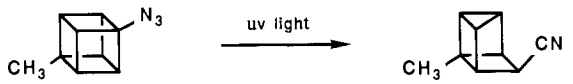

1 4

Nitrile **4** is one of the very few examples of the homoprismane (isoquadricyclane) system[13] and the first, to our knowledge, for which the available spectroscopic information permits an unambiguous assignment of structure:[14] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.18 (m, 2 H), 2.72 (t, 1 H), 2.67 (t, 1 H), 2.58 (m, 2 H), 0.99 (s, 3 H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 120 (s), 55.0 (s), 51.3 (d, J = 161 Hz), 35.2 (d, 188 Hz), 33.5 (d, 145 Hz), 21.1 (d, 184 Hz), 13.9 (q, 125 Hz) ppm; IR (gas) ν 3080, 2236 cm^{-1}.

One obvious possibility for the formation of **4** is that the "expected" azahomocubene **2** forms but is so strained it rearranges before it can be trapped. To examine this possibility, we irradiated azide **1** in a solid argon matrix at ca. 12 K with 290 (±10)-nm light,[11b] following the reaction by infrared spectroscopy. Even at this low temperature, the nitrile appeared immediately. We estimate, using relative extinction coefficients from a spectrum at 12 K of a measured mixture of pure **1** and **4**, that about 65% of the photolyzed azide went directly to **4**.

Infrared absorptions not attributable to **4** also appeared, most conspicuously at 2991, 1140, 802, and 758 (br) cm^{-1} and, less clearly because of overlap with those of **4**, near 1456, 1387, 1268, 1230 (br), and 942 cm^{-1}. All were stable at 12 K in the dark or to further irradiation at 290 nm but diminished very slowly in the dark at 25 K and disappeared after several hours at 32 K. This was accompanied by concomitant growth in the absorptions of **4**. Insofar as could be estimated by integration of the 2240-cm^{-1} CN stretch, at least 15% more **4** was formed.[15] Thus, there appears to be a minor, exceedingly thermally labile compound produced on photolysis of the azide which is precursor to (but not the only source of) nitrile **4**. This might be azahomocubene **2**.[16]

The C=N stretching frequency for **2** has been estimated to be at about 1420 cm^{-1}.[17] Figure 1 shows the changes recorded in the 1400-cm^{-1} region on photolysis of the azide in the matrix at 12 K followed by warming to and holding at 32 K.[18] Absorptions do appear near the predicted value, but these are very weak. Tempting as it may be to assign one of these or one or another of the more prominent absorptions around 1455 or 1385 cm^{-1} to imine **2**, it is not possible to do this with any certainty. In addition to the caveat that the changes seen may be due partly to matrix effects (e.g., annealing), these regions are overly complicated by the symmetric and asymmetric bending absorptions of the methyl substituent on the compounds present. This substituent, deliberately introduced, had otherwise served its purpose well by simplifying the assignment of structures by NMR. Experiments are now underway on the desmethyl compounds derived from cubyl azide itself.

Although future matrix experiments may reveal otherwise, the major path opened by photolysis of azide **1** seems to lead directly to nitrile **4**.[19] Certainly, the direct conversion of **1** to **4** is mechanistically viable.[20] To our knowledge, only azide derivatives of three-membered rings have been reported to give nitriles on photolysis.[21] Sometimes the related imines are also formed[21c] but not as progenitors of the nitriles. Like a cubyl azide, the skeleton of a cyclopropyl azide is severely strained, and the C–C bonds are quite out of the ordinary. Perhaps then, photolysis of **1** does not lead primarily to azahomocubene not because of the difficult geometry of the imine but rather because of the idiosyncratic behavior of highly strained azides.

Acknowledgment. We thank the National Science Foundation (CHE-8118391) and the National Institutes of Health (GM-36436) for support of this work. The NSF and the NIH (CA 14599) provided substantial funding for the departmental instrument facilities. R.E.H. is grateful to the National Institutes of Health for a Pharmacology Training Grant Fellowship.

(13) IUPAC nomenclature: tetracyclo[3.2.0.0^{2,7}.0^{3,6}]heptane.

(14) (a) Cf.: Brember, A. R.; Gorman, A. A.; Sheridan, J. B. *Tetrahedron Lett.* **1973**, *7*, 481. (b) Prinzbach, H.; Herr, H.-J.; Regel, W. *Angew Chem., Int. Ed. Engl.* **1972**, *11*, 131.

(15) Additionally, a new, relatively strong absorption appeared at 755 cm^{-1}. GC/IR and ^{1}H NMR analyses of the photo-/thermolysate, pumped and trapped from the slowly warming matrix, revealed, in addition to **4**, a few percent each of ii and iii, neither responsible for the 755-cm^{-1} band, along with 5–10% of unstable olefins.

(16) Azaadamantene, the most strained of the known azaenes, is stable at least up to 100 K in a polyethylene matrix.[3c]

(17) Calculation courtesy of Prof. J. Michl. The calculated frequencies tend to be higher than those actually observed for the more strained azaenes.[3b,c]

(18) We find no evidence for an imine dimer on further warmup. Cf.: (a) Quast, H.; Eckert, P.; Seiferling B.; Peters, E. M.; Peters, K.; Schnering, H. G. *Chem. Ber.* **1985**, *118*, 3058. (b) Quast, H.; Eckert, P. *Liebigs Ann. Chem.* **1974**, 1727.

(19) We cannot yet eliminate entirely the possibility that inefficient coupling to the monoatomic matrix material delays relaxation of a vibrationally excited imine (cf.: Le Blanc, B. F.; Sheridan, R. S. *J. Am. Chem. Soc.* **1985**, *107*, 4554). However, when the photolysis was repeated with **1** in a 3-methylpentane matrix, **4** still appeared immediately.

(20) Cf.: Jackson, J. E.; Mock, G. B.; Tetef, L.; Zheng, G.; Jones, M., Jr. *Tetrahedron* **1985**, *41*, 1453.

(21) (a) Harrison, A. M., Ph.D. Thesis, University of Chicago, 1975. We thank Prof. G. L. Closs for bringing this to our attention. (b) Wulfman, D. S.; Steinheimer, T. R. *Tetrahedron Lett.* **1972**, *37*, 3933. (c) Szeimies, G. private communication. Cf.: Szeimies, G.; Harnisch, J. *Chem. Ber.* **1979**, *112*, 3914. (d) Vogelbacher, V. J.; Regitz, M.; Mynott, R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 842. (e) Hassner, A.; Levy, A. B.; McEntire, E. E.; Galle, J. E. *J. Org. Chem.* **1974**, *39*, 585.

Total Synthesis of (+)-Phyllanthocin

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Phyllanthocin (**3**),[2] the aglycone of the potent antitumor agent phyllanthoside (**1**), has attracted considerable synthetic interest.[3] Isolated by Kupchan in 1977, the structure was secured via single-crystal X-ray analysis;[2] the structure of the biologically active agent, however, remained unknown until 1982. In that year Pettit[4] announced the structure of phyllanthoside (**1**) as well as the closely related phyllanthostatins.[4,5] We also were intrigued with the spiro ketal architecture embodied in phyllanthoside;[6,7] we report here

(1) Camille and Henry Dreyfus Teacher-Scholar, 1978–1983; National Institutes of Health (National Cancer Institute) Career Development Awardee, 1980–1985; J. S. Guggenheim Fellow, 1985–1986.

(2) Kupchan, S. M.; La Voie, E. J.; Branfman, A. R.; Fei, B. Y.; Bright, W. M.; Bryan, R. F. *J. Am. Chem. Soc.* **1977**, *99*, 3199.

(3) For recent syntheses, see: McGuirk, P. R.; Collum, D. B. *J. Am. Chem. Soc.* **1982**, *104*, 4496. Williams, D. R.; and Sit, S.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 2949. McGuirk, P. R.; Collum, D. B. *J. Org. Chem.* **1984**, *49*, 843. Burke, S. D.; Cobb, J. E.; Takeuchi, K. *J. Org. Chem.* **1985**, *50*, 3420. Dappen, M. S.; Dupré, B.; Murphy, C. J.; Martin, S. F. *Abstracts of Papers*, 192nd National Meeting of the American Chemical Society, Anaheim, CA; American Chemical Society: Washington, DC, September 1986; ORGN 291.

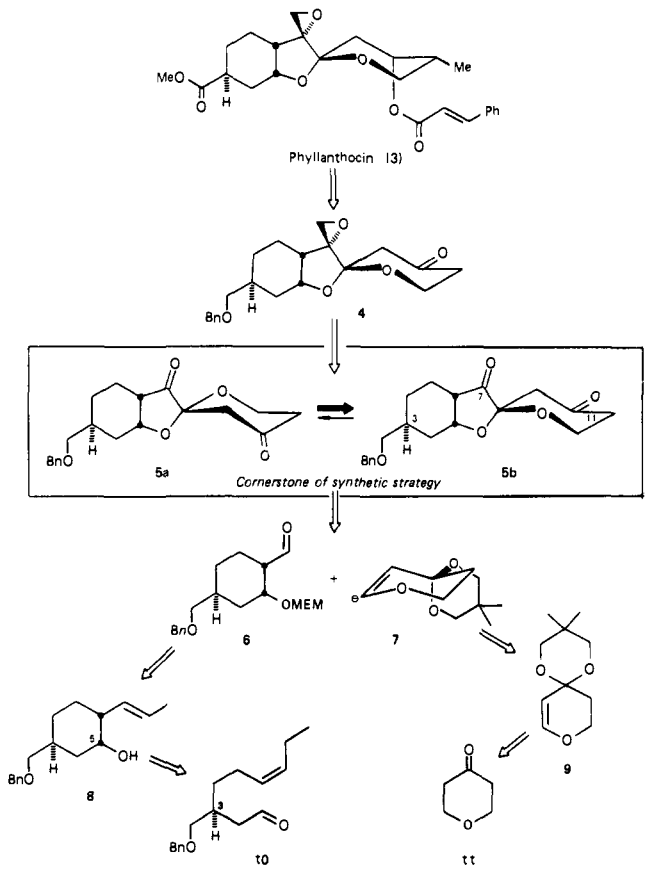
(4) (a) Pettit, G. R.; Cragg, G. M.; Gust, D.; Brown, P. *Can. J. Chem.* **1982**, *60*, 544. (b) Pettit, G. R.; Cragg, G. M.; Gust, D.; Brown, P.; Schmidt, J. M. *Can. J. Chem.* **1982**, *60*, 939. Pettit, G. R.; Cragg, G. M.; Suffness, M. I.; Gust, D.; Boettner, F. E.; Williams, M.; Saenz-Renauld, J. A.; Brown, P.; Schmidt, J. M.; Ellis, P. D. *J. Org. Chem.* **1984**, *49*, 4258. Pettit, G. R.; Cragg, G. M.; Niven, M. L.; Nassimbeni, L. R. *Can. J. Chem.* **1983**, *61*, 2630.

(5) Phyllanthoside was selected for human trials in January 1986. Private communication from Dr. Matthew Suffness, Natural Products Branch, NCI Developmental Therapeutics Program.

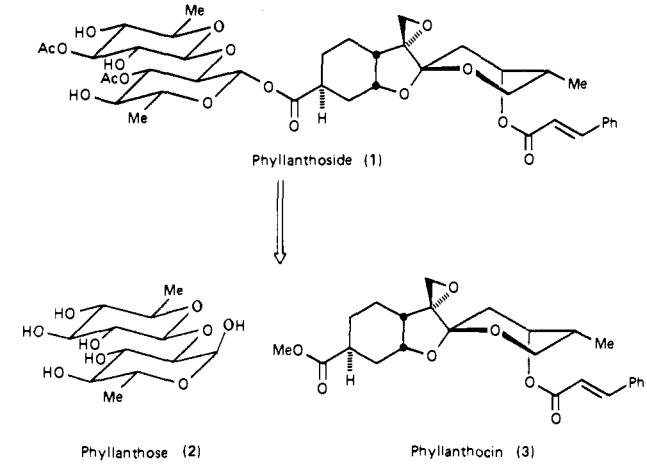
(6) For leading references on the synthesis and chemistry of spiro ketals, see: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Taber, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789. Martinez, G. R.; Grieco, P. A.; Williams, E.; Kanai, K.; Srinivasan, C. V. *Ibid.* **1982**, *104*, 1436. Baker, R.; Herbert, R. H.; Parton, A. H. *J. Chem. Soc., Chem. Commun.* **1982**, 601. Williams, D. R.; Barner, B. A. *Tetrahedron Lett.* **1983**, *24*, 427. Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1983**, *48*, 1303 and references therein. Evans, D. A.; Sacks, C. E.; Whitney, R. A.; Mandel, N. G. *Tetrahedron Lett.* **1978**, 727. Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauve, T.; Saunders, J. K. *Can. J. Chem.* **1981**, *59*, 1105.

0002-7863/87/1509-1269$01.50/0

Scheme I



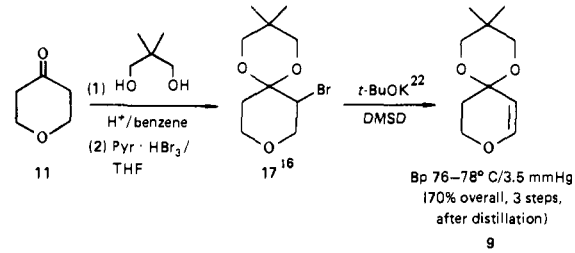
an efficient (4.8%), stereochemically linear strategy (vide infra) which affords (+)-phyllanthocin (**3**). This venture was prelude to completion of the *first* total synthesis of (+)-phyllanthoside (**1**).[8]



Our strategy (Scheme I) is based on a stereoselective intramolecular ene reaction (**10** → **8**)[9,10] to construct aldehyde **6**, followed by a novel, anomerically driven[11] spiroketalization to control the C(8)-spiro center.[12,13] Methylenation at C(7) and introduction of the two substituents at C(10) and C(11) then take advantage of the predictable stereochemical bias of the bicyclic system. Thus, the entire stereochemical problem of (+)-phyllanthocin (**3**) reduces to the preparation of **10** possessing the correct absolute stereochemistry at C(3).[14] For the latter we selected the methodology of Evans.[15]

The synthesis (Scheme II) begins with imide **13**,[16] available in 98% yield from (+)-oxazolidone **12**.[17] Treatment with lithium hexamethyldisilazide (THF, −78 °C) followed by allyl bromide (THF, −78 → 0 °C) afforded **14**[16] and its epimer[16] (96:4) in 92% yield. Reduction ($LiAlH_4$, THF) followed by benzylation (KH, benzyl bromide, THF) and selective ozonolysis led to aldehyde **16**.[16] Aldehyde **10**[16] in turn was prepared via semireduction (H_2, 5% $Pd/CaCO_3$, quinoline). As anticipated, execution of the intramolecular ene reaction (Me_2AlCl, CH_2Cl_2) afforded predominently (83%) alcohol **8**.[16,18,19] Completion of **6**[16] entailed protection of the hydroxyl group[20] followed by ozonolysis.

Dihydropyran **9**,[16] required for spiro ketal construction, was prepared from commercially available tetrahydropyran-4-one (**11**) as indicated.



Union of **6** with **9** involved generation of anion **7** [*t*-BuLi (1.5 equiv), THF] followed by rapid addition of **6** [THF–HMPA (2:1)].[21] Hydrolysis led to a diastereomeric mixture (3:2) of alcohols, which was subjected to Swern oxidation.[23] Spiroketalization was then executed via removal of the MEM group ($ZnBr_2$, CH_2Cl_2)[20] and treatment with a catalytic amount of camphorsulfonic acid (dry benzene). The result was spiro ketal **5b**[16] (71%!) along with a small amount (2%) of the C(8) isomer (**5a**).[16,24] The structure of **5b** was secured by X-ray analysis.[25]

(7) For related work on the synthesis of spiro ketal systems eminating from our laboratory, see: Smith, A. B., III; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015. Smith, A. B., III; Thompson, A. S. *J. Org. Chem.* **1984**, *49*, 1469.

(8) Smith, A. B., III; Rivero, R. A. *J. Am. Chem. Soc.*, following paper in this issue.

(9) For a recent review on the ene reaction, see: Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.

(10) Snider, B. B.; Karras, M.; Price, R. T.; Rodini, D. J. *J. Org. Chem.* **1982**, *47*, 4538. Also see ref 17.

(11) Deslongchamps, P. In *Stereoelectronic Effects in Organic Chemistry*; Baldwin, J. E., Ed.; Pergamon: New York, 1983. Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Hafner, K., Ed.; Springer-Verlag: Berlin, 1983.

(12) To the best of our knowledge, this construction of the [6.5]-spiro ketal framework was previously unknown.

(13) For related examples of acid-promoted spiroketalization of 1-(ω-hydroxyalkyl)dihydropyran derivatives, see: Danishefsky, S. J.; Pearson, W. H. *J. Org. Chem.* **1983**, *48*, 3865. Reference 6.

(14) While convergent strategies are often most attractive, stereochemically linear strategies so designed that a single stereogenic center in a homochiral substrate induces the relative, and thereby absolute, stereochemistry of the remaining centers can in some cases prove more economic overall. That is, only a single resolution, asymmetric induction, or resort to the pool of chiral substrates is required. The price for this economy *may be* an increase in the overall number of steps required to reach the synthetic goal; however, total efficiency maybe enhanced in that only one nonracemic substrate is required.

(15) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

(16) (a) The structure assigned to each new compound is in accord with its infrared and 250-MHz ^1H NMR spectra, as well as appropriate parent ion identification by high-resolution mass spectrometry. (b) In addition, an analytical sample of this new compound, obtained by recrystallization or chromatography (LC or TLC) gave satisfactory C and H combustion analysis within 0.4%.

(17) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

(18) The enantiomeric purity of (−)-**8**, determined via the Mosher ester technique, was 88%; see: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(19) Three additional products (ca. 5% total) were also obtained. Details of this reaction, including full characterization of all products, will be presented in the full account of this work.

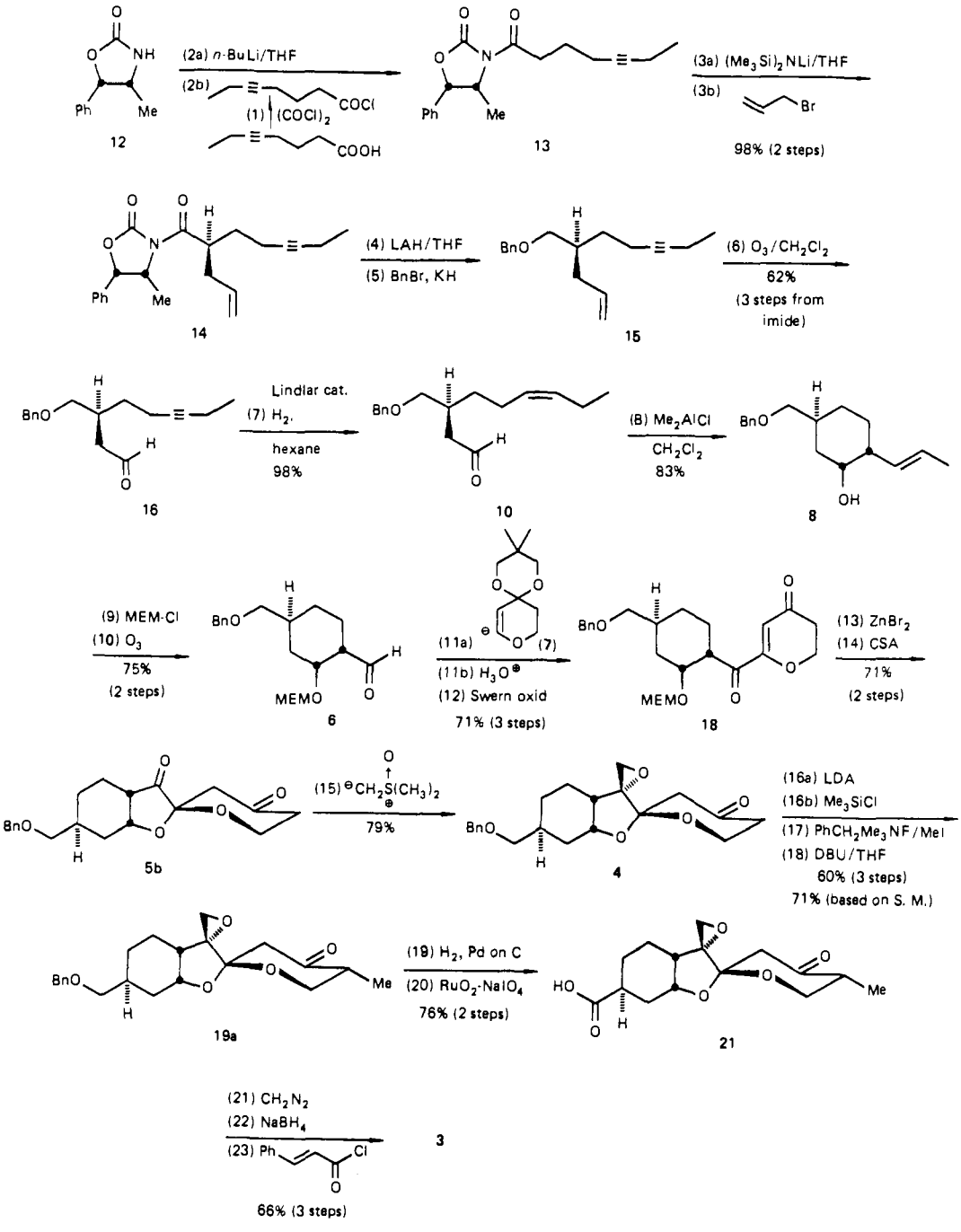
(20) Corey, E. J.; Gras, J.-L.; Ulrich, P. *Tetrahedron Lett.* **1976**, 809.

(21) For examples of unfunctionalized anions of type **7**, see: Boeckman, R. K.; Bruza, K. J. *Tetrahedron* **1981**, *37*, 3997.

(22) E. W. Garbisch, Jr. *J. Org. Chem.* **1965**, *30*, 2109.

(23) Huang, S.-L.; Mancuso, A. J.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480. Also see: Omura, K.; Sharma, A. K.; Swern, D. *J. Org. Chem.* **1976**, *41*, 957.

Scheme II



Three stereochemically demanding operations remained to complete the synthesis: methylenation at C(7),[26] alkylation at C(11), and reduction of the C(10) carbonyl.[27] Toward this end, treatment of **5b** with sodium dimethylsulfoxonium methylide [Me_2SO–THF (1:1)][28] afforded epoxide **4** (79%) as the sole product.[16] Regiocontrolled methylation at C(11) proved more troublesome. Standard kinetic alkylation protocols led predominately to the undesired C(9)-mono- and C(9)-dialkylated products. Fortunately, this problem could be circumvented via the in situ trapping method of Corey[29] to afford an 85:15 mixture (ca. 99%) of enol ethers **20a** and **20b**. Enolate generation with *n*-benzyltrimethylammonium fluoride (4.2 equiv, THF, −78 °C),[30] followed by treatment with excess methyl iodide afforded **19a** and **19b** (1:5), along with a small amount of starting ketone **4**. Without separation this mixture was subjected to equilibration (DBU, THF). Flash chromatography afforded **19a** in 60% yield (three steps), in addition to minor amounts of **19c** (12%) and **4** (17%).

With introduction of the C(11)-methyl complete, the C(3)-benzyloxymethyl unit was converted to the carbomethoxy group in three steps: removal of the benzyl group (H_2 10% Pd/C,

(24) A detailed examination of this spiroketalization process is currently under way in our laboratory. Preliminary results indicate that while **5b** is the thermodynamically more stable isomer, the observed product distribution (35:1) is not the result of equilibration, but instead a kinetic result (Vacarro, H., unpublished results). These observations are consistent with intervention of a kinetic anomeric effect. That is, spiroketalization involves a late transition state stabilized by a combination of stereoelectronic effects including the furanone oxygen and the C(10)-carbonyl group.

(25) Unpublished results of P. Carroll, University of Pennsylvania X-ray Service Center.

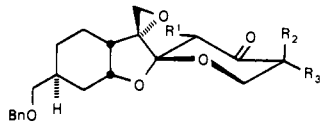
(26) We anticipated that the enhanced electrophilic nature of the C(7)-carbonyl (i.e., two α-oxygen substituents) would facilitate the required chemoselective methylenation. Support for this conjecture derived from the unusually high C(7)-carbonyl frequency of 1775 cm^{-1}.

(27) Ester **21** was reduced with high stereocontrol by Collum; see ref 3.

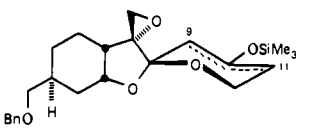
(28) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(29) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(30) Kuwajima, I.; and Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257.



19 a: $R^1 = R^2 = H$, $R^3 = Me$
b: $R^1 = R^3 = H$, $R^2 = Me$
c: $R^1 = Me$, $R^2 = R^3 = H$



20 a: $\Delta^{10,11}$
b: $\Delta^{9,10}$

MeOH), oxidation [RuO_4–$NaIO_4$, $CH_3CN/CCl_4/H_2O$ (6:6:9)], and esterification (CH_2N_2). Following the precedent of Collum,[27] reduction of **21**[16] afforded the axial alcohol.[16,31] Finally, cinnamoylation (*t*-cinnamoylchloride, DMAP, pyr) gave (+)-phyllanthocin (**1**) identical in all respects with an authentic sample of (+)-phyllanthocin provided by Dr. Matthew Suffness (NCI).[32]

In summary, a stereochemically linear, reasonably efficient (4.8%) total synthesis of (+)-phyllanthocin has been achieved.

Acknowledgment. Support for this investigation was provided by the National Institutes of Health (Institutes of General Medical Sciences) through Grant GM 29028.

Supplementary Material Available: Characterization data for compounds **5b**, **6**, **8**, **14**, and **19a** as well as comparison NMR spectra of natural and synthetic (+)-phyllanthocin (3 pages). Ordering information is given on any current masthead page.

(31) Comparison of ester **21** with that prepared by Collum demonstrated their identity. In addition, the enantiomeric excess (Mosher ester method) was 95%.[18] We thank Professor David Collum (Cornell University) for the NMR and IR spectrum of ester **21**.

(32) We thank Dr. Matthew Suffness, Chief, Natural Products Branch NCI Developmental Therapeutics Program, for the generous sample of phyllanthoside.

Total Synthesis of (+)-Phyllanthoside

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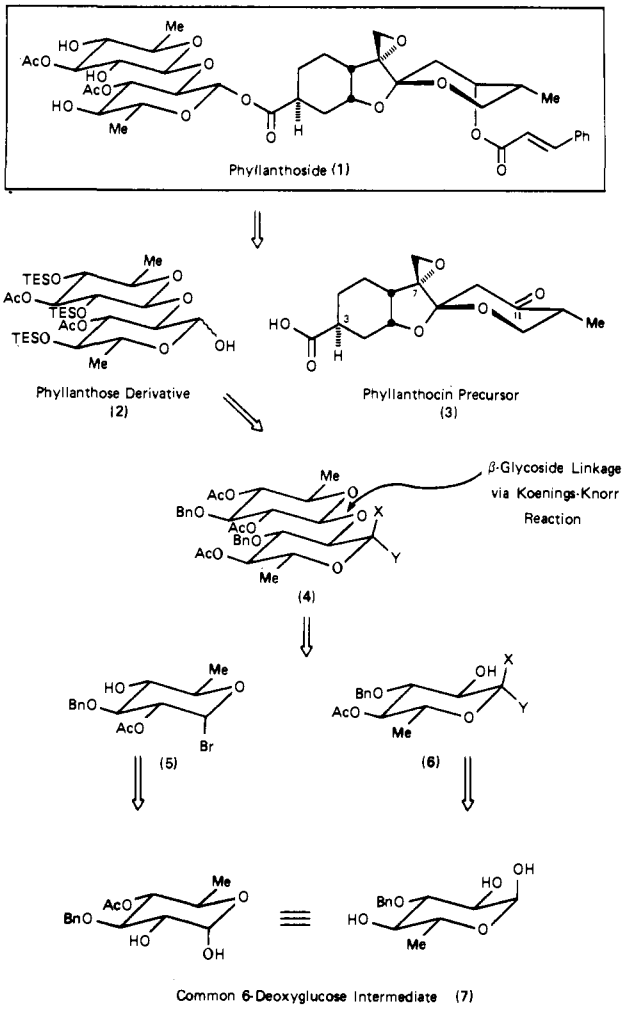
In this paper we report the first total synthesis of (+)-phyllanthoside (**1**), a novel bisabolane glycoside isolated by Kupchan[2a] and structured by Pettit.[2b] Phyllanthoside displays selective cytotoxicity at very low concentrations toward solid tumors of the breast and colon,[3] and as such has recently been selected by NCI as a clinical candidate.[4] No reports on the synthesis and/or approaches to this biologically important glycoside have appeared. The aglycone (phyllanthocin), however, has attracted considerable attention.[5]

With a viable, stereocontrolled synthesis of phyllanthocin secured,[6] the central issue became construction of a disaccharide suitable for coupling to the aglycone.[7,8] Toward this end, we designed our strategy (Scheme I) to take advantage of the well-known Koenigs–Knorr protocol[9a] to couple monosaccharides

Scheme I. Retrosynthetic Analysis of Phyllanthoside[a]



[a] α: X = $OCH_2CH=CH_2$; Y = H. β: X = H; Y = $OCH_2CH=CH_2$.

(1) Camille and Henry Dreyfus Teacher-Scholar, 1978–1983; National Institutes of Health Career Development Award, 1980–1985; J.S. Guggenheim Fellow, 1985–1986.

(2) (a) Kupchan, S. M.; LaVoie, E. J.; Branfman, A. R.; Fei, B. Y.; Bright, W. M.; Bryan, R. F. *J. Am. Chem. Soc.* **1977**, *99*, 3199. (b) Pettit, G. R.; Cragg, G. M.; Gust, D.; Brown, P.; Schmidt, J. M. *Can. J. Chem.* **1982**, *60*, 939. Pettit, G. R.; Cragg, G. M.; Suffness, M.; Gust, D.; Boettner, F. E.; Williams, M.; Saenz-Renauld, J. A.; Brown, P.; Schmidt, J. M.; Ellis, P. *J. Org. Chem.* **1984**, *49*, 4258; Pettit, G. R.; Cragg, G. M.; Suffness, M. *J. Org. Chem.* **1985**, *50*, 5060.

(3) Powis, G.; Moore, D. J. *J. Chromatogr.* **1985**, *342*, 129. Also see: Powis, G.; Moore, D. J. *Proc. Assoc. Cancer Res.* **1985**, *26*, 354.

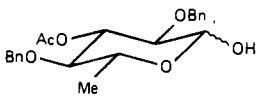
(4) This decision was made in Jan. 1986, with possible initial human studies in early 1987; personal communication from Dr. Matthew Suffness, Chief, Natural Products Branch, Developmental Therapeutics Program, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.

(5) Phyllanthocin is biologically inactive. For recent syntheses of phyllanthocin, see: McGuirk, P. R.; Collum, D. B. *J. Am. Chem. Soc.* **1982**, *104*, 4496. Williams, D. R.; Sit, S.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 2949. McGuirk, P. R.; Collum, D. B. *J. Org. Chem.* **1984**, *49*, 843. Burke, S. D.; Cobb, J. E.; Takeuchi, K. *J. Org. Chem.* **1985**, *50*, 3420. Dappen, M. S.; Dupré, B.; Murphy, C. J.; Martin, S. F. *Abstracts of Papers*, 192nd National Meeting of the American Chemical Society, Anaheim, CA; American Chemical Society: Washington, DC, September 1986; ORGN 291.

(6) Previous communication: Smith, A. B., III; Fukui, M. *J. Am. Chem. Soc.*, preceding paper in this issue.

(7) While seemingly straightforward, several structural–reactivity features of the disaccharide unit, in conjunction with the structure of the aglycone, rendered a direct coupling approach inoperative. Not the least problematic was construction of two β-glycoside bonds, one an unusual $1\rightarrow 2\beta$ glycoside linkage the other the β-glycosidic ester. In addition, we were faced with the known propensity of the acetates in phyllanthoside to undergo facile migration.[2b]

(8) Initial model studies suggested that formation of the β-glycosidic ester would not present a serious problem. Specifically, reaction of 2 equiv of monosaccharide i, shown by NMR to be a 2:1 (β/α) mixture of anomers, with



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the acid chloride derived from **3** afforded an 8:1 mixture of glycosides (β/α). The favorable selectivity presumably derives from the enhanced reactivity of the equatoral (i.e., β) anomer. We recognized that success with disaccharide **3** would directly depend on a similar favorable anomeric ratio (vide infra).

(9) (a) Koenigs, W.; Knorr, E. *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 957. (b) Helferich, B.; Weis, K. *Chem. Ber.* **1956**, *89*, 314.

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