

Synthesis of Vinylic *C*-Glycosides from Telluroglycosides. Addition of Photochemically and Thermally Generated Glycosyl Radicals to Alkynes

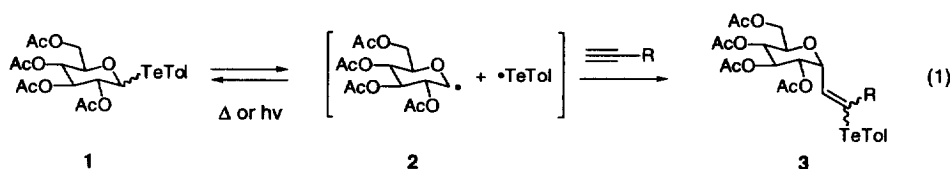
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Abstract: Glycosyl radicals generated from telluroglycosides react with a variety of alkynes to give the corresponding vinylic *C*-glycosides in good to excellent yields. The reaction takes place in an atom transfer manner to form vinyl telluride, and the resulting C-Te bond is transmetalated to the C-Zn bond with Et₂Zn or reduced to the C-H bond with tributyltin hydride. © 1999 Elsevier Science Ltd. All rights reserved.

The synthesis of *C*-glycosides has attracted a great deal of attention because of their numerous and diverse biological functions.¹ Glycosyl radicals play major roles among various methods for the *C*-glycoside synthesis,² because the mild reaction conditions allow the presence of various polar functional groups of sugar derivatives. While the glycosyl radical addition to alkenes is well documented, that to alkynes is not known except for the intramolecular reaction.^{3,4} In the preceding paper, we have reported that the glycosyl radicals **2** are reversibly generated from telluroglycosides **1**.⁵ In this paper, we report that the glycosyl radical so generated reacts with alkynes to form vinylic *C*-glycoside **3** (eq 1). To our knowledge, this is the first example of the intermolecular glycosyl radical addition to alkynes,⁶ providing a new method for the synthesis of a variety of vinylic *C*-glycosides.⁷



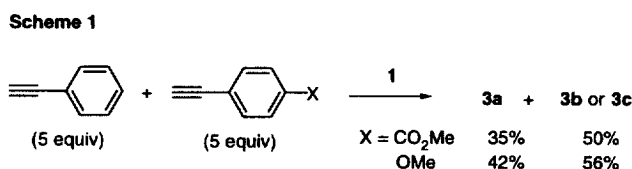
A typical experimental procedure is as follows. A mixture of **1** (2.75 g, 5.0 mmol) and phenylacetylene (2.55 g, 25.0 mmol) in a sealed Pyrex tube was irradiated with a UV lamp [Rayonet RMR-600 equipped with RMR-3500Å lamp (4.5 W x 8)] at 120 °C for 20 h. Purification of the crude mixture by silica gel chromatography afforded the addition product **3a** (R = Ph) in 93% yield (3.02 g, 4.65 mmol) as a 47:29:13:11 mixture of the α -*E*, α -*Z*, β -*E*, and β -*Z* isomers (Table 1, entry 1). The reaction in the dark at 120 °C also gave the adduct in good yield. By the addition of 10 mol% of AIBN,^{6c} the reaction proceeded under milder conditions (80 °C).⁸

Telluroglycoside **1** was also effectively reacted with a variety of alkynes to give the corresponding

vinyllic *C*-glycosides in good to excellent yield (entries 1-8). Aryl- and heteroaryl-substituted alkynes were found to be good acceptors. As the reaction proceeded under neutral conditions, the acid-labile and the base-labile functional groups, such as furanyl, carboxyl, and carbonyl groups, were unaffected. Aromatic alkynes bearing electron-withdrawing and -donating groups served as good acceptors to afford the corresponding *C*-glycosides **3b** ($X = \text{CO}_2\text{Me}$) and **3c** ($X = \text{OMe}$) in good yield (entries 2 and 3), but the reaction of acetylene carboxylic esters gave a moderate yield of the adduct due to competitive side reactions (entry 6). Alkyl-substituted alkynes were less reactive, and the reaction with 1-octyne gave the adduct in low yield (entry 7). Not only the telluroglycosides derived from *D*-glucose **1**, but those from *D*-galactose and 2-deoxy-*D*-glucose also reacted with phenylacetylene to give the corresponding vinyllic *C*-glycoside in good yield (entries 9 and 10). The internal alkynes, e.g., diphenyl acetylene and dimethyl acetylenedicarboxylate, were completely unreactive.

In all cases, the α -isomers were preferentially obtained over the β -isomers.⁹ The observed α -selectivity is consistent with the well-known anomeric effects of the glycosyl radicals;¹⁰ a stabilizing interaction of the SOMO of the glycosyl radical and the electron pair at the pyranose oxygen involves during the α -glycoside formation, while there is no such interaction for the β -glycoside formation. Therefore, the attack of the alkyne preferentially took place from the α -side to give the α -glycosides.

In an effort to gain further insight into the reactivities of the radical **2**, we next examined the intermolecular competition reaction of the radicals with both the electron-deficient and electron-rich alkynes. Since the glycosyl radicals are well known to behave as nucleophilic radicals due to the anomeric effect, the electron-deficient alkynes would be more reactive than the electron-rich ones. However, our expectation notwithstanding, the reactivity was virtually insensitive to the nature of the substituents of the alkynes.¹¹ Thus, the reaction of **1** in the presence of equal amounts of phenylacetylene and *p*-substituted phenylacetylenes ($X = \text{CO}_2\text{Me}$, OMe) revealed that both the electron-deficient and electron-rich alkynes reacted slightly faster than phenylacetylene (Scheme 1).



The C-Te bond of **3** was potentially useful for further synthetic transformation.¹² For example, treatment of **3** with Et_2Zn gave the corresponding zinc species,¹³ which afforded the *C*-vinyl-glycoside **4** after hydrolysis. The same transformation could be achieved under radical conditions by the use of Bu_3SnH . The hydrogenation of **4** gave the corresponding *C*-alkyl-glycoside **5** (Scheme 2).

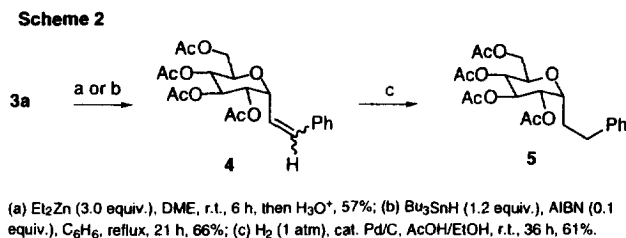
In conclusion, we have demonstrated the intermolecular addition of the glycosyl radical **2** to alkynes provides a powerful strategy for the synthesis of a variety of vinyllic *C*-glycosides. The success in the reaction

Table 1. Telluroglycoside Addition to Alkynes.^a

Entry	Telluroglycoside	Alkyne	Major product	%Yield ^b	$\alpha(E:Z):\beta^c$
1	1			93	75(61:39):25
		X = H	3a	81 ^d 87 ^e 89 ^f	78 (64:36):22 83 (54:46):17 78 (47:53):22
2		X = CO ₂ Me	3b	79	77(58:42):23
3		X = OMe	3c	70	75(61:39):25
4				78	80 (59:41):20
5				48	79 (67:33):21
6 ^g				38 (50) ^h	69 (49:51):31
7				11 (23) ^h 24 ^e (56) ^h	74 (45:55):26 72 (51:49):21
8 ⁱ				41	76 (63:37):24
9				94	90 (50:40):10
10				55	90 (53:37):10

^a The reaction was carried out by UV irradiation of neat telluroglycoside and 5 equiv. of alkynes at 120 °C for 20 h. ^b Isolated yield.

^c Isomeric ratio was determined by the ¹H NMR analysis of the crude reaction mixture. The β -isomer consisted of a *ca.* 1:1 mixture of the *E*- and *Z*-isomers. ^d The reaction was carried out in the dark at 120 °C for 20 h. ^e The reaction was carried out in the presence of 10 mol% of AIBN at 80 °C in the dark for 20 h. See ref. 6c. ^f The reaction was carried out in the presence of 10 mol% of AIBN at 120 °C in the dark for 20 h. ^g The reaction was carried out at 100 °C. ^h Yield based on the converted telluroglycosides. ⁱ Reaction was carried out with 5 equiv. of **1** in toluene, and the yield was based on the alkyne.



is dependent on the reversible generation of **2** from **1** without the use of radical promoters, because competitive additions of the promoter to alkynes are usually serious side reactions. Work on elucidation of the origin of the unique reactivity as well as further synthetic applications is currently underway.

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- We believe that the current reaction proceeds by both a radical chain and a non-chain mechanisms (see ref. 6c).
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