Anionic Activation in Polymer-supported Reactions. Part 2.[1] Stereochemical Studies on the Introduction of Fluorine at Chiral Centres and in Biologically Significant Molecules

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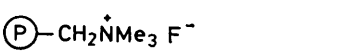
(F^-) Anion exchange resins used as a polymer-supported reagent are a source of 'naked' fluoride and give rise to clean S_N2 reactions as shown by the preparation of epimerically pure 3-fluoro-steroids and of both diastereoisomers of ethyl 2-fluoropropionate. Fluoro-sugars are also prepared from the corresponding toluene-*p*-sulphonates. The remaining water of the resin enhances the basic behaviour of F^-, as in phase-transfer catalyst techniques, but careful dehydration drives the reaction to clean substitution.

THE more recent methods for the preparation of organofluorine compounds involve the reaction of alkyl halides or methanesulphonates with either potassium fluoride under severe phase-transfer conditions in the presence of phosphonium salts [2] or with crown ethers.[3] The use of expensive reagents such as silver(I) or mercury(II) fluorides has also been reported.[4] Fluoro-derivatives have also been prepared by the replacement of hydroxy groups with fluoroalkylamines (FAR),[5] dialkylaminosulphur fluorides,[6] and polyhydrogen fluoride–pyridine,[7] or *via* electrophilic addition of fluorine, hypofluorites, or polyhydrogen fluoride–pyridine.[5,7]

However none of these methods seems to be of general applicability for the synthesis of optically active organofluorine compounds, which are of particular interest in view of their physiological activity.[8]

We have recently reported [1] the use of anion exchange resins as carriers of nucleophilic species. This technique combines the advantage of performing a reaction on a solid phase with the advantages obtained under phase transfer conditions. We now give further examples of the preparation of some monofluoro-derivatives by the substitution reaction of several bromide and sulphonate derivatives with fluoride ion on Amberlite IRA 900 (1a) and Amberlyst-A 26 (1b) anion exchange resins (1). Quaternary ammonium halides in aprotic solvents are known to give rise to an order of nucleophilicity for the halide ions which parallels their electronegativities, *i.e.* $F^- > Cl^- > Br^- > I^-$.[9]

A further advantage of the resin (1) is that among all anions, fluoride exhibits the lowest affinity towards the resin,[10] and the higher affinity of the leaving group X^-



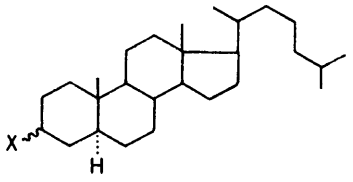
(1)

for the resin provides an additional driving force for the substitution reaction (1). Our interest has been focused

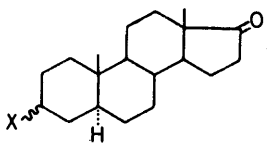
$$F^-\ (\text{resin}) + RX \longrightarrow R\text{–}F + X^-\ (\text{resin}) \quad (1)$$

on the stereochemical aspects of substitution at an asymmetric carbon atom.

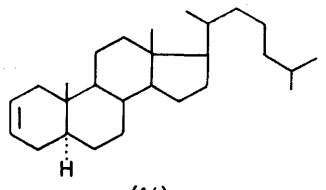
When the diastereoisomerically pure 5α-cholestan-3β-yl (2) and -3α-yl (3) methanesulphonates were treated with (1) in toluene at 100 °C, the epimeric 3α- (4) and 3β-fluoro-5α-cholestanes (5) were obtained in 32 and



(2) X = 3β-MsO
(3) X = 3α-MsO
(4) X = 3α-F
(5) X = 3β-F
(6) X = 3β-TsO
(7) X = 3β-HO
(8) X = 3α-HO
(9) X = 3α-Cl



(10) X = 3α-MsO
(11) X = 3β-MsO
(12) X = 3β-F
(13) X = 3α-F



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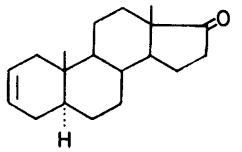


(15)

Ms = methanesulphonyl ; Ts = toluene-*p*-sulphonyl

20% yield, respectively. The values of the optical rotations of (4) and (5) (see Experimental section) were reproducible in our hands but substantially lower than those reported previously.[11,12] The best method to ascertain the diastereoisomeric purity of 3α- and 3β-fluorocholestane was found to be ^1H n.m.r. spectroscopy at 270 MHz. The ^1H n.m.r. spectrum of (5) showed a double multiplet for 3-H centred at δ 4.46, $^1J_{HF}$ 50.7, $J_{H_{ax}-H_{ax}}$ 10, $J_{H_{ax}-H_{eq}}$ 4 Hz. The spectrum of (4) exhibited two broad peaks for 3β-H, centred at

δ 4.80, $^1J_{HF}$ 48.6, $W_{1/2}$ 5.7 Hz. No appreciable amount (<3%) of epimeric impurity was found in either (4) or (5).

The axial and equatorial positions of the fluorine atoms in (4) and (5), respectively, have been confirmed by ^{19}F n.m.r. spectroscopy. The F resonance in (4) occurs at higher field than the corresponding signal in (5).

Nucleophilic substitution by (1) was accompanied by elimination to give cholest-2-ene (14), identified by its physical properties and its i.r. spectrum (see Experimental section). As expected, the elimination : substitution ratio increased with temperature, and the amount of olefin formed was higher starting from the axial ester (3).

In an ancillary experiment 5α-cholestan-3β-yl methanesulphonate (2) was treated with Amberlite IRA (Cl^-) in toluene and gave 3α-chloro-5α-cholestane (9), shown to be diastereoisomerically pure by i.r. spectroscopy.

Less satisfactory results were obtained when 5α-cholestan-3β-yl toluene-*p*-sulphonate (6) was used instead of the methanesulphonate (2). Indeed, the reaction of (6) with (1) in toluene afforded, in lower yield, 3α-fluoro-5α-cholestane of lower optical rotation, together with some olefin and a significant amount of the epimeric 5α-cholestan-3β-ol (7) and 5α-cholestan-3α-ol (8) (see later).

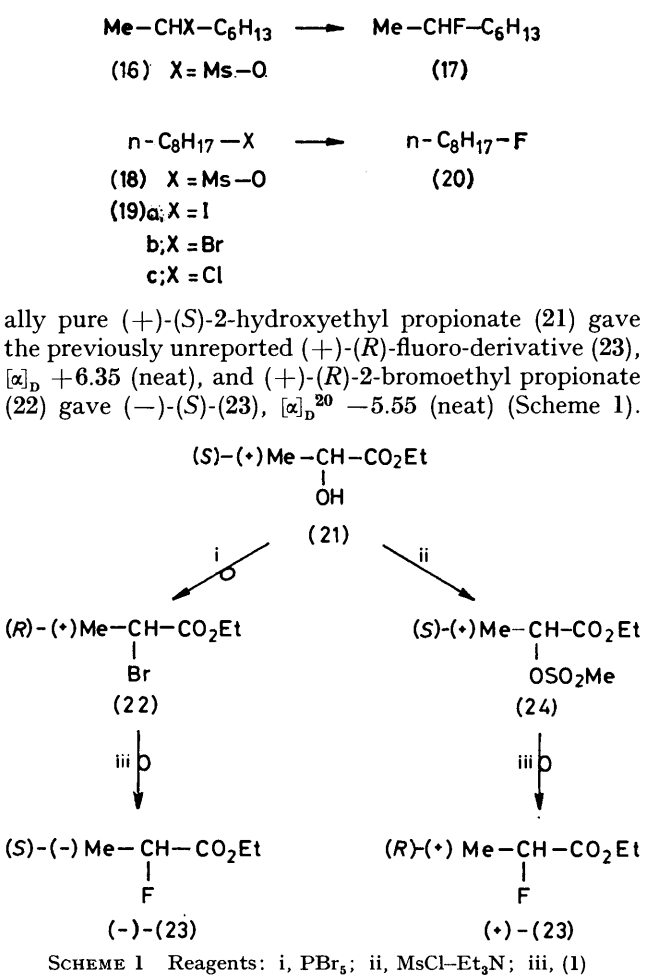
When 3β-methylsulphonyloxy-5α-androstan-17-one (11) was treated with the resin (1) in refluxing toluene, 3α-fluoro-5α-androstan-17-one (13) was obtained in 41% yield (optical rotation in close agreement with that previously reported [13]) together with 57% of 5α-androst-2-en-17-one (15) as the elimination product.

The ^{1}H n.m.r. spectrum of (13) at 100 MHz showed two broad signals centred at δ 4.81 for 3β-H ($^2J_{HF}$ 49.1, $W_{1/2}$ 4 Hz).

Under the same reaction conditions, 3α-methylsulphonyloxy-5α-androstan-17-one (10) gave exclusively the elimination product (15). This is not surprising for a 3α-substituted androstan-17-one,[14] but when using a resin (1) which was subjected to an additional dehydration prior to its use (see later), 3β-fluoro-5α-androstan-17-one (12) was obtained in 26% yield ($[\alpha]_D^{20}$ +34, lit.,[15] +35, $CHCl_3$), together with 37% of 5α-androst-2-en-17-one (15) and 24% of starting material (10). The ^{1}H n.m.r. spectrum of (12) exhibited a system of two seven-line multiplets centred at δ 4.96, $^2J_{HF}$ 54.2 Hz, typical of a 3-H axial proton.[16] The ^{19}F–{^{1}H} n.m.r. spectra of (12) and (13) exhibited signals at 89 and 102.4 p.p.m. (from TFA), respectively. The respective low- and high-field resonances in (12) and (13) can be assigned to equatorial and axial fluorine atoms, respectively.[17]

No appreciable amount greater than 1% of epimeric impurity was found in both the above products.

The high stereospecificity of the reaction with Amberlite IRA 900 (F^-) or with Amberlyst-A 26 (F^-) (1) was confirmed by the conversion of the methanesulphonate (16) of optically pure (−)-(*R*)-octan-2-ol into (+)-(*S*)-2-fluoro-octane (17) having an optical rotation of $[\alpha]_D^{20}$ +10.2 (neat). This value is similar to that reported in the literature [18] for a sample claimed to be optically pure. Similarly, the methanesulphonate (24) of optically pure (+)-(*S*)-2-hydroxyethyl propionate (21) gave the previously unreported (+)-(*R*)-fluoro-derivative (23), $[\alpha]_D$ +6.35 (neat), and (+)-(*R*)-2-bromoethyl propionate (22) gave (−)-(*S*)-(23), $[\alpha]_D^{20}$ −5.55 (neat) (Scheme 1).



SCHEME 1 Reagents: i, PBr_5; ii, MsCl–Et_3N; iii, (1)

The racemization of (22) may occur *via* the attack of bromide ions [19] produced during steps (21) ⟶ (22) and/or (22) ⟶ (23).

All these reactions followed a clean S_N2 mechanism. The lability of the leaving group was examined using the series of n-octyl derivatives (18)—(20).* The sequence observed was I, CH_3SO_2O > Br ⩾ Cl (Table).

Because of the interest in using fluorinated sugars as probes for the metabolism of carbohydrates [21] we prepared two fluoro-sugars [22-24] by reaction of the appropriate protected toluene-*p*-sulphonates with the resin (1). 3-Deoxy-3-fluoro-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (26) and 6-deoxy-6-fluoro-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (28) were obtained, respectively, from 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-allofuranose (25) and 1,2:3,4-di-*O*-isopropylidene-6-*O*-*p*-tolylsulphonyl-α-D-galactopyranose (27) by refluxing in benzene in the presence of the resin

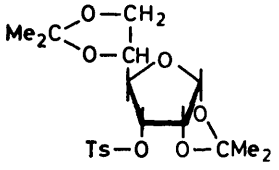
* Alkyl fluorides have been recently prepared [20] by reaction of alkyl halides and methanesulphonates with Amberlyst A-26(F^-).

Synthesis of fluorides with Amberlite IRA 900 (F^-) (4 mol. equiv.)

Substrate	Solvent	T/°C	t/h	Product	Yield (%)	$[\alpha]_D^{20}$ (°)
(2)	Toluene	100	60	(4)	32	+23.5 [a]
(3)		100	24	(5)	20	+18.5 [a]
(3)		75	48	(5)	20	+18.5 [a]
(10)		80	48	(12)	26 [b]	+34 [a]
(11)		80	48	(13)	41	+94.1 [c]
(6)		100	72	(4)	21	+23.5 [a]
(16)	Pentane	36	41	(17)	60	+10.2 [d]
(16)	Benzene	60	21	(17)	55 [e]	
(18)		60	28	(20)	74 [e]	
(19a)		60	28	(20)	74 [e]	
(19b)		60	68	(20)	70 [e]	
(19c)		60	28	(20)	17 [e]	
(24)	Pentane	35	24	(23)	46	+6.49 [a]
(22)		35	24	(23)	46	−5.55 [a]
(25)	Benzene	80	96	(26)	72 [b]	−21.5 [a]
(27)		80	96	(28)	75 [b]	−48.3 [a]

[a] In $CHCl_3$. [b] With Amberlyst-A26 (F^-). [c] In EtOH. [d] Neat. [e] By g.l.c. analysis.

(1). No elimination products [22] were detected and preparative layer chromatography gave compounds (26) ($[\alpha]_D^{20}$ −21.5, lit.,[25] $[\alpha]_D^{30}$ −22, $CHCl_3$) and (28) ($[\alpha]_D^{20}$ −48.3, lit.,[26] $[\alpha]_D^{20}$ −51.4, $CHCl_3$) in 72 and 75% yield, respectively, together with some starting material.



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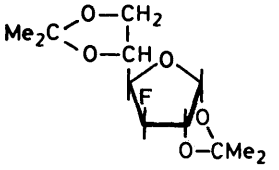

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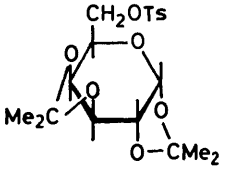

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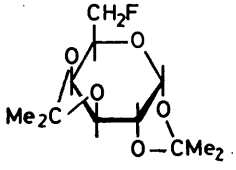
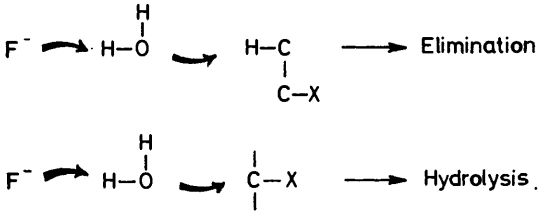


(28)

In these particular examples, as for the preparation of the fluoro-steroid (12), we used an Amberlyst A-26 (F^-) resin (1b) which was subjected to additional dehydration by refluxing in benzene (Soxhlet extractor containing molecular sieves to remove most of the water) without any noticeable decomposition of the resin. The above



SCHEME 2

results indicate that when the resin is treated in the usual manner, the water which remains seems to play an important role in the substitution/elimination and the substitution/hydrolysis behaviour of the fluoride ion.

The formation of the hydrolysis products (7) and (8) from (6) and the exclusive formation of the elimination product (15) from (10) may be explained by equilibrium (2) where the hydroxide anion becomes a competitive reagent * (Scheme 2).

$$F^- + H_2O \rightleftharpoons HF + HO^- \qquad (2)$$

* The hydrogen fluoride formed is then responsible for the observed etching of the walls of the reaction flask.

EXPERIMENTAL

^1H N.m.r. spectra (Me_4Si as internal standard) were recorded on a Varian A-60 and/or a Varian HA 100 and/or a Bruker WH 270 spectrometer and ^{19}F n.m.r. data (trifluoroacetic acid as external standard) on a Varian XL 100 instrument fitted with F.T. capability. I.r. spectra were recorded on a Perkin-Elmer 377 and/or a Perkin-Elmer 621 spectrometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. A Pye 104 chromatograph (2 m × 3 mm silanized glass column; Veas 5% on silanized Chromosorb 100—120 mesh) was used for g.l.c. analysis.

Amberlite IRA 900 (F^-) (1a) *and Amberlyst*-A 26 (F^-) (1b). —The strongly basic quaternary anion exchange resin in the chloride form and packed in a polyethylene column was washed with 1N-NaOH solution until complete removal of chloride ion was achieved and then with water until neutrality, Aqueous 1N-HF was then passed through the column and the resin rinsed with water to neutrality, followed by the addition of 95% aqueous EtOH and C_6H_6, and finally dried in a vacuum oven at 40 °C for 4 h. The exchange capacity of (1), determined according to literature [27] was 3.4 mequiv. g^{-1}. A Karl Fischer titration of water gave one equivalent of H_2O per each F^-. Additional dehydration was performed by refluxing the resin in benzene for 15 h with a Soxhlet extractor containing molecular sieves.

Fluoroaliphatic Compounds.—Alkyl halide or methanesulphonate [25] (5 mmol) and resin (1) (20 mequiv.) were vigorously stirred in toluene, pentane, or benzene. The reaction was followed by g.l.c. or t.l.c. The resin was filtered off, washed, and the solvent was evaporated off. The residue was then purified by bulb-to-bulb distillation or preparative layer or column chromatography.

3α-Fluoro-5α-cholestane (4),—Reaction of 5α-cholestan-3β-yl methanesulphonate (2), m.p. 110° (lit.,[26] 108—110°), $[\alpha]_D^{20}$ +14° (lit.,[28] $[\alpha]_D$ +13.9°, $CHCl_3$) with (1) afforded, after chromatography on silica gel [light petroleum (b.p. 40—60°)–diethyl ether 8 : 2 and then 1 : 1 as solvent], 3α-fluoro-5α-cholestane (4) (32%), m.p. 106—107°, $[\alpha]_D^{20}$ +23.5° (*c* 1, $CHCl_3$) (lit.,[28] m.p. 104—106°, $[\alpha]_D$ +32°, $CHCl_3$), δ($CDCl_3$) 4.80 (1 H, d, $^2J_{HF}$ 48.6, 3β-H, $W_{1/2}$ 7.5 Hz), 0.65 (s, 18-CH_3), 0.78 (s, 19-CH_3), 0.86 (d, 26—27-CH_3), and 0.9 (d, 21-CH_3); $\delta_F(CCl_4)$ 102.4 ($^2J_{HF}$ 47.2, $^3J_{H_{ax}F}$ 14.0 and

14.0, $^3J_{H_{eq}F}$ 5.0 and 5.0 Hz), together with cholest-2-ene (14) (31%), m.p. 66.5—68.5°, $[\alpha]_D^{20}$ +64° (*c* 1, $CHCl_3$). Starting from 5α-cholestan-3β-yl toluene-*p*-sulphonate (6), m.p. 133—134° (lit.,[29] 134—135°), the fluoro-compound (4) was obtained in 21% yield, m.p. 104°, $[\alpha]_D^{20}$ +23.5° (*c* 1, $CHCl_3$), together with cholest-2-ene (14) (49%), 5α-cholestan-3α-ol (8) (18%), m.p. 184—186°, $[\alpha]_D^{20}$ +23° (*c* 1, $CHCl_3$), and 5α-cholestan-3β-ol (7) (2.5%), m.p. 141—143°, $[\alpha]_D^{20}$ +22° (*c* 1, $CHCl_3$).

3β-*Fluoro*-5α-*cholestane* (5).—Reaction of 5α-cholestan-3α-yl methanesulphonate (3), m.p. 117—118°, $[\alpha]_D^{20}$ +23.2° (*c* 1, $CHCl_3$) (lit.,[28] $[\alpha]_D$ +23.2°, $CHCl_3$) with (1) at 75 °C for 48 h and chromatography as above, afforded 3β-fluoro-5α-cholestane (5) (20%), m.p. 78—80°, $[\alpha]_D^{20}$ +18.5° (*c* 1, $CHCl_3$) (lit.,[28] $[\alpha]_D$ +23°, $CHCl_3$); δ($CDCl_3$) 4.46 (1 H, m, $^2J_{HF}$ 50.7, $^3J_{H_{ax}H_{ax}}$ 10, $^3J_{H_{ax}H_{eq}}$ 4 Hz, 3α-H), 0.65 (s, 18-CH_3), 0.83 (s, 19-CH_3), 0.86 (d, 26—27-CH_3), and 0.89 (d, 21-CH_3); $\delta_F(CCl_4)$ 89.0 ($^2J_{HF}$ 36, $^4J_{HF}$ 2 Hz); together with cholest-ene (51%). When the reaction was repeated at 100 °C for 24 h 5β-fluoro-5α-cholestane (5) was obtained in 20% yield, $[\alpha]_D^{20}$ +18.5° (*c* 1, $CHCl_3$), together with cholest-2-ene (70%).

3α-*Chloro*-5α-*cholestane* (9).—Reaction of 5α-cholestan-3β-yl methanesulphonate (2) (5 mmol) with IRA 900 (Cl^-) (20 mequiv.) in toluene at 100 °C for 15 h afforded, after the usual work-up, 3α-chloro-5α-cholestane (9) (70%), m.p. 103—105°, $[\alpha]_D^{20}$ +30.3 (*c* 1, $CHCl_3$) (lit.,[30] m.p. 105°, $[\alpha]_D^{20}$ +31.5° (*c* 1.4, $CHCl_3$), together with cholest-2-ene (20%). I.r. analysis of (9) (CS_2 solvent) showed a peak at 707 cm^{-1} and absence of a peak at 755 cm^{-1}; therefore,[31] 3α-chloro-5α-cholestane was adjudged diastereoisomerically pure.

3β-*Fluoro*-5α-*androstan*-17-*one* (12).—Reaction of 3α-methylsulphonyloxy-5α-androstan-17-one (10), m.p. 125°, $[\alpha]_D^{20}$ +67° (lit.,[14] m.p. 126.5°, $[\alpha]_D^{20}$ +73°, $CHCl_3$), δ($CDCl_3$) 4.97 (m, 3β-H), 2.95 (s, CH_3SO_2), with usually dried resin (1) afforded androst-2-en-17-one (15) as the only product, m.p. 104—105°, $[\alpha]_D^{25}$ +141° (lit.,[32] m.p. 105°, $[\alpha]_D^{20}$ +146°, EtOH), δ($CDCl_3$) 5.62 (m, 2- and 3-H). When Amberlyst A-26 (F^-) resin (1b) (extensively dehydrated—see text) was used, chromatography on a Florisil® column (hexane–ether 8 : 2—1 : 1 as solvent) afforded androst-2-en-17-one (15) (37%) and 3β-fluoro-5α-androstan-17-one (12) in 26% yield, m.p. 125—127°, $[\alpha]_D^{20}$ +34° (lit.,[15] m.p. 130—132°, $[\alpha]_D^{20}$ +35°, $CHCl_3$), δ($CDCl_3$) 4.48 (2 × sept., $^2J_{HF}$ 50.5, $^3J_{H_{ax}H_{ax}}$ 11.0, $^3J_{H_{ax}H_{eq}}$ 5.5 Hz, 3-H), and 0.87 (s, 18- and 19-H); $\delta_F(CCl_4)$ 128.12 ($^2J_{HF}$ 54.20 Hz), and 36% of the recovered methanesulphonate (10).

3α-*Fluoro*-5α-*androstan*-17-*one* (13).—Reaction of 3β-methylsulphonyloxy-5α-androstan-17-one (11), m.p. 152—153°, $[\alpha]_D^{20}$ +66° (lit.,[14] m.p. 153°, $[\alpha]_D^{20}$ +64°, $CHCl_3$), δ($CDCl_3$) 4.65 (2 × sept., 3α-H), 3.0 (s, CH_3SO_2), with resin (1b) afforded, after chromatography, 57% of the elimination product (15) and 41% of 3α-fluoro-5α-androstan-17-one (13), m.p. 111—113°, $[\alpha]_D^{20}$ +94.1° (lit.,[13] m.p. 118—119°, $[\alpha]_D^{20}$ +95°, $CHCl_3$); δ($CDCl_3$) 4.81 (2 × m, $W_{1/2}$ 4, $^2J_{HF}$ 49.1 Hz, 3β-H), and 0.86 and 0.81 (s, 18- and 19-H, respectively); $\delta_F(CCl_4)$ 102.4 ($^2J_{HF}$ 48.0, $^3J_{H_{ax}F}$ 42.0, $^3J_{H_{eq}F}$ 15.1 Hz).

(+)-(S)-2-*Fluoro-octane* (17).—Reaction of the methanesulphonate (16) of the optically pure (−)-(*R*)-octan-2-ol with (1) in pentane gave a mixture of 2-fluoro-octane (17) and octenes (66 and 33% yield, respectively, by g.l.c. analysis). The reaction mixture was then treated with a slight excess of an aqueous solution of bromine and potassium bromide and the organic layer carefully evaporated and distilled to give (+)-(*S*)-2-fluoro-octane (17) (60%), b.p. 85° at 200 mmHg, $[\alpha]_D^{20}$ +10.2° (neat) (lit.,[18] b.p. 55—57° at 43 mmHg); $[\alpha]_D^{20}$ −9.99° (neat) for (−)-(*R*)-(17), δ(CCl_4) 4.50 (1 H, m, J_{HF} 48 Hz, 2-H).

(+)-(R)- *and* (−)-(S)-*Ethyl* 2-*Fluoropropionate* (23).—(+)-(*R*)-Ethyl 2-bromopropionate (22), b.p. 84—86° at 50 mmHg, $[\alpha]_{578}^{20}$ +28.9° (*c* 1.215) (lit.,[33] b.p. 55—57° at 15 mmHg, $[\alpha]_{578}^{17}$ +22.05° (*c* 0.5, $CHCl_3$), δ($CDCl_3$) 4.35 (q, 1 H, 2-H), 1.80 (d, 3 H, 3-H), or (−)-(*S*)-ethyl 2-methylsulphonyloxypropionate [25b] (24), b.p. 126—129° at 0.7 mmHg (q, 1 H, 2-H), 1.80 (d, 3 H, 3-H), or (−)-(*S*)-ethyl 2-methylsulphonyloxypropionate [25b] (24), b.p. 126—129° at 0.7 mmHg, $[\alpha]_D^{22}$ −62.1 (neat), δ($CDCl_3$) 4.99 (q, 1 H, 2-H), 3.02 (s, 3 H, CH_3SO_2), and 1.54 (d, 3 H, 3-H), in dry pentane with 5 equiv. of resin (1) were refluxed for 24 h; after work-up, the residual oil showed [g.l.c. (20% Carbowax 20M–Gas Chrom Q, 3.5m column, 120 °C, Carlo Erba Fractovap)] no more starting material; distillation gave 350 mg (45% yield of isolated product) of (23), b.p. 122—125° at 760 mmHg; $[\alpha]_D^{25}$ −5.55° (*c* 1.84) from (22); $[\alpha]_D^{25}$ +6.49° (*c* 1.4, $CHCl_3$) from (24); δ($CDCl_3$) 4.98 (2 × q, $^2J_{HF}$ 48.6 Hz, 1 H, 2-H), and 1.55 (dd, $^3J_{HF}$ 23.6 Hz, 3 H, 3-H); $\delta_F(CCl_4)$ 104.6 ($^2J_{HF}$ 47.4, $^3J_{HF}$ 21.7 Hz).

3-*Deoxy*-3-*fluoro*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*gluco-furanose* (26).—1,2:5,6-Di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-allofuranose (25), m.p. 119—120°, $[\alpha]_D^{25}$ +86°, $CHCl_3$ (lit.,[22] m.p. 120—121°, $[\alpha]_D^{30}$ +87°, $CHCl_3$), when treated in boiling benzene for 4 days with Amberlyst-A 26 (F^-) (1b) extensively dried, afforded, after chromatography (preparative layer of silica gel, hexane–ether 1 : 1 as solvent), 72% yield of the fluoro-sugar (26) as an oil, b.p. 72—75° at 0.05 mmHg, $[\alpha]_D^{20}$ −21.5°, $CHCl_3$ (lit.,[23] b.p. 66—70° at 0.03 mmHg, $[\alpha]_D^{30}$ −22°, $CHCl_3$), δ(^1H–{^{19}F}) ($CDCl_3$) 5.96 (d, $J_{1-H-2-H}$ 4 Hz, 1-H), 4.95 (dd, $J_{3-H-4-H}$ 5.5, $J_{3-H-2-H}$ 2 Hz, 3-H), 4.6 (dd, 4-H), 1.52, 1.44, 1.34, and 1.32 (s, CH_3); $\delta_F(CCl_4)$ 130.16 ($^2J_{HF}$ 49.87, $^3J_{H_2F}$ 28.22, $^3J_{H_4F}$ 10.70, $^4J_{H_1F}$ 2.4 Hz); and 24% of starting material (25).

6-*Deoxy*-6-*fluoro*-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galacto-pyranose* (28).—1,2:3,4-Di-*O*-isopropylidene-6-*O*-*p*-tolylsulphonyl-α-D-galactopyranose [34] (27) under the same reaction conditions as above afforded a 75% yield of the fluoro-sugar (28) as an oil, b.p. 87—90° at 0.3 mmHg, $[\alpha]_D^{25}$ −48.3° (lit.,[24] b.p. 70—72° at 0.015 mmHg, $[\alpha]_D^{20}$ −51.4°, $CHCl_3$); δ(^1H–{^{19}F}) ($CDCl_3$) 5.53 (d, 1-H), 4.77 (d, 3-H), 4.54 (2 × AB system, 6-H and 6′-H), 4.33 (dd, 2-H), 4.26 (dd, 4-H), 4.06 (ddd, 5-H), 1.68, 1.67, 1.57, and 1.47 (s, CH_3) ($J_{1-H-2-H}$ 5.2, $J_{2-H-3-H}$ 4.95, $J_{3-H-4-H}$ 7.90, $J_{4-H-5-H}$ 1.9, $J_{5-H-6-H}$ 5.5, and 5.8, $J_{6-H-6'-H}$ *ca.* 1.8 Hz); $\delta_F(CDCl_3)$ 152.7 ($^2J_{6-H-F}$ 46.2 and 47.1, $^3J_{5-H-F}$ 13.5, $^4J_{1-H-F}$ and $^4J_{3-H-F}$ 1.0 Hz); and 19% of starting toluenesulphonate (27).

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