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A Convenient Preparation of Sulfines ($R_2C{=}S{=}O$) from Thioketones

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Introduction

Hydrogen peroxide is able to oxidize thiobenzophenones and thiocamphor to their sulfines, when catalyzed by methyltrioxorhenium, CH_3ReO_3 or MTO, according to this general reaction:

$$R_2C{=}S + H_2O_2 \xrightarrow{\text{cat. MTO}} R_2C{=}S{=}O + H_2O \qquad (1)$$

This method has provided a new route to sulfines that is superior to known methods. Peracids are traditionally used, such as perbenzoic acid,[1] monoperoxyphthalic acid,[2,3] and *m*-CPBA.[4−6] Even with a limited peracid concentration to prevent overoxidation, yields were not entirely satisfactory. On the basis of the peracids consumed, conversions were in the range 9−99%, but expressed as the conversion of thione, it was much less satisfactory, even at 0 °C. Ozonation is another common method,[7,8] often carried out at −70 °C under nitrogen. With a 1:1 ratio of thione/O_3 at room temperature, the yield was still quite low, about 3−6% of sulfine, with most of the thione remaining unoxidized or overoxidized to the ketone.[9] The use of $^1O_2$[10] proved unsatisfactory, as did other oxidizing reagents.[11] The conditions used in these reactions and the yields of sulfines thus obtained are summarized in Table 1.

Aside from oxidative methods, one should note the alkylidenation of sulfur dioxide with α-silyl carbanions at −78 °C[12] and the base-induced elimination of alkanesulfinyl derivatives.[13,14]

In this work, reaction 1 was carried out for several thiobenzophenones, with these para substituents: NMe_2, OMe, Me, H, F, Cl, Br, *m*-CF_3, and *m*-NO_2. Thiocamphor was used as well. To obtain the sulfines in high yield on a 1 mmol scale, only the requisite quantity of hydrogen peroxide was used. This method succeeds because the subsequent oxidation of the sulfines occurs $<10^3$ times as rapidly as the rate of reaction 1. With a 1:1 ratio of R_2CS/H_2O_2, no further oxidation or side products were obtained, as judged by ^1H NMR. The reaction was carried out at room temperature in organic solvents (acetonitrile, chloroform, etc.) or in aqueous mixtures.

Table 1. Yields of Sulfines Prepared by Different Methods of Thione Oxidation

oxidizing reagent	conditions	sulfine yield (%)
MTO/H_2O_2	rt, <5 min	>90
perbenzoic acid[1]	rt[a]	80−90[b]
monoperoxyphthalic acid[2,3]	0 °C, 30−45 min[c]	38−89
m-CPBA[4−6]	0 °C, 30−40 min[d]	50−90
ozone[7−9]	−70 to −78 °C, N_2[e]	0−71
$^1O_2$[10]	*hν*, 0.5−48 h	2−25
N-sulfonyloxaziridines[11]	0 °C, N_2, 0.5−1.5 h[f]	70−90

[a] A kinetics investigation. [b] Conversion of the thione to sulfine monitored by UV−vis, not the isolated yield. [c] 1:2 ratio of peracid to thione. [d] *m*-CPBA was the limiting reagent. [e] 1:1 ratio of ozone and thione. [f] Only two sulfines, (1*R*)-(+)-thiocamphor *S*-oxide and (1*S*)-(−)-thiofenchone *S*-oxide, were prepared by this method.

Some of these reactions have now been carried out on a larger scale, starting with 0.7−1.0 g of the thione dissolved in 1:4 aqueous acetonitrile. The solution also contained 0.1 M trifluoromethanesulfonic acid to stabilize MTO. This catalyst was added at 1−10% (usually 1−2%) relative to the thione, followed by hydrogen peroxide (1.0 equiv). The color of solution changed from the dark blue of the thiobenzophenone to light yellow in less than 2 min, signaling the completion of the reaction. The conversion was checked at this point by ^1H NMR; the reactions were found to be completed within 5 min. Acetonitrile was removed from the product solution by rotary evaporation. Hexane and water were added, followed by excess sodium bicarbonate to neutralize the triflic acid and decompose MTO to perrhenate ions.[15] The sulfine appeared in the hexane layer; the aqueous layer contained sodium triflate, excess sodium bicarbonate, and the perrhenate salt. The yellow hexane layer was washed with water several times and then rotary evaporated to remove the solvent. Higher purity material could be obtained by column or thin-layer chromatography on silica gel, eluting with ethyl acetate−hexane. Recrystallization from hexane−isooctane or hexane alone gave the sulfine as light yellow crystals.

The products from 4,4′-dimethoxythiobenzophenone and thiocamphor were isolated in 95−99% isolated yield. The crude sulfines were further purified by column chromatography on silica gel. Elution was with 15% ethyl acetate−hexane. 4,4-Dimethoxythiobenzophenone sulfoxide was recrystallized from hexane, yielding greenish-yellow needles.[16] Thiocamphor sulfine was obtained as a light yellow solid; spectroscopic data for it are given in Table 1.

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(16) ^1H NMR: δ/ppm 0.80 (d, 2H), 7.29 (d, 2H), 7.00 (m, 4H), 3.82 (s, 3H), 3.80 (s, 3H). MS *m*/*z*: 274 (M^+, 67), 258 ($M^+ - O$, 11), 226 ($M^+ - SO$, 8.5), 211 ($M^+ - SO - CH_3$, 10), 196 ($M^+ - SO - OCH_3$, 2.4), 183 ($M^+ - OCH_3 - CSO$, 7), 151 ($M^+ - CSO - 2MeO$, 6), 135 ($M^+ - S - MeOC_6H_4$, 100), 107 ($M^+ - CSO - MeOC_6H_4$, 33).

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Table 2. Spectroscopic and Analytical Data for Previously-Unreported Sulfines[a]

method	(p-FC_6H_4)$_2$CSO	(m-$CF_3C_6H_4$)$_2$CSO
^{1}H NMR ($CDCl_3$)	7.66 (m, 2H), 7.13 (m, 2H), 6.90 (m, 4H)	8.09 (s, 1H), 8.02 (d, 1H), 7.83 (d, 1H), 7.76 (d, 1H), 7.67−7.56 (m, 4H)
^{13}C NMR ($CDCl_3$)	185.26 (CSO), 165.21 (d, ^1J(F, C) = 296), 162.70 (d, ^1J(F, C) = 307), 131.53, 131.44, 130.84 (d, ^4J(F, C) = 15), 126.91 (d, ^4J(F, C)= 14), 116.10 (d, ^2J(F, C) = 88), 115.64 (d, ^2J(F, C) = 88)	185.51 (*C*SO), 134.36, 132.66, 132.16, 131.83, 131.68, 131.60, 130.01, 129.55, 128.08 (q, ^3J(F, C) = 14), 127.87 (q, ^3J(F, C) = 14), 125.98 (q, ^3J(F, C) = 15), 125.73 (q, ^3J(F, C) = 15), 124.82 (CF_3, q, ^1J(F, C) = 35),122.11 (CF_3, q, ^1J(F, C) = 35)
MS	250 (M^+, 75), 234 ($M^+ - O$, 18), 202 ($M^+ - SO$, 100), 183 ($M^+ - SO - F$, 16)	350 (M^+, 66), 334 ($M^+ - O$, 17), 331 ($M^+ - F$, 2), 301 ($M^+ - SO$, 30), 281 ($M^+ - CF_3$, 100), 233 ($M^+ - CF_3 - SO$, 43)
λ_{max} (ϵ) (ethyl acetate)[b]	327 (12 100); 260 (9260)	320 (19 400)
elemental analysis, found (calcd)	C 62.24 (62.38); H 3.15 (3.22); S 12.46 (12.81)	C 51.92 (51.43); H 2.32 (2.30); S 9.18 (9.15)
habit	yellow crystals, mp 75−76 °C	pale yellow, mp 53−55 °C

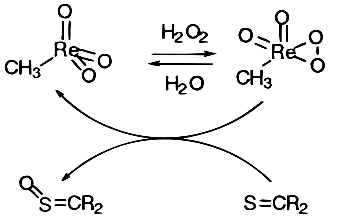
[a] Thiocamphor sulfine, previously reported,[11] has this ^{1}H spectrum [2.94 (d of m, 1H), 2.45 (d, 1H), 2.02 (t, 1H), 1.86 (m, 2H), 1.39 (m, 1H), 1.24 (m, 1H), 1.06 (s, 3H), 0.90 (s, 3H), 0.77 (s, 3H)] and this MS: 184 (M^+, 59), 167 ($M^+ - OH$, 4), 135 ($M^+ - SOH$, 3), 125 (5), 107 (45), 105 (43), 93 (72), 91 (100). [b] UV spectra determined at four concentrations; Beer's law was exactly obeyed.

Most sulfines were obtained as yellow or yellowish crystalline materials. They are mildly photosensitive to room light and to oxygen, but are much more stable than the parent thioketones. Even if exposed to air and light, sulfines can be kept unchanged for days and are stable enough to be isolated and characterized. Some of the sulfines are stable for months when stored in the dark under argon. The melting points, colors, and isolated yields of the other materials have also been noted.[17]

The sulfines with the para substituents NMe_2, OMe, Me, H, Cl, Br, and m-NO_2 were previously known. They were identified by comparing their ^{1}H and ^{13}C NMR spectra, mass spectra, and IR spectra with data previously reported.[8,10,11,18−24]

Two new sulfines were prepared, with p-F and m-CF_3 substituents. They were obtained by the same procedure in >90% yields and purified by thin-layer chromatography on silica gel, eluting with 5% ethyl acetate−hexane. Yellow crystals were grown from hexane−isooctane. The spectroscopic data and elemental analyses for the new compounds are given in Table 2.

Scheme 1. Initial Stage of Oxidation



The success of the method rests, first, on the MTO-catalyzed reaction converting the thioketone to a sulfine. This type of transformation has been verified for a considerable number of substrates, as has recently been reviewed.[25,26] The essence of this chemistry is captured in Scheme 1.

The second stage of oxidation, in which the sulfine, in >1 step, is converted to the ketone, occurs rather more slowly. Under conditions at which a thioketone is oxidized in ca. 10 min, the sulfine required 100−600 h. This timing difference is quite reasonable in that the addition of an oxygen atom to the sulfur will certainly reduce sharply the rate of a subsequent oxidation step by the same reagent. It is just this difference that enables the present procedure to give a high yield of the sulfine with so little loss to the ketone. In the case of thiocamphor, the oxidation stops at the sulfine, even with excess peroxide.

The C═S bond in thioketones is known to be strongly polarized,[2] unlike a C═O bond. A negative charge resides on the carbon atom. The sulfine is formed by the nucleophilic attack of the sulfur atom on the electron-deficient oxygen atom of the peroxorhenium complexes that are the active intermediates in the reaction.

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(17) For (p-XC_6H_4)$_2$CSO, the melting points, colors, and yields are as follows: NMe_2, 181−183 °C, gold 88%; MeO, 84−85, greenish-yellow, 95%; Me, 89−91 °C, yellow, 98%; H, 33−35 °C, greenish yellow, 92%; F, 75−76 °C; yellow, 95%; Cl, 87.5−88 °C; yellow, 95%; Br, 106−108 °C; yellow, 90%. For these meta isomers, CF_3, 53−55 °C, light yellow, 92%; NO_2, 162−164 °C, light yellow, 90%. The sulfine from thiocamphor is a light yellow oily solid, mp 118−120 °C, obtained in 97% yield.

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