

Communications to the Editor

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1-PHENYLSULFONYL-3,3,3-TRIFLUOROPROPENE 1:
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 sodium amalgam 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 sulfonyl chloride (CCl₄, refl., 12 h), oxidized to the sulfone (mCPBA, CH₂Cl₂) and then dehydrochlorinated (DBU, CH₂Cl₂, 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%-H₂O₂ (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

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

Entry	Nucleophile (<u>6</u>)	Base	Solvent	λ Yield (%)
a	$\text{CH}_2(\text{COOEt})_2$	NaH (10% mol)	THF	Quant.
b	CH_3COPh	NaH (10% mol)	THF-t-BuOH	60
c	$\text{CH}_3\text{CH}_2\text{COPh}$	NaH (10% mol)	THF	95
d	$(\text{CH}_3)_2\text{CHCOPh}$	KH	Et_2O	68
e	$\text{NCH}(\text{CH}_3)\text{Ph}$ PhCCH_3	LDA	THF	85*
f	$\text{AcNHCH}(\text{COOEt})_2$	NaH	THF	Quant.
g	$\text{C}_6\text{H}_5\text{CH}_2\text{NH}_2$	—	EtOH	Quant.
h	$\text{CH}_3\text{CH}(\text{NH}_2)\text{COOEt}$	—	EtOH	73**
i	$\text{CH}_3\text{CH}(\text{NH}_2)\text{CH}_2\text{OH}$	—	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.

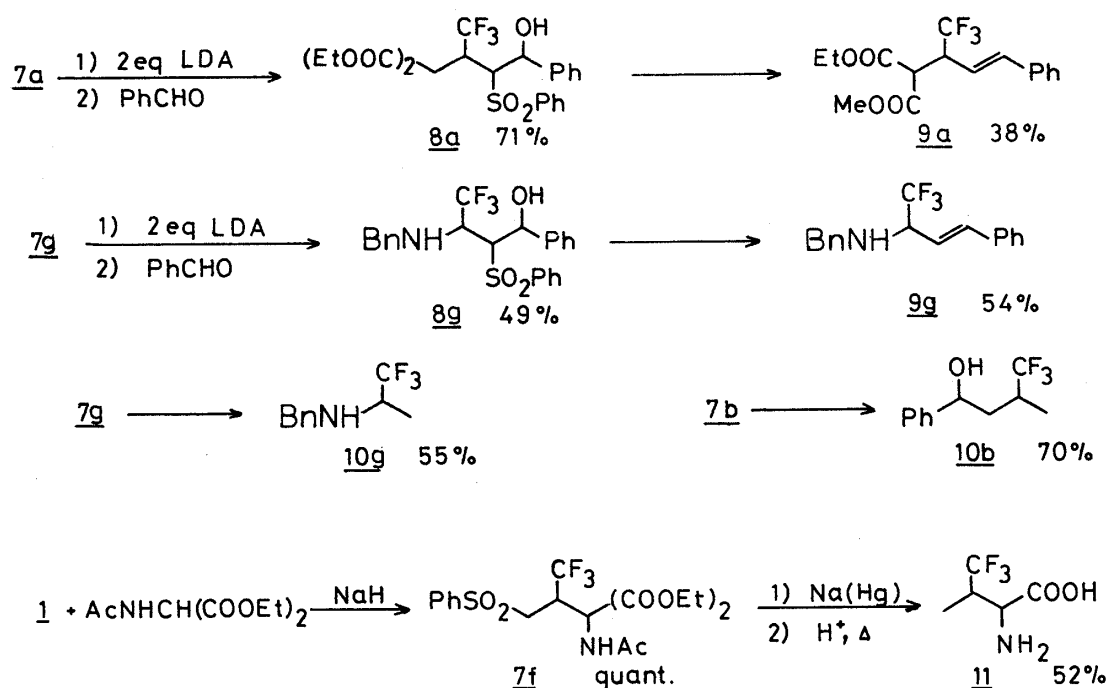


Chart 3

REFERENCES AND NOTES

- 1) Y. Kobayashi and I. Kumadaki, *Acc. Chem. Res.*, **11**, 197 (1978).
- 2) R. Filler and S. M. Naqvi, "Biomedical Aspects of Fluorine Chemistry," ed. by R. Filler and Y. Kobayashi, Elsevier Biomedical Press, 1982, pp. 1-32.
- 3) G. A. Boswell, Jr., W. C. Ripka, R. M. Scribner, C. W. Tullock, "Organic Reactions," **21**, 1 (1974).
- 4) For representative examples: a) Y. Kobayashi, K. Yamamoto, and I. Kumadaki, *J. Chem. Soc., Perkin Trans. 1*, **1980**, 2775; b) T. Kitazume and N. Ishikawa, *Chem. Lett.*, **1982**, 137; c) T. Fuchikami and I. Ojima, *Tetrahedron Lett.*, **25**, 303, 307 (1984); d) T. Umemoto, Y. Kuriu, S. Nakayama, and O. Miyano, *Tetrahedron Lett.*, **23**, 1471 (1982).
- 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 ¹⁹F-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-phenylsulfonyl-3,3,3-trifluoropropene on the bases of its NMR spectrum [¹H-NMR(CDCl₃) δ 6.23 (dq, J_{H-H}=12 Hz, J_{H-F}=9 Hz), 6.83 (d, J_{H-H}=12 Hz); ¹⁹F-NMR -7.5 ppm (d, J_{H-F}=9 Hz)].
- 12) R. M. Babb and F. W. Bollinger, *J. Org. Chem.*, **35**, 1438 (1970).

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