and washed with 100 mL of brine, dried over $MgSO_4$, and concentrated. The resulting oil was flash chromatographed (ether:hexane, 2:1), yielding the product as a yellow oil (0.04 g, 92%). ^1H NMR ($CDCl_3$) δ 7.3 (m, 10 H), 5.86 (pseudo t, J = 2 Hz, 1 H), 4.63, 4.50 (AB quartet, J = 14.7 Hz, 2 H), 3.3 (d, d, J = 12.7, 5.9 Hz, 1 H), 3.05 (d, d, J = 12.7, 6.4 Hz, 1 H), 2.7 (m, 2 H), 2.35 (m, 1 H), 2.1 (m, 2 H), 1.6 (m, 3 H); IR (CCl_4) 2900, 1650, 1440, 690 cm^{-1}; MS, m/e 349 (M^+), 91, 72; exact mass calcd for $C_{22}H_{23}ONS$ 349.1499, found 349.1468.

***N*-Benzyl-4-oxo-*cis*-3-azabicyclo[4.4.0]decan-8-one.** The vinyl sulfide (0.06 g, 0.17 mmol) and $HgCl_2$ (0.049 g, 0.18 mmol) were dissolved in CH_3CN:H_2O (3:1), 0.69 mL) under N_2. The mixture was heated at reflux for 20 h, then cooled to room temperature, diluted with 2 mL of CH_2Cl_2, and filtered through Celite. The solution was concentrated and the resulting oil was taken up in CH_2Cl_2 (5 mL) and filtered through glass wool and Celite. The filtrate was concentrated and purified by flash chromatography (ethyl acetate:hexane, 3:1) on silica gel, yielding 0.029 g (65%) of the ketone: ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H), 4.75, 4.45 (AB quartet, J = 14 Hz, 2 H), 3.4 (d, d, J = 12.7, 5.4 Hz, 1 H), 3.2 (d, d, J = 12.7, 5.9 Hz, 1 H), 2.65–2.4 (m, 3 H), 2.25 (m, 5 H), 1.9 (m, 1 H), 1.8 (m, 1 H); IR (CCl_4) 2920, 1720, 1645, 900 cm^{-1}; MS, m/e 257 (M^+), 106, 92, 91, 88, 86, 84, 65, 49, 47, 43, 41; exact mass calcd for $C_{16}H_{19}O_2N$ 257.1415, found 257.1449.

***cis*-3-Acetoxy-4-vinyl-1-(phenylthio)cyclohexene (18).** The aldehyde **5** (0.1 g, 0.36 mmol) was treated with $CH_2{=}PPh_3$ (0.36 mL of 1 M solution in ether) at room temperature for 15 min and then subjected to a standard aqueous workup. The desired product was obtained by preparative plate chromatography in silica gel (hexane:ether, 2:1), 0.024 g (25%), and immediately carried on to the next reaction: ^1H NMR ($CDCl_3$) δ 7.4 (d, J = 6 Hz, 2 H), 7.3 (m, 3 H), 5.8 (d, d, d, J = 15.8, 6 Hz, 1 H), 5.65 (d, J = 5 Hz, 1 H), 5.25 (pseudo t, J = 5 Hz, 1 H), 5.05 (d, J = 15 Hz, 1 H), 5.04 (d, J = 8 Hz, 1 H), 2.45 (m, 1 H), 2.2 (m, 2 H), 2.0 (5.3 H), 1.75 (m, 2 H); MS, m/e 274 (M^+), 220, 215, 214, 178, 165, 123, 110, 105.

4-[1-[Bis(methoxycarbonyl)methyl]ethyl]-1-(phenylthio)-1,4-cyclohexadiene (20). The allylic acetate **18** (0.03 g, 0.11 mmol), Pd(diphos)$_2$ (0.0098 g, 0.011 mmol), and 0.65 mL of a 1 M DME solution of sodium dimethylmalonate were added to 0.4 mL of DME under N_2. The solution was then heated at 80 °C for 15 min, whereupon it was cooled to room temperature and subjected to preparative plate chromatography on silica gel (hexane:ether, 2:1), yielding 0.045 g of **20** (82%): ^1H NMR ($CDCl_3$) δ 7.4 (d, J = 6 Hz, 2 H), 7.3 (m, 3 H), 5.9 (d, J = 6 Hz, 1 H), 5.7 (d, J = 6 Hz, 1 H), 3.7 (s, 3 H), 3.65 (s, 3 H), 3.45 (d, J = 10 Hz, 1 H), 3.0 (d, t, J = 10, 7 Hz, 1 H), 2.2 (m, 4 H), 1.1 (d, J = 7 Hz, 3 H); *MS*, m/e 346 (M^+), 215, 214, 213, 184, 149, 109, 108, 105, 91, 79, 77, 71, 69, 65, 57, 55, 51, 43.

Registry No. **3**, 90083-78-6; **3** (alcohol), 90083-79-7; **4**, 90083-80-0; **5**, 90083-86-6; **6**, 90083-88-8; **7**, 90083-89-9; **8**, 90084-07-4; **8** (ester lactone), 90083-90-2; **9**, 90083-91-3; **10**, 90084-09-6; **11**, 90084-10-9; **12**, 90083-92-4; **13**, 90083-93-5; **13** (alcohol), 90083-95-7; **14**, 90083-87-7; **14** (mesylate), 90083-94-6; **15**, 90084-02-9; *trans*-**15**, 90084-03-0; **15** (amine), 90084-01-8; **16**, 90084-11-0; **18**, 90084-06-3; **20**, 90084-08-5; Pd(DIPHOS)$_2$, 31277-98-2; TBSCl, 18162-48-6; $NaCH(CO_2Me)_2$, 18424-76-5; (*E*)-$CH_2{=}C(SPh)CH{=}CHOAc$, 90083-81-1; (*Z*)-$CH_2{=}C(SPh)$-$CH{=}CHOAc$, 90083-85-5; $CH_3CH{=}CHCHO$, 4170-30-3; PhSH, 108-98-5; $CH_3CH(SPh)CH_2CHO$, 38160-59-7; $CH_3CH(SPh)$-$CHClCHO$, 90083-82-2; (*E*)-$CH_3C(SPh){=}CHCHO$, 90083-84-4; (*Z*)-$CH_3C(SPh){=}CHCHO$, 90083-83-3; $CH_2{=}CHCHO$, 107-02-8; Et_3NHF, 29585-72-6; LiCl, 7447-41-8; $HgCl_2$, 7487-94-7; $NaCH$-$(SO_2Ar)CO_2Me$, 90083-98-0; $CH_2{=}PPh_3$, 3487-44-3; 3-(phenylthio)cyclohex-2-enone, 75717-39-4; isopropenyl acetate, 108-22-5; *cis*-3-[bis(methoxycarbonyl)methyl]-4-methyl-1-(phenylthio)-cyclohexene, 90083-96-8; 4-methyl-3-[(*p*-tolylsulfonyl)(methoxycarbonyl)methyl]-1-(phenylthio)cyclohexene (isomer 1), 90083-97-9; 4-methyl-3-[(*p*-tolylsulfonyl)(methoxycarbonyl)methyl]-1-(phenylthio)cyclohexene (isomer 2), 90130-47-5; *cis*-3-[(methoxycarbonyl)methyl]-4-methyl-1-(phenylthio)cyclohexene, 90083-99-1; 3-[(methoxycarbonyl)(*p*-tolylsulfonyl)methyl]-4-methylcyclohexanone (isomer 1), 90084-00-7; 3-[(methoxycarbonyl)(*p*-tolylsulfonyl)methyl]-4-methylcyclohexanone (isomer 2), 90130-48-6; *N*-benzyl-4-oxo-8-(phenylthio)-*cis*-3-azabicyclo-[4.4.0]dec-7-ene, 90084-04-1; *N*-benzyl-4-oxo-*cis*-3-azabicyclo-[4.4.0]decan-8-one, 90084-05-2.

Synthesis of Protected 4-Desmethoxy-8-nordaunomycinone

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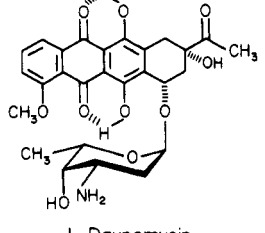
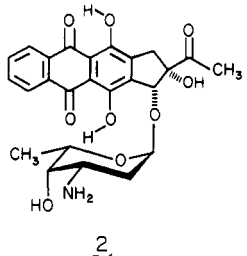
The synthesis of 4-desmethoxy-8-nordaunomycinone in protected form is described. Two separate routes were investigated which share a common strategy for the construction of this new five-membered anthracycline ring system.

The clinical utility of anthracycline antibiotics[1] such as daunomycin **1** has prompted varied approaches to their synthesis[2] and derivatization. The major thrust in analogue development has been to diminish the cumulative cardiotoxic liability of these antitumor agents.[3] Deletion of the 4-methoxyl group in daunomycin has resulted in increased potency.[4] With these thoughts in mind, the desmethoxy-8-nor analogue **2** was chosen as a desirable target whose degradation after glycolysis might be facilitated by the vicinal diol portion of the aglycone.



1 Daunomycin



2

Utilizing existing methodology for the incorporation of the naphthoquinone portion of anthracycline aglycones,[5]

(1) For recent reviews see: Remers, W. A. "The Chemistry of Antitumor Antibiotics"; Wiley Interscience: Somerset, NJ, 1979, Vol. 1, Chapter 2; "Anthracyclines: Current Status and New Developments"; Crooke, S. T., Reich, S. D., Eds.; Academic Press: New York, 1980.

(2) For a recent elegant synthesis of (±)-daunomycinone see: Kelly, T. Ross; Vaya, J.; Ananthasubramanian, L. *J. Am. Chem. Soc.* **1980**, *102*, 5983–5984 and references sited therein.

(3) Israel, M.; Potti, G. *J. Med. Chem.* **1982**, *25*, 187–191.

(4) Arcamone, F. "Doxorubicin-Anticancer Antibiotics"; Academic Press: NY, 1981; Vol. 17; *Cancer. Treat. Rep.* **1976**, *60*, 829.

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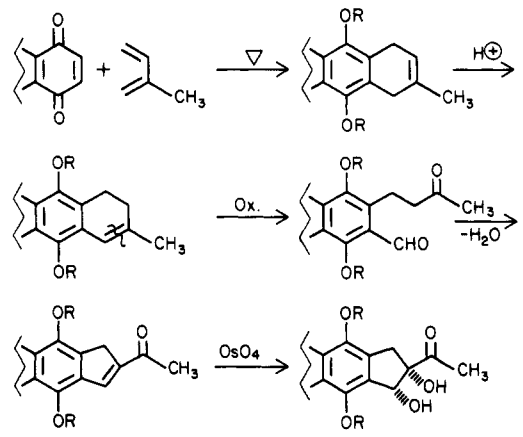
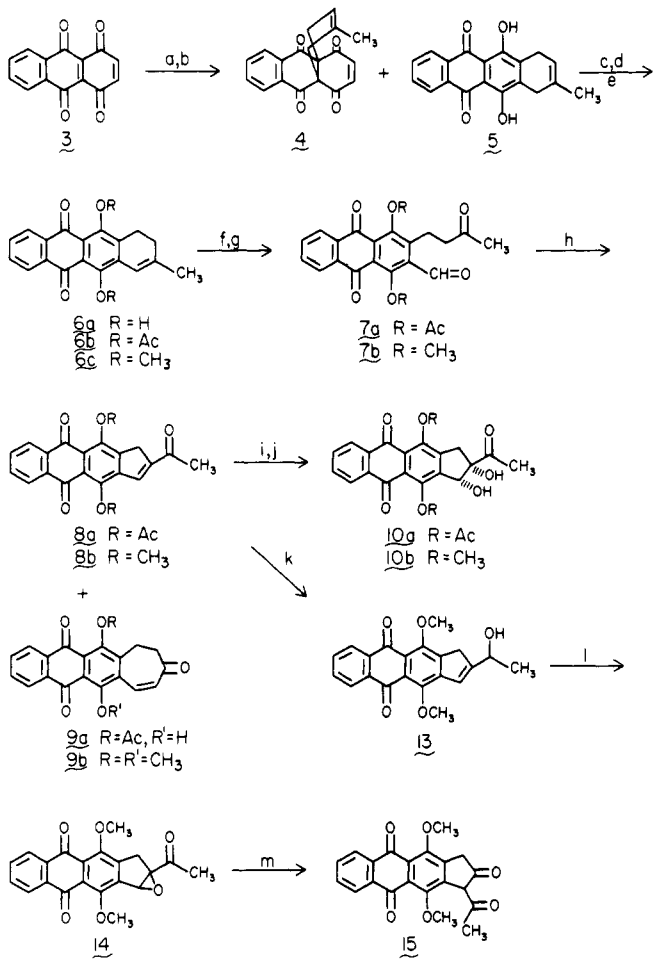
Scheme I



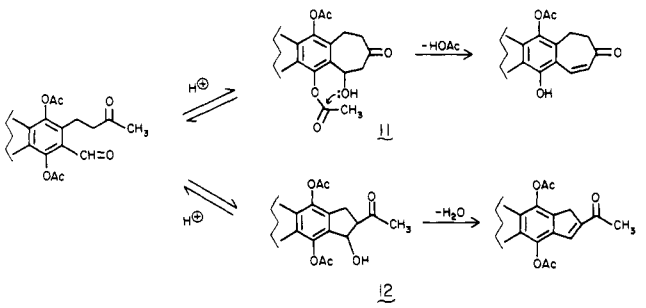
Scheme II[a]



[a] a, Isoprene; b, HOAc, NaOAc, Δ; c, CF_3SO_3H, then H_2O; d, Ac_2O, pyridine; e, Me_2SO_4, K_2CO_3, 2-butanone; f, O_3 in O_2; g, Me_2S; h, TsOH, PhH, $-H_2O$; i, OsO_4; j, H_2S; k, $NaBH_3CN$, aqueous HCl; l, MCPBA, then TMP·HCl + MCPBA; m, $ClCH_2CO_2H$.

construction of the highly functionalized five-membered ring of **2** was envisioned as outlined in Scheme I. Our synthetic efforts began with quinizarin quinone[6] **3** whose insoluble aromatized external isoprene adduct **5** could be readily separated from the predominant internal adduct

Scheme III



4[7] in 27% overall yield, Scheme II. Isomerization of the double bond was quantitatively effected by dissolving olefin **5** in neat trifluoromethanesulfonic acid and quenching with ice water. The resulting conjugated olefin **6a** was converted with acetic anhydride–pyridine to its diacetate **6b**. Ozonolysis and reduction of the ozonide with dimethyl sulfide gave a crude keto aldehyde **7a** which was promptly cyclized with *p*-toluenesulfonic acid in refluxing benzene. The seven-membered deacetylated enone **9a** was isolated in 50% yield accompanied by a 10% yield of the desired five-membered enone **8a**. It appears that in the seven-membered system **11**, acyl migration occurs during the reversible aldol condensation at a rate faster than dehydration of the kinetically favored five-membered aldol **12**, Scheme III.

In order to evaluate the importance of acetyl migration in determining product distribution during the aldol condensation of keto aldehyde **7a**, dimethyl ether derivative **7b** was prepared from hydroquinone **6a** by methylation (K_2CO_3, Me_2SO_4) and ozonolysis of the methylated olefin **6c**. Cyclodehydration of keto aldehyde **7b**, as previously described, provided the five and seven-membered products in 43% and 18% yields, respectively. These results support the active role of acetyl migration in influencing product distribution during the aldol cyclization of **7a**.

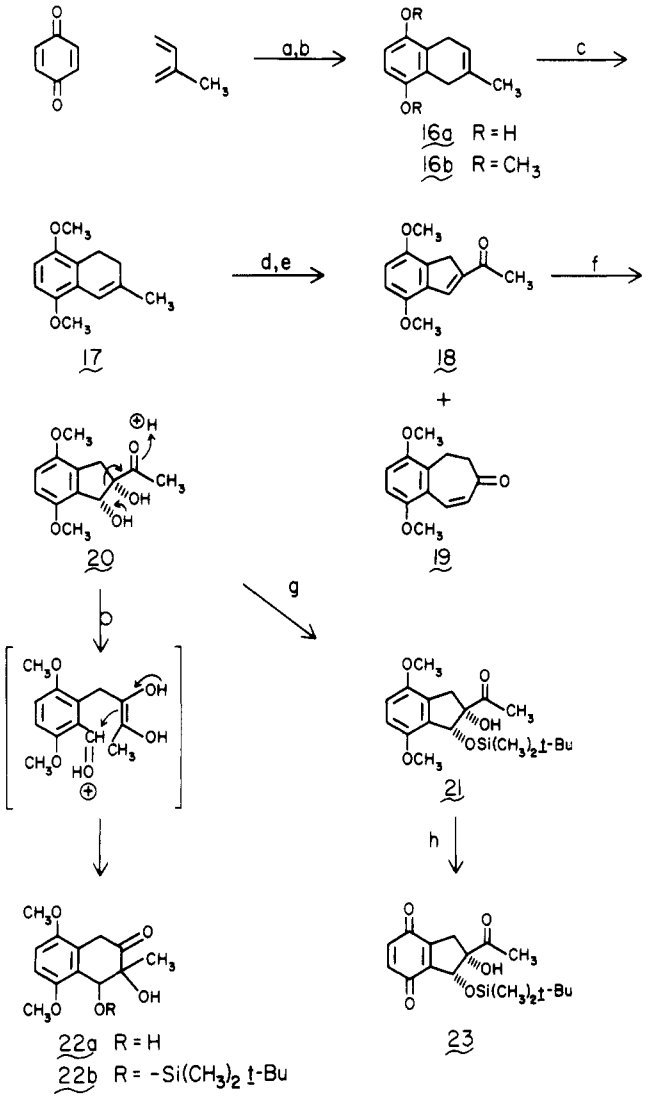
Treatment of either enone **8a** or **8b** with osmium tetroxide (OsO_4) in pyridine appeared to give an osmate, as evidenced by the expected black color, but no organic product was isolated upon attempted osmate cleavage with hydrogen sulfide. It is suspected that properties peculiar to the anthraquinone ring system were responsible for the formation of an intractable osmate complex.

An alternate hydroxylation method involving the acid-catalyzed ring opening[8] of benzylic oxirane **14** was attempted. Epoxy ketone **14** was prepared from enone **8b** by sodium cyanoborohydride reduction, peracid epoxidation of allylic alcohol **13**, and in situ alcohol oxidation catalyzed by 2,2,6,6-tetramethylpiperidinium chloride.[9] Exposure of epoxy ketone **14** to various organic acids in dichloromethane typically resulted in a single rearranged product which gave a positive ferric chloride test. The β-diketone structure **15**, resulting from an epoxy–pinacol rearrangement, has been assigned to this product based on spectral data and literature precedent.[10] Attempts to open epoxide **14** in hydroxylic solvents resulted in complex mixtures which were impractical for our purposes.

The same synthetic strategy outlined in Scheme I was applied to a second synthetic route in which introduction

(5) Kende, A. S.; Tsay, Y.; Mills, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 1967–1969.
(6) Dimroth, O.; Friedemann, O.; Kammerer, H. *Chem. Ber.* **1920**, *53*, 481–487.
(7) Kelly, T. R.; Goerner, J.r., R. N.; Gillard, J. W.; Prazak, B. K. *Tetrahedron Lett.* **1976**, 3869–3872.
(8) Battistini, C.; Crotti, P.; Ferretti, M.; Macchia, F. *J. Org. Chem.* **1977**, *42*, 4067–4070.
(9) Cella, J. A.; McGrath, J. P.; Kelly, J. A.; ElSoukkary, O.; Hilpert, L. H. *J. Org. Chem.* **1977**, *42*, 2077–2080.
(10) House, H. O. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 957.

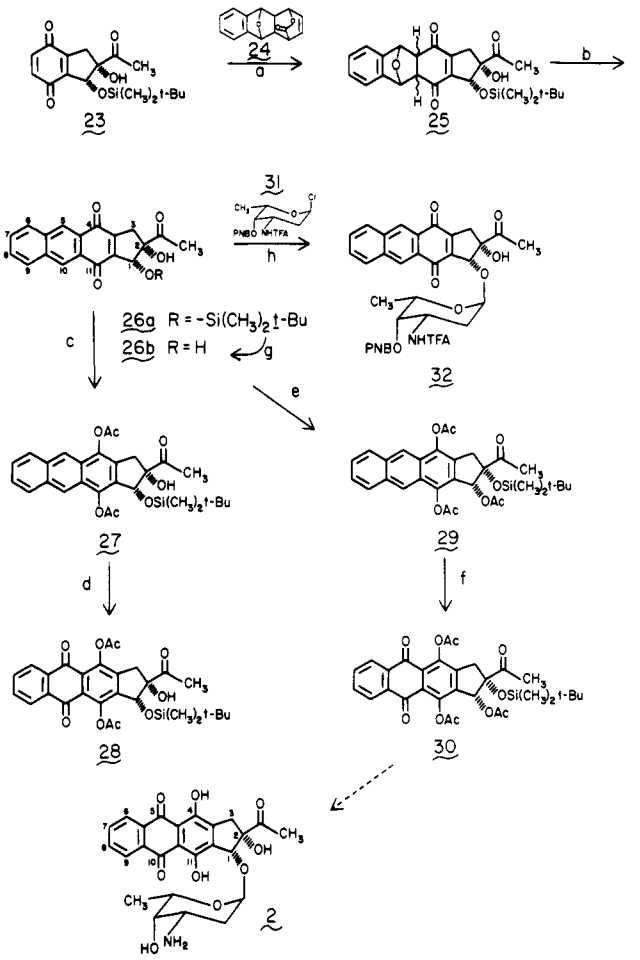
Scheme IV[a]



[a] a, $PhCH_3$, heat, then NaOAc, HOAc; b, Me_2SO_4, KOH, 2-butanone; c, KO-*t*-Bu, Me_2SO; d, OsO_4, $NaIO_4$, dioxane/water; e, TsOH, PhH, $-H_2O$; f, OsO_4, pyridine, then H_2S; g, TBSCl, imidazole, DMF; h, AgO, HNO_3, dioxane.

of the naphthaquinone portion of the molecule[11] was postponed until the functionality in the five-membered ring had been fully elaborated, Scheme IV. Cycloaddition of isoprene with *p*-benzoquinone and aromatization gave hydroquinone **16a** in excellent yield. Methylation of **16a** and double bond isomerization of dimethyl ether **16b** with potassium *tert*-butoxide in Me_2SO gave conjugated olefin **17** in 60% overall yield. Osmium tetroxide-periodate cleavage of **17** and cyclodehydration of the resulting crude keto aldehyde afforded the five- and seven-membered enones **18** and **19** in 33% and 8% yield, respectively. Hydroxylation of enone **18** with OsO_4 occurred smoothly in this instance. Osmate cleavage with H_2S and silylation of the crude glycol with *tert*-butyldimethylsilyl chloride and imidazole gave the desired ether **21** in 56% chromatographed yield along with varying small amounts of an isomer believed to be the six-membered diol **22b**. Isomer **22b** could arise from retroaldol–realdol rearrangement of the initial hydroxylation product **20**. The instability of glycol **20** observed here may in part account for the failure

Scheme V[a]



[a] a, Diglyme, 140 °C; b, NaOAc, HOAc, reflux; c, Zn, Ac_2O, then filter cold, then add pyridine; d, CrO_3, HOAc; e, Zn, Ac_2O, then filter hot and add pyridine; f, CrO_3, HOAc; g, 1 equiv HOAc, 1 equiv $Bu_4N^+ F^-$ in THF; h, AgTf, $CaCO_3$, CH_2Cl_2.

of previous hydroxylation attempts. In contrast, the silylated ketone **21** proved to be quite stable and was cleanly oxidized in 80% yield to quinone **23** by the argentic oxide–nitric acid method.[12]

Heating of the fully elaborated quinone **23** with isobenzofuran precursor **24**[13] in refluxing DME afforded the adducts **25** in quantitative yield, Scheme V. Conversion of the adduct mixture to anthraquinone **26a** with sodium acetate in hot glacial acetic acid proceeded in at best 23% yield. Despite attempts at catalyzing this deoxygenation by different methods,[14] no further improvement in yield was obtained. The inefficiency of this conversion is, again, believed to result from the sensitivity of the functionality in the five-membered ring.

Reduction of anthraquinone **26a** with zinc powder in acetic anhydride was carried out under mild conditions. Filtration to remove the zinc, cooling, and addition of pyridine to promote acetylation gave diacetate **27** in 57% recrystallized yield. Subsequent oxidation of anthracene **27** with chromium trioxide in acetic acid afforded a poor yield of the 5,10-anthraquinone **28**. Oxidation of the α-hydroxy ketone group was thought to account for the material loss. It was discovered that heating of the zinc–acetic anhydride reduction filtrate with pyridine gave

(11) Kende, A. S.; Curran, D. P.; Tsay, Y.-G.; Mills, J. E. *Tetrahedron Lett.* **1977**, *40*, 3537–3540.

(12) Hammer, R. N.; Kleinberg, J. *Inorg. Synth.* **1953**, *4*, 12.
(13) Fieser, L. F.; Haddadin, M. J. *Can. J. Chem.* **1965**, *43*, 1599–1606.
(14) Gras, J.-L. *Tetrahedron Lett.* **1978**, 2111–2114.

triacetate **29** resulting from vacinal silyl migration and acetylation of the liberated secondary hydroxyl group. In this protected form, anthracene **29** was cleaned oxidized in 72% yield to quinone **30**.

The desired aglycone in protected form was finally in hand. Deacetylation, sugar coupling, and further deprotection would be required to prepare the desired target compound **2**. Although transferral of the phenolic acetates of **30** by imidazole in ethyl alcohol was easily effected, all attempts to hydrolyze the secondary acetate of **30** caused extensive decomposition. Even orange peel acetyl esterase[15] failed to yield a tractable product. The inherent instability of this five-membered ring system, although disappointing, is understandable based on previous observations of retroaldol products and low yields.

In contrast, silyl ether cleavage of quinone **26a** by acetic acid buffered tetra-*n*-butylammonium fluoride gave the stable diol **26b** in 75% yield. The electron-withdrawing effect of the adjacent quinone ring in **26b** lends stability to the five-membered ring by disfavoring carbonium ion development at C-1. Further stabilization may arise from hydrogen bonding of the hydroxyl at C-1 to the quinone carbonyl at C-11. Coupling of optically pure protected daunosamine[16] **31** to the racemic glycols **26b** by standard methods[17] yielded the diasteriomeric glycosides **32** which were separable by TLC. Attempted preparative chromatography, quinone reduction, or sugar deprotection of these glycosides resulted in decomposition.

Conclusion

The aglycone portion of 4-desmethoxy-8-nordaunomycin (**2**), representing a new class of anthracyclines, has been prepared. The sensitive functionality of this system has hindered efforts, thus far, to prepare the targeted amino glycoside.

Experimental Section

General Methods. Proton NMR spectra were recorded on a Varian EM390 spectrometer; chemical shifts are reported in δ units with Me_4Si as the internal standard using deuteriochloroform as the solvent unless stated otherwise. IR spectra were taken on a Perkin-Elmer 337 infrared spectrophotometer and are reported in reciprocal centrimeters with polystyrene as the reference standard. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Ozonolyses were carried out by using a Welsbach T-23 ozonator.

7,10-Dihydro-6,11-dihydroxy-8-methyl-5,12-naphthacenedione (5). To a 125-mL Erlenmeyer flask equipped with a magnetic stirring bar was added 4.77 g (20 mmol) of quinizarin quinone,[6] 80 mL of glacial acetic acid, and 20 mL of toluene. The mixture was stirred at −10 °C and 9.0 mL (100 mmoles) of isoprene was added. After stirring at −10 °C for 4 days, the excess isoprene was removed in vacuo. Potassium acetate (1.0 g) was added and the solution was heated at reflux for 5 min. Upon cooling, red crystals formed. Filtration and drying in vacuo gave 1.85 g (5.7 mmol) (27% yield) of the aromatized adduct **5**:[7] mp 273–275 °C; IR (KBr) 3470, 1630, 1590, 1245 cm^{-1}.

Anal. Calcd: C, 74.50; H, 4.61. Found: C, 74.38; H, 4.61.

7,8-Dihydro-6,11-dihydroxy-9-methyl-5,12-naphthacenedione (6a). To a 100-mL beaker submersed in an ice bath was added 730 mg (2.4 mmol) of olefin **5** and 10 mL of trifluforomethanesulfonic acid while stirring with a glass rod. After 30 s, the resulting dark blue solution was diluted with 20 mL of H_2O. The red precipitate was filtered and dried in vacuo to give 715 mg of a cherry red solid (ca. 99% yield): mp 298–300 °C; IR (KBr) 1630, 1590, 1268, cm^{-1}.

Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.46; H, 4.54.

1,2,6,11-Tetrahydro-3-methyl-6,11-dioxo-5,12-naphthacenediol 5,12-Diacetate (6b). To a 100-mL round-bottom flask equipped with a magnetic stirring bar, reflux condenser, and argon inlet was added 715 mg (2.4 mmol) of hydroquinone **6a**, 40 mL of pyridine, and 13 mL of acetic anhydride. The solution was heated to 50 °C under argon for 24 h. The cooled solution was poured onto 100 g of ice and stirred for 1 h. The precipitate was filtered and dried in vacuo to give 890 mg (2.28 mmol) (95% yield) of the diacetate: mp 208–209 °C; IR (KBr) 1770, 1680 cm^{-1}; NMR 2.25 (s, 3 H, C=CCH_3), 2.60 (s, 3 H, $COCH_3$), 2.63 (s, 3 H, $COCH_3$), 6.45 (m, 1 H, C=CH), 7.70 (dd, 2 H, J_a = 6 Hz, J_b = 3 Hz), 8.16 (dd, 2 H, J_a = 6 Hz, J_b = 3 Hz).

Anal. Calcd for $C_{23}H_{18}O_6$: C, 70.76; H, 4.65. Found: C, 70.73; H, 4.64.

2-Acetyl-5,10-dihydro-5,10-dioxo-1*H*-cyclopent[*b*]anthracene-4,11-diol 4,11-Diacetate (8a) and 5,8,9,13-Tetrahydro-5,9,13-trioxo-3*H*-cyclohept[*b*]anthracene-6,12-diol 6-Acetate (9a). To a 500-mL ozonolysis chamber with a submersed gas inlet frit was added 9.8 g (25.0 mmol) of conjugated olefin **6b**, 350 mL of CH_2Cl_2, and 50 mL of CH_3OH. The solution was cooled to −70 °C and a stream of ozone in oxygen was generated and passed through the apparatus until the yellow solution became light green. The solution was purged of excess ozone with oxygen. Dimethyl sulfide (2 mL) and 3 drops of pyridine were added while the solution was allowed to warm to 25 °C slowly and stand for 18 h. The solution was then washed with 100 mL of 10% HCl solution and brine. Drying over Na_2SO_4, filtration, and removal of solvent gave 11.5 g of a yellow foam: NMR 2.16 (s, 3 H, $COCH_3$), 2.46 (s, 6 H, $OCOCH_3$) 7.5–8.2 (m, 4 H, aromatic H).

The sensitive keto aldehyde **7a** was dissolved in 300 mL of benzene containing 250 mg of *p*-toluenesulfonic acid and refluxed with azeotropic removal of water for 3 h. Upon cooling, the dark solution was poured into 300 mL of saturated $NaHCO_3$ solution and extracted with 300 mL of ethyl acetate. The organic layer was dried over Na_2SO_4, filtered, and concentrated to give 8.0 g of a brown solid. Preparative HPLC with 0.5% $EtOH/CH_2Cl_2$ afforded 4.5 g (12.4 mmol), ca. 50% yield, of a light brown crystalline seven-membered product **9a**: mp 228–229 °C; IR (KBr) 3440, 1780, 1685, 1645, 1600 cm^{-1}; NMR δ 2.57 (s, 3 H, $OCOCH_3$), 2.85 (t, 2 H, J = 10 Hz), 2.97 (t, 2 H, J = 10 Hz), 6.42 (d, 1 H, J = 12 Hz), 7.80 (m, 3 H), 8.21 (m, 2 H).

Anal. Calcd for $C_{21}H_{14}O_6$: C, 69.61; H, 3.89. Found: C, 69.29; H, 3.99.

Also isolated was 1.0 g (2.5 mmol, ca. 10% yield) of the yellow five-membered product **8a**: mp 240–242 °C dec; IR (KBr) 1765, 1670, 1300, 1175 cm^{-1}; NMR δ 2.50 (s, 6 H, $OCOCH_3$), 2.53 (s, 3 H, $COCH_3$), 3.76 (d, 2 H, J = 2 Hz), 7.50 (t, 1 H, J = 2 Hz), 7.70 (m, 2 H), 8.10 (m, 2 H).

Anal. Calcd for $C_{23}H_{16}O_7$: C, 68.32; H, 3.96. Found: C, 68.14; H, 4.12.

7,8-Dihydro-9-methyl-6,11-dimethoxy-5,12-naphthacenedione (6c). To a 100-mL round-bottom flask equipped with magnetic stirring bar, reflux condenser, and argon inlet was added 2.53 g (8.3 mmol) of hydroquinone **6a**, 2.76 g (20 mmol) of potassium carbonate, 50 mL of dry 2-butanone, and 2.9 mL (30 mmol) of dimethyl sulfate. This stirred mixture was refluxed under nitrogen for 18 h. The butanone was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 and H_2O. The organic layer was washed with 2.5% KOH solution, dried over Na_2SO_4, and concentrated in vacuo to give 2.8 g of a yellow solid. Recrystallization from $CHCl_3$/hexane gave 1.84 g (5.5 mmol, ca. 66% yield) of yellow needles: mp 170–172 °C; IR (KBr) 1670, 1645, 1330 cm^{-1}; NMR δ 2.05 (s, 3 H, C=CCH_3), 2.22 (t, 2 H, J = 8 Hz), 2.92 (t, 2 H, J = 8 Hz), 3.86 (s, 6 H, OCH_3), 6.60 (s, 1 H, C=CH), 7.65 (m, 2 H), 8.10 (m, 2 H).

Anal. Calcd for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43. Found: C, 75.46; H, 5.48.

2-Acetyl-4,11-dimethoxy-1*H*-cyclopent[*b*]anthracene-5,10-dione (8b) and 6,12-Dimethoxy-7*H*-cyclohept[*b*]-anthracene-5,9,13[8*H*]-trione (9b). To a 500-mL ozonolysis apparatus with gas inlet frit was added 9.0 g (27 mmol) of olefin

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6c, 200 mL of CH_2Cl_2, and 50 mL of CH_3OH. The solution was cooled to −70 °C and treated with a stream of ozone in oxygen until a faint blue color was observed. The excess ozone was removed by bubbling oxygen into the solution. Dimethyl sulfide (5 mL) and 0.2 mL of pyridine were added and the solution was allowed to warm to 25 °C and stand for 18 h. The resulting solution was washed with 10% HCl solution, dried over Na_2SO_4, and concentrated to give 9.0 g of a bright yellow solid: NMR δ 2.16 (s, 3 H), 2.75 (t, 2 H, J = 7 Hz), 3.20 (t, 2 H, J = 7 Hz), 3.90 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 7.75 (m, 2 H), 8.15 (m, 2 H), 10.6 (s, 1 H, CH=O). The crude aldehyde was dissolved in 500 mL of benzene containing 500 mg of *p*-toluenesulfonic acid and refluxed with azeotropic removal of H_2O for 1 h. The cooled reaction mixture was washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, and concentrated in vacuo to give 8.5 g of a light brown solid. Preparative HPLC (20% EtOAc/hexane) gave 4.0 g (11.5 mmol, ca, 43%) of the five-membered product **8b**: mp 201–202 °C; IR (KBr) 1660, 1300 cm^{-1}; NMR δ 2.58 (s, 3 H, $COCH_3$), 3.93 (d, 2 H, J = 2 Hz), 4.05 (s, 3 H, OCH_3), 4.10 (s, 3 H, OCH_3), 7.75 (m, 3 H), 8.15 (m, 2 H).

Anal. Calcd for $C_{21}H_{16}O_5$: C, 72.41; H, 4.63. Found: C, 72.11; H, 4.63.

Also isolated was 1.7 g (49 mmol, 18% yield) of the seven-membered product **9b**: mp 215–216 °C; IR (KBr) 1675, 1655, 1330, 1245 cm^{-1}; NMR δ 2.80 (m, 2 H), 3.20 (m, 2 H), 3.93 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 6.40 (d, 1 H, J = 13 Hz), 7.65 (d, 1 H, J = 13 Hz), 7.75 (m, 2 H), 8.15 (m, 2 H).

Anal. Calcd for $C_{21}H_{16}O_5$: C, 72.41; H, 4.63. Found: C, 72.39; H, 4.85.

2-(1-Hydroxyethyl)-4,11-dimethoxy-1*H*-cyclopent[*b*]anthracene-5,10-dione (13). To a 100-mL round-bottom flask equipped with magnetic stirring bar and argon inlet was added 550 mg (1.58 mmol) of enone **8b**, 20 mL of CH_2Cl_2, 15 mL of CH_3OH, and 400 mg (6.3 mmol) of sodium cyanoborohydride. The stirred reaction mixture was treated with 10% HCl until no starting material was evident by TLC analysis. The solution was poured into saturated $NaHCO_3$ solution and extracted into CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give 550 mg of a brown solid. Recrystallization from $CHCl_3$/hexane gave 440 mg (1.26 mmol, ca. 80% yield) of yellow crystals: mp 190–191 °C; IR (KBr) 3400, 1660, 1300 cm^{-1}; NMR ($CDCl_3/CD_3OD$) δ 1.50 (d, 3 H, J = 7 Hz), 3.63 (d, 2 H, J = 2 Hz), 3.96 (s, 6 H), 4.70 (qd, 1 H, J_a = 7 Hz, J_b = 2 Hz), 6.90 (q, 1 H, J = 2 Hz), 7.65 (m, 2 H), 8.10 (m, 2 H).

Anal. Calcd for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.67; H, 5.17.

2-Acetyl-2,3-dihydro-2,3-epoxy-4,11-dimethoxy-1*H*-cyclopent[*b*]anthracene-5,10-dione (14). The method of Cella et al.[9] was modified. To a 100-ml round-bottom flask equipped with magnetic stirring bar and argon inlet was added 735 mg (2.1 mmol) of allylic alcohol **13**, 50 mL of CH_2Cl_2, 168 mg (2.0 mmol) of $NaHCO_3$, and 470 mg (2.3 mmol) of 85% *m*-chloroperoxybenzoic acid (MCPBA). After the reaction had stirred for 15 h at 25 °C under argon, TLC analysis showed clean conversion to an intermediate epoxy alcohol. 606 mg (3.0 mmol) of additional MCPBA and 1.0 mL of 0.2 M 2,2,6,6-tetramethylpiperidinium chloride (TMP·HCl) in CH_2Cl_2 was added. Stirring was continued for 15 h. The reaction mixture was poured into 50 mL of 1:1 10% $NaHSO_3$ and saturated $NaHCO_3$. Extraction with two 50-mL portions of CH_2Cl_2, drying of the organics over Na_2SO_4, and concentration in vacuo gave 700 mg of a yellow solid. Recrystallization from $CHCl_3$/hexane gave 300 mg (0.82 mmol, ca. 40%) of purified epoxy ketone **14**: mp. 200–201 °C dec; IR (KBr) 1710, 1670, 1585, 1320 cm^{-1}; NMR δ 2.20 (s, 3 H), 3.15 (d, 1 H, J = 20 Hz), 3.80 (d, 1 H, J = 20 Hz), 3.93 (s, 3 H), 4.06 (s, 3 H), 4.80 (s, 1 H), 7.75 (m, 2 H), 8.10 (m, 2 H). Due to the extreme sensitivity of this compound, correct elemental analysis was not obtained.

1-Acetyl-1,3-dihydro-4,11-dimethoxy-2*H*-cyclopent[*b*]anthracene-2,5,10-trione (15). To a solution of 64 mg (0.18 mmol) of epoxy ketone **14** in 3.0 mL of $CHCl_3$ was added 95 mg (1.0 mmol) of chloroacetic acid. The solution was stirred at 25 °C for 15 h during which time the reaction turned reddish brown. The reaction mixture was poured into 10 mL of saturated $NaHCO_3$ solution and extracted into 25 mL of $CHCl_3$. Drying of the organic layer over Na_2SO_4 and concentration in vacuo gave 67 mg of a solid which gave a positive ferric chloride test:[18] IR (KBr) 3400, 1700, 1670, 1570, 1315 cm^{-1}; NMR δ 2.63 (d, 3 H), 3.63 (d, 2 H), 4.0 (s, 6 H), 7.75 (m, 2 H), 8.20 (m, 2 H), 11.55 (s, $^1/_2$ H).

5,8-Dihydro-6-methyl-1,4-naphthalenediol (16a). To a mechanically stirred solution of 540 g (5.0 mmol) of *p*-benzoquinone in 1.5 L of toluene was added 500 g (7.4 mol) of isoprene. The reaction mixture was heated to 50 °C for 72 h. A small aliquot was analyzed and no quinone was present. The volatiles were removed in vacuo, 1.0 L of HOAc and 10 g of NaOAc were added and the resulting solution was heated at reflux for 30 min. White crystals formed upon cooling. Filtration and suction drying gave 775 g (4.4 mol, 88% yield) of aromatized hydroquinone **16a**: mp 177–178 °C (lit.[19] mp 175 °C); (IR KBr) 3280, 1630, 1480, 1240, 1020, 810, 785, 740 cm^{-1}; NMR δ 1.75 (s, 3 H), 3.2 (m, 4 H), 5.55 (m, 1 H), 6.5 (s, 2 H).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.63; H, 6.85.

1,4-Dihydro-5,8-dimethoxy-2-methylnaphthalene (16b). To a 3-L, round-bottom, 3-neck flask equipped with heating mantle, mechanical stirrer, thermometer, and Claisen head with reflux condenser and argon inlet was added 264 g (1.5 mol) of hydroquinone **16a**, 205 g (3.6 mol) of KOH, 1.5 L of 2-butanone, and 170 mL (1.8 mol) of dimethyl sulfate. The stirred mixture was gradually heated to reflux. Initially the reaction was exothermic. After the initial exotherm had subsided, the solution was stirred at gentle reflux for 15 h under positive argon pressure. The cooled solution was filtered and concentrated in vacuo. Kugelrohr distillation (130 °C (1.2 mmHg)) gave 285 g (93% yield) of crude product. Recrystallization from hexane gave 245 g (1.2 mol, 80% yield) of purified product **16b**: mp. 43–44 °C; IR (KBr) 1600, 1485, 1250, 1085, 785, 712 cm^{-1}; NMR 1.70 (s, 3 H), 3.10 (s, 4 H), 3.66 (s, 6 H), 5.40 (m, 1 H), 6.46 (s, 2 H).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.04; H, 7.70.

1,2-Dihydro-5,8-dimethoxy-3-methylnaphthalene (17). To a 2-L, 3-neck, round-bottom flask equipped with magnetic stirring bar, heating mantle, thermometer, condenser, and argon inlet was added 245 g (1.20 mol) of olefin **16b**, 135 g (1.20 mol) of potassium *tert*-butoxide, and 500 mL of dry Me_2SO. The resulting brown solution was stirred at 60 °C for 96 h. The cooled solution was poured into 1.5 L of water and extracted with two 1-L portions of ether and 1-L of hexane. The combined organic layers were washed well with H_2O, shaken with brine, and dried over Na_2SO_4. Filtration and concentration in vacuo gave a crystalline mass which afforded 180 g (73% yield) of white crystals: mp 62–63 °C (lit.[20] mp 66 °C); IR (KBr) 1600, 1490, 1255, 1090, 1075, 795 cm^{-1}; NMR 1.93 (s, 3 H), 2.16 (t, 2 H, J = 8 Hz), 2.80 (t, 2 H, J = 8 Hz), 3.80 (s, 6 H), 6.60 (m, 3 H).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.50; H, 8.03.

1-(4,7-Dimethoxy-1*H*-inden-2-yl)ethanone (18) and 1,4-Dimethoxy-5*H*-benzocyclohepten-7[6*H*]-one (19). The method of Pappo et al.[21] was modified. A stirred solution of 51.0 g (250 mmol) of conjugated olefin **17** in 400 mL of dioxane and 200 mL of water was treated with 20 mL of a stock 20 mg/mL OsO_4 solution in dioxane. After stirring for 5 min at 25 °C under argon, 117 g (275 mmol) of finely powdered sodium metaperiodate was added. The brown mixture was stirred at 25 °C under argon for 5 days. The mixture was filtered and the cake was washed with ether. The filtrate was diluted with ether and washed well with water. The combined aqueous washes were back extracted with 500 mL of ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give 53.2 g of a semisolid: NMR 2.16 (s, 3 H), 2.70 (m, 2 H), 3.10 (m, 2 H), 3.76 (s, 3 H), 3.80 (s, 3 H), 3.76 (d, 1 H, J = 8 Hz), 7.00 (d, 1 H, J = 8 Hz), 10.6 (s, 1 H). The crude keto aldehyde was dissolved in 500 mL of toluene containing 500 mg of *p*-toluenesulfonic acid and heated at 80 °C for 8 h. $NaHCO_3$ (13 g) was added to the cooled solution which was filtered over 300 g of silica

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gel with 25% acetone/toluene. Concentration in vacuo gave 47 g of a brown solid. Recrystallization from $CHCl_3$/hexane gave 15.6 g of the five-membered enone **18**. Chromatography of the mother liquor gave 2.5 g of additional five-membered enone **18** (83 mmol, 33% yield): mp 119–120 °C; IR (KBr) 1665, 1500, 1265 cm^{-1}; NMR 2.40 (s, 3 H), 3.63 (d, 2 H, J = 2 Hz), 3.80 (s, 3 H), 3.85 (s, 3 H), 6.70 (s, 2 H), 7.65 (t, 1 H, J = 2 Hz).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.54; H, 6.47.

Also 4.2 g (19.2 mmol, 7.7% yield) of the seven-membered enone **19** was isolated by chromatography: mp 84–86 °C; IR (KBr) 1650, 1260, 1070, 800, 712 cm^{-1}; NMR 2.55 (m, 2 H), 2.95 (m, 2 H), 3.64 (s, 3 H), 3.68 (s, 3 H), 6.10 (d, 1 H, J = 11 Hz), 6.65 (d, 1 H, J = 9 Hz), 6.84 (d, 1 H, J = 9 Hz), 7.50 (d, 1 H, J = 9 Hz).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.77; H, 6.44.

***cis*-1-[1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2,3-dihydro-2-hydroxy-4,7-dimethoxy-1*H*-inden-2-yl]ethanone (21).** To a solution of 872 mg (4.0 mmol) of enone **18** in 20 mL of dioxane and 5 mL of pyridine was added a solution of 1.01 g (4.0 mmol) of OsO_4 in 40 mL of dioxane. The resulting black solution was stirred for 8 h at 25 °C. A stream of H_2S was bubbled into the solution for 5 min. The mixture was filtered through Celite and the cake was washed with dioxane. The solution was concentrated under high vacuum yielding 920 mg of a light brown oil. This crude diol was dissolved in 7.5 mL of dry DMF and treated with 905 mg (6.00 mmol) of *tert*-butyldimethylsilyl chloride and 680 mg (10.0 mmol) of imidazole. The resulting solution was stirred at 25 °C under argon atmosphere for 18 h. The solution was then poured into 50 mL of H_2O and extracted into three 50-mL portions of ether. The combined organic layers were washed well with H_2O, dried over Na_2SO_4, and concentrated in vacuo to give 1.15 g of a yellow oil. Chromatography on 100 g of silica gel with 10% ethyl acetate:hexane afforded 750 mg (2.04 mmol, 56% yield) of purified silyl ether **21**: bp 190 °C (0.5 mmHg); IR (KBr) 3500, 1705, 1500, 1260 cm^{-1}; NMR δ 0.20 (s, 3 H), 0.23 (s, 3 H), 0.93 (s, 9 H), 2.36 (s, 3 H), 3.10 (s, 2 H), 3.80 (s, 6 H), 4.20 (s, 1 H), 5.53 (s, 1 H), 6.80 (s, 2 H).

Anal. Calcd for $C_{19}H_{30}O_5Si$: C, 62.26; H, 8.25. Found: C, 62.13; H, 8.08.

***cis*-2-Acetyl-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3-dihydro-2-hydroxy-1*H*-indene-4,7-dione (23).** To a stirred suspension of 7.0 g (19.1 mmol) of methyl ether **21** and 9.8 g (80 mmol) of finely ground argentic oxide[12] in 200 mL of *p*-dioxane at 10 °C under argon was added 27 mL (162 mmol) of 6 N nitric acid in dropwise fashion over a 5-min period. Water (25 mL) was added and the homogeneous, orange solution was poured into 1 L of H_2O and extracted with three 350-mL portions of dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give 8.0 g of a viscous oil. Chromatography on 500 g of silica gel with dichloromethane gave 4.8 g of pure quinone **23**, ca. 74% yield. A small sample was Kugelrohr distilled: bp 155 °C (0.15 mmHg); IR (KBr) 3470, 1710, 1665, 1580 cm^{-1}; NMR δ 0.19 (s, 3 H), 0.29 (s, 3 H), 0.93 (s, 9 H), 2.36 (s, 3 H), 2.91 (d, 2 H, J = 2 Hz), 4.0 (s, 1 H, OH), 5.42 (*t*, 1 H, J = 2 Hz), 6.71 (s, 2 H).

Anal. Calcd for $C_{17}H_{24}O_5Si$: C, 60.68; H, 7.19. Found: C, 60.86; H, 7.35.

***cis*-2-Acetyl-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3-dihydro-1*H*-cyclopent[*b*]anthracene-4,11-dione (26a).** The method of Kende[11] was utilized. A solution of 2.4 g (7.0 mmol) of quinone **23** and 1.7 g (7.0 mmol) of isobenzofuran precursor **24**[13] in 100 mL of dry diglyme was heated to 140 °C under argon for 10 min. Evolution of CO_2 ceased and the cooled solution was concentrated in vacuo to give 3.5 g of a viscous oil. The complicated NMR spectrum was consistent with a mixture of adducts **25**. The adduct was dehydrated by two methods.

Method A. To a refluxing solution of 1.0 g of sodium acetate in 100 mL of glacial acetic acid was added a solution of 3.5 g of crude isobenzofuran adduct **24** in 30 mL of glacial acetic acid. After stirring for 1 h, the cooled solution was poured into 500 mL of H_2O and extracted with three 100-mL portions of CH_2Cl_2. The combined organic extracts were washed well with H_2O and saturated $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4 and concentrated to give 4.0 g of a dark oil. Chromatography on 250 g of silica gel with dichloromethane gave 750 mg of pure anthraquinone **25a** (23% yield).

Method B. A solution of 11.4 g (25.0 mmol) of isobenzofuran adduct **25** and 5.53 g (25.0 mmol) of *N*-methylanilinium trifluoroacetate[12] in 250 mL of benzene was refluxed under argon with azeotropic removal of H_2O. After 48 h, no starting material remained. The cooled solution was poured into 500 mL of 10% HCl solution and the aqueous layer was extracted with two 200-mL portions of dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give 10.0 g of a brown foam. Chromatography on silica gel with dichloromethane gave 2.1 g (4.8 mmol) (19.3% yield) of anthraquinone **26a**. A small sample was recrystallized from chloroform/hexane: mp 171–172 °C; IR (KBr) 3470, 1710, 1665, 1630, 1610, 1305 cm^{-1}; NMR δ 0.25 (s, 3 H), 0.35 (s, 3 H), 0.94 (s, 9 H), 2.40 (s, 3 H), 3.06 (s, 2 H), 4.05 (s, 1 H, OH), 5.54 (s, 1 H), 7.62 (m, 2 H), 7.97 (m, 2 H), 8.55 (s, 2 H).

Anal. Calcd for $C_{25}H_{28}O_5Si$: C, 68.78; H, 6.46. Found: C, 68.61; H, 6.42.

***cis*-2-Acetyl-2,3-dihydro-2,3-dihydroxy-1*H*-cyclopent[*b*]anthracene-4,11-dione (26b).** To a solution of 600 mg (1.38 mmol) of silyl ether **26a** in 10 mL of dry THF under argon was added 150 μL (2.5 mmol) of glacial acetic acid and 1.65 mL (1.65 mmol) of 1 M tetra-*n*-butylammonium fluoride in THF. The reaction was monitored by TLC and was complete in 18 h. The solution was taken up in CH_2Cl_2, washed with H_2O, dried over Na_2SO_4, and concentrated to give 600 mg of a light brown solid. Recrystallization from chloroform/hexane and trituration with methyl alcohol gave 300 mg (67% yield) of a yellow solid: mp 212–214 °C dec; IR (KBr) 3430, 1712, 1670, 1620, 1310 cm^{-1}; NMR (Me_2SO-d_6) δ 2.30 (s, 3 H), 2.60 (d, 1 H, J = 20 Hz), 3.15 (d, 1 H, J = 20 Hz), 5.10 (d, 1 H, J = 8 Hz), 5.20 (s, 1 H, OH), 6.10 (d, 1 H, J = 8 Hz), 7.70 (m, 2 H), 8.20 (m, 2 H, 8.60 (s, 2 H).

Anal. Calcd for $C_{19}H_{14}O_5 \cdot {}^1/_2\, H_2O$: C, 68.88; H, 4.56. Found: C, 68.73; H, 4.18.

***cis*-2-Acetyl-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3-dihydro-1*H*-cyclopent[*a*]anthracene-2,4,11-triol 4,11-Diacetate (27).** To a solution of 437 mg (1.0 mmol) of quinone **26a** in 15 mL of acetic anhydride under argon was added 1.0 g of zinc powder. The cooled mixture was stirred at 60 °C for 1 h and then filtered. The zinc solids were washed with 2 mL of Ac_2O and 5 mL of pyridine. The combined filtrates were stirred under argon at 0 °C for 1.5 h. The solution was concentrated under high vacuum and the residue was dissolved in 125 mL of CH_2Cl_2. The organic solution was washed with two 50-mL portions of 10% HCl, 50 mL of saturated $NaHCO_3$ solutions, and brine. After drying over Na_2SO_4, the organics were concentrated to give 500 mg of a yellow oil, which was flash chromatographed on 100 mL of silica gel to give 350 mg of crude product which was recrystallized from CH_2Cl_2/hexane to give 300 mg (0.57 mmol) (57% yield) of yellow crystals: mp 190–191 °C; IR (KBr) 3460, 1770, 1710, 1190 cm^{-1}; NMR δ 0.12 (s, 6 H), 0.94 (s, 9 H), 2.12 (s, 3 H), 2.50 (s, 3 H), 2.54 (s, 3 H), 3.04 (d, 1 H, J = 16 Hz), 3.24 (d, 1 H, J = 16 Hz), 4.00 (s, 1 H), 5.23 (s, 1 H), 7.33 (m, 2 H), 7.92 (m, 2 H), 8.24 (s, 2 H).

Anal. Calcd for $C_{29}H_{34}O_7Si$: C, 66.64; H, 6.56. Found: C, 66.65; H, 6.54.

***cis*-2-Acetyl-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3,5,10-tetrahydro-5,10-dioxo-1*H*-cyclopent[*b*]anthracene-2,4,11-triol 4,11-Diacetate (28).** To a stirred solution of 25 mg of diacetoxyanthracene **27** in 2 mL of glacial acetic acid at 25 °C was added a solution of 20 mg (0.20 mmol) of CrO_3 in 0.5 mL of water. After stirring for 1 h, the solution was poured into 50 mL of saturated $NaHCO_3$ solution and the product was extracted into dichloromethane. The organic extract was dried over Na_2SO_4 and concentrated to give 20 mg of a yellow film. TLC with 2% acetone/CH_2Cl_2 gave 4 mg of a yellow solid (R_f = 0.35) whose NMR was consistent with the expected product: NMR δ 0.15 (s, 3 H), 0.23 (s, 3 H), 0.87 (s, 9 H), 2.20 (s, 3 H), 2.45 (s, 3 H), 2.50 (s, 3 H), 3.20 (s, 1 H), 3.25 (s, 1 H), 3.85 (s, 1 H, OH), 5.34 (s, 1 H), 7.65 (m, 2 H), 8.05 (m, 2 H).

***cis*-2-Acetyl-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3-dihydro-1*H*-cyclopent[*b*]anthracene-1,4,11-triol 1,4,11-Triacetate (29).** To a stirred solution of 1.98 g (4.54 mmol) of quinone **26a** in 50 mL of acetic anhydride was added 6.0 g of zinc powder and the mixture was heated at 60 °C under argon for 1 h. The cooled solution was filtered. Pyridine (15 mL) was added

to the filtrate and the resulting solution was heated at 60 °C under argon for 2 h and then at 25 °C for 18 h. The volatiles were removed in vacuo and the residue was taken up in CH_2Cl_2, washed well with H_2O, dried over Na_2SO_4, and concentrated to give 2.3 g of a semisolid. Flash chromatography on 300 mL of silica gel with 20% EtOAc/hexane gave 1.64 g of pure triacetate (2.9 mmol) (64% yield) as a yellow solid: mp 177–179 °C (hexane); IR (KBr) 1775, 1740, 1718, 1170 cm^{-1}; NMR δ 0.05 (s, 3 H), 0.15 (s, 3 H), 0.80 (s, 9 H), 2.02 (s, 3 H), 2.20 (s, 3 H), 2.40 (s, 3 H, 2.43 (s, 3 H), 3.05 (d, 1 H, J = 16 Hz), 3.40 (d, 1 H, J = 16 Hz), 6.29 (s, 1 H), 7.35 (m, 2 H), 7.80 (m, 2 H), 8.20 (s, 2 H).

Anal. Calcd for $C_{31}H_{36}O_8Si$: C, 65.93; H, 6.43. Found: C, 66.10; H, 6.81.

***cis*-2-Acetyl-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,3,5,10-tetrahydro-5,10-dioxo-1*H*-cyclopent[*b*]anthracene-1,4,11-triol 1,4,11-Triacetate (30).** To a stirred solution of 1.13 g (2.00 mmol) of anthracine **29** in 30 mL of glacial acetic acid at 25 °C under argon was added dropwise over 5 min a solution of 800 mg (8.0 mmol) of CrO_3 in 5 mL of H_2O. After stirring for 15 min, the dark solution was carefully poured into a stirred saturated solution of $NaHCO_3$ (100 mL). The organics were extracted into ethyl acetate, washed repeatedly with bicarbonate solution, dried over Na_2SO_4, filtered, and concentrated to give 1.2 g of an orange oil. Crystallization from hexane gave 720 mg (1.18 mmol) of a yellow solid. The mother liquors were chromatographed on silica gel with 20% ethyl acetate/hexane to give an additional 160 mg of product, 1.45 mmol total (72% yield): mp 110–112 °C; IR (KBr) 1775, 1750, 1715, 1675, 1175 cm^{-1}; NMR δ 0.05 (s, 3 H), 0.12 (s, 3 H), 0.90 (s, 9 H), 2.13 (s, 3 H), 2.28 (s, 3 H), 2.33 (s, 3 H), 2.36 (s, 3 H), 3.12 (d, 1 H, J = 16 Hz), 3.50 (d, 1 H, J = 16 Hz), 6.30 (s, 1 H), 7.70 (m, 2 H), 8.10 (m, 2 H).

Anal. Calcd for $C_{31}H_{34}O_{10}Si$: C, 62.61; H, 5.76. Found: C, 62.93; H, 5.63.

Glycoside Coupling of Protected Daunosamine to Diol 26b. A stirred solution of 326 mg (0.60 mmol) of 2,3,6-trideoxy-1,4-di-*O*-*p*-nitrobenzoyl-3-trifluoroacetamido-α-L-*lyxo*-hexopyranose[17] in 10 mL of dry CH_2Cl_2 at 0 °C under argon was treated with gaseous HCl for 3 min. After standing at 25 °C for 10 min, the *p*-nitrobenzoic acid was removed by filtration and the filtrate was concentrated to dryness yielding 200 mg (ca. 100%) of glycosyl chloride **31**. The chloro sugar (0.60 mmol), diol **26b** (140 mg, 0.44 mmol), and powdered anhydrous $CaCO_3$ (200 mg, 2.0 mmol) were vigorously stirred in 10 mL of dry CH_2Cl_2 under argon while a solution of 154 mg (0.60 mmol) of silver trifluoromethanesulfonate (AgTF) in 5 mL of dry THF was added over a 5-min period. The diol appeared to dissolve and the mixture darkened as addition of AgTf progressed. After stirring for 15 min at 25 °C, TLC (40% EtOAc/hexane) showed two mobile products, R_f 0.50 and R_{f_B} 0.42 with only a trace of starting diol remaining. The reaction mixture was filtered and filtrate was dried over Na_2SO_4. Concentration in vacuo gave 450 mg of a light brown foam. Preparative TLC on eight 20 cm × 20 cm (0.5 mm) silica gel plates with 25% EtOAc/hexane gave 75 mg of isomer A and 60 mg of isomer B. Both isomers gave similar spectra which indicated some decomposition upon chromatography. Isomer A was purified by precipitation from CH_2Cl_2 with hexane: IR (KBr) 3475, 1740, 1715, 1675, 1540 cm^{-1}; NMR δ 1.18 (d, 3 H, J = 7 Hz), 2.25 (m, 3 H), 2.38 (s, 3 H), 3.10 (s, 2 H), 3.60 (m, 1 H), 4.20 (q, 1 H, J = 7 Hz), 4.60 (m, 1 H), 5.35 (m, 2 H), 5.85 (s, 1 H), 6.96 (d, 1 H, J = 7 Hz, NH), 7.60 (m, 2 H), 7.85 (m, 2 H), 8.12 (s, 4 H), 8.35 (s, 2 H).

Effect of the α-Trifluoromethyl Moiety on the Solvolysis of Allylic Sulfonates

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A series of allylic sulfonates bearing aryl substituents on the 2-position and/or trifluoromethyl groups on the 1- and/or 3-positions has been studied under solvolytic conditions in 2,2,2-trifluoroethanol. Nonarylated 1,3-di(trifluoromethyl)-substituted allylic sulfonates did not solvolyze in a conventional manner but instead gave products diagnostic of a complex isomerization–cleavage process. Mono(trifluoromethyl)-substituted allylic sulfonates solvolyzed by normal paths to give k_H/k_{CF_3} ratios of 2×10^6 and 4×10^4 for the substitution at the 1- and 3-positions, respectively. No evidence for 1,3-π interactions was discerned.

Introduction

The study of carbocation intermediates that are destabilized by strongly electron-withdrawing substituents has recently drawn the attention of several groups.[2-8] We have been especially interested in evaluating the influence that these destabilizing substituents have on several classical solvolytic systems.[2,3a] For example, the α-cyano group produced rate retardations relative to α-H (k_H/k_{CN}) of

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