# Alkenylation of C−H Bonds via Reaction with Vinyl and Dienyl Triflones. Stereospecific Synthesis of Trisubstituted Vinyl Triflones via Organocopper Addition to Acetylenic Triflones[1]

Jason Xiang and P. L. Fuchs*

*Department of Chemistry, Purdue University*
*West Lafayette, Indiana 47907*

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We recently reported that reaction of ethers, sulfides, and hydrocarbons with acetylenic triflones such as **2a,b** provides facile access to substituted alkynes **3** (Scheme 1).[2] The reaction proceeds via radical C−H abstraction[3] by the very electrophilic trifluoromethyl radical **4**[4] in a process involving addition of alkyl radical **5** to the α-carbon of the acetylenic triflone **2** followed by elimination of the vinyl radical **6** to alkyne **3** and trifluoromethylsulfonyl radical **7**. Fragmentation[5] of **7** to sulfur dioxide and the trifluoromethyl radical **4** propagates the chain.[6]

Consistent with this mechanism is the finding by Russell that photogenerated cyclohexyl radicals undergo reaction with β-phenylethynyl phenyl sulfone (**8**)[7] to generate phenyl cyclohexyl acetylene (**10**) and phenyl sulfonyl radical (which does not fragment to sulfur dioxide and phenyl radical,[8] thereby unable to propagate a similar C−H activation event). In the same study, Russell made the important observation that radical addition to the vinyl sulfone **11** provides alkene **13** via a similar addition−elimination process (Scheme 2).[7]

The second example suggested that our C−H functionalization protocol shown in Scheme 1 might be extended to the domain of olefins. In order to assess that possibility, we examined the reaction of THF (**15a**) and cyclohexane (**15b**) with the vinyl triflone *E*-**14** and the dienyl triflone *E,E*-**17**, which we had previously prepared via a Peterson olefination protocol.[9] As can be seen in Scheme 3, these reactions provide direct access to C−H functionalized olefins *E*-**16a,b** and dienes *E,E*-**18a,b**.

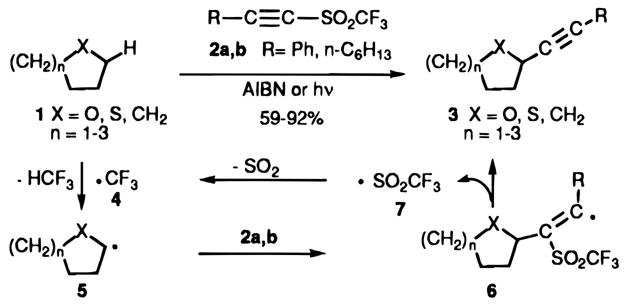
The stereochemistry of the radical addition−elimination reaction was investigated using isomeric vinyl triflone *Z*-**14**.[10] Not surprisingly, reaction with THF (**15a**) again provides adduct *E*-**16a** to the total exclusion of adduct *Z*-**16a**, indicating that intermediate **19** undergoes bond rotation prior to elimination of the trifluoromethyl sulfonyl radical **7** or that **7** can re-add to the *Z*-olefin *Z*-**16a** (Scheme 4).

We next explored the C−H alkenylation reaction with a set of trisubstituted vinyl triflones *Z,E*-**20**, *Z*-**21**, and *Z,E*-**22**. As with previous examples, radical addition−elimination reaction with THF (**15a**) was high yielding, but the products **24**−**26** were *Z*/*E* mixtures of the trisubstituted olefin, consistent with expectations from equilibration of the β-trifluoromethylsulfonyl radical intermediate **23** (Scheme 5).

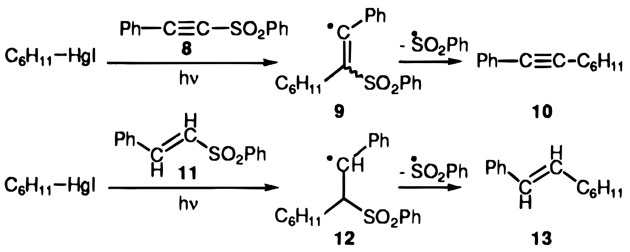
Examination of Table 1 reveals that intermediate **23** retains a substantial memory of the stereochemistry of its vinyl triflone precursor, with fragmentation occurring predominantly via a least motion retention process. The decrease in reaction rate and accompanying increase in stereospecificity as one proceeds down the table is consistent with progressively smaller stability of the β-trifluoromethylsulfonyl radical intermediate **23**.

More interesting is the observation that the reactions of diaryl-substituted vinyl triflones *Z*- and *E*-**20a** initially exhibit high stereospecificity, which is substantially degraded as the reaction proceeds (Table 1, entries 2a−c, 4a−c). Control reactions

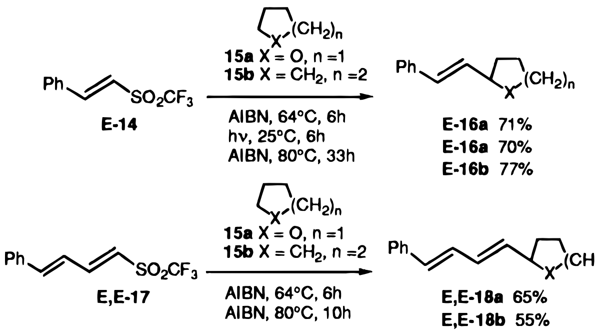
**Scheme 1**



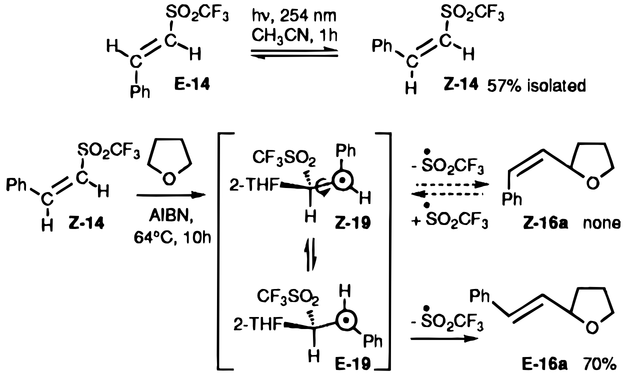
**Scheme 2**



**Scheme 3**



**Scheme 4**



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[1] *Syntheses Via Vinyl Sulfones 68. Triflone Chemistry 7.* For triflone paper 6, see ref 6.

[2] Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4486.

[3] Medebielle, M.; Pinson, J.; Saveant, J.-M. *J. Am. Chem. Soc.* **1991**, *113*, 6872.

[4] Bond dissociation energy $HCF_3$ = 107 kcal/mol: *Handbook of Chemistry and Physics*, 74th ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1993−1994; pp 9−137.

[5] (a) Langlois, B. R.; Laurent, E.; Roidot, N. *Tetrahedron Lett.* **1992**, *33*, 1291. (b) Hu, C.-M.; Qing, F.-L.; Huang, W.-Y. *J. Org. Chem.* **1991**, *56*, 2801. (c) Huang, W.-Y.; Hu, L.-Q. *J. Fluorine Chem.* **1989**, *44*, 25. (d) Langlois, B. R.; Laurent, E.; Roidot, N. *Tetrahedron Lett.* **1991**, *32*, 7525.

[6] Xiang, J.; Fuchs, P. L. *Tetrahedron Lett.* **1996**, *37*, 5269.

[7] Russell, G. A.; Ngoviwatchai, P. *J. Org. Chem.* **1989**, *54*, 1836 and references cited therein. This finding has recently been extended to the additions of α-alkoxy radicals to styryl sulfoximines (Clark, A. J.; Rooke, S.; Sparey, T. J.; Taylor, P. C. *Tetrahedron Lett.* **1996**, *37*, 909). For general references to olefin formation via β-sulfonyl radical chemistry, see: Ono N.; Kamimura, A.; Kaji, A. *J. Org. Chem.* **1987**, *52*, 5111 and references cited therein.

[8] (a) Bertrand, M. P. *Org. Prep. Proc. Int.* **1994**, *26*, 257. (b) Chatgilialoglu, C. Sulfonyl Radicals. In *Chemistry of Sulphones and Sulphoxides*; Patai, S., Ed.; John Wiley: New York, 1988; pp 1089−1113.

[9] Mahadevan, A.; Fuchs, P. L. *Tetrahedron Lett.* **1994**, *35*, 6025.

[10] This material was prepared by photochemical isomerization of *E*-**14**. See ref 12.

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**Scheme 5**

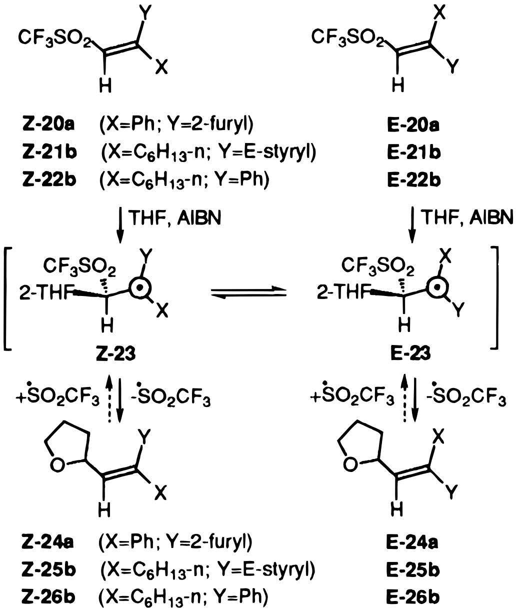
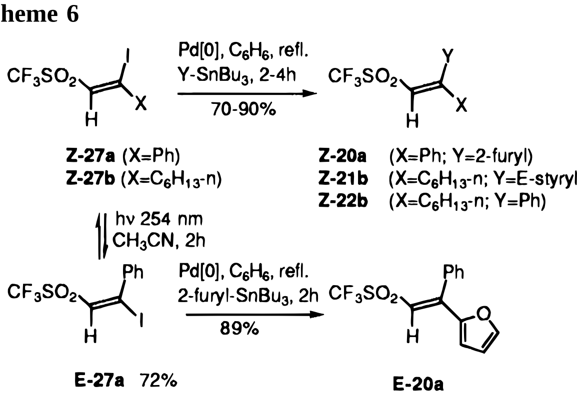


**Table 1.** Reaction of THF with Stereodefined Alkenyl Triflones

| entry | substrate | concn (mM), *t* (h)[a] | SM (%) | products[b] | yield[c] (%) | *Z*:*E* ratio[d] |
|---|---|---|---|---|---|---|
| 1 | *Z*-**20a** | 25, 5 | 0 | *Z*/*E*-**24a** | 91 | 2.3:1 |
| 2a | *Z*-**20a** | 5, 2 | 51 | *Z*/*E*-**24a** | 49 | 7:1 |
| 2b | *Z*-**20a** | 5, 5 | 35 | *Z*/*E*-**24a** | 65 | 4.5:1 |
| 2c | *Z*-**20a** | 5, 12 | 16 | *Z*/*E*-**24a** | 84 | 1.3:1 |
| 3 | *E*-**20a** | 10, 9 | 0 | *Z*/*E*-**24a** | 85 | 1:2.2 |
| 4a | *E*-**20a** | 5, 2 | 68 | *Z*/*E*-**24a** | 32 | 1:19 |
| 4b | *E*-**20a** | 5, 5 | 54 | *Z*/*E*-**24a** | 46 | 1:12 |
| 4c | *E*-**20a** | 5, 10 | 48 | *Z*/*E*-**24a** | 52 | 1:3.2 |
| 5 | *Z*-**21b** | 25, 10 | 0 | *Z*/*E*-**25b** | 71 | 3:1[e] |
| 6 | *Z*-**22b** | 25, 48 | 0 | *Z*/*E*-**26b** | 80 | 5:1[f] |
| 7 | *E*-**22b** | 25, 48 | 0 | *Z*/*E*-**26b** | 81 | 1:5 |
| 8a | *E*-**22b** | 5, 12 | 80 | *Z*/*E*-**25b** | 20 | 1:7 |
| 8b | *E*-**22b** | 5, 24 | 20 | *Z*/*E*-**26b** | 80 | 1:6 |
| 8c | *E*-**22b** | 5, 36 | 1 | *Z*/*E*-**26b** | 99 | 1:5 |

[a] AIBN (10−15%), THF at reflux. [b] Product stereochemistry assigned by NOE experiments; see Supporting Information for the details. [c] Yields of reactions with SM (starting material) remaining are the NMR SM/product ratio of crude reaction mixtures; yields of reactions with 0% SM remaining are isolated yields. [d] Product ratios determined by NMR integration. [e] Product ratio of reaction 5 is shown to be essentially invariant with time. [f] Time-course product ratio of this isomer not studied.

**Scheme 6**



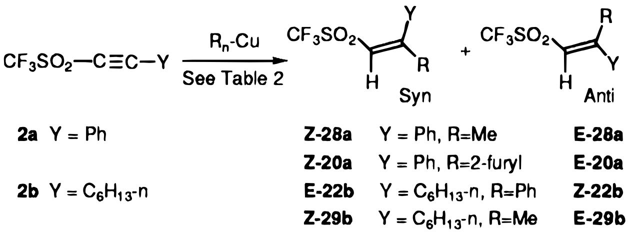
indicate that the equilibration does not result from acid, light, heat, or the 2-methylpropionitrile radical (from AIBN). It is currently believed that the observed equilibration results from the reversible addition of trifluoromethylsulfonyl radical **7**[5] to the product olefins *Z*- and *E*-**24a** which would be expected to be especially reactive radical acceptors.[11]

**Table 2.** Additions of Organocopper Reagents to Acetylenic Triflones

| entry | SM | organocopper | products | yield (%) | *syn*:*anti* |
|---|---|---|---|---|---|
| 1.1 | **2a** | $C_4H_9C{\equiv}CCuMeLi$ | *Z*-**28a**/*E*-**28a** | 84 | 1:2 |
| 1.2 | **2a** | $Me_2CuLi$ | *Z*-**28a**/*E*-**28a** | 85 | 1:1 |
| 1.3 | **2a** | $Me_2CuLi$, −78 °C | *Z*-**28a**/*E*-**28a** | 80 | 1:18 |
| 1.4 | **2a** | $MeCu{\cdot}Me_2S$ | *Z*-**28a**/*E*-**28a** | 78 | 3:1 |
| 1.5 | **2a** | MeCu | *Z*-**28a**/*E*-**28a** | 86 | 6:1 |
| 1.6 | **2a** | MeCu·*n*-$Bu_3B$ | *Z*-**28a**/*E*-**28a** | 85 | 32:1 |
| 2.1 | **2a** | 2-furylCu | *E*-**20a**/*Z*-**20a** | 82 | 12:1 |
| 2.2 | **2a** | 2-furylCu·*n*-$Bu_3B$, −78 °C | *E*-**20a**/*Z*-**20a** | 84 | 17:1 |
| 3 | **2b** | PhCu·*n*-$Bu_3B$ | *E*-**22b**/*Z*-**22b** | 75 | 47:1 |
| 4 | **2b** | MeCu·*n*-$Bu_3B$ | *Z*-**29b**/*E*-**29b** | 90 | 27:1 |

[a] Unless stipulated otherwise, all reactions run in ether at −110 °C for the minimal time (0.5−2 h), followed by quenching with cold ammonium chloride.

**Scheme 7**



The *Z*-configured materials have been made in high overall yield by the stereospecific addition of HI to acetylenic triflone **2a,b** to yield *Z*-**27a,b** followed by Stille coupling.[12] Since it is also known that photoisomerization of *Z*-**27a** affords trisubstituted *β*-iodovinyl triflone *E*-**27a** in 72% isolated yield,[13] we once again applied the Stille coupling reaction to prepare the isomeric trisubstituted vinyl triflone *E*-**20a** (Scheme 6).

The inconvenience associated with the photochemical isomerization−separation−Stille protocol combined with the desire to stereospecifically generate *β*,*β*-dialkyl vinyl triflones, led us to consider an alternative approach to these materials.

Since it is well-known that cuprates undergo *syn* addition to acetylenic sulfones and sulfoxides,[14] we initially investigated the reaction of lithium dimethylcuprate to acetylenic triflones **2a**. Unfortunately, both the mixed acetylenic cuprate[15] and the homocuprate failed to stereospecifically provide the *syn* addition product *Z*-**28a** (Table 2, entries 1.1−1.3), equilibration becoming dominant at higher temperatures. Organocopper reagents gave improved specificity (Table 2, entries 1.4, 1.5, 2.1), but the best condition involved adding 1 equiv of tributylborane, an additive which Yamamoto[16] had used to excellent effect in organocopper additions to acetylenic carbonyl compounds (Scheme 7 and Table 2, entries 1.6, 2.2, 3, 4).

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**Supporting Information Available:** Experimental details and $^1H$ and $^{13}C$ NMR spectra (39 pages). See current masthead page for ordering and Internet access instructions.

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(11) An alternative explanation would involve reversible addition of the THF radical, but this would require equilibration via breaking of C−C bonds and is deemed less likely until a definitive mechanistic study is undertaken.

(12) Compounds shown in Scheme 6 were either recently prepared by the method of Xiang, Mahadevan, and Fuchs (*J. Am. Chem. Soc.* **1996**, *118*, 4284) or were prepared in an analogous fashion (see Supporting Information for synthesis and characterization of *E*-**20a**.)

(13) Although alkylsulfonyl iodides undergo radical trans-addition to acetylenes to generate *E*-*β*-iodovinyl sulfones (Truce, W. E.; Wolf, G. C. *J. Org. Chem.* **1971**, *36*, 1727. Short, K. M.; Ziegler, C. B., Jr. *Tetrahedron Lett.* **1993**, *34*, 71), fluorinated sulfonyl iodides also generate the *E*-*β*-iodovinyl perfluoroalkanes via competitive sulfur dioxide extrusion from the perfluorosulfonyl radical (ref 5c). These facts dictated the selection of a photochemical synthesis for compound *E*-**27a**.

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