Unsaturated Carbohydrates. Part 21.[1] A Carbocyclic Ring Closure of a Hex-5-enopyranoside Derivative

By Robert J. Ferrier,† Department of Pharmacology, University of Edinburgh, 1 George Square, Edinburgh EH8 9JZ

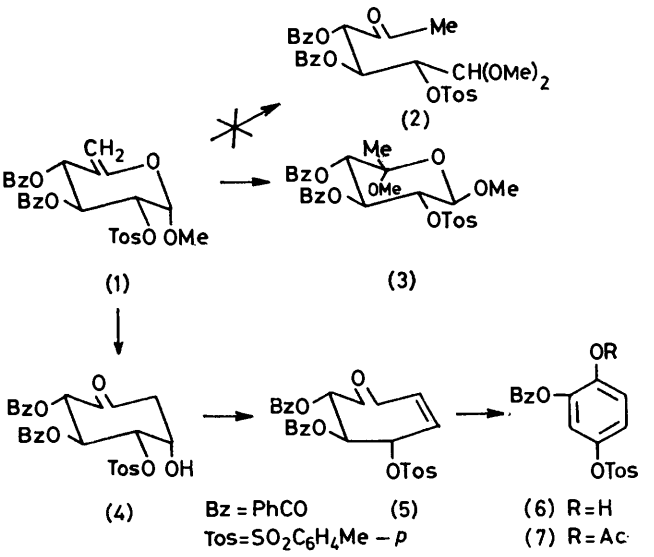
Heating of the unsaturated glycoside triester (1) in refluxing aqueous acetone with mercury(II) chloride gave the cyclohexanone derivative (4) in high yield in a reaction which represents a new means of obtaining functionalised carbocyclic compounds from carbohydrates. From compound (4), the substituted cyclohexenone (5) and thence the phenol (6) were prepared.

INTRAMOLECULAR ring-closure of carbohydrates offers access to highly functionalised carbocyclic compounds, but with the exception of cyclohexane derivatives, few such compounds have been produced by this route. Significant possibilities, however, are suggested by the bonding of C-3′ to C-5′ in nucleosides to give cyclopropyl derivatives,[2] by the photochemical ring closure of 1,3,4,5,6-penta-*O*-acetyl-*keto*-D-fructose and -L-sorbose to give a substituted cyclobutane,[3] and by the conversion of methyl 6-deoxy-2,3-di-*O*-toluene-*p*-sulphonyl-β-D-*xylo*-hexofuranosid-5-ulose into a bicyclic product containing a cyclopentane ring, formed by attack of a carbanion at C-6 on C-2, with displacement of the sulphonyloxy-group at that position.[4] The majority of reported work refers to the synthesis of inositol derivatives and has followed the path by which such compounds are believed to be produced biosynthetically from D-glucose,[5] *i.e.* by ring-closure involving attack of a carbanionic centre at C-6 on the carbonyl centre of the free sugar. Initially Grosheintz and Fischer [6] effected ring-closure by treating 6-deoxy-6-nitro-D-glucose with alkali, and since then it has been shown that inososes and their ethers and esters are obtainable by similar treatment of D-*xylo*-hexos-5-ulose,[7] its 3-benzyl ether,[8] and its 6-phosphate,[9] respectively. The last example duplicates non-enzymically the presumed ring-closure step in the biochemical D-glucose–inositol interconversion.[5] Extension of the initial nitro-sugar procedure has led to the synthesis of a range of inositol derivatives,[10] and extensive use has been made of a variant involving the base-catalysed condensation of dicarbonyl carbohydrate derivatives with nitroalkanes [11] which can lead to a variety of polyhydroxynitrocyclitols having five-,[12] six-,[13] or seven-membered [14] rings. An alternative route to inositols depends upon a carbene reaction which occurred when 3,4,5-tri-*O*-acetyl-1,7-bis(diazo)-1,7-dideoxy-D-*xylo*-hept-2,6-diulose was heated in acetic acid in the presence of copper(II) acetate as catalyst and led to an inosose derivative with an acetoxymethyl branched-group at C-3.[15] In the course of this work, 3,4,5-tri-*O*-acetyl-1,7-dibromo-1,7-dideoxy-*xylo*-hept-2,6-diulose was converted into a rearranged branched cyclohexenone product,[16] but this ring-closure was again base-catalysed, and presumably proceeded by an intramolecular aldol type of reaction.

† *Permanent address:* Department of Chemistry, Victoria University of Wellington, Private Bag, Wellington, New Zealand.

RESULTS AND DISCUSSION

The objective of the present work was to determine whether an acyclic ald-5-ulose derivative with a good leaving group at C-2 would efficiently give a functionalised cyclopentane derivative without the substantial concurrent elimination which occurred with methyl 6-deoxy-2,3-di-*O*-toluene-*p*-sulphonyl-β-D-*xylo*-hexofuranosid-5-ulose.[4] To this end, the 6-deoxy-5-enopyranoside derivative (1), prepared from methyl 3,4-di-*O*-benzoyl-2,6-di-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside [17] which is obtainable directly from methyl α-D-glucopyranoside, was treated with methanolic hydrogen chloride, but no acyclic product (*e.g.* 2) was formed. Instead, a good yield of the cyclic compound (3) was obtained, as evidenced by the presence in the n.m.r. spectrum of resonances for two methoxy-groups (δ 3.35 and 3.43), a *C*-methyl group (δ 1.42) and large ring-proton coupling constants ($J_{1,2} = J_{2,3} = 8$ Hz, $J_{3,4} = 9$ Hz). This is consistent with the findings of Lehmann and his co-workers [18] who treated the triacetate analogue of compound (1) in similar manner and isolated, after acetylation, two ' double glycosides ' varying in stereochemistry at C-5. In this case, however, addition occurred without anomerisation, whereas in the present work inversion at C-1 did occur, the methoxy-group at this position thereby avoiding a destabilising interaction with



Hydrogen-1 n.m.r. parameters [a]

Compound	Chemical shifts (δ) 1-H	2-H	3-H	4-H	6-H	Other protons	Coupling constants/Hz $J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{1,6}$	$J_{2,6}$	$J_{6,6'}$
(1) [b]	5.16	4.8	5.98	5.76	4.65, 4.90	14 Aryl, 3 OMe, 3 CMe	3	9	9	0	0	12
(3) [b]	4.72	4.90	6.02	5.37	1.42	14 Aryl, 6 OMe, 3 CMe	8	8	9	0	0	0
(4) [c]	5.13	6.04	6.99	6.66	3.11, 3.42	14 Aryl, OH, 3 CMe	2.4	10.0	10.0	4.0, 2.4	0	14.4
(5) [d]	7.08	5.60	6.00	5.80	6.32	14 Aryl, 3 CMe	2.0	8.7	11.6	10.6	2.2	

[a] For the purposes of this Table, atom numbering follows the carbohydrate convention *i.e.* C-1 is the anomeric carbon atom in the pyranosides and that derived from it in the cyclohexyl derivatives. [b] Measured at 60 MHz in $CDCl_3$. [c] Measured at 270 MHz in C_5D_5N. [d] Measured at 270 MHz in $CDCl_3$.

the axial substituent at C-5. It is assumed that in compound (3) the methoxy and the methyl groups at C-5 are axial and equatorial, respectively, since in this way (and since the product is presumably formed under thermodynamic control—inversion having occurred at C-1) steric and electrostatic (anomeric effect) requirements are met. In agreement with this, the compound is strongly laevorotatory as is consistent with expectations for a glycoside with ' β-D '-stereochemistry at both C-1 and C-5. Addition of mercury(II) salts to compound (1) in aqueous media would be expected to give products with mercury bonded to C-6 and a hemiacetal centre at C-5,[19] which would lead to ring-opening and loss of the aglycone. During ring-opening, should an unsolvated carbonyl group be liberated at C-5, a very reactive carbanionic centre would result at C-6, since it might be anticipated that the carbonyl group would stabilise such a carbanion in the same way as do 2- and 4- (but not 3-) bonded pyridinium groups in related mercuriated species.[20] Carbanionic character at C-2 has been observed on several occasions in products of mercuriation of glycals.[19,21] Compound (1) was therefore treated with mercury(II) chloride in aqueous acetone, and reaction at room temperature caused a rapid increase in the optical rotation followed by a slow decrease. To accelerate equilibration, the colourless solution was heated under reflux, and, on cooling, a product (4) crystallised from it in good yield. This compound retained the three ester groups of the starting material but had lost the aglycone and contained, instead, an hydroxy-group. In addition, the methylene group now involved an sp^3-hybridised carbon atom, and a ketonic group replaced the alkene double bond. Instead, therefore, of the anticipated carbanion at C-6 attacking C-2, it had taken part in an aldol ring-closure with the carbonyl group which had been liberated at C-1. In this way, the ring-closure reaction resembles the base-catalysed inosose syntheses, but occurred in the acid conditions of aqueous mercury(II) chloride. In a control experiment carried out in aqueous acetone containing hydrochloric acid, of the molarity of the chloride used in the above experiment, no reaction took place, establishing that the mercury ions were required for reaction. The ring-closure also resembles the cyclisations which occur when carbanionic centres of Grignard reagents displace leaving groups within the same molecules.[22]

In the 270 MHz ^1H n.m.r. spectrum of compound (4) (see Table) H-2, H-3, and H-4 (carbohydrate numbering retained for the purposes of this discussion) resonated as a quartet ($J_{1,2}$ 2.4, $J_{2,3}$ 10.0 Hz), a triplet ($J_{3,4}$ 10.0 Hz), and a broad doublet, respectively, indicating that they remained axial on a six-membered ring. The $J_{1,2}$ value shows that H-1 is equatorial; it resonated as a broad singlet ($W_{\frac{1}{2}}$ 8 Hz) at δ 5.13 which is consistent with its being geminal to a hydroxy-group. Two quartets appeared at δ 3.42 and 3.11 with a common splitting of 14.4 Hz and secondary couplings of 2.4 and 4.0 Hz, respectively. Spin-decoupling experiments showed that both these geminal protons were coupled to H-1, which confirms the presence of the cyclohexyl ring system.

On treatment with acetic anhydride in pyridine, the hydroxy-ketone (4) underwent β-elimination to give the conjugated enone (5) which showed resonances for three ring protons bonded to saturated carbon and a vinylic pair at δ 7.08 and δ 6.32 (J 10.6 Hz) consistent with their being H-1 and H-6.[23] The ring adopted the illustrated half-chair conformation with a large $J_{3,4}$ value (11.6 Hz), a $J_{2,3}$ value (8.7 Hz) consistent with ring flattening in the neighbourhood of C-2, and $J_{1,2}$ (2.0 Hz) and $J_{2,6}$ (2.2 Hz) in accord with H-2 being a quasi-axial allylic proton on a cyclohexene ring system.[24] Carbon-13 n.m.r. data on compounds (4) and (5) were consistent with the assigned structures.

Reaction of the enone (5) in benzene solution with 1,5-diazabicyclo[5.4.0]undec-5-ene caused rapid loss of optical activity and the formation of a syrupy product (6) as well as benzoic acid. Aromatisation therefore had occurred by base-catalysed elimination of the acid in similar fashion to the formation of 2,4,6-tribenzyloxyphenol from penta-*O*-benzylinosose.[25] The ^1H n.m.r. spectrum of the phenol (6) showed three aromatic proton resonances in the region δ 6.35—7.1 together with a broad one-proton signal at δ 5.3 which was specifically removed by deuterium exchange. Signals for a *p*-toluenesulphonyl and one benzoyl group were also present.

On acetylation, compound (6) gave the crystalline triester (7) having proton resonances for one acetyl group at δ 2.11, one toluene-*p*-sulphonyl methyl group at δ 2.42, and twelve aromatic hydrogens. The fully decoupled ^{13}C n.m.r. spectrum, run at rapid pulse rate so that quaternary carbon signals were eliminated, showed ten resonances. Acetyl and tolyl methyl carbon signals appeared at δ 20.4 and 21.7, C-4 of the benzoate resonated at δ 134.1, and the eight carbon atoms at C-2, C-3, C-5, and C-6 of the benzoate and toluene-*p*-sulphonate appeared at δ 128.7, 128.8, 130.0, and 130.2 (each twice the intensity of the other signals). Three further

signals were at δ 118.2, 120.4, and 123.9, consistent with their originating from unsubstituted carbon atoms of an oxygenated benzene system.[26] In the C–H coupled spectrum the last of these appeared as a sharp doublet (^1J 157 Hz [27]) indicating that the associated carbon atom had no *meta*-neighbour bonded to hydrogen;[27] this resonance is therefore assigned to C-6. The resonances at δ 120.4 and 118.2 each gave quartets (^1J 157, ^3J 5.6 and ^1J 157, ^3J 5.3 Hz, respectively) consistent with their being derived from C-3 and C-5.[27] On the basis of the shielding effects of oxygenated substituents on benzene rings on *ortho*- and *para*-carbon atoms [26] it would be anticipated that C-3 would resonate upfield from C-5, but the non-additivity of substituent effects [28] makes this assignment uncertain.

The dibenzoylmonotoluene-*p*-sulphonates (1), (3), and (4) showed similar u.v. spectra with maxima at 273 nm (ε 1 950 ± 100, EtOH), less intense peaks at 266 and 280 nm, and well defined minima at 258 nm; however, in the spectrum of the triester (7) the absorptions at 266, 273, and 280 nm were visible only as shoulders on the side of the allowed $\pi \rightarrow \pi^*$ band of the phenolic chromophore. This is consistent with expectations based on the presence of a trihydric phenol triester, since phloroglucinol triacetate has $\lambda_{max.}$ at 267 nm (ε 42 100).[29]

EXPERIMENTAL

Methyl 3,4-*Di*-O-*benzoyl*-2,6-*di*-O-*toluene*-p-*sulphonyl*-α-D-*glucopyranoside*.—Methyl α-D-glucopyranoside (25 g) in pyridine (500 ml) was set aside overnight with toluene-*p*-sulphonyl chloride (50 g, 2.0 mol equiv.). Benzoyl chloride (50 ml) was then added and after a further day the mixture was poured onto ice to give an oil which crystallised on standing. Recrystallisation from methanol gave the dibenzoylditoluene-*p*-sulphonate (35 g, 38%), m.p. 190—191 °C; $[\alpha]_D$ +22.5° (*c* 2.5, $CHCl_3$) [lit.,[17a] m.p. 189—190 °C, $[\alpha]_D$ +25.9° ($CHCl_3$)].

Methyl 3,4-*Di*-O-*benzoyl*-6-*deoxy*-6-*iodo*-2-O-*toluene*-p-*sulphonyl*-α-D-*glucopyranoside*.—The ditoluene-*p*-sulphonate (25 g) was heated in refluxing acetic anhydride (50 ml) for 4 h with sodium iodide (25 g). After removal of the solids and the solvent, the residue was taken up in chloroform (200 ml), washed with aqueous sodium thiosulphate and then water; the solution was then dried and solvent removed to give a solid residue, which was recrystallised from methanol to give the iodo-compound (20 g, 88%), m.p. 179—180 °C; $[\alpha]_D$ +32° (*c* 3.0, $CHCl_3$) (lit.,[17c] m.p. 179.5°, $[\alpha]_D$ +40°). N.m.r. data were consistent with those reported in the literature.[17c]

Methyl 3,4-*Di*-O-*benzoyl*-6-*deoxy*-2-O-*toluene*-p-*sulphonyl*-α-D-xylo-*hex*-5-*enopyranoside* (1).—The iodo-compound (20 g) was shaken with silver fluoride (20 g) in dry pyridine (100 ml) for 2 h. The dark suspension was then poured into ether (1.5 l), and washed with aqueous sodium thiosulphate and then water. After drying of the solution, the solvent was distilled off, traces of pyridine being removed under high vacuum. The residual oil crystallised immediately on trituration with methanol, and recrystallisation from ether–light petroleum (b.p. 60—80 °C) gave the *olefin* (12.2 g, 76%), m.p. 132—133 °C; $[\alpha]_D$ +24° (*c* 1.3, $CHCl_3$) (Found: C, 62.5; H, 4.9; S. 6.2. $C_{28}H_{26}O_9S$ requires C, 62.45; H, 4.8; S, 5.9%); see the Table for the ^1H n.m.r. data.

Methyl 3,4-*Di*-O-*benzoyl*-6-*deoxy*-5-C-*methoxy*-2-O-*toluene*-p-*sulphonyl*-β-D-*glucopyranoside* (3).—The olefin (3.0 g) was heated in a refluxing mixture of methanol (40 ml) and acetyl chloride (3.2 ml) for 1.5 h. Removal of the solvent gave a crystalline residue which, on recrystallisation from methanol, afforded the *dimethoxy-compound* (2.2 g, 69%), m.p. 152—153 °C; $[\alpha]_D$ −95.5° (*c* 2.5, $CHCl_3$) (Found: C, 61.1; H, 5.2; S, 5.8. $C_{29}H_{30}O_{10}S$ requires C, 61.0; H, 5.3; S, 5.6%); see the Table for ^1H n.m.r. data.

2L-2,4,5/3-2,3-*Dibenzoyloxy*-5-*hydroxy*-4-*toluene*-p-*sulphonyloxycyclohexanone* (4) [30].—The olefin (1) (10 g) and mercury(II) chloride (5 g, 1 mol equiv.) were heated under reflux in aqueous acetone (250 ml, 1 : 2) for 4.5 h. On cooling, the product crystallised as silky threads. Filtration gave the *cyclohexanone derivative* (6.1 g) [further material (total 8.1 g, 83%) was obtained by addition of water (100 ml) to the reheated filtrate] which was recrystallised twice from methanol, m.p. 175—176 °C; $[\alpha]_D$ +10° (*c* 2.0, C_5H_5N) (Found: C, 61.6; H, 4.5; S, 6.2. $C_{27}H_{24}O_9S$ requires C, 61.8; H, 4.6; S, 6.1%); see the Table and text for ^1H n.m.r. data; ^{13}C n.m.r. data: δ(C_5D_5N) 198.4 (C-1); 165.65, 165.5 (ester carbonyl); 145.15 (C-1 of sulphonate ring); 134.1—123.8 (other aromatic carbons); 82.05, 78.1, 71.4, 67.8 (C-2—C-5); 44.8 (C-6); and 21.3 (Me).

The olefin (0.5 g) was heated under reflux in acetone (9 ml) and aqueous hydrochloric acid (4 ml, 0.5M) for 5 h. On cooling of the solution, the starting material crystallised and the mother liquors were found by t.l.c. to contain no hydroxyketone (4), but instead contained small amounts of a less mobile product (presumably the 6-deoxy product of acid-catalysed hydrolysis).

2L-2,4/3-2,3-*Dibenzoyloxy*-4-*toluene*-p-*sulphonyloxycyclohex*-5-*enone* (5).[30]—The hydroxyketone (8 g) in pyridine (160 ml) and acetic anhydride (40 ml) was set aside at room temperature for 15 h. The mixture was then poured onto ice (1 l) to give a solid which was recrystallised twice from methanol; the *enone* (3.8 g, 50%) had m.p. 144—145 °C; $[\alpha]_D$ +17° (*c* 1.7, $CHCl_3$) (Found: C, 63.8; H, 4.3; S, 6.3. $C_{27}H_{22}O_8S$ requires C, 64.0; H, 4.3; S, 6.3%); see the Table and text for ^1H n.m.r. data; ^{13}C n.m.r. data: δ($CDCl_3$) 189.3 (C-1); 165.3 and 164.5 (ester carbonyl); 145.3 (C-5); 145.0 (C-1 of sulphonate ring): 133.5—127.8 (other aromatic carbons and C-6); 77.2, 74.6, and 71.8 (C-2—C-4) and 21.6 (Me). The chemical shifts for C-3 and C-2 of cyclohex-2-enone are δ 150.7 and 129.3, respectively.[31]

(2-*Benzoyloxy*-4-*toluene*-p-*sulphonyloxy*)*phenyl Acetate* (7).—Treatment of the enone (0.96 g) in benzene (20 ml) with 1,5-diazabicyclo[5.4.0]undec-5-ene (0.302 g, 1.05 mol equiv.) in benzene (5 ml) caused 99% loss of optical activity of the solution within 10 min. It was then washed with water (2 × 20 ml) and dried and the solvent was removed to leave the phenol (6) as a colourless syrup (0.694 g, 96%). Acidification of the aqueous washings with hydrochloric acid and evaporation of the water gave a solid-containing residue. The solid was removed by addition of a small volume of water and characterised (m.p. and i.r.) as benzoic acid. The phenol was homogeneous on t.l.c. plates (R_F 0.3 in $CHCl_3$ on silica gel; R_F of the enone, 0.6). It was dissolved in pyridine (5 ml) and acetic anhydride (3 ml) and set aside for 16 h. The solution was poured onto ice (25 g), and after 2 h the precipitated oil was extracted into chloroform (25 ml). After drying, the chloroform was removed and the product crystallised from ether–light petroleum (b.p. 60—

80 °C) at 4°. Recrystallised from this solvent the *phenolic triester* (0.3 g, 37%) had m.p. 76—77 °C (Found: C, 62.1; H, 4.2; S, 7.4. $C_{22}H_{18}O_7S$ requires C, 62.0; H, 4.2; S, 7.5%); see text for n.m.r. data.*

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REFERENCES

[1] Part 20; R. J. Ferrier and R. H. Furneaux, *J.C.S. Perkin I*, 1977, 1993.
[2] T. Sasaki, K. Minamoto, and H. Suzuki, *J. Org. Chem.*, 1973, **38**, 598; T. Adachi, T. Iwasaki, M. Miyoshi, and I. Inoue, *J.C.S. Chem. Comm.*, 1977, 248.
[3] R. L. Whistler and L. W. Doner, *J. Org. Chem.*, 1973, **38**, 2900.
[4] R. J. Ferrier and V. K. Srivastava, *Carbohydrate Res.*, 1977, **59**, 333.
[5] D. E. Kiely and H. G. Fletcher, jun., *Ann. New York Acad. Sci.*, 1969, **165**, 559.
[6] J. M. Grosheintz and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 1948, **70**, 1479.
[7] D. E. Kiely and H. G. Fletcher, jun., *J. Amer. Chem. Soc.*, 1968, **90**, 3289; *J. Org. Chem.*, 1969, **34**, 1386.
[8] A. P. Kaplun, V. A. Basharuli, V. E. Kalugin, V. K. Shvets, and R. P. Evstigneeva, *Tr. Mosk. Inst. Tonkoi Khim. Tekhnol.*, 1975, **5**, 82 (*Chem. Abs.*, 1977, **86**, 90, 168p).
[9] D. E. Kiely and W. R. Sherman, *J. Amer. Chem. Soc.*, 1975, **97**, 6810.
[10] *E.g.* T. Iida, M. Funabashi, and J. Yoshimura, *Bull. Chem. Soc. Japan*, 1973, **46**, 3203, 3207; J. Kovář and H. H. Baer, *Carbohydrate Res.*, 1975, **45**, 161.
[11] F. W. Lichtenthaler, *Angew. Chem. Internat. Edn.*, 1964, **3**, 211.
[12] K. Tanado, Y. Emori, M. Ayabe, and T. Suami, *Bull. Chem. Soc. Japan*, 1976, **49**, 1108.
[13] K. Tanado, T. Shiratori, and T. Suami, *Bull. Chem. Soc. Japan*, 1976, **49**, 3193.
[14] I. Dyong and R. Bonn, *Chem. Ber.*, 1973, **106**, 944.
[15] D. E. Kiely and C. E. Cantrell, *Carbohydrate Res.*, 1972, **23**, 155; C. E. Cantrell, D. E. Kiely, G. J. Abruscato, and J. M. Riordan, *J. Org. Chem.*, 1977, **42**, 3562.
[16] C. E. Cantrell, D. E. Kiely, R. A. Hearn, and C. E. Bugg, *Tetrahedron Letters*, 1973, 4379; see also H. J. Bestmann and H. A. Heid, *Angew. Chem. Internat. Edn.*, 1971, **10**, 336 for syntheses of shikimic acid and quinic acid which use a ring-closure undergone by 2,3,4-tri-*O*-benzyl-1,5-di-*O*-toluene-*p*-sulphonyl-D-arabinitol when treated with methylenetriphenylphosphorane.
[17] (*a*) J. J. Willard, J. Sadowski, and W. Vitale, *Canad. J. Chem.*, 1963, **41**, 1223; (*b*) J. Jarý, K. Čapek, and J. Kovár, *Coll. Czech. Chem. Comm.*, 1964, **29**, 930; (*c*) H. B. Sinclair and L. W. Tjarks, *Carbohydrate Res.*, 1971, **19**, 402.
[18] J. Lehmann, E. Pfeiffer, and H. Reinshagen, *Chem. Ber.*, 1969, **102**, 2745.
[19] K. Takiura and S. Honda, *Carbohydrate Res.*, 1972, **23**, 369; F. Gonzalez, S. Lesage, and A. S. Perlin, *ibid.*, 1975, **42**, 267.
[20] J. R. Coad and M. D. Johnson, *J. Chem. Soc.* (*B*), 1967, 633.
[21] T. M. Cheung, D. Horton, and W. Weckerle, *Carbohydrate Res.*, 1977, **59**, 276.
[22] L. N. Ferguson and D. R. Paulson, ' Highlights of Alicyclic Chemistry,' vol. 2, Franklin, Inc., Palisade, New Jersey, 1977, p. 37.
[23] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon Press, Oxford, 1969, p. 188.
[24] E. W. Garbisch, *J. Amer. Chem. Soc.*, 1964, **86**, 5561; R. J. Ferrier, *Adv. Carbohydrate Chem.*, 1969, **24**, 199.
[25] W. Meyer zu Reckendorf, *Chem. Ber.*, 1968, **101**, 3652.
[26] G. C. Levy and G. L. Nelson, ' ^{13}C Nuclear Magnetic Resonance for Organic Chemists,' Wiley–Interscience, New York, 1972, p. 81.
[27] F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, 1967, **89**, 2967.
[28] A. F. Erasmuson, R. J. Ferrier, N. C. Franca, H. E. Gottlieb, and E. Wenkert, *J.C.S. Perkin I*, 1977, 492.
[29] T. W. Campbell and G. M. Coppinger, *J. Amer. Chem. Soc.*, 1951, **73**, 2708.
[30] For nomenclature see *Biochem. J.*, 1976, **153**, 23.
[31] Ref. 26, p. 67.

Note added in proof:* A recent review (B. Ganem, *Tetrahedron*, 1978, **34, 3353) outlines both chemical and biochemical conversions of carbohydrate derivatives into cyclohexane-based compounds related to shikimic acid. The reaction described above by which the cyclohexanone (4) is formed is analogous to that proposed for the ring-closure step in the conversion of 3-deoxy-D-*arabino*-heptulosonic acid 7-phosphate into 3-dehydroquinic acid (P. Le Maréchal and R. Azerad, *Compt. rend.*, 1974, **278**, 1251).