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Sodium Telluride-Mediated Sulfenylation of α-Halo Carbonyl Compounds with Diphenyl Disulfide

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Synopsis. Under mild aprotic conditions α-halo carbonyl compounds react with diphenyl disulfide in the presence of sodium telluride to give the corresponding α-phenylthio derivatives in good to moderate yields. The reaction appears to proceed involving the sulfur-sulfur bond cleavage of diphenyl disulfide by sodium telluride.

Introduction of a phenylthio unit adjacent to a carbonyl function is an important step for achieving facile structural modifications.[1] Generally the sulfenylated compounds are synthesized by reacting metal enolates with organic disulfides[2,3] or thiosulfonates,[4] by the action of sulfenyl chloride on α-diazo ketones,[5] enamines,[6] 1,3,2-dioxaphospholes,[7] and silyl enol ethers,[8] and also from α-halo carbonyl compounds and thiolate ion,[9] thallium(I) benzenethiolate,[10] or α-thio iminium salts.[11] Other methods include the sulfenylation of active methylene carbon with sulfenamides,[12] thermal decomposition of β-keto sulfonium salts,[13] and controlled oxidation of β-hydroxy sulfides.[14] Sulfenylation accompanied by dealkoxycarbonylation of β-keto esters affords α-thio ketones.[15] Sophisticated approaches using [bis(phenylthio)methyl]lithium[16] and α,β-epoxy sulfoxides[17] were also reported.

As part of our continuing efforts to explore the synthetic utility of sodium telluride, we now wish to report a method for preparing monothio carbonyl compounds from α-halo carbonyl compounds and diphenyl disulfide.

$$\underset{\mathbf{1}}{\mathrm{RCOCH_2X}} + \mathrm{Ph_2S_2} \xrightarrow[\text{DMF, }-40\,^\circ\text{C}]{\mathrm{Na_2Te}} \underset{\mathbf{2}}{\mathrm{RCOCH_2SPh}} \qquad (1)$$

When a solution of α-halo carbonyl compounds (**1**) in *N,N*-dimethylformamide (DMF) was added to a mixture of sodium telluride and diphenyl disulfide (excess) in DMF at −40 °C, the monosulfenylated compound (**2**) was obtained in fairly good yields (Table 1). Bissulfenylated compounds and dehalogenation products were also isolated in a few cases. Formation of significant amount of dehalogenated compound from bromodibenzoylmethane could be probably due to the desulfenylation of the monosulfenylated compound initially formed by the thiolate ion. Such desulfenation by thiolate ions has been reported earlier.[18]

The monosulfenylated product **2** arises from the reaction between the thiolate, generated in situ from diphenyl disulfide and sodium telluride, and α-halo carbonyl compound **1**. This was concluded by changing the mode of addition: Addition of phenacyl bromide to sodium telluride at −40 °C generated the enolate anion, which was allowed to react with the added diphenyl disulfide. This resulted in the isolation of bissulfenylated product (**2e**) in addition to acetophenone. Simultaneous formation of these two products can be best explained by assuming the rapid proton removal from the initially formed monosulfenylated compound (**2a**) by the enolate anion present in large excess. Isolation of bissulfenylated products from lithium enolates has been observed earlier.[2] Addition of diphenyl disulfide to sodium telluride at −40 °C resulted in the immediate separation of free tellurium and subsequent addition of ethyl iodide led to the isolation of ethyl phenyl sulfide in 45% isolated yield. Thus the overall reaction (1) can be depicted as follows:

$$\mathrm{PhSSPh + Te^{2-} \longrightarrow 2\,PhS^- + Te}$$
$$\mathrm{RCOCH_2X + PhS^- \longrightarrow RCOCH_2SPh + X^-}$$

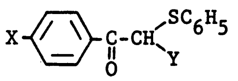
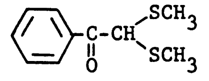
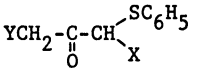
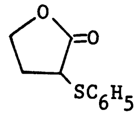
From the reaction of phenacyl bromide with dimethyl disulfide, however, bissulfenylated product and acetophenone were the only major products isolated. This result is very much similar to the one obtained by the addition of diphenyl disulfide to the enolate anion. This indicates that the reaction between phenacyl bromide and dimethyl disulfide may proceed through the nucleophilic attack of the enolate anion on the sulfur atom without any involvement of the reductive cleavage of S-S bond by telluride anion. Trost and co-workers[2] observed that simple ketone enolates are not sufficiently reactive toward dimethyl disulfide. Confirmation of the proposed non-cleavage of S-S bond was provided by an attempted reaction between dimethyl disulfide and benzyl chloride. Formation of benzyl methyl sulfide could not be observed under our conditions from the ^{1}H NMR analysis of the reaction mixture.[19]

It has been reported that the bissulfenylated products can be converted to monosulfenylated compounds with sodium ethanethiolate in the presence of excess base.[20] Any doubt regarding the formation of monosulfenylated compounds by such a possible reduction by sodium telluride in the present study was eliminated by a separate experiment. Reaction of bis(phenylthio)acetophenone with excess of sodium telluride under similar reaction conditions resulted only in the recovery of the starting material in 62% isolated yield and no formation of monosulfenylated product was observed from the ^{1}H NMR of the reaction mixture.

Efforts to effect the selenylation under similar conditions using diphenyl diselenide led to the dehalogenated compounds in most of the cases. Only in the case of ω-bromo-ω-phenylsulfonylacetophenone monoselenylated product was obtained in an acceptable yield.

This paper reports a synthesis of α-phenylthio carbonyl compounds without actually handling the evil-

Table 1. α-Phenylthio and α,α-Bis(phenylthio) Carbonyl Compounds Obtained

Compond			Mp (Bp) °C (°C/mm Hg[a])	Yield[b] %	IR cm^{-1}	^1H NMR ($CDCl_3$/TMS) δ (ppm)
						
	X	Y				
2a:	H	H	49—50 (lit,[22] 53—54)	61	1665, 1590, 1570, 1440, 1270, 1010, 800, 750, 740, 690	4.19 (s, 2H), 7.1—8.0 (m, 10H)
2b:	Br	H	59—60	57 (24)	1680, 1580, 1480, 1395, 1190, 995, 740	4.13 (s, 2H), 7.1—7.4 (m, 5H), 7.48 (d, 2H; J=7.8 Hz), 7.71 (d, 2H; J=7.8 Hz)
2c:[c]	H	$SO_2C_6H_5$	131—134	87	1680, 1440, 1320, 1310, 1275, 1140, 1080, 750, 680	5.73 (s, 1H), 7.2—8.0 (m, 15H)
2d:	H	COC_6H_5	89—91 (lit,[12] 93—94)	38[d]	1690, 1680, 1595, 1580, 1450, 1285, 1250-1260, 1200, 760, 740, 690	5.95 (s, 1H), 6.9—8.0 (m, 15H)
2e:	H	SC_6H_5	94—99 (lit,[22] 99—100	33	1670, 1580, 1470, 1450, 1265, 1180, 1150, 995, 810, 755, 695	5.67 (s, 1H) 7.1—8.1 (m, 15H)
2f:[e]	Br	SC_6H_5	68—69	24	—[f]	5.56 (s, 1H), 7.0—7.8 (m, 14H)
 **2g:**[g]			57—62	30	1650, 1585, 1440, 1310, 1280, 1190, 1170, 1000, 720, 700, 680	2.09 (s, 6H) 5.26 (s, 1H) 7.2—7.6 (m, 3H) 7.8—8.1 (m, 2H)
						
2h:	H	CH_3	115—120/2 (lit,[7] 78—80/0.003)	85	1710, 1480, 1440, 1360, 1030, 750, 690	1.28 (d, 3H) 2.16 (s, 3H) 3.69 (q, 1H) 7.1—7.6 (m, 5H)
2i:	$COOC_2H_5$	H	135—140/3 (lit,[23] 140/1)	74	1730, 1660, 1580, 1485, 1440, 1370, 1320, 1250, 1185, 1090, 1025, 745, 690	1.18 (t, 3H; J=7 Hz) 3.52 (s, 2H) 3.74 (s, 2H) 4.07 (q, 2H: J=7 Hz) 7.23 (s, 5H)
 **2j:**			145—150/3 (lit,[10] 140—145/1.3)	85 (10)	1760, 1475, 1435, 1370, 1200, 1150, 1020, 740, 685	2.0—2.8 (m, 2H) 3.73 (d, 1H; J=6 Hz) 3.88 (d, 1H: J=5.4 Hz) 4.19 (t, 2H; J=6.6 Hz) 7.2—7.6 (m, 5H)

a) Bulb-to-bulb distillation (1 mmHg=133.322 Pa). b) Isolated yields based on α-halo carbonyl compounds are not optimised. The values in parentheses refer to the yields of bissulfenylated products. c) Found: C, 64.99; H, 4.49%. Calcd for $C_{20}H_{16}O_3S_2$: C, 65.22; H, 4.35%. d) Dehalogenated product was obtained in 57% yield. e) Found: C, 57.58; H, 3.76%. Calcd for $C_{20}H_{15}BrOS_2$: C, 57.83; H, 3.64%. f) Not determined. g) Found: C, 56.29; H, 5.66%. Calcd for $C_{10}H_{12}OS_2$: C, 56.60; H, 5.66%.

smelling thiol under mild aprotic conditions in fairly good yields and also discloses one more new property of sodium telluride to cleave the S–S bond in aromatic disulfide, but not in aliphatic one. To the best of our knowledge this is the first report employing both α-halo carbonyl compounds and an organic disulfide in a "one pot" way for preparing the α-phenylthio carbonyl compounds.

Experimental

All melting and boiling points were uncorrected. IR spectra were measured as KBr pellets or as neat films between NaCl plates by using a Hitachi 260-10 spectrophotometer and only prominent peaks between 2000 and 650 cm^{-1} are indicated. ^{1}H NMR spectra were determined on a Hitachi R-600 spectrometer using chloroform-*d* as solvent and TMS as internal standard. Mass spectra were obtained on a Hitachi M-80B spectrometer using 70 eV.

General Procedure for Sulfenylation: To a suspension of sodium telluride (2.0 mmol; prepared from tellurium and sodium hydride[21]) in DMF was added at −40 °C under nitrogen diphenyl disulfide (4.0 mmol) in DMF (5 ml), followed by the addition of α-halo carbonyl compound (2.0 mmol) in the same solvent (3 ml). The dark reaction mixture was kept with stirring at −40 °C for 2 h and then at room temperature for 1 h. The reaction was quenched with saturated aqueous ammonium chloride solution (10 ml) and the mixture was extracted with benzene. The extract was filtered through a thin bed of Celite, washed with 0.5 M (1 M=1 mol dm^{-3}) sulfuric acid and water, and dried over sodium sulfate. The solvent was removed and the crude product was purified by column chromatography on silica gel using hexane as eluent to give the unchanged diphenyl disulfide. Further elution with a mixture of hexane and dichloromethane afforded the sulfenylated compound. Different sulfenylated products prepared and their physical characteristics are given in Table 1.

ω,ω-Bis(phenylthio)acetophenone (2e): To sodium telluride (2.0 mmol) in DMF was added at −40 °C phenacyl bromide (2.0 mmol) in the same solvent (3 ml). The reaction mixture turned black immediately with the separation of free tellurium. After 5 min, diphenyl disulfide (4.0 mmol) in DMF (5 ml) was added. Following the general procedure given above, the bissulfenylated product was isolated in 33% yield. Mp 94—99 °C.

ω,ω-Bis(methylthio)acetophenone (2g) was obtained similarly using dimethyl disulfide instead of diphenyl disulfide. Yield, 30%. Mp 57—62 °C.

ω-Phenylseleno-ω-phenylsulfonylacetophenone: To a mixture of sodium telluride (1.0 mmol) and diphenyl diselenide (2.0 mmol) was added at −40 °C under nitrogen a solution of ω-bromo-ω-phenylsulfonylacetophenone (1.0 mmol) in DMF (2 ml). The reaction mixture was stirred at this temperature for 2 h and then at room temperature for 1 h. After the usual work up the monoselenylated product was isolated in 29% yield in addition to ω-phenylsulfonylacetophenone in 57% yield. The seleno compound was crystallized from ethanol as colorless crystals mp 157—159 °C. MS: *m/z* (rel intensity) 416 (M, 4.4), 275 (21), 167 (23), and 105 (100); IR (KBr): 1690, 1445, 1330, 1315, 1280, 1145, 1085, 745, and 685 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=5.71 (s, 1H) and 7.1—8.0 (m, 15H). Found: C, 57.67; H, 3.98%. Calcd for $C_{20}H_{16}O_3SSe$: C, 57.83; H, 3.86%.

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