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Note

# Chlorodeoxy derivatives from D-galactochloralose

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Polychlorinated compounds often have valuable biological properties, for example as pesticides. Biodegradability of these compounds is normally required for environmental reasons. Since carbohydrate-based compounds usually have high biodegradability, their chloro derivatives are of potential interest in this regard. Several methods for the replacement of a hydroxyl group by chloride ion in carbohydrate chemistry have been described [1–5]. In view of our continuing interest in D-galactochloralose [(*S*)-1,2-*O*-trichloroethylidene-α-D-galactofuranose] [6], we have attempted the OH to Cl conversion in this compound, aiming to obtain a polychlorinated sugar molecule.

Forcing conditions and excess of the Vilsmeier reagent [7] (chloromethylene-*N*,*N*-dimethyliminium chloride) were used. Refluxing of D-galactochloralose (**1**) with this reagent in *N*,*N*-dimethylformamide produced a mixture of chlorinated derivatives, namely, 6-chloro-6-deoxy-1,2-*O*-trichloroethylidene-α-D-galactofuranose (**2**), 5,6-dichloro-5,6-dideoxy-1,2-*O*-trichloroethylidene-β-L-altrofuranose (**3**), and 5,6-dichloro-5,6-dideoxy-3-*O*-formyl-1,2-*O*-trichloroethylidene-β-L-altrofuranose (**5**). Rechlorination of the crude product did not increase the yield of **3** and **5** appreciably. A 3-chloro-3-deoxy derivative was not isolated and probably did not form in a significant amount due to the difficulty for chloride ion to approach C-3. Instead, the 3-*O*-formyl derivative **5** was obtained.

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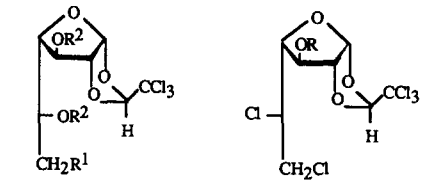

1 $R^1$ = OH ; $R^2$ = H
2 $R^1$ = Cl ; $R^2$ = H
4 $R^1$ = Cl ; $R^2$ = Ac
7 $R^1$ = OTs; $R^2$ = Ts
8 $R^1$ = Cl ; $R^2$ = Ts

3 R = H
5 R = CHO
6 R = Ac
9 R = Ts

The formyl group of compound **5** was clearly indicated by the characteristic chemical shift (7.85 ppm) of the formyl proton and the carbonyl absorptions at 1728 and 1745 $cm^{-1}$ in its IR spectrum. The formyl group of **5** was removed with sodium methoxide in methanol to give compound **3**. Compounds **2** and **3** were characterised as their acetate derivatives **4** and **6**, which were identified by their $^1$H-NMR, mass, and IR spectra (carbonyl absorptions at 1747 $cm^{-1}$ for **4** and at 1732 $cm^{-1}$ for **6**).

In order to confirm the L-*altro* configuration in **3** and **5**, replacement reactions of 3,5,6-tri-*O*-tosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose (**7**) with lithium chloride in *N*,*N*-dimethylformamide were also attempted. Thus, 6-chloro-6-deoxy-3,5-di-*O*-tosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose (**8**) and 5,6- dichloro-5,6-dideoxy-3-*O*-tosyl-1,2-*O*-trichloroethylidene-β-L-altrofuranose (**9**) were obtained as main products, depending on the reaction time. Prolonged reaction using excess of lithium chloride indicated (TLC) slow formation of a faster moving product, probably the trichloro-trideoxy derivative, but this reaction was not further investigated. Compound **9** was also made directly from **3** by tosylation. The tosylated compound was shown to be identical with **9** by their $^1$H-NMR spectra, mp, and mixture mp. The coupling constants of the furanose ring protons agreed with previous results, indicating that there was not a significant change in the ring geometry [6].

## 1. Experimental

TLC was performed on precoated Kieselgel plates (Merck 5554), and column chromatography on Kieselgel (Merck, 7734), with 9:1 toluene–MeOH. Melting points are uncorrected. NMR spectra were recorded with Varian-T 60 (60 MHz) and Bruker AC-200L (200 MHz) instruments, in $CDCl_3$ unless otherwise stated. Mass spectra were recorded with a Finnigan MAT 95 instrument. Optical rotations were determined on a Schmidt and Haensch Polartronic E polarimeter. The IR spectra were recorded on a Bruker IFS-48 spectrometer. Petroleum ether refers to the fraction having bp 60–80 °C.

*Reaction of* **1** *with the Vilsmeier reagent.*—To an ice-cold solution of D-galactochloralose (**1**) [6] (10 g, 0.032 mol) in *N*,*N*-dimethylformamide (60 mL) was added dropwise a solution of chloromethylene-*N*,*N*-dimethyliminium chloride (17 g, 0.133 mol) in the same solvent (40 mL), and the mixture was stirred at room temperature for 3 h, then refluxed for another 3 h. The reaction mixture was poured into water and

extracted with $CH_2Cl_2$ which was evaporated to give a syrupy mixture (11.4 g). This mixture (8 g) was applied to a Kieselgel column, in two parts, eluting with 9:1 toluene–MeOH to give compounds **5**, **3**, and **2** according to their order of elution from the column.

*5,6-Dichloro-5,6-dideoxy-3-*O*-formyl-1,2-*O*-trichloroethylidene-β-*L*-altrofuranose* (**5**).—Yield: 1.30 g; mp 79–80 °C (from petroleum ether); $[\alpha]_D^{18}$ +4.88° (*c* 0.9, pyridine); NMR data: δ 7.85 (s, 1 H, OCHO), 6.17 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.48 (s, 1 H, $CHCCl_3$), 4.87 (d, 1 H, $J_{2,3}$ ~0 Hz, H-2), 5.52 (bs, 1 H, $J_{3,4}$ ~0 Hz, H-3), 4.27 (bd, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.00 (m, 1 H, H-5), 3.85 (m, 2 H, H-6a,6b); MS: *m/z* 275 [$M^+$ – (CHCl–$CH_2Cl$), 94.8%], 255 ($M^+$ – $CCl_3$, 32.5%), 209 (255 – HCOOH, 45.0%), 181 {[($M^+$ + 1) – $CCl_3CHO$] – HCOOH, 100%}, 129 (275 – $CCl_3CHO$, 17.6%). Molecular weight: 372 (FABMS). Anal. Calcd for $C_9H_9Cl_5O_5$: C, 28.87; H, 2.42; Cl, 47.34. Found: C, 28.97, H, 2.32; Cl, 47.28.

*5,6-Dichloro-5,6-dideoxy-1,2-*O*-trichloroethylidene-β-*L*-altrofuranose* (**3**).—Yield: 0.86 g; mp 115–116 °C (from $CHCl_3$); $[\alpha]_D^{18}$ −3.35° (*c* 0.67, pyridine); NMR data: δ 6.43 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.68 (s, 1 H, $CHCCl_3$), 5.10 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 4.90 (bs, 1 H, $J_{3,4}$ ~0 Hz, H-3), 3.80–4.40 (m, 4 H, H-4,5,6a,6b), 2.83 (bs, OH); in $C_6D_6$: δ 6.03 (d, 1 H, $J_{2,3}$ 4 Hz, H-1), 5.33 (s, 1 H, $CHCCl_3$), 4.57 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 4.32 (s, 1 H, $J_{3,4}$ 0 Hz, H-3), 4.15 (d, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.88 (m, 1 H, H-5), 3.67 (m, 2 H, H-6a,6b), 1.83 (bs, 1 H, OH); MS: *m/z* 247 [$M^+$ – (CHCl–$CH_2Cl$), 64.6%], 229 (247 – $H_2O$, 39.3%), 227 ($M^+$ – $CCl_3$, 57%), 209 (227 – $H_2O$, 16.0%), 181 {[($M^+$ + 1) – $CCl_3CHO$] – $H_2O$, 100%}. Molecular weight: 344 (FABMS). Anal. Calcd for $C_8H_9Cl_5O_4$: C, 27.74; H, 2.62; Cl, 51.17. Found: C, 27.89; H, 2.51; Cl, 51.03.

*6-Chloro-6-deoxy-1,2-*O*-trichloroethylidene-α-*D*-galactofuranose* (**2**).—Yield: 2.70 g; mp 179–180 °C (from MeOH); $[\alpha]_D^{18}$ −11.2° (*c* 0.60, pyridine); MS: *m/z* 277 ($M^+$ – $CH_2Cl$, 6.5%), 247 (277 – CHOH, 47.8%), 229 (247 – $H_2O$, 5.4%), 101 (247 – $CCl_3CHO$, 30.1%), 36 (HCl, 100%). Molecular weight: 326 (FABMS). Anal. Calcd for $C_8H_{10}Cl_4O_5$: C, 29.30; H, 3.07; Cl, 43.24. Found: C, 29.26; H, 2.93, Cl, 42.80.

*3-*O*-Acetyl-5,6-dichloro-5,6-dideoxy-1,2-*O*-trichloroethylidene-β-*L*-altrofuranose* (**6**). —Acetylation of **3** (0.5 g) with $Ac_2O$ in pyridine gave the monoacetate **6** (95%), mp 127–128 °C (from petroleum ether; $[\alpha]_D^{18}$ +6.33° (*c* 0.7, $CHCl_3$); NMR data: δ 6.36 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.66 (s, 1 H, $CHCCl_3$), 5.02 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 5.56 (bs, 1 H, $J_{3,4}$ 0 Hz, H-3), 4.40 (bd, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.98–4.15 (m, 3 H, H-5,6a,6b), 2.13 (s, 3 H, Ac); MS: *m/z* 289 [$M^+$ – (CHCl–$CH_2Cl$), 19.2%], 269 ($M^+$ – $CCl_3$, 7.3%), 143 (289 – $CCl_3CHO$, 8.4%), 209 (269 – AcOH, 14.9%), 43 (Ac, 100%). Anal. Calcd for $C_{10}H_{11}Cl_5O_5$: C, 30.92; H, 2.85; Cl, 45.63. Found: C, 30.98; H, 2.71; Cl, 45.45.

*3,5-Di-*O*-acetyl-6-chloro-6-deoxy-1,2-*O*-trichloroethylidene-α-*D*-galactofuranose* (**4**). —Acetylation of **2** gave **4** (90%) as a syrup; $[\alpha]_D^{30}$ +17.97° (*c* 1.0, $CHCl_3$); NMR data: δ 6.52 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 6.05 (s, 1 H, $CHCCl_3$), 5.22 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 5.35 (bs, 1 H, $J_{3,4}$ < 1 Hz, H-3), 4.55 (bd, 1 H, $J_{4,5}$ 6 Hz, H-4), 5.57 (dd, 1 H, $J_{5,6a} = J_{5,6b}$ = 6 Hz, H-5), 3.93, 3.95 (2 d, 2 H, H-6a,6b), 2.18, 2.25 (2 s, 2 × Ac). Anal. Calcd for $C_{12}H_{14}Cl_4O_7$: C, 34.98; H, 3.42; Cl, 34.42. Found: C, 34.90; H, 3.35; Cl, 34.28.

*Deformylation of* **5**.—Deformylation of **5** (0.5 g) with methanolic NaOMe was completed in 2 h at room temperature. The product, 5,6-dichloro-5,6-dideoxy-1,2-*O*-trichloroethylidene-β-L-altrofuranose (**3**) was obtained in 97% yield; mp and mixture mp 115–116 °C.

*3,5,6-Tri-*O*-tosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose* (**7**).—To a cold solution of **1** (7.0 g) in pyridine (70 mL) was added *p*-toluenesulfonyl chloride (13.0 g, 3.015 mol. equiv). The mixture was left at room temperature overnight. TLC indicated the formation of a mixture of four products. The mixture was poured on to crushed ice, the oily product which separated was extracted with $CH_2Cl_2$, the extracts were dried and evaporated to a syrup, and the product was retosylated and worked-up as above to give syrupy **7**. This product was crystallised (8.0 g, 45.8%) from $CCl_4$ containing a little MeOH and petroleum ether; mp 132–134 °C; $[\alpha]_D^{24}$ +22.8° (*c* 1.4, $CHCl_3$); NMR data (200 MHz): δ 6.14 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1), 5.57 (s, 1 H, $CHCCl_3$), 4.95 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 4.83 (bs, 1 H, $J_{3,4}$ ~ 0 Hz, H-3), 4.33 (bs, 1 H, H-4), 4.6 (td, 1 H, $J_{4,5}$ 2.5 Hz, H-5), 4.06 (d, 2 H, $J_{5,6a} = J_{5,6b}$ = 6.6 Hz, H-6a and H-6b), 2.50 (s, 2 × Me), 2.47 (s, Me), 7.85, 7.76, 7.71, 7.43 (4 H), 7.36 (6 doublets for phenyl protons, each *J* 8.0 Hz); MS: *m/z* 770 ($M^+$, 28%), 734 ($M^+ - HCl$, 12%), 653 ($M^+ - CCl_3$, 28%), 600 ($M^+$ – TsOH), 45%). Anal. Calcd for $C_{29}H_{29}Cl_3O_{12}S_3$: C, 45.11; H, 3.78; S, 12.46; Cl, 13.77. Found: C, 44.98; H, 3.69; S, 12.30; Cl, 13.50.

*6-Chloro-6-deoxy-3,5-di-*O*-tosyl-1,2-*O*-trichloroethylidene-α-D-galactofuranose* (**8**). —Tritosyl derivative **7** (2 g) in *N*,*N*-dimethylformamide (50 mL) was stirred with LiCl (0.8 g) at 90 °C for 2.5 h. After evaporation of about half of the solvent, the mixture was poured on to crushed ice to give a white precipitate (1.2 g, 72.8%). This product was contaminated (TLC) with a trace of dichloro derivative **9**. Several crystallisations (from $CHCl_3$ with petroleum ether added until cloudiness) gave pure **8** (0.9 g); mp 95–97 °C; $[\alpha]_D^{24}$ +13.3° (*c* 1.5, $CHCl_3$); NMR data (200 MHz): δ 6.21 (d, 1 H, $J_{1,2}$ 4.1 Hz, H-1), 5.52 (s, 1 H, $CHCCl_3$), 4.96 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 4.84 (bs, 1 H, $J_{3,4}$ ~ 0 Hz, H-3), 4.59 (bs, H-4), 4.56 (m, $J_{5,6b}$ 4.5 Hz, H-5), 3.73 (t, 1 H, $J_{5,6a}$ 10.5 Hz, H-6a), 3.55 (dd, 1 H, $J_{6a,6b}$ 10.5 Hz, H-6b), 2.50 (s, 6 H, 2 × Me), 7.89, 7.81, 7.45, 7.41 (4 doublets for phenyl protons, each *J* 8.0 Hz); MS: *m/z* 634 ($M^+$, 25%), 598 ($M^+ - HCl$, 90%), 517 ($M^+ - CCl_3$, 60%), 401 [($M^+ - CHOTs - CH_2Cl$), 60%]. Anal. Calcd for $C_{22}H_{22}Cl_4O_9S_2$: C, 41.52; H, 3.48; S, 10.07; Cl, 22.28. Found: C, 41.40; H, 3.50; S, 10.22; Cl, 22.00.

*5,6-Dichloro-5,6-dideoxy-3-*O*-tosyl-1,2-*O*-trichloroethylidene-β-L-altrofuranose* (**9**). —Tritosyl derivative **7** (2 g) in *N*,*N*-dimethylformamide (50 mL) was stirred with LiCl (0.8 g) at 90 °C for 20 h. The concentrated mixture was poured on to crushed ice; the precipitate thus formed contained the title compound slightly contaminated with **8** (TLC and NMR). This product was purified by several crystallisations from $CHCl_3$ with added petroleum ether until cloudiness to give **9** (0.9 g, 57.2%); mp 82–84 °C; $[\alpha]_D^{24}$ −48.1° (*c* 1.5, $CHCl_3$); NMR data (200 MHz): δ 6.33 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.56 (s, 1 H, $CHCCl_3$), 5.16 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 5.15 (s, 1 H, $J_{3,4}$ ~ 0 Hz, H-3), 4.29 (bd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 3.92 (m, 1 H, H-5), 3.88 (bs, 2 H, H-6a,6b), 7.85 (d, 2 H, *J* 8.0 Hz, Ph-H), 7.40 (d, 2 H, *J* 8.0 Hz, Ph-H), 2.47 (s, 3 H, Ph-Me); MS: *m/z* 401 [$M^+$–(CHCl–$CH_2Cl$), 100%], 427 [($M^+ - Cl - HCl$), 7%], 381 ($M^+ - CCl_3$, 5%), 255 (401 – $CCl_3CHO$, 75%). Anal. Calcd for $C_{15}H_{15}Cl_5O_6S$: C, 35.99; H, 3.02; S, 6.40; Cl, 35.41. Found: C, 35.82; H, 3.15; S, 6.20; Cl, 35.06.

Tosylation of compound **3** (0.5 g) was carried out with *p*-toluenesulfonyl chloride (0.2 g) in pyridine (10 mL) for 1 h at 60 °C. On completion of the reaction (TLC), the product was isolated and crystallised (0.3 g) as above; mp and mixture mp 80–83 °C; the NMR spectrum of this compound was identical with the NMR spectrum of **9**.

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