



## Synthesis of novel mercury heterocycles

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Dedicated to my Teacher Late Dr. (Smt.)

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### ABSTRACT

*Ortho*-mercurated 4-aryloxymethylcoumarins and 1-azacoumarins have been found to undergo smooth intramolecular metalation in refluxing xylene in the presence of activated neutral alumina and anhydrous potassium carbonate. This is the first report on the synthesis of heterocycles not possessing a metal heteroatom linkage.

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### 1. Introduction

Organic compounds in which the aromatic hydrogens have been replaced by main group metal substituents represent a rare class of molecules [1]. Organomercurials have attracted much attention from the view point of their specific reactivity, attributed to the electropositive character of Hg.

Coumarins and 1-azacoumarins are a pair of isosteric heterocyclic systems, the derivatives of which have exhibited wide ranging biological properties [2]. Earlier work on chloro and acetoxy mercuriation of coumarins has shown that mercuriation was found to occur preferentially at the C-6 and C-8 positions [3]. Subsequently mercurated 3-4'-thiazolylcoumarins were reported for their fungicidal activity [4]. In recent years there has been a growing interest in the application of organomercurials in organic synthesis involving the synthesis of amino acids [5], austamide [6], oxyphenelations [7] and intramolecular annulation of carboxylic acids to triple bonds [8]. In all these reactions mercury is not retained in the final compound but they result in a C–C bond formation *via* halo/acetoxy demercuriation.

4-Aryloxymethylcoumarins and 1-azacoumarins have been of both biological [9,10] and structural interest [11]. Reactivity of *o*-substituted 4-aryloxymethylcoumarins has been explored to synthesize biologically active 4-2'-benzo[b]furanyl coumarins [12], oxygenated triheterocycles [13] and fused polycyclic coumarins [14]. In light of the above observations and paucity

of literature on heterocyclic systems containing mercury it was thought to be of immense interest to study the reactivity of 4-aryloxymethylcoumarins and 1-azacoumarins possessing *o*-halo/acetoxymercury substituents. The present investigation reports probably the first intramolecular mercuriation at the C-3 position on coumarins and 1-azacoumarins leading to a new class of mercury heterocycles.

### 2. Experimental

#### 2.1. Materials and methods

Reactions were performed in oven-dried glassware under nitrogen atmosphere containing a Teflon coated stir bar and dry septum. Butanone was dried over calcium chloride and dry distilled before use. Xylene was dried over Na pressed wire and dry distilled before use. Mercuric acetate was purchased from Fishers Scientific Ltd. TLC analyses were performed on commercial Kieselgel 60 F254 silica gel plates. IR spectra were recorded on a Bruker EQUINOX 55 FTIR. NMR spectra were obtained on Bruker spectrometer using DMSO as solvent, with proton and carbon resonances at 300, 400 and 75 MHz, respectively. Mass spectral data (ESI) were recorded on HCT Ultra ETD II Bruker Daltonics, Germany and FAB mass data were recorded on a JEOL SX 102/DA-6000 mass spectrometer.

#### 2.1.1. Preparation of the 4-(2-chloromercury-phenoxyethyl)-6-chromene-2-ones (general procedure)

To a dry 100 mL flask equipped with a stir bar was added substituted 4-bromomethylcoumarins/1-azacoumarins (0.005 mol),

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o-chloro mercury phenol/o-acetoxy mercurated *p*-cresol (0.005 mol), anhydrous  $K_2CO_3$  (1.72 g, 0.0125 mol) and dry butanone (50 mL). The solution was refluxed for 20–24 h. After this time the reaction was cooled to room temperature, the butanone was concentrated and the solution was poured onto crushed ice. The crude solid obtained was crystallized from warm acetic acid.

**2.1.1.1. 4-(2-Chloromercury-phenoxyethyl)-6-methyl-chromene-2-one (3a).** Yield: 2.20 g (86%). M.p. 238–240 °C. FT-IR (KBr,  $cm^{-1}$ ) 1722.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.45–7.09 (m, 7H), 6.67 (s, 1H,  $C_3$ -H of coum.), 5.27 (s, 2H,  $CH_2O$ ), 2.39 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 152.66, 151.64, 132.62, 131.89, 131.09, 130.69, 125.06, 123.22, 122.10, 121.62, 121.32, 117.32, 113.82, 112.26, 109.19, 67.03, 23.00. MS (ESI+)  $m/z$  = 502.3. Anal. Calc. for  $C_{17}H_{13}ClHgO_3$ : C, 40.73; H, 2.61. Found: C, 40.64; H, 2.53%.

**2.1.1.2. 4-(2-Chloromercury-phenoxyethyl)-7-methyl-chromene-2-one (3b).** Yield: 2.20 g (86%). M.p. 250–252 °C. FT-IR (KBr,  $cm^{-1}$ ) 1728.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.50–7.02 (m, 7H), 6.62 (s, 1H,  $C_3$ -H of coum.), 5.32 (s, 2H,  $CH_2O$ ), 2.46 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 152.45, 151.38, 132.82, 131.55, 130.89, 130.60, 125.08, 123.85, 122.98, 122.26, 121.64, 117.65, 113.82, 112.79, 110.00, 65.07, 22.53. MS (ESI+)  $m/z$  = 502.3. Anal. Calc. for  $C_{17}H_{13}ClHgO_3$ : C, 40.73; H, 2.61. Found: C, 40.72; H, 2.65%.

**2.1.1.3. 4-(2-Chloromercury-phenoxyethyl)-5,7-methyl-chromene-2-one (3c).** Yield: 2.00 g (78%). M.p. 260–262 °C. FT-IR (KBr,  $cm^{-1}$ ) 1714.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.51–7.02 (m, 6H), 6.56 (s, 1H,  $C_3$ -H of coum.), 5.55 (s, 2H,  $CH_2O$ ), 2.70 (s, 3H,  $CH_3$ ), 2.50 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 152.76, 151.24, 131.99, 131.89, 131.09, 130.22, 125.86, 123.82, 122.60, 121.66, 121.22, 117.32, 113.88, 112.32, 109.86, 67.03, 23.52, 23.02. MS (ESI+)  $m/z$  = 516.3. Anal. Calc. for  $C_{18}H_{15}ClHgO_3$ : C, 41.95; H, 2.93. Found: C, 41.98; H, 2.99%.

**2.1.1.4. 4-(2-Chloromercury-phenoxyethyl)-7,8-methyl-chromene-2-one (3d).** Yield: 2.05 g (80%). M.p. 264–266 °C. FT-IR (KBr,  $cm^{-1}$ ) 1704.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.85–7.00 (m, 6H), 6.55 (s, 1H,  $C_3$ -H of coum.), 5.41 (s, 2H,  $CH_2O$ ), 2.37 (s, 3H,  $CH_3$ ), 2.29 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 152.76, 151.24, 131.99, 131.68, 131.14, 130.72, 130.36, 125.86, 123.88, 122.67, 121.66, 117.99, 113.57, 112.72, 109.72, 67.23, 23.02, 23.00. MS (ESI+)  $m/z$  = 516.3. Anal. Calc. for  $C_{18}H_{15}ClHgO_3$ : C, 41.95; H, 2.93. Found: C, 41.98; H, 2.92%.

**2.1.1.5. 4-(2-Chloromercury-phenoxyethyl)-6-methoxy-chromene-2-one (3e).** Yield: 2.12 g (82%). M.p. 216–218 °C. FT-IR (KBr,  $cm^{-1}$ ) 1710.  $^1H$  NMR (400 MHz, DMSO)  $\delta$ : 7.48 (s, 1H,  $C_5$ -H of coum.), 7.46–7.02 (m, 6H), 6.65 (s, 1H,  $C_3$ -H of coum.), 5.45 (s, 2H,  $CH_2O$ ), 3.85 (s, 3H,  $OCH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 153.22, 152.06, 138.22, 132.92, 132.62, 132.09, 125.02, 123.44, 122.82, 121.00, 120.90, 119.22, 115.68, 114.92, 110.00, 67.02, 48.02. MS (ESI+)  $m/z$  = 518.3. Anal. Calc. for  $C_{17}H_{13}O_4HgCl$ : C, 39.47; H, 2.53. Found: C, 39.49; H, 2.60%.

**2.1.1.6. 4-(2-Chloromercury-phenoxyethyl)-6-chloro-chromene-2-one (3f).** Yield: 1.97 g (79%). M.p. 260–264 °C. FT-IR (KBr,  $cm^{-1}$ ) 1716.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.99 (s, 1H,  $C_5$ -H of coum.), 7.31–7.03 (m, 6H), 6.68 (s, 1H,  $C_3$ -H of coum.), 5.44 (s, 2H,  $CH_2O$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 152.49, 151.31, 137.86, 132.54, 130.03, 129.44, 125.05, 122.75, 121.42, 119.27, 119.07, 117.61, 113.80, 112.89, 109.99, 65.76. MS (ESI+)  $m/z$  = 522.7. Anal. Calc. for  $C_{16}H_{10}Cl_2HgO_3$ : C, 36.83; H, 1.93. Found: C, 36.85; H, 1.99%.

**2.1.1.7. 4-(2-Chloromercury-phenoxyethyl)-5,6 benzo-chromene-2-one (3g).** Yield: 2.01 g (75%). M.p. 238–240 °C. FT-IR (KBr,  $cm^{-1}$ ) 1722.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 8.35–7.04 (m, 10H), 6.88 (s, 1H,  $C_3$ -H of coum.), 5.83 (s, 2H,  $CH_2O$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 153.44, 152.16, 138.12, 132.62, 132.32, 132.09, 125.22, 125.16, 123.44, 123.26, 122.96, 122.82, 121.00, 120.90, 120.62, 119.22, 115.68, 114.92, 110.00, 67.08. MS (ESI+)  $m/z$  = 538.3. Anal. Calc. for  $C_{20}H_{13}ClHgO_3$ : C, 44.70; H, 2.44. Found: C, 44.66; H, 2.43%.

**2.1.1.8. 4-(2-Chloromercury-phenoxyethyl)-7,8 benzo-chromene-2-one (3h).** Yield: 1.92 g (72%). M.p. 238–240 °C. FT-IR (KBr,  $cm^{-1}$ ) 1722.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 8.40–7.02 (m, 10H), 6.73 (s, 1H,  $C_3$ -H of coum.), 5.53 (s, 2H,  $CH_2O$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 153.44, 152.12, 138.10, 132.64, 132.62, 132.39, 125.62, 123.34, 123.36, 122.96, 122.68, 121.22, 120.90, 120.58, 119.22, 115.88, 114.92, 114.12, 109.00, 67.10. MS (ESI+)  $m/z$  = 538.3. Anal. Calc. for  $C_{20}H_{13}ClHgO_3$ : C, 44.70; H, 2.44. Found: C, 44.62; H, 2.50%.

**2.1.1.9. 4-(2-Acetoxymercury, 4-methyl-phenoxyethyl)-6-methyl-chromene-2-one (3i).** Yield: 0.87 g (69%). M.p. 216–218 °C. FT-IR (KBr,  $cm^{-1}$ ) 1749, 1723.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.48–7.10 (m, 6H), 6.52 (s, 1H,  $C_3$ -H of coum.), 5.86 (s, 2H,  $CH_2O$ ), 2.42 (s, 3H,  $CH_3$ ), 2.38 (s, 3H,  $CH_3$ ), 2.32 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 169.22, 160.22, 160.02, 157.32, 157.12, 156.22, 155.88, 149.14, 147.04, 126.34, 124.58, 121.47, 118.09, 117.22, 112.10, 108.37, 67.22, 23.82, 23.12, 23.02. MS (ESI+)  $m/z$  = 539.9. Anal. Calc. for  $C_{20}H_{18}HgO_5$ : C, 44.57; H, 3.37. Found: C, 44.56; H, 3.39%.

**2.1.1.10. 4-(2-Acetoxymercury, 4-methyl-phenoxyethyl)-6-methoxy-chromene-2-one (3j).** Yield: 2.24 g (81%). M.p. 236–238 °C. FT-IR (KBr,  $cm^{-1}$ ) 1748, 1729.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 7.36–6.92 (m, 6H), 6.49 (s, 1H,  $C_3$ -H of coum.), 5.30 (s, 2H,  $CH_2O$ ), 3.85 (s, 1H,  $OCH_3$  of coum.), 2.43 (s, 1H,  $CH_3$ ), 2.30 (s, 1H,  $CH_3$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 170.04, 160.96, 160.22, 157.88, 157.33, 156.00, 155.92, 149.88, 147.62, 126.62, 124.72, 122.36, 118.12, 117.55, 112.00, 108.44, 67.28, 48.02, 23.44, 23.00. MS (FAB+)  $m/z$  = 555. Anal. Calc. for  $C_{20}H_{18}HgO_6$ : C, 43.29; H, 3.27. Found: C, 43.29; H, 3.25%.

**2.1.1.11. 4-(2-Chloromercury-phenoxyethyl)-azachromene-2-one (8a).** Yield: 1.94 g (80%). M.p. 230–232 °C. FT-IR (KBr,  $cm^{-1}$ ) 1673.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 11.74 (s, 1H, NH), 7.84–7.00 (m, 8H), 6.67 (s, 1H,  $C_3$ H of coum.), 5.43 (s, 2H,  $CH_2O$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 169.48, 160.49, 160.22, 157.00, 155.86, 148.54, 147.03, 123.44, 119.05, 118.75, 115.42, 113.07, 112.61, 107.80, 106.89, 66.76. MS (ESI+)  $m/z$  = 487.3. Anal. Calc. for  $C_{16}H_{12}ClHgNO_2$ : C, 39.52; H, 2.49; N, 2.88. Found: C, 39.52; H, 2.50; N, 2.86%.

**2.1.1.12. 4-(2-Chloromercury-phenoxyethyl)-6-chloro-azachromene-2-one (8b).** Yield: 1.87 g (72%). M.p. 272–274 °C. FT-IR (KBr,  $cm^{-1}$ ) 1682.  $^1H$  NMR (300 MHz, DMSO)  $\delta$ : 11.78 (s, 1H, NH), 7.89–7.06 (m, 7H), 6.68 (s, 1H,  $C_3$ -H of coum.), 5.72 (s, 2H,  $CH_2O$ ).  $^{13}C$  NMR (75 MHz, DMSO)  $\delta$ : 170.12, 160.82, 160.00, 157.48, 150.62, 147.22, 134.24, 133.26, 129.26, 121.47, 118.88, 118.34, 117.62, 112.22, 108.12, 64.12. MS (ESI+)  $m/z$  = 521.7. Anal. Calc. for  $C_{16}H_{11}Cl_2HgNO_2$ : C, 36.90; H, 2.13; N, 2.69. Found: C, 36.92; H, 2.11; N, 2.62%.

## 2.1.2. Synthesis of substituted 13H-5, 12-dioxo-7-mercurobenzo[4,5]cyclohepta[1,2-a]naphthalene 6-ones (general procedure)

Preparation of activated  $Al_2O_3/K_2CO_3$ : A mixture of neutral  $Al_2O_3$  (1 g, 0.001 mol) and anhydrous  $K_2CO_3$  (2.76 g, 0.002 mol) is ground thoroughly in a glass mortar and heated on the Bunsen flame for 4 h followed by the direct usage into the reaction vessel without allowing the mixture to attain room temperature.

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