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An Expeditious Methodology for the Incorporation of Unsaturated Systems into Carbohydrates via an Enol Triflate

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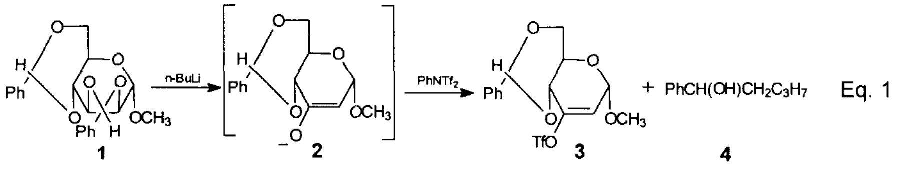
Abstract. *One step synthesis of enal, diene, divinyl ketone and enyne systems on a carbohydrate template via an enol triflate.* © 1997 Elsevier Science Ltd.

The incorporation of enals, dienes, α,β-unsaturated systems and carbocycles into carbohydrates has greatly extended the versatility of the sugar template.[1] In these systems, the sugar moiety serves as an agent for "chirality transfer" in the Diels-Alder, Pauson-Khand, Nazarov and other reactions. However, until recently,[2] introduction of unsaturated systems into carbohydrate templates required many steps with very low overall yields.[1]

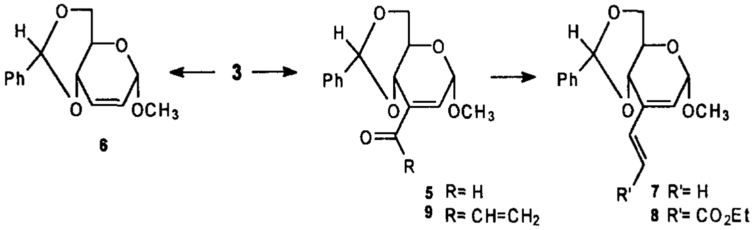
Enol triflates are efficient intermediates for the incorporation of enal, diene, enyne, divinyl ketone and other α,β-unsaturated systems via Pd (0) couplings with a wide variety of organo stannane reagents, or Pd (II) couplings with Michael acceptors.[3] We describe herein, the synthesis of enal, diene, divinyl ketone and enyne systems on pyranoses in two steps starting from **1**.

According to Klemer and Rodemeyer's reaction, the enolate was generated *in situ* upon treament of **1** with *n*-BuLi.[4] Our strategy for the synthesis of enol triflate **3** depends on trapping the enolate (**2**) *in situ* by N-phenyl-bis-tri-fluoromethansulfonimide ($PhNTf_2$). Thus, treatment of **1** with *n*-BuLi in THF at -40 °C for 30 min resulted in the formation of enolate (**2**), as indicated by red



coloration. Trapping of **2** with 4 equivalents of $PhNTf_2$ at -70 °C over 1 h and then at - 18 °C for 12 h gave the desired enol triflate **3** (85% yield).[5] In a previous report, compound **3** was also synthesized in two steps starting from **1**.[6] Furthermore, the coupling of **3** with organo stannane or allylic cuprate to yield respectively, 1,3- or 1,4-diene has been achieved.[6]

The heterodienic system of an unsaturated aldehyde such as **5** is a very useful substrate for the Diels-Alder reaction. Morever, this unsaturated system can serve as a precursor for building a variety of diene systems into carbohydrates via the Wittig reaction. Despite these benefits, the synthesis of this compound in six steps and in an overall yield of 16% was unappealing.[1a] These initial results prompted us to explore a more expeditious approach toward the synthesis of enal **5** via enol triflate **3**. Compound **5** was obtained in 73% yield via Pd(0) coupling of **3** with carbon monoxide (3 atm) at 50 °C with slow addition of *n*-Bu_3SnH during the reaction (4 h). Decreasing the pressure of CO to one atmosphere resulted in the formation of a new product **6**, in addition to compound **5** (25% yield). NMR and MS spectra of **6** were consistent with the product of reductive cleavage of the triflate. Furthermore, the reductive cleavage was obtained quantitatively upon repeating the reaction under argon. Wittig reaction of **5** with $Ph_3P{=}CH_2$ or $Ph_3P{=}CHCO_2Et$ yielded **7** (90%) and **8** (94%), respectively. Alternatively, reaction of **3** with tributylvinylstannane, $(Ph_3P)_4Pd(0)$, and lithium chloride gave a quantitative yield of **7**. Chiral divinylketones such as **9** are useful intermediates for the synthesis of optically active cyclopentenones by the Nazarov reaction. Compound **9** can be prepared in 71% yield from enol triflate **3** by a palladium-catalyzed reaction with tributylvinylstannane and carbon monoxide. The successful insertion of CO was achieved when the reaction was carried out for 12 h at 50 °C.



6

5 R= H

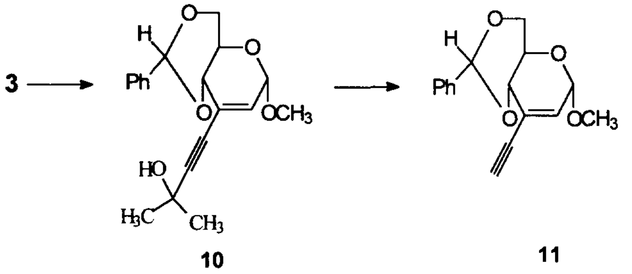
9 R= CH=CH₂

7 R'= H

8 R'= CO₂Et

Eq. 2.

$(Ph_3P)_2Pd(II)Cl_2$ catalyzed the coupling of **3** with 2-methyl-3-butyn-2-ol in the presence of triethylamine in DMF at 70 °C to give **10**, which was transformed to the required enyne (**11**) upon treatment with KOH in benzene.



Eq. 3

In conclusion, this paper describes an expeditious methodology for the incorporation of a carbonyl system into carbohydrates via an enol triflate. Moreover, the divinyl ketone **9**, a useful intermediate for the synthesis of chiral cyclopentenone via the Pauson-Khand reaction, can also be prepared in only three steps giving an overall yield of 57%. This is in contrast to classical methods which rely on 9 steps for the synthesis of this intermediate. Finally, Classical procedures for the incorporation of α,β-unsaturated systems failed to arrive at enyne systems[1a] such as **11**, which are very efficient intermediates for the construction of di- or tricyclic systems via Ad_E reaction and intramolecular Pauson-Khand cycloaddition.[7]

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