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Hydroxynaphthyl *C*-Glycosides via Chromium-Mediated Benzannulation of a Sugar Alkyne[1]

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Abstract:

Benzannulation of *C*-ethynyl glucoside **1** with electrophilic chromium carbene **2** affords $Cr(CO)_3$-coordinated hydroxynaphthyl *C*-glycoside **3**. The metal carbonyl fragment can be shifted by haptotropic migration or removed upon oxidation to give aryl *C*-glycosides **4** and **5**.

Keywords: Benzannulation; Carbenes and carbenoids; Carbohydrates; Chromium carbenes; Glycosides

C-Glycosides receive increasing attention as *O*-glycoside analogues which combine stability to acid hydrolysis with only minor structural changes.[2] *C*-Aryl glycosides play an important role in antibacterial, antitumor, antifungal and antibiotic research.[2] A series of synthetic approaches has been developed over the past decade.[3] The benzannulation of *Fischer*-type chromium carbenes with alkynes provides a straightforward access to oxygenated arenes.[4] It offers a regioselective incorporation of the alkyne, and thus represents a promising novel route to functionalized aryl-*C*-glycosides. As part of our efforts to utilize organometallics in carbohydrate synthesis we focussed on the benzannulation of highly electrophilic chromium diarylcarbenes with ethynyl *C*-glycosides.[5]

The glucose-derived alkyne **1** was obtained as a single diastereomer from the corresponding lactone by addition of ethynyl magnesium bromide followed by reduction with triethylsilane in the presence of boron trifluoride.[6] The configuration at the anomeric centre was established by the coupling constant $^3J_{H(1),H(2)}$ = 9 Hz indicative for a ß-glycoside. While carbene complexes stabilized by an α-heteroatom (O, NR) generally require temperatures above 45°C for the benzannulation, the more electrophilic diphenylcarbene complex **2**[7] reacted with the ethynyl glucose **1** already at room temperature to give the air-sensitive $Cr(CO)_3$-coordinated ß-naphthyl *C*-glycoside **3** (Scheme 1). Chromatography on silica gel resulted in a haptotropic

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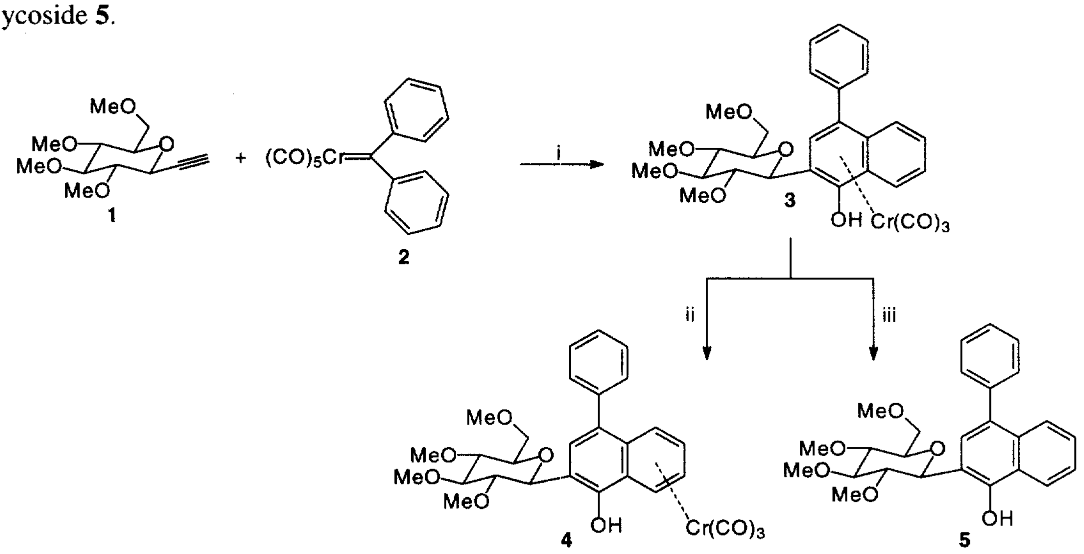
migration of the metal fragment to the unsubstituted naphthol ring to give the thermodynamically more stable aryl *C*-glycoside complex **4** in an overall yield of 30%. The benzannulation occurs with only modest 1.25:1 diastereoselectivity. ^{1}H-NMR analysis indicated the formation of two diastereomers as a consequence of the plane of chirality imposed by the complexation of the naphthol ring. The coordination by the potent acceptor metal fragment may be exploited in subsequent stereoselective functionalization by nucleophilic substitution. Decomplexation was achieved by stirring a solution of **3** on air to give uncoordinated naphthyl glycoside **5**.



Scheme 1: Reagents and conditions: i) THF, r.t., 1h; ii) SiO_2, 10°C, 30 % (overall); iii) O_2, r.t., quantitative.

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[8] Selected spectroscopic data for **5**: ^{13}C-NMR (100 MHz/C_6D_6): δ = 151.1, 132.6, 131.9, 127.3, 126.8, 126.7, 126.3, 125.7, 125.2, 123.1 (10 C, $C_{naphthol}$), 141.3, 130.4, 128.3, 127.6 (6 C, C_{phenyl}), 58.7, 60.1, 60.1, 60.4 (4 C, OCH_3), 70.5 (C-6), 88.1 (C-1), 78.8, 78.8, 80.6, 85.0 (4 C, C-2-C-5) ppm.