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Allyl *C*-Glycosidation of Glycals Mediated by 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ)

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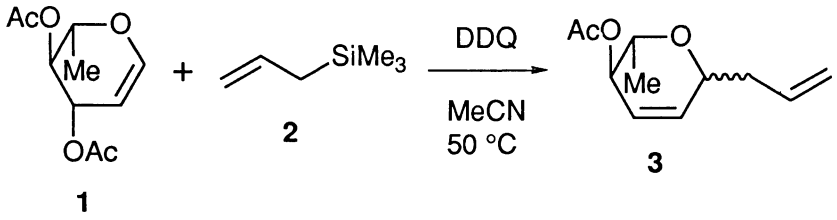
A novel and highly stereoselective method for the synthesis of allyl *C*-glycosides bearing C_2-C_3 unsaturation has been developed using glycal acetate, allyltrimethylsilane and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) as a neutral activator.

Allyl *C*-glycosides are undoubtedly very versatile synthetic intermediates for natural product syntheses.[1] Also, carbon-linked glycosides, stable analogues of naturally occurring *O*- and *N*-glycosides, have become the subject of considerable interest in both bioorganic chemistry and medicinal chemistry.[2] Danishefsky *et al.*[3] and Isobe *et al.*[4] independently reported an effective route to the C_1-allylated glycosides having C_2-C_3 unsaturation from glycal acetates and allyltrimethylsilane [(3-propenyl)trimethylsilane]. A strong Lewis acid such as $TiCl_4$ or BF_3•Et_2O was used as the effective promoter in their methods. Therefore, development of a neutral alternative would extend the scope of the useful allyl *C*-glycosidation reaction. Very recently, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), which is well known as a neutral oxidative reagent, was found to be an effective *O*-glycosidation promoter of 3,4-dimethoxybenzyl glycosides as glycosyl donors by Inanaga *et al.*[5] We also announced the novel *O*-glycosidation of glycals promoted by DDQ.[6] In our extended studies of this project, we have utilized such properties of DDQ in *C*-glycosidation reaction. In this letter, we report a novel and highly stereoselective protocol for the synthesis of 2,3-unsaturated allyl α-*C*-glycosides using glycal acetates, allyltrimethylsilane and DDQ as a neutral activator.

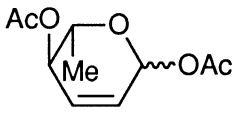
We first examined the *C*-glycosidations of 3,4-di-*O*-acetyl-L-rhamnal (**1**) with allyltrimethylsilane (**2**) using various amounts of DDQ in MeCN at 50 °C.[7] These results are summarized in Table 1. Although this glycosidation reaction proceeded even with 10 mol% of DDQ, a long reaction time was required to get a high yield of the allyl *C*-glycoside **3** (entries 1 and 2). On the other hand, excess amounts of DDQ caused a significant

Table 1. Glycosidations of **1** with allyltrimethylsilane **2** by DDQ [a)]



1 **2** **3**

Entry	Mol% of DDQ	t / h	Yield / % [b)]
1	10	12	63
2	10	36	83
3	30	12	80
4	30	24	86
5	50	12	90
6	70	12	77
7	100	12	67
8	150	12	31



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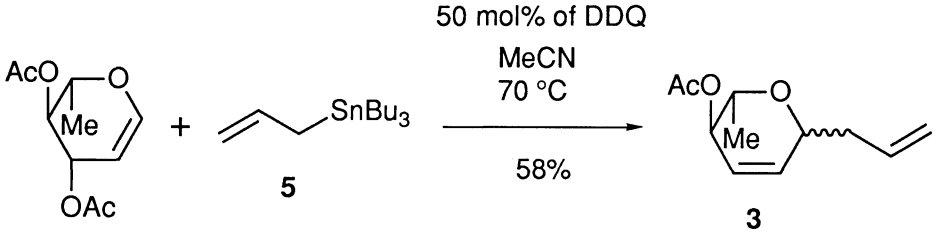
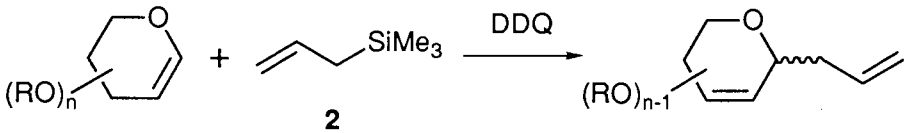
a) All reactions were carried out by use of 1.5 equiv. of **2** to **1**.
b) Isolated yields after purification by column chromatography.

decrease in the yield of the desired glycoside **3** because the allylic rearrangement of the C_3-*O*-acetyl group took place predominantly to give the 1-*O*-acetyl-2,3-unsaturated glycoside **4** (entry 8). Therefore, the use of 30-50 mol% of DDQ was most effective for performing the glycosidation reaction when considering the reaction time and temperature and yield. Indeed, the allyl *C*-glycoside **3** was obtained in high yield after 12 h at 50 °C (entries 3 and 5). Our attention next turned to the effect of the allyl species in this reaction and the glycosidation of **1** with another typical allyl species, allyltributyltin (**5**) (1.5 equiv.), was investigated. Although the reaction also



1 **5** **3**

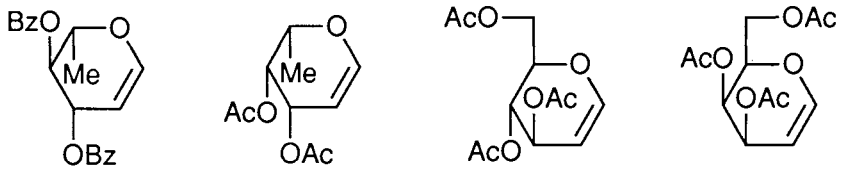
Table 2. Glycosidations of several glycals with **2** by DDQ [a)]



glycal **2** 2,3-unsaturated allyl *C*-glycosides

Entry	Glycal	Mol% of DDQ	T / °C	t / h	Yield / % [b)]	α/β Ratio [c)]
1	**1**	50	50	12	90	15/1
2	**5**	50	70	48	77	10/1
3	**6**	50	70	48	74	>99/1
4	**7**	50	50	48	85	16/1
5	**8**	50	70	48	76	>99/1

a) All reactions were carried out by use of 1.5 equiv. of **2** to the glycal.
b) Isolated yields after purification by column chromatography.
c) α/β Ratios were determined by ^{1}H-NMR (270 MHz) spectroscopy.



5 **6** **7** **8**

Bz = benzoyl

proceeded under similar conditions and the allyl *C*-glycoside **3** was obtained in moderate yield, the glycosidation was much less effective than that with allyltrimethylsilane (**2**).

Finally, the glycosidations of other typical acylated glycals **5**-**8** with **2** mediated by DDQ were examined. The results summarized in Table 2 showed that these glycosidations proceeded under similar conditions to afford the corresponding allyl *C*-glycosides[8)] in high yields. The comparison of entry 1 with entry 2 in Table 2 indicated that the glycosidation of a glycal acetate was more effective than that of the corresponding benzoate. Notably,

the stereoselectivies of these glycosidation reactions were highly α-selective in all cases.[9] Since the configuration of the anomeric position was not isomerized by exposure of the single α-anomer of **3** to the reaction conditions, the high α-stereoselectivity must arise from the kinetic anomeric effect.[10]

In conclusion, although the efficiency of this glycosidation was limited by the long reaction time, the present protocol offers a new method for the *C*-glycosidation of glycals under neutral conditions. Details of the present glycosidation mechanism are now under investigation.

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7) In our previous *O*-glycosylation study of glycal by DDQ, it was found that MeCN was the best solvent and a suitable temperature was 50 °C for the reaction, see Ref. 6.

8) All compounds were purified by silica-gel column chromatography and were fully characterized by spectroscopic means.

9) The stereochemistry of the anomeric center was determined by ^{1}H NOE experiments, see Refs. 3 and 4 for enrties 4 and 5. In the case of the major products in entries 1-3, a clear NOE effect was observed with ~3.5% enhancement between the H-1 signal and the H-6 (methyl) signal; M. Brakta, R. N. Farr, B. Chaguir, G. Massiot, C. Lavaud, W. R. Anderson, Jr., D. Sinou, and G. D. Daves, Jr., *J. Org. Chem.*, **58**, 2992 (1993).

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