Steroidal Cyclobutanones. Part 2.[1] Diastereofacial Selection in the Cycloaddition of Dichloroketene and 3β-Acetoxy-20*a*-homopregna-5,20-diene. Crystal Structure of the Cycloadduct, (20*S*)-3β-Acetoxy-20,24-cyclo-22,22-dichlorochol-5-en-23-one

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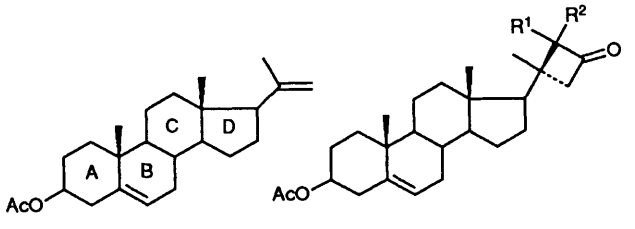
The reaction of dichloroketene and 3β-acetoxy-20*a*-homopregna-5,20-diene **1** is shown to give one diastereoisomeric cycloadduct **2** arising from attack at the rear side of the preferred rotamer **1b** of the steroid skeleton. The structure of dichlorocyclobutanone **2** was determined by X-ray crystallography. Reduction of **2** gives chlorocyclobutanone **3** and cyclobutanone **4**. Examination of the cyclobutanones by CD, ^{1}H and ^{13}C NMR spectroscopy demonstrates that these techniques can be used for the determination of the configuration of **2** and **3**.

The reaction of dichloroketene (DCK) and methylene steroids provides the entry to steroidal spiro cyclobutanones.[1] Depending on the steric crowding around the two faces of the exocyclic double bond, the reaction resulted in formation of one (position 17) or two (positions 3 and 7) spiro cyclobutanone stereoisomers. In the light of these results, it seemed of interest to study the reaction of DCK with 3β-acetoxy-20*a*-homopregna-5,20-diene, **1**. Two points were of interest: (i) the stereoselectivity of cycloaddition, (ii) the conformation of the side chain in compound **1** leading to the cycloadduct.



1

2 $R^1 = R^2 = Cl$
3 $R^1 = Cl$, $R^2 = H$
4 $R^1 = R^2 = H$

The reaction of DCK, generated *in situ* from trichloroacetyl chloride and zinc,[2] with 3β-acetoxy-20*a*-homopregna-5,20-diene **1** in boiling diethyl ether gave a product which, after chromatographic purification, afforded only one cycloadduct (ν_{max} = 1810 cm^{-1}) in 83% yield. This regioisomer was assigned structure **2**. No trace of other diastereoisomeric cycloadducts was observed during the isolation process. The endocyclic double bond in ring B of **1** was found to be unreactive toward DCK under the reaction conditions. Reduction of **2** with zinc in acetic acid at room temperature again afforded one chlorocyclobutanone **3** (ν_{max} = 1788 cm^{-1}) in 85% yield. Reduction of **2** with zinc in boiling acetic acid gave cyclobutanone **4** (98% yield).

The assignment of stereochemistry of compounds **2** and **3** was based on CD, ^{1}H, and ^{13}C NMR spectral data. The presence of two markedly separated signals of protons α to the cyclobutanone ring carbonyl in the ^{1}H NMR spectrum of **2** [δ 2.70 (H_A) and 3.42 (H_B)] is consistent with the non-planar geometry of the cyclobutanone ring. Non-planar geometry appears to be maintained in the chloro compound **3** [δ 2.58 (H_A) and 3.08 (H_B)]. The wide range of absorption (δ 3.35–2.31) of protons α to carbonyl in the ^{1}H NMR spectrum of **4**, as compared with the singlet found for the planar spiro cyclobutanone derivative of cholestane (δ 2.70),[1] also suggests a puckered conformation of the cyclobutanone ring in this compound. Two possible configurational isomers of the dichlorocyclobutanone cycloadduct are represented as **2a** and **2b**. In the ^{13}C NMR spectra (Table 1), the position of the C(21) signal in **2** (δ 21.1) is very close to the value of 21.4 found for **3**. The signal for this carbon is shifted to δ 27.5 in dehalogenated compound **4**. These data are consistent with the removal of pseudo-axial chlorine in monodehalogenation of **2** since in rigid cyclic systems the γ effect of the chlorine atom is close to zero for an antiperiplanar conformation, while a shielding effect (up to 7 ppm) is observed for a synclinal arrangement of chlorine and γ carbon atoms.[3]

Table 1 ^{13}C NMR chemical shifts for steroidal cyclobutanones **2–4**

	Compound		
Atom	**2**	**3**	**4**
C(1)	37.1	37.0	37.1
C(2)	27.7	27.8	27.8
C(3)	73.8	73.8	73.9
C(4)	38.1	38.1	38.2
C(5)	139.8	139.8	139.8
C(6)	122.3	122.3	122.4
C(7)	31.4	31.7	31.8
C(8)	31.6	31.6	31.6
C(9)	50.1	50.0	50.0
C(10)	36.6	36.6	36.6
C(11)	20.6	20.8	20.9
C(12)	39.3	39.5	39.8
C(13)	43.7	43.4	43.7
C(14)	56.0	56.5	56.6
C(15)	24.2	24.0	24.1
C(16)	22.9	23.8	24.1
C(17)	54.8	59.0	57.6
C(18)	15.3	13.6	12.9
C(19)	19.9	19.3	19.3
C(20)	46.1	38.1	31.4
C(21)	21.1	21.4[a]	27.5
C(2′)	94.8	68.1	55.7[b]
C(3′)	192.9	199.6	208.8
C(4′)	53.9	54.7	59.3[b]
CH_3CO_2	21.3	21.3[a]	21.4
CH_3CO_2	170.2	170.3	170.4

[a,b] These signals may be interchanged.

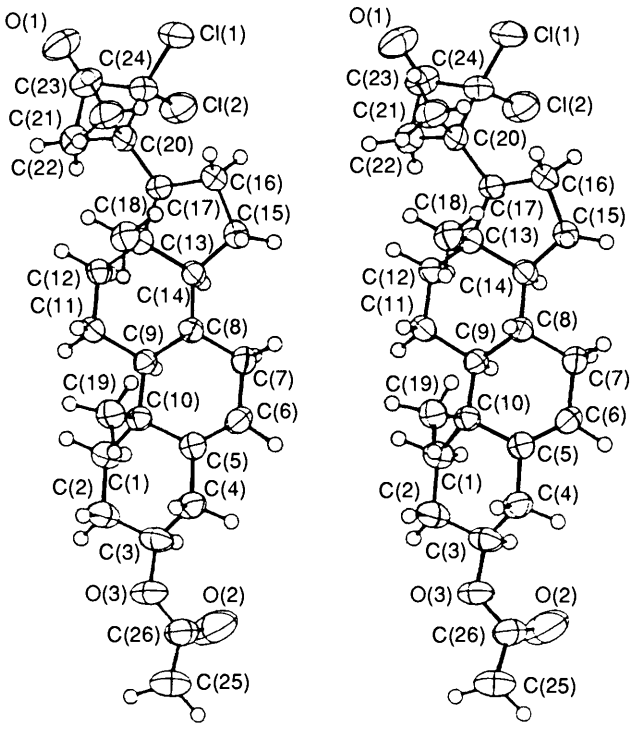


Fig. 1 Stereoscopic view of compound **2** with crystallographic numbering scheme

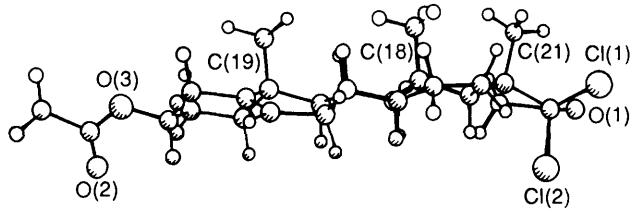


Fig. 2 Perspective view of compound **2**

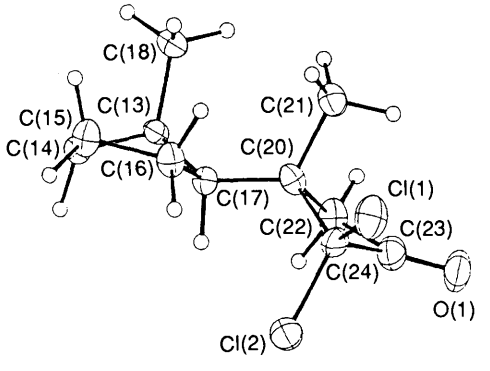


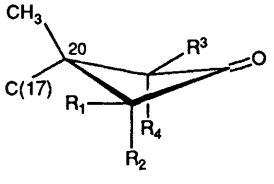
Fig. 3 Conformation of the four-membered ring in compound **2**

Comparison of CD data allowed for differentiation between isomers **2a** and **2b**. In cyclohexanone, $\delta\Delta\varepsilon$ for the α-axial chlorine atom is estimated to the value of 3–3.5 units while the equatorial one has only a very small effect.[4] Comparison of fused steroidal α-chlorocyclobutanones showed that consignate contributions from α quasi-axial chlorine atoms are responsible for the overall Cotton effect.[5] Contribution of the steroid skeleton to the overall Cotton effect in chlorocyclobutanones **2** and **3** is almost negligible as shown by the very weak Cotton effect ($\Delta\varepsilon = -0.25$) recorded for **4**. Thus comparison of $\Delta\varepsilon$ of compounds **2** and **3** ($\Delta\varepsilon = +1.81$ and -0.90, respectively) gives the contribution of the α axial chlorine as -2.7. This is in agreement with structure, **2a**, for which the octant projection indicates the presence of α-axial chlorine atom in the negative

Table 2 Fractional coordinates for non-hydrogen atoms of compound **2**

	x	*y*	*z*
Cl(1)	−0.8899(1)	0.9105(0)	−0.5421(3)
Cl(2)	−0.9141(1)	0.8310(2)	−0.9608(2)
C(1)	−0.7462(3)	0.0240(6)	−1.1570(8)
C(2)	−0.7060(3)	−0.1037(7)	−1.1907(9)
C(3)	−0.6305(4)	−0.0823(6)	−1.2617(9)
C(4)	−0.5827(3)	0.0044(6)	−1.1141(9)
C(5)	−0.6235(3)	0.1280(6)	−1.0728(7)
C(6)	−0.5925(3)	0.2407(6)	−1.0987(9)
C(7)	−0.6252(3)	0.3658(6)	−1.0417(9)
C(8)	−0.6897(3)	0.3472(6)	−0.9073(8)
C(9)	−0.7424(3)	0.2420(6)	−0.9993(8)
C(10)	−0.7014(3)	0.1117(6)	−1.0021(7)
C(11)	−0.8170(3)	0.2337(5)	−0.900(1)
C(12)	−0.8541(3)	0.3634(5)	−0.8763(8)
C(13)	−0.8011(3)	0.4571(5)	−0.7628(7)
C(14)	−0.7321(3)	0.4708(6)	−0.8857(8)
C(15)	−0.6901(3)	0.5855(6)	−0.792(1)
C(16)	−0.7524(3)	0.6718(6)	−0.7168(9)
C(17)	−0.8258(3)	0.5983(6)	−0.7678(8)
C(18)	−0.7783(3)	0.4083(7)	−0.5452(8)
C(19)	−0.6950(4)	0.0488(6)	−0.7888(8)
C(20)	−0.8909(3)	0.6434(5)	−0.6535(8)
C(21)	−0.8830(4)	0.6297(7)	−0.4174(8)
C(22)	−0.9715(3)	0.5973(7)	−0.729(1)
C(23)	−0.9997(4)	0.7305(7)	−0.6940(9)
C(24)	−0.9203(3)	0.7821(6)	−0.7024(9)
C(25)	−0.5154(4)	−0.3578(7)	−1.392(1)
C(26)	−0.5509(4)	−0.2284(8)	−1.414(1)
O(1)	−1.0563(3)	0.7773(5)	−0.6485(8)
O(2)	−0.5429(4)	−0.1553(7)	−1.548(1)
O(3)	−0.5947(2)	−0.2054(4)	−1.2687(6)

octant. Assuming the conformation of compound **3** is the one having pseudo-equatorial chlorine as in **3a**, signal assignment of all the protons of the cyclobutanone ring in the ^{1}H NMR spectrum is possible. The anisotropic effect of the carbonyl



2a $R^1 = R^2 = Cl$, $R^3 = H_A$, $R^4 = H_B$
2b $R^1 = R^2 = H$, $R^3 = R^4 = Cl$
3a $R^1 = Cl$, $R^2 = H_C$, $R^3 = H_A$, $R^4 = H_B$

group allows the assignment of signals of pseudo-equatorial and pseudo-axial protons in **3a** (H_A and H_B, respectively) of the cyclobutanone methylene group. The most deshielded signal at δ 4.86 is assigned to H_C, the signal at δ 3.08 to H_B and signal at δ 2.58 to H_A. Large *geminal* coupling constant (J 18.2 Hz) was found for H_A and H_B. Cross coupling constant J_{trans} (H_A,H_C) is 1.9 Hz and J_{cis} (H_B,H_C) is 2.2 Hz.

The conclusion regarding the stereochemistry of cycloadduct **2** drawn from the spectral data was confirmed by X-ray crystallography.

Figs. 1 and 2 show stereoscopic and perspective views of **2**. The detailed conformation of the four membered ring is shown in Fig. 3. Final positional parameters for non-H atoms are given in Table 2. Bond distances and angles are shown in Table 3. They do not deviate significantly from average values observed in other Δ^5 steroid structures quoted by Duax and Norton.[6] Cramer and Pople puckering parameters[7] using the conformational notation of Boyens[8] and asymmetry and

Table 3 Bond lengths/Å and angles/° for compound **2** (esds in brackets)

Bond	Length/Å	Bond	Length/Å
Cl(1)–C(24)	1.768(6)	C(13)–C(14)	1.550(7)
Cl(2)–C(24)	1.790(6)	C(13)–C(17)	1.549(8)
C(1)–C(2)	1.550(8)	C(13)–C(18)	1.541(7)
C(1)–C(10)	1.546(7)	C(14)–C(15)	1.523(8)
C(2)–C(3)	1.492(8)	C(15)–C(16)	1.555(8)
C(3)–C(4)	1.536(9)	C(16)–C(17)	1.539(8)
C(4)–C(5)	1.527(8)	C(17)–C(20)	1.524(7)
C(5)–C(6)	1.327(8)	C(20)–C(21)	1.555(7)
C(5)–C(10)	1.526(7)	C(20)–C(22)	1.567(8)
C(6)–C(7)	1.501(8)	C(20)–C(24)	1.574(8)
C(7)–C(8)	1.535(7)	C(22)–C(23)	1.513(10)
C(8)–C(9)	1.543(7)	C(23)–C(24)	1.533(9)
C(8)–C(14)	1.518(7)	C(25)–C(26)	1.503(9)
C(9)–C(10)	1.556(7)	O(1)–C(23)	1.194(7)
C(9)–C(11)	1.547(7)	O(2)–C(26)	1.186(8)
C(10)–C(19)	1.547(7)	O(3)–C(3)	1.448(7)
C(11)–C(12)	1.532(7)	O(3)–C(26)	1.315(7)
C(12)–C(13)	1.518(7)		

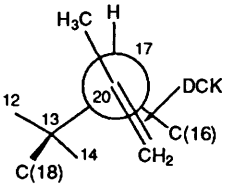
Atom	Angle/°	Atom	Angle/°
Ring A		Extra-nuclear	
C(2)–C(1)–C(10)	112.9(5)	Methyl	
C(1)–C(2)–C(3)	111.3(5)	C(1)–C(10)–C(19)	109.6(5)
C(2)–C(3)–C(4)	111.4(5)	C(5)–C(10)–C(19)	109.4(4)
C(3)–C(4)–C(5)	111.5(5)	C(9)–C(10)–C(19)	111.2(4)
C(4)–C(5)–C(10)	115.4(5)	C(12)–C(13)–C(18)	110.1(5)
C(1)–C(10)–C(5)	107.6(4)	C(14)–C(13)–C(18)	111.0(4)
C(1)–C(10)–C(9)	108.3(4)	C(17)–C(13)–C(18)	112.9(5)
C(4)–C(5)–C(6)	121.4(5)		
		Acetate	
Ring B		C(2)–C(3)–O(3)	107.2(5)
C(5)–C(6)–C(7)	124.8(5)	C(4)–C(3)–O(3)	109.0(5)
C(6)–C(7)–C(8)	111.5(5)	O(2)–C(26)–O(3)	122.8(7)
C(7)–C(8)–C(9)	109.5(4)	C(25)–C(26)–O(3)	111.9(7)
C(8)–C(9)–C(10)	111.1(4)	C(25)–C(26)–O(2)	125.2(7)
C(5)–C(10)–C(9)	110.8(4)		
C(6)–C(5)–C(10)	123.2(5)	2′,2′-Dichloro-3′-methylcyclobutan-1′-one	
C(10)–C(9)–C(11)	112.7(5)	C(13)–C(17)–C(20)	121.3(5)
C(7)–C(8)–C(14)	110.9(4)	C(16)–C(17)–C(20)	114.7(5)
		C(17)–C(20)–C(21)	117.5(5)
Ring C		C(21)–C(20)–C(22)	106.6(5)
C(8)–C(9)–C(11)	113.6(4)	C(21)–C(20)–C(24)	106.8(5)
C(9)–C(11)–C(12)	113.3(5)	C(20)–C(22)–C(23)	88.7(5)
C(11)–C(12)–C(13)	111.5(4)	C(22)–C(23)–C(24)	89.8(5)
C(12)–C(13)–C(14)	107.5(4)	C(22)–C(23)–O(1)	136.4(7)
C(8)–C(14)–C(13)	113.7(4)	C(24)–C(23)–O(1)	133.0(6)
C(9)–C(8)–C(14)	110.7(4)	C(20)–C(24)–C(23)	87.8(5)
C(12)–C(13)–C(17)	116.4(4)	Cl(1)–C(24)–C(23)	119.1(4)
C(8)–C(14)–C(15)	118.7(5)	Cl(2)–C(24)–C(23)	106.0(4)
		Cl(1)–C(24)–Cl(2)	107.8(3)
Ring D		Cl(1)–C(24)–C(20)	120.3(4)
C(14)–C(13)–C(17)	98.1(4)	Cl(2)–C(24)–C(20)	114.3(4)
C(13)–C(14)–C(15)	104.6(4)		
C(14)–C(15)–C(16)	104.3(5)		
C(15)–C(16)–C(17)	105.5(5)		
C(13)–C(17)–C(16)	103.7(4)		

pseudorotation parameters[6] were applied for analyses of the six- and five-membered rings (Table 4). In the steroid backbone, rings A and C have chair conformations. The B ring takes on a half-chair conformation. The endocyclic torsion angles of 5-membered ring D are consistent with a 13β-envelope conformation. The A/B ring junction is quasi-*trans* whereas the B/C and C/D junctions are *trans*. The C(18), C(19) and C(21) methyl groups are in the β-axial positions. The acetate substituent at C(3) and 2′,2′-dichloro-3′-methylocyclobutan-1′-one substituent at C(17) were both found in the β-equatorial positions. Atoms O(3), C(25), C(26) and O(2) of the acetate substituent are coplanar ($\chi^2 = 2.01$). The dihedral angle between this plane and the C(5)···C(17) plane is 54.8°. This group is anticlinal to the C(2)–C(3) bond [C(2)–C(3)–O(3)–C(26) = 144.3(7)°] and its carbonyl is synperiplanar to carbon C(3) [C(3)–O(3)–C(26)–O(2) = −4.6(8)°]. The 4-membered ring at C(17) is greatly distorted from a planar conformation. The torsion angles are as follows:

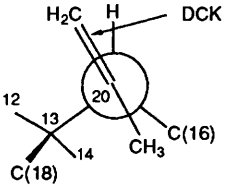
C(24)–C(20)–C(22)–C(23) = −20.0(5)°
C(29)–C(22)–C(23)–C(24) = 20.6(5)°
C(22)–C(23)–C(24)–C(20) = −20.5(5)°
C(22)–C(20)–C(24)–C(23) = 19.8(5)°.

The deviation of C(23) from the plane through C(20), C(22), C(24) is −0.519(6) Å. The torsion angle C(13)–C(17)–C(20)–C(21) is 62.5(6)°. The angle between two planes C(22)–C(20)–C(24) and C(22)–C(23)–C(24) is 28.7°. The deviation of oxygen atom O(1) from the C(22)–C(23)–C(24) plane is −0.14 Å (6.7°). The configuration at the new chiral centre C(20) is of particular interest and is *S*.

In the progesterone side chain, the torsional angle C(16)–C(17)–C(20)–O(20) is estimated to lie between 0 and −46°.[9] Force-field calculations gave values of −20 and −120°.[10] Thus, due to steric hindrance by the 13β-methyl group, pregnan-20-ones exist preferentially in one conformation, with the carbonyl oxygen almost, but not exactly, eclipsing C(16).[11] No precise data characterizing the conformation of 20,22-unsaturated steroids were found. However, the literature clearly shows that the stereochemistry of reactions of 20,22-unsaturated steroids depends on the bulkiness of the reagent involved. For example, catalytic hydrogenation results in formation of equal amounts of C(20) epimers,[12] while stereoselectivity of hydroboration depends strongly on the size of the hydroborating reagent used.[13] As the free rotation around the C(17)–C(20) bond in compound **1** is restricted to some extent by steric hindrance of the



1a



1b

13-methyl group, two rotamers of low energy, **1a** and **1b**, are considered. It seems justified to assume that the approach of DCK to the double bond takes place from the rear side of the steroid skeleton (arrows in **1a** and **1b**). The 20*S*-configuration of cycloadduct **2** clearly indicates that interaction of rotamer **1b** with DCK gives the transition state leading to the final product **2**.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were determined with a Perkin-Elmer 580 grating spectrophotometer for solutions in chloroform. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL FX 90 Q spectrometer, operating in FT mode, using solutions in deuteriochloroform. The chemical shifts (δ) are expressed in ppm relative to tetramethylsilane and *J* values are given in Hz. The SFORD technique along with extensive substituent effect comparison were used for ^{13}C signal assignments. Mass spectra were recorded with a JEOL JMS-D 100 spectrometer using electron impact. CD spectra were recorded with a Jobin–Yvon Dichrograph Mark III for solutions in acetonitrile. Column

Table 4 Ring conformations

Ring	A	B	C	D
Description	Chair	Half-chair	Chair	13β-Envelope
Asymmetry and pseudorotation parameters	$\Delta C_S^1 = 1.84$ $\Delta C_S^2 = 1.60$ $\Delta C_S^3 = 3.16$ $\Delta C_2^{1,2} = 1.00$ $\Delta C_2^{2,3} = 3.58$ $\Delta C_2^{3,4} = 3.99$	$\Delta C_S^6 = 24.55$ $\Delta C_2^{5,6} = 3.31$	$\Delta C_S^8 = 10.03$ $\Delta C_S^9 = 1.32$ $\Delta C_S^{11} = 9.25$ $\Delta C_2^{8,9} = 7.51$ $\Delta C_2^{9,11} = 6.30$ $\Delta C_2^{11,12} = 13.62$	$\Delta C_S^{13} = 2.35$ $\Delta = 31.42$ $\varphi_{max} = 48.72$
Average torsion angle magnitude	54.2	29.2	53.5	25.4
Puckering parameters:	C(1)–C(2)	C(5)–C(6)	C(8)–C(14)	C(13)–C(14)
Q/Å	0.553(6)	0.515(6)	0.556(6)	
Q_2/Å				0.482(6)
φ/°	153.0(12)	333.1(8)	242.0(3)	358.1(8)
θ/°	176.7(7)	125.6(7)	10.4(6)	

chromatography was performed by using 70–230 mesh silica gel 60 (Merck, type 7734). The progress of reactions was monitored by TLC using precoated aluminium-backed silica plates (Merck, type 5554).

(20S)-3β-*Acetoxy*-20,24-*cyclo*-22,22-*dichlorochol*-5-*en*-23-*one* (**2**).—To a stirred mixture of 3β-acetoxy-20*a*-homopregna-5,20-diene[14] (**1**) (300 mg, 0.84 mmol) and activated zinc (165 mg, 2.52 mmol) in anhydrous ether (12 cm^3) refluxed under argon, a solution of trichloracetyl chloride (305 mg, 1.68 mmol) and phosphorus(v) trichloride oxide (257 mg, 1.68 mmol) in anhydrous ether (8 cm^3) was added dropwise over 1 h 45 min. The reaction mixture was refluxed with stirring for 11 h, then stirred at room temperature for 10 h. The mixture was then filtered, the filtrate diluted with benzene and washed with water and 5% aqueous sodium hydrogen carbonate. The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product was purified by column chromatography on silica gel (3 g) to give *compound* **2** (326 mg, 83%), m.p. 212–213 °C (decomp., from acetone); ν_{max}/cm^{-1} 1810, 1725 and 1255; Δε −0.90 (309 nm); δ 5.39 (1 H, m, 6-H), 4.59 (1 H, m, 3α-H), 3.42 (1 H, d, *J* 16.2, CH_2CO), 2.70 (1 H, *J* 16.2, CH_2CO), 2.02 (3 H, s, CH_3COO), 1.34 (3 H, s, 21-H), 1.03 (3 H, s, 19-H) and 0.84 (3 H, s, 18-H); *m*/*z* 364 (M^+ − AcOH − ketene), 213, 145, 105, 91 and 43 (Found: C, 66.8; H, 8.1. $C_{26}H_{36}Cl_2O_3$ requires C, 66.80; H, 7.76%).

(20S,22S)-3β-*Acetoxy*-20,24-*cyclo*-22-*chlorochol*-5-*en*-23-*one* (**3**).—A mixture of compound **2** (65 mg, 0.139 mmol) and zinc (20 mg, 0.306 mmol) in acetic acid (5 cm^3) was stirred at room temperature for 30 min. The solid was filtered off, the filtrate was poured into brine and extracted with a 1:1 mixture of diethyl ether–benzene. The organic layer was washed with water, 5% aqueous sodium hydrogen carbonate, water, dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (1 g) to give *compound* **3** (51 mg, 85%), m.p. 195–198 °C (from acetone); ν_{max}/cm^{-1} 1788, 1723 and 1255; Δε +1.81 (298 nm); δ 5.39 (1 H, m, 6-H), 4.86 (1 H, dd, J_1 2.2 J_2 1.9, CHCl), 4.60 (1 H, m, 3α-H), 3.08 (1 H, dd, J_1 16.2, J_2 2.2, CH_2CO), 2.58 (1 H, dd, J_1 16.2, J_2 1.9, CH_2CO), 2.03 (3 H, s, CH_3CO_2), 1.25 (3 H, s, 21-H), 1.03 (3 H, s, 19-H) and 0.82 (3 H, s, 18-H); *m*/*z* 372 (M^+ − AcOH), 330, 228, 213, 145 and 43 (Found: C, 71.8; H, 8.6 $C_{26}H_{37}ClO_3$ requires C, 72.11; H, 8.61%).

3β-*Acetoxy*-20,24-*cyclochol*-5-*en*-23-*one* **4**.—To a solution of **2** (50 mg, 0.107 mmol) in acetic acid (2.5 cm^3), zinc (100 mg, 1.53 mmol) was added. The mixture was refluxed for 1.5 h. The usual work-up gave a crude product which was filtered through a short column of silica gel to give compound **4** (42 mg, 98%), m.p. 208–210 °C (from acetone); ν_{max}/cm^{-1} 1770, 1720 and 1252; Δε −0.25 (304 nm); δ 5.39 (1 H, m, 6-H), 4.60 (1 H, m, 3α-H), 3.35–2.31 (4 H, m, CH_2CO), 2.03 (3 H, s, CH_3CO_2), 1.38 (3 H, s, 21-H), 1.02 (3 H, s, 19-H) and 0.70 (3 H, s, 18-H); *m*/*z* 338 (M^+ − AcOH), 296 and 43 (Found: C, 78.0; H, 9.9. $C_{26}H_{38}O_3$ requires C, 78.34; H, 9.61%).

Crystal data: *Compound* **2**.—$C_{26}H_{36}Cl_2O_3$, M_r = 467.48, monoclinic, $P2_1$, a = 17.984(5), b = 10.507(2), c = 6.583(3) Å, β = 95.25(3)°, V = 1238.6(7) $Å^3$, Z = 2, D_x = 1.25 g cm^{-3}, (Mo-Kα) = 0.710 69 Å, μ = 2.42 cm^{-1}, $F(000)$ = 500.

Recrystallization was from absolute acetone, at room temperature. Crystal dimensions were 0.4 × 0.3 × 0.6 mm; least-squares refinement of cell dimensions was made with 15 reflections with 18.68° ⩽ 2θ ⩽ 24.25° centred on a Syntex$P2_1$ diffractometer. 2090 intensities were collected with $0 < h < 22$; $0 \leqslant k \leqslant 13$; $-8 \leqslant l \leqslant 8$; [2θ ⩽ 48.0°, (sinθ)/λ ⩽ 0.5723 $Å^{-1}$, Mo-Kα] using the θ–2θ scan technique. Intensity variation of two standard reflections measured every 100 reflections was insignificant. Reflections profiles were analysed according to Lehmann and Larsen.[15] Averaging of 61 symmetry-equivalent reflections (R_{int} = 0.021) gave a unique data set of 2029 reflections; of these 1437 had $I \geqslant 1.96\sigma(I)$ and were regarded as observed. Absorption effect was not corrected. Empirical isotropic extinction parameter x was refined to 7.4(6) × 10^{-7} and F_c multiplied by $(1 - xF_c^2)/\sin\theta$. Lp effect was corrected. The structure was solved by the Patterson method. The positional and anisotropic thermal parameters for non-H atoms were refined on F [$w^{-1} = \sigma^2(F)$] by full-matrix least-squares to R = 0.0417, wR = 0.045. Hydrogen atoms were generated geometrically and included as fixed isotropic contribution to F_c. Methyl hydrogens were refined as rigid groups possessing a local C_3 symmetry. The maximum shift/esd is 0.032. A final difference synthesis showed no peaks greater than 0.19 e $Å^{-3}$, largest hole = −0.18 e $Å^{-3}$. Computer programs used were SHELX76[16] and local programs,[17] and molecular illustrations drawn using PLUTO[18] and ORTEP.[19] Atomic scattering factors were taken from International Tables for X-ray Crystallography.[20]

The list of anisotropic thermal parameters for non-hydrogen atoms and positional parameters for hydrogen atoms have been deposited at the Cambridge Crystallographic Data Centre.*

* For details of the CCDC deposition scheme, see 'Instructions for Authors (1991),' *J. Chem. Soc., Perkin Trans. 2*, 1991, Issue 1.

Table 5 Selected torsion angles/°

Atom	Angle/°	Atom	Angle/°
Ring A		Ring junction	
C(10)–C(1)–C(2)–C(3)	−57.7(6)	C(4)–C(5)–C(10)–C(9)	−170.7(5)
C(1)–C(2)–C(3)–C(4)	55.2(6)	C(6)–C(5)–C(10)–C(1)	127.2(7)
C(2)–C(3)–C(4)–C(5)	−52.7(6)	C(7)–C(8)–C(9)–C(11)	−168.8(5)
C(3)–C(4)–C(5)–C(10)	53.0(6)	C(14)–C(8)–C(9)–C(10)	−174.4(4)
C(4)–C(5)–C(10)–C(1)	−52.5(5)	C(7)–C(8)–C(14)–C(15)	−60.0(6)
C(2)–C(1)–C(10)–C(5)	53.8(5)	C(11)–C(9)–C(10)–C(1)	70.3(5)
		C(12)–C(13)–C(14)–C(15)	167.9(5)
Ring B		C(17)–C(13)–C(14)–C(8)	177.9(4)
C(10)–C(5)–C(6)–C(7)	6.9(7)		
C(5)–C(6)–C(7)–C(8)	12.6(6)	Methyl	
C(6)–C(7)–C(8)–C(9)	−46.2(5)	C(4)–C(5)–C(10)–C(19)	66.4(5)
C(7)–C(8)–C(9)–C(10)	63.0(5)	C(6)–C(5)–C(10)–C(19)	−113.9(6)
C(8)–C(9)–C(10)–C(5)	−43.2(5)	C(18)–C(13)–C(14)–C(8)	59.5(5)
C(6)–C(5)–C(10)–C(9)	9.0(5)	C(18)–C(13)–C(14)–C(15)	−71.6(5)
Ring C		Acetate	
C(14)–C(8)–C(9)–C(11)	−46.1(5)	C(2)–C(3)–O(3)–C(26)	144.3(7)
C(8)–C(9)–C(11)–C(12)	46.7(6)	C(25)–C(26)–O(3)–C(3)	177.1(7)
C(9)–C(11)–C(12)–C(13)	−53.9(5)	O(2)–C(26)–O(3)–C(3)	−4.6(8)
C(11)–C(12)–C(13)–C(14)	58.9(5)		
C(12)–C(13)–C(14)–C(8)	−61.0(5)	2′,2′-Dichloro-3′-methylcyclobutan-1′-one	
C(9)–C(8)–C(14)–C(13)	54.6(5)	C(13)–C(17)–C(20)–C(21)	62.5(6)
		C(13)–C(17)–C(20)–C(24)	−168.9(5)
Ring D		C(16)–C(17)–C(20)–C(22)	166.2(5)
C(17)–C(13)–C(14)–C(15)	46.9(5)	C(21)–C(20)–C(22)–C(23)	86.4(5)
C(13)–C(14)–C(15)–C(16)	−30.6(5)	C(24)–C(20)–C(22)–C(23)	−20.0(5)
C(14)–C(15)–C(16)–C(17)	1.7(5)	C(22)–C(20)–C(24)–C(23)	19.8(5)
C(15)–C(16)–C(17)–C(13)	−45.1(5)	C(22)–C(20)–C(24)–Cl(1)	142.6(5)
		C(22)–C(20)–C(24)–Cl(2)	−86.7(4)
		C(20)–C(22)–C(23)–C(24)	20.6(5)
		C(20)–C(22)–C(23)–O(1)	−149.7(8)
		C(22)–C(23)–C(24)–C(20)	−20.5(5)

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