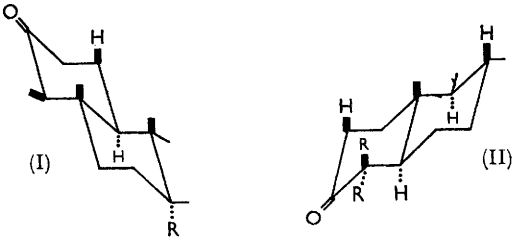
239. *Steroids and Walden Inversion. Part L.* Comparative Studies of α-Bromo- and αα′-Dibromo-ketones derived from Friedelin and from 5α-Cholestan-6-one.*

By C. W. Shoppee and G. A. R. Johnston.

Preparations of the 2α-, 4α-, 2,2-, 2α,4α-, and 2α,4β-bromo-derivatives of friedelin are described; their structures are supported by their ultraviolet, infrared, and rotatory dispersion characteristics, and by appropriate reactions.

The competing Cotton effects exhibited by 2α,4α-dibromofriedelin and 5,7α-dibromo-5α-cholestan-6-one are discussed and the molecular rotatory dispersion contributions of the bromine atoms in 2,2-dibromofriedelin and 7,7-dibromo-5α-cholestan-6-one are examined.

The nuclear configuration of friedelin (I) has been shown by Corey and Ursprung [1] to be conformationally the inverse of that of α- and β-amyrone (as II; R = Me) and 3-keto-5α-steroids (as II; R = H). It was therefore of interest to compare previous studies of



steroid α-bromo- and αα′-dibromo-ketones [2] with a study of analogous bromo-derivatives of friedelin. Some of these compounds (III, XI, XIV) were incidentally described by Corey and Ursprung,[1] and the rotatory dispersion curves of (III and XI) have been recorded by Djerassi *et al.*; [3] the latter authors were unable to prepare the 2α,4α-dibromofriedelin

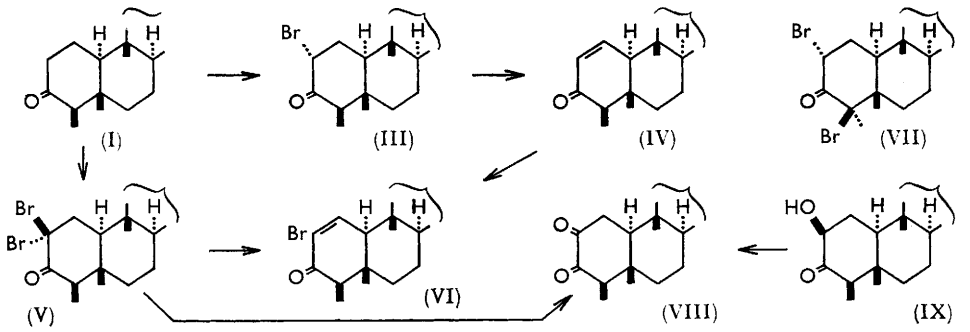
* Part XLIX, *J.*, 1961, 3271.

[1] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041.

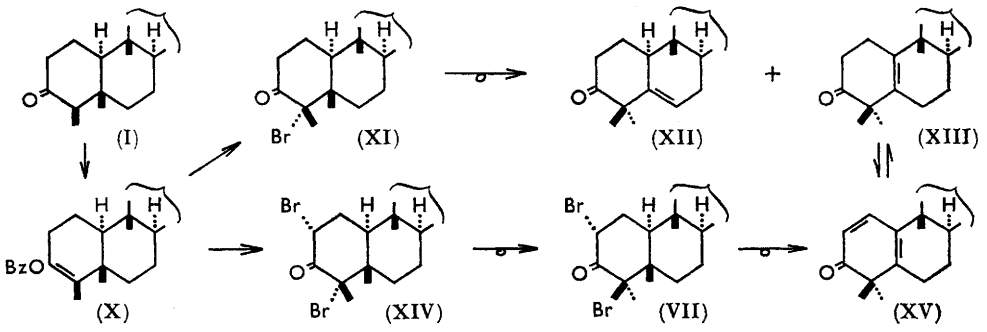
[2] James and Shoppee, *J.*, 1954, 4224; 1956, 1064; Shoppee, Jenkins, and Summers, *J.*, 1958, 1657, 3098; Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630; Shoppee, Rees, Summers, and Phillips *J.*, 1959, 2786; Shoppee and Lack, *J.*, 1961, 3271.

[3] Djerassi, Osieki, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 1216.

(XIV) described by Corey and Ursprung (for a reason disclosed hereunder), obtaining instead a different substance, which they formulated as the 2,2-dibromo-ketone (V) or the 2α,4β-dibromo-ketone (VII), and which we show to be the 2,2-dibromo-ketone.



From the bark of the pimply ash, *Balanops australiana* F. Muell., found mainly in the tropical rain-forests of North Queensland, we have isolated friedelin (I), along with cerin (IX) and other compounds. By monobromination in chloroform in the presence of hydrogen bromide,[1] by base-catalysed monobromination in acetic acid, or by treatment with pyridinium bromide dibromide in pyridine friedelin gave 2α-bromofriedelin (III) dehydrobrominated under nitrogen by 2,4,6-collidine at 200° to friedel-1-en-3-one (IV). Dibromination of friedelin by any of the three foregoing procedures gave 2,2-dibromofriedelin (V); its structure follows from the physical constants listed in Table 1 and from its dehydrobromination under nitrogen by 2,4,6-collidine at 180° to 2-bromofriedel-1-en-3-one (VI), which is also obtained from the αβ-unsaturated ketone (IV) by addition of bromine and treatment of the resulting 1α,2β-dibromofriedelan-3-one with aluminium oxide. The 2,2-dibromo-ketone (V) is identical with the product obtained by Djerassi *et al.*[3] from 2α-bromofriedelin (III) by bromination in acetic acid in the presence of hydrogen bromide; on the basis of its rotatory dispersion curve (negative Cotton effect) Djerassi *et al.* had considered it to have either the 2,2-dibromo- (V) or the 2α,4β-dibromo-structure (VII). We have also prepared the 2,2-dibromo-ketone (V) from 2α-bromofriedelin by base-catalysed bromination in acetic acid and by bromination with pyridinium bromide dibromide in pyridine, and have confirmed its stability[3] to hydrogen bromide; it is converted by refluxing ethanolic potassium hydroxide into friedelane-2,3-dione (VIII), previously prepared by Ruzicka, Jeger, and Ringnes[4] from cerin (IX) by oxidation with chromium trioxide in acetic acid.



Bromination of friedelin (I) by *N*-bromosuccinimide[5] gives 4α-bromofriedelin (XI). Friedel-3-en-3-yl benzoate (X), on monobromination in the presence of pyridine in

[4] Ruzicka, Jeger, and Ringnes, *Helv. Chim. Acta*, 1944, **27**, 972.
[5] Kane and Stevenson, *Chem. and Ind.*, 1960, 1243.

methylene chloride, as reported by Corey and Ursprung,[1] affords the same 4α-bromofriedelin (XI); we have found that dibromination under similar conditions gives 2α,4α-dibromofriedelin (XIV). This substance, with properties corresponding to those of our product, was described by Corey and Ursprung as resulting " by the procedure given above using two equivalents of bromine "; the procedure actually " given above " in their paper is the monobromination of friedelin in chloroform in the presence of hydrogen bromide, which, as Djerassi *et al.*[3] found and we have confirmed, on use of two equivalents of bromine furnishes 2,2-dibromofriedelin (V). We believe that the order of the paragraphs in the experimental section of Corey and Ursprung's paper has become inverted and that the phrase " the procedure given above " refers to the bromination of friedel-3-en-3-yl benzoate in presence of pyridine.

4α-Bromofriedelin (XI), on treatment with silver acetate in pyridine or on brief treatment with 2,4,6-collidine, rearranges with inversion of configuration at the migration terminus ($C_{(4)}$) and elimination of a proton, to yield an inseparable mixture of alnus-5-en-3-one (XII) and alnus-5(10)-en-3-one (XIII), which form mixed crystals.[6] 4α-Bromofriedelin (XI), on bromination in acetic acid in the presence of hydrogen bromide at ~20° or in the presence of an excess of potassium acetate, or on use of pyridinium bromide dibromide, readily affords 2α,4α-dibromofriedelin (XIV); Kane and Stevenson[5] found that attempted bromination of 4α-bromofriedelin with *N*-bromosuccinimide failed to give 2α,4α-dibromofriedelin and led to 4α-bromofriedel-18-en-3-one. 2α,4α-Dibromofriedelin (XIV) is converted by hydrogen bromide in acetic acid at 20° into the thermodynamically more stable 2α,4β-dibromofriedelin (VII). If the temperature exceeds 20°, the solution becomes yellow and the product is alnus-1,5(10)-dien-3-one[6] (XV); this compound can also be obtained from both 2α,4α- (XIV) and 2α,4β-dibromofriedelin (VII) by brief treatment with 2,4,6-collidine at 180°, and it has been prepared[6] from alnus-5(10)-en-3-one (XIII) by bromination and dehydrobromination of the bromination product [probably 2α-bromoalnus-5(10)-en-3-one] with sodium acetate. Hydrogenation of the dienone (XV) with palladium in ethanol yields alnus-5(10)-en-3-one (XIII).

The physical properties of friedelin and its various bromo-derivatives are summarised in Table 1. One general and two special features of this Table deserve mention. (*a*) The bathochromic shifts (Δλ) of the ultraviolet absorption maximum caused by one axial bromine atom (Δλ = +25—28 mμ) or two axial bromine atoms (Δλ = +53 mμ) are reproduced in the displacements (Δλ*) of the rotatory dispersion trough/peak; (*b*) the molecular amplitude, $10^{-2}a$ = +84°, found for 2α,4α-dibromofriedelin (XIV) shows reasonable agreement with that, $10^{-2}a$ = +58°, calculated from the rotatory dispersion contributions Δ*a* of the 2α-bromine atom and the 4α-bromine atom [−109° ($10^{-2}a$, friedelin) − 152°(Δ*a*, 2α-Br) + 319°(Δ*a*, 4α-Br) = +58°]; (*c*) the curiously low frequency of the infrared carbonyl band and the small hypschromic shift Δν caused by the equatorial 2β-bromine atom in 2,2-dibromofriedelin (V), which exhibits normal ultraviolet characteristics.

2α,4α-Dibromofriedelin (XIV) is a representative of a rare type of compound exhibiting competing Cotton effects; the tertiary axial 4α-bromine atom dominates the situation and superimposes its positive Cotton effect contribution, Δ*a* + 319°, on the negative Cotton component, Δ*a* − 152°, of the secondary axial 2α-bromine atom, reducing the molecular amplitude $10^{-2}a$ for (XIV) to +84°. The only previous example has been described by Djerassi *et al.*;[3] 3β-acetoxy-5,7α-dibromo-5α-cholestan-6-one (XVIII; R = OAc) gives a negative Cotton curve of molecular amplitude $10^{-2}a$ = −179°. In the absence of data for 3β-acetoxy-5-bromo-5α-cholestan-6-one (XVI; R = OAc) or 3β-acetoxy-7α-bromo-5α-cholestan-6-one (XVII; R = OAc), comparison was made with 3β-acetoxy-7,7-dibromocholestan-6-one (XIX; R = OAc), the equatorial 7β-bromine atom of which is ineffective; this shows that the contribution of the tertiary axial 5α-bromide atom is dominant in the 5α,7α-dibromo-ketone (XVIII; R = OAc) and imposes

[6] Spring, Beaton, Stevenson, and Stewart, *Chem. and Ind.*, 1955, 1054; *Tetrahedron*, 1958, **2**, 246.

TABLE 1.

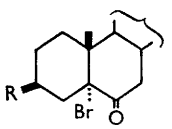
Physical properties of friedelin and its bromo-derivatives.

No.	Compound	M. p.	$[\alpha]_D$	$\lambda_{max.}$ (mμ) in EtOH	Δλ (mμ)	$\nu_{max.}$ (cm.$^{-1}$) in CCl_4	Δν (cm.$^{-1}$)
1.	Friedelin (I)	267°,[1] 264°,[6] 262	−28°,[7] −24°	285	—	1710	—
2.	2α-Bromofriedelin (III)	210,[1] 210	−140,[1] −140	311,[1] 310	+26	1710[1]	0
					+25	1710	0
3.	4α-Bromofriedelin (XI)	196,[1] 197—198	+90,[1] +92	310,[1] 310	+25	1715[1]	+5
					+25	1712	+2
4.	2,2-Dibromofriedelin (V)	231—233,[3] 228—231	−123,[3] −124	310,[3] 308	+25	—	—
					+23	1718	+8
5.	2α,4α-Dibromofriedelin (XIV)	203,[1] 203	−60,[1] −60	332,[1] 338	+47	1712[1]	+2
					+53	1712	+2
6.	2α,4β-Dibromofriedelin (VII)	213—216		315 §	+30	1723	+13

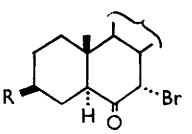
No.	Cotton curve sign and molecular amplitude ($10^{-2}a$)	Molar dispersion contribn. of subst., Δa †	Position of first trough (or peak) λ* (mμ)	Δλ* (mμ)	Halogen confign.
1.	−107° (d),[8] −109(d)	—	315	—	—
2.	−261 (d)[3]	−152° (2α)	335	+20	*ax*
3.	+210 (d),[3] +209 (c)	+319 (4α)	335	+20	*ax*
4.	−280 (c, d)[3]	−171 (2α)	333	+18	*eq, ax*
5.	+84 (c)	−126 (2α)	365	+50	*ax, ax*
		+345 (4α)			
6.	−218 (c), −227(m)	−109 (2α)	332	+17	*ax, eq*

Δλ* represents the difference (mμ) between the first trough (peak) of the derivative and the parent ketone. § Broad band. c = Chloroform. d = Dioxan. m = Methanol. † Only axial bromine is considered in calculating these values.

its negative Cotton effect, Δa − 205°, over the positive Cotton component of the secondary axial 7α-bromine atom, thereby reducing the molecular amplitude $10^{-2}a$ = −291° for (XIX; R = OAc) to −179° for (XVIII; R = OAc).



(XVI)



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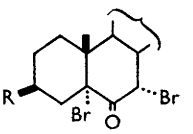
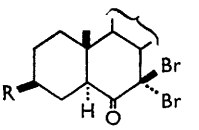


(XVIII)



(XIX)

5,7α-Dibromo-5α-cholestan-6-one (XVIII; R = H) likewise exhibits competing Cotton effects. Shoppee, Jenkins, and Summers[9] have described the set of bromo-ketones (XVI—XIX; R = H) derived from 5α-cholestan-6-one, and we now report their rotatory dispersions. The physical characteristics of these compounds are collected in Table 2. In the 5α,7α-dibromo-ketone (XVIII; R = H), the tertiary axial 5α-bromine atom superimposes its negative rotatory dispersion contribution, Δa − 290°, on the positive component of the secondary axial 7α-bromine atom, Δa + 203°, reducing the molecular amplitude to $10^{-2}a$ = −120°, compared with $10^{-2}a$ = −323° for 5-bromo-5α-cholestan-6-one (XVI; R = H). It should be noted, however, that the negative rotatory dispersion contribution for the isolated tertiary axial 5α-bromine atom in the 5α-bromo-ketone (XVI; R = H), Δa − 247°, is effectively equal* to that for the isolated secondary axial 7α-bromine atom in the 7α-bromo-ketone (XVII; R = H), Δa + 246°. The Δλ and Δλ* values for the isomeric 5α- and 7α-bromo-ketones (XVI, XVII; R = H) are also strikingly similar.

* The only other published[3] example shows unequal rotatory dispersion contributions: 9α-bromo-3β-acetoxy-5α-ergostan-11-one, $10^{-2}a$ − 148°, Δa − 160°; 12α-bromo-3β-acetoxy-5α-ergostan-11-one, $10^{-2}a$ + 253°, Δa + 241° (3β-acetoxy-5α-ergostan-11-one, $10^{-2}a$ + 12°).

[7] White, *Rev. Pure and App. Chem.* (*Australia*), 1956, **6**, 191.
[8] Djerassi, Halpern, Halpern, and Rinehart, *J. Amer. Chem. Soc.*, 1958, **80**, 4001.
[9] Shoppee, Jenkins, and Summers, *J.*, 1958, 1657.

TABLE 2.

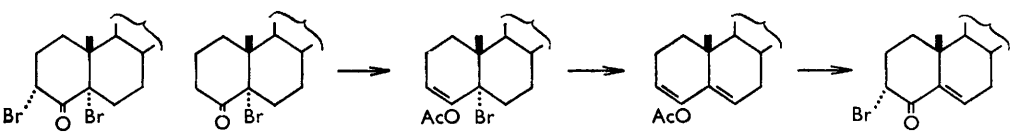
Physical properties of 5α-cholestan-6-one and its bromo-derivatives.

No.	Compound	M. p.	$[\alpha]_D$	$\lambda_{max.}$ (mμ) in EtOH	Δλ (mμ)	$\nu_{max.}$ (cm.$^{-1}$) in CCl_4	Δν (cm.$^{-1}$)
7.	5α-Cholestan-6-one	98°	−7° (c)	284	—	1711	—
8.	5-Bromo-5α-cholestan-6-one (XVI)	101 ‡	−146‡(c)	308	+24	1712	+1
9.	7α-Bromo-5α-cholestan-6-one (XVII)	82	+51(c)	308	+24	1711	0
10.	5,7α-Dibromo-5α-cholestan-6-one (XVIII)	115	−101(c)	334	+50	1713	+2
11.	7,7-Dibromo-5α-cholestan-6-one (XIX)	167	−28(c)	292	+8	1725	+14

No.	Cotton curve sign and molecular amplitude ($10^{-2}a$)	Molar dispersion contribn. of subst. Δa †	Position of first trough (or peak) λ* (mμ)	Δλ (mμ)	Halogen confign.
7.	−76° (m)	—	307·5	—	—
8.	−323 (m)	−247° (5α)	330	+22·5	*ax*
9.	+170 (m)	+246 (7α)	332	+24·5	*ax*
10.	−120 (m)	−290 (5α), +203 (7α)	360	+52·5	*ax*, *ax*
11.	−98 (m)	−22 (7α)	312	+4·5	*ax*, *eq*

Footnotes as for Table 1. ‡ Henbest and Wrigley (*J.*, 1958, 4596) record m. p. 101°, $[\alpha]_D$ −134°.

3α,5-Dibromo-5α-cholestan-4-one (XX) should also exhibit competing Cotton effects. The reputed compound of this structure, described by Shoppee, Howden, Killick, and Summers,[10] has been shown [11] to be a solid solution of 3α-bromo- and 3,3-dibromo-5α-cholestan-4-one; we have therefore made further attempts to prepare the 3α,5α-dibromo-ketone (XX) but without success. Treatment of 5-bromo-5α-cholestan-4-one (XXI) with acetic anhydride and toluene-*p*-sulphonic acid at 140° led to enol-acetylation (cf. XXII) but also to dehydrobromination to give 4-acetoxycholesta-3,5-diene (XXIII), converted by bromine in acetic acid into 3α-bromocholest-5-en-4-one (XXIV) and its 5α,6β-dibromide, these two compounds not being completely separable. Use of isopropenyl acetate and toluene-*p*-sulphonic acid at 97° for 24 hr. was ineffective. It appears therefore that our failure to prepare the 3α,5α-dibromo-ketone (XX) must be attributed to the difficulty of enolisation of the 5α-bromo-ketone (XXI) or to the ease of dehydrobromination of the intermediate allylic bromide (XXII).



(XX) (XXI) (XXII) (XXIII) (XXIV)

The spectroscopic properties of 7,7-dibromo-5α-cholestan-6-one (XIX; R = H) are unexpected and interesting. The equatorial 7β-bromine atom exhibits normal behaviour in the infrared spectrum, leading to a displacement of the carbonyl stretching frequency Δν + 14 cm.$^{-1}$; in the ultraviolet and rotatory dispersion spectra, the axial 7α-bromine atom simulates the usual behaviour of an equatorial bromine atom. Thus the increments Δλ and Δλ* are small (+8, +4·5 mμ) compared with those (12—15 mμ) normally found [12] for axial bromine atoms in *gem*-dibromo-ketones (cf. also Table 1), whilst the molecular rotatory dispersion contribution Δ*a* of the 7α-bromine atom is only −22°, *i.e.*, effectively zero, compared with values of +246° for compound (XVII; R = H) and +203° for (XVIII; R = H). These results suggest that ring B in (XIX; R = H) is distorted; Dreiding models show that the normal chair-conformation of ring B in (XIX; R = H) can pass

[10] Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630.
[11] Shoppee and Lack, *J.*, 1961, 3271.
[12] Cookson, *J.*, 1954, 282; cf. ref. 3.

over a rather small energy barrier into a distorted chair-conformation in which $C_{(6)}$, $C_{(7)}$, $C_{(8)}$, and $C_{(9)}$ are roughly coplanar and the 7α- and 7β-bromine atoms are inclined at approximately equal angles to that plane.

Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to $CHCl_3$ solutions at room temperature. Unless otherwise stated, ultraviolet absorption spectra were determined for EtOH solutions in a Hilger Uvispec spectrophotometer, and infrared absorption spectra were measured for CCl_4 solutions by use of a Perkin–Elmer model 21B spectrophotometer. Chromatography was effected on silica gel (Davison 40—200 mesh), aluminium oxide (Spence type H, activity II), or neutralised aluminium oxide (Woelm). M. p.s were determined on a Kofler block and are corrected.

Monobromination of Friedelin.—(a) *Acid-catalysed (method described by Corey and Ursprung* [1]). A solution of friedelin (1·28 g.) in chloroform (50 c.c.) was treated with a saturated solution of hydrogen bromide in chloroform (1 c.c.), followed by bromine (0·55 g.) in chloroform (5 c.c.). The decolorisation of bromine was almost instantaneous. The chloroform was removed under reduced pressure and the residue recrystallised from chloroform–methanol to give 2α-bromofriedelin (0·85 g.), m. p. 210°, $[\alpha]_D$ −140° (*c* 1·0), $\nu_{max.}$ 1710 cm.$^{-1}$, $\lambda_{max.}$ 311 mμ.

(b) *Base-catalysed.* Friedelin (426 mg.) was dissolved in anhydrous acetic acid (100 c.c.) at 90°. A solution of sodium acetate (1·0 g.; dried at 100°) in acetic acid (15 c.c.) at 90° was added, followed by bromine (165 mg.) in acetic acid (3 c.c.). Heating was continued on the steam bath until the bromine colour disappeared (*ca.* 1 hr.). The solution was then rapidly cooled to room temperature, and was set aside for 5 hr. during which 2α-bromofriedelin crystallised as needles (385 mg.), m. p. 210°, $[\alpha]_D$ −140° (*c* 1·0).

(c) *With pyridinium bromide dibromide.* To a solution of friedelin (426 mg.) in acetic acid (130 c.c.) at 60° was added one of pyridinium bromide dibromide (325 mg.) in acetic acid (25 c.c.), also at 60°. After 5 min. at 60°, the mixture was set aside at room temperature overnight, 2α-bromofriedelin (30 mg.), m. p. 210°, $[\alpha]_D$ −140° (*c* 1·0), separating.

Dehydrobromination of 2α-Bromofriedelin with Collidine.—2α-Bromofriedelin (100 mg.) was heated at 200° with freshly distilled 2,4,6-collidine (1 c.c.) for 2 hr. under nitrogen. The usual working up gave a yellow solid, which was chromatographed on silica gel (6 g.) in pentane. Elution with 1% ether–pentane afforded *friedel-1-en-3-one* (73 mg.), having m. p. 247—248°, $\lambda_{max.}$ 230 mμ, $\nu_{max.}$ 1680 cm.$^{-1}$, after crystallisation from chloroform–methanol [Found (after drying at 80°/0·05 mm. for 12 hr.): C, 84·9; H, 11·2. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%].

Dibromination of Friedelin.—(a) *Acid-catalysed.* To a solution of friedelin (426 mg.) in chloroform (15 c.c.) was added a saturated solution of hydrogen bromide in chloroform (0·2 c.c.) followed by bromine (330 mg.) in chloroform (6 c.c.). After 10 min., the chloroform was removed under reduced pressure at 15°, and the crystalline residue taken up in pentane and chromatographed on silica gel (40 g.) prepared in the same solvent. Elution with 1% ether–pentane and crystallisation from chloroform–methanol afforded 2,2-dibromofriedelin [3] (349 mg.), m. p. 228—231°, $[\alpha]_D$ −124° (*c* 1·0), $\lambda_{max.}$ 308 mμ, $\nu_{max.}$ 1718 cm.$^{-1}$. Elution with 5% ether–pentane yielded 2α-bromofriedelin (108 mg.), m. p. 210°.

(b) *Base-catalysed.* Friedelin (426 mg.) in anhydrous acetic acid (100 c.c.) was treated at 90° with sodium acetate (1·0 g.; dried at 100°) in acetic acid (15 c.c.), followed by bromine (330 mg.) in acetic acid (6 c.c.). After 3 hr. at 90°, most of the acid was removed under reduced pressure, and the residue worked up in the usual way by ether extraction. The crystalline product was chromatographed on silica gel (40 g.), as above, to yield 2,2-dibromofriedelin (310 mg.), m. p. 228—231°, and 2α-bromofriedelin (130 mg.), m. p. 210°.

(c) *With pyridinium bromide dibromide.*—Friedelin (426 mg.) in acetic acid (130 c.c.) was treated at 60° with a solution of pyridinium bromide dibromide (650 mg.) in acetic acid (50 c.c.). After 1 hr. at 60°, the acid was removed under reduced pressure and the residue worked up by the usual ether extraction. The crystalline product was chromatographed on silica gel (40 g.), as above, to yield 2,2-dibromofriedelin (301 mg.), m. p. 228—231°, and 2α-bromofriedelin (135 mg.), m. p. 210°.

Dehydrobromination of 2,2-Dibromofriedelin with Collidine.—2,2-Dibromofriedelin (82 mg.) was heated at 180° with freshly distilled 2,4,6-collidine (1 c.c.) for 10 min. under nitrogen. The usual isolation procedure gave a solid (63 mg.), which, by crystallisation from chloroform–methanol, yielded 2-*bromofriedel*-1-*en*-3-*one*, m. p. 206—208°, $\lambda_{max.}$ 258 mμ, $\nu_{max.}$ 1690 cm.$^{-1}$

[Found (after drying at 80°/0·05 mm. for 12 hr.): C, 71·4; H, 9·5. $C_{30}H_{47}OBr$ requires C, 71·55; H, 9·4%].

Preparation of 2-Bromofriedel-1-en-3-one from Friedel-1-en-3-one.—Friedel-1-en-3-one (50 mg.) in ether (5 c.c.) was treated dropwise at 0° with bromine (20 mg.) in acetic acid (1 c.c.). After being kept overnight at room temperature, the mixture was poured into water, and the ethereal extract worked up in the usual way to give crude 1α,2β-dibromofriedelan-3-one (63 mg.); dissolution in ether–pentane (1 : 1) and filtration through aluminium oxide (2·5 g.) gave 2-bromofriedel-1-en-3-one, which had m. p. and mixed m. p. 206—208°, $\lambda_{max.}$ 258 mμ, $\nu_{max.}$ 1690 cm.$^{-1}$, after crystallisation from chloroform–methanol.

Monobromination of 2α-Bromofriedelin.—(a) *Acid-catalysed* (cf. Djerassi *et al.*[3]). To a solution of 2α-bromofriedelin (505 mg.) in acetic acid (100 c.c.) was added a saturated solution of hydrogen bromide in acetic acid (0·2 c.c.), followed by bromine (165 mg.) in acetic acid (3 c.c.). After 10 min., most of the acetic acid was removed under reduced pressure, and the residue worked up in the usual way. The crystalline product was chromatographed on silica gel (50 g.) in pentane. Elution with 1% ether–pentane and crystallisation from chloroform–methanol afforded 2,2-dibromofriedelin (375 mg.), m. p. 228—231°. Elution with 5% ether–pentane yielded unchanged 2α-bromofriedelin (125 mg.).

(b) *Base-catalysed.* 2α-Bromofriedelin (505 mg.) in anhydrous acetic acid (100 c.c.) was treated at 90° with sodium acetate (1·0 g.; dried at 100°) in acetic acid (15 c.c.), followed by bromine (165 mg.) in acetic acid (3 c.c.). After 3 hr. at 90°, most of the acetic acid was removed under reduced pressure and the residue worked up in the usual way. The crystalline product was chromatographed on silica gel (50 g.), as above, yielding 2,2-dibromofriedelin (360 mg.), 228—231°, and unchanged 2α-bromofriedelin (136 mg.), m. p. 210°.

(c) *With pyridinium bromide dibromide.* 2α-Bromofriedelin (505 mg.) in acetic acid (150 c.c.) was treated at 60° with a solution of pyridinium bromide dibromide (325 mg.) in acetic acid (25 c.c.). After 1 hr. at 60°, the acetic acid was removed under pressure and the residue worked up in the usual way. The crystalline product was chromatographed on silica gel (50 g.), as above, to yield 2,2-dibromofriedelin (345 mg.), m. p. 228—231°, and unchanged 2α-bromofriedelin (136 mg.), m. p. 210°.

Attempted Equilibration of 2,2-Dibromofriedelin by Hydrogen Bromide.—2,2-Dibromofriedelin (27 mg.) in chloroform (5 c.c.) was treated with a saturated solution of hydrogen bromide in chloroform (5 drops). After 5 days at room temperature the chloroform was removed under reduced pressure and the residue crystallised from chloroform–methanol, to yield unchanged 2,2-dibromofriedelin (23 mg.), m. p. 228—231°, $[\alpha]_D$ −124° (*c* 1·0).

Treatment of 2,2-Dibromofriedelin with Refluxing Ethanolic Potassium Hydroxide.—2,2-Dibromofriedelin (170 mg.) was refluxed with 20% ethanolic potassium hydroxide (50 c.c.) for 1 hr. Dilution with water and acidification with dilute hydrochloric acid gave a product (165 mg.), which was collected and was chromatographed on aluminium oxide (5 g.) in ether. Elution with methanol afforded friedelane-2,3-dione (90 mg.), having m. p. and mixed m. p. 267—269°, $[\alpha]_D$ +19° (*c* 1·0), $\lambda_{max.}$ 275 mμ, $\nu_{max.}$ (in CS_2) 1670 and 1645 cm.$^{-1}$, after crystallisation from chloroform–methanol. Authentic friedelane-2,3-dione for mixed m. p. and comparison of infrared spectra was prepared by oxidation of cerin according to the directions of Ruzicka, Jeger, and Ringnes.[4]

Monobromination of Friedel-3-en-3-yl Benzoate (modification of procedure described by Corey and Ursprung [1]).—Friedel-3-en-3-yl benzoate [1] (1·941 g.), suspended in anhydrous acetic acid (500 c.c.)–pyridine (10 c.c.), was treated at 40° with bromine (650 mg.) in acetic acid (25 c.c.). Dissolution was complete after 5 min. at 40°. The solvents were removed under reduced pressure; the product, isolated by the usual ether extraction and recrystallised several times from chloroform–methanol, yielded 4α-bromofriedelin (965 mg.), m. p. 197—198° (decomp.), $[\alpha]_D$ +92° (*c* 1·3), $\lambda_{max.}$ 310 mμ, $\nu_{max.}$ 1715 cm.$^{-1}$. Optical rotatory dispersion in chloroform: peak +9300° (333 mμ); trough −11,600° (285 mμ); amplitude +209°.

Dibromination of Friedel-3-en-3-yl Benzoate.—Friedel-3-en-3-yl benzoate (1·446 g.), suspended in anhydrous acetic acid (300 c.c.)–pyridine (10 c.c.), with bromine (970 mg.) in acetic acid (25 c.c.) afforded, exactly as in the preceding paragraph, 2α,4α-dibromofriedelin (1·269 g.), m. p. 203—204°, $[\alpha]_D$ −60° (*c* 0·9), $\lambda_{max.}$ 338 mμ, $\nu_{max.}$ 1712 cm.$^{-1}$. Optical rotatory dispersion in chloroform: peak +2880° (365 mμ); trough −5550° (313 mμ); amplitude −84°.

Dehydrobromination of 4α-Bromofriedelin with Collidine.—4α-Bromofriedelin (85 mg.) was heated at 180° (bath) under nitrogen with freshly distilled 2,4,6-collidine (1 c.c.) for 5 min.

Working up as usual gave a solid (69 mg.), which by crystallisation from chloroform–methanol yielded alnus-5(10)-en-3-one and -5-en-3-one [6] as mixed crystals, m. p. 247—248°, $[\alpha]_D$ −51° (*c* 0·9), $\nu_{max.}$ 1710 cm.$^{-1}$, $\lambda_{max.}$ 290 mμ.

Monobromination of 4α-*Bromofriedelin.*—(a) *Acid-catalysed.* To a solution of 4α-bromofriedelin (505 mg.) in acetic acid (100 c.c.) was added a saturated solution of hydrogen bromide in acetic acid (0·05 c.c.), followed by bromine (165 mg.) in acetic acid (3 c.c.). After 3 min. the acid was removed at 15° *in vacuo*, and the product, isolated by ether extraction, was chromatographed on silica gel (50 g.) in pentane. Elution with 1% ether–pentane gave 2α,4α-dibromofriedelin (295 mg.), m. p. 203—204°, $[\alpha]_D$ −60° (*c* 1·1). Elution with 5% ether–pentane afforded unchanged 4α-bromofriedelin (185 mg.), m. p. 197—198° (decomp.).

(b) *Base-catalysed.* 4α-Bromofriedelin (505 mg.) in anhydrous acetic acid (100 c.c.) was treated at 90° with potassium acetate (0·8 g.; dried at 100°) in acetic acid (15 c.c.), followed by bromine (165 mg.) in acetic acid (3 c.c.). After 3 hr. at 90°, most of the acid was removed under reduced pressure, and the residue extracted with ether and worked up in the usual way. The crystalline product was chromatographed on silica gel (50 g.), as above, to yield 2α,4α-dibromofriedelin (356 mg.), m. p. 203—204°, and unchanged 4α-bromofriedelin (130 mg.), m. p. 197—198° (decomp.).

(c) *With pyridinium bromide dibromide.* 4α-Bromofriedelin (505 mg.) in acetic acid (150 c.c.) was treated at 60° with pyridinium bromide dibromide (325 mg.) in acetic acid (25 c.c.). After 5 min. at 60°, the acid was removed under reduced pressure, and the residue worked up in the usual way by ether extraction. The crystalline product was chromatographed on silica gel (50 g.), as above, to yield 2α,4α-dibromofriedelin (280 mg.), m. p. 203—204°, and unchanged 4α-bromofriedelin (195 mg.), m. p. 197—198 (decomp.).

Equilibration of 2α,4α-*Dibromofriedelin by Hydrogen Bromide.*—2α,4α-Dibromofriedelin (25 mg.) in chloroform (5 c.c.) was treated with a saturated solution of hydrogen bromide in chloroform (5 drops). After 5 days at 15°, the chloroform was removed under reduced pressure at 15°, and the residue crystallised from chloroform–methanol to yield 2α,4β-*dibromofriedelin* (18 mg.), m. p. 213—216°, $\lambda_{max.}$ 315 mμ (broad), $\nu_{max.}$ 1723 cm.$^{-1}$ [Found (after drying at 60°/0·05 mm. for 12 hr.): C, 61·8; H, 8·2. $C_{30}H_{48}Br_2O$ requires C, 61·4; H, 8·3%]. Optical rotatory dispersion in chloroform: trough −10,100° (333 mμ); peak, +11,700° (288 mμ); amplitude −218°. If the temperature of the equilibration mixture was allowed to rise above *ca.* 20°, or if the equilibrating agent was perchloric acid instead of hydrogen bromide, a yellow colour gradually developed, and alnus-1,5(10)-dien-3-one,[6] m. p. 215—217°, $\lambda_{max.}$ 207, 322 mμ, was isolated in poor yield.

Dehydrobromination of 2α,4α-*Dibromofriedelin with Collidine.*—2α,4α-Dibromofriedelin (80 mg.) was heated at 180° (bath) under nitrogen with freshly distilled 2,4,6-collidine (1 c.c.) for 10 min. Working up in the usual way and crystallisation of the product from chloroform–methanol gave alnus-1,5(10)-dien-3-one (53 mg.), m. p. 215—217°, $[\alpha]_D$ −28° (*c* 0·8), $\lambda_{max.}$ 207, 332 mμ, identical with a specimen prepared by the method of Spring *et al.*[6] from alnus-5(10)-en-3-one by bromination and dehydrobromination of the bromination product with sodium acetate.

Dehydrobromination of 2α,4β-*Dibromofriedelin with Collidine.*—2α,4β-Didormofriedelin (10 mg.) and 2,4,6-collidine (0·05 c.c.) gave, as above but after two recrystallisations from chloroform–methanol, friedel-1,5(10)-dien-3-one (3 mg.), m. p. and mixed m. p. 213—216°, $\lambda_{max.}$ 207, 322 mμ.

Hydrogenation of Alnus-1,5(10)-*dien*-3-*one.*—Alnus-1,5(10)-dien-3-one (35 mg.) in ethanol (100 c.c.) was shaken in hydrogen in the presence of 10% palladium–charcoal for 1 hr. Filtration and evaporation *in vacuo* gave alnus-5(10)-en-3-one (26 mg.), having m. p. 249—251°, $[\alpha]_D$ −86° (*c* 0·8), after two crystallisations from chloroform–methanol.

4-*Acetoxycholesta*-3,5-*diene and* 3α-*Bromocholest*-5-*en*-4-*one* [*by* R. Lack].—A solution of 5-bromo-5α-cholestan-4-one (500 mg.) and toluene-*p*-sulphonic acid (285 mg.) in acetic anhydride (15 c.c.) was slowly distilled through a short column, acetic anhydride being added from time to time to keep the volume approximately constant. After 8 hr. the solution was evaporated to small volume at 10 mm. and worked up in the usual way to give a brown oil, which was chromatographed on silica gel (40 g.) prepared in pentane. Elution with 2% ether–pentane (3 × 20 c.c.) gave 4-acetoxycholesta-3,5-diene (150 mg.) as a pale yellow oil, $\lambda_{max.}$ 240 mμ (log ε 4·23); elution with 5% ether–pentane gave only decomposition products. 4-Acetoxycholesta-3,5-diene (75 mg.) in pyridine–acetic acid (1 : 10, 5 c.c.) was treated with bromine

(47 mg.; 1·5 mol.) in acetic acid (1 c.c.) at 20° for 3 hr. The usual isolation procedure gave impure 3α-bromocholest-5-en-4-one (42 mg.), m. p. 133—134°, $\lambda_{max.}$ 259 (log ε 4·23) (Found: C, 66·4; H, 8·9. Calc. for $C_{27}H_{43}BrO$: C, 69·9; H, 9·3%). Despite its sharp m. p. and high extinction coefficient, the compound appears to be contaminated with its 5α,6β-dibromide and there was insufficient material for complete purification; it may be noted that cholest-5-en-4-one readily forms a 5α,6β-dibromide.[11] The material depressed the m. p. of 3-bromo-5α-cholest-2-en-4-one [11] (131—132°) to 118—121°.

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