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Facile Synthesis of Allyl, γ-Iodoallyl, and Cyclopropyl Triflones via Radical-Mediated Atom-Transfer Addition of Iodomethyl Triflone to Olefins and Acetylenes[1]

Anu Mahadevan and P. L. Fuchs*

Department of Chemistry, Purdue University
West Lafayette, Indiana 47907

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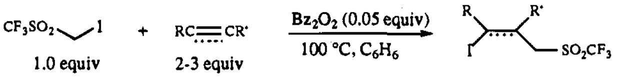
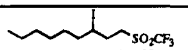
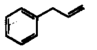
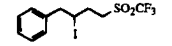
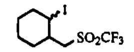
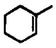
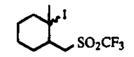
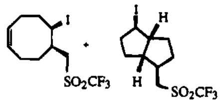
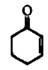
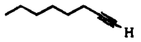
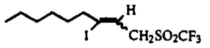
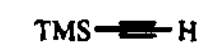
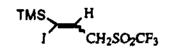
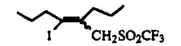
In connection with our interest in extending the synthetic potential of the sulfone moiety, we have recently expanded our focus to include the synthetic chemistry of triflones (trifluoromethyl sulfones).[2] The potent electron-withdrawing property which renders the triflone moiety so attractive unfortunately mitigates against efficient synthesis where the carbon–sulfur bond is constructed via nucleophilic protocols.[3]

Recent attention has been focused on atom-transfer reactions since they produce valuable *difunctionalized* products.[4] Curran has pioneered the development of halogen-transfer radical cyclizations;[4] examples utilizing α-halo esters, α-halo ketones, and α-halo sulfones are noteworthy.[5] We have exploited this concept to provide the first examples of atom-transfer radical additions of the now readily available[2b] iodomethyl triflone (IMT) to alkenes and alkynes.

IMT adds regioselectively, and in synthetically useful yields, to substituted alkenes and alkynes, as shown in Table 1. In most of the cases observed, the reaction is complete within 5–10 h on heating a benzene solution of iodomethyl triflone (1.0 equiv) and alkene or alkyne (2.0–3.0 equiv, to ensure an excess of the volatile substrate) at 100 °C in the presence of 5–10 mol % of benzoyl peroxide or AIBN in a sealed tube.

Table 1



entry	substrate	product	time (h)	yield (%) Bz$_2$O$_2$ (AIBN)
1			5	85 (90)
2			10	80 (69)
3			10	69 cis:trans = 1:2
4			10	47 cis:trans = 1:5
5			5	25+66 (22+64)
6		nr[a]	10	-
7		nr[a]	10	-
8			5	71 E:Z = 1:3
9			4	99 (99) E:Z = 1:7.5
10			10	75 (69) E:Z = 1:1.7

[a] No reaction.

When a terminal alkene was used (entries 1 and 2, Table 1), the sole product was the isomer obtained from attack of α-((trifluoromethyl)sulfonyl)methyl radical at the least substituted end of the alkene. The reaction was successful even with 1,2-disubstituted and trisubstituted alkenes (entries 3 and 4, Table 1), although the reaction time was longer and yield was lower with the trisubstituted alkene. Examination of the ^{1}H NMR spectra of the crude reaction mixture in the case of addition to cyclohexene reveals a 1:2 ratio of the cis and trans addition products. The trans isomer was identified on the basis of the 11.1-Hz coupling constant. The ability of the α-((trifluoromethyl)sulfonyl)methyl radical to undergo a tandem addition–cyclization reaction is seen in entry 5, Table 1. Based on the literature precedent[6] for 1,5-octadiene radical cyclizations, we have assigned the isomer formed in this reaction as the cis isomer ($J = 3.3$ Hz; $J = 8.4$ Hz; $J = 3.3$ Hz). The minor product obtained in the cyclooctadiene reaction arose via competitive iodination of the initial adduct. In the reaction with 1,3-hexadiene (entry 6, Table 1), a major amount of unreacted IMT remained. This observation is consistent with literature examples in which the lack of reactivity is explained by the disruption of the conjugated π-system combined with generation of a resonance-stabilized allylic radical which would be expected to be inefficient at maintaining the chain process.[7]

When cyclohexenone (entry 7, Table 1) was used, there was no reaction; this observation was not unexpected, as this lack of reactivity is characteristic of reactions of electron-deficient olefins with electrophilic radicals.[4g] The procedure was next extended to internal and terminal alkynes. Addition to 1-octyne and 4-octyne resulted in a mixture of *E* and *Z* isomers (entries 8 and 10, Table 1). Mechanistically, addition of the α-((trifluoromethyl)sulfonyl)methyl radical to an alkyne results in the formation of isomeric vinyl radicals. The vinyl radical then abstracts an iodine atom from IMT, generating the *E*/*Z* mixture. Literature precedents on alkyl- and silyl-substituted alkenyl radicals suggest that the inversion of the radical is faster than atom transfer.[4c] It was hoped that the TMS substituent might impose sufficient steric constraints on the radical reaction, resulting in better *E*/*Z* selectivity. In this regard, we investigated the addition of a silyl-substituted alkyne. The result (entry 9, Table 1) suggests that the silyl substituent plays only a relatively small role in the stereochemistry of the atom-transfer reaction.

The high efficiency of the radical reaction coupled with the versatility of the iodo and ((trifluoromethyl)sulfonyl)methyl groups in the product makes this method very useful. Encouraged by the success of the atom-transfer reaction, we were

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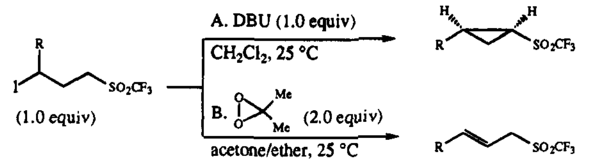
Table 2



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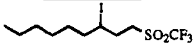
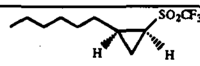
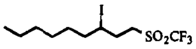
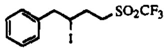
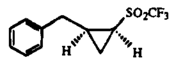
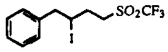
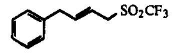
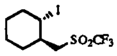
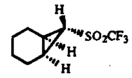
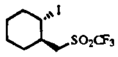
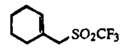
1			A	1	94
2			B	1	80
3			A	1	83
4			B	1	93
5			A	1	91
6			B	1	58

prompted to investigate the conversion of these substrates to cyclopropyl and allyl triflones.

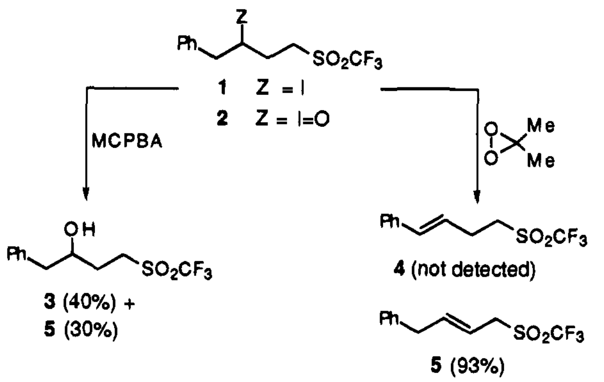
Currently, no general method exists for the synthesis of cyclopropyl triflones.[2] The γ-iodo triflones were converted to the corresponding isomeric cyclopropyl triflones via treatment with DBU (1.0 equiv) in dichloromethane. The cyclopropyl triflones were obtained as isomers (>10:1), the major isomer being assigned the cis configuration based upon coupling constants of cyclopropyl phenyl sulfones[8] (J = 8.1 Hz; entries 1 and 3 Table 2).

In order to confirm the stereochemistry of the isomeric addition products in the cyclohexene case (entry 3, Table 1), we investigated the conversion of these isomers to cyclopropyl triflones. The trans isomer, upon treatment with DBU, would be expected to give the desired cyclopropyl triflone, whereas the cis isomer would not. When the major isomer (J = 11.1 Hz) was treated with DBU, the trans cyclopropyl triflone was obtained (J = 3 Hz; entry 5, Table 2). When the minor (cis) isomer was subjected to the same conditions, it did not yield the cyclopropyl triflone, but rather produced allyl triflone along with starting material (3:7).

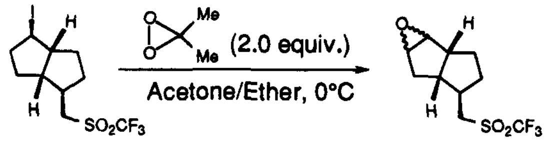
Due to the difficulty associated with the preparation of allyl triflones,[2] attempts were made to introduce the olefin functionality by elimination of the iodide. Since the above reaction of γ-iodo triflones with base to generate cyclopropyl triflones needed to be avoided, we elected to investigate oxidation of the iodide moiety[9] in the hopes that the inductive effect of the triflone would direct 1,2-elimination of the putative iodoso intermediate. The elimination reaction likely proceeds via syn elimination of hypoiodous acid from the iodoso intermediate, a reaction originally developed by Reich.[9a]

Initial attempts to employ this strategy were disappointing since use of mCPBA gave the corresponding alcohol, a common mode of failure in oxidations of iodides.[9a,10] As shown in

Scheme 1



Scheme 2



6 (1.0 eq.) **7** (77%)

Scheme 1, when 3-iodo-4-phenylbutyl triflone (**1**) was treated with mCPBA, alcohol **3** was obtained along with the allyl triflone **5**. When dimethyldioxirane was used, however, the corresponding allyl triflone **5** was the only product observed. Interestingly, the olefin isomer **4** was not formed even in small amounts. We were delighted to note that in all cases dimethyldioxirane[11] gave the corresponding allyl triflone regio- and stereoselectively (entries 2, 4, and 6, Table 2) with no sign of alcohol production. Presumably this is a consequence of the neutral reaction conditions.

However, when *exo*-2-(((trifluoromethyl)sulfonyl)methyl)-*exo*-6-iodo-*cis*-bicyclo[3.3.0]octane (**6**) (Scheme 2) was treated with dimethyldioxirane, a mixture of epoxides **7** (1:4.6) was generated. The facility with which the epoxidation occurred suggests that the elimination reaction is slow relative to epoxidation. The reason for this observation presumably lies in the literature precedence for the low reactivity of ring substituents in bicyclo[3.3.0]octane toward elimination[6b] reactions. It should be noted that for the examples shown in Table 2 (entries 2, 4, and 6), epoxidation was not observed, presumably due to inductive deactivation by the proximal triflone moiety.

In conclusion, the strategy outlined here provides a mild and general method for preparation of allyl, γ-iodoallyl, cyclopropyl, and γ-iodo triflones. Furthermore, the improved method of iodide elimination via oxidation with dimethyldioxirane suggests considerable generality.

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Supplementary Material Available: Proton and carbon spectra for all new compounds (36 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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