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## Note

# Synthesis of α-(2→9)-disialic acid*

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Oligosialyl structures have been found to occur in glycoproteins, glycolipids, and bacterial polysaccharides[2]. The α-(2→8) and α-(2→9) linkages between sialic acids are present in the sialic acid polysaccharide antigens of pathogenic bacteria[3]. Recently, the α-(2→9)-linked polysialyl phosphoglycerolipid structure (**1**) was proposed for the meningococcal serogroup C polysaccharide[4].

We now describe a regioselective synthesis of α-(2→9)-disialic acid (**3**) as a key intermediate for the synthesis of oligosialyl phosphoglycerolipids (**1**). A similar compound (**2**) was synthesized by Ogawa and Sugimoto[5].

The allyl compound (**4**)‡ was stereoselectively prepared from the chloride[6] (**9**) in the presence of silver salicylate and 2-propenol. Deacetylation of **4** with 0.1M sodium methoxide in methanol afforded the 4,7,8,9-tetrahydroxy derivative (**5**)‡ [81.4%; m.p. 133–.135°, $[\alpha]_D^{24}$ −3.26° (*c* 1.02, EtOH)]. Treatment of **5** with acetone plus IR-120 ($H^+$) ion-exchange resin gave the 8,9-isopropylidene derivative (**6**)‡ [81.8%; m.p. 173–175°, $[\alpha]_D^{22}$ −9.40° (*c* 1.00, $CHCl_3$)].

Regioselective benzylation of **6** was achieved with benzyl bromide, silver oxide, and tetrabutylammonium iodide in 1,2-dichloroethane, to yield the 7-*O*-benzyl derivative (**7**)‡ [58.4%; m.p. 122–125°, $[\alpha]_D^{23}$ +12.5° (*c* 1.00, $CHCl_3$)]. The isopropylidene group of **7** was removed by heating in 80% AcOH to give a glycosyl acceptor, the 4,8,9-trihydroxy derivative (**8**)‡ [93.8%; amorphous, $[\alpha]_D^{22}$ +9.28° (*c* 1.02, $CHCl_3$)].

Glycosation of **8** with the chloride **9** in the presence of $Hg(CN)_2$–$HgBr_2$–molecular sieves 4A afforded the (2→9)-disialyl derivatives (**10α**:**10β** = 2:1), which were separated by p.l.c.; total yield 82.9%; **10α**‡: m.p. 96–99°, $[\alpha]_D^{22}$ −6.1° (*c* 1.0, $CHCl_3$); $\delta_H$ ($CDCl_3$): 2.62 (dd, 1 H, *J* 4.4, 12.9 Hz, H-3*e*); **10β**‡: m.p. 92–95°, $[\alpha]_D^{22}$ −3.5° (*c* 0.8, $CHCl_3$); $\delta_H$ ($CDCl_3$): 2.50 (dd, 1 H, *J* 6.1, 13.9 Hz, H-3*e*).

*Neuraminic Acid and Related Compounds, Part II. For Part I, see ref. 1.
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‡Satisfactory analytical and spectral data were obtained for these compounds.

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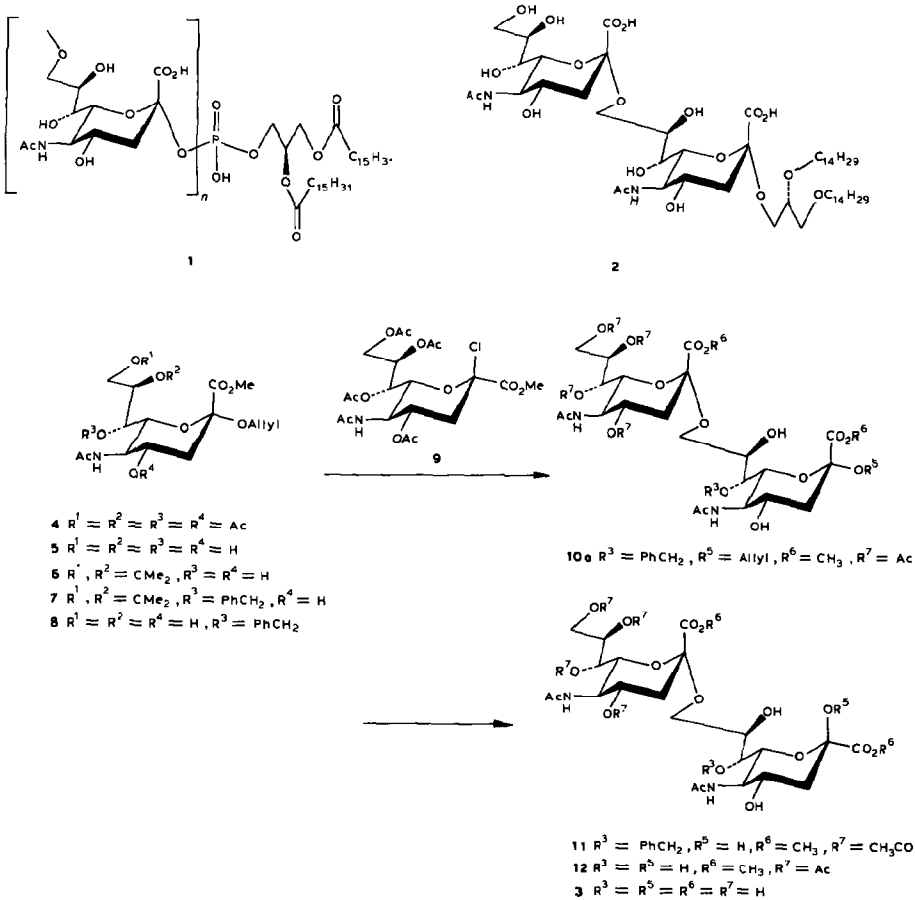

*O*-Deallylation of the disialyl compound **10α** was performed as follows. The allyl group of **10** was isomerized with $[(COD)Ir\text{-}(PMePh_2)_2]^+PF_4^-$ catalyst into the 1-propenyl compound, which was then saponified with THF–$H_2O$–$I_2$, to give the 2-hydroxy compound **11**‡ [39%; m.p. 131–133°, $[\alpha]_D^{19}$ −14.1° (*c* 0.28, $CHCl_3$)].

The use of $Pd(OH)_2$ in the hydrogenolysis of **11** afforded the 7-hydroxy derivative (**12**)‡ [86%; m.p. 146–148°, $[\alpha]_D^{19}$ −31.7° (*c* 0.2, $CHCl_3$)]. *O*-Deacetylation of **12**, followed by saponification of the methyl ester groups, yielded the potassium salt of (2→9)-disialic acid (**3**)‡ [94%; m.p. 162–165°, $[\alpha]_D^{19}$ −14° (*c* 0.14, $H_2O$)].

Use of the 7-*O*-benzyl-8-hydroxy derivative (**7**), instead of the 7,8-di-*O*-acetyl derivative[5], gave the (2→9)-linked compounds in surprisingly high yield.

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