crude 26: yield 1.0 g; M^+ 366.

6-(Methylthio)-9-[2-(tosyloxymethyl)pyrrolidin-1-yl]-9*H*-purine (28). A solution of 11 (0.55 g) in anhydrous pyridine (14 ml) containing *p*-toluenesulfonyl chloride (0.75 g) was stirred at room temperature for 18 hr. The reaction mixture was diluted with H_2O (125 ml) and extracted with $CHCl_3$ (3 × 50 ml). After drying ($MgSO_4$), the combined extracts were evaporated to dryness and the resulting residue was triturated with Et_2O: yield 0.37 g (45%); mp 137°. Anal. ($C_{18}H_{21}N_5O_3S_2$) C, H, N.

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Synthesis of 6α-Methyldigitoxigenin 3-Acetate

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In order to determine the influence of a 6α-methyl group activity, the 6α-methyl derivative of digitoxigenin 3-acetate 14 was prepared and pharmacologically tested in comparison with digitoxigenen 3-acetate. The synthesis of 6α-methyldigitoxigenin 3-acetate (14) was performed starting from 21-hydroxy-4-pregnene-3,20-dione (1). According to the cardiac activity determined on guinea-pig isolated heart and by slow infusion in the cat, the 6α-methyldigitoxigenin 3-acetate (14) is not more active than digitoxigenin 3-acetate.

Many methyl derivatives of steroid hormones and of adrenocortical steroids were prepared and pharmacologically tested; some of them (6α-, 16α-, or 16β-methyl derivatives) were far more active than the nonmethylated parent compounds (perhaps influencing the metabolism of the drugs) and are today widely used in human therapy as progestative or antirheumatic compounds.[1,2]

On the contrary, although cardenolides have been used for more than two centuries in human therapy as cardioactive compounds, no methyl or other alkyl derivatives of digitoxigenin have yet been prepared and pharmacologically tested. This may be due to some difficulties in the synthesis of such methyl derivatives of cardenolides. Here we report the synthesis of the 6α-methyl derivative of digitoxigenin 3-acetate 14.

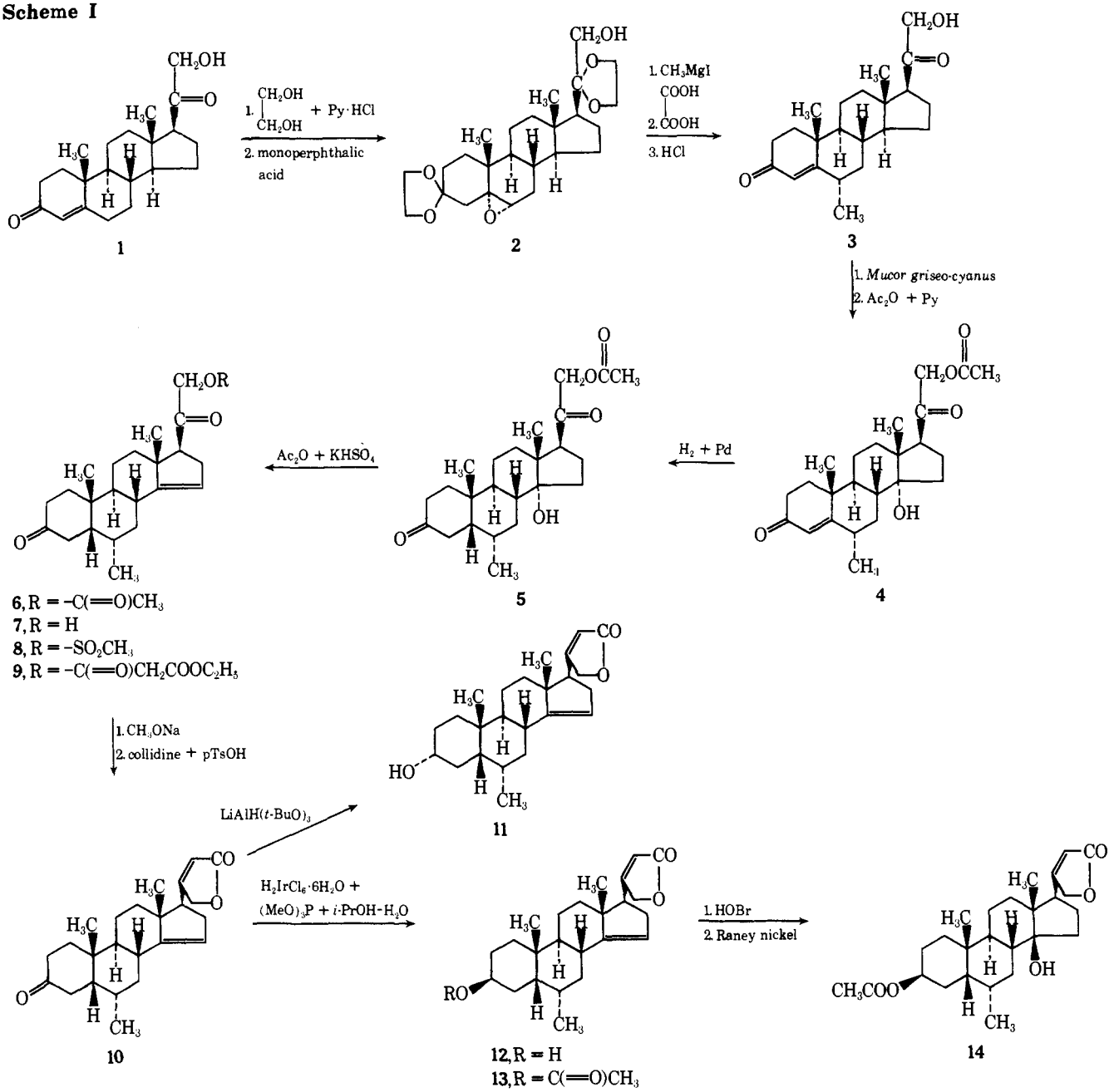
Chemistry. The 21-hydroxy-6α-methyl-4-pregnene-3,20-dione (**3**, previously obtained starting from 3β-hydroxy-5-pregnen-20-one with many steps and with low yield[3]) was obtained by us[4] in five steps starting from easily disposable 21-hydroxy-4-pregnene-3,20-dione (**1**). In order to synthetize the 6α-methyldigitoxigenin 3-acetate (**14**), involving 12 biological–chemical steps, it was extremely important to produce easily the starting compound **3**. The 21-hydroxy-4-pregnene-3,20-dione (**1**) was treated with ethylene glycol and pyridine hydrochloride giving the 3,20-diethyleneketal derivative which was transformed with monoperphthalic acid into the 5α,6α-epoxy compound **2**. Compound **2** was treated with methylmagnesium iodide giving the 6β-methyl-5α-hydroxy intermediate (trans-diaxial opening of the oxirane ring[1]) which was hydrolized with oxalic acid into the 5α,21-dihydroxy-6β-methylpregnane-3,20-dione; this last compound was treated with hydrochloric acid giving (by means of water elimination from the 5α-hydroxyl group and isomerization of the methyl group from the 6β-axial into the 6α-equatorial position) compound **3**, which was identical (ir, uv, TLC, melting point, NMR) with the compound obtained by another synthetic approach.[3]

Compound **3**, when incubated with *Mucor griseo-cyanus* ATCC 1207 a(+), gave a 60% yield of the 14α-hydroxy derivative[5] which was acetylated to give the 21-acetate **4**. Compound **4** was catalytically reduced to the 5β-dihydro derivative **5**; the 5β configuration was assigned to compound **5** because catalytic hydrogenation of 3-keto-4-pregnene compounds gave, as the chief products, the 5β-dihydro derivatives,[6-11] because in compound **4** the 6α-methyl group may furthermore hinder the approach of the catalyst from the rear α-side of the steroid nucleus and because compound **5** showed a single positive Cotton effect at 310 nm (the same of the 6α-nonmethylated compound 14α,21-dihydroxy-5β-pregnane-3,20-dione 21-acetate of known configuration[11]) (see Scheme I).

Compound **5** was dehydrated with $KHSO_4$ and acetic anhydride to give the 14-dehydro derivative **6**; the 14,15 positions were assigned to the double bond because compound **7** was catalytically reduced with platinum in methanol at room temperature and a pressure of 1 atm to the 21-hydroxy-6α-methyl-5β-pregnene-3,20-dione, identical with the product obtained by the same reduction and in the same conditions as compound **3** (the $\Delta^{8(14)}$-steroids are resistant to hydrogenation[1]).

Compound **6** was hydrolyzed to the 21-alcohol **7** which, on treatment with methanesulfonyl chloride in acetone–pyridine, gave the 21-mesilate **8**. Treatment of the 21-mesilate **8** with the monoethyl ester potassium salt of malonic acid in dimethylformamide gave the 21-ethylmalonyl derivative **9** which was cyclized with sodium methoxide in methanol and then was decarboxylated with *p*-toluenesulfonic acid to give the butenolide **10**. To compound **10** the 17β configuration was assigned because between compounds **10** and **6** there is a difference in the molecular opti-

Scheme I



cal rotation of −363° which is very similar to the difference in the molecular optical rotation (−357°) between the nonmethylated compounds[11] (14-dehydrodigitoxigenone and 21-hydroxy-5β-pregn-14-ene-3,20-dione 21-acetate), because compound **13** has an NMR signal of H in the 17α position at a normal value δ 2.76, because in the 14α or Δ^{14}-steroids the 17β configuration is thermodynamically more stable,[1] and because the same cyclization applied to the nonmethylated compound gave digitoxigenin 3-acetate[11] having the 17β configuration. The butenolide **10** was then reduced with chloroiridic acid and trimethyl phosphite in isopropyl alcohol–water to give the 3β-axial alcohol **12**. The 3β-axial configuration was assigned because it is known[11,12] that chloroiridic acid reduction of 3-keto steroids gives the corresponding 3-axial alcohol and because compound **12** was different from the 3α-equatorial compound **11**, prepared by reduction of the 3-keto derivative **10** with tri-*tert*-butoxylithium aluminum hydride (this hydride gives nearly exclusively the 3-equatorial alcohol[1]).

The butenolide **12** was acetylated to the 3β-acetate **13**. The structure of compound **13** was confirmed by NMR (CH_3 at the 6α position as a doublet at δ 0.91, H at the 17α position as a triplet at δ 2.76, H at the 3α position as a multiplet at δ 4.96, H at the 15 position as a triplet at δ 5.18, H at the 22 position as a singlet at δ 5.75). Compound **13** was treated with *N*-bromoacetamide and perchloric acid in dioxane to give the crude bromohydrin which, when reduced with Raney nickel in boiling methanol, gave the 6α-methyldigitoxigenin 3-acetate (**14**).

Biological Evaluation. The cardiac activity of compound **14** was determined in comparison with the nonmethylated parent compound (digitoxigenin 3-acetate) on guinea-pig isolated heart[13] and with slow infusion in the cat.[14] It seems therefore (see Table I) that the 6α-methyl group in compound **14** does not increase the cardiac activity (at least according to the used pharmacologically tests) of digitoxigenin 3-acetate. It may be not excluded that the influence of the 6α-methyl group on the cardiac activity is,

Table I

Compd	Inotropic activity on guinea-pig isolated heart[a] Concn (mM) of perfusion liquid	Max increase (%) of contractility, medium value ± SE	Total quantity (mg) necessary for max increase of contractility, medium value ± SE	Total quantity (mg) necessary for cardiac arrest, medium value ± SE	Slow infusion in cat,[b] lethal dose in mg/kg, medium value ± SE
14	From 0.0093 to 0.0116	59.2 ± 24.062%[c]	0.20125 ± 0.069262[d]	0.807 ± 0.119[e]	1.973 ± 0.260[f]
Digitoxigenin 3-acetate	From 0.006 to 0.072	41.4 ± 20.946%	0.08033 ± 0.010837	0.457 ± 0.072	0.645 ± 0.021

[a]Determined on the guinea-pig isolated heart prepared according to Langendorff,[13] using the apparatus for the isolated heart, oxygenated liquid Ringer-Locke, at 37°, with hydrostatic pressure of 40 cm of water; the cardiac arrest was obtained between 20 and 40 min; the myocardial contractility was measured with a Battaglia-Rangoni apparatus TR-B/100. [b]Determined according to Chen[14] using an anaesthetized cat with 40 mg of pentobarbital sodium/kg; the respiration was maintained by a Terzano pump; the liquid was infused in the femoral vein with a constant quantity of 0.96 ml/min using the slow infusion apparatus of Scientific Research Instruments Ltd., Croydol, and using such a concentration of digitalic compound to have the death between 30 and 60 min. [c]In comparison to digitoxigenin 3-acetate, $t = 0.530$, not significative. [d]In comparison to digitoxigenin 3-acetate, $t = 1.466$, not significative. [e]In comparison to digitoxigenin 3-acetate, $t = 2.266$, $p = 0.05$–0.02. [f]In comparison to digitoxigenin 3-acetate, $t = 3.830$, $p = 0.01$–0.0001.

in compound **14**, masked by the 3β-acetoxy group; nevertheless, it must be considered that the digitoxigenin 3-acetate and the 6α-methyldigitoxigenin 3-acetate (**14**), by incubation in vitro at 37° with guinea-pig and cat blood, are quickly hydrolyzed to digitoxigenin or 6α-methyldigitoxigenin, respectively (the half-life of both the compounds is less than 30 min).

Experimental Section

Melting points were determined in an open capillary tube with a Mel-Temp apparatus and are uncorrected. Analytical results indicated by symbol only of an element were within ±0.4% of their calculated values; ir spectra were determined in Nujol, uv spectra in methanol, optical rotation in $CHCl_3$ at 1% concentration (except where otherwise stated), and circular dichroism in dioxane at 0.1% concentration using a Perkin-Elmer Model 141; NMR spectra were taken on a Varian HA-100 instrument in deuteriochloroform with tetramethylsilane as internal standard (s = singlet, d = doublet, t = triplet, m = multiplet).

21-Hydroxy-5-pregnene-3,20-dione 3,20-Diethyleneketal. A solution of 13.98 g (0.0423 mol) of 21-hydroxy-4-pregnene-3,20-dione (**1**) in 1360 ml of benzene was treated with 140 ml of ethylene glycol and 2.1 g of pyridine hydrochloride. The reaction mixture was refluxed for 24 hr with stirring and continuously removing with a Dean-Stark trap[15] the water formed in the reaction. The solvent was removed in vacuo, the residue was treated with 1.4 ml of NaOH (50% of H_2O), diluted with 1000 ml of H_2O, and the solid product was filtered and crystallized from benzene to yield 8.3 g (46%) of the 3,20-diethyleneketal derivative: mp 186–190°; no absorption in uv; ν 3400, 1050, 950, 873 cm^{-1}. Anal. ($C_{25}H_{38}O_5$) C, H.

21-Hydroxy-5α,6α-epoxypregnane-3,20-dione 3,20-Diethyleneketal (2). To a solution of 7 g (0.0167 mol) of 21-hydroxy-5-pregnene-3,20-dione 3,20-diethyleneketal in 78 ml of $CHCl_3$ was added a solution of 4.67 g of monoperphthalic acid in 111 ml of ethyl ether. After 20 hr at 20° in the dark, the mixture was diluted with 780 ml of $CHCl_3$, washed with KOH (5% in H_2O) and with NaCl saturated with H_2O, and evaporated to dryness. The residue was crystallized from acetone to yield 2.2 g (30%) of **2**: mp 223–225°; ν 3400, 1260, 1220, 1050, 995, 952, 862, 805, 725 cm^{-1}. Anal. ($C_{25}H_{38}O_6$) C, H.

5α,21-Dihydroxy-6β-methylpregnane-3,20-dione. A solution of 1 g (0.0023 mol) of **2** in 30 ml of benzene was added to a stirred solution of CH_3MgI (obtained from 0.6 g of Mg, 1.54 ml of CH_3I, and 50 ml of ethyl ether); the reaction mixture was stirred 6 hr at 20° and poured into 100 ml of NH_4Cl saturated with H_2O. After extraction with benzene and evaporation in vacuo, the residue was refluxed 0.5 hr in 20 ml of MeOH with 0.33 g of oxalic acid. The solvent was removed in vacuo and the residue was diluted with H_2O and filtered to yield 0.83 g (100%) of 5α,21-dihydroxy-6β-methylpregnane-3,20-dione: mp 205–207°; ν 3350, 1690, 1260, 1060, 1025, 807 cm^{-1}. Anal. ($C_{22}H_{34}O_4$) C, H.

21-Hydroxy-6α-methyl-4-pregnene-3,20-dione (3). A solution of 1.1 g (0.00304 mol) of 5α,21-dihydroxy-6β-methylpregnane-3,20-dione in 103 ml of MeOH was refluxed 1 hr with 0.85 ml of HCl (36% in H_2O); the reaction mixture was cooled and treated with $NaHCO_3$ and the solvent was removed in vacuo. The residue was diluted with H_2O and extracted with $CHCl_3$, and the solvent was removed in vacuo. The residue was crystallized from ethyl ether to give 0.6 g (57%) of **3**: mp 114–115°; λ_{max} 241 nm (ε 14700); ν 3400, 1720, 1670, 1610, 1270, 1070, 900, 870, 680 cm^{-1}. Anal. ($C_{22}H_{32}O_3$) C, H. **3** (1 g) was treated with 10 ml of pyridine and 1 ml of acetic anhydride for 20 hr at room temperature and worked up to give 1 g (89%) of the 21-acetate of **3**: mp 124–126°; λ_{max} 241 nm (ε 15000); ν 1725, 1700, 1660, 1225 cm^{-1}; NMR δ 0.68 (s, 3 H, CH_3 at C_{13}), 1.05 (d, 3 H, CH_3 at C_6), 1.14 (s, 3 H, CH_3 at C_{10}), 2.08 (s, 3 H, CH_3COO–), 2.30 (m, 2 H, CH_2 at C_2), 4.50 (d, 2 H, CH_2 at C_{21}, AB system), 5.66 (s, 1 H, CH at C_4). Anal. ($C_{24}H_{34}O_4$) C, H.

14α,21-Dihydroxy-6α-methyl-4-pregnen-20-one 21-Acetate (4). *Mucor griseo-cyanus* ATCC 1207 a(+) was maintained on slants containing potato starch; the spores of *Mucor* obtained from such slants, after 2 weeks at 28°, were suspended in 5 ml of water. Such a suspension of spores was used to inoculate 250 ml of broth (20 g of lactabulmin hydrolysate, 50 g of glucose, 3 g of corn steep liquor, 1000 ml of water, pH 4.3–4.5) in a 1000-ml flask. After incubation for 24 hr at 28° on a reciprocating shaker (118 strokes/min with width of 5 cm) the content of the flask was used to inoculate a 20 l. Fomel fermentor containing 15 l. of broth of the same composition as above indicated. After 24 hr of incubation at 28° with 0.9 l. of air/l. of broth/min and 650 rpm of agitation, the mycelium was filtered on gauze, washed with water, and resuspended in 10 l. of water in a Fomel fermentor. To this suspension 4 g (0.0116 mol) of **3** in 400 ml of acetone was added; after 5 hr of incubation at 28° with 0.9 l. of air/l. of broth/min and 650 rpm of agitation, 2 l. of $CHCl_3$ was added; the mycelium was filtered, suspended in 2 l. of acetone, and filtered. The mycelium was again suspended in 2 l. of $CHCl_3$ and filtered again. The organic phase was separated and the water phase was extracted with $CHCl_3$. The combined organic phase was washed with $NaHCO_3$ (5% in H_2O) and with H_2O, dried on Na_2SO_4, and evaporated in vacuo. The residue was worked up with hexane and then with ethyl ether to yield 2.6 g (62%) of 14α,21-dihydroxy-6α-methyl-4-pregnene-3,20-dione: mp 150–158°. A sample crystallized from ethyl ether had mp 155–156°; λ_{max} 241 nm (ε 15800); $[\alpha]^{20}D$ +159°; ν 3550, 3450, 1700, 1670, 1650, 1600, 1068, 1055 cm^{-1}. Anal. ($C_{22}H_{32}O_4$) C, H. A solution of 5 g (0.0138 mol) of 14α,21-dihydroxy-6α-methyl-4-pregnene-3,20-dione (mp 150–158°) in 50 ml of pyridine was treated with 5 ml of acetic anhydride for 15 hr at room temperature. After dilution with H_2O, the solid product was filtered and crystallized from MeOH–H_2O to yield 4.5 g (80%) of **4**: mp 149–151°; λ_{max} 241 nm (ε 15900); $[\alpha]^{20}D$ +157°; ν 3550, 1750, 1720, 1650, 1590, 1280, 1200, 1070, 1055 cm^{-1}; NMR δ 0.79 (s, 3 H, CH_3 at C_{13}), 1.05 (d, 3 H, CH_3 at C_6), 1.11 (s, 3 H, CH_3 at C_{10}), 2.08 (s, 3 H, CH_3COO–), 2.30 (m, 2 H, CH_2 at C_2), 3.15 (s, 1 H, OH at C_{14}), 4.50 (d, 2 H, CH_2 at C_{21}, AB system), 5.66 (s, 1 H, CH at C_4). Anal. ($C_{24}H_{34}O_5$) C, H.

14α,21-Dihydroxy-6α-methyl-5β-pregnane-3,20-dione 21-Acetate (5). A solution of 2.68 g (0.00666 mol) of **4** in 155 ml of MeOH was hydrogenated with 0.518 g of Pd (10%) on $BaSO_4$ at 20° and 1 atm of H_2 for 1 hr. The catalyst was filtered, the solvent was removed in vacuo, and the residue was worked up with ethyl ether and crystallized from MeOH–H_2O to yield 1.5 g (55%) of **5**: mp 164–166°: no uv absorption; $[\alpha]^{20}D$ +98° (1% of MeOH); ν 3350, 1760, 1745, 1715 cm^{-1}; circular dichroism 260 (MD = −20000), 295 (MD = 0), 310 (MD = +3800), 350 nm (MD = 0) [in comparison the nonmethylated compound 14α,21-dihydroxy-5β-pregnane-3,20-dione 21-acetate gave 260 (MD = −17700), 295 (MD = 0), 310 (MD = +5400), 350 nm (MD = 0)]. Anal. ($C_{24}H_{36}O_5$) C, H.

21-Hydroxy-6α-methyl-5β-pregn-14-ene-3,20-dione 21-Acetate (6). A solution of 4 g (0.0099 mol) of **5** in 40 ml of acetic anhydride was treated with 4 g of $KHSO_4$ at 95–100° for 3 min; the solvent was removed in vacuo, the residue was diluted with H_2O, and the solid product was filtered and worked up with ether to yield 3.8 g (100%) of **6**: mp 148–151°; $[\alpha]^{20}D$ +61° (1% in MeOH); ν 1750, 1720 cm^{-1}; no uv absorption. Anal. ($C_{24}H_{34}O_4$) C, H.

21-Hydroxy-6α-methyl-5β-pregn-14-ene-3,20-dione (7). To a solution of 4.4 g (0.01139 mol) of **6** in 324 ml of MeOH was added 19.2 ml of K_2CO_3 (10% in H_2O); after 1 hr at 20°, acetic acid was added to neutral pH, the solvent was removed in vacuo, H_2O was added, and the solid product was filtered, dried, and worked up with hexane to yield 3.6 g (91%) of **7**: mp 147–149°. A sample crystallized from hexane–EtOAc gave mp 148–150°: $[\alpha]^{20}D$ +23°; ν 3400, 1700, 1260, 1060 cm^{-1}. Anal. ($C_{22}H_{32}O_3$) C, H.

6α-Methyl-14-dehydrodigitoxigenone (10). To a solution of 1 g (0.0029 mol) of **7** in 11.45 ml of acetone and 3.5 ml of pyridine at 0°, 1.7 ml of methanesulfonyl chloride was added. The resultant mixture was stirred at 0° for 6 hr and then 100 ml of H_2O was added. After extraction with $CHCl_3$ and solvent evaporation, 1.45 g of the crude 21-mesilate **8** was obtained. A solution of 1.45 g of crude **8** in 12.2 ml of dimethylformamide was treated with 1.7 g of the potassium salt of the monoethyl ester of malonic acid. The reaction mixture was slowly heated in 2.5 hr to 55° and then stirred at 55° for 4 hr. After cooling, dilution with 100 ml of H_2O, and extraction with $CHCl_3$, the solvent was evaporated to yield 1.16 g of crude **9** which was dissolved in 15 ml of MeOH and treated at 0° with 2.23 ml of MeONa (1 *M* in MeOH). The reaction mixture was stirred at 0° for 10 min, treated with HCl in MeOH to pH 2, and diluted with H_2O. The solid product was filtered, dried, and dissolved in 10.65 ml of collidine. After stirring 1 hr at room temperature, 0.13 ml of H_2O and 2.7 g of *p*-toluenesulfonic acid were added. The reaction mixture was refluxed 2 hr in a nitrogen atmosphere; the solvent was removed in vacuo; after cooling the mixture was acidified with 26 ml of HCl (2 *N*) and the solid product was filtered, dried, and chromatographed on 100 g of Florisil eluting with hexane–EtOAc (6:4), collecting 50-ml fractions. The chromatographic fractions 11–23 gave, after crystallization from MeOH, 0.22 g (20% from **7**) of **10**: mp 210–212°; $[\alpha]^{20}D$ −35°; λ_{max} 214 nm (λ 16400); ν 1770, 1740, 1680, 1620 cm^{-1}. Anal. ($C_{24}H_{32}O_3$) C, H.

6α-Methyl-14-dehydrodigitoxigenin 3-Acetate (13). To a solution of 31.2 mg of $H_2IrCl_6 \cdot 6H_2O$ in 12.5 ml of *i*-PrOH–H_2O (9:1), 0.5 g (0.00135 mol) of **10** and 1 ml of trimethyl phosphite were added. The reaction mixture was refluxed 48 hr, cooled, and poured into 100 ml of ice–H_2O. The solid product was filtered to yield 0.45 g (89%) of **12**: mp 180–183°; λ_{max} 217 nm (ε 15500); $[\alpha]^{20}D$ −41°; ν 3418, 1785, 1750, 1630, 1038, 890, 855 cm^{-1}; TLC [hexane–EtOAc (1:1) or C_6H_6–EtOH (97:3)] compound **12** resulted less polar than the 3α-equatorial compound **11** (prepared as below indicated). To a solution of 1.3 g (0.00351 mol) of **12** in 13 ml of pyridine, 1.3 ml of acetic anhydride was added. After 72 hr at room temperature, the solution was poured in 130 ml of ice–H_2O, and the solid product was filtered to yield 1.35 g (93%) of **13**: mp 128–130°; $[\alpha]^{20}D$ −21°; λ_{max} 219 nm (ε 14000); ν 1785, 1753, 1732, 1630, 1250, 1235, 1033 cm^{-1}; NMR δ 0.82 (s, 3 H, CH_3 at C_{13}), 0.91 (d, 3 H, CH_3 at C_6), 0.96 (s, 3 H, CH_3 at C_{10}), 1.97 (s, 3 H, CH_3COO–), 2.76 (t, 1 H, H at 17α), 4.63 (s, 2 H, CH_2 at C_{21}), 4.96 (m, 1 H, H at 3α), 5.18 (t, 1 H, H at C_{15}), 5.75 (s, 1 H, H at C_{22}). Anal. ($C_{26}H_{36}O_4$) C, H.

6α-Methyl-14-dehydro-3-epidigitoxigenin (11). To a solution of 0.1 g (0.0002/ mol) of **10** in 12 ml of THF, 0.83 g of $LiAlH(t\text{-}BuO)_3$ in 5 ml of THF was added at 0°. The reaction mixture was stirred 2 hr at 0° and treated with 43.3 ml of AcOH (5% in H_2O). The THF was removed in vacuo and the product was extracted with CH_2Cl_2. After evaporation of the solvent 0.07 g (70%) of **11** was obtained: mp 178–183°; $[\alpha]^{20}D$ −23°; ν 3430, 1785, 1750, 1630 cm^{-1}. Anal. ($C_{24}H_{34}O_3$) C, H.

6α-Methyldigitoxigenin 3-Acetate (14). To a solution of 0.33 g (0.0008 mol) of **13** in 12 ml of dioxane at 0°, 1.57 ml of $HClO_4$ (3.5% in H_2O) was added. The reaction mixture was treated in the dark with 0.21 g of *N*-bromoacetamide; after stirring 2 hr in the dark at 0° the solution was poured into 100 ml of ice–H_2O containing 0.1% $Na_2S_2O_5$. The solid product was filtered and the wet crude bromohydrin so obtained was dissolved in 15 ml of MeOH and treated with 2.6 g of Raney nickel deactivated with AcOH (to a solution of 124 g of NaOH in 500 ml of H_2O, in 2.5 hr, 100 g of Ni–Al was added at 0–10°; the suspension was decanted and washed with H_2O; the Ni catalyst was suspended in H_2O, neutralized with AcOH, washed with H_2O, and MeOH). To the slurry 0.28 ml of water was added and the mixture was refluxed 4 hr in the dark. After dilution with 25 ml of $CHCl_3$, filtration, and washing with $CHCl_3$, the filtrate was evaporated in vacuo. The residue was dissolved in 100 ml of $CHCl_3$, washed with H_2O, and dried on Na_2SO_4 and the solvent was removed in vacuo. The residue was worked up with ethyl ether and the solid product was crystallized from ethyl ether to yield 0.065 g (19%) of **14**: mp 178–182°; $[\alpha]^{20}D$ −72°; λ_{max} 216–219 nm (ε 13300); ν 3450, 1775, 1740, 1730, 1620, 1260, 1020, 960, 895, 860 cm^{-1}. Anal. ($C_{26}H_{38}O_5$) C, H.

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