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# Scope and Limitations of Functionalized Acetylenic Triflones in the Direct Alkynylation of C-H Bonds.[1]

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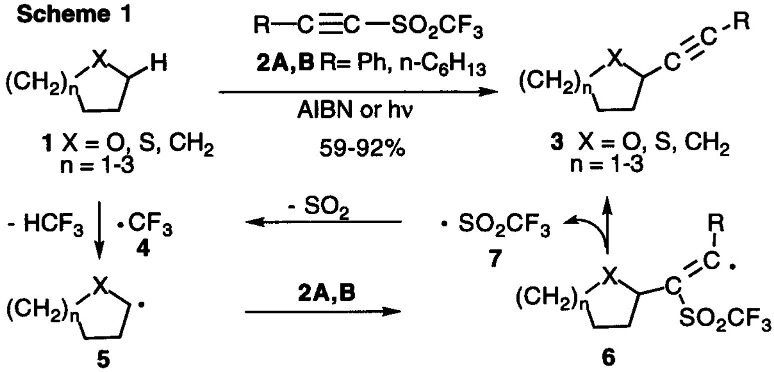
**Abstract:** Reactions of TIPS-substituted acetylenic triflones extends the versatility of the trifluoromethyl radical mediated C-H alkynylation reaction. Alkynes bearing acetylenic or propargylic oxygen functionality cannot be prepared, but silyl ethers or chlorides in remote positions may be carried through the reaction. Crown ethers are successfully monofunctionalized and distal bis-acetylenes may be employed in the title reaction. © 1997 Elsevier Science Ltd.

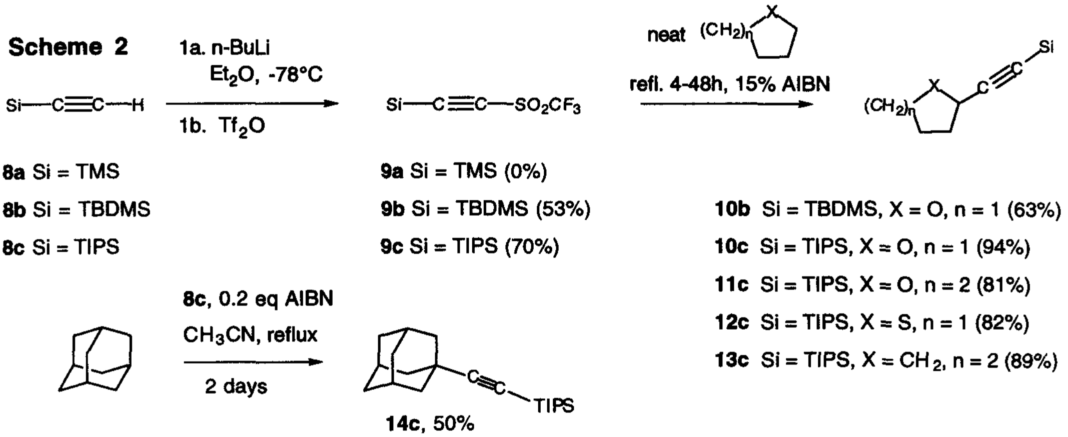
We recently reported that reaction of ethers, sulfides, and hydrocarbons with acetylenic triflones such as **2A,B** provides facile access to substituted alkynes **3** (Scheme 1).[2] The reaction proceeds via radical C-H abstraction by the very electrophilic trifluoromethyl radical **4** in a process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

**Scheme 1**



In order to delineate the scope and limitations of reagents bearing additional functionality we undertook the synthesis of acetylenic triflones bearing a silane. The exceptional electron-withdrawing ability of the triflone imparts considerable lability to the β-silylacetylenic triflones, attempts at synthesis of TMS-substituted reagent **9a** leading to black tars. TBDMS-alkynyl triflone **9b** was also somewhat sensitive, but could be isolated and employed in the alkynylation reaction, affording THF adduct **10b** in a moderate yield of 63%. The TIPS-substituted reagent **9c** was far more satisfying, providing excellent yields of C-H alkynylated products **10c**-**13c** (Scheme 2). As previously observed,[2] reactions conducted in acetonitrile solution are somewhat slower and loweryielding than those run in neat substrate. For example, adamantane is converted to acetylenic silane **14c** in 50% yield after heating in acetonitrile with reagent **8c** for 48h (Scheme 2).

**Scheme 2**



**8a** Si = TMS
**8b** Si = TBDMS
**8c** Si = TIPS

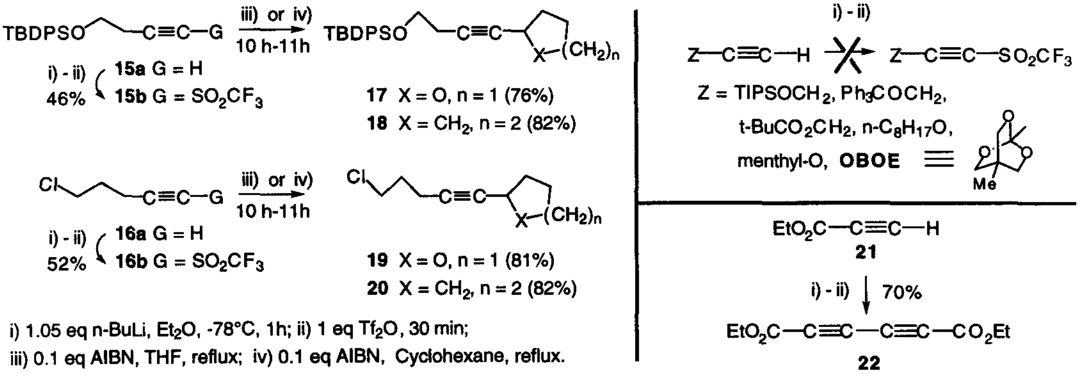
**9a** Si = TMS (0%)
**9b** Si = TBDMS (53%)
**9c** Si = TIPS (70%)

**10b** Si = TBDMS, X = O, n = 1 (63%)
**10c** Si = TIPS, X = O, n = 1 (94%)
**11c** Si = TIPS, X = O, n = 2 (81%)
**12c** Si = TIPS, X = S, n = 1 (82%)
**13c** Si = TIPS, X = $CH_2$, n = 2 (89%)

**14c**, 50%

Distal substituents such as homopropargyl ether **15b** and bishomopropargyl chloride **16b** undergo the alkynylation reaction with test substrates tetrahydrofuran and cyclohexane affording the adducts **17-20** in 76-82% yield (Scheme 3, left). Unfortunately all attempts with substrates bearing functionality in closer proximity to the alkyne moiety, such as protected propargyl alcohols, acetylenic ethers, or the indicated bicyclooctyl orthoester (OBOE[3]), were uniformly disastrous. While the acetylenic anions could be prepared in each instance, addition of triflic anhydride generated a reaction mixture which began to darken even at low temperature and upon further warming only produced intractable tarry mixtures (Scheme 3, top right). The only substrate which yielded an identifiable product was ethyl propiolate **21**, which afforded dimer **22**, via addition-elimination of the acetylenic anion to the incipient acetylenic triflone (Scheme 3, bottom right).

**Scheme 3**



i) - ii) 46% **15a** G = H
**15b** G = $SO_2CF_3$

**17** X = O, n = 1 (76%)
**18** X = $CH_2$, n = 2 (82%)

i) - ii) 52% **16a** G = H
**16b** G = $SO_2CF_3$

**19** X = O, n = 1 (81%)
**20** X = $CH_2$, n = 2 (82%)

Z = $TIPSOCH_2$, $Ph_3COCH_2$, $t\text{-}BuCO_2CH_2$, $n\text{-}C_8H_{17}O$, menthyl-O, **OBOE**

$EtO_2C—C{\equiv}C—H$ **21**

$EtO_2C—C{\equiv}C—C{\equiv}C—CO_2Et$ **22**

i) 1.05 eq n-BuLi, $Et_2O$, -78°C, 1h; ii) 1 eq $Tf_2O$, 30 min;
iii) 0.1 eq AIBN, THF, reflux; iv) 0.1 eq AIBN, Cyclohexane, reflux.

Acetylenic triflones **2A** and **9c** are also excellent reagents for the alkynylation of crown ethers. As can be seen in Scheme 4 and Table 1, both 12-crown-4 **23** and 15-crown-5 **24** were effectively monoalkynylated to provide functionalized crowns **25-26**. Desilylation of **25c** and **26c** could be effected in near-quantitative yield (1.1equiv TBAF, 25°C, 2h). This represents an extremely efficient access to molecules of this nature.[4]

**Scheme 4**

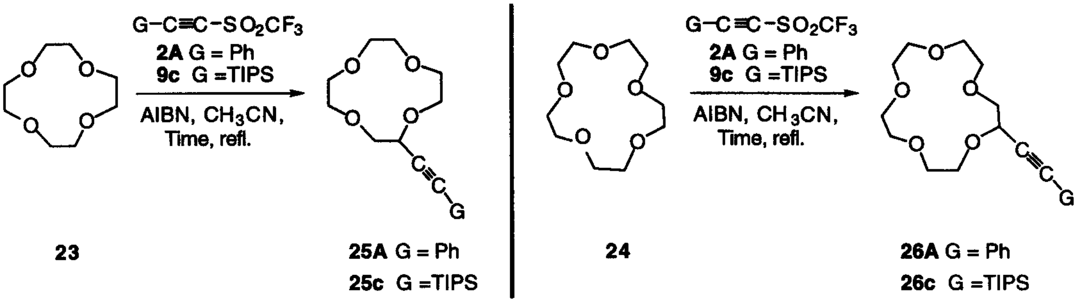


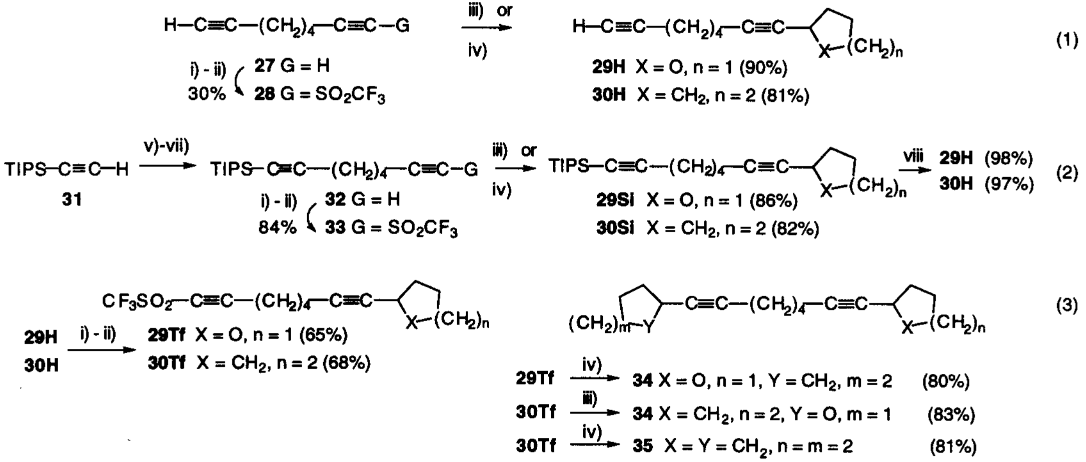
**Table 1.** Comparison of reactions of Crown ethers with Acetylenic Triflones **2A** and **9c**.

| Run | Crown (#equiv) | Conditions# | Products | Yield |
|---|---|---|---|---|
| 1 | **23** (10eq) | **2A**, 3h, 0.10M | **25A** | 70% |
| 2 | **23** (1.5eq) | **2A**, 48h, 0.05M | **25A** | 55%* |
| 3 | **23** (5eq) | **9c**, 6h, 0.06M | **25c** | 70% |
| 4 | **23** (1.5eq) | **9c**, 48h, 0.08M | **25c** | 50% |
| 5 | **24** (10eq) | **2A**, 2h, 0.10M | **26A** | 80% |
| 6 | **24** (1.5eq) | **2A**, 24h, 0.05M | **26A** | 60%* |
| 7 | **24** (5eq) | **9c**, 5h, 0.06M | **26c** | 70% |
| 8 | **24** (1.5eq) | **9c**, 48h, 0.05M | **26c** | 53% |

#AIBN (20 mol%), acetonitrile at reflux,; *20% $PhCOCH_2SO_2CF_3$ also isolated.

The final class of reagents investigated were the bis-acetylenes. As might now be expected, the 1,3 and 1,4 diacetylenes were not satisfactory substrates. However the 1,7-diynes shown in Scheme 5 were perfectly well-behaved materials. Although direct monofunctionalization of **27** proceeded in only 30% yield, the alkynylation reactions of the resulting **28** proved that the C-H functionalization proceeds in the presence of the unprotected terminal acetylene (Scheme 5, rxn 1). A higher-yielding, but longer sequence involves starting with TIPS-acetylene **31** and provides **29Si** and **30Si**, the TIPS-protected derivatives of compounds **29H** and **30H**. Fluoride-mediated cleavage of these materials then affords **29H** and **30H** in near-quantitative yield (Scheme 5, rxn 2). Application of the metalation/sulfonylation sequence gives acetylenic triflones **29Tf** and **30Tf** in reasonable yield (Scheme 5, rxn 3). Reaction of **29Tf** with cyclohexane or **30Tf** with THF provide the identical bis-functionalized bis-acetylene **34** in >80% yield in each instance. Treatment of **30Tf** with cyclohexane provides the expected symmetrical bis-acetylene **35** in similar yield (Scheme 5, rxn 3).

**Scheme 5**



i) 1.05 eq n-BuLi, $Et_2O$, -78°C, 1h; ii) 1 eq $Tf_2O$, 30 min; iii) 0.15 eq AIBN, THF, reflux, 14h; iv) 0.15 eq AIBN, Cyclohexane, reflux, 24h; v) n-BuLi -78°C THF/HMPA, add 1,4-dibromobutane 5eq., warm to 23°C (98%); vi) TMS-C≡C-Li, warm to 23°C, (97%); vii) $K_2CO_3$ 1eq, MeOH, 0°C to 23°C, 3 h (83%); viii) TBAF, THF, 23°C, 2 h, (98%)

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