisubstituted double bond, a quaternary methyl, and an isopropyl moiety strictly represents the 5/7 ring system for aphanamol I as in formula **1**. The stereochemistry was determined by proton NOE experiments. Upon irradiation of the angular methyl protons (H-11) at δ 1.27, significant enhancement was observed of the H-4 (δ 2.27) and H-8β (δ 2.81) signals. Another strong NOE was detected between H-3 (δ 1.66) and the sole vinyl proton (H-5, δ 5.51). Structure **1b** is the conformation consistent with the spectral observations.

Aphanamol II (**2**) was obtained as colorless oil in 0.005% yield [LC_{50} 27 ppm (48 h); $[\alpha]^{18}{}_D$ +6.9° (*c* 0.94, $CHCl_3$); IR (neat) 3450, 2720, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (3 H, d, *J* = 7 Hz), 0.93 (3H, d, *J* = 7 Hz), 1.04 (3H, s), 3.40 (1 H, dd, *J* = 11, 6 Hz), 6.62 (1H, d, *J* = 5 Hz), 9.37 (1H, s); ^{13}C NMR shown in formula **2**]. From this evidence, combined with the spectral correlation with aphanamol I (**1**), an α,β-unsaturated aldehyde structure **2** is derived.

When aphanamol II (**2**) was treated with $LiAlH_4$ in ether, diol **3** was obtained quantitatively. The identical diol was formed from aphanamol I (**1**) by $LiAlH[OC(CH_3)_3]_3$ reduction as a minor product along with the epimeric diol **4** (1:4 ratio). Considering the conformation of the parent ketone **1b**, preferential hydride attack on the carbonyl group should take place from the less hindered β-face, affording α-alcohol **4** as the major product. Therefore, the *sec*-hydroxyl group of **2** is assigned the β-orientation. These assignments are also in agreement with the coupling pattern of the carbinyl protons of the epimers (δ 3.43, dd, *J* = 11, 6 Hz for **3**, and δ 3.51, dd, *J* = 5, 3 Hz for **4**) and the observed NOE (3.13%) between H-11 (δ 1.06) and H-9 (δ 3.51) in the major alcohol **4**.

The structure of the aphanamols represents a very rare type of carbon skeleton for naturally occurring sesquiterpenoids. Recently, the structure of a component of peppermint oil, mintsulphide, was established as **5** by X-ray analysis.[6] A sexual stimulant of the American cockroach, periplanone A (**6**), is also postulated to have the same carbon framework.[7] In connection with the possible biogenesis of the aphanamols, it may be noted that the skeletally related compounds **7** and **8** are produced by acidic rearrangement of humulene[8] or epoxygermacrene D,[9] respectively.

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Registry No. **1**, 91410-61-6; **2**, 91410-62-7; **3**, 91410-63-8; **4**, 91464-56-1.

Supplementary Material Available: Full spectral data of compounds **1**–**4** (4 pages). Ordering information is given on any current masthead page.

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Heteroannulation via Intramolecular (π-Allyl)palladium Displacement

Summary: Conjugated and nonconjugated dienes, as well as vinylcyclopropanes, react with $LiPdCl_3$ and organomercurials bearing carboxylic acid, phenol, alcohol, and amide functionality to generate (π-allyl)palladium compounds which readily undergo intramolecular displacement of palladium upon addition of an appropriate base to give a wide variety of oxygen and nitrogen heterocycles.

Sir: (π-Allyl)palladium compounds have recently become very valuable intermediates in organic synthesis.[1,2] The majority of synthetic applications have involved displacement of the palladium moiety by either stabilized carbon nucleophiles[3-8] or amines.[9-15] Relatively little work has been reported on analogous alkoxide,[16-18] aryl oxide,[16] or carboxylate[19,20] processes. We report a convenient, new,

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