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# Mechanistic Aspects of the C-H Alkynylation Reaction of Acetylenic Triflones. Determination of Phenyl Versus Cyclohexyl Migratory Aptitude for a Vinylidine Carbene.[1]

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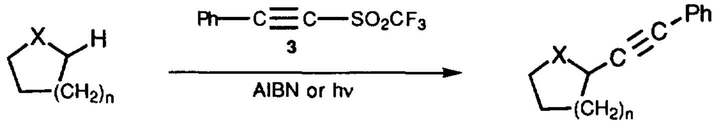
**Abstract:** $^{13}$C-2 labeled phenyl ethynyl triflone undergoes regiospecific C-H alkynylation upon reaction with cyclohexane. The $^{13}$C label is found to be exclusively adjacent to the phenyl group in the product phenyl cyclohexyl acetylene, consistent with cyclohexyl radical addition at the α-position. Control studies show preferential phenyl migration from a vinylidine carbene, thus excluding the presence of such an intermediate.

**Scheme 1**

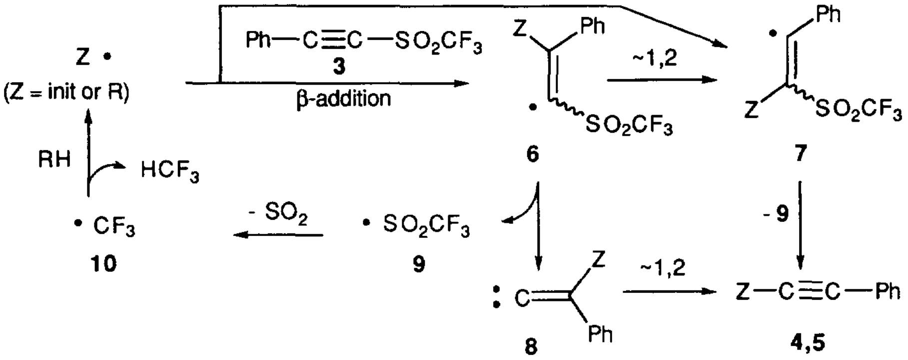


**1** X = O, n = 1
**2** X = $CH_2$, n = 2

**4** X = O, n = 1, 92%
**5** X = $CH_2$, n = 2, 83%

We recently reported that reaction of ethers, sulfides, and hydrocarbons with acetylenic triflones such as **3** provides facile access to substituted alkynes (Scheme 1).[2] The reaction is postulated to proceed via radical intermediates which are generated via C-H abstraction by the very electrophilic trifluoromethyl radical (bond dissociation energy $HCF_3$ = 107 Kcal/mole[3]). While it seems clear that the reaction is initiated (Z = init•) and propagated (Z = R•) by radical addition-elimination to acetylenic triflone **3** (Scheme 2), the regiochemistry of addition needed to be established.

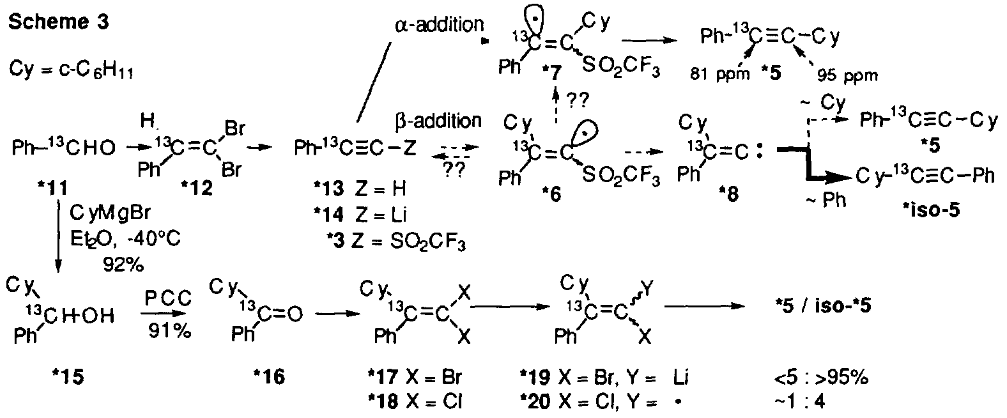
**Scheme 2**



Arguments in favor of either addition mode can be made (Scheme 2). For example, radical addition to the β-carbon of acetylenic triflone **3** could generate α-trifluoromethylsulfonyl vinyl radical **6** which might fragment to vinylidine carbene **8** and trifluoromethylsulfonyl radical **9**. Vinylidine carbenes **8** are well-known to undergo the Fritch-Buttenberg-Weichell rearrangement to afford acetylenes.[4] An alternative mechanism involves either direct α-addition to produce vinyl radical **7**[5] or the unprecedented 1,2-rearrangement of **6** to this species prior to scission of the carbon-sulfur bond. Finally, formation of β-addition intermediate **6** may be a *rapid and reversible* process, thereby allowing the α-addition intermediate **7** to ultimately generate the alkynes **4,5**. Completion of the process involves the known fragmentation[6] of trifluoromethylsulfonyl radical **9** to sulfur dioxide and the highly reactive trifluoromethyl radical **10** which propagates the chain by abstraction of a hydrogen atom from the reaction substrate.[7]

In order to delineate the above regiochemical question, a C-13 labeling study was undertaken. C-13 benzyl alcohol (99% Aldrich) was oxidized in 99% yield to C-13 benzaldehyde ***11** using the Dess-Martin periodinane[8] reagent. Reaction of ***11** with dibromomethylenetriphenylphosphorane[9] afforded dibromide ***12** in 87% yield (vinyl H = 7.5δ, $J_{CH}$ = 160Hz; $\mathrm{Ph\underline{C}H{=}CBr_2}$ = 137.4δ; $\mathrm{PhCH{=}\underline{C}Br_2}$ = 89.7δ, $J_{CC}$ = 87Hz). Treatment of ***12** with excess n-BuLi followed by isolation of phenyl acetylene ***13** in 73% yield revealed the labeled carbon to be adjacent to the phenyl moiety as expected (ipso C = 122.7δ, $J_{CC}$ = 89Hz; terminal acetylenic C = 77.0δ, $J_{CC}$ = 176Hz). Reaction of intermediate acetylide ***14** with triflic anhydride[2] afforded the key reagent ***3** in 51% yield (ipso C = 116.2δ, $J_{CC}$ = 88Hz; $\mathrm{Ph\underline{C}{\equiv}CTf}$ = 101.8δ; $\mathrm{PhC{\equiv}\underline{C}Tf}$ = 77.7δ; $\mathrm{SO_2\underline{C}F_3}$ = 119.6δ, $J_{CF}$ = q, 323Hz). Photochemical reaction of ***3** with cyclohexane afforded cyclohexyl phenylacetylene ***5** in 71% yield. Regioisomer ***iso-5** was not detected in the 13C spectrum. The unlabeled compound **5** has the two acetylenic carbons well separated (81, 95 ppm) and the chemical shifts have been assigned (Scheme 3).[10]

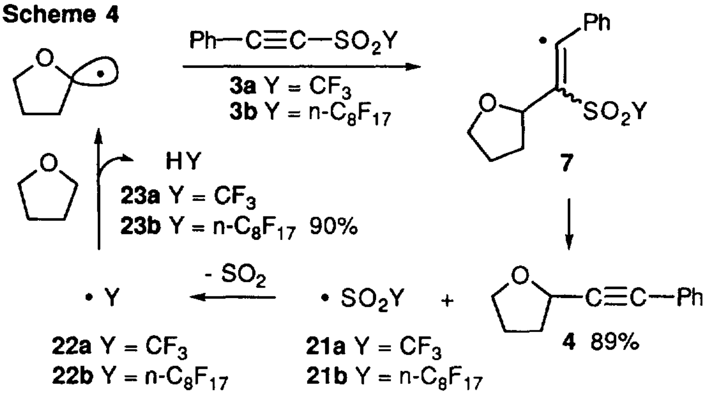
The β-addition/rearrangement manifold (***6** → ***8**) introduces the need for a further control study. It was not known whether phenyl or cyclohexyl would undergo preferential rearrangement[11] through the intermediacy of carbene ***8**. Therefore, we converted labeled benzaldehyde *11 to ketone *16 followed by reaction with dibromomethylenetriphenylphosphorane under forcing conditions[12] to afford bis-bromoolefin *17 in ~10% yield, accompanied by much starting ketone *16. Reaction of *17 with n-butyl lithium affords α-lithiovinylbromide intermediate *19 which regiospecifically undergoes rearrangement of the phenyl moiety to only generate *iso-5 within the limits imposed by 13C NMR analysis. The low yield for preparation of *17 necessitated the preparation of *18 for further studies related to vinylidene carbene intermediate *8. In contrast to the dibromomethylenetriphenylphosphorane reaction, ketone *16 was smoothly transformed to *18 upon treatment with dichloromethylenetriphenylphosphorane ($CCl_4$, reflux, 20h, 72%). Reaction of *18 with tributyl tinhydride (1.0eq, $C_6H_6$, hv 254nm, 10h) afforded 46% of an 1:4 mixture of *5/iso-*5 in addition to significant amounts of three over-reduction products. The finding that intermediates *19 and *20 undergo preferential or exclusive phenyl migration excludes vinylidine carbene *8 as the intermediate in the triflone alkynylation reaction, but does not unambiguously eliminate the possibility that intermediate *6 undergoes stereospecific cyclohexyl rearrangement to afford *7 which then proceeds further to *5.



The second mechanistic study involves identification and quantitation of the fluorocarbon species **23** resulting from propagation of the radical cascade. In the case of the parent reagent **3a** this means we would be obliged to isolate trifluoromethane **23a**, a compound having a boiling point of -82°C. Consequently, we have prepared perfluorooctylsulfonyl phenylacetylene **3b** in order to more feasibly realize this goal.

Synthesis of **3b** was accomplished in 42% yield by the reaction of phenyl acetylide anion with commercially available perfluorooctylsulfonyl fluoride (Aldrich). As can be seen in Scheme 4, reaction of THF with **3b** affords a high yield of the known fluorinated octane derivative **23b** $^1$H NMR (6.1δ, tt, 52, 5Hz).[13]

**Scheme 4**



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