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ADDITION TO STEROID POLYENES—II

REACTION OF 7-DEHYDROCHOLESTERYL ACETATE WITH DIMETHYL ACETYLENEDICARBOXYLATE

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Abstract—Dimethyl acetylenedicarboxylate reacts with 7-dehydrocholesteryl acetate (I) by nucleophilic addition at C_7. Two products are obtained, resulting from subsequent hydrogen abstraction from C_9 (II) and from C_{14} (III) respectively. Addition-abstraction, hitherto unreported for esters of acetylenedicarboxylic acid, appears to be the sole reaction mode with this highly hindered diene-system. Structure proof is supported by NMR spectroscopy as well as by chemical transformations of the adducts. On treatment with base one of the adducts undergoes a prototropic rearrangement.

THE unexpected course of the reaction of 7-dehydrocholesterylacetate (I) with esters of diazodicarboxylic acid[2*] prompted us to investigate the reaction of this tetrasubstituted diene with other reactive dienophiles.

Dimethyl acetylenedicarboxylate, first used in the diene synthesis by Diels and Alder in 1931,[3] reacts with simple dienes such as butadiene and cyclohexadiene exothermally at room temperature with exclusive formation of 1,4-adducts.[4] No other reaction modes have thus far been reported for this dienophile.

7-Dehydrocholesteryl acetate (I) did not react as readily with dimethyl acetylenedicarboxylate as with diethyl diazodicarboxylate.[2] After refluxing for 20 hr in *p*-xylene however, the reaction appeared to be complete, as indicated by UV and thin-layer chromatographic (TLC) analyses. By fractional crystallization two one-to-one adducts were obtained. They show different crystal forms but similar IR spectra with one broadened absorption in the carbonyl-region and an intense band at 1640 cm^{-1} which is assigned to the stretching mode of a conjugated double bond. The adducts are not interconvertible under the reaction conditions. Furthermore the fact that the two adducts were separately crystallizable from the same solvent (MeOH) at the same temperature excluded the occurrence of crystal isomers. The UV spectra [λ_{max}^{EtOH}: 219 nm ($\varepsilon = 10{,}000$)] confirm the presence of an α,β-unsaturated ester and exclude allylic-addition. In contrast to what is known about the behaviour of 1,4-adducts of dimethyl acetylenedicarboxylate, all of which pyrolyse easily with

* Note. In a recent publication titled "*Adducts of Maleic Anhydride with Ergosteryl Acetate, J. Chem. Soc.* 5206 (1964) by D. Neville Jones and I. Thomas, the authors have assigned incorrect structures to the addition products obtained by them. This was pointed out by one of us (A. van der Gen) in a private communication to Dr. D. Neville Jones. On the basis of a re-interpretation of the NMR evidence as well as on the basis of new chemical evidence presented, the authors will revise their originally described structures in a forthcoming paper in the Tetrahedron.

[1] Part of the Thesis of A. van der Gen, Amsterdam (1964).

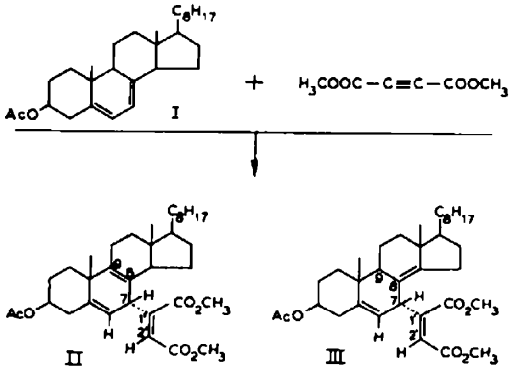
[2] Part I of this series. A. van der Gen, J. Lakeman, M. A. M. P. Gras and H. O. Huisman, *Tetrahedron* **20**, 2521 (1964).

[3] O. Diels and K. Alder, *Liebigs Ann.* **486**, 191 (1931).

[4] O. Diels and K. Alder, *Liebigs Ann.* **490**, 236 (1931).

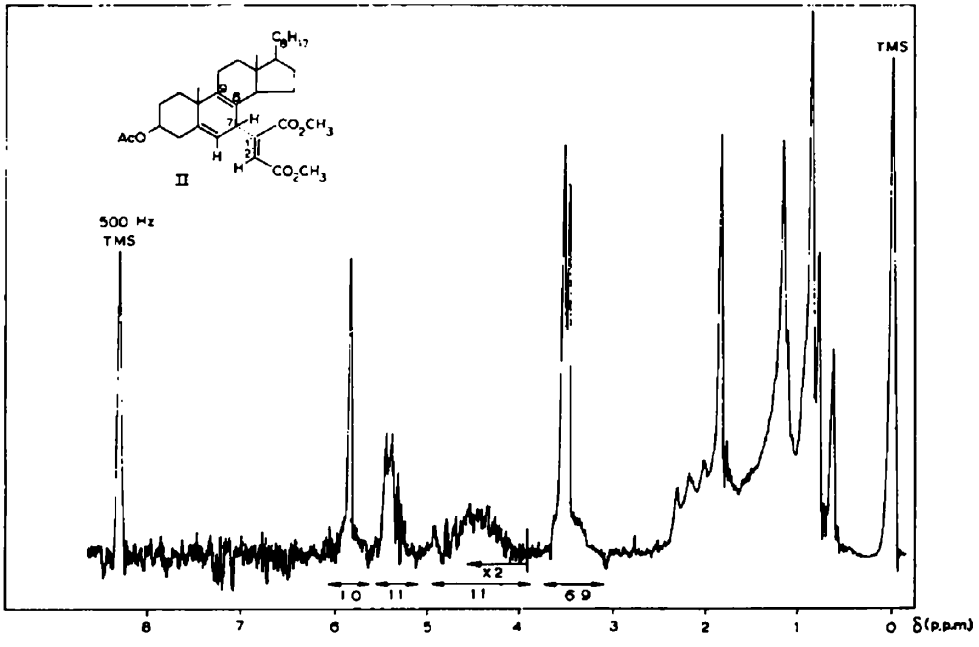
formation of substituted phthalates,[5,6] both adducts are recovered unchanged after being heated at 265° under reduced pressure for two hours.

The low-field parts of the NMR spectra of the two adducts are quite similar. In addition to the methyl ester signals (pairs of singlets in the region δ 3·5–4·0) and the broad absorption of the 3α-proton (around δ 4·5) there are absorptions corresponding to the presence of three protons, two of which are in the vinyl proton-region



7α-(1′,2′-cis-dicarbomethoxyvinyl)-3β-acetoxycholesta-5, 8-diene.

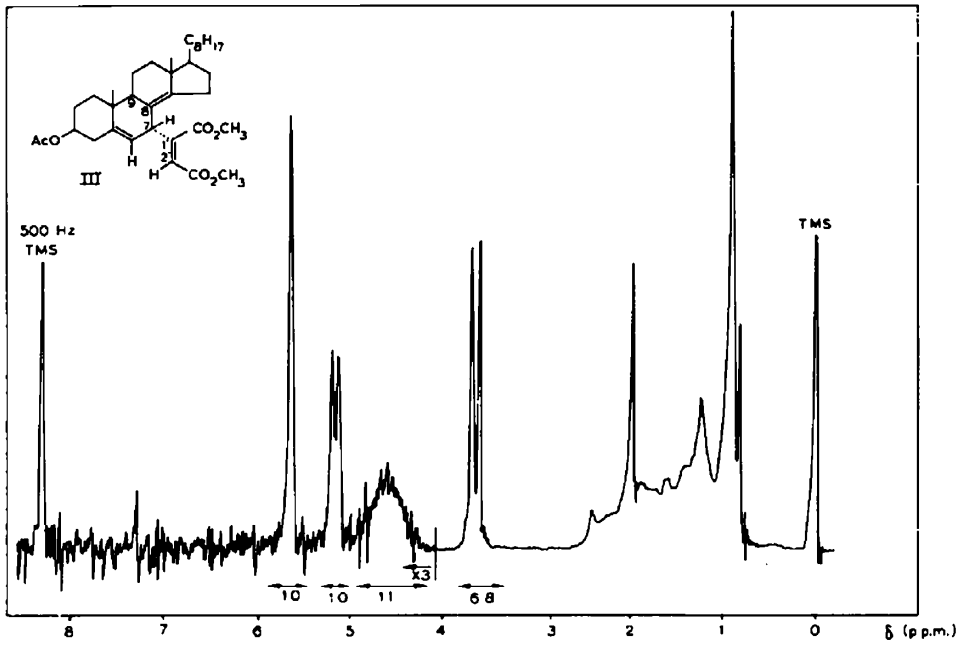
7α-(1′,2′-cis-dicarbomethoxyvinyl)-3β-acetoxycholesta-5, 8(14)-diene.



m.p. 13.3 – 134.5° α_D – 1.19°
Yield 19.2%

II

[5] H. Pines and R. H. Kozlowski, *J. Amer. Chem. Soc.* 78, 3776 (1956).
[6] R. S. Davidson, P. S. Littlewood, T. Medcalfe, S. M. Waddington-Feather, D. H. Williams and B. Lythgoe, *Tetrahedron Letters* 1413 (1963).



m.p. 96 – 98° α_D – 2.14°
Yield 49.7%

III

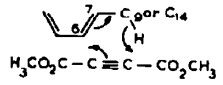
(δ 5·0–6·0) while the third one coincides with the methyl ester signals.[7] The singlet-doublet pattern of the vinyl-proton absorptions give another indication that the adducts have not been formed by 1,4-addition.[8] Before interpreting the high-field portions of the NMR spectra the catalytic reduction of the adducts will be discussed. On reduction of both compounds with Adam's catalyst at atmospheric pressure, the hydrogen absorption stops after uptake of 1 mole. The IR and UV spectra of the products show distinctly that in each case the ester-activated double bond has been reduced. The NMR spectra show that the single proton absorption between δ 3·0 and δ 4·0 has disappeared and that only one vinyl proton is left. This last observation is only compatible with structures for the original adducts in which the ester-activated double bond also carries one hydrogen atom. Such structures can only arise from asymmetric addition to the triple bond in the acetylene-ester. Allylic-addition to the steroid-diene system already being excluded, this leaves addition-abstraction reactions at C_6 or C_7 as the remaining possibilities. Of these, only addition at C_7 gives rise to the formation of products with two vinylic protons, one being located at C_6 and the second on the C_7-side chain.

Addition of the acetylene ester may in principle occur at either the α- or the β-side of the steroid molecule. However, attack from the β-side can be excluded both on mechanistic grounds (no β-hydrogen atoms are available at the two possible reaction sites C_9 and C_{14}) and from an evaluation of the chemical shifts of the C_{18}- and C_{19}-

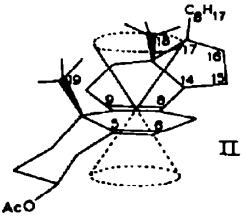
[7] Assuming a total of 52 protons, the absorptions between δ 3·0 and δ 4·0 integrate for 6·9 and 6·8 protons respectively.

[8] The vinylene bridge protons of a 1,4-addition product would give rise to a pair of doublets each with a coupling constant of about 8 c/s.

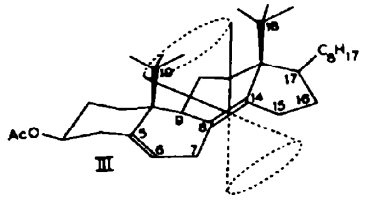
methyl groups.[9] The foregoing considerations leave the subjoined structures II and III for the two adducts. The *cis*-structure in the C_7-side chain of both adducts follows from consideration of the most likely mechanism of the addition-abstraction reaction[10]



Assignment of structures II and III to the two adducts can unambiguously be made by examination of the chemical shifts of the C_{18}- and C_{19}-methyl groups in the NMR spectra, which are completely different in both cases. Whereas the adduct with m.p. 133–134·5° shows, in addition to the side-chain absorptions at δ 0·82 and δ 0·90, clearly separated signals at δ 0·65 and δ 1·20 from the C_{18}- and the C_{19}-methyl groups respectively, the adduct with m.p. 96–98° shows only one strong absorption at δ 0·90.[11] Thus, with respect to the former, the C_{18}-methyl signal of the latter adduct is shifted considerably downfield while the C_{19}-methyl signal is shifted in the opposite direction. The effects that the diamagnetic anisotropy of the 8(9)- and 8(14)-double bonds will have on the chemical shifts of the axial methyl groups in structures II and III respectively are indicated in the following Figs.



II



III

In structure II the C_{18}-methyl group lies within the "shielding cone" of the 8(9)-double bond and its NMR signal will appear at higher field. The C_{19}-methyl signal on the other hand will be shifted towards lower field. In structure III the 8(14)-double bond will bring about shifts in opposite directions. Here the C_{19}-methyl group lies within the "shielding cone" of the 8(14)-double bond and the C_{18}-methyl group lies in the area where this double bond brings about a downfield shift. Thus structure II must be assigned to the adduct with m.p. 133–134·5° which has its C_{18}- and C_{19}-methyl absorptions at δ 0·65 and δ 1·20 respectively while structure III is assigned to the adduct with m.p. 96–98° whose axial-methyl absorptions coincide at δ 0·90.

Confirmation of the above structural assignment was found in a study of the alkaline hydrolysis of the adducts II and III and their reduction products.

Hydrolysis of the high-melting adduct (II) with 10% KOH in methanol followed by

[9] If the adducts had comprised a pair of C_7-epimers both axial methyl absorptions of the β-isomer would be expected to be shifted downfield relative to the corresponding absorptions of the α-isomer.

[10] The high degree of stereospecifity and the transfer of optical asymmetry from one of the reactants to a different site in the adduct seem to provide sufficient proof for assuming a concerted "four centre" mechanism in this "substitutive-addition" type of reactions. R. K. Hill and M. Rabinovitz, *J. Amer. Chem. Soc.* **86**, 965 (1964) and Ref. cited therein.

[11] The ratio of the number of protons at low field to the total number of protons is the same for both adducts.

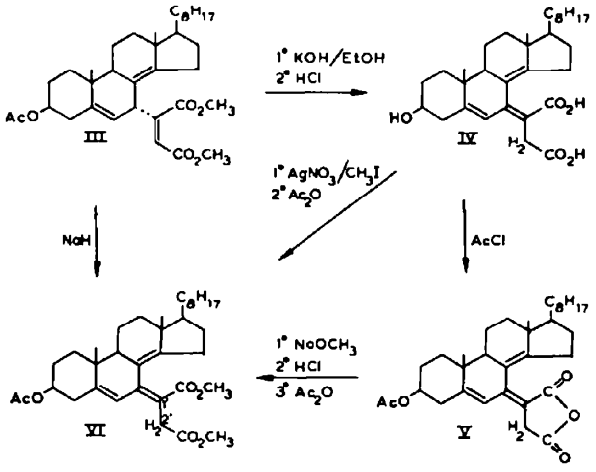
acidification provided the corresponding hydroxy-dicarboxylic acid.[12] No rearrangement occurred during this hydrolysis as was shown by the fact that the original acetoxy-dimethylester could be recovered in 85% yield on treatment of the hydroxy-dicarboxylic acid with silver nitrate, methyl iodide and acetic anhydride in sequence.

Hydrolysis of the low-melting adduct (III) in methanol gave mixtures with UV absorptions at 282 nm. When however the hydrolysis was carried out in boiling ethanol a pure potassium salt precipitated almost quantitatively in 5 min. Both this salt and its corresponding acid show bands at 1635 and 1585 cm^{-1} indicating formation of a new conjugated system. Thus is confirmed by the UV absorption [λ_{max}^{EtOH}: 210 (ε = 10,000); 224 (ε = 9,600) and 282 nm (ε = 15,000)]. The broad maximum at high wavelength without fine-structure is indicative of a cross-conjugated system. An NMR spectrum in deuteromethanol shows the presence of only one vinyl-proton at very low field (δ 7·05).

Hydrolysis of the adducts obtained on catalytic reduction of II and III gave the corresponding hydroxy-dicarboxylic acids with no UV absorption over 220 nm.

In summary it can be said that on basic hydrolysis adduct (III) undergoes a rearrangement in the course of which the number of vinyl protons decreases by one and a highly conjugated system is formed. The presence of the 1′(2′)-double bond seems to be a prerequisite. The obvious start for a base catalysed rearrangement would be the abstraction of the triply-allylic 7β-proton. The only shift which decreases the number of vinyl-protons is that of the 1′(2′)-double bond to the 7(1′)-position resulting in formation of IV. This supposition was confirmed by the following experiments:

a. Conversion of IV into an acetoxy-dimethylester (VI) differing from III and with spectral properties that are in complete agreement with the proposed structure.

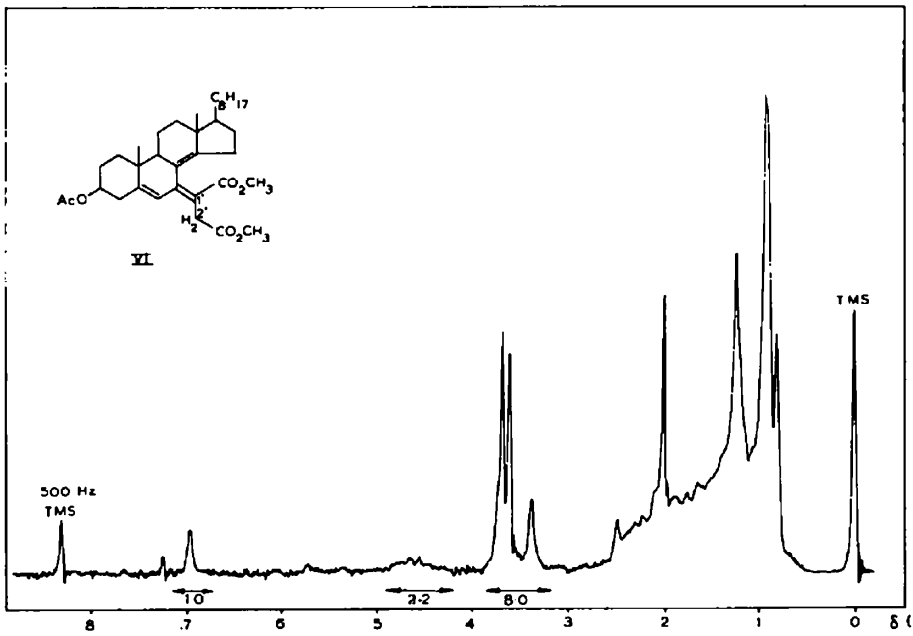


Compound VI was obtained by several different routes. Although most of the intermediates, as for example the acetoxy-anhydride (V) were obtained in a crystalline form, the ultimate product was not crystallizable because of its great solubility in all

[12] When hydrolysis was carried out in EtOH, a mixture of acids was formed that crystallized with difficulty and showed UV absorption at 278 nm.

common organic solvents. The NMR spectrum of VI shows a singlet at δ 6·98 for the C_6-vinyl-allylic-proton, the 3α-proton at δ 4·68 and the ester methyl groups at δ 3·70 and δ 3·62. The two hydrogen atoms at C_2' appear as a singlet absorption at δ 3·39.

b. Prototropic rearrangement of III under non-hydrolytic conditions. This could be accomplished by refluxing III in benzene solution with sodium hydride. The



reaction product was shown to be identical with VI by comparison of the IR, UV and NMR spectra.

The dissimilarity between adducts II and III in undergoing the prototropic rearrangement may possibly be explained by considering the interaction between the 7α-side chain and the C_{15}-methylene group. Examination of Dreiding-models indicate that this interaction is considerably smaller in II, where the bulky 7α-substituent occupies an almost axial position, than in III where this group possesses a more equatorial configuration.[13] Dreiding models clearly show that in both adducts rearrangement of the 1'(2')-double bond is accompanied by a considerable increase in spatial interaction. Since the transition state for the rearrangement of II involves a greater steric compression (relative to that for III) a decrease in tendency of the prototropic shift would be the expected consequence.

EXPERIMENTAL

7α-(1',2'-cis-Dicarbomethoxyvinyl)-3β-acetoxycholesta-5,8-diene (II) *and 7α-(1',2'-cis-dicarbomethoxyvinyl)-3β-acetoxycholesta-5,8(14)-diene* (III). 7-Dehydrocholesteryl acetate (30 g; 0·07 mole) was

[13] The coupling constant of 2·9 c/s observed in the doublet-signal of the C_6-vinylproton of II suggests, that in this adduct the 7α-substituent "dips" to a more axial position, thereby "flattening" ring B, reducing the steric interaction of the 7α-side chain with the C_{15}-methylene group and declining the dihedral angle between the C_6- and C_7-β-protons.

dissolved in 300 ml *p*-xylene, dimethyl acetylenedicarboxylate (20 g; 0·14 mole) was added and the mixture was refluxed in a N_2 atm. for 20 hr. After removal of the solvent and the excess ester under red. press. at temp not exceeding 100° the pale yellow glassy residue was dissolved in 150 ml boiling MeOH. On slow cooling to room temp II crystallized in colourless needles with m.p. 133–134·5°, yield 6·9 g, 19·2%. α_D^{20*} −1·19° ($CHCl_3$). λ_{max}^{EtOH}: 218·5 nm (ε = 10,800).

The volume of the mother liquor of II was reduced to 60 ml. On storage at 0° III slowly crystallized in colourless leaflets with m.p. 96–98°, yield 17·9 g, 49·7%. α_D^{20*} −2·14° ($CHCl_3$). λ_{max}^{EtOH}: 219 nm (ε = 9,800). (Found II: C, 73·95; H, 9·08; O, 16·98. Found III: C, 74·01; H, 9·29; O, 16·92; $C_{36}H_{52}O_8$ requires: C, 73·91; H, 9·22; O, 16·87%.)

Catalytic reduction of adducts II *and* III

In a closed system, flushed with H_2, II (1000 mg; 1·8 mmoles) was added to a previously hydrogenated suspension of 20 mg Adam's catalyst in 20 ml ethyl acetate and hydrogenated at atm. press. The H_2 uptake stopped after 10 hr and was at that time 45 ml (1·05 moles). After filtration of the catalyst and evaporation of the solvent the reaction product was crystallized from MeOH, yielding 900 mg (90%) of 7α-(1′,2′-dicarbomethoxyethyl)-3β-acetoxycholesta-5,8-diene as needles with m.p. 158–159°. λ_{max}^{EtOH}: 213 nm (ε = 3,400). The IR spectrum shows no absorption maxima between 1500 and 1700 cm^{-1}.

Likewise reduction of adduct III provided 7α-(1′,2′-dicarbomethoxyethyl)-3β-acetoxycholesta-5, 8(14)-diene as a colourless glass. This compound was recovered unchanged after attempted purification by TLC and column chromatography. λ_{max}^{EtOH}: 215 nm (ε = 3,400). The IR spectrum is identical with that of the 8(9)-isomer.

Alkaline hydrolysis of adducts II *and* III *and their reduction products*

7α-(1′,2′-cis-*Dicarboxyvinyl*)-3β-*hydroxycholesta*-5,8-*diene*. Adduct II (2000 mg; 3·5 mmoles) was dissolved in 75 ml of a 10% soln. of KOH in 95% MeOH. After refluxing 3 hr the white precipitate was filtered and dried. This gave 1200 mg (59%) of the di-potassium salt of 7α-(1′,2′-*cis*-dicarboxyvinyl)-3β-hydroxycholesta-5,8-diene. The IR spectrum displayed bands at 3500, 1640, 1565 and 1085 cm^{-1}. The salt was dissolved in 50 ml water and, after addition of 50 ml ether, the soln. was acidified with 2 N HCl. The water layer became turbid and after shaking again clear. The ether layer afforded, after shaking with sat. NaCl aq and drying on molecular sieves, 850 mg (78%) 7α-(1′,2′-*cis*-dicarboxyvinyl)-3β-hydroxycholesta-5,8-diene with m.p. 167–169°. λ_{max}^{EtOH}: 217 nm (ε = 9,300). The NMR spectrum (taken in a MeOD soln.) shows absorptions at δ 5·75 (s, 1p, 2′-H),[14] δ 5·36 (d, 1p, 6-H), δ 4·99 (s, 3·6p, 1′ acid; 2′ acid; 3-OH; CD_3OH), δ 3·62 (d, 1·2p, 7β-H), δ 3·1–3·9 (m, 3α-H), δ 3·32 (m, CD_2HOD). (Found: C, 74·48; H, 9·43; O, 15·98, $C_{31}H_{44}O_8$ requires: C, 74·66; H, 9·30; O, 16·04%.)

7-(1′,2′-*Dicarboxyethylidene*)-3β-*hydroxycholesta*-5,8(14)-*diene* (IV). Adduct III (3000 mg; 5·3 mmoles) was dissolved in 100 ml of a 10% soln. of KOH in 95% EtOH. After 5 min boiling the di-potassium salt of IV was precipitated almost quantitatively. This salt yielded the corresponding acid in 92% yield; m.p. 184–187°. λ_{max}^{EtOH}: 210 (ε = 10,000), 224 (ε = 9,600) and 282 nm (ε = 15,000). ν_{max} at 3500, 2700, 1730, 1695, 1635, 1585, 1165 and 1040 cm^{-1}. The NMR spectrum (taken from a hexadeutero-acetone soln.) shows absorption at δ 7·05 (s, 1p, 6-H), δ 5·22 (s, 3p, 1′ acid; 2′ acid; 3-OH), δ 3·3–4·0 (m, 3p, 2′-CH_2; CD_2HCOCD_3). (Found: C, 74·37; H, 9·33; O, 16·12, $C_{31}H_{46}O_8$ requires: C, 74·66; H, 9·30; O, 16·04%.)

7α-(1′,2′-*Dicarboxyethyl*)-3β-*hydroxycholesta*-5,8-*diene*. On saponification of the reduced adduct II (500 mg; 1 mmole) in a manner similar to that employed for the hydrolysis of the unreduced adduct II the di-potassium salt was formed as a crystalline precipitate in 76% yield. This salt was converted into the acid in 94% yield; m.p. 212–216°. λ_{max}^{EtOH}: 209 nm (ε = 5,200). No IR absorptions are observed between 1500 and 1650 cm^{-1}. NMR absorptions (hexadeutero acetone) are found at δ 5·10 (d, 1p, 6-H). (Found: C, 74·19; H, 9·76;O, 15·73, $C_{31}H_{48}O_8$ requires: C, 74·36; H, 9·66; O, 15·98%.)

* Concentration: 100 mg/10 ml.

[14] The symbols in parenthesis denote the multiplicity [singlet (s), doublet (d) or multiplet (m)], the number of protons and the kind of protons to which the signal is assigned.

7α-(1',2'-Dicarboxyethyl)-3β-hydroxycholesta-5,8(14)-diene. The di-potassium salt of this acid was obtained from the reduced adduct III in a way analogous to that used with the unreduced adduct III in 64% yield and converted into the acid in 90% yield; m.p. 225–226° λ_{max}^{EtOH}: 211 nm (ε = 7,000). No IR absorptions were displayed between 1500 and 1650 cm^{-1}. The NMR spectrum was not recorded because of insufficient solubility in the available solvents. (Found: C, 74·26; H, 9·59; O, 15·95, $C_{31}H_{48}O_5$ requires: C, 74·36; H, 9·66; O, 15·98%.)

Conversion of the hydroxy-dicarboxylic acids into the corresponding acetoxy-dimethyl esters

A. *Esterification of the hydroxy-dicarboxylic acid obtained from* II

Hydroxy-di-silver salt. To a soln. of the di-potassium salt of the hydroxy-dicarboxylic acid obtained from II (630 mg; 1·1 mmoles) in 20 ml water was added dropwise a soln. of $AgNO_3$ (510 mg; 3 mmoles) in 10 ml water. After shaking mechanically for 5 min the reaction mixture was centrifuged at 2600 rpm and decanted. The precipitate was washed twice with water and once with acetone. On drying at red. press. 740 mg (95%) purple hydroxy-di-silver salt was obtained.

Hydroxy-dimethyl ester. The hydroxy-di-silver salt (740 mg; 1·1 mmoles) was added to a mixture of 15 ml MeI and 15 ml ether.[15] After refluxing for 4 hr the reaction mixture was centrifuged at 2600 rpm and the colourless supernatant liquid was decanted. Evaporation of the solvent yielded 7α-(1',2'-*cis*-dicarbomethoxyethylene)-3β-hydroxycholesta-5,8-diene, 505 mg (87%), m.p. 132–137°. $\lambda_{max}^{cyclohex}$: 217 nm (ε = 12,700). ν_{max} at 3600, 3350, 1730, 1695, 1655, 1295, 1255, 1210 1160 and 1060 cm^{-1}. NMR signals were displayed at δ 5·79 (s, 1p, 2'-H), δ 5·34 (d, 1p, 6-H), δ 3·3–3·8 (d + m, 8p, 1' and 2' ester-CH_3, 3α-H, 7β-H). The analytical sample was crystallized once from MeOH. (Found: C, 75·18; H, 9·38; $C_{32}H_{50}O_5$ requires: C, 75·24; H, 9·57%.)

Acetoxy-dimethyl ester (II). The hydroxy-dimethyl ester (220 mg; 0·4 mmole) was dissolved in 1 ml acetic anhydride by heating at 100° and was kept at 145° for 1 hr. On cooling and scratching a precipitate was formed. Filtration and washing with cold acetic anhydride yielded 220 mg (98%) II as needles with m.p. 130–133·5°. Crystallization from MeOH gave 180 mg adduct II with m.p. 134–135·5°.

B. *Esterification of the hydroxy-dicarboxylic acid obtained from* III

Hydroxy-dimethyl ester. A suspension of IV (1000 mg; 2 mmoles) in 25 ml ether was stirred at 0° for 1 hr with a soln. of approx. 8 mmole of diazomethane in 16 ml ether. During the reaction period the acid dissolved and work-up in the usual way gave 7-(1',2'-dicarbomethoxyethylidene)-3β-hydroxycholesta-5,8(14)-diene (970 mg; 92%) as a pale yellow powder, very soluble in all common organic solvents. $\lambda_{max}^{cyclohex}$: 215 (ε = 11,000), 218 (ε = 11,000) and 289 nm (ε = 16,500). ν_{max} at 3600, 2950, 1720, 1700, 1620, 1560, 1255, 1190, 1165 and 1105 cm^{-1}. NMR absorptions are found at δ 7·01 (s, 1p, 6-H), δ 3·40–3·90 [(9p), two OCH_3, δ 3·74 s δ 3·65 s, + 2'-CH_3, δ 3·43 s + 3α-H, δ 3·40–3·90, m].

An identical product was obtained when the transformation was carried out by Fisher-esterification with HCl in dry MeOH or by subsequent treatment of the hydroxy-dicarboxylic acid with $AgNO_3$ and MeI.

Acetoxy-dimethyl ester. Acetylation of the hydroxy-dimethyl ester (800 mg; 1·5 mmoles) with either acetyl chloride or acetic anhydride in pyridine and work-up in the usual way yielded VI (730 mg; 85%) as a powder, which gave one spot in TLC and was very soluble in all common organic solvents. $\lambda_{max}^{cyclohex}$: 211 (ε = 9,600), 224 (ε = 9,200) and 286 nm (ε = 15,600). ν_{max} at 3000, 1750, 1720, 1635, 1580, 1265, 1200, 1170, 1115 cm^{-1}. NMR absorptions were displayed at δ 6·98 (s, 1p, 6-H), δ 4·68 (m, 1p, 3α-H), δ 3·70 and 3·67 (s, 6p, ester-CH_3), δ 3·39 (s, 2p, 2'-CH_2).

Acetoxy-dicarboxyanhydride (V). Compound IV (500 mg; 1 mmole) was added at −5° in small portions to 15 ml acetyl chloride. After addition of 1 ml pyridine the reaction mixture was allowed to warm up slowly and was finally refluxed for 1 hr. Solvent and excess reagent were then removed at red. press. The residue was taken up in ether and washed twice with 1 N HCl and twice with 1 N NaOH soln. Drying and evaporation of the solvent yielded the acetoxy-dicarboxyanhydride

[15] The ether was added to make the reaction product soluble.

(370 mg; 71%). The compound is crystallizable from MeOH without dec. giving V with m.p. 168–170°. λ_{max}^{EtOH}: 213 (ε = 9,700), 224 (ε = 9,300) and 284 nm (ε = 13,500). ν_{max} at 1830, 1755, 1725, 1625, 1585 and 1250 cm^{-1}. NMR signals were observed at δ 7·38 (s, 1p, 6-H), δ 4·68 (m, 1p, 3α-H), δ 3·40 (s, 2p, 2'-CH_2). (Found: C, 75·58; H, 8·96; O, 15·30, $C_{33}H_{46}O_6$ requires: C, 75·82; H, 8·87; O, 15·31%.)

Acetoxy-monomethyl ester. Compound V (320 mg; 0·6 mmole) was dissolved in 10 ml ether and added to a soln. of 162 mg (3 mmole) of MeONa in a mixture of 20 ml ether and 0·5 ml MeOH. Immediately a precipitate appeared. Filtration and drying gave the sodium salt of the acetoxy-monomethyl ester (200 mg; 57%). Acidification of a soln. of this salt in water and extraction with ether yielded 7-(1'-carbomethoxy-2'-carboxyethylidene)-3β-acetoxycholesta-5,8(14)-diene (150 mg; 78%) [m.p. 140–143°]. λ_{max}^{EtOH}: 216 (ε = 14,000), 226 (ε = 12,800) and 281 nm (ε = 16,000).

Acetoxy-dimethyl ester. Esterification of the acetoxy-monoethyl ester with diazomethane at 10° yielded the acetoxy-dimethyl ester as a colourless oil with $\lambda_{max}^{cyclohex}$ 286 nm (ε = 15,600). Identical in IR, NMR and TLC analyses with VI described earlier.

Rearrangement with sodium hydride.

Sodium hydride suspension (500 mg) was shaken mechanically for 5 min with 50 ml ether abs. After settling, the ether with the dissolved oil was decanted. The 250 mg NaH thus obtained was added to a soln. of 1000 mg (2 mmoles) of adduct III in 25 ml benzene. After refluxing for 18 hr the base was removed by filtration. On evaporation of the solvent an acetoxy-dimethyl ester was obtained as a colourless oil that solidified on standing. This material was shown to be identical in IR, NMR and TLC analyses with VI obtained previously. $\lambda_{max}^{cyclohex}$: 213 (ε = 9,400), 225 (ε = 8,700) and 284 nm (ε = 15,400).

M.ps are uncorrected. UV spectra were measured on a Zeiss RPQ 20C spectrophotometer with quartz monochromator. IR spectra were taken from KBr discs on a Unicam SP 200 spectrophotometer with NaCl optics. NMR spectra have been recorded on a Varian HR 60 spectrometer, using 0·5% tetramethylsilane as an internal standard. Unless otherwise stated NMR spectra were taken from $CDCl_3$ solns.

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