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USE OF N-LITHIOETHYLENEDIAMINE IN THE DOUBLE BOND ISOMERIZATION AND DEGRADATION OF STEROL SIDE CHAINS

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Abstract—Double bond isomerization of stigmasterol ((24*S*)-24-ethylcholesta-5,22-dien-3β-ol) with N-lithioethylenediamine produced stigmasta-5,17(20)-dien-3β-ol, stigmasta-5,20(22)-dien-3β-ol, stigmasta-5,23-dien-3β-ol and stigmasta-5,24-dien-3β-ol. Some starting material was also present in the isomerization mixture along with a small amount of stigmast-5-en-3β-ol. Similar treatment of 3α,5-cyclo-6β-methoxystigmast-22-en (stigmasterol i-methyl ether) followed by ozonization and removal of the ring A-protecting group yielded predominantly 3β-hydroxyandrost-5-en-17-one and 3β-hydroxypregn-5-en-20-one. The isomerization products of fucosterol (24-ethylcholesta-5,24(28)*E*-dien-3β-ol) and 23,24-bisnorchola-5,20-dien-3β-ol are also reported.

Double bond migration and degradation of the side chains of steroids has been an interesting area of research in recent years. Iodine in benzene was used for obtaining double bond isomers of the acetates of 24-methylenecholesterol (3a),[1] fucosterol (4a),[2] dehydroepiysterol (5a)[3] and strongylosterol (6a).[4] N-Lithioethylenediamine solution in ethylenediamine (LEDA/EDA) was recently utilized[5] for the same purpose in tetracyclic triterpenes, in order to degrade the side chain after ozonolysis. Such a double bond migration in sterols with unsaturated side chains followed by oxidative degradation of the isomerized product could be of considerable utility for the structural elucidation of new marine sterols since they differ primarily in their side chain substitution patterns.[6] Furthermore, these steps could be of potential industrial utility for the production of important hormone derivatives such as 3β-hydroxyandrost-5-en-17-one (1a) and 3β-hydroxypregn-5-en-20-one (pregnenolone; 2a) in view of the dramatic shift[7] in availability of starting materials from steroidal sapogenins to plant sterols such as stigmasterol (7a).

A recent article[8] dealing with the reaction of stigmasterol (7a) with N-lithioethylenediamine prompts us to report our own results in this area. The Indian authors[8] found that on prolonged refluxing (72 hr) stigmasterol (7a) was converted completely into a mixture of two double bond isomers, stigmasta-5,17(20)-dien-3β-ol (8a) and stigmasta-5,20(22)-dien-3β-ol (9a) which were separated by argentic column chromatography.

We had also selected stigmasterol as a substrate for our experiments since it is widely distributed in nature, especially in soybeans, and has been utilized as a starting material[9,10] for several steroidal hormones. During our preliminary investigations, iodine in benzene, potassium-t-butoxide in DMSO,[11] potassium-3-aminopropylamide in 1,3-diaminopropane[12] (KAPA) were not found to be effective for isomerizing the side chain of stigmasterol (or its acetate). The only reactive system was N-lithioethylenediamine in excess ethylenediamine as solvent. The reaction was carried out with free stigmasterol (7a) and its i-Me derivative (7b), and in both cases roughly the same distribution of side chain double bond isomers was encountered, indicating that the reagent does not affect the Δ^5 double bond. To confirm this result, cholesterol was subjected to the same reaction conditions with LEDA/EDA and was totally recovered.

Most of the reaction products of stigmasterol with the base gave the same or very similar retention times on glc. However, the components could be separated and purified by preparative high pressure liquid chromatography (hplc) using a reversed phase column. For this purpose the mixture was applied to the hplc column and enriched mixtures were obtained. These mixtures were repeatedly subjected to hplc separation to obtain pure compounds. Reaction products were characterized by NMR and mass spectrometry and by their glc and hplc retention time comparisons in the case of known compounds. As can be seen from Table 1, which contains the gas and hplc retention times as well as the yields of the various products, we were able to demonstrate the presence of three additional components aside from the two (8a and 9a) encountered by the Indian group.[8] As can be noted from Table 1, the gas chromatographic retention times of stigmasta-5,17(20)-dien-3β-ol (8a), stigmasta-5,20(22)-dien-3β-ol (9a) and stigmast-5-en-3β-ol (12a) are very close and they give a broad peak as a mixture, especially when injected in more concentrated amounts.

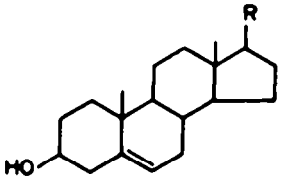
Stigmasta-5,23-dien-3β-ol (10a) has recently[13] been isolated from the sponge *Calix nicaaencis* and stigmasta-5,24-dien-3β-ol (11a) has been encountered among double bond migration products of fucosterol acetate with iodine in benzene.[2] The 100 MHz NMR spectrum of the latter (11a) gives a singlet signal at 1.63 ppm (6H) corresponding to the C-26 and C-27 methyls while a 360 MHz NMR spectrum affords better resolution with two 3H absorptions at 1.625 and 1.629 ppm. As expected[14,15] the mass spectrum of 11a shows a base peak at *m/z* 314 due to a McLafferty rearrangement (11a → *m/z* 314) typical of 24-alkyl-Δ^{24}-steroids. The Indian authors[8] mentioned that stigmasta-5,17(20)-dien-3β-ol (8a) also has such an *m/z* 314 McLafferty rearrangement peak of appreciable (34%) intensity. In our hands the same compound purified by hplc shows only a very weak (4% intensity) peak at *m/z* 314 and we ascribe this difference

Table 1. Chromatographic data and yields of double bond isomers of stigmasterol

Compound	GLC ret.time[a] (min)	HPLC ret.time[a] (min)	Yield[b] %
Stigmasta-5,17(20)-dien-3β-ol (8a)	14.6	36.3	24
Stigmasta-5,20(22)-dien-3β-ol (9a)	14.8	36.7	23
Stigmasta-5,23-dien-3β-ol (10a)	12.8	47.4	13
Stigmasta-5,24-dien-3β-ol (11a)	16.8	44.4	14
Stigmasterol (7a)	12.6	50.4	9
Stigmast-5-en-3β-ol (12a)	14.7	54.6	6

[a] Chromatographic conditions are given in the Experimental section.

[b] The yields were calculated roughly by GLC and HPLC analysis. In addition to the six listed compounds 11% of less polar impurities were also isolated.



a

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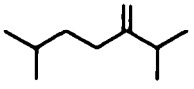
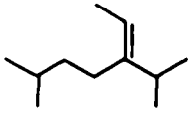
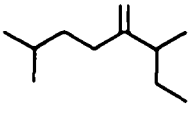
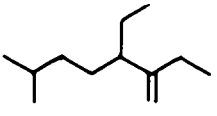
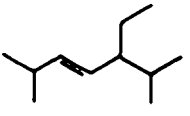
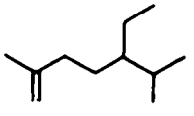
3 R = 

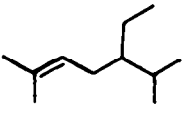
4 R = 

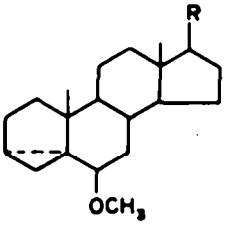
5 R = 

6 R = 

7 R = 

8 R = 

9 R = 



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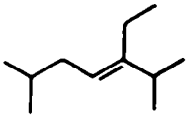
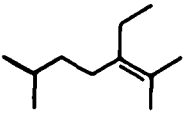
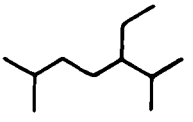
10 R = 

11 R = 

12 R = 

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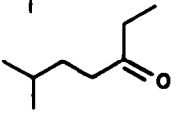
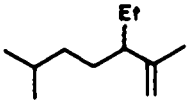
15 R = 

16 R = 

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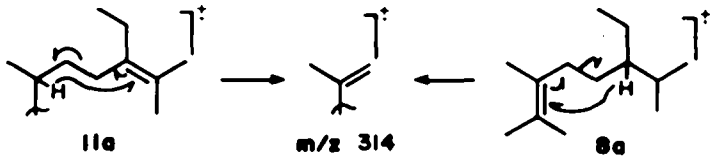
18 R = 



to some impurity (such as stigmasta-5,24-dien-3β-ol which has a base peak at *m/z* 314) in the specimen of the Indian group.

Ozonization was used for the degradation of the double bonds in the side chain, the Δ^5-3β-hydroxy system being protected via the i-methyl ether (b) prior to LEDA/EDA double bond isomerization. Analysis of the reaction mixture by high resolution gc/MS demonstrated the presence of 1b (M^+ 302.21748, $C_{20}H_{30}O_2$), 2b (M^+ 330.25582, $C_{22}H_{34}O_2$), 13b (M^+ 344.26850, $C_{23}H_{36}O_2$), 14b (M^+ 358.28439, $C_{24}H_{38}O_2$), 15b (M^+ 400.33137, $C_{27}H_{44}O_2$) and 12b (M^+ 428.39523, $C_{30}H_{52}O$) which showed that compounds 8b, 9b, 7b, 10b, 11b and 12b were present as reaction products in the stigmasterol i-methyl ether base-catalyzed isomerization. For further confirmation the ozonization mixture was treated with *p*-toluenesulfonic acid in dioxane-water to obtain Δ^5-3β-hydroxy compounds. The major reaction products were identified by combined gas chromatographic and mass spectrometric comparison with authentic samples.

Fucosterol (4a) was also subjected to a double bond isomerization with LEDA/EDA under the same conditions used for stigmasterol (7a). Stigmasta-5,23-dien-3β-ol (10a), stigmasta-5,24-dien-3β-ol (11a) were obtained along with some starting material and stigmasta-5,25-dien-3β-ol (16a). Other investigators, using fucosterol acetate and iodine in benzene reported[2] the same side chain rearrangement products.

As a further example 23,24-bisnorchola-5,20-dien-3β-ol (17a) (obtained from 3β-hydroxypregn-5-en-20-one (2a) by Wittig condensation) was subjected to double bond migration using LEDA/EDA. Equilibrium was reached in two hours, the Δ^{17}-derivative (23,24-bisnorchola-5,17(20)-dien-3β-ol) (18a) being formed as the major product with some starting material and an unidentified compound.

In summary, our results confirm earlier[5,8] observations that base-catalyzed isomerization of steroids with unsaturated side chains offers a route to the most highly substituted olefin, but other less substituted double bond isomers are invariably also present.

EXPERIMENTAL

General. The following instruments and conditions were used for chromatographic separations of reaction products and for securing appropriate physical data:

Analytical glc: Hewlett-Packard 402 high-efficiency chromatograph equipped with "U" shaped glass column (4 mm i.d. × 1.5 m); packing material: 3% OV-25 on 100–120 mesh GCQ (Applied Sci., Inc.); oven temp. for stigmasterol and fucosterol double bond isomers: 270°, for i-methyl ethers and other compounds: 250°, for ozonization products: 230–260° (programmed temp., 5°/min, program delay: 5 min). Carrier gas and flow rate: helium, 100 ml/min. A standard 402A flame ionization detector was used throughout this work.

Analytical and preparative hplc; a Whatman partisil M9 10/50 ODS-2 column (8 mm i.d. × 50 cm) equipped with a Haskel model 28388 pump, a 0–5000 psi Ashrof gauge, and a Waters Associates dual cell refractometer detector. Mobil phase: abs. methanol, pressure: 980 psi, flow rate: 6 ml/min.

Low resolution gc/MS: Varian MAT-44 gc/MS system equipped with a spiral glass column (2.7 mm i.d. × 2 m), packing material: 3% OV-17 on GCQ (Applied Sci., Inc.), oven temp.: 220–270° (programmed temp., 5°/min, program delay: 5 min).

High-resolution gc/MS: Hewlett-Packard 7610A gas chromatograph equipped with a "U" shaped glass column (2 mm i.d. × 3 m), packing material: 3% OV-17 on GCQ and interfaced with a Varian MAT 711 double focusing mass spectrometer connected to a PDP-11 computer for data acquisition and reduction, temp.: 220–265° (programmed temp., 6°/min, program delay: 5 min).

NMR spectra: Bruker HXS 360 MHz NMR spectrometer and Varian Associates HA-100 NMR spectrometer equipped with a NTCFT-1180 computer for Fourier Transform process and data acquisition or a Varian Associates T-60 NMR spectrometer. Shift values are given in ppm (δ) with TMS as internal reference.

M.ps: Thomas-Hoover "Uni-Melt" capillary m.p. apparatus, uncorrected.

Isomerization of sterols

As a general procedure, to a stirred soln of N-lithioethylenediamine (prepared from 0.5 g Li and 18 ml anhyd. ethylenediamine, 90–100°, N_2) 0.5 g sterol was added (100–120°, N_2, 30–40 hr for stigmasterol (7a), stigmasterol i-methyl ether (7b) and fucosterol (4a); 2 hr for 23,24-bisnorchola-5,20-dien-3β-ol (17a). The final mixture was cooled, poured into ice-water (25 ml), extracted with ether (20 ml × 3), the organic layer washed with 10% HCl aq, 10% $NaHCO_3$ aq and water, respectively, and the ether removed by evaporation under reduced pressure. The products were subjected to subsequent glc analysis, hplc separation and crystallization as indicated earlier.

Stigmasta-5,17(20)-dien-3β-ol (8a), m.p. 105–107° (lit.[9] m.p. 98–100°); MS: *m/z* 412 (M^+, 24%), 397 (18), 379 (10), 300 (26), 299 (100), 281 (22), 271 (23), 230 (18), 175 (10), 159 (11), 157 (11), 147 (19), 145 (17), 133 (19), 131 (10), 123 (12), 121 (38), 119 (21), 109 (14), 107 (29), 105 (19), 97 (20), 95 (55), 93 (20), 91 (18), 85 (11), 83 (22), 81 (25), 79 (15), 71 (14), 69 (46), 67 (14); NMR: 0.77 (s, 3H, C-18 Me), 0.99 (s, 3H, C-19 Me), 1.68 (s, 3H, =C–CH₃, C-21 Me), 3.45 (m, 1H, CH–OH), 5.31 (d, 1H, =CH).

Stigmasta-5,23-dien-3β-ol (10a), m.p. 149–151°; MS: *m/z* 412 (M^+, 49%), 369 (14), 351 (19), 314 (31), 301 (11), 300 (24), 299 (14), 281 (10), 273 (12), 272 (19), 271 (36), 256 (11), 255 (45), 229 (14), 215 (11), 213 (21), 199 (10), 161 (17), 159 (36), 151 (15), 149 (11), 147 (27), 145 (33), 137 (11), 135 (18), 133 (37), 131 (16), 123 (25), 121 (21), 119 (23), 117 (10), 110 (12), 109 (25), 107 (34), 105 (30), 97 (45), 96 (12), 95 (40), 93 (32), 91 (28), 83 (64), 82 (14), 81 (59), 79 (28), 77 (10), 71 (12), 69 (54), 67 (31), 57 (19), 55 (100), 43 (32), 41 (39); NMR: 0.696 (s, 3H, C-18 Me), 1.009 (s, 3H, C-19 Me), 0.788–0.851 (9H, C-21, C-26 and C-27 Me's), 1.011 (t, 3H, J 4.1, C-29 Me), 3.52 (m, 1H, CH–OH), 5.08 (t, 1H, J 6.3, CH_2–CH=C), 5.34 (d, 1H, =CH).

Stigmasta-5,24-dien-3β-ol (11a), m.p. 125–127°: MS: *m/z* 412 (M^+, 15%), 315 (27), 314 (100), 300 (12), 299 (31), 296 (14), 281 (27), 272 (12), 271 (26), 255 (10), 231 (12), 229 (27), 213 (20), 211 (14), 199 (10), 173 (11), 161 (15), 159 (22), 158 (13), 157 (11), 147 (16), 145 (25), 143 (11), 135 (14), 133 (33), 131 (16), 123 (15), 121 (19), 120 (12), 119 (22), 110 (12), 109 (19), 107 (29), 105 (28), 97 (48), 95 (32), 93 (26), 91 (24), 83 (22), 82 (14), 81 (38), 79 (24), 69 (51), 67 (25), 57 (13), 55 (92), 43 (21), 41 (36); NMR: 0.681 (s, 3H, C-18 Me), 1.008 (s, 3H, C-19 Me), 0.929–1.01 (6H, C-21 and C-29 Me's), 1.625 and 1.629 (two singlets, 3H each, C-26 and C-27 Me's).

Ozonization

Compound 7b was prepared by treating 7a with *p*-toluenesulfonyl-chloride in pyridine to yield the tosylate followed by methanolysis in the presence of anhyd. KOAc in the usual manner.[10] The product was subjected to isomerization reaction with LEDA/EDA as described above. The mixture of isomers

(200 mg) was dissolved in 15 ml of dry CH_2Cl_2 and a few drops of dry pyridine were added. O_3 was bubbled into the stirred soln at −78° until a blue color persisted. Zn dust (0.2 g) and glacial AcOH (0.5 ml) was added and this mixture was stirred at room temp. for 1 hr. The mixture was filtered to remove the Zn, the filtrate was concentrated, diluted with water and extracted with pentane–ether (1:1) (3 × 100 ml). The combined organic layers were washed with 10% $NaHCO_3$ aq, water and dried over anhyd. $MgSO_4$. The high resolution mass spectral results of the major ozonolysis products of the double bond isomers were obtained by direct gc–MS determinations.

3α,5-Cyclo-6β-methoxyandrostan-17-one (1b), M^+ 302.21748 (22, $C_{20}H_{30}O_2$), 288.20107 (10, $C_{19}H_{28}O_2$—probably contamination by 1a), 287.19860 (37, $C_{19}H_{27}O_2$), 271.19844 (10, $C_{19}H_{27}O$), 270.19339 (46, $C_{19}H_{26}O$), 248.17379 (16, $C_{16}H_{24}O_2$), 247.16744 (100, $C_{16}H_{23}O_2$), 244.18267 (11, $C_{17}H_{24}O$), 145.10109 (16, $C_{11}H_{13}$), 137.09548 (11, $C_9H_{13}O$), 131.08602 (14, $C_{10}H_{11}$), 123.08019 (15, $C_8H_{11}O$), 121.10107 (13, C_9H_{13}), 120.09442 (13, C_9H_{12}), 119.08666 (17, C_9H_{11}), 107.08869 (27, C_8H_{11}), 105.07021 (33, C_8H_9).

3α,5-Cyclo-6β-methoxypregnane-20-one (2b): M^+ 330.25582 (12, $C_{22}H_{34}O_2$), 315.23371 (16, $C_{21}H_{31}O_2$), 298.22990 (22, $C_{21}H_{30}O$), 275.20130 (35, $C_{18}H_{27}O_2$), 159.11796 (11, $C_{12}H_{15}$), 145.10012 (13, $C_{11}H_{13}$), 133.10211 (12, $C_{10}H_{13}$), 121.10068 (10, C_9H_{13}), 119.08566 (16, C_9H_{11}), 107.08659 (21, C_8H_{11}), 105.07066 (30, C_8H_9).

3α,5-Cyclo-6β-methoxy-23,24-bisnorcholan-22-al (3b), M^+ 344.26850 (25, $C_{23}H_{36}O_2$), 329.25163 (45, $C_{22}H_{33}O_2$), 313.25211 (24, $C_{22}H_{33}O$), 312.24301 (83, $C_{22}H_{32}O$), 297.22757 (16, $C_{21}H_{29}O$), 289.21552 (100, $C_{18}H_{29}O_2$), 286.23067 (22, $C_{20}H_{30}O$), 253.19776 (11, $C_{16}H_{25}$), 239.17847 (11, $C_{16}H_{23}$), 231.17433 (15, $C_{16}H_{23}O$), 187.14769 (11, $C_{14}H_{19}$), 173.13349 (16, $C_{13}H_{17}$), 163.11452 (11, $C_{11}H_{15}O$), 161.13202 (28, $C_{12}H_{17}$), 160.12586 (15, $C_{12}H_{16}$), 159.11747 (25, $C_{12}H_{15}$), 157.09916 (12, $C_{12}H_{13}$), 147.11685 (28, $C_{11}H_{15}$), 146.10909 (13, $C_{11}H_{14}$), 145.10170 (21, $C_{11}H_{13}$), 139.11115 (24, $C_9H_{15}O$), 137.09605 (23, $C_9H_{13}O$), 135.11573 (14, $C_{10}H_{15}$), 135.07979 (13, $C_9H_{11}O$), 134.10823 (14, $C_{10}H_{14}$), 133.09962 (33, $C_{10}H_{13}$), 123.07993 (20, $C_8H_{11}O$), 121.10088 (52, C_9H_{13}), 120.09422 (22, C_9H_{12}), 119.08607 (37, C_9H_{11}), 108.09000 (16, C_8H_{12}), 107.08619 (65, C_8H_{11}), 106.07753 (20, C_8H_{10}), 105.06925 (64, C_8H_9).

3α,5-Cyclo-6β-methoxy-24-norcholan-23-al (4a), M^+ 358.28439 (8, $C_{24}H_{38}O_2$), 343.25068 (16, $C_{23}H_{35}O_2$), 326.26313 (25, $C_{23}H_{34}O$), 314.22183 (30, $C_{21}H_{30}O_2$), 303.22835 (45, $C_{20}H_{31}O_2$), 296.21231 (10, $C_{21}H_{28}O_1$), 232.18499 (11, $C_{16}H_{24}O$), 161.13151 (20, $C_{12}H_{17}$), 159.11910 (26, $C_{12}H_{15}$), 157.10042 (11, $C_{12}H_{13}$), 147.11748 (19, $C_{11}H_{15}$), 143.08925 (13, $C_{11}H_{11}$), 137.09694 (13, $C_9H_{13}O$), 136.09027 (38, $C_9H_{12}O$), 131.08560 (17, $C_{10}H_{11}$), 123.07973 (28, $C_8H_{11}O$), 121.10257 (26, C_9H_{13}), 120.09284 (20, C_9H_{12}), 119.08466 (28, C_9H_{11}), 117.07062 (16, C_9H_9), 108.09406 (13, C_8H_{12}), 107.08589 (54, C_8H_{11}), 106.07637 (10, C_8H_{10}), 105.07066 (10, C_8H_9), 43.01866 (100, C_2H_3O).

3α,5-Cyclo-6β-methoxy-26-norcholestan-24-one (5b), M^+ 400.33137 (70, $C_{27}H_{44}O_2$), 386.30960 (14, $C_{26}H_{42}O_2$—probably due to contamination by 15a), 353.27676 (17, $C_{25}H_{37}O$), 346.27510 (19, $C_{26}H_{34}$), 345.27034 (93, $C_{25}H_{37}O_2$), 313.25207 (12, $C_{25}H_{37}O$), 285.22355 (13, $C_{20}H_{29}O$), 255.21192 (44, $C_{19}H_{27}$), 229.18834 (18, $C_{17}H_{25}$), 228.18470 (15, $C_{17}H_{24}$), 214.16828 (18, $C_{16}H_{22}$), 213.16158 (40, $C_{16}H_{21}$), 185.13321 (29, $C_{14}H_{17}$), 173.13464 (26, $C_{13}H_{17}$), 159.11589 (44, $C_{12}H_{15}$), 157.10039 (25, $C_{12}H_{13}$), 147.11753 (31, $C_{11}H_{15}$), 145.09883 (47, $C_{11}H_{13}$), 139.11120 (27, $C_9H_{15}O$), 135.11670 (30, $C_{10}H_{15}$), 133.10149 (28, $C_{10}H_{13}$), 131.08685 (23, $C_{10}H_{11}$), 123.08209 (22, $C_9H_{11}O$), 120.09134 (15, C_9H_{12}), 119.08267 (35, C_9H_{11}), 118.07573 (12, C_9H_{10}), 117.07051 (22, C_9H_9), 113.09544 (44, $C_7H_{13}O$), 109.10040 (30, C_8H_{13}), 108.09381 (24, C_8H_{12}), 107.08586 (66, C_8H_{11}), 106.07830 (15, C_8H_{10}), 105.07029 (76, C_8H_9).

To obtain the Δ^5-3β-hydroxy alcohols, the ozonization mixture (25 mg) was dissolved in 10 ml of dioxane–water (8:2) with 4 mg of *p*-toluenesulfonic acid and the mixture was heated under reflux for 1 hr. The soln was cooled and extracted with ether (4 × 10 ml). the organic solvent was evaporated under reduced pressure. The major free alcohols were compared with authentic samples as indicated earlier.

Isomerization of 23,24-bisnorcholo-5,20-dien-3β-ol (17a). 3β-Hydroxyprega-5-en-20-one (0.5 g) was treated with methyltriphenylphosphonium bromide (1.42 g in 35 ml dry THF) under N_2 for 2 hr, the resulting mixture was poured into H_2O and extracted with ether to provide 70% of 17a.[17] This compound was subjected to double bond migration with LEDA/EDA as described earlier and 18a separated by hplc and repeated crystallization from MeOH. Gas chromatographic analysis indicated the formation of 70% 18a.

23,24-Bisnorcholo-5,17(20)-dien-3β-ol (18a), m.p. 127.5–128.5°, MS: 314 (M^+, 60%), 299 (36), 281 (36), 271 (14), 230 (20), 229 (18), 213 (20), 212 (11), 211 (18), 199 (14), 197 (16), 187 (11), 185 (16), 175 (16), 175 (16), 173 (18), 171 (20), 161 (18), 159 (34), 158 (25), 157 (27), 147 (30), 145 (41), 144 (14), 143 (27), 135 (27), 134 (14), 133 (36), 132 (14), 131 (30), 129 (18), 123 (14), 122 (14), 121 (73), 120 (25), 119 (45), 118 (14), 117 (25), 109 (23), 108 (14), 107 (55), 106 (18), 105 (66), 95 (73), 94 (16), 93 (66), 92 (18), 91 (93), 83 (41), 82 (18), 81 (64), 79 (80), 77 (45), 69 (32), 68 (14), 67 (59), 65 (18), 57 (36), 55 (100), 53 (32); NMR: 0.86 (s, 3H, C-18 Me), 1.02 (s, 3H, C-19 Me), 1.59 and 1.71 (two singlets, 3H each, C-21 and C-22 methyls), 3.5 (m, 1H, CH–OH), 5.4 (d, 1H, =CH).

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REFERENCES

[1]W. J. S. Lockley, D. P. Roberts, H. H. Rees and T. W. Goodwin, *Tetrahedron Lett.* 43, 3373 (1974).
[2]N. Ikekawa, Y. Honma, N. Morisaki and K. Sakai, *J. Org. Chem.* 38(12), 4145 (1970).
[3]P. DeLuca, M. DeRosa, L. Minale and G. Sodano, *J. Chem. Soc., Perkin I* 2132 (1972).
[4]M. Bortolotto, J. C. Braekman, D. Daloze and B. Tursch, *Bull. Soc. Chem. Belg.* 87, 539 (1978).
[5]C. Singh, J. Singh and S. Dev, *Tetrahedron* 33, 1759 (1977).
[6]F. J. Schmitz, In *Marine Natural Products* (Edited by P. J. Scheuer), Chap. 5. Academic Press, New York (1978).
[7]C. Djerassi, *Proc. Roy. Soc. Lond. B* 198, 175 (1976).
[8]P. Balakrishnan, R. Seshadri, K. K. Chakravarti and S. C. Bhattacharya, *Indian J. Chem.* 16B, 253 (1978).
[9]E. Fernholz, *Liebigs Ann.* 507, 128 (1933).
[10]P. W. Heyl and M. E. Herr, *J. Am. Chem. Soc.* 72, 2617 (1970).
[11]W. H. Pasl, A. Pailli and C. Djerassi, *J. Org. Chem.* 35, 2571 (1970).
[12]C. A. Brown, *Chem. Comm.* 222 (1975).
[13]E. Steiner, C. Djerassi, E. Pattorusso, S. Magno, L. Mayol, C. Santacroce and D. Sica, *Helv. Chim. Acta* 60, 475 (1977).
[14]C. Djerassi, *Pure Appl. Chem.* 50, 171 (1978).
[15]S. G. Wyllie and C. Djerassi, *J. Org. Chem.* 33, 305 (1968).
[16]J. A. Stocle and E. Mosettig, *J. Org. Chem.* 28, 571 (1963).
[17]J. P. Dauza and W. Bergmann, *J. Org. Chem.* 25, 79 (1960).