ESTERS OF ARYLPROPIONIC ACIDS WITH 1,2 : 5,6-DI-O--ISOPROPYLIDENE- AND 1,2-O-ISOPROPYLIDENE-α-D--GLUCOFURANOSE

Jiří SVOBODA[a], Karel ČAPEK[b] and Jaroslav PALEČEK[c]

[a] *Department of Organic Chemistry and*
[b] *Laboratory of Monosaccharides,*
Prague Institute of Chemical Technology, 166 28 Prague 6

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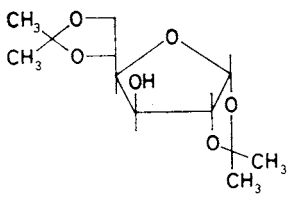
On fractional crystallization of 3-O-(2-(2-fluoro-4-biphenylyl)propionyl-, 3-O-(2-(4-isobutylphenyl)propionyl)- and 3-O-(2-(6-methoxy-2-naphthyl)propionyl)-1,2 : 5,6-di-O-isopropylidene--α-D-glucofuranoses *V*—*VII* optically pure *R*-diastereoisomers were isolated. The derivatives of 1,2-O-isopropylidene-α-D-glucofuranose obtained on partial deacetylation of esters *V*—*VII* were separated chromatographically to *R* and *S*-diastereoisomers. Their hydrolysis or transesterification afforded optically pure arylpropionic acids or their methyl esters, respectively. Kinetic resolution of the acids gives rise to esters *V*—*VII* enriched in *R*-diastereoisomer.

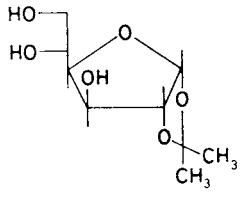
One of the procedures[1] for the resolution of racemic acids to enantiomers is based on the conversion of the racemic acid to a mixture of diastereoisomeric esters and the resolution of this mixture by crystallization or chromatography. Menthol[2,3] was used, for example, as an optically active alcohol, further 2-octanol[4] or α-methylfenchol[5]; however, the derivatives of the saccharides were omitted, as far as we know. One of them, deserving attention in this respect, is 1,2 : 5,6-di-O-isopropylidene-α-D--glucofuranose (*I*)[6,7]. In addition to its low price and easy availability this compound has the advantage that in esters of compound *I* with carboxylic acids the acetal groups can be eliminated from the glucofuranose skeleton under preservation of the ester bond; often partial deacetalization[8,9] can be carried out. Hence, from one racemic acid three pairs of diastereoisomeric esters can be obtained, differing in polarity; this should increase the variability and the probability of their successful resolution. We tried to check a part of this procedure with 2-arylpropionic acids of which it is known[10–12] that their therapeutically important analgetic and antiinflammatory effect are dependent in some instances on the configuration at the chiral carbon atom. Moreover, some esters of these acids are more active than the acids alone[13], which cannot be excluded for the substances investigated by us either.

From racemic arylpropionic acids *II*—*IV* we prepared corresponding chlorides on reaction with thionyl chloride or oxalyl chloride. On reaction of these chlorides with compound *I* in pyridine or in the dichloromethane–triethylamine system we

obtained a mixture of diastereoisomeric esters *V – VII*. The addition of a catalytic amount of 4-dimethylaminopyridine[14] greatly accelerates the esterification course and increases the yield of esters *V – VII*. The spectral data of the compounds prepared are in agreement with the proposed structure.

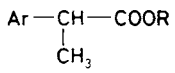


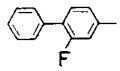
I



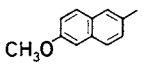
IX

From the mixture of diastereoisomeric 3-O-(2-(6-methoxy-2-naphthyl)propionyl)--1,2 : 5,6-di-O-isopropylidene-α-D-glucofuranoses (*VIIa*, *VIIb*) we obtained the(−)--diastereoisomer *VIIa* in pure form by fractional crystallization from light petroleum, and we have demonstrated that this contained the *R*-(−)-enantiomer of acid *IV* in the following two ways: Acid catalysed hydrolysis of ester *VIIa* in aqueous acetone afforded 2-(6-methoxy-2-naphthyl)propionic acid (*IVa*), the optical rotation of which ($[\alpha]_D$ −65·2°) is practically identical with the absolute rotation value given for the *S*-(+)-isomer[15]. On transesterification of compound *VIIa* in methanol, under catalysis with potassium carbonate, we also obtained optically pure methyl 2-(6--methoxy-2-naphthyl)propionate (*XIVa*) with an optical rotation value of $[\alpha]_D$ −76·3° and of *R*-(−) configuration[15]. In the same manner as in the case of ester *VII* we separated from the diastereoisomeric pairs *Va*, *Vb* and *VIa*, *VIb* optically

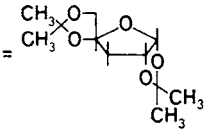


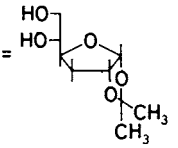
II, *V*, *VIII*, *XII*, Ar = 

III, *VI*, *IX*, *XIII*, Ar = $(CH_3)_2CHCH_2$

IV, *VII*, *X*, *XIV*, Ar = 

II – IV, R = H

V – VII, R = 

VIII – X, R = 

XII – XIV, R = CH_3

In formulae *IIa – Xa*, *XIIa – XIVa*, ***R*** enantiomer; *IIb – Xb*, *XIIb – XIVb*, ***S*** enantiomer.

pure diastereoisomers *Va* or *VIa*, respectively, containing the *R*-enantiomer of acid *II* or *III*, respectively, by crystallization from light petroleum. We then converted ester *Va* by acid catalysed hydrolysis to *R*-acid *IIa* and also by transesterification in methanol to corresponding *R*-methyl ester *XIIa* (Table I). We assigned the probable configuration *R* to these substances on the basis of the sense of the rotation coinciding with that of known analogous arylpropionic acids and their methyl esters[15,16] with *R* configuration. To our knowledge compounds *IIa* and *XIIa* have not been described yet. Corresponding diastereoisomeric derivatives *Vb*–*VIIb* of *S* absolute configuration could not be isolated in pure state by crystallization so far.

When acting with an ion exchanger in H^+-cycle on a mixture of diastereoisomers *Va*, *Vb* in aqueous acetone we could isolate from the reaction mixture two compounds by column chromatography: R_F 0·43, $[\alpha]_D$ −7·0° and R_F 0·40, $[\alpha]_D$ +16·6°. Interpretation of the mass and ^1H NMR spectra indicated that both substances contained a single isopropylidene protecting group and two hydroxyl groups only. Transesterification of compounds *VIIIa*, *VIIIb* with methanol under the above mentioned conditions gave the enantiomeric methyl esters *XIIa* ($[\alpha]_D$ −49·0°), *XIIb* ($[\alpha]_D$ +49·1°) and 1,2-O-isopropylidene-α-D-glucofuranose (*XI*)[17]. From this it follows that the isopropylidene protecting group from the 5,6-position of the glucofuranose skeleton is split off preferentially from the starting mixture of the diastereoisomeric esters *Va*, *Vb*. An analogous selective splitting off of the isopropylidene group from the position 5,6 has already been observed earlier in other compounds[18–20]. Acid catalysed hydrolysis of compound *VIIIa* or *VIIIb* gave optically pure isomer of acid *IIa* or *IIb*, respectively (see Table II). From the above it follows that 3-O-(2-(2-fluoro-4-biphenyl)propionyl)-1,2-O-isopropylidene-α-D-glucofuranose (*VIIIa*, *VIIIb*) are optically pure diastereoisomers, while ester *VIIIa* with the higher R_F value is formed by the acid with an *R*-configuration. By optimizing the reaction conditions we found that this partial deacetalisation can be carried out quantitatively

TABLE I

Esters *Va*–*VIIa* and their transformation

Ester	M.p. °C	$[\alpha]_D$[a]	Methyl ester			Acid		
				$[\alpha]_D$[a]	Ref.		$[\alpha]_D$[a]	Ref.
Va	120–124	−43·0	*XIIa*	−48·5	–	*IIa*	−43·5	+44·7[c]
VIa	70–74	−46·1	*XIIIa*	−65·2	+64·6[b]	*IIIa*	−56·5	−56·9[d]
VIIa	143–144	−50·1	*XIVa*	−75·3	+76·9[b]	*IVa*	−65·9	+66·4[b]

[a] Measured in chloroform; [b] *S*-(+)-isomer, ref.[15]; [c] (+)-isomer, ref.[26]; [d] ref.[15].

when acting with 80% aqueous acetic at 40°C. Under these conditions we carried out partial deacetalisation of the mixture of diastereoisomers *VI* or *VII*. In these cases too we obtained the corresponding monoisopropylidene derivatives *IXa*, *IXb*, or *Xa*, *Xb*, respectively (Scheme 1), which we separated chromatographically to optically pure diastereoisomers (Table II). Transesterification of these esters gave the known optically active esters *XIIIa*, *XIIIb*, or *XIVa*, *XIVb*, respectively. Acid catalysed hydrolysis of individual diastereoisomeric esters *IXa*, *IXb*, *Xa*, *Xb* also afforded optically active acids *IIIa*, *IIIb*, *IVa*, and *IVb* (Table II). Deacetalisation of the mixture of esters *V*–*VII*, prepared according to procedure *a* followed by column chromatography, failed in all cases to yield equimolar amounts of diastereomeric esters *VIIIa*, *VIIIb*, *IXa*, *IXb*, or *Xa*, *Xb*, respectively The content of esters *VIIIa*–*Xa* in the reaction mixture always predominated over the content of esters *VIIIb*–*Xb*. In view of the fact that the conversion of the starting esters *V*–*VII* during partial deacetalisation was always complete, it means that the content of isomers *VIIIa*–*Xa* and *VIIIb*–*Xb* corresponds to the relative representation of diastereoisomeric esters *Va*–*VIIa* or *Vb*–*VIIb*, respectively, in the starting mixtures *V*–*VII*. Hence, during the acylation of glucofuranose *I*, chlorides of acids of configuration *R* *II*–*IV* react preferentially. The differing reactivity of *R* and *S* derivatives of acids *II*–*IV* has already been observed and used for the so-called kinetic resolution[21,22] of arylpropionic acids with optically active 1-(4-pyridyl)ethanol. We used this finding for the resolution of acids *II*–*IV* under the conditions of kinetic resolution, *i.e.* in the reaction of acid chloride with compound *I* in a 1 : 0·55 molar ratio. From the diastereoisomeric esters *V*–*VII* isolated chromatographically, we obtained by transesterification with methanol methyl esters *XII*–*XIV* which displayed optical activity (Table III). From these results it is evident that *R*-isomers

TABLE II

Esters *VIII*–*X* and their transformation

Ester	M.p. °C	$[\alpha]_D^a$	Configuration	$[\alpha]_D^a$			
				Methyl ester		Acid	
VIIIa	118–123	−7·0	*R*	*XIIa*	−49·0	*IIa*	−43·1
VIIIb	72–76	+16·6	*S*	*XIIb*	+49·1	*IIb*	+44·9
IXa	48–54	−22·9	*R*	*XIIIa*	−63·2	*IIIa*	−54·5
IXb	oil	+28·1	*S*	*XIIIb*	+63·6	*IIIb*	+56·0
Xa	125–126	−6·6	*R*	*XIVa*	−73·2	*IVa*	−64·1
Xb	103–106	+23·8	*S*	*XIVb*	+75·0	*IVb*	+65·0

[a] Measured in chloroform.

of acids *II*–*IV* react preferentially with glucofuranose *I*. This kinetic effect also appeared in the esterification of acid *II* by the method of mixed anhydride[23]. Under these conditions acid *II* afforded optically active ester *V* in 43% yield, having $[\alpha]_D$ −33·5°, *i.e.* 76% e.e.

Finally it may be stated that the protected glucofuranose *I* used represents a useful substrate for the resolution of racemic mixtures of carboxylic acids.

EXPERIMENTAL

The temperature data were not corrected. The melting points were determined on a Boetius block (C. Zeiss, Jena). The infrared spectra were measured on a Perkin–Elmer 325 (Bodenseewerk) instrument, in chloroform. The ^{1}H NMR spectra were recorded on a Varian XL-100-15 instrument (Palo Alto), in chloroform, using tetramethylsilane as reference. The mass spectra were measured on a Jeol DX 300 spectrometer (70 eV electron energy). The following chemicals were prepared by standard procedures[24,25]: 1,2 : 5,6-di-O-isopropylidene-α-D-glucofuranose (*I*), (m.p. 110–111°C) and 1,2-O-isopropylidene-α-D-glucofuranose (*XI*) m.p. 160–161°C).

3-O-(2-(Subst. aryl)propionyl)-1,2 : 5,6-di-O-isopropylidene-α-D-glucofuranose (*V*– *VII*)

a) A mixture of 2·08 g (9 mmol) of acid *IV*, 3·2 g (27 mmol) of thionyl chloride and benzene (90 ml) was refluxed for 3 h. The solvent was evaporated and the residue dissolved in pyridine (30 ml) under cooling at 0°C. Glucofuranose *I* (2·34 g; 9 mmol) was added to the stirred solution and after 48 h stirring at 20°C the mixture was decomposed with ice water (100 ml) and extracted with chloroform (2 × 50 ml). The organic layer was washed with dilute sulfuric acid (5%, 50 ml), ice water (100 ml) and dried over anhydrous magnesium sulfate. After evaporation of the solvents the mixture was submitted to flash chromatography (silica gel, benzene–ethyl acetate as eluent), to give 2·70 g (5·7 mmol) of ester *VII*; yield, 63%.

b) In the same manner as under *A* 3·7 g (16 mmol) of acid *IV* was reacted with 7·44 g (59 mmol) of oxalyl chloride in benzene (50 ml) to give the corresponding chloride which was dissolved in dichloromethane (20 ml). The solution was added dropwise over 15 min to a mixture of 4·18 g (16 mmol) of glucofuranose *I*, 2·42 g (24 mmol) of triethylamine and dichloromethane (50 ml). Using the procedure as under *A* 5·85 g (12·4 mmol) of compound *VII* were obtained, yield, 77%.

TABLE III
Results of kinetic resolution of acids *II*–*IV*

Ester	$[\alpha]_D$[a]	% e.e.
XII	−21·6	44
XIII	−35·1	50
XIV	−43·5	56

[a] Measured in chloroform.

c) Proceeding as under *B* and taking 3·7 g (16 mmol) of acid *IV* and 0·1 g (0·1 mmol) of 4-dimethylaminopyridine as catalyst ester *VII* (7·1 g; 15 mmol) was obtained after 6 h reaction time in 94% yield.

d) Proceeding as under *B*, *i.e.* using 2·44 g (10 mmol) of acid *II* and 2·60 g (10 mmol) of glucofuranose *I*, 3·20 g (7·6 mmol) of ester *V* was obtained in 76% yield.

e) Using the same procedure as under *B* 2·06 g (100 ml) of acid *III* reacted with 2·60 g (10 mmol) of glucofuranose *I* to give 3·27 g (7·3 mmol) of ester *VI* in a 73% yield.

For compound *V* $C_{27}H_{31}FO_7$ (486·5) calculated: 66·66% C, 6·42% H; found: 66·36% C, 6·44% H. For compound *VI* $C_{25}H_{36}O_7$ (448·6) calculated: 66·93% C, 8·09% H; found: 66·77% C, 8·01% H. For compound *VII* $C_{26}H_{32}O_7$ (472·5) calculated: 66·09% C, 6·83% H; found: 65·89% C, 6·90% H. Infrared spectra (cm^{-1}): compound *V*: ν(C=O) 1 742 s; *VI*: ν(C=O) 1 740 s; *VII* ν(C=O) 1 740 s. ^1H NMR spectra: compound *V*: 1·14 s (3 H, CH_3), 1·29 s (3 H, CH_3), 1·33 s (3 H, CH_3), 1·52 s (3 H, CH_3), 1·54 d (3 H, CH_3, $J = 7$), 3·84 q (1 H, CH), 3·88—4·26 m (4 H), 4·32 d and 4·46 d (1 H, CH, $J = 4$), 5·32 d (1 H, CH, $J = 4$, 5·75 d and 5·86 d (1 H, CH, $J = 4$), 7·10—7·51 m (8 H, nucleus); *VI*: 0·90 d (6 H, CH_3, $J = 7$), 1·15 s (3 H, CH_3), 1·27 s (3 H, CH_3), 1·34 s (3 H, CH_3), 1·49 s (3 H, CH_3), 1·50 d (3 H, CH_3, $J = 7$), 1·81 m (1 H, CH), 2·44 d (2 H, CH_2), 3·80 q (1 H, CH), 3·75—4·20 m (4 H), 4·40 d and 4·52 d (1 H, CH, $J = 4$), 5·20 d and 5·28 d (1 H, CH, $J = 4$), 5·62 d and 5·80 d (1 H, CH, $J = 4$), 7·10 dd (4 H, nucleus); *VII*: 1·15 s (3 H, CH_3), 1·29 s (3 H, CH_3), 1·31 s (3 H, CH_3), 1·48 s (3 H, CH_3), 1·57 d (3 H, CH_3, $J = 6·5$), 3·83 q (1 H, CH), 3·89 s (3 H, OCH_3), 3·90—4·25 m (4 H), 4·40 d and 4·50 d (1 H, CH, $J = 4$), 5·23 d and 5·31 d (1 H, CH, $J = 4$), 5·58 d and 5·80 d (1 H, CH, $J = 4$), 7·05—7·72 m (6 H, nucleus). Mass spectra (*m/z*/% rel. int. (ionic species)): compound *V*: 486/9 ($M^{+\cdot}$), 471/62 ($M - CH_3$), 200/17, 199/100 (M — COOR), 101/93, 43/15; *VI*: 448/2 ($M^{+\cdot}$), 434/12, 433/61 ($M - CH_3$), 390/7 ($M - (CH_3)_2CO$), 289/10, 161/73 (M — COOR), 118/18, 101/100 ($C_5H_9O^+$), 43/17; *VII*: 488/11 ($M^{+\cdot}$), 473/56 ($M - CH_3$), 186/15, 185/100 (M — COOR), 170/10, 141/11, 115/9, 101/86.

Fractional Crystallization of Compounds *V*— *VII*

a) From 0·9 g of a mixture of diastereoisomeric esters *V* 0·26 g of ester *Va* (Table I) were obtained by five crystallizations from light petroleum (25 ml each time).

b) Using the same procedure as under *A* 0·95 g of ester *VIa* were obtained from 2·6 g of ester *VI* by 3 crystallizations.

c) Using the same procedure as above 0·65 g of ester *VIIa* (Table I) were obtained from 2·2 g of ester *VII* after 5 crystallizations.

3-O-(2-(Subst. aryl)propionyl)-1,2-O-isopropylidene-α-D-glucofuranose (*VIII*—*X*)

a) A mixture of 1·0 g (2 mmol) of ester *V*, acetone (25 ml), water (10 ml) and cation exchanger Dowex 50 W × 8 in H^+-cycle (5 ml) was stirred at 20°C, filtered, evaporated and the residue chromatographed (silica gel, benzene–ethanol as eluent) to give 190 mg (0·39 mmol, 20%) of the starting *V*, 315 mg (0·7 mmol, 35%) of ester *VIIIa* and 300 mg (0·67 mmol, 34%) of ester *VIII* (Table II).

b) A mixture of 373 mg (0·79 mmol) of ester *VII*, acetic acid (24 ml) and water (6 ml) was stirred at 40°C for 5 h, then diluted with water (50 ml) and extracted with chloroform (3 × 10 ml). The extract was washed with a saturated sodium hydrogen carbonate solution (10 ml), water (10 ml) and dried over magneisum sulfate. After evaporation of the solvent 323 mg (0·75 mmol,

95%) of the mixture of diastereoisomeric esters *X* were obtained, which were separated as under *a*. The yield was 170 mg (0·39 mmol) of ester *Xa* and 132 mg (0·31 mmol) of ester *Xb* (Table II).

c) Using the same procedure as under *b* 1·0 g (2·23 mmol) of ester *VI* gave after chromatography 735 mg (1·80 mmol, 80%) of ester *IXa* and 136 mg (0·33 mmol, 15%) of ester *IXb* (Table II).

For compound *VIII* $C_{21}H_{23}FO_7$ (406·4) calculated: 62·06% C, 5·70% H; found: 61·88% C, 5·81% H. For compound *IX* $C_{22}H_{32}O_7$ (408·5) calculated: 64·69% C, 7·90% H; found: 64·44% C, 7·88% H. For compound *X* $C_{23}H_{28}O_8$ (432·5) calculated: 63·87% C, 6·53% H; found: 63·49% C, 6·46% H. Infrared spectra (cm^{-1}): *VIIIa*: 3 540 m ν(OH), 1 740 s ν(C=O); *VIIIb*: 3 540 m ν(OH), 1 732 s ν(C=O); *IXa*: 3 580 m ν(OH), 1 740 s ν(C=O); *IXb*: 3 500 m ν(OH); 1 738 s ν(C=O); *Xa*: 3 580 m ν(OH), 1 728 s ν(C=O), *Xb*: 3 500 m ν(OH), 1 730 s ν(C=O). ^{1}H NMR spectra: compound *VIIIa*: 1·30 s (3 H, CH_3), 1·49 s (3 H, CH_3), 1·54 d (3 H, CH_3, $J = 7$), 2·20 s (1 H, OH), 2·36 s (1 H, OH), 3·36–3·64 m (2 H, CH_2), 3·78 q (1 H, CH), 4·15 dd (1 H, CH, $J = 3$, $J = 8$), 4·50 d (1 H, CH, $J = 4$), 5·27 d (1 H, CH, $J = 2·5$), 5·85 d (1 H, CH, $J = 4$), 7·04–7·50 m (8 H, nucleus); *VIIIb*: 1·28 s (3 H, CH_3), 1·49 s (3 H, CH_3), 1·56 d (3 H, CH_3, $J = 7$), 2·38 s (2 H, OH), 3·50–3·90 m (4 H), 4·16 dd (1 H, CH, $J = 2·5$, $J = 8$), 4·34 d (1 H, CH), 5·25 d (1 H, CH, $J = 2·5$), 5·80 d (1 H, CH, $J = 4$), 7·04–7·50 m (8 H, nucleus); *IXa*: 9·90 d (6 H, CH_3), 1·29 s (3 H, CH_3), 1·48 s (3 H, CH_3), 1·50 d (3 H, CH_3, $J = 7$), 1·84 m (1 H, CH), 2·32 s (2 H, OH), 2·44 d (2 H, CH_2), 3·66 t (2 H, CH_2), 3·80 q (1 H, CH), 4·12 dd (1 H, CH, $J = 2·5$, $J = 8$), 4·52 d (1 H, CH), 5·28 d (1 H, CH, $J = 2·5$), 5·82 d (1 H, CH, $J = 4$), 7·10 dd (4 H, nucleus); *IXb*: 0·90 d (6 H, CH_3, $J = 7$), 1·28 s (3 H, CH_3), 1·50 s (3 H, CH_3), 1·54 d (3 H, CH_3), 1·84 m (1 H, CH), 2·40 s (2 H, OH), 2·44 d (2 H, CH_2), 3·52–3·88 (4 H), 4·16 dd (1 H, CH, $J = 2·5$, $J = 8$), 4·31 d (1 H, CH), 5·22 d (1 H, CH, $J = 2·5$), 5·76 d (1 H, CH, $J = 4$), 7·11 dd (4 H, nucleus); *Xa*: 1·29 s (3 H, CH_3), 1·48 s (3 H, CH_3), 1·60 d (3 H, CH_3, $J = 7$), 2·20 s (2 H, OH), 3·46 m (2 H, CH_2), 3·88 q (1 H, CH), 3·94 s (3 H, OCH_3), 4·14 dd (1 H, CH, $J = 3$, $J = 8$), 4·54 d (1 H, CH, $J = 4$), 5·29 d (1 H, CH), 5·89 d (1 H, CH, $J = 4$), 7·15–7·82 m (6 H, nucleus); *Xb*: 1·22 s (3 H, CH_3), 1·50 s (3 H, CH_3), 1·60 d (3 H, CH_3, $J = 7$), 2·30 s (2 H, OH), 3·60–3·90 m (4 H), 3·94 s (3 H, OCH_3), 4·16 dd (1 H, CH, $J = 3$, $J = 8$), 4·34 d (1 H, CH), 5·28 d (1 H, CH, $J = 3$), 5·76 d (1 H, CH, $J = 4$), 7·14–7·80 m (6 H, nucleus). Mass spectra (*m*/*z*/% rel. int. (ionic species)): compound *VIII*: 462/0·2 (M^+), 447/12 (M – CH_3), 327/27 (M – $C_5H_{11}O_3$), 200/28, 199/100 (M – COOR), 127/9, 113/12, 85/18, 43/17; *IX*: 408/2 ($M^{+\cdot}$), 393/10 (M – CH_3), 351/42 (M – C_4H_9), 350/31 (M – $(CH_3)_2CO$), 347/10 (M – $C_2H_5O_2$), 289/35, 162/15, 161/100 (M – COOR), 145/10, 118/19, 43/10; *X*: 433/12, 432/51 ($M^{+\cdot}$), 186/20, 185/100 (M – COOR), 170/10, 141/5, 115/7.

Transesterification of Esters *V*–*VII*, *VIII*–*X*

A mixture of 200 mg of ester, methanol (10 ml) and freshly annealed potassium carbonate (15 mg) was stirred at 20°C and the reaction course followed by thin-layer chromatography. One drop of concentrated hydrochloric acid was added to the solution and the mixture evaporated. The residue was dissolved in chloroform (20 ml), washed with water, saturated sodium chloride solution and dried over anhydrous magnesium sulfate. After evaporation the residue was separated by column chromatography (silica gel, chloroform as eluent). Esters *XII* and *XIII* were isolated in the form of an oil, ester *XIV* had m.p. 90·5–92°C (ref.[15] 92°C). For compound *XII* $C_{16}H_{15}FO_2$ (258·3) calculated: 74·40% C, 5·85% H; found: 74·26% C, 5·76% H. For compound *XIII* $C_{14}H_{20}O_2$ (220·3) calculated: 76·33% C, 9·15% H; found: 76·31% C, 9·32% H. For compound *XIV* $C_{15}H_{16}O_3$ (244·3) calculated: 73·75% C, 6·60% H; found: 73·46% C, 6·55% H. Infrared spectra (cm^{-1}): compound *XII*: 1 733 s ν(C=O); *XIII*: 1 740 ν(C=O); *XIV*: 1 733 s ν(C=O). ^{1}H NMR spectra: compound *XII*: 1·60 d (3 H, CH_3, $J = 7$), 3·84 q (1 H, CH), 3·96 s (1 H, OCH_3), 7·04–7·56 m (8 H, nucleus); *XIII*: 0·91 d (6 H, CH_3), 1·60 d (3 H, CH_3,

$J = 7$), 1·84 m (1 H, CH), 2·44 d (2 H, CH_2), 3·88 q (1 H, CH), 3·98 s (3 H, OCH_3), 7·22 dd (4 H, nucleus); *XIV*: 1·60 d (3 H, CH_3, $J = 7$), 3·84 s (3 H, OCH_3), 3·98 s (3 H, OCH_3) 4·06 q (1 H, CH), 7·15—7·78 m (6 H, nucleus). Mass spectra (*m/z*/% rel. int. (Ionic species)): compound *XII*: 258/49 ($M^{+\cdot}$), 200/17, 199/100 ($M - C_2H_3O_2$), 184/8, 179/8, 178/13, 175/5; *XIII*: 221/3, 220/23 ($M^{+\cdot}$), 187/34 ($M - C_3H_7$), 162/14, 161/100 ($M - C_2H_3O_2$), 121/10, 119/17, 118/17, 117/33, 105/7, 91/15, 43/4; *XIV*: 244/47 ($M^{+\cdot}$), 186/17, 185/100 ($M - C_2H_3O_2$), 170/10, 141/8, 115/6.

Hydrolysis of Esters *V*—*VII* and *VIII*—*X* to Acids *II*—*IV*

A mixture of 300 mg of ester, acetone (5 ml), water (1 ml) and hydrochloric acid (1 ml) was refluxed for 3 h, evaporated and the residue dissolved in chloroform (20 ml), washed with water (2 × 20 ml), saturated sodium chloride solution and dried over anhydrous magnesium sulfate. After evaporation the residue was crystallized from hexane. The acids *II*—*IV* isolated in this way displayed identical spectral data with the starting racemic acids.

Kinetic Esterification of Acids *II*—*IV*

a) Chloride of acid *II*, prepared from 1·564 g (6·4 mmol) of acid *II* in the above mentioned manner, was isolated and diluted with dichloromethane (10 ml). Triethylamine (0·65 g; 6·4 mmol) was then added dropwise to the ice-cooled solution, followed by dropwise addition under stirring and cooling at 0°C over 45 min of a solution of 0·916 g (3·32 mmol) of glucofuranose *I* in dichloromethane (20 ml). The mixture was stirred for 1 h, diluted with ice water (50 ml), washed with sodium hyroxide solution (5%, 50 ml), water (50 ml) and dried over anhydrous magnesium sulfate. Chromatography on a silica gel column (benzene–ethyl acetate as eluent) gave 1·51 g (3·19 mmol) of ester *V*, yield 91% (referred to glucofuranose *I*), which was converted by transesterification with methanol (Table III).

b) Using the same method as under *A* 1·5 g (7·3 mmol) of acid *III* was reacted with 0·81 g (8 mmol) of triethylamine and 1·04 g (4 mmol) of glucofuranose *I* to give 1·516 g (3·38 mmol) of ester *VI*, yield 85%.

c) Applying the procedure as under *A* 0·876 g (3·8 mmol) of acid *IV* was reacted with 0·38 g (3·8 mmol) of triethylamine and 0·544 g (2·09 mmol) of glucofuranose *I* to afford 0·842 g (1·78 mmol) of ester *VII* (85% yield).

Esterification of Acid *II* According to ref.[23]

Triethylamine (2·02 g, 20 mmol) and 1·15 g (10 mmol) of methanesulfonyl chloride were added under stirring to a cooled (to −25°C) mixture of 2·44 g (10 mmol) of acid *II* and dichloromethane (25 ml). After 2 h of stirring at −20°C 2·45 g (9·4 mmol) of glucofuranose *I* and 0·1 g of 4-dimethylaminopyridine in dichloromethane (25 ml) were added to the mixture which was stirred for another 2 h at 0°C. After decomposition with a saturated sodium hydrogen carbonate solution (50 ml) the organic layer was washed with water (2 × 50 ml) and dried over anhydrous magnesium sulfate. The residue after evaporation of the solvent was separated by column chromatography (silica gel, benzene–ethyl acetate as eluent). Yield, 2·1 g (4·3 mmol; 43%) of ester *V*, $[\alpha]_D$ −33·5° (*c* 0·7, $CHCl_3$).

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