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# A MILD AND CONVENIENT SYNTHESIS OF FUNCTIONALIZED METHYL TRIFLONES AND VINYL TRIFLONES.[1]

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**Abstract:** A general route for the synthesis of methyl triflone derivatives utilizing triflic anhydride is described. Stereoselective synthesis of E-vinyl and dienyl triflones has been accomplished by the Peterson olefination reaction of $\alpha$-silyl triflone anions.

The trifluoromethyl sulfone (triflone) functional moiety is regarded as the strongest neutral electron-withdrawing group,[2] and is attractive in connection with our interest in synthetic strategies involving sulfones. The seminal contributions of Hendrickson have established that the triflone's amphoteric nature can be admirably exploited both for $\alpha$-anion stabilization as well as serving as a leaving group in 1,2 elimination reactions and intramolecular nucleophilic displacements.[3,4]

Functionalized methyl triflones serve as versatile reagents in synthesis.[4] Literature precedence on the synthesis of these triflone derivatives have generally relied on the use of trifluoromethanesulfonyl fluoride as the electrophilic source of the triflyl group.[5a,4d] No general methods are known for the synthesis of these compounds, although difunctionalized triflones **2a,b** have been synthesized earlier by indirect methods.[4e,5b-e] We wish to report a convenient protocol for the preparation of several members of this interesting class of compounds. The procedure described in **Scheme 1** utilizes the sulfonylation of metalated compounds **1a-d** with triflic anhydride as the key step. The results are summarized in **Table 1**.

**Scheme 1**

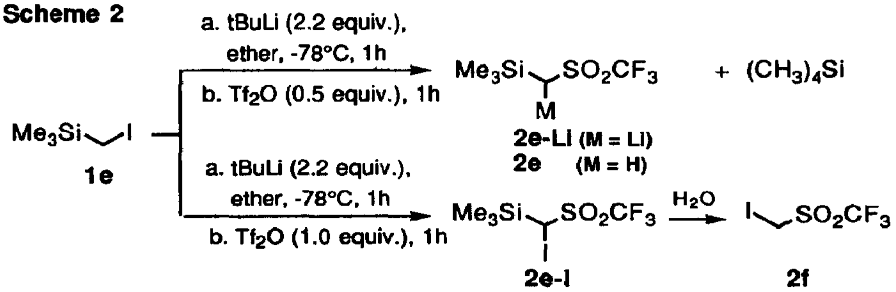
$$\underset{\textbf{1a-d}}{RCH_2R'} \xrightarrow[\text{b. } Tf_2O \text{ (0.5 equiv.), 1h}]{\text{a. nBuLi (1.1 equiv.), ether, -78°C, 1h}} \underset{\textbf{2a-d}}{RR'CHSO_2CF_3}$$

**Table 1**. Preparation of functionalized methyl triflones.

| Substrate | R' | R | Product | Yield (%) |
|---|---|---|---|---|
| **1a** | H | $SO_2Ph$ | **2a** | 69 |
| **1b** | $CH_3$ | $SO_2Ph$ | **2b** | 53 |
| **1c** | H | $P(O)(OMe)_2$ | **2c** | 60 |
| **1d** | H | CN | **2d** | 50 |

Application of this strategy to iodomethylsilane **1e** provided some interesting results as shown in **Scheme 2**. As expected, halogen-metal exchange of **1e** with t-BuLi followed by addition of 0.5 equivalent of triflic anhydride provides a stock solution of **2e-Li**, formed by in situ deprotonation of **2e** with the extra 0.5 equivalent of $TMSCH_2Li$.[6] While acidification of the reaction mixture allows characterization of **2e** in only moderate yield (42%), subsequent reactions demonstrate ~85% solution yield of **2e** based upon the Peterson chemistry. Repeating the reaction as previously but using 1.0 equivalent of triflic anhydride provided iodomethyl triflone **2f** in 65% yield after an aqueous workup (3g scale). This seemingly improbable reaction apparently occurs via the reaction of lithium iodide with triflic anhydride to generate $ISO_2CF_3$ which either directly serves as the electrophilic iodinating agent or suffers further attack by iodide ion to produce $I_2$ and triflinate. While we cannot currently distinguish which species reestablished the carbon-iodine bond, control studies affirm that iodide ion is rapidly and quantitatively oxidized to $I_2$ by triflic anhydride in ether at low temperature.

**Scheme 2**



Vinyl triflones are superb Michael acceptors, and their reaction with a variety of heteroatom, organometallic and stabilized carbon nucleophiles has been well documented.[3] Unfortunately vinyl triflones are not readily available. The existing methods for the preparation of vinyl triflones include: (i) The condensation of primary triflones with aldehydes and ketones; (ii) Tautomerization of allylic triflones by base - a method only applicable in selected instances; and (iii) addition of trifluoromethanesulfenyl chloride to alkenes followed by oxidation and elimination - another method of selected applicability. All of the above methods suffer from low to moderate yields.[7] For the preparation of the precursor triflones, heating and long reaction times are sometimes required.[3] Other problems are associated with the difficulty of obtaining trifluoromethanesulfenyl chloride and trifluoromethanesulfonyl fluoride (gas).

Attempts to synthesize vinyl triflones using Wadsworth-Emmons phosphonate reagent **2c** were largely unsuccessful as seen in **Scheme 3, Eq. B**. The failure presumably results from the low nucleophilicity of the stabilized anion, thereby permitting the aldehyde to undergo competitive side reactions. To overcome the lack of reactivity of the reagent **2c**, the corresponding Peterson reagent **2e** was next investigated, which provided an anion capable of undergoing successful reaction with the aldehyde. The present methodology allows for the stereoselective synthesis of vinyl triflones using the Peterson olefination reaction.[8] It appears to be substantially more advantageous than existing methods, proceeding via a one-pot operation requiring low temperatures and short reaction times. The reaction proceeds well with different aldehydes resulting in stereoselective formation of the E-olefins as shown in **Scheme 3**. The results obtained are summarized in **Table 2**. The yields presented in **Table 1** and **2** are for isolated, purified products. All compounds were characterized using $^1H$, $^{13}C$ and $^{19}F$ NMR. The physical data of all known compounds were in excellent agreement with literature values.[4h,3e,f] Extension of this methodology to synthesize more substituted vinyl triflones from ketone precursors was unsuccessful. This failure likely results from the diminished reactivity of **2e-Li** with ketones in combination with the superb Michael acceptor properties of the product triflones which appear to foster complicated side reactions.

**Scheme 3**

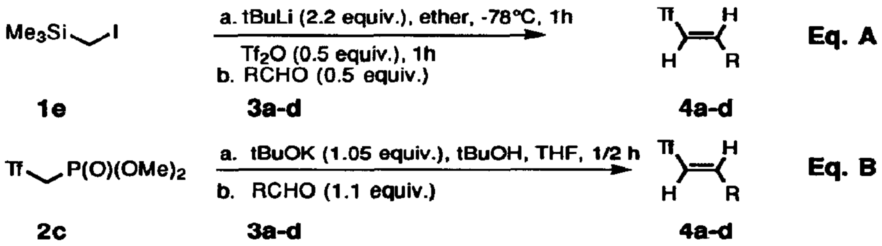


**Table 2.** Preparation of Vinyl triflones.

| Product | R | Yield Eq. A | Yield Eq. B | $^{19}F$; $^{13}C$ Shift* |
|---|---|---|---|---|
| **4a** | Ph | 56% | 80% | -77.74; 119.66 |
| **4b** | PhCH=CH | 70% | <5% | -77.99; 119.67 |
| **4c** | $CH_3(CH_2)_4$ | 84% | 21% | -78.17; 119.59 |
| **4d** | $CH_3(CH_2)_2CH=CH$ | 50% | <5% | -78.23; 119.64 |

*Chemical shift of triflone fluorines and trifluoromethyl carbon, respectively (1:3:3:1 q, J~322 Hz)

## General Procedure:

### Synthesis of functionalized methyl triflones

To a solution of compound **1a-d** (1.0 equiv.) in ether at -78°C was added n-BuLi in hexane (1.1 equiv.) dropwise. The reaction mixture was allowed to stir for 1 h followed by addition of triflic anhydride (0.5 equiv.). On completion of reaction, the reaction mixture was quenched with 5% HCl. The aqueous layer was extracted with ether and the combined organic extracts were washed with brine. Drying and concentration afforded a crude mixture which was purified by column chromatography. Yields reported in Table 1 have been calculated with respect to 0.5 equiv. of $Tf_2O$.

### Synthesis of Vinyl triflones

To a solution of **1e** (1.0 equiv.) in ether at -78°C was added t-BuLi in pentane (2.1 equiv.) dropwise. The reaction mixture was allowed to stir for 1 h followed by addition of triflic anhydride (0.5 equiv.). Aldehyde **3a-d** (0.5 equiv.) was added to the reaction mixture after 1 h. On completion of reaction, the reaction mixture was quenched with water. The aqueous layer was extracted with ether and the combined organic extracts were washed with brine. Drying and concentration afforded a crude mixture which was purified by column chromatography.

In conclusion, we have developed a general method of preparation for the synthesis of functionalized methyl triflones and have applied the Peterson reaction of reagent **2e-Li** for the stereoselective synthesis of E-vinyl triflones and dienyl triflones. To our knowledge, reagents **2c,e,f** reported in **Table 1** have not been previously prepared.

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