

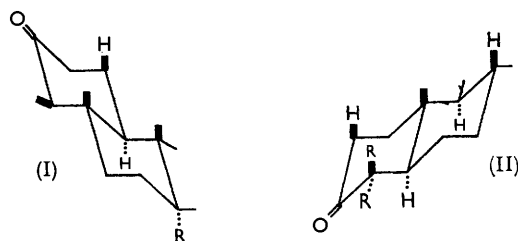
239. *Steroids and Walden Inversion. Part L.* Comparative Studies of α -Bromo- and $\alpha\alpha'$ -Dibromo-ketones derived from Friedelin and from 5 α -Cholestan-6-one.*

By C. W. SHOPPEE and G. A. R. JOHNSTON.

Preparations of the 2 α -, 4 α -, 2,2-, 2 α ,4 α -, and 2 α ,4 β -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 2 α ,4 α -dibromofriedelin and 5,7 α -dibromo-5 α -cholestan-6-one are discussed and the molecular rotatory dispersion contributions of the bromine atoms in 2,2-dibromofriedelin and 7,7-dibromo-5 α -cholestan-6-one are examined.

THE nuclear configuration of friedelin (I) has been shown by Corey and Ursprung¹ to be conformationally the inverse of that of α - and β -amyrone (as II; R = Me) and 3-keto-5 α -steroids (as II; R = H). It was therefore of interest to compare previous studies of



steroid α -bromo- and $\alpha\alpha'$ -dibromo-ketones² 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 2 α ,4 α -dibromofriedelin

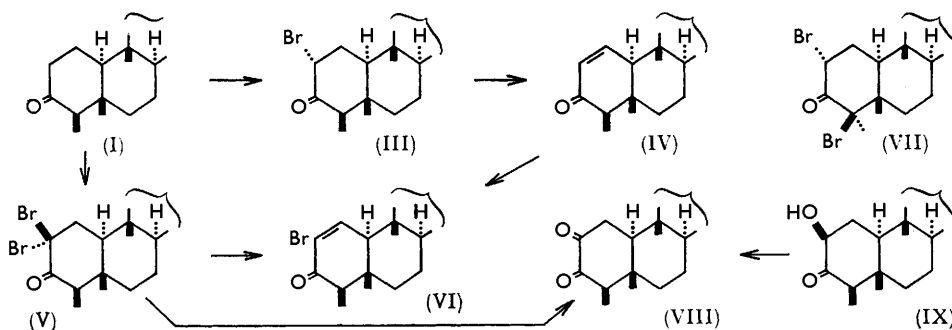
* Part XLIX, *J.*, 1961, 3271.

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

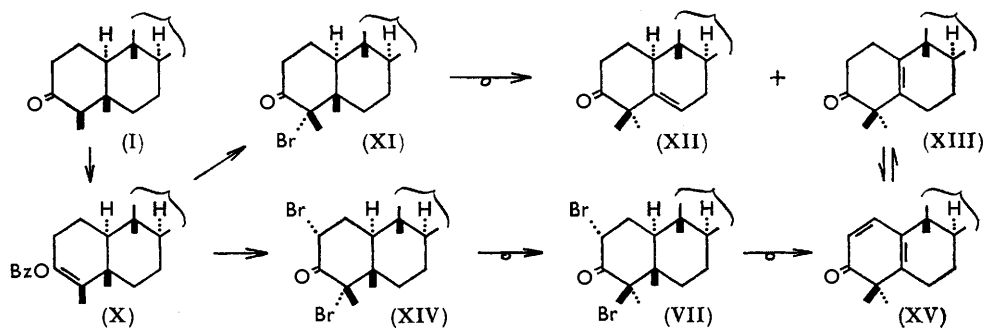
² James and Shoppee, *J.*, 1954, 4224; 1956, 1064; Shoppee, Jenkins, and Summers, *J.*, 1958, 1657, 3098; Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630; Shoppee, Rees, Summers, and Phillips *J.*, 1959, 2786; Shoppee and Lack, *J.*, 1961, 3271.

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 2 α ,4 β -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 2 α -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 $\alpha\beta$ -unsaturated ketone (IV) by addition of bromine and treatment of the resulting 1 α ,2 β -dibromofriedelan-3-one (VII) with aluminium oxide. The 2,2-dibromo-ketone (V) is identical with the product obtained by Djerassi *et al.*³ from 2 α -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 2 α ,4 β -dibromo-structure (VII). We have also prepared the 2,2-dibromo-ketone (V) from 2 α -bromofriedelin by base-catalysed bromination in acetic acid and by bromination with pyridinium bromide dibromide in pyridine, and have confirmed its stability³ to hydrogen bromide; it is converted by refluxing ethanolic potassium hydroxide into friedelane-2,3-dione (VIII), previously prepared by Ruzicka, Jeger, and Ringnes⁴ from cerin (IX) by oxidation with chromium trioxide in acetic acid.



Bromination of friedelin (I) by *N*-bromosuccinimide⁵ gives 4 α -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 4 α -bromofriedelin (XI); we have found that dibromination under similar conditions gives 2 α ,4 α -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.

4 α -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 (C₄) 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 4 α -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 2 α ,4 α -dibromofriedelin (XIV); Kane and Stevenson⁵ found that attempted bromination of 4 α -bromofriedelin with *N*-bromosuccinimide failed to give 2 α ,4 α -dibromofriedelin and led to 4 α -bromofriedel-18-en-3-one. 2 α ,4 α -Dibromofriedelin (XIV) is converted by hydrogen bromide in acetic acid at 20° into the thermodynamically more stable 2 α ,4 β -dibromofriedelin (VII). If the temperature exceeds 20°, the solution becomes yellow and the product is alnus-1,5(10)-dien-3-one⁶ (XV); this compound can also be obtained from both 2 α ,4 α - (XIV) and 2 α ,4 β -dibromofriedelin (VII) by brief treatment with 2,4,6-collidine at 180°, and it has been prepared⁶ from alnus-5(10)-en-3-one (XIII) by bromination and dehydrobromination of the bromination product [probably 2 α -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 ($\Delta\lambda$) of the ultraviolet absorption maximum caused by one axial bromine atom ($\Delta\lambda = +25$ — 28μ) or two axial bromine atoms ($\Delta\lambda = +53\mu$) are reproduced in the displacements ($\Delta\lambda^*$) of the rotatory dispersion trough/peak; (b) the molecular amplitude, $10^{-2}a = +84^\circ$, found for 2 α ,4 α -dibromofriedelin (XIV) shows reasonable agreement with that, $10^{-2}a = +58^\circ$, calculated from the rotatory dispersion contributions Δa of the 2 α -bromine atom and the 4 α -bromine atom [-109° ($10^{-2}a$, friedelin) $- 152^\circ$ (Δa , 2 α -Br) $+ 319^\circ$ (Δa , 4 α -Br) $= +58^\circ$]; (c) the curiously low frequency of the infrared carbonyl band and the small hypsochromic shift $\Delta\nu$ caused by the equatorial 2 β -bromine atom in 2,2-dibromofriedelin (V), which exhibits normal ultraviolet characteristics.

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

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

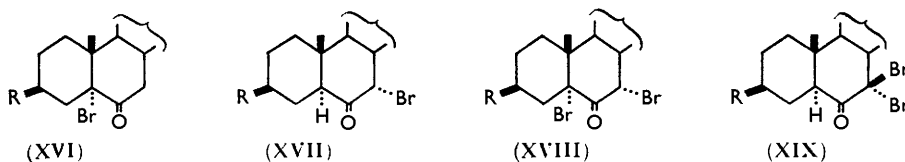
TABLE I.
Physical properties of friedelin and its bromo-derivatives.

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

No.	Cotton curve sign and molecular amplitude ($10^{-2}a$)	Molar dispersion contribution of subst., Δa †	Position of first trough (or peak) λ^* ($m\mu$)	$\Delta\lambda^*$ ($m\mu$)	Halogen confgn.
1.	-107 ^o (d), ⁸ -109(d)	—	315	—	—
2.	-261 (d) ³	-152 ^o (2 α)	335	+20	<i>ax</i>
3.	+210 (d), ³ +209 (c)	+319 (4 α)	335	+20	<i>ax</i>
4.	-280 (c, d) ³	-171 (2 α)	333	+18	<i>eq, ax</i>
5.	+84 (c)	-126 (2 α) +345 (4 α)	365	+50	<i>ax, ax</i>
6.	-218 (c), -227(m)	-109 (2 α)	332	+17	<i>ax, eq</i>

$\Delta\lambda^*$ represents the difference ($m\mu$) 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, $\Delta a - 205^\circ$, over the positive Cotton component of the secondary axial 7 α -bromine atom, thereby reducing the molecular amplitude $10^{-2}a = -291^\circ$ for (XIX; R = OAc) to -179° for (XVIII; R = OAc).



5,7 α -Dibromo-5 α -cholestan-6-one (XVIII; R = H) likewise exhibits competing Cotton effects. Shoppee, Jenkins, and Summers⁹ have described the set of bromo-ketones (XVI—XIX; R = H) derived from 5 α -cholestan-6-one, and we now report their rotatory dispersions. The physical characteristics of these compounds are collected in Table 2. In the 5 α ,7 α -dibromo-ketone (XVIII; R = H), the tertiary axial 5 α -bromine atom superimposes its negative rotatory dispersion contribution, $\Delta a - 290^\circ$, on the positive component of the secondary axial 7 α -bromine atom, $\Delta a + 203^\circ$, reducing the molecular amplitude to $10^{-2}a = -120^\circ$, compared with $10^{-2}a = -323^\circ$ for 5-bromo-5 α -cholestan-6-one (XVI; R = H). It should be noted, however, that the negative rotatory dispersion contribution for the isolated tertiary axial 5 α -bromine atom in the 5 α -bromo-ketone (XVI; R = H), $\Delta a - 247^\circ$, is effectively equal* to that for the isolated secondary axial 7 α -bromine atom in the 7 α -bromo-ketone (XVII; R = H), $\Delta a + 246^\circ$. The $\Delta\lambda$ and $\Delta\lambda^*$ values for the isomeric 5 α - and 7 α -bromo-ketones (XVI, XVII; R = H) are also strikingly similar.

* The only other published⁸ example shows unequal rotatory dispersion contributions: 9 α -bromo-3 β -acetoxy-5 α -ergostan-11-one, $10^{-2}a - 148^\circ$, $\Delta a - 160^\circ$; 12 α -bromo-3 β -acetoxy-5 α -ergostan-11-one, $10^{-2}a + 253^\circ$, $\Delta a + 241^\circ$ (3 β -acetoxy-5 α -ergostan-11-one, $10^{-2}a + 12^\circ$).

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.

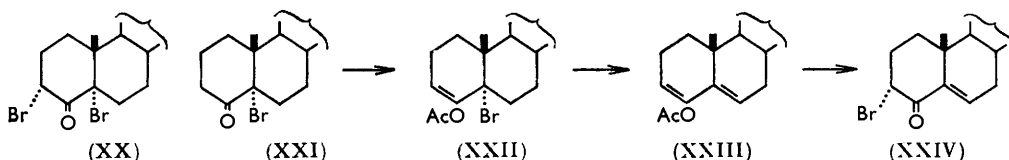
TABLE 2.
Physical properties of 5 α -cholestan-6-one and its bromo-derivatives.

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

No.	Cotton curve sign and molecular amplitude ($10^{-3}a$)	Molar dispersion contribution of subst. Δa †	Position of first trough (or peak) λ^* ($m\mu$)	$\Delta\lambda$ ($m\mu$)	Halogen confign.
7.	-76° (m)	—	307.5	—	—
8.	-323 (m)	-247° (5 α)	330	+22.5	<i>ax</i>
9.	+170 (m)	+246 (7 α)	332	+24.5	<i>ax</i>
10.	-120 (m)	-290 (5 α), +203 (7 α)	360	+52.5	<i>ax, ax</i>
11.	-98 (m)	-22 (7 α)	312	+4.5	<i>ax, eq</i>

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

3 α ,5-Dibromo-5 α -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 shown¹¹ to be a solid solution of 3 α -bromo- and 3,3-dibromo-5 α -cholestan-4-one; we have therefore made further attempts to prepare the 3 α ,5 α -dibromo-ketone (XX) but without success. Treatment of 5-bromo-5 α -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 3 α -bromocholest-5-en-4-one (XXIV) and its 5 α ,6 β -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 3 α ,5 α -dibromo-ketone (XX) must be attributed to the difficulty of enolisation of the 5 α -bromo-ketone (XXI) or to the ease of dehydrobromination of the intermediate allylic bromide (XXII).



The spectroscopic properties of 7,7-dibromo-5 α -cholestan-6-one (XIX; R = H) are unexpected and interesting. The equatorial 7 β -bromine atom exhibits normal behaviour in the infrared spectrum, leading to a displacement of the carbonyl stretching frequency $\Delta\nu + 14$ cm^{-1} ; in the ultraviolet and rotatory dispersion spectra, the axial 7 α -bromine atom simulates the usual behaviour of an equatorial bromine atom. Thus the increments $\Delta\lambda$ and $\Delta\lambda^*$ are small (+8, +4.5 $m\mu$) compared with those (12—15 $m\mu$) normally found¹² for axial bromine atoms in *gem*-dibromo-ketones (cf. also Table 1), whilst the molecular rotatory dispersion contribution Δa of the 7 α -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 7 α - and 7 β -bromine atoms are inclined at approximately equal angles to that plane.

EXPERIMENTAL

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to CHCl₃ 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 CCl₄ 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 Ursprung¹)*. 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 2 α -bromofriedelin (0.85 g.), m. p. 210°, $[\alpha]_D -140^\circ$ (c 1.0), ν_{\max} 1710 cm.⁻¹, λ_{\max} 311 m μ .

(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 2 α -bromofriedelin crystallised as needles (385 mg.), m. p. 210°, $[\alpha]_D -140^\circ$ (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, 2 α -bromofriedelin (30 mg.), m. p. 210°, $[\alpha]_D -140^\circ$ (c 1.0), separating.

Dehydrobromination of 2 α -Bromofriedelin with Collidine.—2 α -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°, λ_{\max} 230 m μ , ν_{\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. C₃₀H₄₈O 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-dibromofriedelin³ (349 mg.), m. p. 228—231°, $[\alpha]_D -124^\circ$ (c 1.0), λ_{\max} 308 m μ , ν_{\max} 1718 cm.⁻¹. Elution with 5% ether-pentane yielded 2 α -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 2 α -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 2 α -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°, λ_{\max} 258 m μ , ν_{\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 1 α ,2 β -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°, λ_{max} 258 m μ , ν_{max} 1690 cm.⁻¹, after crystallisation from chloroform-methanol.

Monobromination of 2 α -Bromofriedelin.—(a) *Acid-catalysed* (cf. Djerassi *et al.*³). To a solution of 2 α -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 2 α -bromofriedelin (125 mg.).

(b) *Base-catalysed.* 2 α -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 2 α -bromofriedelin (136 mg.), m. p. 210°.

(c) *With pyridinium bromide dibromide.* 2 α -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 2 α -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°, $[\alpha]_D -124^\circ$ (*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°, $[\alpha]_D +19^\circ$ (*c* 1.0), λ_{max} 275 m μ , ν_{max} (in CS₂) 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 Ursprung¹).—Friedel-3-en-3-yl benzoate¹ (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 4 α -bromofriedelin (965 mg.), m. p. 197—198° (decomp.), $[\alpha]_D +92^\circ$ (*c* 1.3), λ_{max} 310 m μ , ν_{max} 1715 cm.⁻¹. Optical rotatory dispersion in chloroform: peak +9300° (333 m μ); trough -11,600° (285 m μ); 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, 2 α ,4 α -dibromofriedelin (1.269 g.), m. p. 203—204°, $[\alpha]_D -60^\circ$ (*c* 0.9), λ_{max} 338 m μ , ν_{max} 1712 cm.⁻¹. Optical rotatory dispersion in chloroform: peak +2880° (365 m μ); trough -5550° (313 m μ); amplitude -84°.

Dehydrobromination of 4 α -Bromofriedelin with Collidine.—4 α -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-one⁶ as mixed crystals, m. p. 247—248°, $[\alpha]_D -51^\circ$ (*c* 0.9), ν_{\max} 1710 cm^{-1} , λ_{\max} 290 $\text{m}\mu$.

Monobromination of 4 α -Bromofriedelin.—(a) *Acid-catalysed.* To a solution of 4 α -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 2 α ,4 α -dibromofriedelin (295 mg.), m. p. 203—204°, $[\alpha]_D -60^\circ$ (*c* 1.1). Elution with 5% ether-pentane afforded unchanged 4 α -bromofriedelin (185 mg.), m. p. 197—198° (decomp.).

(b) *Base-catalysed.* 4 α -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 2 α ,4 α -dibromofriedelin (356 mg.), m. p. 203—204°, and unchanged 4 α -bromofriedelin (130 mg.), m. p. 197—198° (decomp.).

(c) *With pyridinium bromide dibromide.* 4 α -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 2 α ,4 α -dibromofriedelin (280 mg.), m. p. 203—204°, and unchanged 4 α -bromofriedelin (195 mg.), m. p. 197—198 (decomp.).

Equilibration of 2 α ,4 α -Dibromofriedelin by Hydrogen Bromide.—2 α ,4 α -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 2 α ,4 β -dibromofriedelin (18 mg.), m. p. 213—216°, λ_{\max} 315 $\text{m}\mu$ (broad), ν_{\max} 1723 cm^{-1} [Found (after drying at 60°/0.05 mm. for 12 hr.): C, 61.8; H, 8.2. $\text{C}_{30}\text{H}_{48}\text{Br}_2\text{O}$ requires C, 61.4; H, 8.3%]. Optical rotatory dispersion in chloroform: trough $-10,100^\circ$ (333 $\text{m}\mu$); peak, $+11,700^\circ$ (288 $\text{m}\mu$); 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°, λ_{\max} 207, 322 $\text{m}\mu$, was isolated in poor yield.

Dehydrobromination of 2 α ,4 α -Dibromofriedelin with Collidine.—2 α ,4 α -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°, $[\alpha]_D -28^\circ$ (*c* 0.8), λ_{\max} 207, 332 $\text{m}\mu$, 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 2 α ,4 β -Dibromofriedelin with Collidine.—2 α ,4 β -Dibromofriedelin (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°, λ_{\max} 207, 322 $\text{m}\mu$.

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°, $[\alpha]_D -86^\circ$ (*c* 0.8), after two crystallisations from chloroform-methanol.

4-Acetoxycholesta-3,5-diene and 3 α -Bromocholest-5-en-4-one [by R. LACK].—A solution of 5-bromo-5 α -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 \times 20 c.c.) gave 4-acetoxycholesta-3,5-diene (150 mg.) as a pale yellow oil, λ_{\max} 240 $\text{m}\mu$ ($\log \epsilon$ 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 3 α -bromocholest-5-en-4-one (42 mg.), m. p. 133—134°, λ_{max} 259 (log ϵ 4.23) (Found: C, 66.4; H, 8.9. Calc. for C₂₇H₄₈BrO: C, 69.9; H, 9.3%). Despite its sharp m. p. and high extinction coefficient, the compound appears to be contaminated with its 5 α ,6 β -dibromide and there was insufficient material for complete purification; it may be noted that cholest-5-en-4-one readily forms a 5 α ,6 β -dibromide.¹¹ The material depressed the m. p. of 3-bromo-5 α -cholest-2-en-4-one¹¹ (131—132°) to 118—121°.

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