96999-21-2; **7e**, 13169-74-9; **7f**, 96999-22-3; **7g**, 1003-29-8; **8** (R = Ph), 75400-63-4; **8** (R = $C_{15}H_{31}$), 96999-23-4; **9**, 35563-07-6; **10a**, 7126-41-2; **10b**, 96999-24-5; **10b** (*N*-phenylsulfonyl deriv), 96999-30-3; **11**, 13754-86-4; **12a**, 33234-57-0; **12b**, 97011-45-5; **13**, 13618-91-2; **14**, 75233-98-6; **15**, 93363-39-4; **16**, 75234-04-7; **17**, 96999-25-6; **18**, 22186-60-3; **19**, 96999-26-7; **20a**, 37496-06-3; **20b**, 93304-03-1; **21a**, 52293-26-2; **21b**, 86012-92-2; **22**, 16851-82-4; **23**, 96999-27-8; **24**, 96999-28-9; **25**, 96999-29-0; $NaBH_4$, 16940-66-2; $Me(CH_2)_{14}C(O)Cl$, 112-67-4; $PhCH_2C(O)Cl$, 103-80-0; 3,4-dimethoxybenzoyl chloride, 3535-37-3; *N*-(3,4-dimethoxybenzoyl)morpholine, 22792-13-8; 3,4-bis(benzyloxy)benzoyl chloride, 1486-54-0; *N*-[3,4-bis(benzyloxy)benzoyl]morpholine, 93363-32-7; 3,4-(methylenedioxy)benzoyl chloride, 25054-53-9; *N*-[3,4-(methylenedioxy)benzoyl]morpholine, 63916-59-6; pyrrole, 109-97-7; 2-pyrrolyloxalyl chloride, 3768-70-5.

**Supplementary Material Available:** Table of elemental analyses and high resolution mass spectra of pyrrole derivatives (1 page). Ordering information can be found on any current masthead page.

# [2,3]-Sigmatropic Rearrangement of an in Situ Prepared Ylide and a Thioether to Thio Ester Conversion as Key Steps in Short Syntheses of Sarkomycin and Its Phenylthio Ester

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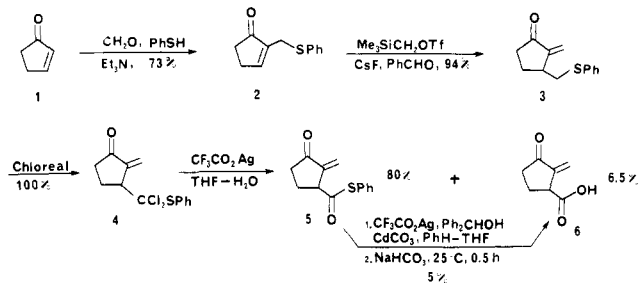
2-[(Phenylthio)methyl]cyclopent-2-en-1-one (**2**), which is readily available by the reaction of 2-cyclopentenone with thiophenol, formaldehyde, and triethylamine, is transformed, in high yield and moderate conversion by treatment with (trimethylsilyl)methyl triflate, cesium fluoride, and benzaldehyde, to 2-methylene-3-[(phenylthio)methyl]cyclopentanone (**3**), which, by the use of trichloroisocyanuric acid (Chloreal), can be quantitatively dichlorinated on the sulfur-bearing carbon atom to 3-[(phenylthio)dichloromethyl]-2-methylenecyclopentanone (**4**). This dichloro thioether could be hydrolyzed in good yield to a mixture of sarkomycin phenyl thio ester (**5**) and sarkomycin (**6**), containing mainly the former; an additional small amount of sarkomycin can be obtained by hydrolysis of the thio ester in the presence of silver trifluoroacetate and benzhydrol. This procedure represents one of the shortest extant syntheses of sarkomycin and a sarkomycin ester. Model studies of the dichlorination of *n*-octyl phenyl sulfide (**8**) to 1-(phenylthio)-1,1-dichlorooctane (**9**) and various transformations of the latter are also reported.

Our interest in the one-flask conversion of allylic phenyl thioethers to rearranged and homologated phenyl thioethers by means of the [2,3]-sigmatropic rearrangement of an in situ generated ylide[1] prompted us to attempt the synthesis of the antitumor antibiotic sarkomycin[2] (**6**) from 2-[(phenylthio)methyl]cyclopent-2-en-1-one (**2**)[3] (see Scheme I) which is readily available by a modification of the Petrow reaction[4] (see below). Although the carboxylic acid **6** is one of the simplest antitumor compounds known, the few syntheses[2,5,6] that were extant prior to 1984 are rather long, the shortest being at least eight steps, and the last step, the generation of the carboxylic acid itself, had proved troublesome.[5,7] The work reported by Thebtaranonth,[9] which largely overcomes these problems, appeared after the present work had been completed and prepared for submission.[10] We envisioned the dichlorination of **3** by the use of trichloroisocyanuric acid (Chloreal)[11] and the hopefully mild hydrolysis of **4** to sarkomycin (**6**).

**Scheme I**




When cyclopent-2-en-1-one (which is now available in one step from cyclopentene[12]) is treated with 1 molar equiv each of formaldehyde (as a 37% aqueous solution), thiophenol, and triethylamine in ethanol at 25 °C, a high yield of 3-(phenylthio)cyclopentanone, is produced in 2 h, but this material is gradually converted to **2**. The best yield

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0022-3263/85/1950-2965$01.50/0 

was obtained by heating at reflux an ethanol solution of equimolar quantities of reactants for 58 h, adding an additional 10 mol % of aqueous formaldehyde, heating for 24 h, adding an additional 10 mol % of formaldehyde, heating for an additional 28 concentrating, performing the usual water–ether workup, and distilling the concentrated organic extract.

As we suspected, treatment of **2** with diethylzinc and $CH_2I_2$[1] did not yield **3**. On the other hand, the ethylene ketal of **2**[13] could be converted by this treatment to the ketal of **3**; however, deprotection of the ketone function could not be successfully executed presumably because of the considerable sensitivity of the $\alpha$-methylene ketone group of the product to acid. Finally, it was found that the requisite methylide of **2** could be generated by the elegant procedure of Vedejs[15] involving treatment of **2**, in acetonitrile, with 3 molar equiv of (trimethylsilyl)methyl triflate[16] and desilylating the resulting sulfonium salt with 3 equiv of cesium fluoride. We have found that good yields of **3** could be obtained if the fluoride was present along with the alkylating agent as long as benzaldehyde was also present in order to demethylenate **7**, the ylide of **3**, which was presumably also produced (Scheme II). However, somewhat better yields were obtained by adding the cesium fluoride after the 2-h alkylation period and stirring for an additional 1 h at 25 °C; the presence of benzaldehyde was still found to be beneficial during the desilylation. In this way a 94% yield of **3** was produced based on the 57% of **2** consumed; larger quantities of reagents led to decreased yields.

Model studies of the chlorination step showed that *n*-octyl phenyl sulfide (**8**) could be dichlorinated cleanly with an excess of Chloreal[11] to produce 1-(phenylthio)-1,1-dichlorooctane (**9**) (NCS only gave monochlorination product). This model geminal dichloride readily lost HCl to yield 1-(phenylthio)-1-chloro-1-octene (**10**) when it was added to aqueous carbonate or merely chloroform; however, it was hydrolyzed largely to the thio ester phenyl octanethioate (**11**) upon treatment with acetone–water

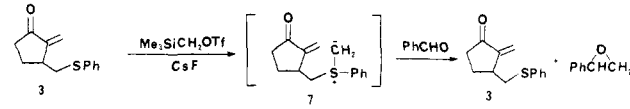
$$\underset{8}{HexCH_2CH_2SPh} \xrightarrow{\text{Chloreal}} \underset{9}{HexCH_2CCl_2SPh}$$

$$9 \xrightarrow[CO_3^{-2}(aq)]{CHCl_3 \text{ or}} \underset{10}{PentCH{=}CClSPh}$$

$$9 \xrightarrow[HCO_3^-]{\text{acetone-water}} \underset{11}{HexCH_2COSPh}$$

containing sodium bicarbonate. Although methods for the hydrolysis of the model thio ester (**11**) were not extensively investigated, it was found that hydrolysis to octanoic acid occurred in 74% yield upon treatment with barium hydroxide. The types of easily executed transformations exemplified by the conversions of **8** to **10** and **11** are of considerable potential synthetic value and are worthy of closer experimental scrutiny. A related study, which appeared after the model studies reported here were largely complete, reports a similar dichlorination using sulfuryl chloride in the presence of pyridine; in that report, chloroalkenes such as **10** were produced by performing the chlorinations at reflux and these chloroalkenes could be converted to carboxylic acids by hydrolysis at an elevated temperature with mercuric acetate and formic acid.[17]

**Scheme II**




Treatment of **3** with excess (2 mol) Chloreal at 5 °C for 20 h in $CCl_4$ followed by filtration cleanly produced the unstable dichloro compound **4**, the decomposition of which could be somewhat retarded by the presence of the radical inhibitor 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide. As expected, **4** (without purification) could be hydrolyzed readily to the thio ester **5** by treatment with acetone–water (3:2) containing sodium bicarbonate. Not surprisingly, attempts at traditional acid- and base-induced hydrolysis, including the barium hydroxide method which was used in the model system, were unsuccessful when applied to **5**. Since it has been shown that phenyl thio esters undergo *alcoholysis* under mild conditions in the presence of silver, cuprous, or mercuric salts,[18] a number of attempts were made to *hydrolyze* the thio ester **5** and its precursor **4** under such conditions; it should be noted that cuprous triflate could not be used in aqueous solution because of its ready disproportionation. Whereas in the case of the model thio ester **11**, it was found that benzhydrol could be used successfully as a surrogate for water, the ester solvolyzing upon workup to produce the acid, this procedure was only marginally successful in the case of **5**. The best conditions found involved the hydrolysis of **4** in the presence of silver trifluoroacetate in water–THF for 2 h at 25 °C; this procedure yielded 80% of the thio ester **5** and 6.5% of sarkomycin (**6**) (isolated by bicarbonate extraction, acidification, and chloroform extraction). The great sensitivity of **5** and **6** to rearrangement precluded a high-yield hydrolysis to sarkomycin; for example, treatment of the thio ester with ammonia in order to generate the lactam, which should be converted under mild nitrosation conditions to sarkomycin (**6**), caused a prototropic rearrangement resulting in a shift of the double bond to the endo position. The best yield of sarkomycin (**6**) from the thio ester **5** was 5% obtained by treatment with silver trifluoroacetate in the presence of cadmium carbonate and benzhydrol. Although the total yield (10.5%) of sarkomycin from the chlorination product **4** is unimpressive, the preparation of **4** is so brief and proceeds in such high yield that the overall yield of the acid (7.2%) from cyclopentenone compares favorably with all previous syntheses except the very latest[9] and the synthesis of the thio ester **5** is far more efficient than any of the previous syntheses[6] of esters of sarkomycin. There are two notable features of this synthesis which may be of general utility: (1) the one-flask transformation of an allylic thioether in which the olefinic component is conjugated with a ketone into a homologous enone in which the thioether group is homoallylic, which is successful even though the product is a sensitive $\alpha$-methylenecyclopentanone; (2) the highly efficient conversion of the $CH_2SPh$ group to a thio ester or, as shown in the model system, to a potentially useful 1-chloro-1-(phenylthio)alkene or a carboxylic acid.

## Experimental Section

Flash chromatography[19] was performed with 40–63-$\mu$m silica gel 60 (E. Merck). Thin-layer chromatogram (TLC) was performed on glass-supported silica gel 60 plates (0.25-mm layer,

(13) This compound was prepared from the ethylene ketal of 2-(hydroxymethyl)cyclopent-2-en-1-one[14] by sequential treatment with butyllithium, tosyl chloride, and sodium thiophenoxide.
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F-254, E. Merck). Proton NMR spectra were determined in $CDCl_3$ (unless otherwise stated) using $Me_4Si$ as an internal standard.

**2-[(Phenylthio)methyl]cyclopent-2-en-1-one (2).** A solution of cyclopent-2-en-1-one (**1**, 5.58 g, 71.3 mmol), triethylamine (9.95 mL, 71.5 mmol), 37% aqueous formaldehyde solution (5.79 g, 71.3 mmol), and benzenethiol (7.33 mL, 71.4 mmol) in 245 mL of absolute ethanol was heated at reflux for 58 h. To the cooled solution was added 0.58 g of 37% aqueous formaldehyde. Refluxing was continued for another 24 h. Additional formaldehyde (0.58 g) was added and the solution was heated for additional 28 h. The cooled solution was concentrated in vacuo to remove ethanol. The residue was partitioned between ether and water. The aqueous layer was extracted with ether. All etheral layers were combined, washed with 5% aqueous sodium hydroxide to remove benzenethiol and then with water and brine, and dried over anhydrous magnesium sulfate. Fractional distillation of the concentrated residue yielded 10.6 g (73%) of 2-[(phenylthio)-methyl]cyclopent-2-en-1-one (**2**): bp 145–150 °C (0.8 mm); $^1H$ NMR $\delta$ 2.42–2.48 (m, 2 H), 2.53–2.56 (m, 2 H), 3.68 (d, $J$ = 1.21 Hz, 2 H, $CH_2SPh$), 7.17–7.51 (m, 6 H, Ph and vinyl); IR (neat) 1702 (CO), 1635 (C=C) $cm^{-1}$; mass spectrum (15 eV), $m/e$ 204 ($M^+$, 100%), 110 ($PhSH^+$, 9%), 95 ($M^+ - PhS$, 4%); exact mass calcd for $C_{12}H_{12}OS$ 204.0609, found 204.0608.

**3-[(Phenylthio)methyl]-2-methylenecyclopentan-1-one (3).** To a solution of sulfide **2** (4.1 g, 20 mmol) in 300 mL of dry acetonitrile was added (trimethylsilyl)methyl triflate[14] (14.2 g, 60 mmol) at room temperature under argon. The resulting solution was stirred for 2 h before the addition of cesium fluoride (9.1 g, 60 mmol) and benzaldehyde (6.1 mL, 60 mmol). The mixture was stirred for another 1 h and quenched with water. The residue from concentration was partitioned between ether and saturated aqueous sodium bisulfite solution. The etheral layer was washed throughly with the latter to remove benzaldehyde completely. All aqueous layers were combined and extracted with ether. All organic extracts were washed with water and brine and were dried over anhydrous magnesium sulfate. Flash chromatography of the concentrated residue yielded 2.34 g (53.8%) of the rearranged sulfide **3** and 1.76 g (43%) of the starting sulfide **2**. **3**: $^1H$ NMR $\delta$ 1.60–1.80 (m, 1 H), 2.20–2.40 (m, 3 H), 2.95–2.98 (m, 2 H, allylic and $CH_2SPh$), 3.28–3.30 (m, 1 H, $CH_2SPh$) 5.44 (d, $J$ = 1.62 Hz, 1 H, OCC=$CH_2$ (trans)), 6.10 (d, $J$ = 2.22 Hz, 1 H, OCC=$CH_2$ (cis)), 7.20–7.40 (m, 5 H, Ph); IR ($CCl_4$) 1725 (CO), 1636 (C=C) $cm^{-1}$; mass spectrum, $m/e$ 218 ($M^+$, 38%), 123 ($PhSCH_2^+$, 100%), 109 ($PhS^+$ or M – SPh, 35%); exact mass calcd for $C_{13}H_{14}OS$ 218.0765, found 218.0765.

**Preparation and Reactions of 1,1-Dichloro-1-(phenylthio)octane (9).** To a solution of *n*-octyl phenyl sulfide (**8**) (445 mg, 2.00 mmol) in carbon tetrachloride (20 mL) was added trichloroisocyanuric acid (930 mg, 4.00 mmol). The resulting mixture was stirred, under argon, at 5 °C for 20 h in the dark. The solid was removed by filtration and the filtrate was concentrated to provide the dichloro sulfide **9** which was subjected to further reaction without purification. Dichloro sulfide **9**: $^1H$ NMR ($C_6D_6$) $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.05–1.23 (m, 8 H), 1.76–1.86 (m, 2 H), 2.38–2.43 (m, 2 H, $CH_2CCl_2SPh$), 7.02–7.16 (m, 3 H, Ph), 7.69–7.72 (m, 2 H, Ph).

The dichloro sulfide **9** was treated with a cold mixture of acetone (3 mL) and water (2 mL) containing sodium bicarbonate (504 mg, 6.00 mmol). After being stirred at 25 °C for 0.5 h, the mixture was concentrated in vacuo to remove acetone. The remaining aqueous layer was extracted with benzene. Column chromatography of the dried and concentrated extracts gave phenylthio octanoate (**11**) and 1-chloro-1-(phenylthio)-1-octene (**10**, mixture of *E* and *Z* isomers) in 57% and 32% yield, respectively. Phenylthio octanoate (**11**): $^1H$ NMR $\delta$ 0.89 (br t, $J$ = 7 Hz, 3 H), 1.22–1.40 (m, 8 H), 1.67–1.78 (m, 2 H), 2.65 (t, $J$ = 7.4 Hz, 2 H, $CH_2CO$), 7.41 (s, 5 H, Ph); IR (neat) 1681 (CO) $cm^{-1}$; mass spectrum (15 eV), $m/e$ 236 ($M^+$, 14%), 127 ($M^+ - PhS$, 100%) exact mass calcd for $C_{14}H_{20}OS$ 236.1235, found 236.1235. 1-Chloro-1-(phenylthio)-1-octene (**10**): $^1H$ NMR $\delta$ 0.86–0.92 (m, 3 H), 1.23–1.49 (m, 8 H), 2.29 (q, $J$ = 7.28 Hz), 2.37 (q, $J$ = 7.28 Hz, total 2 H for the latter two peaks, allylic), 6.30 (t, $J$ = 7.68 Hz), 6.31 (t, $J$ = 7.28 Hz, total 1 H for the latter two peaks, vinyl), 7.26–7.41 (m, 5 H, Ph); IR (neat) 1584 (C=C) $cm^{-1}$; mass spectrum (15 eV), $m/e$ 254 ($M^+$, 73%), 219 ($M^+ - Cl$, 9%), 110 ($PhSH^+$, 100%), 109 ($PhS^+$, 64%); exact mass calcd for $C_{14}H_{19}ClS$ 254.0896, found 254.0896.

When the dichloro sulfide **9** was treated with methanol–water (2:1) or THF–water (2:1) in the presence of sodium carbonate at 5 °C for 0.5 h or simply allowed to sand in chloroform at 25 °C, elimination product **10** was obtained in almost quantitative yield.

**Hydrolysis of Phenyl Octanethioate (11).** To a solution of phenyl thio ester **11** (118 mg, 0.50 mmol) in 10 mL of THF–benzene (1:1) was added benzhydrol (92 mg, 0.50 mmol), silver trifluoroacetate (331 mg, 1.50 mmol), and cadmium carbonate (517 mg, 3.00 mmol). The mixture was stirred at 25 °C for 5 h and then filtered. The concentrated filtrate was dissolved in dry ether (10 mL) and then filtered again. Sodium bicarbonate (504 mg in 4 mL of water, 6.0 mmol) was added to the etheral filtrate and the mixture was stirred for 0.5 h at 25 °C. The aqueous layer was acidified with concentrated hydrochloric acid and was extracted with chloroform; the extract was concentrated to provide 33 mg (46%) of octanoic acid. No optimization experiments were performed.

In another experiment, thio ester **11** (118 mg, 0.50 mmol) was treated with barium hydroxide hydrate (946 mg, 3.00 mmol) and methyl iodide (142 mg, 3.00 mmol) in 10 mL of THF–water (4:1) at 0 °C for 2 h. The concentrated filtrate was partitioned between benzene and water. The aqueous layer was acidified and extracted with chloroform; concentration of the extract yielded 50 mg (69%) of octanoic acid. The concentrated benzene fraction provided a solid precipitate which was dissolved in water and acidified. Chloroform extraction of the resulting aqueous layer gave 3.8 mg of octanoic acid. The total yield for this hydrolysis was 74%.

**3-[[(Dichlorophenyl)thio]methyl]-2-methylene-1-cyclopentanone (4).** To a solution of sulfide **3** (109 mg, 0.50 mmol) in 10 mL of carbon tetrachloride was added trichloroisocyanuric acid (232 mg, 1.00 mmol). The mixture was stirred at 5 °C, under argon, in the dark for 20 h. The reaction mixture was filtered and the filtrate was concentrated at 0 °C to give an unstable, spectroscopically pure compound **4** in quantitative yield without purification. **4**: $^1H$ NMR $\delta$ 2.30–2.70 (m, 4 H), 3.72–3.76 (m, 1 H, $CHCCl_2SPh$), 6.10 (dd, $J$ = 2.0, 0.8 Hz, 1 H, OCC=$CH_2$ (trans)), 6.44 (dd, $J$ = 2.3, 0.8 Hz, 1 H, OCC=$CH_2$ (cis)), 7.40–7.60 (m, 3 H, Ph) 7.70–7.80 (m, 2 H, Ph); IR ($CCl_4$) 1755 (CO), 1630 (C=C) $cm^{-1}$.

**Hydrolysis of Dichloro Sulfide 4.** The dichloro sulfide **4** obtained as above was dissolved in a mixture of water (2 mL) and THF (8 mL) containing 3.6 mg (0.010 mmol) of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide as a radical inhibitor. Silver trifluoroacetate (331 mg, 1.50 mmol) was added to this solution with vigorous stirring. Stirring was continued for 2 h at 25 °C and the mixture was concentrated in vacuo to remove THF. The residue was shaken vigorously with a mixture of benzene (10 mL) and 2 mL of aqueous potassium bicarbonate (300 mg, 3.00 mmol) solution in the presence of hydroquinone (1.1 mg, 0.005 mmol). After filtration, the aqueous layer was acidified with concentrated hydrochloric acid. The aqueous layer was then extracted with chloroform (5 × 2 mL + 1 × 5 mL) to which 3.6 mg (0.010 mmol) of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide was added. The dried and concentrated residue which contained a trace of sarkomycin phenyl thio ester (**5**) was subjected to NMR measurement. The yield of sarcomycin (**6**) was determined to be 6.5% by integration of the ratio of the peak at 6.24 (cis methylene proton) of **6** to the hydroxyl peak of the radical inhibitor. Sarkomycin (**6**): $^1H$ NMR $\delta$ 2.20–2.60 (m, 4 H), 3.76–3.86 (m, 1 H, allylic), 5.71 (d, $J$ = 2.43 Hz, 1 H, OCC=$CH_2$ (trans)), 6.24 (d, $J$ = 2.63 Hz, 1 H, OCC=$CH_2$ (cis)). The spectrum matches the published one.[2]

The benzene layer obtained as above was dried and concentrated to give spectroscopically pure sarkomycin phenyl thio ester (**5**) in 80% yield. **5**: $^1H$ NMR $\delta$ 2.20–2.66 (m, 4 H), 4.02–4.06 (m, 1 H, $CHCOSPh$), 5.76 (d, $J$ = 2.02 Hz, 1 H, OCC=$CH_2$ (trans)), 6.29 (d, $J$ = 2.22 Hz, 1 H, OCC=$CH_2$ (cis)), 7.44–7.76 (m, 5 H, Ph); IR ($CCl_4$) 1734, 1705 (CO), 1638 (C=C) $cm^{-1}$; mass spectrum (15 eV), $m/e$ 232 ($M^+$, 15%), 204 ($M^+ - CO$, 100%), 123 ($M^+ - PhS$, 78%), 122 ($M^+ - PhSH$, 30%), 95 ($M^+ - COSPh$, 76%), 110 ($HSPh^+$, 25%), 109 ($PhS^+$, 9%); exact mass calcd for $C_{13}H_{12}O_2S$ 232.0558, found 232.0560. This compound was also characterized as its 1,4-adduct with thiophenol.

The phenyl thio ester **5** could also be obtained by the following procedure. The dichloro compound **4** prepared by the same procedure as above from 0.50 mmol of sulfide **3** was treated with a mixture of acetone (12 mL) and water (8 mL) in the presence

of sodium bicarbonate (252 mg, 3.00 mmol) at 0 °C for 0.5 h. Acetone was evaporated in vacuo and the remaining aqueous portion was extracted with ether. All ethereal extracts were combined and washed with water and brine and were concentrated to provide the phenyl thio ester **5** in 64% yield.

**Hydrolysis of Sarkomycin Phenyl Thio Ester (5).** The phenylthio ester obtained by acetone–water–bicarbonate hydrolysis of the dichloro compound **4** prepared from 0.50 mmol of sulfide **3** was dissolved in a solution of benzene (5 mL) and THF (5 mL) and treated with silver trifluoroacetate (331 mg, 1.50 mmol), cadmium carbonate (517 mg, 6.00 mmol), and benzhydrol (92 mg, 0.50 mmol). The mixture was stirred at 25 °C for 24 h and filtered, the filtrate was dissolved in carbon tetrachloride, and the resulting solution was filtered again. To an ethereal solution of the concentrated filtrate was added an aqueous solution containing 504 mg (6.00 mmol) of sodium bicarbonate and a small amount of hydroquinone. The mixture was stirred at 25 °C for 0.5 h. The separated aqueous layer was acidified with hydrochloric acid and extracted with chloroform (15 mL + 3 × 5 mL) to which 3.6 mg of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide had been added. The overall yield of sarkomycin (**6**) from the concentrated extracts was 3% from the sulfide **3**; since the yield of thio ester starting from **3** and using the water–acetone–bicarbonate method is 64%, it follows that the yield of sarcomycin (**6**) starting from the thioester **5** is 5%.

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# The Equilibrium between an Areneselenenic Acid and Its Anhydride[1]

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The equilibrium constants ($K_{eq}$ = [ArSeOH]$^2$/[$H_2O$][ArSeOSeAr]) associated with the equilibrium (eq 1) between *o*-nitro- and *o*-benzoylbenzeneselenenic anhydrides (**2a** and **2b**) and the corresponding selenenic acids (**1a** and **1b**) have been determined in dioxane containing 0.25–1.5% water. For the **2b**–**1b** equilibrium, $K_{eq}$ = 0.16 (25 °C) and $\Delta H°$ = +0.6 kcal/mol. The equilibrium constant for the **2a**–**1a** system is ~10 times larger. That $\Delta H°$ for the hydrolysis of **2b** is slightly *endothermic* contrasts sharply with the exothermic nature of the hydrolysis of most common acid anhydrides. The values of $K_{eq}$ for both **2b** and **2a** are such that conditions can easily be encountered in media of low water content, where a significant fraction of the selenenic anhydride will remain unhydrolyzed at equilibrium, a situation without precedent in the chemistry of typical acid anhydrides.

Previous research[2] has shown that the compounds thought by Rheinboldt and Giesbrecht[3] to be *o*-nitro- and *o*-benzoylbenzeneselenenic acids (**1a** and **1b**) are, in actuality, the corresponding selenenic anhydrides (**2a** and **2b**).

$$\underset{\textbf{2a},\ Ar = o\text{-}O_2NC_6H_4}{ArSeOSeAr} + H_2O \overset{H^+}{\rightleftharpoons} \underset{\textbf{1a},\ Ar = o\text{-}O_2NC_6H_4}{2ArSeOH} \quad (1)$$

**2b**, Ar = *o*-$PhC(O)C_6H_4$ **1b**, Ar = *o*-$PhC(O)C_6H_4$

In aqueous organic solvents these selenenic anhydrides undergo acid-catalyzed hydrolysis (eq 1) to afford stable solutions of the selenenic acids.[2] In the absence of water, however, **1a** and **1b** revert readily to anhydrides **2a** and **2b**,[2a] indicating the easily reversible nature of the equilibrium between **2** and **1**.

Since most areneselenenic acids, such as PhSeOH, are quite unstable and disproportionate (3PhSeOH → PhSeSePh + $PhSeO_2H$ + $H_2O$) so readily as to preclude any quantitative investigation of the equilibrium between acid and selenenic anhydride, the **1a**–**2a** and **1b**–**2b** systems offer a unique opportunity to probe the details of the equilibrium between an areneselenenic acid and the corresponding anhydride.

The kinetics and mechanisms of the acid-catalyzed hydrolyses of **2a** and **2b** in 60% aqueous dioxane were explored earlier.[2b] The objective of the present work was to determine the equilibrium constants and the enthalpy of reaction associated with the equilibria shown in eq 1 and to compare them, where possible, with equivalent data for other anhydride–acid equilibria.

Most measurements of $K_{eq}$ for eq 1 were done by starting with the selenenic anhydride and allowing the system to proceed to equilibrium. Some, however, were done by starting from a solution of the selenenic acid, the latter being prepared by allowing a sample of the appropriate ethyl aryl selenoxide (**3**) to undergo fragmentation[4] into ethylene and the selenenic acid (eq 2). In connection with

$$ArSe(O)CH_2CH_3 \rightarrow ArSeOH + CH_2{=}CH_2 \quad (2)$$

**3a**, Ar = *o*-$O_2NC_6H_4$ **1a**
**3b**, Ar = *o*-$PhC(O)C_6H_4$ **1b**

this aspect of the work the kinetics of the decomposition of both **3a** and **3b** were measured over a range of temperatures in dioxane as solvent. The results and the ac-

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