Carbohydrate Research, 124 (1983) 215–224
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

A RAPID, STEREOSELECTIVE SYNTHESIS OF FLUORINATED CARBOHYDRATES: ADDITION OF ACETYL HYPOFLUORITE TO VINYL ETHER DERIVATIVES OF SUGARS*

MICHAEL J. ADAM†, BRIAN D. PATE,
TRIUMF and UBC/TRIUMF Programme on Positron Emission Tomography, University of British Columbia, Vancouver V6T 2A3 (Canada)

JEAN-RICHARD NESSER‡, AND LAURANCE D. HALL
Department of Chemistry, University of British Columbia, Vancouver V6T 1Y6 (Canada)
(Received June 28th, 1983; accepted for publication, July 27th, 1983)

ABSTRACT

Acetyl hypofluorite has been added to six unsaturated carbohydrates that contain a vinyl ether moiety. All reactions were rapid (<5 min at −78°) and gave, with one exception, high yields of isomerically pure products. The hypofluorite was shown to add exclusively in the *cis* mode, with a strong tendency to attack on a particular "face" of the double bond. As well as the syntheses, n.m.r. data and favored conformations of the fluorinated products are discussed.

INTRODUCTION

The synthesis of fluorinated carbohydrates has been a very active area for many years, principally because of the interesting biological properties associated with these compounds[2–4]. Recently, there has been a renewed interest, because of the use of 2-deoxy-2-[^{18}F]fluoro-D-glucose, a proven D-glucose analog[5], as an imaging agent in studies of regional, cerebral, D-glucose metabolism by positron-emission tomography (PET)[6].

Previous electrophilic routes to fluorinated carbohydrates, such as the addition of trifluoromethyl hypofluorite[7] (CF_3OF), elemental fluorine[8], and xenon difluoride[9] to glycals, are less than ideal. Generally, yields of products are low, and the reactions lead to mixtures of isomeric products, and to difluorinated compounds. These approaches have further disadvantages in the context of ^{18}F-

*For a preliminary communication, see ref. 1.
†To whom correspondence should be addressed.
‡Current address: Research Department, NESTEC S.A., Lausanne, Switzerland.

0008-6215/83/$ 03.00

radiolabelling, in that these reagents, with the exception of F_2, are difficult to produce* routinely with ^{18}F.

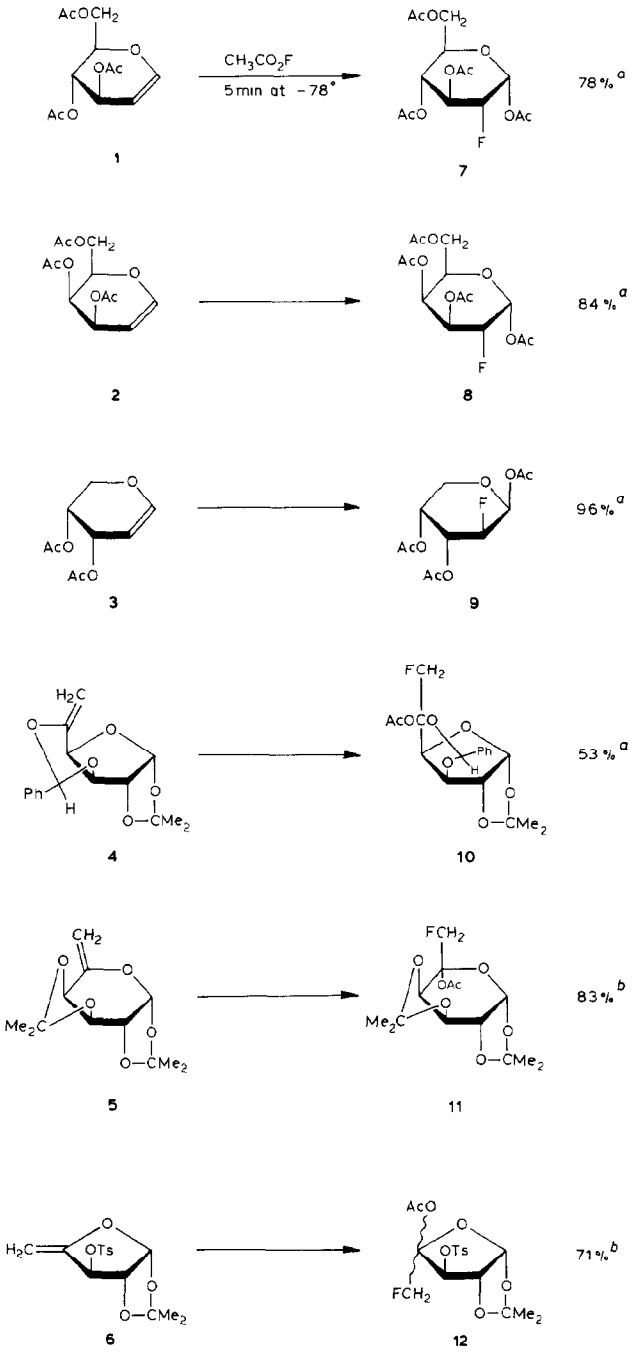
Prompted by a recent report[10] of a simple preparation of acetyl hypofluorite ($MeCO_2F$) from F_2, we have investigated the reaction of this electrophilic fluorinating agent with a number of unsaturated sugars (**1–6**). These substrates impart various degrees of steric hindrance with regard to attack by the incoming acetyl hypofluorite on a particular face of the double bond. In all but one case, that of compound **6**, a favored face can be determined; hence, information about the stereoselectivity of acetyl hypofluorite can be obtained. N.m.r. data and favored conformations for the fluorinated products are also discussed.

RESULTS AND DISCUSSION

Synthesis. — There is precedent in the literature for the exclusive, *cis* addition of acetyl hypofluorite to such unsaturated systems as stilbenes[10]. The addition of acetyl hypofluorite to sugars **1, 2,** and **3** also occurs in the *cis* mode, to give the fluorinated sugars **7, 8,** and **9** (see Scheme 1). This behavior is not unique in itself, as other electrophilic fluorinating agents, including CF_3OF, are known to add to unsaturated sugars to give *cis* products exclusively. However, the addition of acetyl hypofluorite to **1, 2,** and **3**, as well as to the terminal double-bonds in **4, 5,** and **6**, reveals a greater degree of stereoselectivity, because these reactions not only afford *cis* products, but also involve addition to a favored face of the double bond. Thus, reaction of $MeCO_2F$ at $-78°$ with **1, 2,** and **3** occurs exclusively by *cis* addition to the less-hindered face, to give the isomerically pure products **7, 8,** and **9** in 78, 84, and 96% yield, respectively, in <5 min; in each case, the other isomer was not detected in the final mixture. Essentially all three of these products could be crystallized directly from the reaction mixtures, after washing of the organic layer, and evaporation. The 2-fluoro-D-glucose derivative **7** required further purification, either by column chromatography or recrystallization, to remove impurities having lower R_F values (see Experimental section). Compounds **7** and **8**, as shown by the ^1H-n.m.r. data (see Table I), have the α-anomeric configuration. Surprisingly, these compounds have never been fully characterized, as they were previously synthesized only as either an α,β mixture, or in pure β-anomeric form, by acetylation of the "free" 2-fluoro sugars[7,11]. In the context of PET chemistry, this method constitutes a significant improvement in the synthesis of 2-deoxy-2-fluoro-D-glucose, and is currently being used[12] at some PET centers to synthesize ^{18}F-2FDG.

Addition of $MeCO_2F$ to the terminal double-bonds in **4, 5,** and **6**, although not quite so stereospecific as the previous examples, is also highly selective, and generally occurs in high yield (see Scheme 1). Compound **10** was obtained in the lowest yield (53%), in isomerically pure form after column chromatography. Of

*Although the use of $[^{18}F]F_2$ has become routine in the production of 2-deoxy-2-[^{18}F]fluoro-D-glucose, only ~10% of the ^{18}F used is incorporated into the desired product[20].



Scheme 1 [Key. [a]Isolated yields in pure form [b]Isolated yields after column chromatography; contaminated with a minor by-product (see text)]

the crude reaction-mixture, ~22% by weight contains two by-products having lower R_F values. From the n.m.r. spectra (^1H and ^{19}F), it appears that neither of these is a simple, isomeric form of **10**, and may, instead, be the result of the addition of fluorine to the terminal carbon atom (C-6) of the double bond, and addition of the acetate to the asymmetric, tertiary carbon atom of the benzylidene group, followed by ring opening, and formation of a carbonyl group at C-5*.

Reaction of $MeCO_2F$ with **5** gives **11** in 83% yield, mixed with a by-product after purification by column chromatography; ^1H-n.m.r. spectroscopy of this column-purified material revealed the anomeric ratio of the mixture to be 93:7. Although the by-product was not positively identified, the n.m.r. spectrum and the similar chromatographic behavior strongly suggest that this is the other *cis* isomer; if this is so, the aforementioned ratio gives the relative ease of addition of $MeCO_2F$ to the two faces of the double bond. Fortunately, a second columnar purification gave a sample of **11** in analytically pure form. Similarly, $MeCO_2F$ reacts with **6** to give, after chromatography, 71% of a crystalline mixture (87:13) of **12** and a by-product. The major compound (**12**) was further purified by recrystallization. Again, although the by-product was not positively identified, it appears from the n.m.r. spectrum that this is the other *cis* isomer.

Owing to the variable production yields of $MeCO_2F$, and the difficulties in its quantification, it was deemed prudent to use an ~2-fold excess of the hypofluorite. However, separate experiments showed that, when a known 1:1 ratio of **1** to the hypofluorite is used, the product yield is unaffected, and the proportion of impurities is also the same. From this result, it seems reasonable to conclude that an excess of $MeCO_2F$ does not cause the overfluorination problems that normally result when an excess of F_2 is used as the fluorinating agent.

N.m.r. spectroscopy, and proof of structure, of 2-deoxy-2-fluoro derivatives. — Examination of the ^{19}F chemical-shift values for compounds **7–9** (see Table I) immediately shows that all are secondary fluorine-containing derivatives[13]. Furthermore, the values of $J_{F2,H2}$ in these three cases are compatible only with a geminal ^2J value[13]. Analysis of the $^3J_{H,H}$, $^3J_{F,H}$, and long-range $J_{F,H}$ values (see Table I) permits unambiguous assignments of the configurations at both the C-1 and C-2 centers, together with the conformational assignments depicted. Thus, the $^3J_{F2,H3}$ values are in good agreement with that expected for vicinal, *gauche*-related, coupled nuclei in pyranose derivatives[4], as are the $^3J_{H2,H3}$ values with the expected coupling constant for vicinal, *trans*-diaxially related, coupled protons. In addition, the zero value of $^3J_{F2,H1}$ for compounds **7–9** can be attributed to the high electronegativity of substituents at C-1 and C-2, together with the antiplanar orienta-

*This impurity mixture was not fully characterized; however, its proposed structure is strongly supported by the n.m.r. spectra (^1H and ^{19}F). Similarly, there are good analytical data (n.m.r.-spectral, elemental analysis, and m.s.) that suggest that the major impurity resulting from the reaction of $MeCO_2F$ with **1** is formed by the normal addition of fluorine to C-2, accompanied by addition of the acetate group, not to C-1, but to C-5. This yields the acyclic sugar in the hydrated-aldehyde form, with fluorine at C-2 and acetates at C-3,4,5 and 6.

TABLE I

N.M.R. DATA FOR COMPOUNDS **7–12**[a]

Compound	*^{1}H Chemical shifts*[b]							
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*OAc*	*CMe_2*
7	6.42	4.66	5.55	5.09	4.09	Ha 4.06 Hb 4.29	2.05;2.08; 2.09;2.21	—
8	6.47	4.90	5.41	5.52	4.32	4.09	2.04;2.06; 2.15;2.19;	—
9[d]	6.44	4.92	(5.38–5.46)		Ha 3.80 Hb 4.03	—	2.09;2.15; 2.18	—
10[e]	6.02	4.66	4.23 or 4.62	4.23 or 4.62	—	Ha 4.90 Hb 5.13	2.19	1.35;1.54
11	5.55	4.13	4.52 or 4.62	4.52 or 4.62	—	Ha 4.69 Hb 5.13	2.07	1.35;1.39; 1.44;1.48
12[f]	6.08	4.83	5.28	—	Ha 4.48 Hb 4.73	—	2.05	1.32;1.54

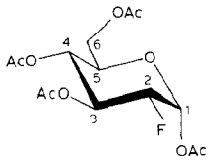
Table I (continued)

Compound	*^{19}F Chemical*[c] *shifts*	*Coupling constants* ($J_{H,H}$)					
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6a,6b}$
7	202.8	4.0	9.6	9.6	10.0	$J_{5,6a}$ 2.3 $J_{5,6b}$ 4.1	12.5
8	207.1	3.9	10.2	1.2	3.4	6.5 (virtual)	6.5 (virtual)
9[d]	207.8	3.7	9.3	?	$J_{4,5a}$ ~1.5 $J_{4,5b}$ 0	—	—
10[e]	240.2	3.4	0	~0	—	—	9.7
11	236.0	3.9	0	6.2	—	—	9.6
12[f]	236.1	3.8	0	—	—	—	—

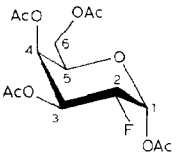
Table I (continued)

Compound	*Coupling constants* ($J_{F,H}$)
7	$J_{F2,H1}$ 0, $J_{F2,H2}$ 48.5, $J_{F2,H3}$ 12.1
8	$J_{F2,H1}$ 0, $J_{F2,H2}$ 49.1, $J_{F2,H3}$ 10.8, $J_{F2,H4}$ 3.5
9[d]	$J_{F2,H1}$ 0, $J_{F2,H2}$ 48.4, $J_{F2,H3}$ $J_{F2,H4}$ 5–7, $J_{F2,H5a}$ 1.5
10[e]	$J_{F6,H6a}$ 45.1, $J_{F6,H6b}$ 46.7
11	$J_{F6,H6a}$ 46.0, $J_{F6,H6b}$ 46.8
12[f]	$J_{F5,H5a}$ 45.7, $J_{F5,H5b}$ 46.4

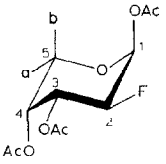
[a]In $CDCl_3$. [b]In p.p.m. downfield from Me_4Si. [c]In p.p.m relative to external $CFCl_3$. [d]$J_{H5a,H5b}$ 13.2 Hz. [e]≥C*H*-Ph, 5.88 p.p.m.; ≥*CH*-Ph, 7.35–7.47 p.p.m. [f]-SO_2-*Ph*-Me, 7.39–7.86 p.p.m.; -SO_2-Ph-*Me*, 2.48 p.p m., $J_{H5a,H5b}$ 10.1.



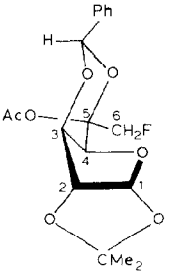
7



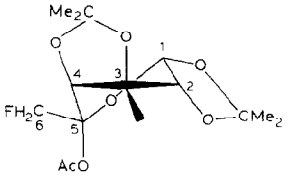
8



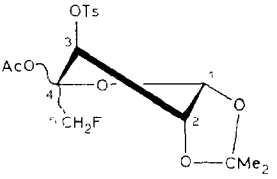
9



10



11



12

tion between the C-2–F-2 and C-1–O-5 bonds[7,14]. Finally, it is interesting that the $^4J_{F2,H4}$ value for long-range coupling for compounds **8** and **9** occurs *via* "W-coplanar" coupling routes; similarly, the $^5J_{F2,H5a}$ value observed in the p.m.r. spectrum of **9** can be rationalized by the existence of two different coupling routes, each of them implying two groups of three coplanar bonds.

N.m.r. spectroscopy, and proof of structure, of fluorinated, primary-center derivatives. — Again, examination of the ^{19}F chemical-shift values, together with the $^2J_{F,Ha}$ and $^2J_{F,Hb}$ geminal values, for compounds **10–12** (see Table I) clearly shows that all are primary, fluorine-containing derivatives[13]. Configurational assignment for a quaternary center is probably one of the problems that n.m.r. spectroscopy cannot readily solve in the structural analysis of small molecules. For this reason, configurational assignment of C-5 for compounds **10** and **11** is proposed on the basis of the following chemical evidence. Both of the vinyl ether starting-derivatives (**4** and **5**) are well known to undergo hydrogenation to give two products, one of which is strongly favored[15], because the 3,4-*cis*-fused, bicyclic systems presented by these substrates define *endo* and *exo* faces with respect to the double bond. Obviously, in such hydrogenations starting from **4** and **5**, the *exo* face is favored. Furthermore, a recent study on hydroboration–halogenation reactions[16], starting from

the same substrates, showed unequivocally that, in both cases, the same *exo* face of these vinyl ether derivatives is favored in these additions.

Considering, now, the results obtained in the synthesis of the 2-deoxy-2-fluoro sugars **7–9**, it is clear that the *cis*-addition of acetyl hypofluorite shows an unusually high degree of selectivity in approach to the less-hindered face of the glycal derivatives **1–3**. The very high susceptibility of acetyl hypofluorite to steric hindrance, together with previous results on the stereochemistry of other *cis*-addition reactions (hydrogenation or hydroboration) to the double bond of **4** and **5**, both provide strong evidence supporting the configurational assignment of C-5 for compounds **10** and **11**, as resulting from attack by acetyl hypofluorite on the *exo* face of each of the (vinyl ether) starting-derivatives **4** and **5**.

Because inspection of a Dreiding model of **6** did not indicate a favored direction for attack on the double bond, and because no previous study of *cis*-addition to this substrate has been reported, we have not assigned the configuration of C-4 in **12**.

Analysis of the $^3J_{H,H}$ values for compounds **10–12** permits assignment of the favored conformations depicted. Interestingly, the conformations of compounds **10** and **11** allow an equatorial orientation of the -CH_2F substituent on C-5 and an axial one for the -OAc substituent on the same carbon atom. In this regard, the $^1S_5$(D) conformer (assigned on the basis of the zero value of $J_{2,3}$) of **11** allows the maximum distance between O-1 and OAc-5.

EXPERIMENTAL

General. — Melting points were determined either on a hot stage, or a capillary–oil bath instrument, and are uncorrected. The $[\alpha]_D$ values were determined with a Perkin–Elmer 241 MC polarimeter. ^{1}H-N.m.r. spectra were recorded with a homebuilt, 270-MHz, pulse Fourier-transform, n.m.r. spectrometer. All chemical shifts are reported in parts per million downfield from Me_4Si. ^{19}F-N.m.r. spectra were recorded with a Varian XL-100 spectrometer, and chemical shifts are given relative to Freon-11 ($CFCl_3$).

Tri-*O*-acetyl-D-glucal (**1**) was purchased from Aldrich Chemical Co., Milwaukee, WI. Tri-*O*-acetyl-D-galactal (**2**) was purchased from Terochem. Laboratories, Ltd., Edmonton, Canada, and was distilled before use. Di-*O*-acetyl-D-arabinal (**3**) was purchased from Raylo Chemical, Ltd., Edmonton, Canada, and was distilled before use. Compound **5** was prepared by the published procedure[17] from the 6-deoxy-6-iodo-D-galactopyranose derivative, and purified by crystallization and sublimation. In the same way, **4** (ref. 18) and **6** (ref. 19) were obtained in good yields by the action of AgF in pyridine on the 6-deoxy-6-iodo-D-glucofuranose and 5-deoxy-5-iodo-D-xylofuranose derivatives, respectively.

General procedure for preparation of acetyl hypofluorite, and of the fluoro sugars (**7–12**). — Acetyl hypofluorite (1.4–2 mmol) was prepared as described by Rozen *et al.*[10]. Sodium acetate (6.8 g, 83 mmol) was added to a stirred solution of

Freon-11 ($CFCl_3$) (180 mL) in glacial acetic acid (20 mL), and the mixture was cooled to −78° under an atmosphere of nitrogen gas. After cooling, F_2 (1% of He) was bubbled through the suspension at ~50 mL/min. After 2 h, the flow of F_2 was stopped, and the mixture was purged with an inert gas for 2 min (to remove any unreacted F_2).

The unsaturated-sugar substrate (0.75 mmol) was then added as a solution in either $CHCl_3$ or $CFCl_3$ (5 mL). After 5 min, the mixture was treated with aqueous KI, and titrated with $Na_2S_2O_3$ to determine the excess of acetyl hypofluorite. After titration, the organic layer was washed successively with saturated Na_2CO_3 and H_2O (twice), dried ($MgSO_4$), filtered, and evaporated to dryness.

1,3,4,6-Tetra-O-*acetyl-2-deoxy-2-fluoro-α*-D-*glucopyranose* (**7**). — After evaporation of the solvent, the organic residue was purified by flash chromatography using 3:2 ether–hexane, to give **7** in 78% (isolated) yield; m.p. 78–79°, $[\alpha]_D^{24}$ +146° (*c* 1, $CHCl_3$); *m/z* 350 (≪1) (M^+), 291 (4), 230 (3), 188 (6), 160 (2), 145 (8), 115 (4), 103 (10), 73 (2), 44 (3), 43 (100), 32 (3), and 28 (14).

Anal. Calc. for $C_{14}H_{19}FO_9$: C, 48.02; H, 5.43. Found: C, 47.99; H, 5.68.

1,3,4,6-Tetra-O-*acetyl-2-deoxy-2-fluoro-α*-D-*galactopyranose* (**8**). — After evaporation of the solvent, the syrup crystallized from 1:1 ether–hexane, to give **8** in 84% yield. An analytical sample was obtained by recrystallization from ethanol; m.p. 126–127°, $[\alpha]_D^{24}$ +150° (*c* 1, $CHCl_3$); *m/z* 291 (5), 230 (2), 188 (7), 160 (3), 145 (6), 130 (3), 117 (3), 115 (3), 103 (8), 73 (2), 44 (2), 43 (100), 32 (6), and 28 (26).

Anal. Calc. for $C_{14}H_{19}FO_9$: C, 48.02; H, 5.43. Found: C, 47.99; H, 5.54.

1,3,4-Tri-O-*acetyl-2-deoxy-2-fluoro-β*-D-*arabinopyranose* (**9**). — After evaporation of the solvent, the organic layer yielded 200 mg (96%) of **9** as a single, pure crystalline compound. An analytical sample was obtained by recrystallization from methanol; m.p. 129–131°, $[\alpha]_D^{24}$ −186.5° (*c* 1, $CHCl_3$); *m/z* 219 (6), 176 (12), 131 (15), 117 (6), 103 (6), 99 (7), 88 (7), 44 (4), 43 (100), 32 (3), and 28 (10).

Anal. Calc. for $C_{11}H_{15}FO_7$: C, 47.49; H, 5.43. Found: C, 47.68; H, 5.35.

5(S)-*5*-C-*Acetoxy-3,5*-O-*benzylidene-6-deoxy-6-fluoro-1,2*-O-*isopropylidene-α*-D-xylo-*hexo-1,4-furanos-5-ulose* (**10**). — After evaporation of the solvent, the organic layer yielded a crude mixture which showed two major spots in t.l.c. Column chromatography on silica with 2:1 hexane–ether as the eluant permitted the isolation of **10** (145 mg, 53%) in the first fraction, and 40 mg of an unresolved mixture of two byproducts in the second fraction. Compound **10** was obtained crystalline after evaporation of the first fraction. Recrystallization from methanol did not improve the micro-analytical results; m.p. 102–104°, $[\alpha]_D^{24}$ +46.39° (*c* 0.8, $CHCl_3$); *m/z* 308 (22), 145 (16), 113 (53), 107 (22), 105 (78), 100 (12), 77 (10), 61 (15), 59 (22), 43 (100), and 28 (16).

Anal. Calc. for $C_{18}H_{21}FO_7$: C, 58.69; H, 5.75. Found: C, 58.30; H, 5.69.

5(R)-*5*-C-*Acetoxy-6-deoxy-6-fluoro-1,2:3,4-di*-O-*isopropylidene-β*-L-arabino-*hexo-1,5-pyranos-5-ulose* (**11**). — After evaporation of the solvent, the organic layer yielded the crude product, which was purified by chromatography on a column of silica, with 3:1 hexane–ether as the eluant; 200 mg (83%) of a syrupy

mixture (93:7) of **11** plus a minor by-product was obtained. An analytically pure sample of **11** was obtained after an additional purification by 101-kPa liquid chromatography in an open column of silica, using 6:1 hexane–ether as the eluant; a syrup; $[\alpha]_D^{24}$ −42.9° (*c* 1.5, $CHCl_3$); *m/z* 305 (12) (M^+ − Me), 203 (13), 145 (12), 117 (8), 113 (14), 103 (37), 100 (32), 97 (8), 85 (13), 61 (9), 59 (24), 43 (100), 41 (8), 31 (8), and 28 (12).

Anal. Calc. for $C_{14}H_{21}FO_7$: C, 52.50: H, 6.61. Found: C, 52.47; H, 6.70.

*4-O-Acetyl-5-deoxy-5-fluoro-1,2-O-isopropylidene-3-O-tosyl-β-*L-threo-*pento-1,4-furanos-4-ulose* (**12**). — After evaporation of the solvent, the organic layer yielded a crude product which was purified by 101-kPa liquid chromatography in an open column of silica, with 2:1 hexane–ether as the eluant; 215 mg (71%) of a crystalline mixture (87:13) of **12** and a minor by-product was obtained. An analytically pure sample of **12** was obtained by recrystallization from methanol; m.p. 84–85°, $[\alpha]_D^{24}$ −83.2° (*c* 0.6, $CHCl_3$); *m/z* 389 (18) (M^+ − Me), 347 (8), 287 (7), 213 (7), 175 (17), 155 (59), 90 (34), 87 (7), 71 (7), 65 (7), 59 (18), 43 (100), 32 (10), and 28 (29).

Anal. Calc. for $C_{17}H_{21}FO_8S$: C, 50.49; H, 5.23. Found: C, 50.35; H, 5.14.

ACKNOWLEDGMENTS

We thank several funding agencies for their generous support: The Medical Research Council of Canada and the Mr. & Mrs. P. A. Woodward's Foundation (operating grants to B.D.P. and M.J.A.), the Fonds National Suisse de la Recherche Scientifique (a grant to J.-R.N.), and the Natural Sciences and Engineering Research Council of Canada (A 1905, to L.D.H.). It is a pleasure also to thank Salma Jivan for her capable, experimental assistance, and Mr. K. F. Damji for helping to prepare some of the unsaturated sugars.

REFERENCES

1 M. J. ADAM, *J. Chem. Soc., Chem. Commun.*, (1982) 730–731.
2 A. B. FOSTER AND J. H. WESTWOOD, *Pure Appl. Chem.*, 35 (1973) 147–168.
3 P. W. KENT, *Ciba Found. Symp. Carbon Fluorine Compd.*, Elsevier, New York, 1972, pp. 169–238.
4 A. A. E. PENGLIS, *Adv. Carbohydr. Chem. Biochem.*, 38 (1981) 195–285.
5 M. REIVICH, D. KUHL, A. P. WOLF, J. GREENBERG, M. E. PHELPS, T. IDO, V. CASELLA, J. S. FOWLER, E. HOFFMAN, A. ALAVI, P. SOM, AND L. SOKOLOFF, *Circ. Res.*, 44 (1979) 127–137.
6 A. P. WOLF, *Semin. Nucl. Med.*, 11 (1981) 2–12; M. E. PHELPS, *ibid.*, 32–49.
7 J. ADAMSON, A. B. FOSTER, L. D. HALL, R. N. JOHNSON, AND R. H. HESSE, *Carbohydr. Res.*, 15 (1970) 351–359.
8 T. IDO, C. N. WAN, J. S. FOWLER, AND A. P. WOLF, *J. Org. Chem.*, 42 (1977) 2341–2342.
9 W. KORYTNYK AND S. VALENTEKOVIC-HORVAT, *Tetrahedron Lett.*, (1980) 1493–1496.
10 S. ROZEN, O. LERMAN, AND M. KOL, *J. Chem. Soc., Chem. Commun.*, (1981) 443–444.
11 J. ADAMSON AND D. M. MARCUS, *Carbohydr. Res.*, 22 (1972) 257–264.
12 C. SHIUE, P. A. SALVADORI, A. P. WOLF, J. S. FOWLER, AND R. R. MACGREGOR, *J. Nucl. Med.*, 23 (1982) 899–903.
13 L. D. HALL, *High Resolution Nuclear Magnetic Resonance Spectroscopy*, in W. PIGMAN AND D. HORTON (Eds.), *The Carbohydrates: Chemistry/Biochemistry*, 2nd edn., Vol. IB, Academic Press, New York, 1980, pp. 1299–1326.

14 J. ADAMSON, A. B. FOSTER, L. D. HALL, AND R. H. HESSE, *J. Chem. Soc., Chem. Commun.*, (1969) 309–310.
15 R. J. FERRIER, *Unsaturated Sugars*, in ref. 13, pp. 843–879.
16 J.-R. NESSER, L. D. HALL, AND J. A. BALATONI, *Helv. Chim. Acta*, 66 (1983) 1018–1027.
17 B. HELFERICH AND E. HIMMEN, *Ber.* 62 (1929) 2136–2141.
18 A. S. MEYER AND T. REICHSTEIN, *Helv. Chim. Acta*, 29 (1946) 139–152.
19 L. HOUGH, R. KAHN, AND B. A. OTTER, in *Deoxy Sugars, Adv. Chem. Ser.*, 74 (1968) 120–140.
20 J. S. FOWLER, R. R. MACGREGOR, A. P. WOLF, A. A. FARRELL, K. I. KARLSTROM, AND T. J. RUTH, *J. Nucl. Med.*, 22 (1981) 376–380.