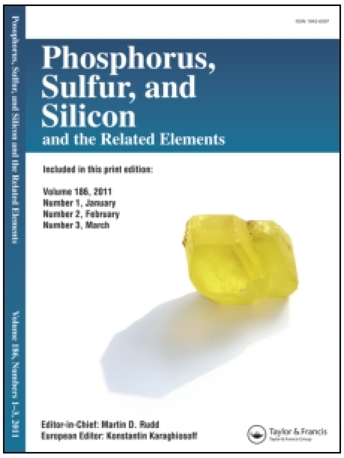


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

FLUOROALKYLTHIO SUBSTITUTED BENZOYL DERIVATIVES

Thomas S. Croft[a]
[a] Central Research Laboratories 3M Co., St. Paul, Minnesota, U.S.A.

To cite this Article Croft, Thomas S.(1976) 'FLUOROALKYLTHIO SUBSTITUTED BENZOYL DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 2: 1, 129 — 132

To link to this Article: DOI: 10.1080/03086647608078937

URL: http://dx.doi.org/10.1080/03086647608078937

Phosphorus and Sulfur
1976, Vol. 2, pp. 129-132

FLUOROALKYLTHIO SUBSTITUTED BENZOYL DERIVATIVES

by

Thomas S. Croft

Central Research Laboratories, 3M Co.,
St. Paul, Minnesota 55133, U.S.A.

Received September 20, 1975

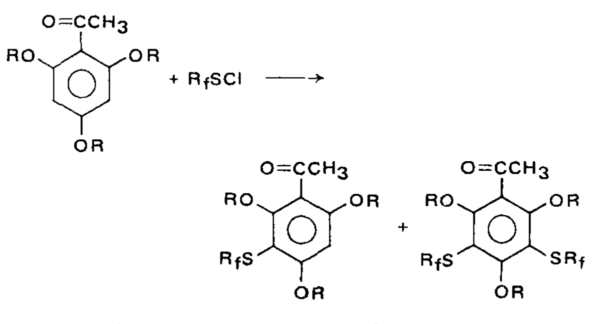
ABSTRACT

Electrophilic substitution with fluoroalkanesulfenyl chlorides on appropriately activated acetophenones, benzophenones, benzaldehydes, and benzoates is described.

Results and Discussion

The trifluoromethylthio (also referred to as trifluoromethylmercapto or trifluoromethyl sulfur) substituted benzoyl derivatives known to date were synthesized by the chlorination of aryl methyl sulfides with subsequent replacement of chlorine by fluorine. Due to the laborious and restrictive nature of this procedure, only the mono-trifluoromethylthioacetophenone,[1] -benzophenone,[2] -benzaldehyde,[3] and -benzoate[4] have been reported. A few references have appeared[5,6,7] which involve electrophilic substitution with trifluormethanesulfenyl chloride but the electron withdrawing effect of the carbonyl or keto function[8] does not allow reaction with the simple benzoyl derivatives. However, the introduction of powerful electron donating groups to overcome this deactivation is shown by this paper to lead to direct substitution with fluorosulfenyl chlorides. Even multiple fluoroalkylthio substitution was possible by judicious location of these groups so as to activate a specific position and by the use of a catalyst in some cases.

SCHEME I

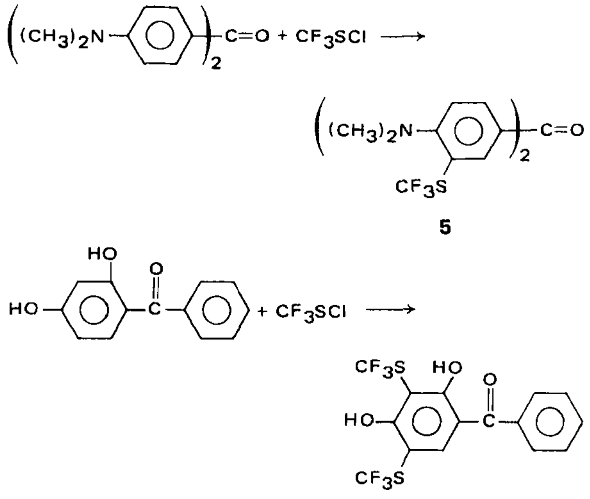


1, R = H, $R_f = CF_3$ 2, R = H, $R_f = CF_3$
3, R = CH_3, $R_f = CF_3$ 4, R = H, $R_f = C_7F_{15}$

Acetophenones and benzophenones undergo ring substitution with fluoroalkanesulfenyl chlorides only if sufficient electron-donating substituents are present. Thus, with 2,4,6-trihydroxy or 2,4,6-trimethoxyacetophenone in chloroform and pyridine, the introduction of trifluoromethanesulfenyl chloride gave the corresponding mono aryl trifluoromethyl sulfide, compounds **1** and **3** of Scheme I. The addition of iron powder allowed a second substitution on the more activated acetophenone with both trifluoromethyl and perfluoroheptysulfenyl chloride to produce compounds **2** and **4**.

With 4,4′-bis(dimethylamino)-benzophenone, substitution took place in both rings to give 4,4′-bis-(dimethylamino)-3,3′-bis(trifluoromethylthio)-benzophenone (**5**). In this system, the presence of two hydroxy groups in one ring was sufficient for disubstitution (see compound **6** of Scheme II).

SCHEME II

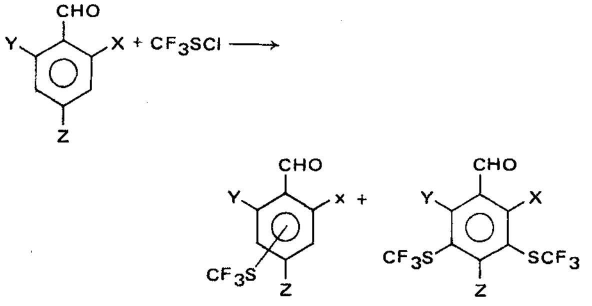


5

6

For benzaldehydes, mono-substitution occurred with a 4-dimethylamino group present to give compound 7 of Scheme III or with 2,4,6-trimethoxy substituents to yield compound **8**. Similarly, 2-hydroxy-4,6-dimethoxy benzaldehyde yielded a 3- or 5-trifluoromethylthio aryl sulfide, compound **9**. However, with either 2,4-dihydroxy or 2,4,6-trihydroxybenzaldehyde, two trifluoromethylthio groups were introduced into the ring, giving compounds **10** and **11**, respectively.

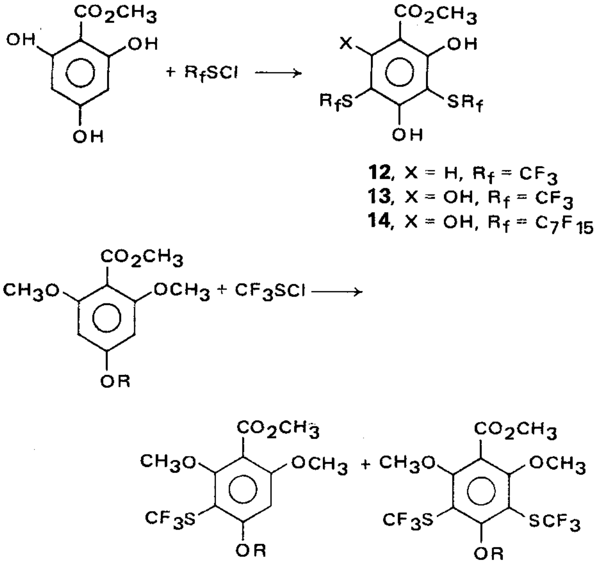
SCHEME III



7, X = Y = H, Z = N(CH$_3$)$_2$
8, X = Y = Z = —OCH$_3$
9, X = OH, Y = Z = —OCH$_3$
10, Y = H, X = Z = OH
11, X = Y = Z = OH

A similar situation was noted with methyl benzoates in that a bis(trifluoromethylthio) product resulted

SCHEME IV



12, X = H, R$_f$ = CF$_3$
13, X = OH, R$_f$ = CF$_3$
14, X = OH, R$_f$ = C$_7$F$_{15}$

15, R = H
17, R = CH$_3$
16, R = H

TABLE I

Analytical and Spectral Data for New Aceto- and Benzophenones

Cpn (Method-Yield %)	Mp (°C)	IR*	Analysis (%)				NMR†		
			Calculated		Found				
			C	F	C	F	φ‡	τ	Group
1 (A-33)	139–140	6.1	40.3	21.3	40.3	21.2	43.9	1.45, 3.37	OH
								3.79	ring CH
									7.28 CH$_3$
2 (B-40)	113-5	6.1	32.6	31.0	32.9	30.6	43.5	−0.5	OH
								7.24	CH$_3$
3 (A-74)	68–71	5.74	46.5	18.4	46.3	18.7	43.0	3.62	ring CH
								6.03, 6.09, 6.15	OCH$_3$
								7.50	CH$_3$
4 (B-39)	106–108	6.1	27.3	58.9	27.4	58.7	87.4	−1.72, 2.63	OH
							(—CF$_2$S—)	7.23	CH$_3$
5 (A-80)	93-5	6.1	48.7	24.3	48.5	24.9	43.0	1.98, 2.22, 2.95	ring CH
								7.01	CH$_3$
6 (A-80)	91-5	6.1	43.5	27.5	43.8	27.2	43.9	−3.87	OH
								1.87, *ca.* 2.39	ring CH

*C=O (μ) † in CDCl$_3$/CFCl$_3$ ‡ CF$_3$S—.

with both 2,4-dihydroxy or 2,4,6-trihydroxy substituents, yielding compounds **12** and **13** (see Scheme IV). Perfluoroheptanesulfenyl chloride also led to disubstitution, compound **14**, when iron powder was introduced as a catalyst. With methyl-2,4,6-trimethoxy or 2,6-dimethoxy-4-hydroxybenzoate, a single substitution took place to yield compounds **17** and **15** respectively, although the latter compound underwent an additional reaction in the presence of iron powder to produce **16**.

Consequently, multiple substituted benzoyl derivatives are available from simple electrophilic substitution with fluoroalkanesulfenyl halides.

Experimental Section

The nmr spectra were obtained using a Varian XL-100 spectrometer, utilizing internal standards of fluorotrichloromethane and tetramethylsilane, with chemical shifts reported as ϕ and τ values. When possible, analytical samples were collected from a F and M Model 700 gas chromatograph employing 6 ft by 1/4 in columns packed with 15% OV-17 on ABS. Infrared spectra were measured on a Perkin-Elmer Model 21 spectrophotometer. Trifluoromethanesulfenyl chloride was prepared by the method of Tullock and Coffman[9] and perfluoroheptanesulfenyl chloride as previously described.[10] The sulfenyl chlorides should be treated as hazardous materials and suitable precautions taken to prevent contact.[11] All other reagents were obtained from chemical supply houses, largely Aldrich Chemical Co.

In general, these products can be prepared by the following method, designated as Method A. A solution of the appropriate aromatic compound and a slight excess of pyridine is dissolved in chloroform and cooled to –40°, with the low-boiling trifluoromethanesulfenyl chloride, bp –2°: an excess of this reagent was bubbled into the solution using a dry-ice condenser to retain the sulfenyl chloride in the reaction vessel until reaction had taken place. With the higher boiling perfluoroheptanesulfenyl chloride, a dropping funnel and water condenser was used. This addition was carried out in an unlighted hood in the case of the acetophenone derivatives. The temperature was slowly raised to 60° by external heating and held three or more hours before washing the resulting mixture while hot three times with dilute (about five percent) hydrochloric acid. Then distillation or recrystallization, after drying with $MgSO_4$, led to the desired products. The addition of 100 mg of iron powder (Baker) to facilitate the reaction will be indicated as Method B. The analytical, physical, and spectral data for the new aceto- and benzophenones are listed in Table I, for the new benzaldehydes in Table II, and for the new methyl benzoates in Table III.

TABLE II

Analytical and Spectral Data for New Benzaldehydes

Cpn (Method-Yield %)	Mp (°) (bp*)	IR†	Analysis (%) Calculated C	Calculated F	Found C	Found F	NMR‡ ϕ§	τ	Group
7 (A-55)	(131-6)	5.86	48.2	22.9	48.3	23.0	43.3	0.22	CHO
								2.03, 2.26, 2.98	ring CH
								6.99	CH_3
8 (A-80)	97-8	6.0	44.6	19.2	44.7	19.1	42.5	−0.28	CHO
								3.27	ring CH
								5.94, 6.12	CH_3
9 (A-44)	133-4	6.13	42.6	20.2	42.5	20.5	43.1	−0.13	CHO
							44.2	−3.22	OH
								3.53	ring CH
								5.91	CH_3
10 (B-21)	74-5	6.04	32.0	33.7	32.0	33.7	42.4	0.03	CHO
							43.8	1.67	ring CH
								4.50	OH
11 (A-30)	140-1	6.10	30.5	32.2	30.5	31.9	43.4	−0.2	CHO

* At *ca.* 1 mm or less † C=O (μ) ‡ in $CD_3COCD_3/CFCl_3$ except for cpn **7** which was in $CDCl_3/CFCl_3$ § CF_3S–.

TABLE III

Analytical and Spectral Data for New Benzoates

Cpn (Method-Yield %)	Mp (°) (bp*)	IR†	Analysis (%) Calculated C	Analysis (%) Calculated F	Analysis (%) Found C	Analysis (%) Found F	NMR‡ ϕ§	NMR‡ τ	NMR‡ Group
12 (A-20)	134–137	5.93	32.6	31.0	32.8	30.8	42.8	1.70	ring CH
							44.2	6.01	CH_3
13 (A-55)	149–152	5.84	31.3	29.7	31.4	29.4	43.4	−1.08, 2.36	OH
								5.85	CH_3
14 (B-35)	70–8	5.95	26.8	57.9	26.7	57.8	87.5	−1.10, 2.40	OH
							($-CF_2S$)	5.85	CH_3
15 (A-65)	(129–130)	5.70	42.3	18.3	42.2	18.0	43.4	2.90	OH
								3.57	ring CH
								6.07, 6.18	CH_3
16 (B-60)	102–3	5.80	35.0	27.6	35.2	27.5	42.5	5.99, 6.03	CH_3
17 (A-70)	97–9	5.68	44.2	17.5	44.3	17.4	42.9	3.67	ring CH
								6.10	CH_3

* At *ca.* mm or less † C=O (μ) ‡ in $CDCl_3/CFCl_3$ except for cpns **12**, **14**, and **16** which were run in $CD_3COCD_3/CFCl_3$ § CF_3S

Acknowledgements

The author wishes to thank Dr. J. J. McBrady for interpretation of the nmr spectra, Mr. P. Olson and Mr. J. G. Gagnon for the elemental analyses, and Mr. G. B. Jefson for experimental assistance.

References

1. L. M. Yagupolskii and B. E. Gruz, *Zhur. Obsch. Khim.*, **31**, 1315 (1961).
2. W. J. Middleton, U.S. Patent 3,732,307 (1973).
3. J. B. Buchanon and W. A. Gregory, U.S. Patents 3,061, 645 (1962), 3,207,792 (1965) and 3,387,037(1968).
4. L. M. Yagupolskii and M. S. Marenets, *Zhur. Obsch. Khim.*, **24**, 887 (1954).
5. S. Andreades, J. F. Harris, Jr., and W. A. Sheppard, *J. Org. Chem.*, **29**, 898 (1964).
6. H. Richert, U.S. Patent 3,132,182 (1964).
7. R. M. Scribner, *J. Org. Chem.*, **31**, 3671 (1966).
8. A general reference to the electronic effect of substituents and electrophilic substitution is: R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Co., New York, N.Y., 1965
9. C. W. Tullock and D. D. Coffman, *J. Org. Chem.*, **25**, 2016 (1960).
10. T. S. Croft and J. J. McBrady, *J. Heterocyclic Chem.*, in press.
11. PCR, Inc., Gainesville, Fla., Bulletin on Toxic Fluorine Compounds dated July 1, 1968.