Communications to the Editor

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1-PHENYLSULFONYL-3,3,3-TRIFLUOROPROPENE I: THE MICHAEL-TYPE ADDITION REACTION

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The reaction of 1-phenylsulfonyl-3,3,3-trifluoropropene (1) with active methylene compounds gave the corresponding adducts in good yields.

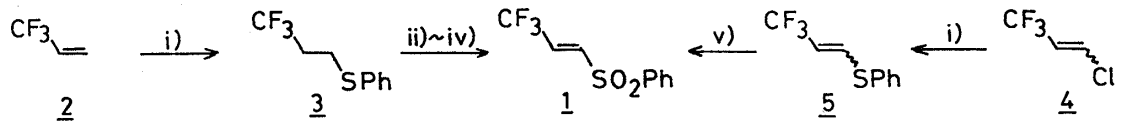
KEYWORDS—— trifluoromethyl; propene; phenylsulfonyl; Michael-type addition; sodium amalgam

Trifluoromethylated compounds, particularly trifluoromethylated bioactive compounds, have attracted attention recently because of their characteristic properties. The trifluoromethyl group is one of the most important groups in drug design.[1,2]

Methods for synthesizing trifluoromethylated compounds are of three types: (1) conversion of carboxylic acid or the trichloromethyl group using toxic and gaseous sulfur tetrafluoride or hydrogen fluoride,[3] (2) substitution or addition reactions using reactive trifluoromethyl intermediates which involve trifluoromethyl radical or ions (e.g. trifluoromethyl metals),[4] and (3) using functionalized molecules having a trifluoromethyl group as building units for such compounds.[5] We have found 1-phenylsulfonyl-3,3,3-trifluoropropene (1) to be a versatile building unit for trifluoromethylated compounds because it is highly reactive as a Michael acceptor as well as a dienophile.[6] The phenylsulfonyl group has the following features: (1) α-carbanion stabilized by this group can be generated by treating the adduct formed by the above reactions with LDA, and this reacts with electrophiles, (2) the phenylsulfonyl group can be reductively removed by sodiumamalgam without any effect on the trifluoromethyl group, and (3) in some cases good crystallinity due to the presence of this group facilitates the separation of the diastereomers by recrystallization. In this paper, we wish to report on the synthesis of 1 and its reactions with nucleophiles as a Michael acceptor.

1 was synthesized from 3,3,3-trifluoropropene (2): addition of benzenethiol (NaOH, EtOH, 90°C, 4 days) gave the sulfide 3 (51%),[9] which was then treated with sulfuryl chloride (CCl_4, refl., 12 h), oxidized to the sulfone (mCPBA, CH_2Cl_2) and then dehydrochlorinated (DBU, CH_2Cl_2, r.t.) to provide 1 (46% from 3). As an alternative route, a stereoisomeric mixture of 1-chloro-3,3,3-trifluoropropene (4) was treated with benzenethiol (NaOH, EtOH, 50°C, 1 day then 100°C, 1 day) to give the vinylsulfide (80%) as a stereoisomeric mixture and the following oxidation with 30%-H_2O_2 (AcOH, 40°C, 40 h) gave 1 in 82% yield as a single product. The E-stereochemistry of 1 prepared by either procedure was confirmed by its NMR spectrum

[^{1}H-NMR ($CDCl_3$) δ 6.87 (dq, J_{H-H}=15 Hz, J_{H-F}=4.7 Hz), 7.15 (d, J_{H-H}=15 Hz); ^{19}F-NMR +0.7 ppm (d, J_{H-F}=4.7 Hz)][10,11] (Chart 1).



i) PhSH, NaOH, EtOH ii) SO_2Cl_2, CCl_4 iii) mCPBA, CH_2Cl_2
iv) DBU, CH_2Cl_2 v) 30%-H_2O_2, AcOH

Chart 1

1 reacted with active methylene compounds or primary amines to give Michael-type addition products in good yields (Table). For example, treatment of 1 with diethyl malonate (6a) in the presence of a catalytic amount of NaH (10 mol%, THF, r.t., 5 min) gave the adduct (7a) in a quantitative yield (Chart 2).

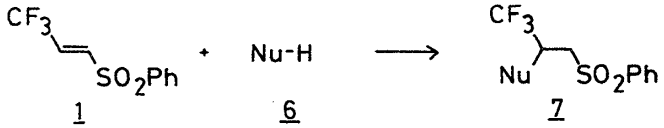


Chart 2

Both diastereoisomeric mixtures (7h and 7i) formed by the reaction of 1 with alanine methyl ester (6h) and alaninol (6i) could be separated by recrystallization or by column chromatography. It should be noted that the reaction of 1 with the Grignard reagent (CH_3MgBr or CH_3MgBr in the presence of CuI) or alkyl lithium (n-BuLi) did not give the adduct.

The formation of the α-carbanion stabilized by the phenylsulfonyl group and the reductive desulfonylation of the Michael adducts formed by the above mentioned reactions proceeded smoothly without any effect on the trifluoromethyl group. For example, treatment of 7a or 7g with 2 eq. of LDA followed by the reaction with benzaldehyde gave the adduct 8a or 8g in 71% and 49% yield, respectively. Na(Hg) reduction of 8a or 8g in THF-MeOH at room temperature gave the corresponding olefinic compound 9a or 9g in 38% and 54% yield, respectively.

Similar desulfonylation with 7b gave the carbinol (10b) in 70% yield as a 1:1 diastereoisomeric mixture.

According to these reactions, 4,4,4-trifluorovaline (11) was effectively synthesized:[12] reaction of 1 with diethyl acetoamidomalonate and NaH in THF for 14 h at room temperature gave the adduct (7f), which was treated with 5%-Na(Hg) in THF-MeOH in the presence of Na_2HPO_4 for 4 h at room temperature and the following decarboxylation by refluxing in c-HCl for 14 h gave 11 in 52% yield as a 1:1 diastereoisomeric mixture (Chart 3).

In conclusion 1-phenylsulfonyl-3,3,3-trifluoropropene (1) is a versatile building unit for the construction of trifluoromethylated compounds due to its high reactivity as a Michael acceptor.

Table. Reaction of 1-Phenylsulfonyl-3,3,3-trifluoropropene with Nucleophiles

Entry	Nucleophile (6)	Base	Solvent	7 Yield (%)
a	$CH_2(COOEt)_2$	NaH (10% mol)	THF	Quant.
b	CH_3COPh	NaH (10% mol)	THF-t-BuOH	60
c	CH_3CH_2COPh	NaH (10% mol)	THF	95
d	$(CH_3)_2CHCOPh$	KH	Et_2O	68
e	$PhC(=NCH(CH_3)Ph)CH_3$	LDA	THF	85*
f	$AcNHCH(COOEt)_2$	NaH	THF	Quant.
g	$C_6H_5CH_2NH_2$	——	EtOH	Quant.
h	$CH_3CH(NH_2)COOEt$	——	EtOH	73**
i	$CH_3CH(NH_2)CH_2OH$	——	EtOH	75***

* Isolated as 7b by treating the adduct with 1N-HCl. ** 5:2 diastereoisomeric mixture. The major isomer was isolated by recrystallization of the mixture from ethyl acetate and n-hexane. *** 6:5 diastereoisomeric mixture.

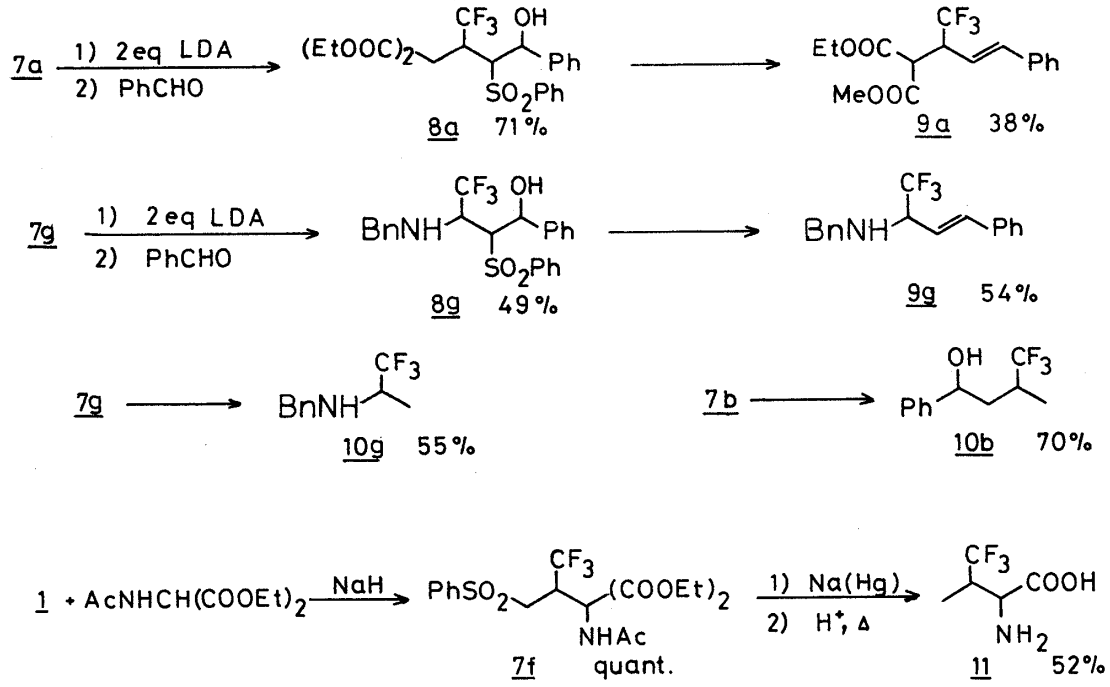


Chart 3

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5) For example: 3,3,3-trifluoropropene was shown as a versatile intermediate for the syntheses of various trifluoromethylated compounds: a) Y. Kobayashi, N. Nagai, I. Kumadaki, M. Takahashi and T. Yamauchi, Chem. Pharm. Bull., 32, 4382 (1984); b) I. Ojima and T. Fuchikami, J. Am. Chem. Soc., 104, 3527 (1982); c) I. Ojima, M. Yatabe, and T. Fuchikami, J. Org. Chem., 47, 2051 (1982).
6) 1 showed a high reactivity as dienophile, while the 3,3,3-trifluoropropene itself was reported to have rather low reactivity as a dienophile.[7,8] For example, the reaction of 1 with cyclopentadiene proceeded within 10 min at room temperature to give the adduct in 80% isolated yield. The Diels-Alder reaction of 1 with various dienes and the synthetic applications will be reported elsewhere.
7) B. Gaeda and T. M. Balthazor, J. Org. Chem., 48, 276 (1983).
8) Ref. 5c.
9) M. Shimagaki, H. Koshiji, and T. Oishi, Phosphorous and Sulfur, 16, 45 (1983).
10) In ^{19}F-NMR benzotrifluoride was used as an internal standard. + means high field.
11) Photoisomerization of 1 (acetone, high pressure Hg lamp) gave a mixture of 1 and the stereoisomer of 1. The latter was tentatively identified as (Z)-1-phenyl-sulfonyl-3,3,3-trifluoropropene on the bases of its NMR spectrum [^{1}H-NMR($CDCl_3$) δ 6.23 (dq, J_{H-H}=12 Hz, J_{H-F}=9 Hz), 6.83 (d, J_{H-H}=12 Hz); ^{19}F-NMR -7.5 ppm (d, J_{H-F}=9 Hz)].
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