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The Efficient Oxidation of Thiols to Disulfides with Thallium(III) Acetate

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The treatment of various kinds of alkane- and arenethiols with thallium(III) acetate in chloroform at 20—30 °C readily affords the corresponding disulfides almost quantitatively, without affecting other functional groups, such as the hydroxyl, amino, and carboxyl in the thiols. Under similar conditions, the reaction of thiobenzoic *S*-acid with thallium(III) acetate gives thallium(III) thiobenzoate, while that of thioacetic *S*-acid yields diacetyl disulfide and thallium(I) thioacetate.

It is generally known that a large variety of metal ions and oxides oxidize thiols to disulfides.[1] However, although the oxidation with lead(IV) acetate has been fully studied,[2,3] there have been no reports on that with thallium(III) salt, which is also a good oxidizing reagent and which shows some resemblance to lead(IV) salt in many organic reactions.[4] We wish now to describe a facile oxidation of thiols to disulfides with thallium(III) acetate.

TABLE 1. THE OXIDATION OF BUTANETHIOL WITH VARIOUS OXIDANTS IN CHLOROFORM[a]

Oxidant (mmol)		*n*-BuSH (mmol)	Temp (°C)	Time (h)	Yield (%)[b] of *n*-BuSS-*n*-Bu
$Tl(OAc)_3$	10	30	25—35	1	104[c,d]
$Tl(OAc)_3$	5	10	20—27	1	100[e]
Tl_2O_3	5	15	26—34	1	61
TlOAc	10	10	25—27	5	30
$Hg(OAc)_2$	5	20	20—27	1	32
$Pb(OAc)_4$	5	20	20—27	1	74
—		10	20	2	trace

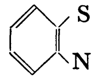
a) $CHCl_3$ (15 ml). b) Based on the amount of oxidant charged and determined by GLC. c) Isolated yield. d) TlOAc (91%) was isolated. e) TlOAc (95%) was isolated as TlCl by the addition of aq NaCl to the reaction mixture.

First, the oxidation of 1-butanethiol was examined with various thallium salts and lead(IV) and mercury(II) acetate as oxidants in chloroform. The results are shown in Table 1. It is clear that thallium(III) acetate is a more effective reagent than lead(IV) and mercury(II) acetate for disulfide formation, and also that the stoichiometric reduction of thallium(III) acetate to thallium(I) one occurs thus (Scheme 1):

$$2RSH + Tl(OAc)_3 \longrightarrow RSSR + TlOAc + 2AcOH \quad (1)$$

Since thallium(III) acetate was revealed to be a good oxidizing reagent for disulfides, the reaction was applied to various alkane- and arenethiols. It was found that the oxidation proceeded almost quantitatively without affecting other functional groups, such as the hydroxyl, amino, and carboxyl in the thiols. Some typical results are summarized in Table 2, together with some data obtained using lead(IV) acetate. In the case of 2-methyl-2-propanethiol, the oxidation with thallium(III) acetate gave disulfide selectively, while a further oxidized compound, sulfone, was obtained as the major product by the use of lead(IV) acetate. In the case of *o*-aminobenzenethiol, it has been reported that the oxidation with lead(IV) acetate gave disulfide in a low yield, probably because of the oxidation of the amino group by lead(IV) salt.[2] The oxidation with thallium(III) acetate, however, yielded only disulfide quantitatively. In the case of L-cysteine, the oxidation by lead(IV) acetate was very slow compared to that by thallium(III) acetate under nearly the same reaction conditions.

TABLE 2. THE OXIDATION OF THIOL WITH THALLIUM(III) AND LEAD (IV) ACETATES[a]

RSH R	Time (h)	Yield (%) of RSSR[b] oxidant $Tl(OAc)_3$	$Pb(OAc)_4$
n-Bu	1	100[c]	74[c]
t-Bu	2	73	
t-Bu	5	100[c]	37[c,d](46)
i-Pr	2	100[c]	(76)
$HOCH_2CH_2$	2	80	(91)
EtO_2CCH_2	1	76	66
Ph	1	100	(88)
o-$H_2NC_6H_4$	1	100	(29)
o-$HO_2CC_6H_4$	3	100	(95)
	1	100	(81)
$PhCH_2$	1	89	(89)
(L)-$HO_2CCH(NH_2)CH_2$	5	68	4[e]

a) RSH (10 mmol), $M(OAc)_n$ (5 mmol), $CHCl_3$ (15 ml) at 20—30 °C. b) Isolated yield unless otherwise stated. The values in parentheses are from Ref. 2. c) Determined by GLC. d) Other product: *t*-$BuSO_2S$-*t*-Bu (50% yield). e) More than 90% of the lead (IV) salt was recovered (by iodometry).

In the oxidation of arenethiols, when the reaction was carried out in the presence of more than two equivalents of thiols to one of thallium(III) acetate, yellow thallium(I) thiolate was formed as well as disulfide, as has previously been reported in the cases with lead(IV) acetate[3] (See Experimental section). The stoichiometry (using three mol of thiols) is shown in Scheme 2. On the other hand, in the cases of alkanethiols, no such thiolate was formed and thallium(I) salt was obtained as the acetate.

$$3ArSH + Tl(OAc)_3 \longrightarrow ArSSAr + TlSAr + 3AcOH \quad (2)$$

Although thiocarboxylic *S*-acids have reacted with lead(IV) acetate to yield diacetyl disulfides,[2,3] the reaction of them with thallium(III) acetate gave slightly different results. That is, the reaction of thiobenzoic

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S-acid with thallium(III) acetate in chloroform at room temperature resulted in the formation of thallium(III) thiobenzoate in a good yield (Scheme 3), while that of thioacetic *S*-acid gave diacetyl disulfide and thallium(I) thioacetate (Scheme 4). In the latter case, unstable thallium(III) thioacetate seemed to be formed at first; it then decomposed to give the products. In fact, thallium(III) thiobenzoate also decomposed to thallium(I) salt and dibenzoyl disulfide upon heating in chloroform or carbon tetrachloride, or even upon standing at room temperature for several days.

$$3PhCOSH + Tl(OAc)_3 \longrightarrow Tl(SCOPh)_3 + 3AcOH \qquad (3)$$

$$3CH_3COSH + Tl(OAc)_3 \longrightarrow TlSCOCH_3 + (CH_3COS)_2 + 3AcOH \qquad (4)$$

Experimental

The NMR spectra were taken with a Varian EM-360 spectrometer, using $CDCl_3$ as the solvent. The IR and mass spectra were recorded on Hitachi EPI-S2 and JEOL JMS-01SG spectrometers respectively. The GLC analyses were carried out on a Shimadzu 4BMPF apparatus, using an EGSS-X (30%)-Chromosorb W (1 m or 3 m) column. Commercial organic and inorganic materials were used without further purification. The thallium(III) acetate was prepared from thallium(III) oxide and acetic acid.[5]

Reaction of Thiols with $Tl(OAc)_3$. The following is a typical example. To a stirred chloroform (15 ml) solution of 1-butanethiol (2.7 g, 30 mmol) we added solid thallium(III) acetate (3.81 g, 10 mmol) in several portions at 25 °C over a 10-min period. The reaction was exothermic, and the temperature rose to 35 °C during the addition. The resulting yellowish orange mixture was stirred for 1 h. The subsequent evaporation of the chloroform by means of a vacuum evaporator at room temperature left white thallium(I) acetate (2.4 g, 9.1 mmol; mp 130 °C) and organic products, the latter of which was distilled to afford acetic acid (0.5 g, 8.3 mmol; bp 25—35 °C/22 Torr) and dibutyl disulfide (1.85 g, 10.4 mmol; bp 110—118 °C/22 Torr).

Reaction of Benzenethiol with $Tl(OAc)_3$. To a chloroform (15 ml) solution of benzenethiol (3.3 g, 30 mmol) we added several portions of solid thallium(III) acetate (3.81 g, 10 mmol) at 25 °C over a 10-min period. The temperature of the mixture rose to 30 °C during the addition, and a yellow solid of thallium(I) benzenethiolate was precipitated. After 1 h, the solid was filtered off [C_6H_5STl, 2.90 g, 9.3 mmol, 93% yield; mp 255—260 °C (lit,[6] mp 258—260 °C)] and the filtrate was concentrated to give diphenyl disulfide [2.18 g, 10 mmol, 100% yield; mp 59—60 °C (lit,[2] mp 59—61 °C)]. When benzenethiol (20 ml) was added, drop by drop, to a suspension of thallium(III) acetate (10 mmol) in chloroform (15 ml), diphenyl disulfide and thallium(I) acetate were obtained quantitatively. The further addition of the thiol in this case resulted in the formation of thallium(I) benzenethiolate instead of the acetate.

Reaction of Thiobenzoic S-*Acid with* $Tl(OAc)_3$. The addition of thallium(III) acetate (1.15 g, 3 mmol) to a chloroform (8 ml) solution of thiobenzoic *S*-acid (1.38 g, 10 mmol) at 20—25 °C readily afforded a yellow heterogeneous mixture. After 20 mins' stirring a yellow solid was filtered off and washed with ether. It was revealed to be thallium(III) thiobenzoate [1.55 g, 2.5 mmol, 84% yield; mp (decomp) 113—114 °C]. IR (hexachlorobutadiene and paraffin mulls), 3070 (w), 1660 (s), 1630 (m), 1590 (m), 1575(m), 1445 (m), *1310* (w), *1195* (s), *1170* (s), 1000 (w), 900 (s), 890 (s), 765 (m), and 675 (s) cm^{-1}. Found: C, 41.10; H, 2.51%. Calcd for $C_{21}H_{15}O_3S_3Tl$: C, 40.95; H, 2.45%. Dibenzoyl disulfide was not detected in the organic extract.

By heating thallium(III) thiobenzoate (0.61 g, 1 mmol) in CCl_4 (15 ml) under reflux for 3 h, dibenzoyl disulfide [0.24 g, 0.88 mmol, mp 125 °C (lit,[3] mp 125—127 °C)] and thallium(I) thiobenzoate (0.33 g, 0.97 mmol) were isolated. The latter thallium(I) salt was also prepared by the reaction of equimolar amounts of thallium(I) acetate and thiobenzoic acid in ethanol at room temperature for 2 h: mp (decomp) 200—202 °C; Found: C, 24.52; H, 1.30%. Calcd for C_7H_5OSTl: C, 24.60; H, 1.46%.

Reaction of Thioacetic S-*Acid with* $Tl(OAc)_3$. To a stirred chloroform (10 ml) solution of thioacetic *S*-acid (1.14 g, 15 mmol), we added several portions of solid thallium(III) acetate (1.90 g, 5 mmol) at 25—30 °C. The color of the mixture soon became bright yellow and then gradually changed to pale yellow. After 5 h, a pale yellow solid was filtered off. It was revealed to be thallium(I) thioacetate (1.35 g, 4.82 mmol, 96% yield; mp 76—78 °C). IR (hexachlorobutadiene and paraffin mulls), 1645 (s), 1638(s), 1565 (s), 1545 (sh), 1410 (w), 1348 (m), 1150 (w), 1130 (m), 1110 (s), 950 (m), and 865 (m) cm^{-1}. Found: C, 8.64; H, 1.21%. Calcd for C_2H_3OSTl: C, 8.60; H, 1.08%. The evaporation of chloroform from the organic filtrate left 0.4 g of a residue which was revealed by NMR to consist of almost pure diacetyl disulfide. The distillation of the residue, accompanied by a slight decomposition, gave diacetyl disulfide (0.2 g, 1.33 mmol, 27% yield; bp 40—65 °C/3 Torr), the NMR and IR spectra being identical with those of an authentic sample prepared by the oxidation with $Pb(OAc)_4$.[2]

Reaction of 2-Methyl-2-propanethiol with $Pb(OAc)_4$. The oxidation of 2-methyl-2-propanethiol (0.9 g, 10 mmol) with lead(IV) acetate [2.46 g (90% purity), 5 mmol] in chloroform (15 ml) was carried out at 25—30 °C for 5 h, as in the case with thallium(III) acetate. The lead(II) acetate thus formed (1.40 g, 4.31 mmol) was filtered off, and the subsequent GLC analysis of the filtrate revealed the presence of di-*t*-butyl disulfide (1.85 mmol, 37% yield) and *S*-*t*-butyl 2-methyl-2-propanethiosulfonate, *t*-$BuSO_2S$-*t*-Bu (2.50 mmol, 50% yield). Even when the reaction was stopped within 1 h, the yield of each compound was nearly the same to that described above. The reaction with PbO_2 in place of $Pb(OAc)_4$ was sluggish, and only disulfide was formed. Pure thiosulfonate was isolated by the distillation of the filtrate after the solvent had been removed. Thiosulfonate: bp 122 °C/35 Torr; NMR δ 1.37 (s); MS, (m/e) 210 (M^+); IR 1362 (s, ν_{as} SO_2), 1165 (s, ν_s SO_2); Found: C, 45.59; H, 8.92%. Calcd for $C_8H_{18}O_2S_2$: C, 45.68; H, 8.62%. Disulfide: NMR δ 1.30 (s); MS, (m/e) 178 (M^+).

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