Total Synthesis of (+)-(1,2,3/4,5)-2,3,4,5-Tetrahydroxycyclohexane-1-methanol and (+)-(1,3/2,4,5)-5-Amino-2,3,4-trihydroxycyclohexane-1-methanol [(+)-Validamine]. *X*-Ray Crystal Structure of (3*S*)-(+)-2-*exo*-Bromo-4,8-dioxatricyclo[4.2.1.O^{3,7}]nonan-5-one[1]

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The optical resolution of (±)-7-*endo*-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid (±)-(**1**) has been accomplished by use of (*R*)-(+)- and (*S*)-(−)-α-methylbenzylamine, respectively. The absolute configuration of (−)-(**1**) has been determined on the basis of *X*-ray analysis of the bromo lactone (**2**) derived from it. The title branched-chain cyclitol (**6**), the antibiotic produced by *Streptomyces* sp. MA-4145, has been totally synthesized from (−)-(**1**), its absolute configuration being established. Synthesis of the penta-*N,O*-acetyl derivative (**12**) of (+)-validamine, the branched-chain aminocyclitol obtained by degradation of the antibiotic validamycin A, has also been carried out from (−)-(**1**).

In the course of a series of studies on pseudo-sugars,[2] carbocyclic analogues of hexopyranose, it became necessary to prepare optically active compounds for extensive biochemical and biological tests. Since we had been utilising a Diels–Alder adduct of furan and acrylic acid, (±)-7-*endo*-oxabicyclo-[2.2.1]hept-5-ene-2-carboxylic acid (±)-(**1**),[3] as a common starting material for synthesis of all pseudo-sugars and derivatives thereof, it seemed most desirable to provide optically active acids for this purpose.

Attempts were thus made to resolve the racemic acid (±)-(**1**) by use of commercially available resolving agents, and (*R*)-(+)- and (*S*)-(−)-α-methylbenzylamine were found to be effective agents to offer (−)-(**1**) and (+)-(**1**), respectively. Thus, a mixture of (*R*)-(+)-amine salts of (−)-(**1**) and (+)-(**1**) was fractionally crystallised from ethanol to give, in 42% yield, the (*R*)-(+)-amine salt of (−)-(**1**), from which the free acid (−)-(**1**) ($[\alpha]_D$ −112°) was obtained by treatment with mineral acid or acidic ion-exchange resin. In a similar way, the acid (+)-(**1**) ($[\alpha]_D$ +111°) was obtained by the use of the (*S*)-(−)-amine. The absolute configuration of the acid (−)-(**1**) could be established by *X*-ray analysis of the crystalline bromo lactone (**2**) derived from it in the usual way (Figure).

To demonstrate the versatility of the acid (−)-(**1**) for synthesis of an optically active branched-chain cyclitol, (+)-(1,2,3/4,5)-2,3,4,5-tetrahydroxycyclohexane-1-methanol (**6**) was first synthesized. It is the only naturally occurring pseudo-sugar,† isolated as an antibiotic from *Streptomyces* sp. MA-4145,[5] whose absolute structure had not then been fully established.[4]

The synthesis was carried out in the following sequence, previously used for the preparation of the racemic modification.[6] Treatment of the acid (−)-(**1**) with 90% formic acid and 35% hydrogen peroxide gave the hydroxy lactone (**3**) in 66% yield. Compound (**3**) was reduced with lithium aluminium hydride in tetrahydrofuran (THF) and then acetylated to give the triacetate (**4**) which, without purification, was directly subjected to acetolysis to give a mixture of fully acetylated derivatives of pseudo-sugars. Fractionation of the mixture on a silica gel column gave the penta-acetates (**5**) and (**7**) in 27% and 34% yield, respectively. Their structures were confirmed by comparison of their n.m.r. spectra with those of authentic racemic modifications.[6] *O*-Deacetylation of compounds (**5**) and (**7**) with sodium methoxide gave the pentaols (**6**) and (**8**), respectively. Compound (**6**) was identical with an authentic sample[5] in all respects. Therefore, the absolute configuration of C-1 was established to be *R*.

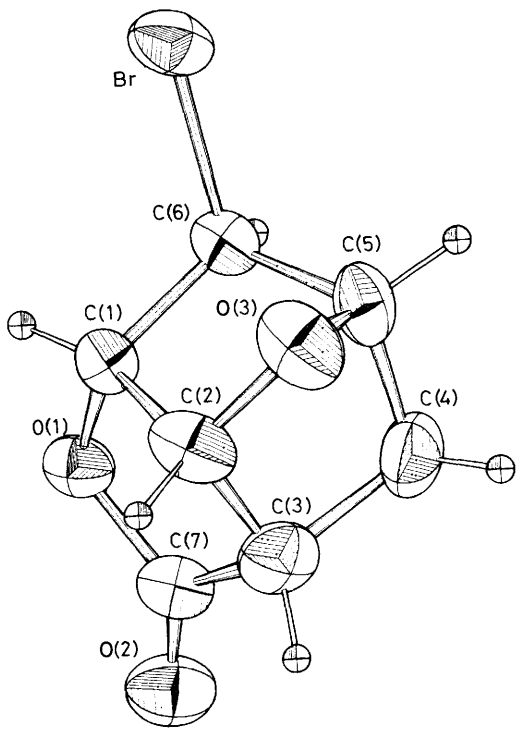
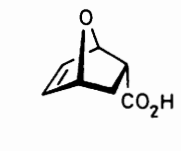


Figure. Molecular structure of the bromo lactone (**2**)

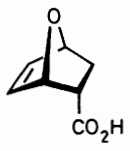
Next, optically active validamine penta-*N,O*-acetate (**12**) was prepared. Validamine was first isolated by hydrogenolysis of the antibiotic validamycin A[7] and the structure was determined by *X*-ray analysis of its hydrochloride.[8] Synthesis of the racemic modification was achieved by us[3,9] and the enantiomers were obtained by separation of the diastereoisomeric β-glucosides, followed by decomposition.[10]

Treatment of the triacetate (**4**) with 20% hydrogen bromide at

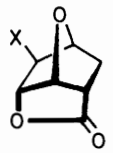
† Very recently, Paulsen and his co-workers have succeeded in synthesizing compound (**6**) starting from L-quebrachitol.[4]



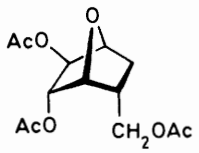
(+)-(1)



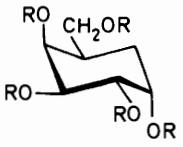
(−)-(1)



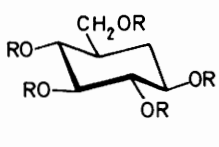
(2) X = Br
(3) X = OH



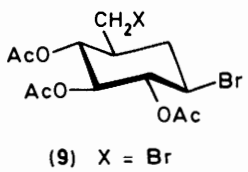
(4)



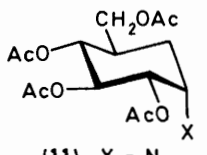
(5) R = Ac
(6) R = H



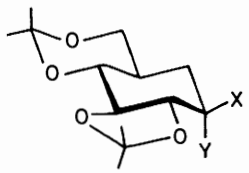
(7) R = Ac
(8) R = H



(9) X = Br
(10) X = OAc



(11) X = N_3
(12) X = NHAc



(13) X = Br, Y = H
(14) X = H, Y = N_3
(15) X = H, Y = NH_2

85 °C for 20 h gave the crystalline dibromide (**9**) in 53% yield. Compound (**9**) was selectively converted into the bromide (**10**) by treatment with sodium acetate in 90% aqueous 2-methoxyethanol at 85 °C, followed by acetylation. The secondary bromo group was then displaced with an azide ion *via* S_N2 reaction to give the azide (**11**), which was hydrogenated in the presence of Raney nickel and acetylated to give the penta-*N*,*O*-acetate (**12**) in 50% yield. This compound was identical with an authentic sample[10] in all respects.

Alternatively, the synthetically useful, protected validamine (**15**) was prepared in the following way. The bromide (**10**) was *O*-deacetylated and successively treated with 2,2-dimethoxypropane in *NN*-dimethylformamide (DMF) in the presence of toluene-*p*-sulphonic acid to give the diacetonide (**13**) in 98% yield. Azidolysis of compound (**13**) gave the azide (**14**), in 71% yield, which was reduced with hydrogen sulphide in aqueous pyridine to give the amine (**15**) in 78% yield. Compound (**15**) was convertible into the penta-*N*,*O*-acetate (**12**).

Experimental

M.p.s were determined on a Mel-temp capillary melting point apparatus and are uncorrected. The n.m.r. spectra were measured in deuteriochloroform solutions with a Varian EM-390 (90 MHz) instrument.* Optical rotations were measured with a Hitachi HPL-225 instrument. (*R*)-(+)- and (*S*)-(−)-α-methylbenzylamine were purchased from Tokyo Kasei Kogyo Co. Ltd. (Tokyo) and showed specific rotations of +38.4 and −38.4° (neat), respectively, corresponding to *ca.* 96% optical purity. Light petroleum refers to that fraction boiling in the range 75—120 °C. Microanalyses were carried out by Mr. Saburo Nakada, to whom our thanks are due.

Optical Resolution of (±)-7-endo-*Oxabicyclo*[2.2.1]*hept*-5-*ene*-2-*carboxylic Acid* [(±)-(**1**)].—To a solution of the acid (±)-(**1**) (3.33 g, 23.8 mmol) in ethanol (40 ml) was added (*R*)-(+)-α-methylbenzylamine (3.07 ml, 23.8 mmol), and the mixture was kept in a refrigerator (0—5 °C) overnight. The precipitate was collected by filtration and washed with propan-2-ol to give a crystalline mixture of the salts (2.54 g, 82.0%). Three recrystallisations from ethanol afforded the pure (R)-(+)-*amine salt* of (−)-(**1**) (1.31 g, 42%) as white needles, m.p. 137.5—138.5 °C (Found: C, 68.9; H, 7.3; N, 5.3. $C_{15}H_{19}NO_3$ requires C, 68.95; H, 7.3; N, 5.4%); $[\alpha]_D^{27}$ −66.4° (*c* 1.05 in MeOH).

Similarly, by use of (*S*)-(−)-α-methylbenzylamine, the (S)-(−)-*amine salt* of (+)-(**1**) was obtained, m.p. 137.5—138.5 °C (from EtOH) (Found: C, 69.0; H, 7.25; N, 5.2%); $[\alpha]_D^{27}$ +66.7° (*c* 0.99 in MeOH).

A portion (2.0 g, 7.7 mmol) of the (*R*)-(+)-amine salt of (−)-(**1**) was treated with 1M aqueous sodium carbonate (20 ml) at room temperature for 0.5 h, and then the solution was extracted with ether (20 ml × 2). The solvent was removed to leave recovered (*R*)-(+)-amine (0.85 g, 92%). The aqueous layer was acidified with 1M hydrochloric acid and extracted with ether (20 ml × 5). The extracts were dried and concentrated to give a crystalline residue (0.99 g, 92%). Recrystallisation from ethyl acetate–light petroleum (1:10, v/v) gave needles of the *acid* (−)-(**1**), m.p. 97—98.5 °C (Found: C, 59.95; H, 5.7. $C_7H_8O_3$ requires C, 60.0; H, 5.75%); $[\alpha]_D^{22}$ −112° (*c* 1.01 in EtOH).

From the (*S*)-(−)-amine salt of (+)-(**1**), the *free acid* (+)-(**1**) was obtained as needles, m.p. 97—99 °C (from AcOEt–light petroleum) (Found: C, 59.9; H, 5.7%); $[\alpha]_D^{22}$ +111° (*c* 1.0 in EtOH).

Both the acids (−)-(**1**) and (+)-(**1**) were also obtained easily by treatment of aqueous solution of the corresponding amine salts with Dowex 50W X2 (H^+) resin.

(3S)-(+)-2-exo-*Bromo*-4,8-*dioxatricyclo*[4.2.1.$0^{3,7}$]*nonan*-5-*one* (**2**).—To a stirred solution of the acid (−)-(**1**) (250 mg, 1.90 mmol) and sodium hydrogen carbonate (250 mg, 3.0 mmol) in water (3 ml) was added bromine (0.23 ml, 4.5 mmol) and the reaction mixture was stirred at room temperature for 1 h and then extracted with ethyl acetate (10 ml × 2). The extract was dried and concentrated to give the *bromo lactone* (**2**) (372 mg, 89%) as prisms, m.p. 117.5—118.5 °C (from AcOEt) (Found: C, 38.1; H, 3.3; Br, 36.3. $C_7H_7BrO_3$ requires C, 38.4; H, 3.2; Br, 36.5%); $[\alpha]_D^{25}$ +92° (*c* 0.99 in $CHCl_3$).

(3R)-(+)-2-exo-*Hydroxy*-4,8-*dioxatricyclo*[4.2.1.$0^{3,7}$]*nonan*-5-*one* (**3**).—A mixture of the acid (−)-(**1**) (1.61 g, 11.5 mmol), 90% formic acid (3 ml), and 35% hydrogen peroxide (3.5 ml) was heated at 70 °C for 20 min. The reaction mixture was concentrated to give the *hydroxy lactone* (**3**) (1.19 g, 66%) as prisms, m.p. 107—108 °C (from EtOH) (Found: C, 53.6; H, 5.1. $C_7H_8O_4$ requires C, 53.85; H, 5.2%); $[\alpha]_D^{22}$ +47.9° (*c* 1.0 in EtOH).

Acetolysis of (1S)-2-exo,3-endo-*Diacetoxy*-5-endo-*acetoxymethyl*-7-*oxabicyclo*[2.2.1]*heptane* (**4**).—To a slurry of lithium aluminium hydride (0.20 g) in THF (5 ml) was added dropwise a solution of the hydroxy lactone (**3**) (1.05 g, 6.73 mmol) in THF (20 ml), and the mixture was stirred at room temperature for 30 min. Water (2.5 ml) was added to the reaction mixture which was then neutralised with 1M-hydrochloric acid, and con-

* The structures of all new optically active compounds were assigned by comparison of their spectral data with those of the corresponding known racemic modifications.

centrated. The residue was treated with acetic anhydride (15 ml) and pyridine (15 ml) at room temperature for 1 h. The mixture was concentrated and extracted with ethyl acetate. The extract was washed successively with 1M-hydrochloric acid, saturated sodium hydrogen carbonate, and water, and dried. The solvent was removed to leave the triacetate (**4**) (1.47 g, 76%) as a syrup. Without further purification this compound was heated with acetic acid (4.5 ml), acetic anhydride (2.6 ml), and conc. sulphuric acid (0.3 ml) in a sealed tube at 80 °C for 20 h. The reaction mixture was poured into ice–water (50 ml) and, after neutralisation with sodium hydrogen carbonate, the solution was extracted with ethyl acetate (30 ml × 3). The extract was dried and concentrated to afford a syrup (1.57 g) which was chromatographed on a silica gel column (80 g) with acetone–hexane (2:9, v/v) as eluant. The first fraction gave (1R)-(+)-(1,2,3/4,5)-2,3,4,5-*tetrahydroxycyclohexane*-1-*methanol penta-acetate* (**5**) (525 mg, 27%) as prisms, m.p. 143—144 °C (from EtOH) (Found: C, 52.6; H, 6.2. $C_{17}H_{24}O_{10}$ requires C, 52.6; H, 6.2%); $[\alpha]_D^{20}$ +43.2° (*c* 1.06 in $CHCl_3$).

The second fraction gave (1R)-(+)-(1,3,5/2,4)-2,3,4,5-*tetrahydroxycyclohexane*-1-*methanol penta-acetate* (**7**) (660 mg, 34%) as prisms, m.p. 115—116 °C (from EtOH) (Found: C, 52.7; H, 6.2%); $[\alpha]_D^{20}$ +13.8° (*c* 1.0 in $CHCl_3$).

The n.m.r. spectra of the penta-acetate (**5**) and (**7**) were shown to be superimposable on those of their authentic racemic modifications,[6] respectively.

(1R)-(+)-(1,2,3/4,5)-2,3,4,5-*Tetrahydroxycyclohexane*-1-*methanol* (**6**).—The penta-acetate (**5**) (140 mg, 0.36 mmol) was treated with 1M methanolic sodium methoxide (4 ml) at room temperature for 2 h. After neutralisation with Dowex 50W X2 (H^+) resin (0.5 ml), the solution was concentrated to give the pentaol (**6**) (45 mg, 70%) as prisms, m.p. 161.5—162.5 °C (from MeOH) (Found: C, 47.4; H, 7.8. Calc. for $C_7H_{14}O_5$: C, 47.2; H, 7.9%); $[\alpha]_D^{23}$ +66.3° (*c* 1.48 in water) (lit.,[5] m.p. 164 °C; $[\alpha]_D^{22}$ +61.5 ± 4° in water).

(1R)-(+)-(1,3,5/2,4)-2,3,4,5-*Tetrahydroxycyclohexane*-1-*methanol* (**8**).—The penta-acetate (**7**) (140 mg, 0.36 mmol) was similarly *O*-deacetylated with sodium methoxide to give the *pentaol* (**8**) (75 mg, 100%) as a syrup (Found: C, 44.8; H, 8.1. $C_7H_{14}O_5 \cdot 0.5H_2O$ requires C, 44.9; H, 8.1%); $[\alpha]_D$ +13.0° (*c* 2.1 in water).

(1R)-(−)-(1,3,5/2,4)-2,3,4-*Triacetoxy*-1-*bromo*-5-*bromomethylcyclohexane* (**9**).—A mixture of the triacetate (**4**) (2.0 g, 7.0 mmol) and 20% hydrogen bromide–acetic acid (15 ml) was heated in a sealed tube at 85 °C for 20 h. The reaction mixture was poured into ice–water, and the solution was neutralised with sodium hydrogen-carbonate and extracted with ethyl acetate (20 ml × 2). The extract was washed with water, dried, and concentrated to give a syrup which was crystallised to give the *dibromide* (**9**) (1.58 g, 53%) as prisms, m.p. 99—100 °C (from EtOH) (Found: C, 36.1; H, 4.2; Br, 36.8. $C_{13}H_{18}Br_2O_6$ requires C, 36.3; H, 4.2; Br, 37.2%); $[\alpha]_D^{16}$ −3.6° (*c* 1.07 in $CHCl_3$).

(1R)-(−)-(1,3,5/2,4)-2,3,4-*Triacetoxy*-1-*acetoxymethyl*-5-*bromocyclohexane* (**10**).—The dibromide (**9**) (2.51 g, 5.83 mmol) was treated with sodium acetate in aqueous 2-methoxyethanol, followed by acetylation, as in the preparation of the racemic product (**10**).[9] The product was purified on a silica gel column to give the *bromide* (**10**) (1.15 g, 48%), m.p. 94.5—95.5 °C (from EtOH) (Found: C, 43.9; H, 5.05; Br, 19.3. $C_{15}H_{21}BrO_8$ requires C, 44.0; H, 5.2; Br, 19.5%); $[\alpha]_D^{14}$ −15.7° (*c* 1.05 in $CHCl_3$).

(1R)-(+)-(1,3/2,4,5)-2,3,4-*Triacetoxy*-1-*acetoxymethyl*-5-*azidocyclohexane* (**11**).—The bromide (**10**) (87 mg, 0.21 mmol) was treated with sodium azide in DMF as in the preparation of the racemic product (**11**).[9] The product was purified on a silica gel column to give the *azide* (**11**) (70 mg, 89%) as a syrup (Found: C, 48.7; H, 5.7; N, 11.1. $C_{15}H_{21}N_3O_8$ requires C, 48.5; H, 5.7; N, 11.3%); $[\alpha]_D^{28}$ +44.8° (*c* 0.98 in $CHCl_3$).

(1S)-(+)-(1,2,4/3,5)-1-*Acetamido*-2,3,4-*triacetoxy*-5-*acetoxymethylcyclohexane* [(+)-Penta-N,O-*acetylvalidamine*] (**12**).—A solution of the azide (**11**) (49 mg, 0.13 mmol) in methanol (1.5 ml) containing acetic anhydride (36 μl) was hydrogenated in the presence of Raney nickel T-4[11] (0.2 ml) in a Parr shaker-type apparatus at room temperature for 20 h. The product was purified on a silica-gel column to give the penta-acetyl derivative (**12**) (29 mg, 57%) as needles, m.p. 144—146 °C (from chloroform–ether) (Found: C, 53.0; H, 6.6; N, 3.6. Calc. for $C_{17}H_{25}NO_9$: C, 52.7; H, 6.5; N, 3.6%); $[\alpha]_D^{26}$ +44° (*c* 0.75 in $CHCl_3$) {lit.,[10] m.p. 147—149 °C; $[\alpha]_D^{20}$ +60.2° (*c* 0.60 in $CHCl_3$)}.

(1R,2S,6R,7R,9R)-(−)-7-*Bromo*-4,4,12,12-*tetramethyl*-3,5,11,13-*tetraoxatricyclo*[7.4.0.0^{2,6}]*tridecane* (**13**).—A mixture of the bromide (**10**) (866 mg, 2.12 mmol), 2M-hydrobromic acid (5.2 ml), and ethanol (5.5 ml) was heated at 80 °C for 3 h. The mixture was concentrated to give a syrupy tetraol which was directly treated with 2,2-dimethoxypropane (8 ml) in dry DMF (11 ml) in the presence of toluene-*p*-sulphonic acid (5 mg) at 60 °C for 3 h. After neutralisation with sodium hydrogen carbonate, the mixture was concentrated to give the *diacetonide* (**13**) (665 mg, 98%), m.p. 175—176 °C (from EtOH) (Found: C, 48.7; H, 6.6; Br, 24.7. $C_{13}H_{21}BrO_4$ requires C, 48.6; H, 6.6; Br, 24.9%); $[\alpha]_D^{18}$ −43.5° (*c* 0.95 in $CHCl_3$).

(1R,2S,6S,7S,9R)-(−)-7-*Azido*-4,4,12,12-*tetramethyl*-3,5,11,13-*tetraoxatricyclo*[7.4.0.0^{2,6}]*tridecane* (**14**).—A mixture of the diacetonide (**13**) (628 mg, 1.96 mmol), sodium azide (660 mg), and dry DMF (14 ml) was stirred at 110 °C for 16 h. Ethyl acetate (30 ml) was added, and the solution was washed with water, dried and concentrated to give the *azide* (**14**) (397 mg, 71%), m.p. 137—138 °C (from EtOH) (Found: C, 55.0; H, 7.4; N, 14.8. $C_{13}H_{21}N_3O_4$ requires C, 55.1; H, 7.5; N, 14.8%); $[\alpha]_D^{16}$ −33.3° (*c* 1.02 in $CHCl_3$).

(1R,2S,6S,7S,9R)-(+)-7-*Amino*-4,4,12,12-*tetramethyl*-3,5,11,13-*tetraoxatricyclo*[7.4.0.0^{2,6}]*tridecane* (**15**).—To a solution of the azide (**14**) (389 mg, 1.37 mmol) in pyridine (4 ml) and water (4 ml) was bubbled hydrogen sulphide at room temperature for 8 h. The mixture was then concentrated and the residue was dissolved in toluene and the solution was charged on a short column of neutral alumina. Sulphur was removed by elution with toluene and then the product was eluted with ethanol to give the *amine* (**15**) (276 mg, 78%) as prisms, m.p. 170—171 °C (from EtOH) (Found: C, 60.7; H, 8.9; N, 5.2. $C_{13}H_{23}NO_4$ requires C, 60.7; H, 9.0; N, 5.4%); $[\alpha]_D^{18}$ +8.9° (*c* 0.99 in EtOH).

Treatment of the amine (**15**) (30 mg, 0.12 mmol) with 70% aqueous acetic acid (1 ml) at 80 °C for 2 h, followed by acetylation in the usual way, gave the penta-acetyl derivative (**12**) (50 mg, 100%) as a syrup; $[\alpha]_D^{17}$ +57.6° (*c* 1.55 in $CHCl_3$). The n.m.r. spectrum was superposable on that of an authentic racemic modification.[9,10]

X-Ray Crystal Structure of the Bromo Lactone (**2**).—*Crystal data.* $C_7H_7BrO_3$, M = 219.0. Monoclinic, a = 10.137(2), b = 5.447(1), c = 6.770(2) Å, β = 90.88(2)°, V = 373.8(1) Å^3 (by least-squares refinement of diffractometer angles for 20 automatically centred reflections, λ = 0.710 69 Å), space group $P2_1$, Z = 2, D_x = 1.95 g cm^{-3}. Colourless prismatic crystals, crystal dimensions (distance to faces from centre): 0.30 × 0.30 × 0.50 mm, μ(Mo-K_α) = 59.5 cm^{-1}.

Data collection and processing. Rigaku four-circle diffractometer with ω/2θ mode with ω scan width 1.30 + 0.5 tanθ, ω scan speed 2° (ω) min^{-1}, graphite-monochromated Mo-K_α radiation,

Table 1. Positional parameters ($\times 10^4$; for Br $\times 10^5$) and equivalent isotopic temperature factors[a] for compound (**2**)

	x	y	z	B_{eq} (Å^2)
Br	10 6210(4)	5 0000(28)	2 0110(7)	3.9
O(1)	6 961(3)	2 644(5)	454(4)	2.8
O(2)	4 982(3)	1 356(8)	1 486(6)	4.2
O(3)	7 940(4)	7 449(7)	3 461(6)	4.3
C(1)	7 869(4)	4 523(8)	897(6)	2.5
C(2)	7 089(5)	6 563(10)	1 968(8)	3.6
C(3)	6 088(4)	5 000(15)	3 000(7)	3.8
C(4)	6 940(5)	4 173(12)	4 831(7)	4.2
C(5)	8 275(5)	5 289(11)	4 326(6)	3.4
C(6)	8 856(4)	3 882(9)	2 561(7)	2.8
C(7)	5 875(4)	2 883(10)	1 626(7)	3.2

[a] W. C. Hamilton, *Acta Crystallogr.*, 1959, **12**, 609.

Table 2. Intramolecular bond distances and angles for compound (**2**)

Atoms	Distance (Å)	Atoms	Distance (Å)
Br–C(6)	1.931(5)	C(1)–C(6)	1.536(6)
O(1)–C(1)	1.406(5)	C(2)–C(3)	1.505(8)
O(1)–C(7)	1.373(5)	C(3)–C(4)	1.566(7)
O(2)–C(7)	1.232(6)	C(3)–C(7)	1.495(9)
O(3)–C(2)	1.404(6)	C(4)–C(5)	1.527(7)
O(3)–C(5)	1.355(7)	C(5)–C(6)	1.544(7)
C(1)–C(2)	1.550(7)		

Atoms	Angle (°)	Atoms	Angle (°)
C(1)–O(1)–C(7)	109.6(0.3)	C(3)–C(4)–C(5)	100.9(0.4)
C(2)–O(3)–C(5)	99.2(0.4)	O(3)–C(5)–C(4)	103.0(0.4)
O(1)–C(1)–C(2)	106.5(0.3)	O(3)–C(5)–C(6)	101.1(0.4)
O(1)–C(1)–C(6)	114.1(0.4)	C(4)–C(5)–C(6)	109.0(0.4)
C(2)–C(1)–C(6)	98.7(0.3)	Br–C(6)–C(5)	112.5(0.3)
O(3)–C(2)–C(1)	105.7(0.4)	Br–C(6)–C(1)	111.0(0.3)
O(3)–C(2)–C(3)	105.8(0.4)	C(1)–C(6)–C(5)	101.7(0.4)
C(1)–C(2)–C(3)	99.4(0.4)	O(1)–C(7)–O(2)	119.1(0.4)
C(2)–C(3)–C(4)	99.4(0.4)	O(1)–C(7)–C(3)	108.9(0.4)
C(2)–C(3)–C(7)	103.9(0.4)	O(2)–C(7)–C(3)	131.9(0.4)
C(4)–C(3)–C(7)	110.1(0.6)		

2 663 reflections measured, 1 241 unique ($2\theta < 65°$; $0 \leqslant h \leqslant 15$, $0 \leqslant k \leqslant 8$, $-10 \leqslant l \leqslant 10$) and 606 Bijvoet pairs ($2\theta < 50°$; $-10 \leqslant h \leqslant 0$, $0 \leqslant k \leqslant 5$, $-7 \leqslant l \leqslant 7$) with $I > 3\sigma(I)$. Absorption correction (max., min. transmission factors = 0.25, 0.18).

Structure analysis and refinement. A normal heavy-atom method was used, followed by successive Fourier syntheses calculations. Block diagonal least-squares refinement was performed with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The weighting scheme $w^{-1} = \sigma(|F_o|) + (0.015|F_o|)^2$, with $\sigma(|F_o|)$ from counting statistics, gave satisfactory agreement analyses, using standard scattering factors and the UNIX-III program system. Convergence was achieved for both possible absolute configurations (by inverting the molecule). The weighted (R_w) and unweighted (R) factors for correct (incorrect) configurations were 0.043 (0.044), 0.050 (0.049), respectively, indicating >99.6% assignment probability. The absolute configuration was also confirmed by comparison of the 606 more relevant Bijvoet pairs. All the calculations were performed using the UNIX-III system[12] of programs.

Atomic co-ordinates, bond lengths and angles (non-hydrogen atoms), and selected torsion angles are given in Tables 1—3. Observed and calculated structure factors, and thermal parameters, are listed in Supplementary Publication No. SUP. 56169 (16 pp.).*

Table 3. Torsion angles (°) for compound (**2**) looking from atom 2 to 3; the clockwise rotation of bond 3—4 with reference to bond 2—1 is given

C(7)–O(1)–C(1)–C(2)	−19.1(0.4)
C(7)–O(1)–C(1)–C(6)	88.7(0.4)
C(1)–O(1)–C(7)–O(2)	−178.1(0.4)
C(1)–O(1)–C(7)–C(3)	−2.3(0.5)
C(5)–O(3)–C(2)–C(1)	−51.6(0.4)
C(5)–O(3)–C(2)–C(3)	53.2(0.5)
C(2)–O(3)–C(5)–C(4)	−55.2(0.4)
C(2)–O(3)–C(5)–C(6)	57.5(0.4)
O(1)–C(1)–C(2)–O(3)	141.2(0.4)
O(1)–C(1)–C(2)–C(3)	31.8(0.4)
C(6)–C(1)–C(2)–O(3)	22.8(0.4)
C(6)–C(1)–C(2)–C(3)	−86.6(0.4)
O(1)–C(1)–C(6)–Br	139.1(0.3)
O(1)–C(1)–C(6)–C(5)	−102.1(0.4)
C(2)–C(1)–C(6)–Br	−108.3(0.3)
C(2)–C(1)–C(6)–C(5)	10.5(0.4)
O(3)–C(2)–C(3)–C(4)	−27.8(0.5)
O(3)–C(2)–C(3)–C(7)	−141.3(0.4)
C(1)–C(2)–C(3)–C(4)	81.6(0.4)
C(1)–C(2)–C(3)–C(7)	−31.9(0.5)
C(2)–C(3)–C(4)–C(5)	−4.6(0.5)
C(7)–C(3)–C(4)–C(5)	104.0(0.5)
C(2)–C(3)–C(7)–O(1)	23.2(0.5)
C(2)–C(3)–C(7)–O(2)	−161.7(0.5)
C(4)–C(3)–C(7)–O(1)	−82.4(0.5)
C(4)–C(3)–C(7)–O(2)	92.7(0.7)
C(3)–C(4)–C(5)–O(3)	36.8(0.5)
C(3)–C(4)–C(5)–C(6)	−69.9(0.5)
O(3)–C(5)–C(6)–Br	77.5(0.4)
O(3)–C(5)–C(6)–C(1)	−42.4(0.4)
C(4)–C(5)–C(6)–Br	−174.5(0.3)
C(4)–C(5)–C(6)–C(1)	65.7(0.5)

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* For details of the Supplementary Publications Scheme, see Instructions for Authors (1985), *J. Chem. Soc., Perkin Trans 1*, 1985, Issue 1. Structure factors are available from the editorial office on request.