Tetrahedron Vol. 43, No. 18, pp. 4133 to 4140, 1987
Printed in Great Britain

0040-4020/87 $3.00 + .00
Pergamon Journals Ltd.

SYNTHESES OF THE METHYL GLYCOSIDES OF CURACIN, *A-B* FRAGMENT FOUND IN AVILAMYCIN-A AND -C, CURAMYCIN-A, FLAMBAMYCIN AND EVERNINOMICIN-2, AND OF ITS ARTIFICIAL REGIOISOMER ISOCURACIN

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(*Received in Germany* 15 *May* 1987)

Abstract - Methyl 4-O-dichloroisoeverninyl-α-D-arabino-hexopyranoside, the methyl glycoside of curacin, **2**, which is the chromophoric A-B terminus of orthosomycins, was synthesized by esterification of methyl 3-O-benzyl-2,6-dideoxy- α-D-arabino-hexopyranoside (**9**) with 4-benzyloxy-3,5-dichloro-2-methoxy-6-methylbenzoyl chloride (**12**) with the help of n-butyl lithium, followed by hydrogenolytic debenzylation. The esterification of methyl 2,6-dideoxy- α-D-arabino-hexopyranoside (**8**) with 4-benzyloxy-3,5-dichloro-2-hydroxy-6-methylbenzoic acid (**13**) in the presence of CBI/DBN afforded after methylation with diazomethane and hydrogenolytic debenzylation the methyl glycoside of isocuracin, the artificial regioisomer of curacin, **5**. Derivatives of dichloroisoeverninic acid (**10**) decomposed under the reaction conditions of various esterification methods.

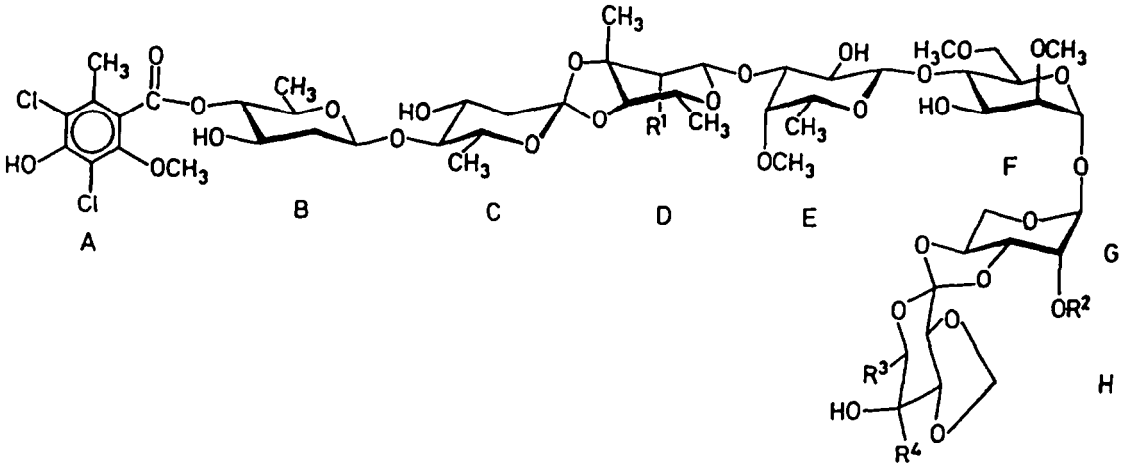
Curacin (everninocin) **1**, which is the chromophoric terminus of several orthosomycin antibiotics[1], e.g. curamycin[2], flambamycin[3], avilamycins[4] and everninomicins[5], has been proved to be the 4-O-ester[6] of 2,6-dideoxy-D-arabino-hexose (canarose, chromose C, olivose)[7] **7** (residue *B*) and dichloroisoeverninic acid[8] **10** (residue *A*) (Scheme 1 and 2).

The methyl glycoside of methyl curacin **3** has been claimed to be synthesized[9]. However, orthosomycins and their degradation products, whose phenolic hydroxyl group of the dichloroisoeverninyl residue have been substituted, are reported to be pharmacologically inactive[1,10]. Obviously, this phenolic hydroxyl group influences the structure-relationship considerably. A selective cleavage of the aryl methyl ether **3** leading to methyl α–curacinoside **2** does not seem to be promising, since methyl ethers of phenols adjacent to a carbonyl group are cleaved more easily[11].

Till now curacin **1** was only accessible by the decomposition of natural orthosomycin specimen. We have now achieved the first syntheses of the methyl glycosides of curacin and of the alternate 3-O-regioisomer isocuracin (**4**), whose tri-O-methyl ether **6** is described as an artificial degradation product of flambamycin[3].

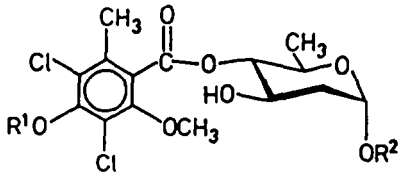
As methyl 2,6-dideoxy-α-D-arabino-hexopyranoside[7] **8** is predominantly acylated in the 3-O-position[12,13], a protection of this hydroxyl group during the esterification reaction leading to methyl α-curacinoside **2** is necessary. The acidic para-phenolic hydroxyl group of dichloroisoeverninic acid[8] **10** has to be blocked in order to avoid the formation of polyesters[14]. Protecting groups which are removed in neutral or mild acidic media without cleaving the alkali-labile ester and acid-labile glycosidic linkage are suitable. The benzyl ether protecting group[15] turned out to be most successful in both cases; the hydrogenolytic debenzylation did not affect the chlorine substituents in the dichloroisoeverninyl residue.

Synthetic routes to methyl curacinoside **2** and methyl isocuracinoside **5**, involving 4-O-protected and

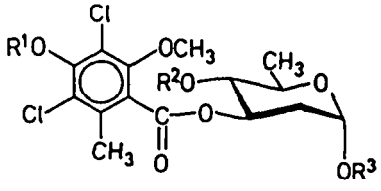


	R_1	R_2	R_3	R_4
Flambamycin	OH	$COCH(CH_3)_2$	CH_3	$COCH_3$
Curamycin-A	H	$COCH_3$	CH_3	$COCH_3$
Avilamycin-A	H	$COCH(CH_3)_2$	CH_3	$COCH_3$
Avilamycin-C	H	CH_3	CH_3	(S)-$CH(OH)CH_3$
Everninomicin-2	H	CH_3	H	(S)-$CH(OH)CH_3$

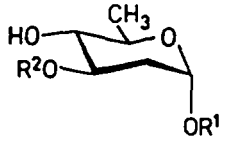
Scheme 1



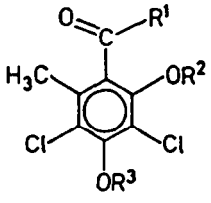
1 $R^1=R^2=H$ *Curacin*
2 $R^1=H, R^2=CH_3$
3 $R^1=R^2=CH_3$



4 $R^1=R^2=R^3=H$ *Isocuracin*
5 $R^1=R^2=H, R^3=CH_3$
6 $R^1=R^2=R^3=CH_3$

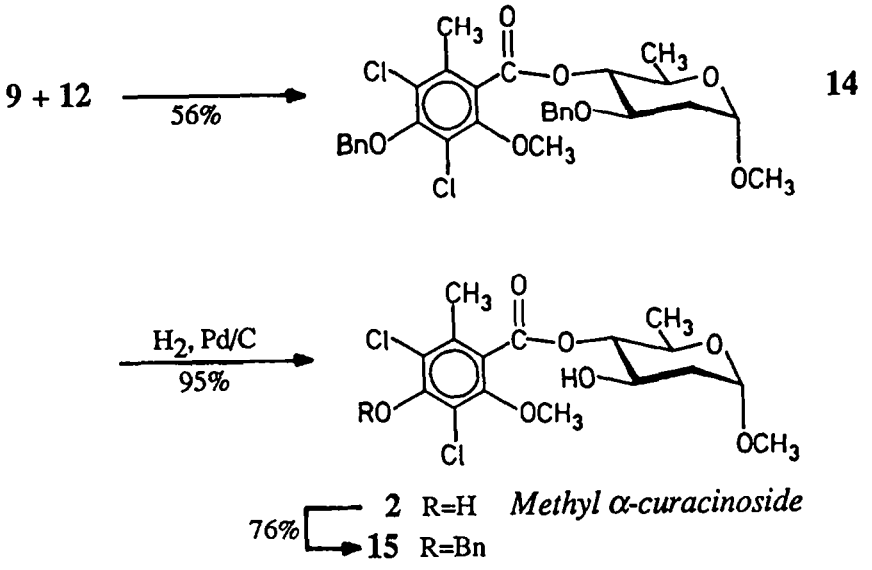


7 $R^1=R^2=H$
8 $R^1=CH_3, R^2=H$
9 $R^1=CH_3, R^2=Bn$

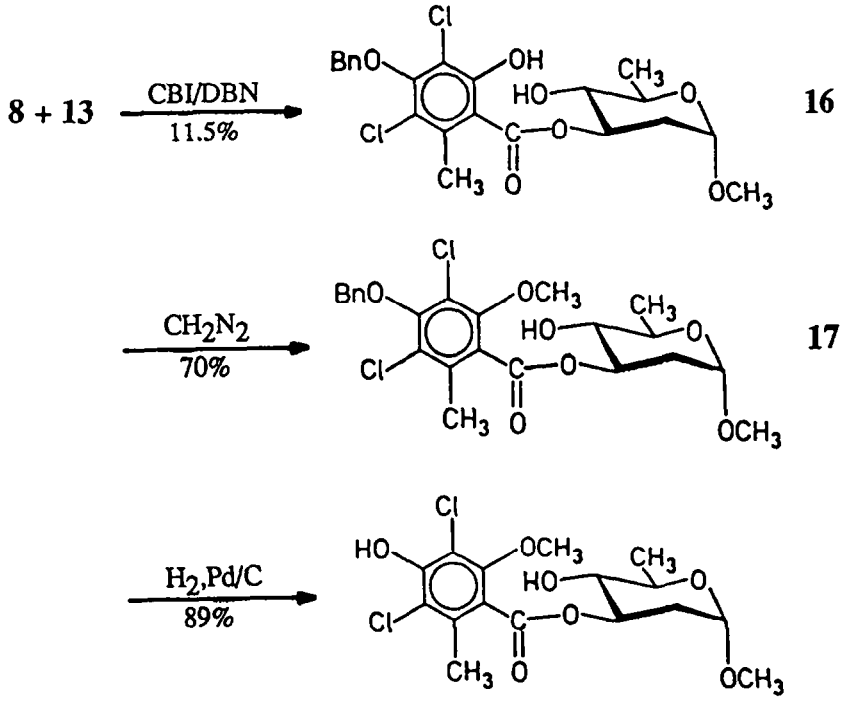


10 $R^1=OH, R^2=CH_3, R^3=H$
11 $R^1=OH, R^2=CH_3, R^3=Bn$
12 $R^1=Cl, R^2=CH_3, R^3=Bn$
13 $R^1=OH, R^2=H, R^3=Bn$

Scheme 2



Scheme 3



Scheme 4

carboxyl-activated derivatives of dichloroisoeverninic acid **10**, demonstrate the peculiar behaviour of multifunctionalised aromates. The activation of the benzyl ether **11** with various reagents, e.g. α,α-dichloromethyl methyl ether, oxalyl chloride, thionyl chloride and phosphor halides[16], and other mild in situ-methods failed. Employing the reagents N,N-dimethylchloroformamidinium chloride/pyridine, DMAP or PPY[17], cyanuric chloride/NEt_3[18], thionyl chloride/DMAP[19], methane sulphonyl chloride/DMAP[20], 2-halopyridium salts[21], dicyclohexylcarbodiimide/DMAP or PPY[22], N,N´-carbonyldiimidazole (CBI)/1,8-diaza-bicyclo[5,4,0]-7-undecene (DBU)[23], S-2-pyridyl-chloroformate/$CuBr_2$[24] and 1,1´-(carbonyldioxy)-dibenzotriazole/NEt_3[25] decomposed the acid. Recently we observed how pyridine solutions of dichloroisoeverninic acid **10** decarboxylate on standing[8]. Even the benzyl ether **11** could not be prepared via the direct etherification of methyl dichloroisoeverninate, but had to be initially introduced during the synthesis[8] of dichloroisoeverninic acid **10**.

Tetramethyl-α-halogenamines are reported to be very effective in preparing acyl halides from carboxylic acids under essentially neutral conditions[26]. The 4-O-benzyl-dichloroisoeverninic acid[8] **11** was converted into the acyl chloride **12** with 1-chloro-N,N,2-trimethylpropenylamine[27] in fairly good yield (82%). The crude product obtained after evaporation of volatile material is pure enough for further preparations. Methyl 3-O-benzyl-2,6-dideoxy-α-D-arabino-hexopyranoside[13] **9** was easily obtained by regioselective benzylation of methyl α-D-olivoside **8** via the O-di-n-butylstannylene acetal[28] in high yield (85%). The esterification reaction of the sterically demanding 3-O-benzyl sugar **9** with the sterically hindered acyl chloride **12** required an efficient method. We transfered **9** with n-butyl lithium[29] into the alkoxide and afforded the expected ester **14** in a satisfactory yield (56%). Subsequent hydrogenolytic debenzylation provided the methyl glycoside of curacin **2** in excellent yield (95%) (Scheme 3). Regioselective benzylation of **2** with phenyldiazomethane[30] resulted in the formation of **15** (76%).

For the synthesis of methyl α-isocuracinoside **5** we used the 4-O-benzyl protected ortho-O-unsubstituted aromatic[8] **13** as precursor. Ortho-hydroxyl groups of hydroxybenzoic acids do not interfere in esterification reactions, because the ortho-hydroxyl functions form strong intramolecular hydrogen bonds with the carboxyl group[31]. So we allowed unprotected **8** to react with the acid **13**, which was best activated with N,N´-carbonyl-diimidazole/1,5-diazabicyclo[4,3,0]-5-nonene (DBN). This reaction proceeds selectively to the 3-O-ester **16** (11.5%). Regioselective methylation of the phenolic hydroxyl group to **17** was accomplished with diazomethane in good yield (70%). Hydrogenolytic debenzylation produced the methyl glycoside of isocuracin **5** in high yield (89%) (Scheme 4).

EXPERIMENTAL

General.- Melting points were determined with a Büchi 510 K melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. ^{1}H-NMR spectra were recorded on a Varian VXR 300 (300 MHz) resp. on a Varian EM-390 (90 MHz) spectrometer, and ^{13}C-NMR spectra using a Varian VXR 300 (75 MHz) or a Varian CFT-20 (20 MHz) instrument. Mass spectra were obtained by using a Finnigan MAT 212 spectrometer (70 eV). TLC was carried out on Merck 0.2 mm silica gel 60 F_{254} analytical aluminium plates. For column chromatography silica gel 60 (140-270 mesh, Macherey & Nagel) was used.

Methyl 3-O-benzyl-2,6-dideoxy-α-D-arabino-hexopyranoside (9).- A mixture of **8** (2.07g, 12.76mmol) and di-n-butyltinoxide (3.81g, 15.32 mmol) in 10:1 benzene-methanol (88ml) was boiled under reflux for 2h. The solvent was evaporated, and the solid residue was stirred with DMF (22ml) and benzyl bromide (21ml) for 2h at 110°C

[TLC,1:1 EtOAc-cyclohexane; R_f= 0.63 (**9**); R_f= 0.26 (**8**)], cooled, evaporated in high vacuo, and the residual oil chromatographed on silica gel with 1:10 EtOAc-cyclohexane to remove faster moving impurities (about 1-1.5g), yielding 2.74g (85%) of **9**, colourless syrup, $[\alpha]_D^{26}$= +53° (c=1.39, $CHCl_3$) [lit.[13]: $[\alpha]_D^{20}$= +32° (c=0.23, CH_3OH]. ^{1}H-NMR data (300 MHz, $CDCl_3$): δ 1.27 (d,3H,CH_3-6), 1.58 (ddd,H-2a), 2.23 (ddd,H-2e), 2.9 (bs,4-OH), 3.18 (t,H-4,J=9.2 Hz), 3.28 (s,3H,OCH_3), 3.63 (dq, H-5), 3.71 (ddd, H-3), 4.46 and 4.61 (AB,2H,CH_2,Bn), 4.72 (d,H-1,J=2.7 Hz), 7.42 (m,5H,Aryl-H); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.3, $J_{2a,2e}$=12.9, $J_{2a,3}$= 11.5, $J_{2e,3}$= 4.9, $J_{3,4}$= 8.9, $J_{4,5}$= 9.4, $J_{5,6}$= 6.3, J_{AB}= 11.5 Hz. ^{13}C-NMR data (75 MHz, $CDCl_3$): δ 17.88 (C-6), 34.79 (C-2), 54.49 (OCH_3), 67.43, 76.08, 77.06 (C-3,-4,-5), 71.08 (CH_2,Bn), 98.39 (C-1), 127.69, 127.73, 128.46 (C_{ortho},C_{meta},C_{para},Bn), 138.41 (C_1,Bn).

(Found: C, 66.43; H, 8.21. Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99).

4-Benzyloxy-3,5-dichloro-2-methoxy-6-methylbenzoyl chloride (**12**).- 1-Chloro-N,N,2-trimethylpropenylamine (2.20g, 16.47mmol) is added to a solution of **11** (5.62g, 16.47mmol) in abs. dichloromethane (100ml) at -10°C and stirred for 4h (→0°C). Solvent and N,N-dimethylisobutyramide are evaporated in vacuo (15 Torr), at least in high vacuo, to yield 4.86g (82%) **12** as a yellow oil. IR ($CDCl_3$): ν 1775 cm^{-1} (C=O). MS: 358/360/362/364 (M^+,97:100:34:4), 323/325/237 (M^+-Cl,100:63:13), 232/234/236 (323-C_7H_7, 100:66:12), 91 ($C_7H_7^+$,basepeak).

Methyl 3-O-benzyl-4-O-(4-benzyloxy-3,5-dichloro-2-methoxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (**14**).- To a solution of **9** (2.62g, 10.38mmol) in anhydrous THF (15ml) was added under nitrogen and under exclusion of light during 15min 5.0ml (12.5mmol) of 2.5M n-butyl lithium in hexane. After 30min the resulting solution was treated during 5min at 20°C by the dropwise addition of **12** (4.48g, 12.46mmol) in anhydrous THF (10ml), refluxed for 16h [TLC, 2:5 EtOAc-cyclohexane; R_f= 0.56 (**14**); R_f= 0.25 (**9**)], cooled in an ice bath, and hydrolyzed by the addition of water (10ml). The aqueous phase was extracted with diethyl ether, the combined organic phases were dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel with 1:10 EtOAc-cyclohexane, yielding 3.33g (56%) of **14**, m.p. 98-100°C, $[\alpha]_D^{21}$= +25.9° (c=1.04, $CHCl_3$). ^{1}H-NMR data (300 MHz, $CDCl_3$): δ 1.38 (d,3H,CH_3-6), 1.76 (ddd,H-2a), 2.18 (s,3H,$ArCH_3$), 2.34 (ddd,H-2e), 3.30 (s,3H,1-OCH_3), 3.84 (s,3H,$ArOCH_3$), 3.85 (dq,H-5), 3.98 (ddd,H-3), 4.47 and 4.61 (AB,2H,CH_2,3-O-Bn), 4.80 (d,H-1,J=2.5 Hz), 5.00 (s,2H,CH_2,4'-O-Bn), 5.05 (t,H-4,J=9.5 Hz), 7.25-7.58 (m,10H,Aryl-H,Bn); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.1, $J_{2a,2e}$= 13.0, $J_{2a,3}$= 11.4, $J_{2e,3}$= 5.1, $J_{3,4}$= 9.3, $J_{4,5}$= 9.8, $J_{5,6}$= 6.3,J_{AB}=11.6 Hz. ^{13}C-NMR data (75 MHz, $CDCl_3$): δ 17.35 ($ArCH_3$), 17.60 (C-6), 35.19 (C-2), 54.70 (1-OCH_3), 62.18 ($ArOCH_3$), 65.84, 74.14, 77.34, (C-3,-4,-5), 70.58, 74.83 (CH_2,3- and 4'-O-Bn), 98.16 (C-1), 121.36, 126.08 (C-3',-5'), 127.34, 127.49, 128.23, 128.46, 128.49 (C_{ortho},C_{meta}, C_{para},3- and 4'-O-Bn), 127.51 (C-1'), 133.63 (C-6'), 136.06 (C_1,4'-O-Bn), 138.16 (C_1,3-O-Bn), 152.12, 152.72 (C-2',-4'), 165.81 (COO).

(Found: C, 62.81; H, 5.60. Calcd. for $C_{30}H_{32}O_7Cl_2$: C, 62.61; H, 5.60).

Methyl 4-O-(3,5-dichloro-4-hydroxy-2-methoxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (methyl α-curacinoside) (**2**).- A solution of **14** (3.22g, 5.59mmol) in methyl tert.butyl ether (600ml) was shaken with 10% Pd on charcoal (1.00g) at 20°C for 2.5h under hydrogen (1.2 bar). After filtration of the catalyst, the filtrate was concentrated to yield 2.10g (95%) of **2**, m.p. 151-153°C (1:1 methanol-water) [lit.: 145-146°C [6], 148-150°C[3,9]], $[\alpha]_D^{23}$ = +70.8° (c=1,06, $CHCl_3$) <lit.[9]: $[\alpha]_D^{24}$ = +54.5° ($CHCl_3$)>. ^{1}H-NMR data (300 MHz, D_5-pyridine): δ 1.58 (d,3H,CH_3-6), 2.09 (ddd,H-2a), 2.49 (ddd,H-2e), 2.53 (s,3H,$ArCH_3$), 3.33 (s,3H,1-OCH_3), 4.04 (s,3H,$ArOCH_3$), 4.10 (dq,H-5), 4.53 (ddd,H-3), 4.88 (d,H-1,J=2.9 Hz), 5.36 (t,H-4,J=9.6 Hz), 8.9 (bs,2H,3-and 4´-OH); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.0, $J_{2a,2e}$= 13.1, $J_{2a,3}$= 11.6, $J_{2e,3}$= 5.2, $J_{3,4}$= 9.3, $J_{4,5}$= 9.8, $J_{5,6}$= 6.3 Hz. ^{13}C-NMR data (75 MHz, D_5-pyridine): δ 17.90 ($ArCH_3$), 18.17 (C-6), 39.74 (C-2), 54.60 (1-OCH_3), 62.21 ($ArOCH_3$), 66.40, 66.48 (C-3,-5), 80.40 (C-4), 98.83 (C-1), 115.11 (C-3´), 119.85 (C-1´), 123.12 (C-5´), 133.54 (C-6´), 152.84 (C-2´), 153.07 (C-4´), 166.91 (COO) [lit. ref. 32]. MS: 394/ 396/398(100:72:13), M^+ for $^{35}Cl_2$,$^{35}Cl^{37}Cl$,$^{37}Cl_2$.

(Found: C, 48.82; H, 5.31. Calcd. for $C_{16}H_{20}O_7Cl_2$: C, 48.62; H, 5.10).

Methyl 4-O-(4-benzyloxy-3,5-dichloro-2-methoxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (**15**).- To a solution of **2** (1.00g, 2.53mmol) in ether (50ml) was added at 0°C under exclusion of light during 20min an ethereal solution of phenyldiazomethane [prepared from N-nitroso-N-benzyl-p-toluenesulfonamide (6.12g, 21.08mmol), sodium methoxide (1.14g, 21.10mmol) in a mixture of methanol (4ml)-ether (100ml); s.ref. 30]. The mixture was stirred for 19h at 20°C [TLC, 1:1 EtOAc-cyclohexane; R_f= 0.51 (**15**); R_f= 0.30 (**2**)], absorbed on silica gel (10g) and chromatographed on silica gel with 1:10 EtOAc-cyclohexane to give 932mg (76%) of **15**, m.p. 135-137°C, $[\alpha]_D^{22}$ = +54.9° (c=1.01, $CHCl_3$). ^{1}H-NMR data (300 MHz, $CDCl_3$): δ 1.34 (s,3H,CH_3-6), 1.80 (ddd,H-2a), 2.23 (ddd,H-2e), 2.38 (s,3H,$ArCH_3$), 2.7 (bs,1H,3-OH), 3.31 (s,3H,1-OCH_3), 3.81 (dq,H-5), 3.89 (s,3H,$ArOCH_3$), 4.12 (ddd,H-3), 4.78 (d,H-1,J=3.0 Hz), 4.84 (t,H-4, J=9.5 Hz), 5.02 (s,2H,CH_2,Bn), 7.32-7.58 (m,5H,Aryl-H,Bn); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.0, $J_{2a,2e}$= 13.2, $J_{2a,3}$= 11.8, $J_{2e,3}$= 5.2, $J_{3,4}$= 9.2, $J_{4,5}$= 9.7, $J_{5,6}$= 6.3 Hz. ^{13}C-NMR data (75 MHz, $CDCl_3$): δ 17.44 ($ArCH_3$), 17.63 (C-6), 37.86 (C-2), 54.74 (1-OCH_3), 62.38 ($ArOCH_3$), 65.25, 67.21 (C-3,-5), 74.93 (CH_2,Bn), 80.40 (C-4), 98.24 (C-1), 121.41, 126.36 (C-3´,5´), 127.20 (C-1´), 128.49, 128.51, 128.53 (C_{ortho},C_{meta},C_{para}, Bn), 133.30 (C-6´), 135.99 (C_1,Bn), 151.93, 152.94 (C-2´,-4´), 166.41 (COO).

(Found: C, 57.13; H, 5.29. Calcd. for $C_{23}H_{26}O_7Cl_2$: C, 56.92; H, 5.40)

Methyl 3-O-(4-benzyloxy-3,5-dichloro-2-hydroxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (**16**).- To a solution of **13** (2.30g, 7.03mmol) in THF (50ml) was added N,N´-carbonyldiimidazole (1.20g, 7.41mmol) and stirred at 25°C for 40min. A solution of **8** (1.14g, 7.04mmol) in THF (20ml) and 1,5-diazabicyclo[4,3,0]-5-nonene (0.9ml, 7.25mmol) was boiled under reflux for 28h. The cooled reaction mixture was poured into ether (200ml), washed with brine, dried (Na_2SO_4) and chromatographed on silica gel with 1:10 EtOAc-hexane producing 380.6mg (11.5%) of **16**, colourless oil, $[\alpha]_D^{25}$= +49.1° (c=0.935, $CHCl_3$). ^{1}H-NMR data (90 MHz, $CDCl_3$): δ 1.32 (d,3H,CH_3-6), 1.82 (ddd,H-2a), 1.94 (dd,H-2e), 2.61 (s,3H, $ArCH_3$), 3.34 (s,3H,1-OCH_3),

3.39 (t,H-4), 3.72 (dq,H-5), 4.75 (d,H-1), 5.00 (s,2H,CH_2,Bn), 5.39 (ddd,H-3), 7.25 (m,5H,Aryl-H,Bn), 10.50 (s,1H,ArOH); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.3, $J_{2a,2e}$= 13, $J_{2a,3}$=11, $J_{2e,3}$= 5, $J_{3,4}$=$J_{4,5}$= 9.0, $J_{5,6}$= 6 Hz. ^{13}C-NMR data (20 MHz, $CDCl_3$): δ 17.66 (q,C-6,^{1}J=128 Hz), 19.50 (q,$ArCH_3$, ^{1}J=129 Hz), 35.26 (t,C-2,^{1}J=132 Hz), 54.71 (dq,1-OCH_3,^{1}J=142, ^{3}J=4 Hz), 67.88 and 74.75 (d,C-3,-4, ^{1}J=148 Hz), 74.78 (t, CH_2,Bn,^{1}J=147 Hz), 75.04 (t,C-5,^{1}J=148 Hz), 97.78 (d,C-1,^{1}J=168 Hz), 112.22 (q,C-5',J=4 Hz),, 115.56 (s,C-3'), 122.12 (q,C-1',J=5 Hz), 128.49 (d,C_{ortho},C_{meta},C_{para},Bn,^{1}J=160 Hz), 135.98 (s,C_1,Bn), 137.49 (q,C-6',J=6 Hz), 155.21 (s,C-4'), 156.34 (s,C-2'), 169.85 (d,COO,J=3 Hz).

(Found: C, 55.90; H, 5.22. Calcd. for $C_{22}H_{24}O_7Cl_2$: C, 56.06; H, 5.13).

Methyl 3-O-(4-benzyloxy-3,5-dichloro-2-methoxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (**17**).- To a stirred solution of **16** (380mg, 0.81mmol) in ether (10ml) was added a solution of diazomethane (20mmol) in ether (40ml) at 0°C and stirred at 0°C for 15h. The reaction mixture was concentrated, and chromatography on silica gel with 1:5 EtOAc-hexane yielded 276.4mg (70%) of **17**, m.p. 87-88°C, $[\alpha]_D^{25}$ = +42.5° (c=1.03, $CHCl_3$). ^{1}H-NMR data (90 MHz, CCl_4): δ 1.27 (d,3H,CH_3-6), 1.69 (dt,H-2a), 2.26 (dd,H-2e), 2.32 (s,3H,$ArCH_3$), 2.74 (d,1H,4-OH), 3.17 (dt,H-4), 3.32 (s,3H,1-OCH_3), 3.66 (dq,H-5), 3.84 (s,3H,$ArOCH_3$), 4.66 (d,H-1), 4.95 (s,2H,CH_2,Bn), 5.26 (ddd,H-3), 7.25-7.52 (m,5H,Aryl-H,Bn); $J_{1,2a}$= 3.5, $J_{1,2e}$= 3, $J_{2a,2e}$= 12, $J_{2a,3}$= 11.5, $J_{2e,3}$= 5, $J_{3,4}$= $J_{4,5}$= 9, $J_{4,4\text{-}OH}$= 4.7, $J_{5,6}$= 6 Hz. ^{13}C-NMR data (20 MHz, CCl_4+1% C_6D_6): δ 17.05 ($ArCH_3$), 17.65 (C-6), 35.03 (C-2), 54.20 (1-OCH_3), 61.83 ($ArOCH_3$), 67.63, 73.87, 74.45, 75.06 (C-3,-4,-5 and CH_2,Bn), 97.50 (C-1), 121.31, 125.89, 127.18, 133.11 (C-1',-3'-5',-6'), 128.04, 128.12 (C_{ortho}, C_{meta},C_{para},Bn), 136.00 (C_1,Bn), 152.09, 152.80 (C-2',-4'), 165.70 (COO).

(Found: C, 57.09; H, 5.43. Calcd. for $C_{23}H_{26}O_7Cl_2$: C, 56.92; H, 5.40).

Methyl 3-O-(3,5-dichloro-4-hydroxy-2-methoxy-6-methylbenzoyl)-2,6-dideoxy-α-D-arabino-hexopyranoside (methyl α-isocuracinoside) (**5**).- A solution of **17** (276mg, 0.57mmol) in methyl tert.butyl ether (100ml) was shaken with 10% Pd on charcoal (100mg) at 25°C for 5h under hydrogen (1.2 bar). After filtration of the catalyst, the filtrate was concentrated and the residue recrystallized from chloroform-hexane to yield 200mg (89%) of **5**, m.p. 169-170°C $[\alpha]_D^{25}$ = +37.8° (c=0.502, $CHCl_3$). ^{1}H-NMR data (90 MHz, D_5-pyridine): δ 1.55 (d,3H,CH_3-6), 1.97 (dt,H-2a), 2.40 (s,3H,$ArCH_3$), 2.62 (ddd,H-2e), 3.32 (s,3H,1-OCH_3), 3.67 (t,H-4), 3.98 (s,3H,$ArOCH_3$), 4.06 (dq,H-5), 4.87 (dd,H-1), 5.60 (ddd,H-3), 8.2 (bs,1H,ArOH); $J_{1,2a}$= 3.6, $J_{1,2e}$= 1.2, $J_{2a,2e}$=$J_{2a,3}$= 12.6, $J_{2e,3}$= 5.2, $J_{3,4}$=$J_{4,5}$= 9.3, $J_{5,6}$= 6.3 Hz. ^{13}C-NMR data (20 MHz, D_5-pyridine): δ 17.68 (C-6), 18.49 ($ArCH_3$), 35.97 (C-2), 54.50 (1-OCH_3), 62.19 ($ArOCH_3$), 69.12, 74.29, 74.72 (C-3,-4,-5), 98.40 (C-1), 115.16 (C-3'), 119.67 (C-5'), 123.04 (C-1'), 133.29 (C-6'), 152.97 (C-4'), 153.04 (C-2'), 166.69 (COO).

(Found: C, 48.71; H, 5.22. Calcd. for $C_{16}H_{20}O_7Cl_2$: C, 48.62; H, 5.10).

Acknowledgements.- This work was supported by the Deutsche Forschungsgemeinschaft. We thank Degussa (Hanau) for palladium catalyst and Dr. Jan Runsink for recording the NMR spectra.

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