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Palladium-Catalyzed Rearrangement and Substitution Reactions of Acyclic Vinylogous Carbonates and Sulfonates: Development of a New Leaving Group for Pd-Allyl Chemistry

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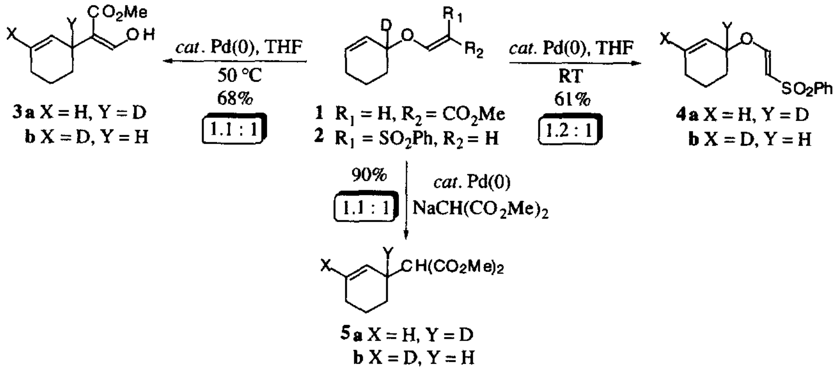
Abstract: *Palladium-catalyzed rearrangement of the deuterium labeled vinylogous carbonate 1 furnished the β-formyl esters 3a/b in 68% yield, while the Z-vinylogous sulfonate (Z-VINS) 2 under analogous reaction conditions led to reversible O-alkylation and isomerization to afford the* E-*VINS 4a/b in 61% yield. This observation prompted the development of the vinylogous sulfonate as an improved leaving group for a variety of palladium-catalyzed allylic substitution reactions.*

The transition metal-catalyzed allylic substitution reaction is an important transformation that remains the focus of intense synthetic and mechanistic interest.[1] This may be attributed, at least in part, to its immense synthetic utility in carbon-carbon bond formation. Asymmetric catalysis has further increased the synthetic utility of this reaction, through the development of chiral ligands which furnish transition-metal complexes that produce highly enantiomerically enriched products.[2,3] In a program aimed at the development of new metal-catalyzed allylic substitution reactions, we have examined the merit of acyclic vinylogous carbonates and sulfonates in a series of palladium-catalyzed rearrangement and substitution reactions.



Scheme 1

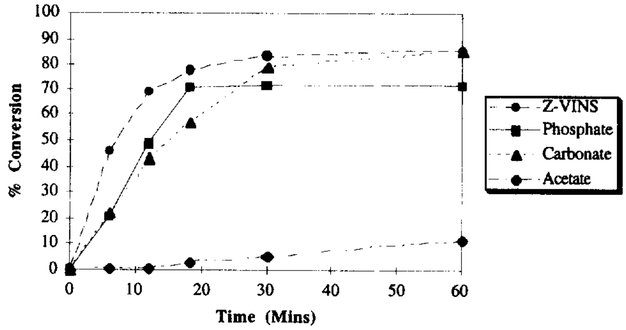
PII: S0040-4039(99)00475-X

The *intramolecular* palladium-catalyzed *O*- to *C*-alkylation of *cyclic* vinylogous carbonates and sulfonates, has been described independently by Trost[4] and Tsuji.[5] We now report the corresponding palladium-catalyzed allylic rearrangement and substitution reactions of *acyclic* vinylogous carbonates and sulfonates, in which the latter provides an effective new leaving group with enhanced rate of reaction.

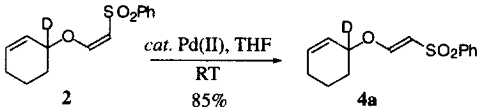
Preliminary investigations established that the deuterium labeled *E*-vinylogous carbonate **1**[6,7] and *Z*-vinylogous sulfonate (VINS) **2**[7,8] undergo complementary allylic-type rearrangements, as outlined in **Scheme 1**. Palladium-catalyzed isomerization of **1** afforded the *C*-substituted products **3a/b**[7] in 68% yield, while *Z*-VINS **2** furnished the *E*-VINS **4a/b**[7] in 61% yield, as a mixture of regioisomers in both cases. The deuterium scrambling demonstrates that the rearrangement of acyclic vinylogous carbonates and sulfonates is consistent with the intermediacy of a fluxional π-allyl palladium complex.[1] Hence, it was envisioned that the π-allyl palladium intermediate derived from the vinylogous sulfonate **2** could be intercepted by an external nucleophile. As expected, treatment of **2** with catalytic palladium(0) in the presence of the sodium salt of dimethyl malonate, rapidly (*ca.* 5 min.), furnished the diesters **5a/b**[7] in 90% yield. These preliminary observations provided the impetus to develop the vinylogous sulfonate as a new leaving group for palladium-catalyzed allylic substitution reactions.

Table 1 summarizes the results for this study using the acyclic *Z*-VINS **6a/b** with a range of stabilized carbon and nitrogen nucleophiles. The leaving group facilitates the rapid formation ($\leq$ 20 min.) of the substitution products **7a/b** in 78-90% isolated yield in each case examined (entries 1-12).[7] The excellent turnover rates are particularly noteworthy, especially for the nitrogen nucleophiles (entries 9-12), since this type of transformation often requires elevated temperatures and extended reaction times.[9] The improved reactivity of the vinylogous sulfonate was further supported by direct comparison of its reaction rate (by HPLC) in the allylic amination with the phosphate (LG = $P(O)OEt_2$), carbonate (LG = CO_2Me), and acetate (LG = $COCH_3$) derivatives of **6b** using the lithium anion of *N*-tosylallylamine as the nucleophile (**Fig. 1**).

Figure 1: *Comparison of the Relative Rates of Reaction for the Pd(0)-Catalyzed Allylic Amination (Nu = $TsNLiCH_2CH{=}CH_2$) using Various Leaving Group Derivatives of* ***6b****.*



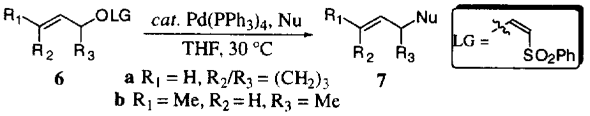
Attempted palladium-catalyzed Claisen rearrangement of the Z-VINS **2** was expected to provide the complementary *C*-alkylation product.[11] However, treatment of **2** with catalytic palladium(II)chloride bis(benzonitrile) complex at room temperature led to *E/Z*-isomerization furnishing the *E*-VINS **4a**[7] in 85% yield as a *single regio- and geometrical isomer* (eq. 1).[12]



(1)

This result may provide insight into the possible mechanistic course of the Pd(0)-catalyzed oxidative addition process, and thus account for the excellent rate enhancements observed with vinylogous sulfonates. It is plausible, that provided Pd(0) can reversibly bind the vinylogous sulfonate in a similar fashion to Pd(II), the oxidative addition may occur through either a cooperative or intramolecular pathway.

Table 1: Allylic Alkylation of the Acyclic Z-VINS **6a/b**[7] with Stabilized Carbon and Nitrogen Nucleophiles



Entry	Z-VINS **6**	Nucleophile[a]	Equiv.	Base	Solvent.	Time (min.)[b]	Yield of **7** (%)[c]
1	**a**	$CH_3COCH_2COCH_3$	3	NaH	THF/DMF (10:1)	4	82
2	**b**	“	2	“	“	5	90
3	**a**	$CH_3COCH_2CO_2CH_3$	3	NaH	THF/DMF (20:1)	10	90
4	**b**	“	2	“	THF	6	90
5	**a**	$PhSO_2CH_2CO_2CH_3$	3	NaH	THF/DMF (10:1)	17	87
6	**b**	“	“	“	“	10	81
7	**a**	$NCCH_2CO_2Bn$	2	NaH	THF	5	89
8	**b**	“	“	“	“	10	84
9	**a**	$PhCH_2NHTs$	2	LiHMDS	THF	15	78
10	**b**	“	“	“	“	20	82
11	**a**	$CH_2{=}CHCH_2NHTs$	2	LiHMDS	THF	13	81
12	**b**	“	“	“	“	15	85

[a] Reactions were all carried out with 5 mol% of $Pd(PPh_3)_4$ at 30 °C on a 0.5 mmol reaction scale.[10] [b] Reactions were monitored by t.l.c. [c] Isolated yields.

In conclusion, we have demonstrated that vinylogous sulfonates provide excellent leaving groups for a variety of palladium-catalyzed substitution reactions. In the course of these studies, we also delineated the Pd(0)-catalyzed allylic rearrangement and substitution reactions of vinylogous carbonates and sulfonates. Studies are underway to determine the merit of vinylogous sulfonates in asymmetric metal-catalyzed substitution reactions, and elucidate the mechanism for oxidative addition.

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10. *Representative Experimental Procedure*: *p*-Tolylsulfonylallylamine (0.212 g, 1.0 mmol) was dissolved in anhydrous THF (3.0 mL) and stirred at 30 °C under an atmosphere of argon using a constant temperature bath. Lithium hexamethydisilylazide (1.0 mL, 1.0 mmol, 1.0 M in tetrahydrofuran) was added dropwise and the resulting anion allowed to form over *ca.* 30 minutes. The Z-vinylogous sulfonate **6a** (0.133 g, 0.5 mmol) was dissolved in anhydrous THF (1.0 mL) and added to the anion solution *via* teflon® cannula rinsing the flask with THF (2 x 0.5 mL). $Pd(PPh_3)_4$ (0.029 g, 0.025 mmol, 5 mol%) was then added in a single portion and the resulting reaction mixture stirred for *ca.* 13 minutes at 30 °C (t.l.c. control). The reaction mixture was then concentrated *in vacuo* and purified by flash chromatography (eluting with a 10-20% gradient of ethyl acetate/hexane) furnished the allylic amination product **7a** (Nu = $TsNCH_2CH{=}CH_2$; 0.118 g, 81%) as a colorless oil.
11. Overman, L. E. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 579.
12. Palladium-catalyzed isomerization of *E*-VINS **4a** furnished the isomeric *E*-VINS **4a/b** (1.5:1) in 84% yield, which is consistent with a dynamic equilibration through a palladium π-allyl intermediate.