REACTIONS OF ACID ANHYDRIDES—III[1]

DIMERIZATIONS OF 3-OXO-STEROIDS

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Abstract—Steroidal ketone 1 reacts with trichloroacetyl *p*-toluenesulphonate to give in addition to the enol tosylate 3 a dimeric ketone 4 together with its enol esters 5 and 6. The dimeric ketone 4 was also obtained when ketone 1 was treated with trichloroacetic anhydride and *p*-toluenesulphonic acid. High concentrations of reactants and presence of acid favoured the formation of the dimeric products. It is suggested, that the dimerization occurs by an acid catalysed aldol-type condensation, while the anhydrides act as dehydrating agents converting the initially formed dimeric ketol to the β,γ-unsaturated ketone 4. Formation of dimeric ketone 4 was also observed when the α-bromoketone 8 was treated with zinc and ethyl chlorocarbonate. In the presence of zinc and zinc chloride however, ketone 8 yielded the dimeric β-diketone 12.

WE HAVE reported in the preceding paper the reaction of ketones with trichloroacetyl *p*-toluenesulphonate. When the 3-oxo-steroid 1 was treated with this mixed anhydride, the enol tosylate 3 was obtained in addition to dimeric products. In this paper we wish to define the structure of these dimeric compounds and describe similar dimerization reactions of the steroidal ketone 1.

Dimerization in the presence of trichloroacetyl p-*toluenesulphonate*
  In an initial experiment, a solution of ketone 1 in carbon tetrachloride was heated with a tenfold excess of the mixed anhydride to give, in addition to the monomeric enol tosylate 3, two high melting products in 11% yield.[1] These products were identified as the enol trichloroacetate 5 and the enol tosylate 6, both derived from the dimeric ketone 4. The reaction was repeated using only twofold excess of mixed anhydride in a 30% solution of ketone 1 in carbon tetrachloride. After 16 hr of heating dimers 5 and 6 were obtained in 15% and 32% yield respectively, whereas only minute amounts of monomeric products could be isolated (Chart I).
 That the monomeric enol tosylate 3 is not an intermediate in the formation of the dimeric products 5 and 6 was proved by conducting an experiment with an equimolar mixture of enol tosylate 3 and ketone 1 as reactants using a twofold excess of mixed anhydride under the same conditions. The enol tosylate 3 was recovered unchanged from this experiment and the yield of dimers 5 and 6 indicated that they had been formed by exclusive dimerization of ketone 1, without involving participation of enol tosylate 3.
  Dimeric ketone 4 was isolated in 28% yield in addition to 11% enol tosylate 3

Chart I
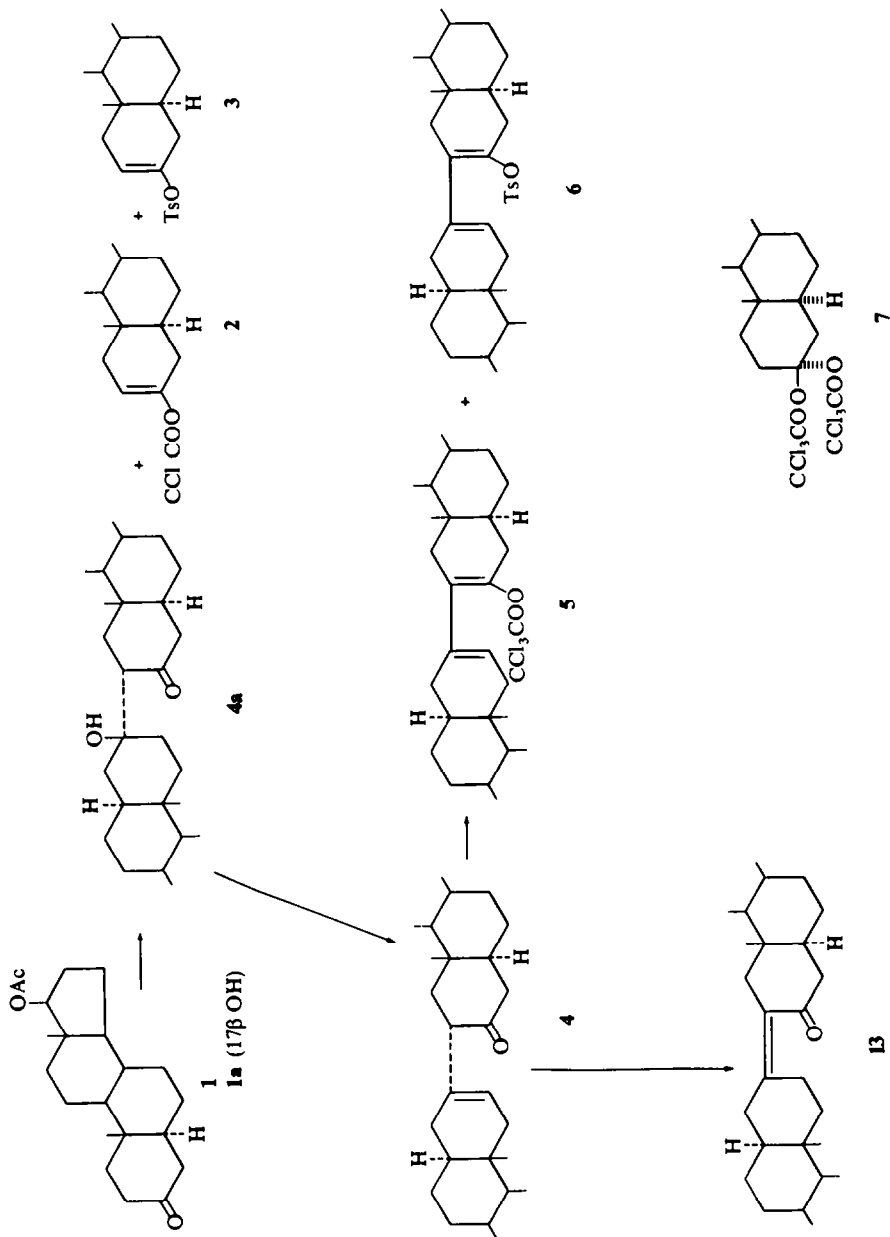
using similar reaction conditions, but higher temperature and much shorter reaction period.

It is thus conceivable, that the dimeric enol esters 5 and 6 are formed by an acid catalyzed aldol-type condensation of ketone 1, resulting in the β,γ-unsaturated ketone 4, which subsequently reacts with the mixed anhydride leading to the enol esters 5 and 6.

The acid catalyst necessary for this aldol condensation may be generated in the first stages of the reaction, when ketone 1 is converted to the corresponding enol ester. Accordingly, when small amounts of triethylamine, to remove any such acid as formed, where added to the reaction mixture the yield of the dimeric products decreased considerably, while that of the monomeric enol tosylate 3 increased. On the other hand, when the reaction was performed in the presence of traces of sulfuric acid, almost quantitative conversion to the dimeric products was recorded after $2\frac{1}{2}$ hr, as determined from the NMR spectrum of the crude reaction mixture.

Thus the reaction scheme for the formation of the dimeric enol esters 5 and 6 may be written as shown in Chart I. The mixed anhydride is likely to be the dehydrating agent, which converts the primarily formed ketol 4a to the β,γ-unsaturated ketone 4, and which by this transformation leads the condensation to completion.

Dimerization in the presence of trichloroacetic anhydride

The formation of the ketonic dimer 4 from the reaction of the ketone 1 with mixed anhydride in the presence of acid suggests that the same ketonic dimer may be formed when ketone 1 is treated with another acid anhydride, trichloroacetic anhydride, and *p*-toluenesulphonic acid. However, when ketone 1 was treated with an excess of trichloroacetic anhydride in the presence of *p*-toluenesulphonic acid, the enol trichloroacetate 2 was obtained as the sole product.[2] Since the formation of a dimer is favoured in highly concentrated solutions, we repeated this reaction using molar equivalents of ketone 1 and trichloroacetic anhydride. As expected, both the enol trichloroacetate 2 and the dimeric ketone 4 were obtained from this reaction.

The dimeric ketone 4 is also in this case most probably formed by an acid catalyzed aldol condensation of the ketone 1. That neither the *gem* bis-trichloroacetate 7 nor the enol trichloroacetate 2 participate in this condensation reaction was shown by the following experiments.

The geminal bistrichloroacetate 7 and the enol trichloroacetate 2 were separately treated with a mixture of trichloroacetic anhydride and *p*-toluenesulphonic acid under conditions which convert ketone 1 to dimer 4. From both reactions the enol trichloroacetate 2 was the only compound isolated. Equimolar mixtures of ketone 1 with *gem* bistrichloroacetate 7 or with enol trichloroacetate 2 were then subjected to the same reaction conditions. The yield of the dimer 4 isolated from these reactions corresponded only to the dimerization of the monomeric ketone 1 present in the reaction mixture, and not to dimerization of the ketone with either 7 or 2.

Dimerization of steroidal α-bromoketone

In this context we would like to report also on another reaction leading to the formation of the dimeric ketone 4. During attempted preparation of an enol carbonate by treatment of the α-bromoketone 8 with zinc in dimethoxyethane with subsequent addition of ethyl chlorocarbonate we isolated dimer 4 in addition to

Chart II

a: Zn + CH₃COCl
b: Zn + HCl
c: Zn + C₂H₅OCOCl
d: Zn + ZnCl₂
e: NaOH + H₂O
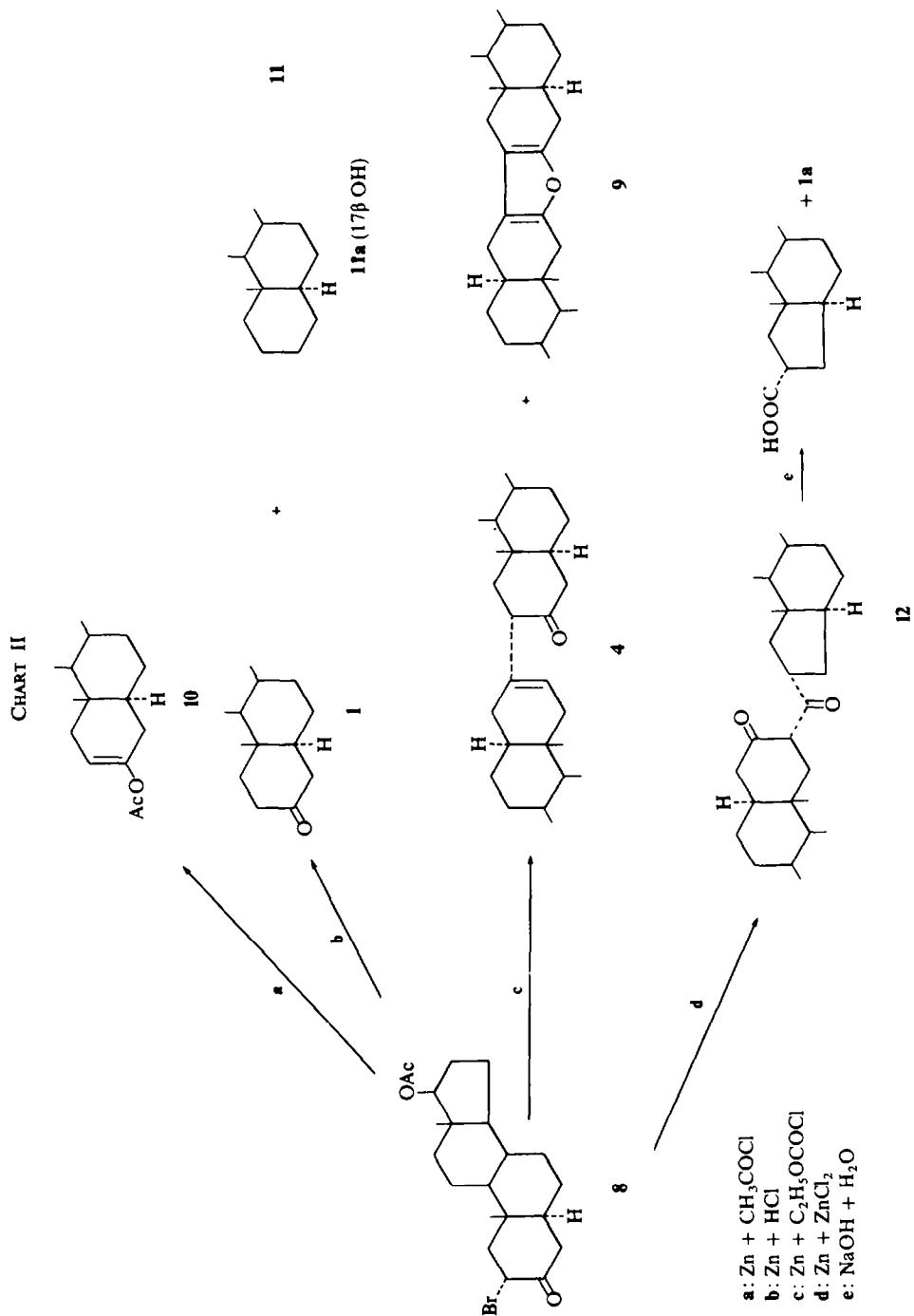
another high melting product. We assigned to the second product structure **9** possessing a furan chromophore. Analogous dimerizations of α-bromoketones with magnesium alone in an inert solvent leading to ketols, α,β-unsaturated ketones and furan derivatives have been reported previously.[3] In addition, formation of ketols and furan derivatives from the reaction of α-bromoketone with unsubstituted ketone in the presence of magnesium was also described.[4]

However, when we treated the α-bromoketone **8** with zinc in 1,2-dimethoxyethane without adding ethyl chlorocarbonate, most of the starting material was recovered unchanged.

It appears, thus, that in addition to zinc the presence of ethyl chlorocarbonate or hydrogen chloride as catalysts is necessary for the dimerization reaction. The latter could well have been present in the reaction mixture, being formed by partial decomposition of the ethyl chlorocarbonate.

However, when we treated α-bromoketone **8** with zinc in dimethoxyethane and gaseous hydrogen chloride, we obtained only the reduction products **1**, **11** and **11a**.

The hydrogen chloride present in the reaction mixture containing ethylchlorocarbonate might also have reacted with zinc to give zinc chloride, which might constitute the active catalyst. We therefore performed the reaction of α-bromoketone **8** with zinc in the presence of zinc chloride. But neither dimer **4** nor dimer **9** were obtained from this reaction. Instead we isolated a β-diketone, to which we assigned structure **12**.

We assume that in the reaction of α-bromoketone **8** with zinc the dimeric ketone **4** is formed by an aldol-type condensation of the zinc enolate species with ketone **1** (Chart III). The presence of a reactive zinc enolate species was indicated by the formation of enol acetate **10**, when acetyl chloride was added to a mixture of the α-bromoketone **8** and zinc in dimethoxyethane. The ketone **1** might have been produced by reduction of the α-bromoketone **8**. The furan derivative **9**, on the other hand, might have been formed by condensation of the zinc enolate species with the α-bromoketone **8** (Chart III). Both the formation of the enolate species from the α-bromoketone **8** and zinc and its subsequent reaction with either the ketone **1** or the α-bromoketone **8** are reversible processes, the latter two being acid catalysed. These equilibria may be displaced by the ethyl chlorocarbonate, possibly by irreversible formation of a carbonate ester and its subsequent decomposition leading to the isolated products **4** and **9**.

In the reaction of the α-bromoketone **8** with zinc and zinc chloride, the latter acts as Lewis acid, which renders the carbonyl-carbon of the α-bromoketone **8** more susceptible to nucleophilic attack by the zinc enolate. The intermediate undergoes pinacol-type rearrangement with ring contraction resulting in the β-diketone **12** (Chart III).

Identification of the products

β,γ-*unsaturated ketone* **4**. The presence of a ketonic group in **4** was indicated by its IR spectrum [(C=O) at 1715 cm^{-1}] and its UV spectrum (λ_{max} 285 mμ, ε 50). A molecular ion peak was observed in its mass spectrum (*m/e* 646) and intense peaks at *m/e* 332 and *m/e* 314, corresponding to fragments derived from the molecular ion by C2—C3′ bond cleavage. The NMR spectrum of **4** shows one resonance line in the

CHART III
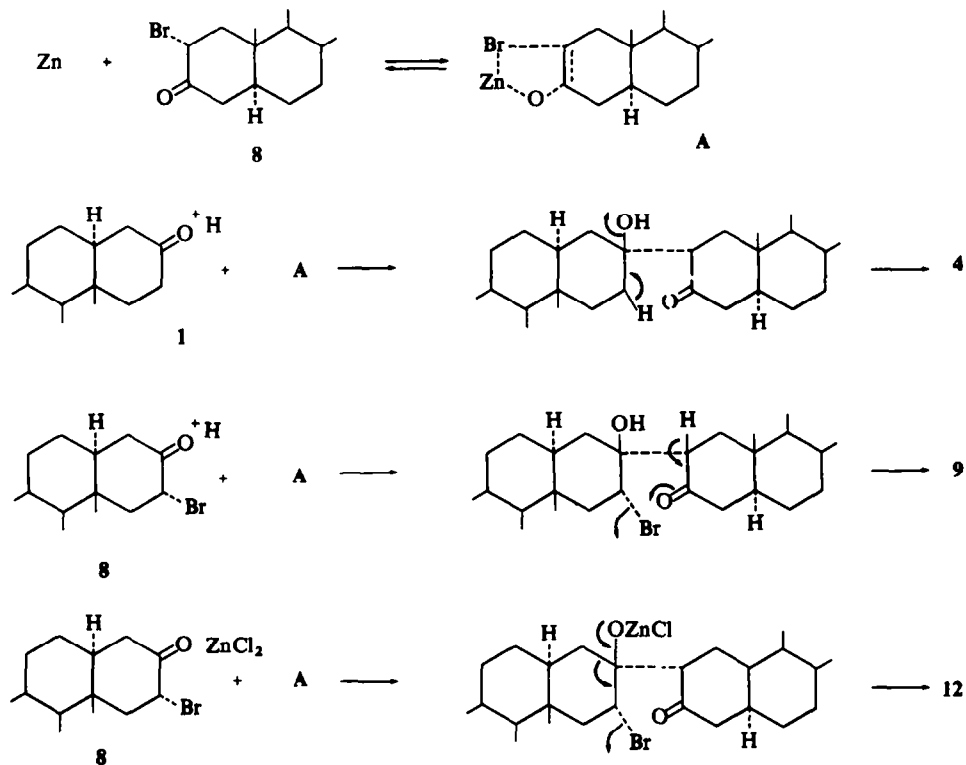
vinylic region, whose relative intensity corresponds to one proton, and separate signals for the two C19—Me groups.

The double bond in ketone 4 was located at the β,γ-position to the CO group, since it partially isomerized on treatment with acid to the α,β-position (4 → 13) as seen by the appearance of a new band in the UV spectrum at 258 mμ (E_1^1 1, 36). The incomplete isomerization of 4 to 13 indicates the sterically unfavoured position of the double bond in the α,β-unsaturated ketone 13 and the reduced overlap of the π-electrons in this system. The location of the double bond in the β,γ-unsaturated ketone 4 at Δ² position was supported by the broad signal of the vinylic proton at C2′ in the NMR. For steric reasons the androstenyl moiety is likely to assume 2α-configuration in compound 4.

The ORD spectrum of 4 shows a small positive Cotton effect in the n → π* region, which is superimposed on the more intense positive Cotton effect appearing at shorter wavelength. The latter may be due to a π → π* transition of the double bond. Since no significant enhancement of the n → π* transition was observed, a planar arrangement of the two chromophors in 4 may be postulated.

Treatment of ketone 1 with hydrogen bromide in acetic acid according to a procedure[5] described for dimerization of cholestan-3-one led to the dimeric ketol 4a. Dehydration of 4a with p-toluenesulphonic acid in di–n-butyl ether yielded a β,γ-unsaturated ketone, identical with product 4.

Dimeric enol esters **5** *and* **6**. The presence of the enol trichloroacetate grouping in **5** and that of the enol tosylate grouping in **6** were indicated by comparison of their UV, IR and NMR spectra with those of the enol trichloroacetate **2** and enol tosylate **3**. The characteristic spectral features of enol trichloroacetates **2** and **5** are: UV band (shoulder) at λ_{max} 220 mμ (in cyclohexane) and chemical shift of vinylic protons at ca. 5·45 ppm and those of enol tosylates **3** and **6** are: UV max at λ 224–227 mμ (in cyclohexane) and chemical shift of the vinylic proton at ca. 5·20 ppm. The analytical data and the integration values for the NMR peaks of both compounds were in accord with structures **5** and **6** respectively. The dimeric enol trichloroacetate **5** was converted to the parent ketone **4** by treatment with aqueous base and subsequent reacetylation. However, enol tosylate **6** was recovered unchanged when subjected to the same conditions.

Furan derivative **9**. The structural assignment of compound **9** was based on its spectroscopic properties. Its mass spectrum shows a molecular ion peak of m/e 644, and its UV spectrum an absorption at 225 mμ (ε 7100). Only one signal for its two C18—Me groups and one for its two C19—Me groups were observed in the NMR spectrum.

β-Diketone **12**. The presence of a partially enolized β-diketone grouping in **12** was evident from its UV spectrum in ethanol, showing a strong band at 290 mμ (ε 11,000), which is shifted to 315 mμ (ε 20,400) upon addition of aqueous base. That the β-diketone **12** exists in deuteriochloroform also partially in the ketonic form was indicated by the relative intensity of the signal at δ 3·1 ppm (m, ½H), assigned to the proton at the C2. Two signals for the two C19—Me groups and one for the two C18–Me groups were observed in the NMR spectrum of **12**. The presence of a β-diketone grouping was also supported by appearance of a strong enol band at 1600 cm^{-1} (C=C) in the IR spectrum. A molecular ion peak was recorded in its mass spectrum (m/e 662) and intense peaks at m/e 387 and m/e 359, corresponding to the following fragmentation:
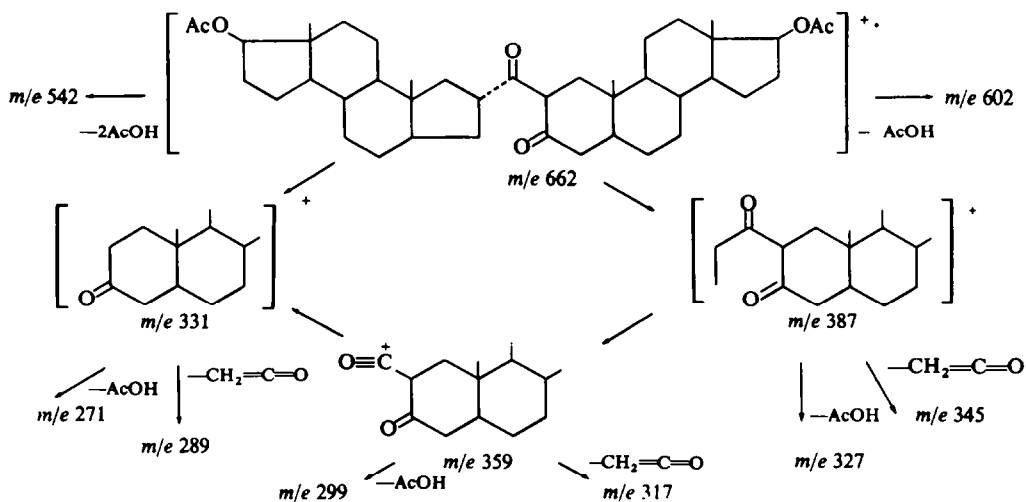
When β-diketone **12** was treated with aqueous sodium hydroxide two products were obtained: 5α-androstane-17β-ol-3-one (**1a**) and the A-nor-acid **14**.* The latter was identified by comparison with an authentic sample.[6]

EXPERIMENTAL

All m.ps were taken in capillaries and are uncorrected. UV spectra were determined on a Cary 14 spectrophotometer and the IR spectra on a Perkin–Elmer Infracord. The NMR spectra were recorded on a Varian A-60 spectrometer, using TMS as internal standard. The ORD spectra were determined on a Jasco ORD/UV-5 instrument. Mass spectra were measured with an Atlas CH-4 instrument, samples being introduced directly into the ion source.

Dimerization of ketone 1 in the presence of trichloroacetic anhydride

(a) Ketone **1**, 500 mg, was treated for 1 hr with 0·3 ml trichloroacetic anhydride and 35–45 mg *p*-toluenesulphonic acid at 125–135°. Liberated trichloroacetic acid and excess trichloroacetic anhydride were evaporated under reduced press (1 mm) and the residue chromatographed on silicagel. Elution with pentane–ether (95:5) gave 150 mg (22%) **2**, m.p. 169–171°. Elution with pentane–ether (8:2) furnished 175 mg (36%) of **4**, m.p. 252–255°; UV max (cyclohexane) 288 mμ (ε 50); IR (KBr) 1735 cm^{-1} (acetoxy C=O), 1715 cm^{-1} (ketone C=O), 1245 cm^{-1} (acetoxy C—O—C); NMR (CDCl$_3$) δ 5·3 (m, 1, C=C—$\underline{H}$), 0·76, 0·79 (each s, 3, CH$_3$ at C13), 0·73, 1·04 ppm (each s, 3, CH$_3$ at C10). Mass spectrum *m/e* 646, 586, 526, 332, 314, 273, 255; ORD (dioxan, 25°) [α]$_{330}$ +162°, [α]$_{305}$ +25°, [α]$_{226}$ +1180°. (Found: C, 77·71; H, 9·89. Calcd. for C$_{42}$H$_{62}$O$_6$: C, 77·97; H, 9·66%).

(b) **7**, 500 mg, was treated for 1 hr with 0·15 ml trichloroacetic anhydride and 25 mg *p*-toluenesulphonic acid at 125–135°. The volatile fractions were distilled off and the residue chromatographed. Elution with ether–pentane gave as only product 288 mg (77%) of **2**, m.p. 169–171°.

(c) Enol trichloroacetate **2**, 250 mg, was heated at 125–135° for 1 hr with 0·1 ml trichloroacetate anhydride in the presence of 20 mg *p*-toluenesulphonic acid. The volatile fractions were distilled off under reduced press. Chromatography of the residue on silicagel and elution with ether–pentane gave 170 mg (68%) of **2**, m.p. 169–171°. No dimerization product could be isolated.

(d) A mixture of **1**, 110 mg, and **7**, 212 mg, was heated for 1 hr at 125–135° with 0·15 ml trichloroacetic anhydride and 20 mg *p*-toluenesulphonic acid. The volatile fractions were distilled off under reduced press and the residue was chromatographed on silicagel. Elution with ether–pentane gave 100 mg (32%) of **2**, m.p. 169–171°, followed by 25 mg (8%) of **3**, m.p. 166–168°, and 32 mg (16%) of **4**, m.p. 252–255°.

(e) A mixture of **1**, 110 mg, and **2**, 158 mg, was heated for 1 hr at 125–135° with 0·15 ml trichloroacetic anhydride and 20 mg *p*-toluenesulphonic acid. The volatile fractions were distilled off under reduced press and the residue was chromatographed on silicagel. Elution with ether–pentane gave 197 mg (60%) of **2**, m.p. 169–171°, 16 mg (6%) of **3**, m.p. 166–168°, and 25 mg (12%) of **4**, m.p. 251–254°.

Dimerization of ketone 1 in the presence of trichloroacetyl-p-toluene sulphonate

(a) *Ketone* **1**. 1·0 g, was treated for 16 hr at 85–95° with 2·0 g trichloroacetyl *p*-toluenesulphonate in 2 ml CCl$_4$. The reaction mixture was cooled, diluted with 300 ml CCl$_4$, washed with 5% NaHCO$_3$ aq, then with water and dried. Evaporation of the solvent gave an oily residue, which was chromatographed on silicagel. Elution with ether–pentane (5:95) gave 25 mg (2%) monomeric **2**, m.p. 167–169°. Elution with ether–pentane (2:8) yielded 180 mg (15%) dimeric **5**, which was recrystallized from ether–pentane. M.p. 224–226°; UV max (EtOH) 215 mμ (ε 6700), shoulder; IR (KBr) 1770 cm^{-1} (trichloroacetoxy C=O), 1735 cm^{-1} (acetoxy C=O), 1250 cm^{-1} (acetoxy C—O—C), 1235 cm^{-1} (trichloroacetoxy C—O—C), several bands between 790–880 cm^{-1} (C—Cl); NMR (CDCl$_3$) δ 5·43 (m, 1, C=CH), 0·80, 0·72 (each s, 3, CH$_3$ at C13), 0·72, 0·87 ppm (each s, 3, CH$_3$ at C10). (Found: C, 66·63; H, 7·49; Calcd. for C$_{44}$H$_{61}$O$_6$Cl$_3$: C, 66·70; H, 7·76%). Further elution with ether–pentane (2:8) furnished 390 mg (32%) dimeric **6**, which was recrystallized from ether–pentane, m.p. 184–186°; UV max (EtOH) 224 mμ (ε 15,400); IR (KBr) 1735 cm^{-1} (acetoxy C=O), 1600 cm^{-1} (Ph), 1245 cm^{-1} (acetoxy C—O—C), 1190 and 1180 cm (OSO$_2$); NMR (CDCl$_3$) δ 7·80 (d, *J* = 8 c/s, 2, phenyl-$\underline{H}$), 7·30 (d, *J* = 8 c/s, 2, phenyl-$\underline{H}$), 5·2 (m, 1, C=CH), 2·25 (s, 3, CH$_3$C$_6$H$_4$), 0·78

(s, 9, CH$_3$ at C13, C13′ and C10) and 0·63 ppm (s, 3, CH$_3$ at C′10). (Found: C, 73·52; H, 8·63; S, 3·82. Calcd. for C$_{49}$H$_{68}$O$_7$S: 73·46; H, 8·56; S, 4·00%).

(b) *Ketone* 1, 750 mg, was heated for 24 hr at 85–95° with 1·5 g trichloroacetyl *p*-toluenesulphonate and 0·10 ml dry Et$_3$N in 1·5 ml CCl$_4$. The products were isolated by extraction with ether and chromatography on silicagel. Elution with ether–pentane (1 :9) gave 240 mg (25%) monomeric 3, m.p. 168–169°, which was identified by comparison with an authentic sample. Elution with ether–pentane (15:85) furnished 280 mg of a mixture. Crystallization of it from ether yielded 30 mg dimeric 4, m.p. 252–255°, recrystallization of the mother liquid from ether–pentane gave 90 mg dimeric 6, m.p. 184–186°.

(c) A mixture of 1, 850 mg, and 3, 1·2 g, was treated with 4·25 g trichloroacetyl *p*-toluenesulphonate in 4·25 ml CCl$_4$ for 20 hr at 85–95°. The products were again isolated by extraction with ether and chromatography on silicagel. Elution with ether–pentane (5:95) yielded 20 mg (1%) monomeric enol trichloroacetate 2, m.p. 168–170°. Elution with ether–pentane (1 :9) gave 140 mg (7%) dimeric 5, m.p. 224–226°, followed by 1·29 g (54%) monomeric 33, m.p. 166–167°. Further elution with ether–pentane (2:8) furnished 330 mg (17%) dimeric 6, m.p. 184–186°. The yields are calculated in respect to the total amount of steroidal reactant used.

Reactions of 17β-*acetoxy*-2α-*bromo*-5α-*androstan*-3-*one* (8)

(a) A soln of 8, 3·0 g, in 45 ml abs dimethoxyethane (distilled over LAH) was treated with 1·92 g Zn dust. The mixture was heated under reflux for 1 hr. Then 45 ml chloroethyl carbonate were added and the mixture stirred for 2 days at room temp under N$_2$ atm. The suspension was filtered off, the filtrate evaporated to dryness, and the residue chromatographed on silicagel (Merck, type H, for TLC). The products were eluted with benzene–dioxan (95:5) and 200 fractions were collected. Fractions 34–36 contained 111 mg (7%) of 9, which was recrystallized from ether-pentane. M.p. 240° (dec); UV max (cyclohexane) 225 mμ (ε 7100); IR (KBr) 1735 cm^{-1} (acetoxy C=O), 1245 cm^{-1} (acetoxy C—O—C); NMR (CDCl$_3$) δ 0·8 ppm (s, 12, CH$_3$ at C10 and C13). Mass spectrum *m/e* 644, 388. Fractions 38–42 contained 644 mg (40%) dimeric 4, m.p. 252–255°, which was identified by comparison with an authentic sample. Fractions 47–51 consisted of 248 mg (15%) of 1, m.p. 158–159°, and fractions 115–135 of 42 mg (3%) of 1a; m.p. 180–182°.

(b) A soln of 8, 1·0 g, in 15 ml dimethoxyethane was treated with 600 mg Zn dust and heated under reflux for 1 hr under N$_2$ atm. The mixture was then stirred for 1 day at room temp under N$_2$ atm, filtered and the filtrate evaporated to dryness. The residue contained in addition to unreacted material 8 small amounts of 1 as determined by TLC, NMR and IR spectroscopy.

(c) A soln of 8, 865 mg, in 13 ml dimethoxyethane was treated with 500 mg Zn dust and heated under reflux for 3 hr under N$_2$. Then 15 ml acetylchloride (freshly distilled before use) were added and the mixture stirred for 40 hr at room temp under N$_2$ atm. The suspension was then filtered off, the filtrate evaporated to dryness and the residue chromatographed on silicagel (Merck, type H, for TLC). The material was eluted with benzene–dioxan (98:2) and 200 fractions were collected. Fractions 65–78 contained 570 mg (75%) of 10, m.p. 177–178°, fractions 85–92 120 mg (17%) of 1, m.p. 158–159°. Both compounds were identified by comparison with authentic samples.

(d) A soln of 8, 1·0 g, in 30 ml dimethoxyethane was treated with 640 mg Zn dust. The mixture was heated under reflux for 3 hr. Then dry HCl gas was passed through the soln for 1 hr. The reaction mixture was filtered, the filtrate diluted with 300 ml ether, washed with 10% NaHCO$_3$ aq, then with water, dried and evaporated. The residue was chromatographed on silicagel (Merck, type H, for TLC) and the material eluted with benzene–dioxan (98:2). 200 Fractions were collected. Fractions 41–45 contained 70 mg (9–10%) of 11, m.p. 76–77°, which was identified by comparison with an authentic sample. Fractions 85–95 consisted of 37 mg (5%) of 1, m.p. 159–160°, and fractions 106–116 contained 135 mg (20%) of 11a, m.p. 165–166°, which was also identified by comparison with an authentic sample.

(e) A soln of 8, 1·0 g, in 15 ml dimethoxyethane was treated with 600 mg Zn dust and with 200 mg ZnCl$_2$. The mixture was then heated under reflux for 3 hr under N$_2$ atm. The suspension was filtered, the filtrate evaporated to dryness and chromatographed on silicagel (Merck, type H, for TLC). The products were eluted with benzene-dioxan (98:2) and 200 fractions were collected. Fractions 81–95 contained 366 mg (45%) dimeric 12, which was recrystallized from CHCl$_3$-hexane, m.p. 294–295°; UV max (EtOH) 290 mμ (ε 11,000), (OH) (EtOH) 315 mμ (ε 20,400); IR (KBr) 1735 cm^{-1} (acetoxy C=O), 1600 cm^{-1} (enol C=C), 1250 cm^{-1} (acetoxy C—O—C); NMR (CDCl$_3$) δ 3·1 (m, ½, CH at C2), 0·77, 0·78 (each s, 3, CH$_3$ at C10) and 0·75 (s, 6, CH$_3$ at C-13); mass spectrum *m/e* 662, 602, 542, 387, 359, 345, 331, 327, 299, 317, 289, 271. (Found: C, 76·43; H, 9·28. Calcd for C$_{42}$H$_{62}$O$_6$: C, 76·09; H, 9·43%). Fractions 120–140 contained 200 mg (25%) of 1 157–158°, which was identified by comparison with an authentic sample.

Preparation of dimer 4 according to Corey's procedure[5]

A soln of **1**, 1·0 g, in 29 ml abs di-n-butyl ether was treated for 4 hr at 70–80° with 3·5 ml of 3·3% HBr in AcOH. Crystalline **4a**, 112 mg (12%), precipitated from the cold reaction mixture, m.p. 195–200°; IR (KBr) 3450 cm^{-1} (OH), 1735 cm^{-1} (acetoxy C=O), 1715 cm^{-1} (ketone C=O), 1245 cm^{-1} (acetoxy C—O—C); NMR (CDCl$_3$) δ 1·12, 0·9 (each s, 3, CH$_3$ at C10), 0·78, 0·8 ppm (each s, 3, CH$_3$ at C13); mass spectrum m/e 645, 602, 585, 526, 524, 332, 314, 273, 255.

A soln of 30 mg **4a** in 25 ml abs di-n-butyl ether was treated for 3½ hr under reflux with ca. 10 mg p-toluenesulphonic acid. The mixture was extracted with ether, washed with 10% NaHCO aq, then with water, dried and evaporated to give 25 mg of **4**, m.p. 252–255°. It was identical with a sample prepared by reaction of **1** with anhydride or α-bromo-ketone **8** with Zn and chloroethyl carbonate.

Isomerization of dimer 4

Dimeric **4**, 4·3 mg, was dissolved in 4·5 ml EtOH and 0·5 ml 10% H$_2$SO$_4$ aq. The mixture was heated under reflux and the UV spectrum of the soln recorded after several time intervals. After 1 hr the UV spectrum showed an absorption max at 258 mμ (ε 790). Reflux of the reaction mixture for additional 2 hr resulted in only a slight increase of the intensity of this absorption to $\varepsilon = 870$.

Treatment of β-diketone 12 with sodium hydroxide

A soln of 500 mg **12** in 100 ml EtOH and 50 ml 10% NaOH aq was heated for 3 hr under reflux. The EtOH was then evaporated under reduced press, the aqueous residue acidified with HCl and extracted with ether. The organic layer was washed with water, dried, evaporated and the residue chromatographed on silicagel. Elution with ether–pentane (4:6) gave 105 mg of **1a**, m.p. 181–182°. Elution with ether–pentane (8:2) furnished 111 mg of **14**, m.p. 274–277°, which was identified by comparison with an authentic sample.[6]

Hydrolysis of enol trichloroacetate 5

A soln of dimeric **5**, 40 mg, in 50 ml MeOH, 10 ml dioxan and 12 ml 10% NaOH aq was heated for 2 hr under reflux. The organic solvents were evaporated under reduced press, and the aqueous mixture extracted with ether, washed with water, dried and evaporated. The residue was treated overnight at room temp with 1 ml Ac$_2$O and 1 ml pyridine. Isolation of the product by extraction with ether and recrystallization from ether gave dimeric **4**, m.p. 252–255°, which was identical with an authentic sample.

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