# Aminomercuration-Demercuration of Divinyl Sulfone: Synthesis of 4-Aryltetrahydro-1,4-thiazine 1,1-Dioxides

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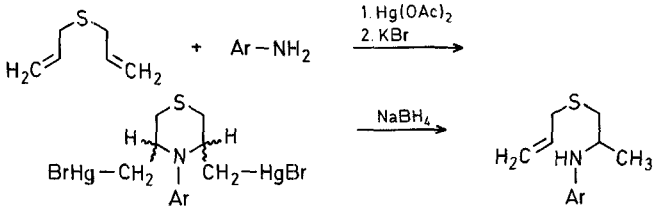
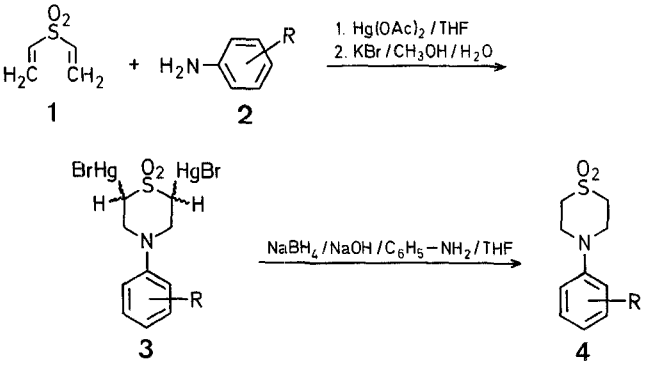
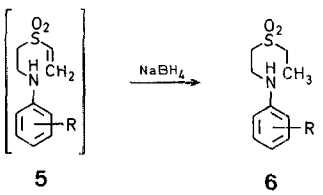
The solvomercuration-demercuration reaction is the most important synthetic method using organomercury compounds as intermediates[1]. In particular, the aminomercuration-demercuration process has been shown to be a convenient procedure for the synthesis of bifunctional aminated compounds[2] and saturated *N*-heterocycles[3]. Thus, mercurated substituted tetrahydro-1,4-thiazines can be obtained from diallyl sulfide but the corresponding mercury-free heterocycles have never been obtained by reduction. Instead, allyl 2-arylaminoalkyl sulfides are generated resulting from a single deaminomercuration reaction[4].




In connection with these results, we report here the preparation by this method of tetrahydro-1,4-thiazine derivatives from commercially available divinyl sulfone. When divinyl sulfone (**1**) is allowed to react with primary aromatic amines[5] (**2**) in the presence of mercury(II) acetate, followed by anion exchange with potassium bromide, 4-aryl-2,6-bis[bromomercurio]-tetrahydro-1,4-thiazine 1,1-dioxides (**3**) are obtained[6]. Sodium borohydride reduction of the mercurated heterocycles **3** in aqueous basic media using aniline and tetrahydrofuran as co-solvents leads to the expected 4-aryltetrahydro-1,4-thiazine 1,1-dioxides (**4**) via mercury/hydrogen exchange.




The reaction products **4** are contaminated (< 15% according to $^1$H-N.M.R. analysis) with ethyl 2-arylaminoethylsulfones (**6**) resulting from mono-deaminomercuration of **3** and reduction of the intermediate **5**.




*The substituted tetrahydro-1,4-thiazine 1,1-dioxides* **4** *thus* obtained can be reduced to 4-aryltetrahydro-1,4-thiazines by means of lithium alanate[7] or diisobutylaluminum hydride[8]; the 4-aryltetrahydro-1,4-thiazines are of potential physiological activity[9].

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**Table 1.** ,6-Bis[bromomercurio]-4-aryltetrahydro-1,4-thiazine 1,1-Dioxides (**3**)

| 3 | R | Reaction time | Yield[a] [%] | m.p. (dec.)[b] [°C] | Molecular formula[c] | | I.R. (nujol) [cm$^{-1}$][d] $\nu_{SO_2}$ | $\nu_{arom}$ |
|---|---|---|---|---|---|---|---|---|
| **a** | H | 8 h | 88 | 98–100° | $C_{10}H_{11}Br_2Hg_2NO_2S$ | (770.3) | 1290, 1120 | 3020, 1600, 1500, 760, 700 |
| **b** | 2-H C | 42 h | 79 | 138–140° | $C_{11}H_{13}Br_2Hg_2NO_2S$ | (784.3) | 1300, 1110 | 3020, 1600, 1580, 1510, 760 |
| **c** | 3-H C | 9 h | 84 | 105–107° | $C_{11}H_{13}Br_2Hg_2NO_2S$ | (784.3) | 1280, 1110 | 3020, 1600, 1580, 1500, 780, 700 |
| **d** | 4-H C | 21 h | 82 | 130–132° | $C_{11}H_{13}Br_2Hg_2NO_2S$ | (784.3) | 1280, 1110 | 3020, 1620, 1610, 1510, 820 |
| **e** | 4-H CO | 8 h | 72 | 125–127° | $C_{11}H_{13}Br_2Hg_2NO_3S$ | (800.3) | 1280, 1120 | 3020, 1610, 1510, 1500, 830 |
| **f** | 2-Cl | 13 h | 76 | 122–124° | $C_{10}H_{10}Br_2ClHg_2NO_2S$ | (804.7) | 1290, 1120 | 3020, 1600, 1590, 1510, 760 |
| **g** | 4-Cl | 20 h | 78 | 68–70° | $C_{10}H_{10}Br_2ClHg_2NO_2S$ | (804.7) | 1290, 1120 | 3020, 1600, 1570, 1500, 820 |

[a] Based o sulfone **1**.
[b] Uncorre ted; compounds **3** could not be recrystallized.
[c] The microanalyses were in satisfactory agreement with the calculated values: H, ±0.36; N, ±0.09.
[d] Recorded on a Pye-Unicam SP-1000 spectrometer.

**Table 2.** 4 Aryltetrahydro-1,4-thiazine 1,1-dioxides (**4**)

| 4 | R | Reaction time [h] | Yield [%] of | | m.p.[b] [°C] (solvent) | Molecular formula[c] or Lit. m.p. [°C] | |
|---|---|---|---|---|---|---|---|
| | | | **4**[a] | Hg(0)[a] | | | |
| **a** | H | 21 | 64 | 79 | 122–123° (ether/THF) | 123.5°[10] | |
| **b** | 2-$H_3C$ | 13 | 31 | 82 | 129–131° ($CCl_4$) | $C_{11}H_{15}NO_2S$ | (225.3) |
| **c** | 3-$H_3C$ | 24 | 59 | 74 | 69–71° ($CCl_4$) | $C_{11}H_{15}NO_2S$ | (225.3) |
| **d** | 4-$H_3C$ | 14 | 73 | 87 | 130–132° ($CCl_4$) | $C_{11}H_{15}NO_2S$ | (225.3) |
| **e** | 4-$H_3CO$ | 6 | 63 | 89 | 128–129° ($CCl_4$) | $C_{11}H_{15}NO_3S$ | (241.3) |
| **f** | 2-Cl | 8 | 66 | 63 | 110–112° ($CCl_4$) | $C_{10}H_{12}ClNO_2S$ | (245.7) |
| **g** | 4-Cl | 24 | 35 | 64 | 140–142° ($CCl_4$) | $C_{10}H_{12}ClNO_2S$ | (245.7) |

[a] Based o starting organomercury compound **3**.
[b] Uncorre ted.
[c] The mic analyses were in satisfactory agreement with the calculated values: C, ±0.33; H, ±0.10; N, ±0.10.

**Table 3.** S ectral Data of Compounds **4**

| 4 | I.R. ( ujol) [cm$^{-1}$][a] | | $^1$H-N.M.R. ($CDCl_3$/$TMS_{int}$) $\delta$ [ppm][b] | | | | $^{13}$C-N.M.R. ($CDCl_3$/$TMS_{int}$) $\delta$ [ppm][b] | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\nu_{SO_2}$ | $\nu_{arom}$ | $CH_2N$ | $CH_2S$ | Ar | other | $CH_2N$ | $CH_2S$ | Ar | other |
| **a** | 1300<br>1130 | 3040, 1600, 1580, 1500, 770, 700 | 3.2 (m) | 3.9 (m) | 6.6–7.6 (m)[c] | — | 47.5 (t) | 50.4 (t) | 116.2, 120.6, 129.5, 147.6 | — |
| **b** | 1300<br>1120 | 3040, 1590, 1570, 1490, 770 | 3.15 (m) | 3.4 (m) | 7.1 (m) | 2.3 (s) | 50.4 (t) | 52.4 (t) | 120.1, 124.5, 126.6, 131.0, 132.4, 150.0 | 17.5 (q) |
| **c** | 1310<br>1120 | 3030, 1600, 1580, 1510, 780, 700 | 3.1 (m) | 3.8 (m) | 6.4–7.4 (m) | 2.4 (s)[c] | 46.7 (t) | 49.7 (t) | 112.6, 116.3, 120.6, 128.7, 138.6, 147.0 | 21.0 (q) |
| **d** | 1310<br>1130 | 3020, 1610, 1580, 1510, 820 | 3.2 (m) | 3.9 (m) | 6.9–7.5 (m) | 2.45 (s)[c] | 48.1 (t) | 50.5 (t) | 116.7, 130.0, 130.4, 145.6 | 20.2 (q) |
| **e** | 1310<br>1130 | 3020, 1600, 1570, 1510, 820 | 3.1 (m) | 3.65 (m) | 6.8 (s) | 3.7 (s) | 49.3 (t) | 50.8 (t) | 114.7, 119.2, 142.5, 154.6 | 55.4 (q) |
| **f** | 1310<br>1120 | 3020, 1590, 1500, 770 | 3.2 (m) | 3.5 (m) | 7.2 (m) | — | 49.9 (t) | 52.1 (t) | 121.4, 124.9, 127.5, 130.2, 130.5, 148.1 | —[d] |
| **g** | 1310<br>1130 | 3010, 1590, 1570, 1500, 830 | 3.1 (m) | 3.8 (m) | 6.7–7.4 (m) | — | 47.6 (t) | 50.3 (t) | 117.6, 128.8, 129.4, 146.3 | — |

[a] Recorde with a Pye-Unicam SP-1000 I.R. spectrometer.
[b] Recorde with a Varian CFT-80 spectrometer.
[c] TMS capillary.
[d] $CCl_4/D_2O$ capillary.

**2,6-Bis[bro omercurio]-4-phenyltetrahydro-1,4-thiazine 1,1-Dioxide (3a); Typic l Procedure:**

To a well s irred solution of divinyl sulfone (**1**; 1.2 g, 10 mmol; Aldrich) and niline (10.0 ml, ~100 mmol) in tetrahydrofuran (50 ml), mercury(II acetate (6.4 g, 20 mmol) is added. After 8 h, the solvent and the exc ss of amine are removed under reduced pressure (15 and then 0.001 orr), the resultant oil is dissolved in methanol (100 ml) and the produc then precipitated by the addition of a solution of potassium brom de (3.0 g, ~25 mmol) in water (20 ml); yield: 6.8 g (88%), pink powd r; m.p. 98–100°C (dec.).

| $C_{10}H_{11}Br_2Hg_2NO_2S$ | calc. | N 1.82 | Hg 52.08 |
|---|---|---|---|
| (770.3) | found | 1.84 | 52.30 |

**4-Phenyltet ahydro-1,4-thiazine 1,1-Dioxide (4a); Typical Procedure:**

2,6-Bis[bro omercurio]-4-phenyltetrahydro-1,4-thiazine 1,1-dioxide (**3a**; 6.2 g, 8 mmol) is suspended in tetrahydrofuran (50 ml) + aniline (10 ml) + 0.5 normal aqueous sodium hydroxide (50 ml). Then, a solution of sodium borohydride (0.38 g, 10 mmol) in 2.5 normal aqueous sodium hydroxide (10 ml) is added with stirring. After 21 h, the mixture is extracted with ether (2×50 ml), the organic layer is washed with water (50 ml), and dried with sodium sulfate. The solvent is removed in vacuo and the residue is distilled at 0.001 torr and recrystallized; yield: 1.1 g (64%); m.p. 122–123°C (from THF/ether 1:1); yellow crystals.

| $C_{10}H_{13}NO_2S$ | calc. | C 56.85 | H 6.20 | N 6.63 |
|---|---|---|---|---|
| (211.3) | found | 56.57 | 6.11 | 6.55 |

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