Journal of Natural Products
Vol. 48, No. 3, pp. 357-362, May-Jun 1985

PREPARATION OF GLUCOSIDIC DERIVATIVES OF STEGANOL

RICKEY P. HICKS and ALBERT T. SNEDEN*

Department of Chemistry, Virginia Commonwealth University, Richmond, Virginia 23284

ABSTRACT.—Glucoside derivatives of steganol (**1**) analogous to the semisynthetic podophyllotoxin derivative, VP 16-213, were prepared. Glucosidation of steganol (**1**) with 2,3,4,6-tetra-*O*-benzylglucopyranose gave the α-anomer (**7**) of the glucoside as the major product. Subsequent removal of the benzyl groups and reaction with acetaldehyde dimethyl acetal gave the ethylidene derivative **10**. The β-anomer (**8**) of the glucoside was similarly converted to **12**. All derivatives prepared were screened for activity in the DNA breakage assay.

The bioassay guided fractionation of plants has provided a large number of potential antineoplastic agents during the past twenty years, but few of these active plant principles have proven effective in advanced animal cancer systems or clinical trials. Modification of active plant principles has, in several cases, provided clinically useful agents. Among the premier examples of such successful modifications are the glucosidic derivatives of 4′-demethyl-*epi*-podophyllotoxin, VM-26 and VP-16-213 (1,2). As part of a continuing effort to investigate plant-derived principles as potential chemotherapeutic agents, glucosidic derivatives of the bisbenzocyclooctadiene lignan lactone steganol (**1**) analogous to VP-16-213 have been prepared.

RESULTS AND DISCUSSION

In order to obtain sufficient steganol (**1**) for this work, stem wood and stem bark of *Steganotaenia araliacea* Hochst. (Apiaceae) were fractionated according to literature procedures (3,4). In addition to the small amount of steganol (**1**) thus obtained, larger amounts of steganacin (**2**), steganangin (**3**), and steganone (**4**) were also isolated. Hydrolysis of either steganacin (**2**) or steganangin (**3**) with 5% NH_4OH in MeOH gave steganol (**1**) in 75% yield with only minor amounts of side products resulting from epimerization of the lactone. Steganone (**4**) was reduced with sodium borohydride according to literature procedures (3) to obtain *epi*-steganol (**5**).

In the studies with the podophyllotoxin lignans, glucosidation of either podophyllotoxin or *epi*-podophyllotoxin resulted in the formation of the *epi*-glucoside exclusively (5). To examine the stereochemical consequences of the reaction conditions for glucosidation with steganol (**1**), preparation of the ethyl ether (**6**) of steganol (**1**) was investigated. Excess EtOH was added to a solution of **1** in 1,2-dichloroethane at −20°. After addition of BF_3-etherate, the resulting mixture was stirred at −20° for 4 h, then quenched with pyridine. The ethyl ether (**6**) was isolated by preparative tlc.

The stereochemistry at C-5 in the steganol-derived lignans may be determined from examination of the ^{1}H-nmr spectra, in particular the chemical shift and coupling of the 8α-H. In the ^{1}H-nmr spectrum of steganol (**1**), the 8α-H appears as a doublet (J= 14.5 Hz) at δ 3.04. This same coupling and chemical shift (δ 3.00-3.08) is seen for the 8α-H in the ^{1}H-nmr spectra of steganacin (**2**) and steganangin (**3**), and, from examination of Dreiding models, would be expected to be the case whenever the C-5 substituent is α (5*R*). On the other hand, the 8α-H appears as a doublet of doublets (J=8, 15 Hz) at δ 3.22 in the spectrum of *epi*-steganol (**5**). This multiplicity, again from examination of Dreiding models, is consistent with a 5-β substituent. The chemical shifts and coupling of the 7, 8β, 13α, and 13β protons (Table 1) are also indicative of and may be used to confirm the stereochemistry at C-5.

The ^{1}H-nmr data of the ethyl ether (**6**) prepared from steganol (**1**) suggested that the stereochemistry at C-5 was "normal;" the 8α-H appeared as a doublet at δ 3.07

TABLE 1. [1]H-nmr Resonances for the Aliphatic Stegane Skeletal Protons of **1**, **5**, and **7**-**10**.

Compound	H (*J* in Hz)						
	5	6	7	8α	8β	13α	13β
1	4.50 m	2.38 m	2.58 dd (9,14)	3.04 d (14.5)	2.48 dd (14.5,9)	4.50 m	3.92 m
5	4.98 d (8)	2.94 m	2.28 m	3.22 dd (8,15)	2.68 dd (10,15)	4.32 dd (7.5,8)	4.08 dd (7.5,12.5)
7	4.38 d (7)	2.67 dd	2.45 dd (9,15)	3.04 d (13)	2.53 dd (9,12)	3.91 dd (7,10)	3.71 dd (7,10)
8	obscured	2.64 m	2.44 dd (9,15)	3.03 (13)	2.56 dd (9,13)	3.99 dd (7,10)	3.22 dd (7,10)
9	4.36 d (9)	2.16 m	2.44 dd (6.5,13)	3.05 d (13)	2.58 dd (6.5,13)	3.94 dd (7,10)	3.20 dd (7,10)
10	4.32 d (8)	2.22 m	2.45 dd (9,14)	3.03 d (13)	2.62 dd (9,14)	3.95 m	obscured

($J = 12$ Hz). This stereochemistry was confirmed by the preparation of **6** from steganol (**1**), using triethyloxonium tetrafluoroborate, a reagent which will not affect the stereochemistry of the hydroxyl-bearing carbon (6). These results suggested that epimerization at C-5 of steganol (**1**) would not occur under the conditions required to prepare the glucosides.

With these results in hand, glucosides of steganol (**1**) were then prepared by a slightly modified procedure. 2,3,4,6-Tetra-*O*-benzylglucose (2 eq.) was dissolved in 1,2-dichloroethane containing BF_3-etherate under N_2 at $-78°$. Steganol (**1**) (1 eq.) was added, and the mixture was stirred at $-78°$ for 6 h. After workup, two isomeric tetra-*O*-benzylglucosides, **7** and **8**, of steganol (**1**) were isolated in a 4:1 ratio. The [1]H-nmr spectra (Table 1) of each isomer exhibited a one-proton doublet ($J = 13$ Hz) at δ 3.04 for the 8α-H, indicating that both isomers retained the configuration of steganol

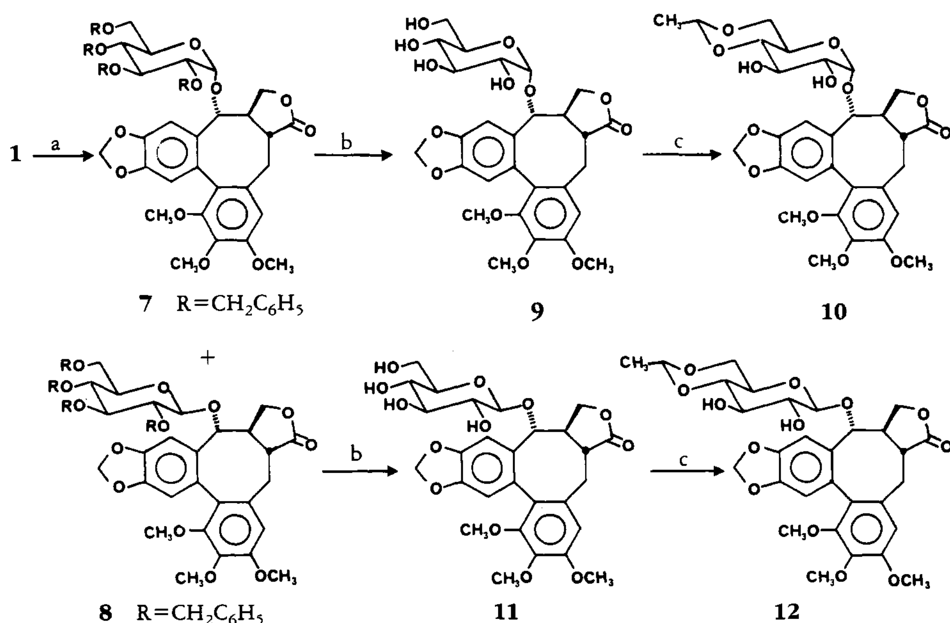


FIGURE 1. Conversion of steganol (**1**) into **10** and **12**. (a) 2,3,4,6-tetra-*O*-benzylglucopyranose, BF_3-Et_2O, $ClCH_2CH_2Cl$, $-78°$, 6h; (b) H_2, Pd-C, EtOH, rt, 72h; (c) $CH_3CH(OCH_3)_2$, *p*-TsOH, CH_3NO_2, rt, 96h.

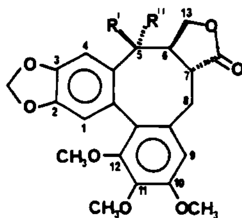
(**1**) at C-5, i.e., 5β-H. This, in conjunction with the other ^{1}H- and ^{13}C-nmr spectral data, suggested that the isomers differed at the anomeric carbon of the glucose. The ^{1}H-nmr of the major isomer (**7**) exhibited a one-proton doublet at δ 4.98 (J=3 Hz) which was assigned to the anomeric proton.[1] The coupling constant of this resonance was consistent with that expected for the α-anomer (7). The ^{1}H-nmr resonance of the anomeric proton of the minor isomer (**8**) was obscured by the resonances for the benzyl protons.

Hydrogenolysis of the benzyl groups of **7** gave 5α-(glucopyranosyl) stegane (**9**). The stereochemistry at C-5 and the anomeric carbon was clearly indicated in the ^{1}H-nmr spectrum of **9**. The 8α-H appeared as a doublet at δ 3.05 (J=12-13 Hz), and the 5β-H appeared as a doublet at δ 4.3 (J=9 Hz) while the anomeric 1′-H appeared as a doublet at δ 4.78 (J=3 Hz).[1] These data indicated that **9** was the α-anomer of 5α-(glucopyranosyl)stegane.

The ethylidene derivative of **9** was then prepared by the method developed for the podophyllotoxin derivatives (8). Treatment of **9** with a molar excess of acetaldehyde dimethyl acetal and a catalytic amount of *p*-toluenesulfonic acid yielded ethylidene derivative **10**. Formation of the ethylidene derivative was indicated by a three-proton doublet (J=5 Hz) at δ 1.35 and a one-proton quartet (J=5 Hz) at δ 4.70 in the ^{1}H-nmr spectrum of **10**. The 8α-H appeared as a doublet (J=13 Hz) at δ 3.03, and the 5β-H appeared as a doublet (J=8 Hz) at δ 4.32, again indicating that the stereochemistry at C-5 was "normal." This assignment was confirmed by the chemical shifts and couplings of the 7, 8β, 13α, and 13β protons (Table 1). The anomeric proton appeared as a doublet (J=3 Hz) at δ 4.78 confirming that **10** retained the α-configuration of the anomeric carbon of the glucoside.

The minor tetra-*O*-benzylglucoside (**8**) was converted in an analogous manner into its ethylidene derivative (**12**) via its free glucoside (**11**). This glucoside also had the "normal" stereochemistry at C-5 as indicated by the 8α-H resonance at δ 3.04 (d, J=12 Hz). The ^{1}H nmr of **12** was identical to the ^{1}H nmr of the steganol ethylidene-β-D-glucoside (**12**) prepared by Robin and co-workers (9).

Ethyl ether **6** and glucoside derivatives **7-12** were all screened in the DNA breakage assay (10) by Bristol Laboratories, an assay in which the 4′-demethyl-*epi*-podophyllotoxin derivatives show activity. Unfortunately, none of the steganol derivatives were active in this assay. This may be due to the presence of the C-11 methoxyl moiety in the steganol derivatives or the rigid conformation of the biaryl ring system. Further investigations are in progress to resolve this question.



	R′		R″
1	H		OH
2	H		$OCOCH_3$
3	H		$OCOC(CH_3)=CHCH_3$
4		=O	
5	OH		H
6	H		OCH_2CH_3

[1]This assignment was confirmed by decoupling experiments.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Ir spectra were measured on a Perkin-Elmer 283 instrument, and uv spectra were measured on a Beckman Acta MVII recording spectrophotometer. ^{1}H-nmr spectra were recorded on a JEOL FX90Q spectrometer at 89.56 MHz or on a Bruker 360 MHz spectrometer at Bristol Laboratories in Syracuse, New York, in $CDCl_3$ with TMS as an internal standard. ^{13}C-nmr spectra were recorded on a JEOL FX90Q spectrometer at 22.5 MHz in $CDCl_3$ with TMS as an internal standard. Mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Center. DNA breakage assays were carried out by Bristol Laboratories. All known steganins were compared to authentic samples from the collection of the late Dr. S.M. Kupchan.

PLANT MATERIAL.—Stem wood and stem bark of *S. araliacea* (B643452, PR-20777) collected in Ethiopia in 1971, was supplied by the Medicinal Plant Resources Laboratory, USDA, Beltsville, Maryland, where voucher specimens are preserved.

ISOLATION PROCEDURE.—The dried, ground stem wood and stem bark of *S. araliacea* was extracted with 95% EtOH, and the steganins were isolated as previously described (3,4).

HYDROLYSIS OF STEGANACIN (**2**) AND STEGANANGIN (**3**).—A mixture of steganacin (**2**) and steganangin (**3**) (984.7 mg) was dissolved in absolute MeOH (50 ml) and NH_4OH (3 ml), and stirred at room temperature for 62 h. The MeOH was concentrated in vacuo to yield a white solid. This solid was dissolved in $CHCl_3$ (50 ml), washed twice with saturated NaCl (30 ml), then dried (Na_2SO_4). The $CHCl_3$ was concentrated in vacuo to yield crude product (884 mg). This material was subjected to flash chromatography over silica gel eluted with 20% Et_2O in C_6H_6 to give steganol (**1**) (734.8 mg) (75%).

REDUCTION OF STEGANONE (**4**).—Steganone (**4**) (244 mg) in freshly distilled THF (20 ml) was cooled to 0° and $NaBH_4$ (43.4 mg) was added at once. The solution was stirred at 0° for 3 h, and the reaction terminated by addition of HOAc. The solution was diluted with CH_2Cl_2 (20 ml), washed with 1N HCl (10 ml) and H_2O (2× 10 ml), and dried (Na_2SO_4). The CH_2Cl_2 was concentrated in vacuo to yield a yellow-white residue. Preparative tlc of this residue on silica gel eluted (twice) with 30% Et_2O in C_6H_6 gave epi-steganol (**5**) (65.2 mg), steganol (**1**) (50 mg), and recovered steganone (**4**) (47.7 mg).

STEGANOL-5-ETHYL ETHER (**6**).—Steganol (**1**) (91.8 mg) and absolute EtOH (0.5 ml) in 1,2-dichloroethane (15 ml) were cooled to −20°. BF_3-etherate (0.4 ml) was added, and the mixture was stirred for 4 h while slowly warming to room temperature. Dry pyridine (0.6 ml) was added, and the mixture was diluted with 1,2-dichloroethane (25 ml) and washed four times with 1N HCl (50 ml) and dried (Na_2SO_4). The solvent was concentrated in vacuo to give 100 mg of crude product. Preparative tlc of this material on silica gel eluted (twice) with 40% Et_2O in C_6H_6 gave **6** (45.4 mg, 46%); mp 190-193° (EtOH); ir ν max (KBr) 2980, 2940, 1760, 1605, 1485, 1375, 1230, 1070 cm^{-1}; uv λ max (EtOH) 248 nm (ϵ 3450); ^{1}H nmr δ 6.64 (s, 1H, 9-H), 6.54 (s, 1H, 4-H), 6.33 (s, 1H, 1-H), 5.95 (s, 2H, O-CH_2-O), 3.82 (s, 3H, 10-OCH_3), 3.77 (s, 3H, 11-OCH_3), 3.60 (s, 3H, 12-OCH_3), 3.24 (q, 2H, J=7 Hz, 1'-CH_2), 0.99 (t, 3H, J=7 Hz, 2'-CH_3); ^{13}C nmr 178.1 s (C=O), 153.3 s, 152.0 s, 147.6 s, 146.5 s, 147.4 s, 133.3 s, 131.0 s, 130.4 s, 127.8 s, 113.1 d, 112.4 d, 107.8 d, 101.6 t (OCH_2O), 85.4 d (C-5), 72.5 t (C-13), 63.2 t (C-1'), 61.1 q (OCH_3), 60.8 q (OCH_3), 56.2 q (OCH_3), 44.6 d (C-7), 42.0 d (C-6), 30.8 t (C-8), 15.1 q (C-2') ppm; ms m/z 442.1 [M$^+$], 396, 366, 358, 314, 313, 290, 283, 282.

Steganol (**1**) (41.5 mg) was dissolved in CH_2Cl_2 (4 ml) and treated with 0.15 ml Et_3OBF_4 (1.0M in CH_2Cl_2). After 45 min at room temperature, the solution had turned reddish-orange. After stirring for 2.5 h at room temperature, the reaction mixture was poured into H_2O (25 ml) and extracted with Et_2O (2×30 ml). The combined Et_2O layers were washed with 5% $NaHCO_3$ (2×50 ml) and H_2O (50 ml) and dried (Na_2SO_4). The Et_2O was removed in vacuo, and the residue was subjected to preparative tlc on silica gel eluted with 20% Et_2O in C_6H_6 to give 4.1 mg (9.3%) of **6**, identical with the material prepared in the first procedure.

GLUCOSIDATION OF STEGANOL (**1**).—2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranose (**11**) (941 mg) in 1,2-dichloroethane (50 ml) was cooled to −78° under N_2 and BF_3-etherate (3 ml) was added. After 15 min, steganol (**1**) (395 mg) was added. The reaction was stirred at −78° for 6 h, dry pyridine (4 ml) was added, and the reaction mixture was diluted with CH_2Cl_2 (100 ml). The solution was washed with H_2O (3× 100 ml), dried (Na_2SO_4), and the solvent was concentrated in vacuo. The resulting residue was subjected to flash chromatography over silica gel eluted with 20% Et_2O in C_6H_6 to give 850 mg of crude material. Preparative tlc of 243.5 mg of this material on silica gel developed (twice) with CCl_4-$C_6H_5CH_3$-EtOAC (2:1:1) gave two isomers, **7** (87.7 mg) and **8** (19.4 mg).

5-(2,3,4,6-TETRA-*O*-BENZYL-α-GLUCOPYRANOSYL)STEGANE (**7**).—Mp 79-81° (EtOH-CH_2Cl_2); ir ν max ($CHCl_3$) 2900, 1760, 1600, 1450, 1420, 1360, 1050 cm^{-1}; uv λ max (EtOH) 274 (ϵ 2294), 244

nm (ε 4300); 360 MHz ^{1}H nmr δ 7.30-7.04 (m, 20H), 6.85 (s, 1H, 9-H), 6.67 (s, 1H, 4-H), 6.43 (s, 1H, 1-H), 6.02, 5.91 (2d, 2H, *J*=2 Hz, OCH_2O), 4.98 (d, 1H, *J*=3 Hz, 1′-H), 4.38 (d, 1H, *J*=7 Hz, 5β-H), 4.8-4.4 (m, 9H), 3.91 (dd, 1H, *J*=7, 10Hz, 13α-H), 3.84 (s, 6H, 10-OCH_3, 11-OCH_3), 3.71 (dd, 1H, *J*=7, 10 Hz, 13β-H), 3.63 (s, 3H, 12-OCH_3), 3.3-3.5 (m, 4H), 3.04 (d, 1H, *J*=13Hz, 8α-H), 2.67 (m, 1H, 6α-H), 2.53 (dd, 1H, *J*=12,9Hz, 8β-H), 2.45 (dd, 1H, *J*=9, 15Hz, 7β-H); ^{13}C nmr 177.6 (C=O), 153.3, 151.8, 147.7, 146.5, 139.6, 138.5, 138.0, 137.8, 132.9, 131.2, 129.2, 128.3, 127.9, 127.7, 113.6, 112.6, 107.3, 101.5 (OCH_2O), 94.1 (C-1′), 82.6, 81.8, 78.0, 77.7, 75.1, 73.6, 72.5, 72.3 (C-13), 71.3, 68.8, 61.3 (OCH_3), 60.9 (OCH_3), 56.0 (OCH_3), 43.3 (C-7), 42.3 (C-6), 30.5 (C-8).

5-(2,3,4,6-TETRA-*O*-BENZYL-β-GLUCOPYRANOSYL)STEGANE (**8**).—Mp 146-149° (EtOH); ir ν max ($CHCl_3$) 2900, 1770, 1600, 1460, 1040 cm^{-1}; uv λ max (EtOH) 265 (ε 2300), 235 nm (ε 4300); 360 MHz ^{1}H nmr δ 7.30-7.04 (m, 20H), 6.96 (s, 9-H), 6.53 (s, 4-H), 6.43 (s, 1-H), 5.99, 5.88 (2d, *J*=2 Hz, OCH_2O), 5.0-4.4 (m, 10H), 3.99 (dd, *J*=7, 10 Hz, 13α-H), 3.83 (s, 10-OCH_3), 3.80 (s, 11-OCH_3), 3.78 (s, 12-OCH_3), 3.75-3.25 (m, 6H), 3.22 (dd, *J*=7, 10 Hz, 13β-H), 3.03 (d, *J*=12-13 Hz, 8α-H), 2.64 (m, 6α-H), 2.56 (dd, *J*=13, 9 Hz, 8β-H), 2.44 (dd, *J*=9, 15 Hz, 7β-H); ^{13}C nmr 177.6 (C=O), 153.3, 146.4, 138.5, 138.1, 132.7, 130.7, 128.4, 127.7, 112.8, 112.2, 107.4, 102.2, 101.4, 85.7, 84.7, 82.4, 77.8, 74.9, 74.6, 73.6, 71.7, 69.2, 61.2 (OCH_3), 60.9 (OCH_3), 56.0 (OCH_3), 44.1 (C-7), 42.6 (C-6), 30.5 (C-8) ppm.

5-(α-GLUCOPYRANOSYL)STEGANE (**9**).—5-(2,3,4,6-Tetra-*O*-benzyl-α-glucopyranosyl)stegane (**7**) (400 mg) was treated with 10% Pd/C (500 mg) in absolute EtOH (50 ml) and H_2 gas at atmospheric pressure at room temperature for 72 h. The Pd/C was removed by filtration, and the EtOH was concentrated in vacuo to yield 300 mg of a white residue. The residue was subjected to preparative tlc on silica gel plates developed with 5% MeOH in CH_2Cl_2 to give 160 mg (66%) of 5-(α-glucopyranosyl)stegane (**9**), mp 149-151°; ir ν max (KBr) 3450, 2940, 1770, 1600, 1040 cm^{-1}; 360 MHz ^{1}H nmr δ 6.72 (s, 9-H), 6.62 (s, 4-H), 6.45 (s, 1-H), 6.06 (d, *J*=2 Hz, O-CH_2-O), 4.78 (d, *J*=3 Hz, 1′-H), 4.47 (m, 1H), 4.36 (d, *J*=9 Hz, 5βH); 4.0-3.6 (m, 6H), 3.94 (dd, *J*=7, 10 Hz, 13α-H), 3.87 (s, 10-OCH_3, 11-OCH_3), 3.81 (s, 12-OCH_3), 3.25 (m, 1H), 3.20 (dd, *J*=7, 10Hz, 13β-H), 3.05 (d, *J*=13 Hz, 8α-H), 2.87 (d, *J*=11 Hz), 2.58 (dd, *J*=6.5, 13 Hz, 8β-H), 2.44 (dd, *J*=6.5, 13 Hz, 7β-H), 2.16 (m, 6α-H); ^{13}C nmr 177.6 (C=O), 153.6, 150.7, 148.1, 146.7, 141.0, 134.2, 131.4, 129.9, 127.2, 111.9, 108.2, 101.8 (O-CH_2-O), 95.4 (C-1′), 81.3 (C-5), 74.6, 74.2, 72.3, 72.8, 71.8, 70.3, 61.8 (OCH_3), 61.0 (OCH_3), 56.2 (OCH_3), 45.2 (C-7), 42.0 (C-6), 30.7 (C-8) ppm; ms *m/z* 576 (M^+), 414, 399, 398, 366, 330, 300, 299, 151.

5-[(4,6-*O*-ETHYLIDENE)-α-GLUCOPYRANOSYL]STEGANE (**10**).—5-(α-Glucopyranosyl)stegane (**9**) (17 mg, 0.03 mmoles) in dried CH_3NO_2 (5 ml) was treated with *p*-toluenesulfonic acid (2 mg) and acetaldehyde dimethyl acetal (26 μl) under N_2 at room temperature for 96 h. The reaction was terminated by dilution with CH_2Cl_2 (10 ml), washed with H_2O (3× 10 ml), and dried (Na_2SO_4). The solvent was concentrated in vacuo to yield a white residue. This residue was subjected to preparative tlc on silica gel developed with 5% MeOH in CH_2Cl_2 to give 7.8 mg (43%) of 5-[(4,6-*O*-ethylidene)-α-glucopyranosyl]stegane (**10**); mp 148-150° (CH_2Cl_2); ir ν max (KBr) 3460, 2950, 1733, 1600, 1510, 1035 cm^{-1}; uv λ max (EtOH) 266 nm (ε 1700); 360 MHz ^{1}H nmr δ 6.71 (s, 9-H), 6.63 (s, 4-H), 6.45 (s, 1-H), 6.07 (d, *J*=2 Hz, O-CH_2-O), 4.78 (d, *J*=3 Hz, 1′-H), 4.70 (q, *J*=5 Hz, 1″-H), 4.47 (dd, *J*=6.5, 6.5 Hz, 1H), 4.32 (d, *J*=8 Hz, 5β-H), 3.95 (m, 13α-H), 3.89 (s, 10-OCH_3), 3.87 (s, 11-OCH_3), 3.86 (s, 12-OCH_3), 3.6-3.2 (m, 6H), 3.03 (d, *J*=13 Hz, 8α-H), 2.62 (dd, *J*=9, 14 Hz, 8β-H), 2.55 (m, 1H), 2.45 (dd, *J*=9, 14 Hz, 7β-H), 2.22 (m, 6α-H), 1.56 (s, 1H), 1.35 (d, *J*=5 Hz, 2″-CH_3); ^{13}C nmr 177.3 (C=O), 153.8, 150.7, 148.2, 146.8, 140.4, 134.2, 131.5, 129.8, 127.1, 111.8, 108.2, 101.8, (O-CH_2-O), 99.8 (C-1″), 96.1 (C-1′), 81.8 (C-5), 80.4, 72.5, 71.5 (C-13), 72.5, 68.3, 63.4, 61.6 (OCH_3), 61.0 (OCH_3), 56.2 (OCH_3), 45.2 (C-7), 42.0 (C-6), 30.7 (C-8), 20.3 (C-2″) ppm; ms *m/z* 602 [M^+] 398, 366, 300, 263, 261.

5-(β-GLUCOPYRANOSYL)STEGANE (**11**).—5-(2,3,4,6-Tetra-*O*-benzyl-β-glucopyranosyl)stegane (**8**), (100 mg) was treated with 10% Pd/C (130 mg) in absolute EtOH (20 ml) and H_2 gas at atmospheric pressure at room temperature for 72 h. The Pd/C was removed by filtration, and the EtOH was concentrated in vacuo to yield a white residue. This residue was subjected to preparative tlc on silica gel developed with 5% MeOH in CH_2Cl_2 to give 30 mg (50%) 5-(β-glucopyranosyl)stegane (**11**); ir ν max ($CHCl_3$ 3450, 2940, 1770, 1600, 1040 cm^{-1}; uv λ max (EtOH) 266 (ε 4032), 246 nm (ε 6719); 360 MHz ^{1}H nmr δ 6.84 (s, 9-H), 6.55 (s, 4-H), 6.45 (s, 1-H), 6.02 (s, O-CH_2-O), 4.66 (d, *J*=9 Hz, 1′-H), 4.48 (m, 1H), 4.32 (d, *J*=9 Hz, 5β-H), 3.92 (s, 10-OCH_3), 3.87 (s, 11-OCH_3), 3.85 (s, 12-OCH_3), 3.03 (d, *J*=12-13 Hz, 8α-H). The other resonances were poorly resolved.

5-[(4,6-*O*-ETHYLIDENE)-β-GLUCOPYRANOSYL]STEGANE (**12**).—Following the procedure outlined for the preparation of **10**, 5-[(4,6-*O*-ethylidene)-β-glucopyranosyl]stegane (**12**) (1.8 mg) was prepared

from 5-(β-glucopyranosyl)stegane (**11**) (6 mg, 0.01 mmoles), 360 MHz ^{1}H nmr δ 6.80 (s, 9-H), 6.52 (s, 4-H), 6.45 (s, 1-H), 6.04 (s, O-CH_2-O), 4.72 (d, *J*=10-11 Hz, 1′-H), 4.67 (q, *J*=5 Hz, 1″-H), 4.46 (dd, *J*=6.5, 6.5 Hz, 1H), 4.35 (d, *J*=8 Hz, 5β-H), 3.92 (s, 10-OCH_3), 3.85 (s, 11-OCH_3), 3.82 (s, 12-OCH_3), 3.60 (m, 1H), 3.44 (m, 1H), 3.2 (m, 3H), 3.04 (d, *J*=12-13 Hz, 8α-H), 2.6-2.3 (m, 8β-H), 1.5 (s, 2(H)), 1.34 (d, *J*=5 Hz, 2″-H).

ACKNOWLEDGMENTS

This work was supported by a grant from Bristol-Myers Company. RPH acknowledges support by the MCV/VCU Cancer Center Summer Fellowship Program and by fellowships from the School of Graduate Studies of VCU. We would also like to thank Dr. T.W. Doyle of Bristol-Myers Company for arranging for the 360 MHz ^{1}H-nmr spectra and Dr. Byron Long of Bristol-Myers for the DNA breakage assays.

LITERATURE CITED

1. H. Stahelin, *Eur. J. Cancer,* **6**, 303 (1970).
2. H. Stahelin, *Eur. J. Cancer,* **9**, 215 (1973).
3. S.M. Kupchan, R.W. Britton, M.F. Ziegler, C.J. Gilmore, R.J. Restivo, and R.F. Bryan, *J. Am. Chem. Soc.,* **95**, 1335 (1973).
4. M. Taafrout, F. Rouessac, J.P. Robin, R.P. Hicks, D.D. Shillady, and A.T. Sneden, *J. Nat. Prod.,* **47**, 600 (1984).
5. M. Kuhn and A. von Wartburg, *Helv. Chim. Acta,* **51**, 1631 (1968).
6. M.J. Diem, D.F. Burow, and J.L. Fry, *J. Org. Chem.,* **42**, 1801 (1977).
7. J.F. Stoddart, "Stereochemistry of Carbohydrates," New York: Wiley-Interscience, 1971, pp. 137-145.
8. C. Keller-Juslen, M. Kuhn, A. von Wartburg, and H. Stahelin, *J. Med. Chem.,* **14**, 936 (1971).
9. J.P. Robin, Departement de Chimie, Institut Universitaire de Technologie, LeMans, France, personal communication.
10. J.D. Loike and S.B. Horwitz, *Biochem.,* **15**, 5443 (1976).
11. T.D. Perrine, C.P.J. Glaudemans, R.K. Ness, J. Kyle, and H.G. Fletcher, *J. Org. Chem.,* **32**, 664 (1967).

Received 8 October 1984