# Synthesis of Sugar–Organometallic Conjugates: Ferrocenyl Derivatives

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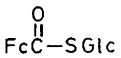
*Summary* Ferrocenylcarbonyl chloride (**1**) reacts with 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**2**) to form the thio ester (**3**), and the reaction of *NN*-dimethylaminomethylferrocene methiodide (**4**) with 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (**5**) yields the *NN*-bis-complex (**6**); the reaction of (**2**) with the ferrocenyl reagent (**7**) yields the sugar–ferrocenyl conjugate (**8**) *via* the versatile coupling reagent cyanuric chloride.

As part of a general programme to develop methods for the synthesis of various types of metal–sugar conjugates we have previously described the synthesis of salicylideneamine Schiff's base sugar–metal chelate complexes.[1] We now demonstrate the ease with which organometallic species, *e.g.* ferrocene (**9**), can be covalently attached to sugars in a variety of ways. Such substances are of interest for a number of reasons including the possible development of new iron-containing drugs,[2] optically active catalysts,[3] new ferrocene modified polymers,[4] metal compounds for new immunoassay techniques,[5] and their possible use as heavy metal probes for electron microscopy.[6] Although systematic studies were not made, the formation of ferrocenyl glycosides[7] and of ferrocenyl acetyls[8] has been reported previously.

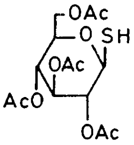
A wide variety of ferrocene derivatives are susceptible to nucleophilic attack by the amino, hydroxy, or thiol groups of suitably blocked carbohydrate derivatives. For example, ferrocenylcarbonyl chloride[9] (**1**) readily reacts† (15 min) with the 1-thio sugar (**2**) in chloroform–pyridine at room temperature to give (**3**) as orange needles in 70% yield, m.p. 186 °C (from EtOH), $[\alpha]^{25}_{D}$ + 35° (*c* 1, $CHCl_3$). Reactions of (**1**) with hydroxy or amino groups are equally easy.

When 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (**5**) was heated under reflux (13 h) in acetonitrile

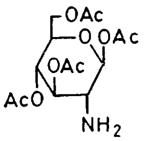
FcCOCl
(1)


$Fc\overset{O}{\overset{\|}{C}}-SGlc$
(3)

$FcCH_2\overset{+}{N}Me_3$
(4)

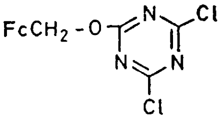


(HSGlc)
(2)

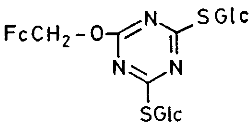


$(H_2NGlc)$
(5)

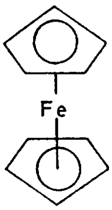
$(FcCH_2)_2NGlc$
(6)



(7)



(8)



(FeH)
(9)

$FcCH_2OH$
(10)

$FcCH_2-O-CH_2Fc$
(11)

with 2 equiv. of *NN*-dimethylaminomethylferrocene methiodide[10] (**4**) and anhydrous sodium carbonate, compound (**6**) was produced in 66% yield [from benzene, hexane, and light petroleum (b.p. 30—60 °C)], m.p. 95 °C, $[\alpha]_D^{22}$ + 77° (*c* 1, $CHCl_3$). We have found that the reagent (**4**) also reacts with thiol nucleophiles but not with hydroxy groups.

An alternative strategy for the preparation of ferrocene–sugar conjugates involves the intermediacy of a 'covalent locus', and we exemplify this approach here using cyanuric chloride. The ferrocene reagent (**7**) was prepared by adding dropwise to an acetone solution of cyanuric chloride at 0 °C, over 45 min, an acetone solution of hydroxymethylferrocene[11] (**10**) and aqueous sodium hydroxide. Compound (**11**), a by-product, was removed by filtration; on standing, the filtrate became acidic and the desired product (**7**) separated as an orange solid in 50% yield, m.p. 120 °C (decomp.) (from ether, hexane). This material displayed essentially the same reactivity as the other substituted *s*-triazine reagents we recently reported elsewhere,[12] suggesting that it will find use, for example, in grafting ferrocene to solid support matrices.[13]

When (**7**) was stirred at room temperature with 2 equiv. of the 1-thio sugar (**2**) and $NEt_3$ in acetonitrile solution the compound (**8**) was obtained in 74% yield, m.p. 120 °C (from $Pr^iOH$), $[\alpha]_D^{22}$ + 25·4 (*c* 1, $CHCl_3$).

The structures of the compounds reported here were confirmed by 270 MHz $^1H$ n.m.r. measurements. The protons of the unsubstituted cyclopentadienyl ring appear as a sharp singlet at *ca.* 4 p.p.m., whereas the substituted cyclopentadienyl ring protons are split and shifted slightly down-field. It is interesting to note that proximity to a sugar group renders inequivalent all the four protons of the substituted cyclopentadienyl ring, as previously observed by Kursanov *et al.*[14] for other chiral species.

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† All derivatives reported here have satisfactory elemental analysis and/or mass spectra.

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