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An Analysis of the Structures and Electronic Properties of the Isomeric 1,2-Bis(cyanomethylene)cyclobutanes

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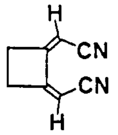
In the Ni(0)-complex-mediated reactions of cyanoallene (CNA) and the cycloaddition reactions of CNA with dienophiles, cyclodimers of CNA have been isolated possessing the 1,2-bis(cyanomethylene)cyclobutane structure. Differentiation between the *E,E* and *Z,Z* stereoisomers was not possible on the basis of NMR or UV spectral data. As it was necessary to distinguish between the two stereoisomers for mechanistic reasons, X-ray diffraction studies have been carried out. The results of the X-ray diffraction studies surprisingly show that the *Z,Z* isomer (1) exists in an all-planar conformation in which considerable bond-angle distortions are present. Geometry optimization MO calculations affirm that the all-planar structure of 1 represents an energy minimum and predict bond angles very close to the experimental values. The experimental and theoretical results indicate that in 1 the CC≡N and CH_2C=C angles are distorted in an outward manner. The experimental and theoretical data for the *E,E* isomer 2 indicate all bond angles to be of more normal magnitude. Theoretical calculations have been carried out on model fragments of 1 and 2 in order to assess the various bond angle deformation energies and the long-range repulsion energy between the two cyano groups of 1. It is concluded that the bond-angle deformations, which total a surprisingly small 1.60 kcal/mol in 1 compared to 2, and the long-range electronic repulsion are less than the loss in π delocalization and induced ring strain incurred on skewing the diene chromophore and/or twisting about the double bonds.

Recent investigations in our laboratories have focused on features of the cycloaddition reactions of substituted allenes[1] and coupling reactions induced by tris(triphenylphosphine)nickel(0).[2] In the cycloaddition reactions with cyanoallene (CNA) competitive cyclodimerization of CNA occurs to produce a mixture of three cyclodimers. In the reaction of CNA with the Ni(0) complex two cyclodimers are formed.[2] The NMR spectra of the cyclodimers indicated that two possessed an internal plane or axis of symmetry, while the third did not. The UV spectra indicated that all three cyclodimers contained a conjugated diene system, limiting the possible structures of those shown as 1–3. Although the NMR spectrum of the unsymmetrical isomer 3 showed the characteristic difference between cis and trans long-range allylic coupling constants,[3] the long-range coupling constants in the spectra of the two symmetrical isomers were within experimental error, and an unambiguous assignment of stereochemistry was not possible. It was initially thought that perhaps the diene chromophore of 1 was skewed which might affect the magnitude of the long-range coupling constant between the vinyl and ring-methylene hydrogens. The presence of skewing of the diene chromophore, however, was not evident from the UV data. The unsymmetrical isomer 3 showed extensive fine structure with maximum absorption at 281 nm (see paragraph at the end of paper about supplementary material). The UV spectrum of one of the symmetrical isomers was virtually identical, showing the same fine structure with maximum absorption at 281 nm. The UV spectrum of the other symmetrical isomer did not show any vibrational fine structure, but displayed a maximum at 280 nm. If the diene chromophore of 1 is appreciably skewed, its maximum absorption would have appeared at a much shorter wavelength. Thus, the available NMR and UV data did not allow for an unambiguous distinction between 1 and 2. As it was necessary to know the stereochemistries of the cyclodimers derived from the two reactions for mechanistic reasons, it was necessary to differentiate between the two symmetrical cyclodimers by X-ray diffraction techniques. The interestingly distorted, all-planar structure derived for 1 prompted further PES and theoretical studies on 1–3, the results of which are reported herein.



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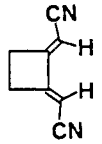

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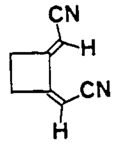

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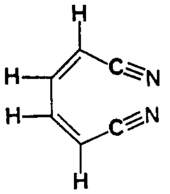

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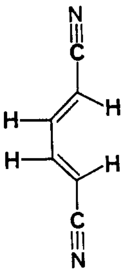

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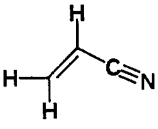

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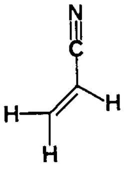

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X-ray Diffraction Results. The results of X-ray diffraction studies on 2 show that the molecule is planar, deviations from the least-squares planes being about 0.01 Å (see paragraph at the end of paper about supplementary material). The observed bond lengths and angles are given in Table I. The CC≡N average bond angle of 178 (1)° suggests a very slight nonlinearity. (For average values the number in parentheses is the standard deviation for the average). The CH_2C=C average bond angle of 134 (1)° is close to that expected for a nondistorted methylenecyclobutane of 135°. The C=CCN average bond angle of 118.9 (7)° indicates very little distortion about this bond angle.

The results of the X-ray diffraction studies on 1 indicate that this structure is also completely planar (as is required by the symmetry of the space group). The CC≡N bond angles are slightly distorted in an outward manner, having

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[1] For the most recent article see: Pasto, D. J.; Yang, S.-H *J. Am. Chem. Soc.* **1984**, *106*, 152.

[2] Pasto, D. J.; Huang, N.-Z. *J. Am. Chem. Soc.* **1985**, *107*, 3160.

[3] See ref 1 for examples.

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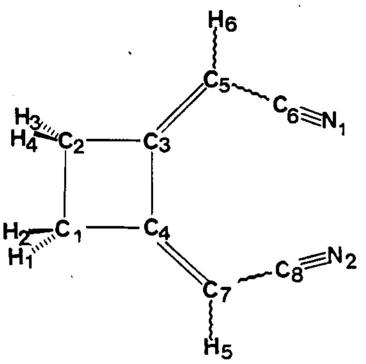
Table I. Experimental and Calculated Structural Parameters for 1, 2, and 3



	1		2[a]		3
	exptl[b]	STO-3G	exptl	STO-3G	STO-3G
			Bond Lengths (Å)		
C_1–C_4	1.499 (4)	1.533	1.519 (5), 1.514 (5)	1.533	1.524
C_4–C_7	1.335 (5)	1.322	1.333 (5), 1.319 (5)	1.321	1.322 (*Z*)
C_7–C_8	1.395 (4)	1.454	1.441 (6), 1.415 (6)	1.455	1.456
C_8–N_2	1.137 (4)	1.157	1.142 (5), 1.176 (5)	1.157	1.157
C_1–C_2	1.560 (6)	1.558	1.572 (6), 1.575 (6)	1.560	1.559
C_3–C_4	1.487 (4)	1.501	1.462 (5), 1.460 (5)	1.494	1.496
C_2–C_3	1.492 (5)	1.533	1.524 (5), 1.542 (5)	1.533	1.524
C_3–C_5	1.343 (5)	1.322	1.333 (5), 1.320 (5)	1.322	1.321 (*E*)
C_5–C_6	1.402 (6)	1.454	1.441 (6), 1.405 (5)	1.454	1.455
C_6–N_1	1.139 (5)	1.157	1.140 (6), 1.156 (6)	1.157	1.157
$C_{1(2)}$–$H_{1,2(3,4)}$		1.088		1.089	1.088
C_7–H_5		1.084		1.085	1.085
C_5–H_6		1.084		1.085	1.085
			Bond Angles (deg)[b]		
C_2–C_1–C_4	88.4 (3)	88.92	88.0 (3) 88.3 (3)	88.77	88.81
C_1–C_2–C_3	88.8 (3)	88.92	87.9 (3) 87.3 (3)	88.77	88.90
C_1–C_4–C_3	91.3 (3)	91.08	92.2 (3) 92.7 (3)	91.23	91.20
C_1–C_4–C_7	130.6 (3)	126.85	135.6 (4) 132.3 (4)	135.21	134.11
C_4–C_7–C_8	126.9 (3)	126.85	119.1 (4) 118.8 (4)	122.64	122.93
C_7–C_8–N_2	175.0 (4)	176.73	179.1 (5) 177.4 (5)	180.00	179.88
C_2–C_3–C_4	91.4 (3)	91.08	92.0 (3) 91.6 (3)	91.23	91.19
C_2–C_3–C_5	131.6 (3)	130.58	133.3 (4) 133.0 (4)	135.31	134.90
C_3–C_4–C_7	138.1 (3)	138.34	132.2 (4) 134.9 (3)	133.56	134.71
C_3–C_5–C_6	128.0 (3)	126.35	118.0 (4) 119.6 (4)	122.64	122.31
C_4–C_3–C_5	137.0 (3)	138.34	134.7 (4) 135.4 (3)	133.56	133.91
C_5–C_6–N_1	176.5 (4)	176.73	177.0 (5) 178.6 (4)	180.00	180.00
C_1–C_2–$H_{1(2)}$		110.93		114.79	114.75
C_1–C_2–$H_{3(4)}$		110.93		110.93	114.75
C_4–C_7–H_5		118.86		121.25	121.11
C_3–C_5–H_6		118.86		121.25	121.62

[a] Values provided are for molecule 1 of the two molecules in the asymmetric unit and the analogous values for molecule 2. [b] Values in parentheses are estimated standard deviations in the least significant digit. [c] The C_3–C_2–C_1–$H_{1(2)}$ and C_4–C_1–C_2–$H_{3(4)}$ dihedral angles in 1, 2, and 3 are, respectively, 60.92, 63.79, and 63.73°.

values of 176.5 (4) and 175.0 (4)°. The C=CCN bond angles (C_4–C_7–C_8 and C_3–C_5–C_6 angles in Table I) are significantly distorted, being 126.9 (3) and 128.0 (3)° compared to the average of 118.9 (7)° in 2. The CH_2C=C bond angles (C_1–C_4–C_7 and C_2–C_3–C_5) also show an outward distortion, being reduced in value to 130.6 (3) and 131.6 (3)° compared to the average of 134 (1)° in 2. Even with these distortions the N_1–N_2 nonbonded distance is a rather short 3.185 (5) Å. It is obvious that for 1 to exist in an all-planar conformation the observed distortions are necessary to increase the N_1–N_2 nonbonded distance. The all-planar structure of 1 in the crystalline state does not appear to be due to packing forces in the crystal lattice as the results of theoretical studies also indicate that the all-planar structure of 1 is an energy minimum structure.

Photoelectron Spectroscopic (PES) Studies. The PES spectra of 1–3 have been recorded in order to determine what effect the proximity of the two cyano groups in 1 has on the electronic structure of 1 compared to 2 and 3. The PES spectra are reproduced in Figure 1, and the ionization potentials (IP) of the first four bands are given in Table II. The vertical IP's of the first two bands of 1–3 are all quite similar, and show extensive vibrational fine structure (see paragraph at the end of paper about supplementary material). There is an obvious large splitting in the order of 1400–1500 cm^{-1} characteristic of a C=C vibration suggesting ionization from a π MO having dominant C=C character. Further analysis and assignment of the vibrational fine structure is not reasonable or warranted in view of the large number of modes available to 1–3.[4]

Table II. Ionization Potentials of the First Four Bands of 1–3

	ionization potential, eV[a]		
band	1	2	3
1	9.41 (9.35)	9.59 (9.40)	9.60 (9.50)
2	11.02 (10.66)	11.45 (10.95)	11.19 (10.99)
3	11.34	11.66	11.60
4	11.9	12.0	12.0

[a] Adiabatic IP's are given in parentheses.

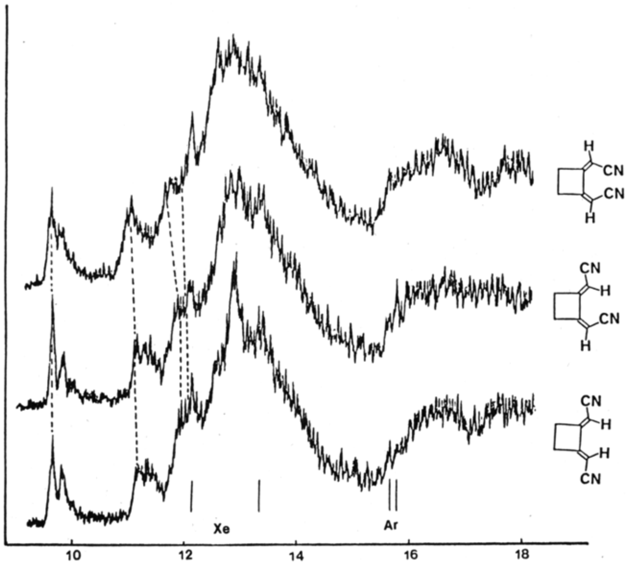


Figure 1. Photoelectron spectra of **1**, **2**, and **3**.

Table III. Total Energies (3-21G/STO-3G) for 1–11

structure	total energy, au	
	STO-3G (opt)	3-21G/STO-3G
1	−410.094 36	−412.922 86
2	−410.106 61	−412.935 77
3	−410.106 52	−412.936 64
4		−336.430 79
5		−336.436 87
6		−168.795 75
7		−168.790 07
8		−92.352 41
9		−92.352 58
10		−230.498 10
10 (distorted)		−230.491 60
11		−184.698 74

The IP of the third band is much lower in **1** than in **2** and **3**, and shows prominant vibrational fine structure. The large change in the IP of this band in **1** suggests the presence of a large long-range interaction between more localized MO's on the two cyano groups, specifically the antisymmetric combination of the in-plane π MO's. The fourth band changes only little in energy and also shows little vibrational fine structure. This band is assigned to ionization from the symmetric combination MO of the in-plane π MO's of the cyano groups. These band assignments are supported by the results of theoretical calculations described in the following section.

Theoretical Calculations on 1–3 and Partial Fragments. Theoretical calculations have been carried out on **1**, **2**, and **3**. Complete geometry optimization calculations were carried out on **1**, **2**, and **3** at the STO-3G level. Single-point calculations were then carried out at the 3-21G level on the STO-3G optimized structures (see paragraph at the end of paper about supplementary material). The total energies of **1–3** are given in Table III, and the calculated geometrical parameters are given in Table I.

The calculated geometries for **1** and **2** compare very favorably with those determined by the X-ray diffraction studies, particularly the C–C–C and C–C–N bond angles (see the bold-face values in Table I). The calculations on **1** indicate that the all-planar structure is an energy minimum structure, which in turn indicates that the all-planar structure of **1** in the crystalline state is not due to crystal packing forces. At the optimized STO-3G level **2** and **3** differ only very slightly in energy, with **2** being lower in energy. The single-point 3-21G/STO-3G calculations indicate that **3** is slightly lower in energy. The *Z,Z* isomer **1** lies 8.10 kcal/mol above the *E,E* isomer **2**.

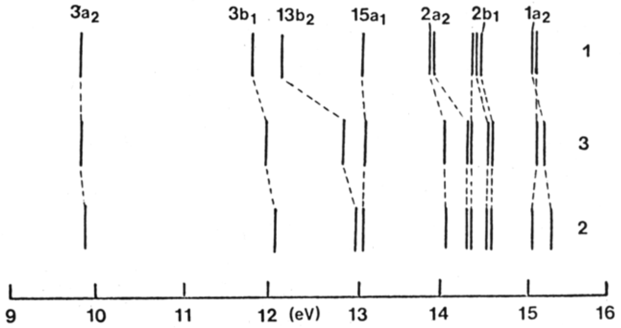
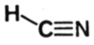


Figure 2. Correlation of π MO's of **1**, **2**, and **3**.

The energies of the higher lying occupied MO's are graphically presented in Figure 2. The changes in energy of the four highest occupied MO's correspond very closely with those observed in the PE spectra supporting the proposed assignment of these bands.

In order to derive an estimation of the strain energies involved in the bond angle distortions in **1** and to gain an understanding of the orbital interactions in **1–3**, single-point calculations were carried out at the 3-21G level on the model fragments **4–11** in which hydrogen atoms have replaced carbon atoms in **1** and **2** with r_{C-H} of 1.08 Å and the H–C–X (X = C or N) angles being the same as the C–C–X angles in **1** and **2**. The remaining bond lengths and angles were kept the same as in the optimized structures for **1** and **2**. The total energies of **3–11** are given in Table III.



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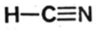

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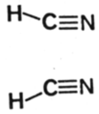

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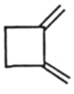

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The calculations on bent (from **1**) and linear HCN (from **2**) indicate an energy difference of only 0.11 kcal/mol.[5] Fragments **6** and **7** differ by only 0.20 kcal/mol. If the $CC{\equiv}N$ bond angle deformation energy is assumed to be same as in HCN, the $C{=}CC$ bond angle deformation energy is 0.09 kcal/mol. In order to estimate the exocyclic bond angle deformation energy, STO-3G optimization calculations were carried out on 1,2-dimethylenecyclobutane (**10**). The calculations give a value of 134.66° for the $CH_2C{=}C$ bond angle, which is quite close to the experimental and calculated values of 135.6° and 135.21° for **2**. Single-point calculations were carried out on **10** and a distorted **10** in which the $CH_2C{=}C$ angle was distorted by 4.62 (the difference in the optimized angles in **1** and **2**). The calculated bond angle deformation energy is 1.20 kcal/mol, which represents the distortion energy of both double bonds in **10**. The total bond angle deformation energy in **1** relative to **2** is therefore 2(0.11 + 0.09) + 1.20, or 1.60 kcal/mol; a rather surprisingly small value.

The calculated difference in energy between fragments **4** and **5** is 3.81 kcal/mol which is the sum of the bond angle

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(4) The distortions present in **1** are not evident in the IR spectrum of **1** compared to the IR spectra of **2** and **3**. The $C{\equiv}N$ and $C{=}C$ stretching frequencies are virtually identical (see Experimental Section), and the bending deformation frequencies show no correlatable trend.

(5) The $={CC}{\equiv}N$ bending frequency in acrylonitrile is at 242 cm^{-1} (Halverson, F.; Stamm, R. F.; Whalen, J. J. *J. Chem. Phys.* **1948**, *16*, 808) indicative of a rather small force constant and consistent with the small calculated bending deformation energy.

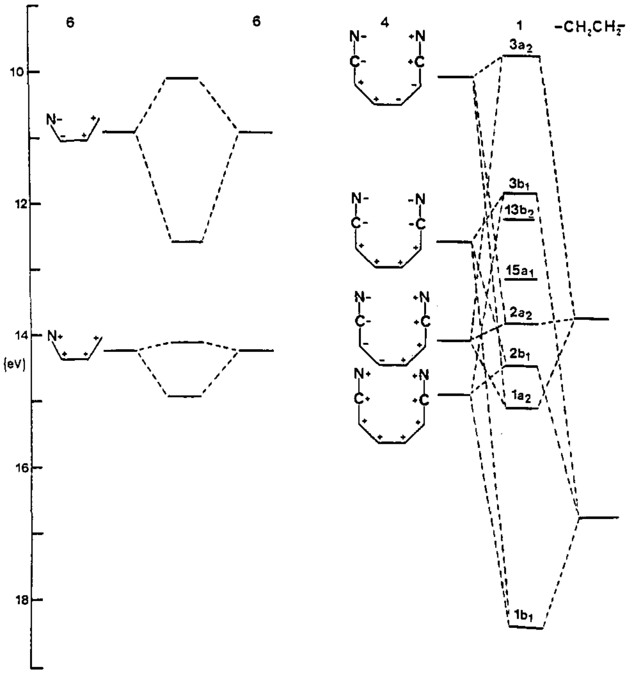

Figure 3. π MO correlation diagram for fragment interactions in 1.

deformation energies and the through-space and through-bond electronic interactions. Subtracting the bond angle deformation energies gives a value of 2.21 kcal/mol for the repulsive electronic interactions. The resulting splitting between the symmetric (CN_+) and antisymmetric (CN_-) combinations of the in-plane π MO's of the cyano groups in 4 is 0.908 eV. A comparison of the results of calculations on 11 and 8 indicate a through-space repulsive interaction of 4.02 kcal/mol, with a splitting between the CN_+ and CN_- MO's of 1.15 eV, and between the π_+ and π_- MO's of 0.182 eV. (The 2p AO coefficients in 11 are considerably larger than 4 resulting in a larger long-range interaction).

The calculated energy difference between 1 and 2 is 8.10 kcal/mol. Subtracting the bond angle deformation energy gives a value of 6.50 kcal/mol for the long-range repulsion energy in 1. This value is significantly larger than in 4 and 11. The splitting beteen the CN_+ and CN_- MO's is 0.899 eV, essentially the same as in 4. The summed Mulliken populations for the in-plane AO interactions between the C and N atoms are also virtually identical, being −0.003 17 in 1 and −0.003 13 in 4. The cause of the increase in the long-range repulsion in 1 is not immediately evident, but must be of a through-bond nature arising from the mixing of the orbitals of the $-CH_2CH_2-$ fragment with those of 4.

The interactions between the π MO's of the fragments are illustrated in Figure 3. Although the figure is based on the formation of the π MO's of 1, the π interactions shown are representative of 2 and 3 also, in that there is little difference in the energies of the π MO's of 1, 2, and 3. It is important to note the strong interactions between the π-type MO's of the $-CH_2CH_2-$ fragment with the π MO's of 4 which elevate the energies of the $3b_1$ and $3a_2$ MO's. In the absence of these interactions the $13b_2$ MO of 1 would lie above the $3b_1$ MO and would be very close to the energies of the $3b_1$ MO's in 2 and 3.

Summary

The total "strain" energy in 1 is relieved to a certain extent by bond angle deformations. The remaining "strain" energy is not sufficient to cause skewing of the diene or twisting about the double bonds resulting in a nonplanar structure. Skewing and twisting would result in a loss in π delocalization energy, as well as inducing strain energy due to a resultant twisting of the four-membered ring. These sacrifices in energy must be greater than the resulting "strain" energy in the all-planar structure of 1.

Experimental Section

Cyclodimerization of Cyanoallene (CNA). A solution of 44 mg of CNA and 40 mg of hydroquinone in 0.5 mL of toluene was placed in a heavy-walled glass tube. The contents of the tube were triply freeze degassed and sealed under vacuum. The tube was heated in a sand bath at 140 °C for 24 h, during which time a small amount of a dark viscous oil separated.

The contents of the tube were removed and the toluene solution was decanted from the dark oil. The toluene was removed under reduced pressure. The residue was separated by rotating disk chromatography using a 1-mm thick silica gel plate eluting with pentane–methylene chloride mixtures giving three fractions.

Fraction 1 (3): mp 75–77 °C (from pentane–methylene chloride); NMR ($CDCl_3$) δ 2.95 (m, 2 H), 3.05 (m, 2 H), 5.30 (br t, J = 2.12 Hz, 1 H), and 6.19 (br t, J = 2.65 Hz, 1 H); UV (95% ethanol) 272 (sh, log ϵ 4.17), 281 (log ϵ 4.26), and 294 nm (log ϵ 4.15); IR ($CHCl_3$ and CH_3CN) 2218, 1630 (br), 1418, 1410, 1316, 1191, 1125, 831, 722, 304 cm^{-1}; MS, exact mass calcd for $C_8H_6N_2$ 130.053, found 130.052.

Fraction 2 (1): mp 101–103 °C from (pentane–methylene chloride); NMR ($CDCl_3$) δ 2.87 (br d, J = 1.37 Hz, 4 H) and 5.36 (br s, 2 H); UV (95% ethanol) 280 nm (log ϵ 3.94); IR ($CHCl_3$ and CH_3CN) 2221, 1624 (br), 1414, 1347, 1109, 822, 722, 527, 489, and 280 cm^{-1}; MS, exact mass calcd for $C_8H_6N_2$ 130.053, found 130.053.

Fraction 3 (2): mp 98–100 °C (from pentane–methylene chloride); NMR ($CDCl_3$) δ 2.97 (br t, $J \approx$ 1.0 Hz, 4 H) and 5.62 (br s, 2 H); UV (95% ethanol) 273 (sh, log ϵ 4.18), 280 (log ϵ 4.22), and 293 nm (log ϵ 4.10); IR ($CHCl_3$ and CH_3CH) 2219, 1624 (br), 1436, 1419, 1409, 1310, 1193, 1190, 812, 722, 696, 543, and 322 cm^{-1}; MS, exact mass calcd for $C_8H_6N_2$ 130.053, found 130.052.

X-ray Crystallographic Study of 1. An irregularly shaped, clear, colorless crystal (approximately 0.3 × 0.3 × 0.2 mm) was glued to a glass fiber and mounted on a Enraf-Nonius CAD4 diffractometer. It was oriented and cell parameters were calculated by the least-squares fit of 25 reflections between 18° and 30° in 2θ. (Mo K$\bar{\alpha}$ = 0.710 73 Å). Axial photographs confirmed orthorhombic symmetry. From the systematic absences of $0kl$ ($k + 1 = 2n$), $hk0$ ($h = 2n$), $h00$ ($h = 2n$), $0k0$ ($k = 2n$, and 001 ($1 = 2n$), the space group was determined to be either $Pnma$ or $Pn2_1a$. The structure was solved and refined satisfactorily in $Pnma$ (no. 62). A summary of crystal and data collection appear in the supplementary material.

A total of 993 (888 unique) $-h,+k,+l$ refections were collected to 2θ = 54.9° using the $\theta/2\theta$ scan technique. Intensity standards showed no significant trend. No absorption correction was applied. The 502 reflections having $F_o^2 > 2.0\sigma(F_o^2)$ were used in the final refinement.

X-ray Crystallographic Study of 2. An irregularly shaped, colorless crystal (approximately 0.4 × 0.2 × 0.1 mm) was glued to a glass fiber and oriented as described above using 25 reflections between 20 and 27° in 2θ. The crystal system proved to be triclinic. The structure was solved and refined in $P\bar{1}$ (No. 2).

Two crystals were required to complete data collection due to decay. A total of 1462 $+h,\pm k,\pm l$ reflections were collected on the first crystal to 2θ = 39.7° using the $\theta/2\theta$ scan technique. Approximately 100 extra data were collected between 39.7° and 45.7° in 2θ and were used to calculate a scaling factor for data from a second crystal (approximately 0.3 × 0.3 × 0.1 mm). The 1462 reflections were corrected for linear decay (maximum correction factor 1.0943) and equivalent reflections averaged. (R = 1.0% based on F_o). A total of 1085 $+h,\pm k,\pm l$ reflections were collected on the second crystal between 39.7° and 48.3° in 2θ. The 1085 reflections were corrected for linear decay (maximum correction factor 1.0914) and equivalent reflections averaged (R = 4.7% based on F_o). Ten strong reflections common to both data sets were used to calculate the rescaling factor $F_o(1)/F_o(2)$ = 0.89. All F_o's and $\sigma(F_o)$'s from the second crystal were multiplied by this factor.

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As a check on the rescaling, the two partial data sets from which the rescaling factor was calculated were averaged. The 160 averaged reflections have $R = 5.5\%$ based on F_o. The merged data sets provided 2363 unique data. No absorption correction was applied. The 1302 reflections having $F_o^2 > 3.0\sigma(F_o^2)$ were used in the final refinement.

Structure Solution and Refinement. Both structures were solved by direct methods. Hydrogen atoms were not included in either structure. For **1**, all atoms were treated anisotropically. For **2**, only one of the two molecules present in the asymmetric unit was treated anisotropically. Atomic scattering[6] and anomolous depression[7] factors were from usual sources. The final full-matrix least-squares refinements converged to $R = \sum||F_o| - |F_o||/\sum|F_o| = 0.102$ for **1** and 0.100 for **2** and $R_w = [\sum w(|F_o| - |F_o|)^2|\sum w/F_o|^2]^{1/2} = 0.135$ for **1** and 0.138 for **2**. For **1** there were 61 parameters and 502 observations; for **2** there were 131 parameters and 1302 observations. The weighting scheme used in the minimization of $\sum w(|F_o| - |F_o|)^2$ is defined as $w = 1/\sigma^2(F_o)$ where $\sigma^2(F_o)$ includes a factor ($p = 0.06$) introduced to downweight intense reflections, in addition to the contribution from counting statistics. In both structures, the residuals showed no anomalies. The largest peak in the final difference Fourier map was 0.30 e/Å^3 for **1** and 0.47 e/Å^3 for **2**.

Measurement of the Photoelectron Spectra. The He I (21.2 eV) photoelectron spectra were recorded using a spectrometer whose configuration has been described previously.[8,9] The instrument was initially calibrated using a 50/50 mixture of Xe/Ar gas and in all cases a resolution of 35 meV or better was achieved relative to Xe (fwhm). Individual band positions were determined using Xe (12.13 and 13.44 eV) and Ar (15.76 eV) as *A* references. All three samples were air-stable at room temperature and it was necessary to apply heat in order to produce sufficient vapor pressure to obtain a spectrum. Minimal temperatures necessary to achieve sublimation were used. These temperatures were 75 °C for **1**, 50 °C for **2**, and 30 °C for **3**. In all cases, samples sublimed cleanly with no evidence of decomposition being seen, i.e., production of HCN.

Supplementary Material Available: A figure showing the UV absorption spectra of **1**–**3**, ORTEP drawings of **1** and **2**, expansions of the first bands of the PE spectra of **1**–**3**, tables of the MO energies of **1**–**11**, table of crystal data for **1** and **2**, and tables of positional parameters, general temperature factor expressions (*B*'s and *U*'s), refined temperture factor expressions (*β*'s), and root-mean-square applitudes of thermal vibrations (12 pages). Ordering information is given on any current masthead page.

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Phyllanthostatin 1-Phyllanthoside Orthoacid Rearrangement[1]

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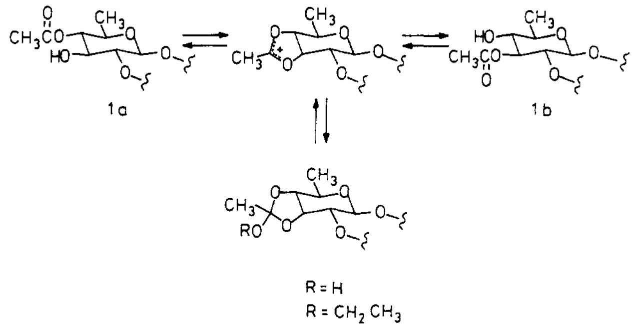
Solvolysis of phyllanthoside (**1b**) in 1:9 ethanol–water (14 days at room temperature) consumed about 54% of the starting glycoside and afforded the S3′-monoacetyl derivative **1f** and phyllanthostatins 1 (**1a**) and 4 (**1e**) in 8–10% yields accompanied by five related products of orthoacid rearrangement and/or deacetylation. Several additional minor transformation products were detected by HPLC analyses. When phyllathostatin 1 (**1a**) was subjected to the same solvolysis reaction for 21.5 h, approximately half rearranged to phyllanthoside (**1b**). After 4 days the product composition resembled that from phyllanthoside. Discovery of the phyllanthostatin 1 ⇄ phyllanthoside orthoacid rearrangement revealed a very important aspect of *Phyllanthus* glycoside chemistry and provided the first examples of O-3 ⇄ O-4 acetyl migrations in a glucopyranoside.

The central American tree *Phyllanthus acuminatus* Vahl (Euphorbiaceae) has been found[2] to contain a series of potentially useful antineoplastic (murine P388 lymphocytic leukemia and B16 melanoma) glycosides. Presently, we have completed the isolation and structural elucidation of four principal members, namely, phyllanthostatins 1–3 (**1a**,**c**, **2**) and phyllanthoside (**1b**).[2] Glycosides **1a** and **1b** have been undergoing detailed evaluation by the U.S. National Cancer Institute (NCI). The major glycoside **1b** has recently been selected for further development toward an eventual clinical trial. During our structural studies of glycosides **1a** and **1b** it became clear that both substances were interconvertible by virtue of intramolecular acetyl group migrations[3] of the orthoacid[4] type (Scheme I). Such neighboring group participation reactions involving acetoxonium ion[5] intermediates (Scheme I) are well known,[6] and recent examples include a very pertinent and interesting study by Weidmann[7] and colleagues of O-4 → O-6 and O-3 ⇄ O-4 acetyl migrations

Scheme I



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