Heck Reactions Starting from Silyl Enol Ethers - A Simple One-Pot Nonaflation-Coupling Procedure for the Synthesis of 1,3-Dienes

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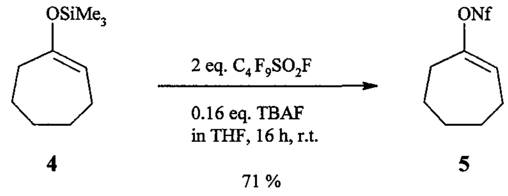
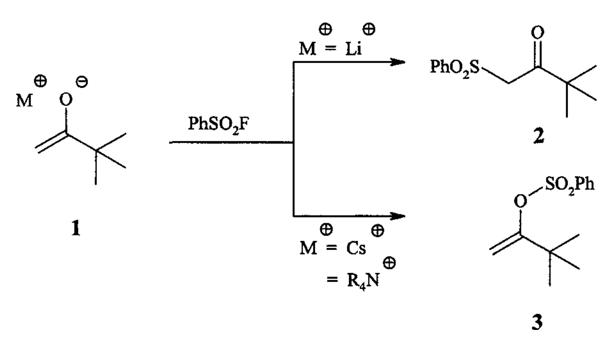
Abstract: Starting from silyl enol ether **4** the corresponding alkenylnonaflate **5** was generated by treatment with nonafluorobutanesulfonyl fluoride (NfF) and a catalytic amount of tetra-*n*-butylammonium fluoride (TBAF). By Pd-catalysis **5** was directly Heck-coupled with a variety of olefins to furnish functionalized 1,3-dienes **6** - **12**. This one-pot procedure could be extended to other silyl enol ethers and provides new synthetic options.



In 1982 Hirsch, Hünig, and Reissig reported an interesting cation effect observed with enolate **1**.[1] A smooth C-sulfonylation of the lithium enolate occurs with benzenesulfonyl fluoride to give **2** whereas the corresponding cesium or ammonium enolates provide the O-sulfonylation product **3** exclusively. This effect could be exploited to prepare various alkenylsulfonates starting from silyl enol ethers and applying catalytic amounts of tetraalkylammonium fluorides. A few nonafluorobutanesulfonates (nonaflates) had been among the examples.[2]



Due to our interest in Pd-catalyzed coupling reactions[3] we disclose here our results of a one-pot nonaflation-Heck-reaction[4] which starts from silyl enol ethers and provides substituted and functionalized 1,3-dienes in a simple and flexible manner.

1-Trimethylsiloxycycloheptene (**4**) served as model substrate for the procedure. Its reaction with commercially available nonafluorobutanesulfonyl fluoride (NfF) in the presence of catalytic amounts of tetra-*n*-butylammonium fluoride (TBAF) furnished nonaflate **5** after careful distillation in 71% yield. The quality of the fluoride source is crucial for the success of this transformation. Good results were obtained when a THF solution of TBAF was further dried with molecular sieves.[5]

Having established the first step of the two-step one-pot procedure **5** was directly coupled to several monosubstituted olefins without isolation (Table). For the Heck step we employed $Pd(OAc)_2$ as catalyst (0.035 eq.), K_2CO_3/KOAc as base and DMF as solvent.[6] These ingredients were just added to the solution containing **5** and then the mixture was heated to 65 - 85 °C. This unoptimized protocol provided 1,3-dienes **6** - **10** in the range of 40 - 65% overall yield. The reaction with acrylonitrile as olefin furnished diene **7** as a mixture of *E*/*Z*-isomers (4:1) whereas all other isolated 1,3-dienes of the table were pure *E*-isomers.[7]

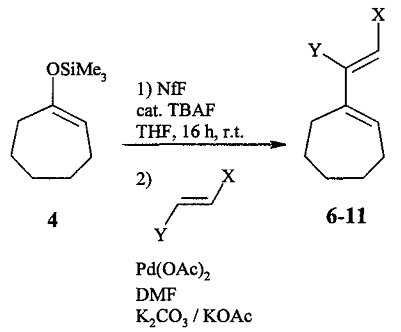
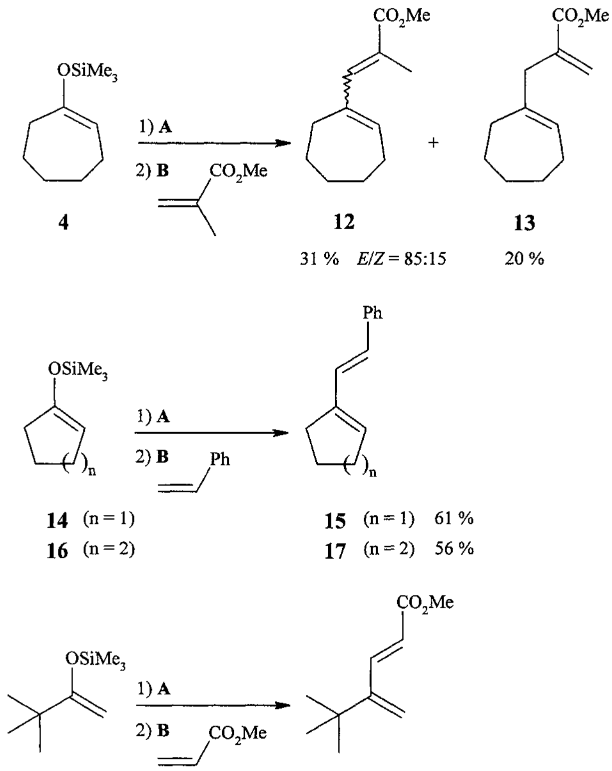


Table. Synthesis of 1,3-Dienes **6-11**

Alkene		Conditions		Product	Yield
X	Y	Time [h]	Temp. [°C]		[%]
CO_2Me	H	6	85	**6**	64
CN	H	6	65	**7**[a]	43
Ph	H	6	80	**8**	64
SO_2Ph	H	6	85	**9**	39
$PO(OMe)_2$	H	6	85	**10**	56
CO_2Me	Me	6	80	**11**	40

[a] Mixture of *E*/*Z*-isomers (4 : 1)

The examples of Scheme 1 show that disubstituted olefins can be used with somewhat reduced efficiency, whereas silyl enol ethers **14** and **16** behave in a way similar to that of **4**. Their coupling to styrene succeeded in ca. 60% yield. Only pinacolone based silyl enol ether **18** provided the expected diene ester **19** in lower yield.[8]



A NfF, cat. TBAF, THF, 16 h, r.t.

B cat. $Pd(OAc)_2$, DMF, K_2CO_3 / KOAc, 6 h, 80 °C

Scheme 1

Alkenyltriflates, which are equivalent to alkenylnonaflates, are usually generated from carbonyl compounds, bases and triflating reagents such as $PhNTf_2$, OTf_2, and therefore at least 50% of the valuable Tf group is lost.[2,9] What are the advantages of our method? First, it employs the technical product NfF, which is a considerably cheaper sulfonating agent. Second, the resulting nonaflates should even be slightly more reactive than the corresponding triflates due to the better leaving group quality.[10] Third, our method should allow to exploit all the advantages of silyl enol ether properties, as are their regio- and stereoselective preparation or the possibility to purify by distillation or chromatography.[11] This gives additional synthetic options compared with the direct sulfonylation of enolates. We are currently exploring these possibilities and extend the one-pot protocol to other Pd-catalyzed couplings.

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References and Notes

(1) Hirsch, E.; Hünig, S.; Reissig, H.-U. *Chem. Ber.* **1982**, *115*, 3687. For a very similar O-acylation of enolates employing acyl fluorides, see: Limat, D.; Schlosser, M. *Tetrahedron* **1995**, *51*, 5799.

(2) For alternative syntheses of alkenylnonaflates and the more commonly used alkenyltriflates as well as their reactions, see: Stang, P.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85. - Ritter, K. *Synthesis* **1993**, 735. - For the use of perfluoroalkanesulfonyl fluorides, see: Subramanian, L. R.; Bentz, H.; Hanack, M. *Synthesis* **1973**, 293. - Zhu, Z.; Tian, W.; Liao, Q. *Tetrahedron Lett.* **1996**, *37*, 8553.

(3) Khan, F. A.; Czerwonka, R.; Reissig, H.-U. *Synlett* **1996**, 533.

(4) Reviews: 4a) Heck, R. F. in *Palladium Reagents in Organic Synthesis*, Academic Press, Orlando FL, **1985**. - 4b) Heck, R. F. in *Comprehensive Organic Synthesis* (Eds.: Trost, B. M.; Fleming, I.), Vol. **4**, p. 833, Pergamon Press, Oxford, **1991**. - 4c) de Meijere, A.; Meyer, F. E. *Angew. Chem.* **1994**, *106*, 2473; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379. - 4d) Tsuji, J. in *Palladium Reagents and Catalysts*, J. Wiley & Sons, Chichester, **1995**.

(5) TBAF was purchased from ABCR as 1 M solution in THF. It was dried with freshly activated pulverized molecular sieves (4 X). See: Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas E. *Helv. Chim. Acta* **1982**, *65*, 1102.

(6) For Heck reactions of alkenyltriflates, see: Scott, W. J.; Peña, M. R.; Swärd, K.; Stoessel, S. J.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2302. - We employed conditions as described by Burini, A.; Cacchi, S.; Pace, P.; Pietroni, B. R. *Synlett* **1995**, 677.

(7) Typical procedure **4** → **8** (performed under Ar): To 1-trimethylsiloxycycloheptene (**4**) (0.92 g, 5.00 mmol) were first added at 0 °C ca. 80 mg of pulverized, freshly activated molecular sieves (4 X), then nonafluorobutanesulfonyl fluoride (3.02 g, 10.0 mmol), and finally 0.9 ml of a 1 M solution of TBAF in THF (0.90 mmol). The resulting two-phase mixture was stirred for 16 h at room temperature and then diluted with dry DMF (6 ml). After addition of $Pd(OAc)_2$ (39 mg, 0.175 mmol), K_2CO_3 (0.60 g, 4.43 mmol), KOAc (0.34 g, 3.50 mmol), and styrene (0.546 g, 5.25 mmol) the mixture was heated to 80 °C for 6 h. Extractive workup (H_2O/ethyl acetate) provided crude **8** which was purified by chromatography (SiO_2, hexane/ethyl acetate, 10:1) thus furnishing 0.63 g (64%) of pure **8** as colorless liquid (Tamura, R.; Kato, M.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* **1987**, *52*, 4121).

(8) The lower yield may be due to the steric hindrance in the coupling step. We are not aware of a similar example bearing a *tert*-butyl group.

(9) For recent alternatives, see: Comins, D. L.; Benjelloun, N. R. *Tetrahedron Lett.* **1994**, *35*, 829.

(10) There are only singular examples of the use of aryl- and alkenylnonaflates in Pd-catalyzed coupling reactions, see ref. 4c and Bräse, S.; de Meijere, A. *Angew. Chem.* **1995**, *107*, 2741; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2545.

(11) Review: Chan, T.-H. in *Comprehensive Organic Synthesis* (Eds.: Trost, B. M.; Fleming, I.), Vol. **2**, p. 595, Pergamon Press, Oxford, **1991**.