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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.<sup>1</sup>

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Abstract: <sup>13</sup>C-2 labeled phenyl ethynyl triflone undergoes regiospecific C-H alkynylation upon reaction with cyclohexane. The <sup>13</sup>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  $\alpha$ -position. Control studies show preferential phenyl migration from a vinylidine carbene, thus excluding the presence of such an intermediate.

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We recently reported that reaction of ethers, sulfides, and hydrocarbons with acetylenic triflones such as **3** provides facile access to substituted alkynes (Scheme 1).<sup>2</sup> 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  $HCF_3 = 107 \text{ Kcal/mole}^3$ ). 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.



Arguments in favor of either addition mode can be made (Scheme 2). For example, radical addition to the  $\beta$ -carbon of acetylenic triflone **3** could generate  $\alpha$ -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.<sup>4</sup> An alternative mechanism involves either direct  $\alpha$ -addition to produce vinyl radical **7**<sup>5</sup> or the unprecedented 1,2-rearrangement of **6** to this species prior to scission of the carbon-sulfur bond. Finally, formation of  $\beta$ -addition intermediate **6** may be a *rapid and reversible* process, thereby allowing the  $\alpha$ -addition intermediate **7** to ultimately generate the alkynes **4**,**5**. Completion of the process involves the known fragmentation<sup>6</sup> 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.<sup>7</sup>

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<sup>8</sup> reagent. Reaction of \*11 with dibromomethylenetriphenylphosphorane<sup>9</sup> afforded dibromide \*12 in 87% yield (vinyl H = 7.58,  $J_{CH} = 160Hz$ ; PhCH=CBr<sub>2</sub> = 137.48; PhCH=CBr<sub>2</sub> = 89.78,  $J_{CC} = 87Hz$ ). 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 = 122.78,  $J_{CC} = 89Hz$ ; terminal acetylenic C = 77.08,  $J_{CC} = 176Hz$ ). Reaction of intermediate acetylide \*14 with triffic anhydride<sup>2</sup> afforded the key reagent \*3 in 51% yield (ipso C = 116.28,  $J_{CC} = 88Hz$ ; PhC==CTf = 101.88; PhC=CTf = 77.78; SO<sub>2</sub>CF<sub>3</sub> = 119.68,  $J_{CF} = q$ , 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).<sup>10</sup>

The  $\beta$ -addition/rearrangement manifold (\*6  $\rightarrow$  \*8) introduces the need for a further control study. It was not known whether phenyl or cyclohexyl would undergo preferential rearrangement<sup>11</sup> through the intermediacy of carbene \*8. Therefore, we converted labeled

benzaldehyde \*11 to ketone \*16 followed by reaction with dibromomethylenetriphenylphosphorane under forcing conditions<sup>12</sup> to afford bis-bromoolefin \*17 in ~10% yield. accompanied by much starting ketone \*16. Reaction of \*17 with n-butyl lithium affords  $\alpha$ lithiovinvibromide intermediate \*19 which regiospecifically undergoes rearrangement of the phenyl mojety 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 vinvlidene carbene intermediate \*8. In contrast to the dibromomethylenetriphenylphosphorane reaction, ketone \*16 was smoothly transformed to \*18 upon treatment with dichloromethylenetriphenylphosphorane (CCl<sub>4</sub>, reflux, 20h, 72%). Reaction of \*18 with tributyl tinhydride (1.0eq, C<sub>6</sub>H<sub>6</sub>, 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** <sup>1</sup>H NMR (6.18, tt, 52, 5Hz).<sup>13</sup>



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