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# Chlorination of 3-Arylsydnones with Iodine Monochloride

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Sydnones undergo electrophilic aromatic substitution at the 4-position<sup>1,2</sup> and bromination has been the most studied reaction of this type. For the latter, a number of methods, including Br<sub>2</sub> / NaHCO<sub>3</sub>,<sup>3</sup> Br<sub>2</sub> / Ac<sub>2</sub>O,<sup>4</sup> NBS<sup>5,6</sup> or KBrO<sub>3</sub> / HBr,<sup>7</sup> have been used for the conversion of the parent sydnones 1 to their 4-bromo congeners 2. While methods for the chlorination of sydnones ( $1 \rightarrow 3$ ) are available (*inter* alia Cl<sub>2</sub>,<sup>4</sup> NCS/DMF,<sup>5</sup> KClO<sub>3</sub>/HCl,<sup>7</sup> electrochemical chlorination,<sup>8,9</sup> PhICl<sub>2</sub><sup>10</sup>), most of them suffer from one or more major drawback and, accordingly, there is room for improvement of the process. We now report that iodine monochloride in dichloromethane converts 4-unsubstituted 3-arylsydnones (*cf.* 1) to the corresponding 4-chloro analogs 3 in moderate to good yields under very mild conditions.



The present discovery stems from our need to prepare 4-iodo-3-arylsydnones **4** for subsequent alkynyl coupling studies. Dumitrascu *et al.*<sup>11</sup> had reported that the use of iodine monochloride in acetic acid gave good yields of the corresponding 4-iodo sydnone **4** from the 4-unsubstituted compound **1** and we utilized this approach for the preparation of a number of 4-iodosydnones. However, it was observed that the efficiency of the process diminished over time, undoubtedly due to breakdown of the reagent and, accordingly, instead of the neat reactant we elected to use a solution of ICl in dichloromethane, which was available commercially. When the reaction of 3-phenylsydnone (**1a**) with this reagent was reexamined using dichloromethane as solvent, we were surprised to find that a mixture of

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two products was obtained, the minor component being the expected 4-iodo species 4a. The major product was isolated and identified as the 4-chloro congener 3a and, intrigued by this result, we endeavored to optimize the parameters leading to its formation.



**a**, R = H; **b**, R = 3,4-diMe; **c**, R = 2,3-diMe; **d**, R = 2,4-diMe; **e**, R = 3-MeO; **f**, R = 4-MeO; **g**, R = 4-Me; **h**, R = 4-Br; **i**, R = 4-Cl

Accordingly, using 3-phenylsydnone (1a) as our model reactant we modified both the reaction time and the number of equivalents of iodine monochloride employed in order to optimize the conversion to the chlorosydnone 3a. Thus, reaction of 1a with one equivalent of ICl gave a mixture of 1a, 3a and 4a, a mixture of 3a and 4a with two equivalents of ICl and complete conversion to the 4-chloro product 3a in 72% yield with three equivalents of ICl in under 1 hour at room temperature. The latter protocol was extended to the study of a series of 3-arylsydnones 1b-i and, in all cases, complete reaction occurred in less than 2 hours at room temperature. The corresponding 4-chloro species 3b-i were obtained in 51-81% yields after recrystallization from absolute ethanol. No consistent pattern emerged from the yields obtained with different aryl substituents but the reaction was successful in the presence of alkyl, alkoxy, bromo or chloro groups and the position of the substituent did not appear to affect the outcome of the reaction. The identities of the products were confirmed by the presence of the sydnone C = O stretching vibration at  $\sim 1750 \text{ cm}^{-1}$  and the absence of the sydnone C-H stretching vibration at  $\sim$ 3150 cm<sup>-1</sup> and the expected chemical shifts and splitting patterns in their proton and carbon NMR spectra. The most informative observation was the absence of the signal for the hydrogen at the C-4 position of the sydnone ring (typically *ca*.  $\delta$  6.8), indicating substitution at that location.

Arene chlorination by ICl has been observed occasionally prior to the present work. Thus, chloro products were obtained by reaction of ICl with phenolic species in glacial acetic acid,<sup>12</sup> an imidazole nucleoside,<sup>13</sup> 8,16-dimethyl[2.2]metacyclophane,<sup>14</sup> HAT6,<sup>15</sup> methoxybenzenes,<sup>16</sup> and polycyclic aromatic hydrocarbons.<sup>17,18</sup> It has been suggested that an electron transfer pathway involving radical cation intermediates occurs and subsequent chlorination or iodination results from reaction of the latter with chloride ion or iodine atom.<sup>16,18</sup> It is unclear whether this mechanism is operative in the present case and confirmation of this speculation will require further studies. Overall, however, a useful process for the chlorination of sydnones has been developed.

# **Experimental Section**

3-Phenylsydnone (**1a**) was synthesized from *N*-phenylglycine using a literature procedure. <sup>19</sup> The other starting sydnones, 3-(3,4-dimethylphenyl)sydnone (**1b**)<sup>20</sup>, 3-(2,3-dimethylphenyl)-sydnone (**1c**)<sup>20</sup>, 3-(2,4-dimethylphenyl)sydnone (**1d**)<sup>20</sup>, 3-(3-methoxyphenyl)sydnone (**1e**)<sup>21</sup>,

3-(4-methoxyphenyl)sydnone  $(\mathbf{1f})^{22}$ , 3-(4-tolyl)sydnone  $(\mathbf{1g})^{23}$ , 3-(4-bromophenyl)sydnone  $(\mathbf{1h})^{24}$  and 3-(4-chlorophenyl)sydnone  $(\mathbf{1i})^{23}$  were prepared according to the reported procedure. <sup>20</sup> All other starting materials and reagents were purchased commercially and used without purification unless otherwise noted. Melting points were determined on a Mel-Temp melting point device and are uncorrected. The infrared spectra were taken as KBr pellets on a Nicolet 6700 FTIR. NMR spectra were obtained on a Bruker Avance 300 MHz NMR and are reported relative to tetramethylsilane (TMS) as an internal standard. Elemental analyses were carried out by Midwest Microlab LLC, Indianapolis, IN 46250.

# Preparation of 4-Chloro-3-arylsydnones 3a-i from Reaction of 3-Arylsydnones 1a-i with ICI: General Procedure

Iodine monochloride (1M in dry dichloromethane, 3 equiv.) was added dropwise at room temperature to a stirred solution of the 3-arylsydnone (1 equiv.) and anhydrous sodium acetate (3 equiv.) in dry dichloromethane (4 mL / 0.1 g) under an atmosphere of nitrogen gas. After the reaction was complete (usually 0.5 h to 1 h, monitored by TLC on silica gel, dichloromethane: ethyl acetate (25:1 v.v) as eluant), the reaction mixture was poured into aqueous sodium sulfite (2%, 30 mL / 0.1 g), extracted 3 times with dichloromethane and the combined extracts were washed with saturated aqueous sodium bicarbonate (25 mL / 0.1 g), dried with magnesium sulfate, filtered and evaporated *in vacuo*. The resultant solid was recrystallized from hot ethanol.

### 4-Chloro-3-phenylsydnone (3a)

3-Phenylsydnone (**1a**) [0.204 g, 1.258 mmol] for 1 h by the general procedure gave **3a** as colorless crystals (0.182 g, 0.926 mmol, 72%), mp. 116.5–117 °C, identical to an authentic sample.<sup>10</sup>

# 4-Chloro-3-(3,4-dimethylphenyl)sydnone (3b)

3-(3,4-Dimethylphenyl)sydnone (**1b**) [0.100 g, 0.524 mmol] for 1 h by the general procedure gave **3b** as colorless crystals (0.074 g, 0.323 mmol, 62%), mp. 130–2 °C. IR: 3055, 1761 (sydnone C = O), 1500, 1461 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  7.39 (d, 1 H), 7.38 (d, 1 H), 7.11 (s, 1 H), 2.40 (s, 3 H), 2.24 (s, 3 H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  164.1 (sydnone C = O), 142.3, 139.3, 139.2, 131.1, 130.8, 126.1, 98.3 (sydnone C-4), 20.2, 20.0.

Anal. Calcd for  $C_{10}H_9ClN_2O_2 \bullet 0.5 H_2O$ : C, 51.41; H, 4.31; N, 11.99. Found: C, 51.65; H, 3.98; N, 11.73.

# 4-Chloro-3-(2,3-dimethylphenyl)sydnone (3c)

3-(2,3-Dimethylphenyl)sydnone (**1c**) [0.100 g, 0.524 mmol] for 2 h by the general procedure gave **3c** as colorless crystals (0.082 g, 0.365 mmol, 70%), mp. 120–122 °C, identical to an authentic sample.<sup>25</sup>

#### 4-Chloro-3-(2,4-dimethylphenyl)sydnone (3d)

3-(2,4-Dimethylphenyl)sydnone (**1d**) [0.100 g, 0.524 mmol] for 2 h by the general procedure gave **3d** as colorless crystals (0.072 g, 0.319 mmol, 61%), mp. 120–122 °C, identical to an authentic sample.<sup>26</sup>

#### 4-Chloro-3-(3-methoxyphenyl)sydnone (3e)

3-(3-Methoxyphenyl)sydnone (**1e**) [0.201 g, 1.046 mmol] for 0.5 h by the general procedure gave **3e** as colorless crystals (0.174 g, 0.77 mmol, 74%), mp. 93–94 °C, identical to an authentic sample.<sup>10</sup>

### 4-Chloro-3-(4-methoxyphenyl)sydnone (3f)

3-(4-Methoxyphenyl)sydnone (**1f**) [0.202 g, 1.05 mmol] for 0.5 h by the general procedure gave **3f** as colorless crystals (0.161 g, 0.710 mmol, 68%), mp. 101–102 °C, identical to an authentic sample.<sup>6</sup>

### 4-Chloro-3-(4-tolyl)sydnone (3g)

3-(4-Tolyl)sydnone (**1g**) [0.202 g, 1.144 mmol] for 0.5 h by the general procedure gave **3g** as colorless crystals (0.194 g, 0.923 mmol, 81%), mp. 138.5–139 °C, identical to an authentic sample.<sup>10</sup>

### 4-Chloro-3-(4-bromophenyl)sydnone (3h)

3-(4-Bromophenyl)sydnone (**1h**) [0.202 g, 0.839 mmol] for 0.75 h by the general procedure gave **3h** as colorless crystals (0.164 g, 0.596 mmol, 71%), mp. 111–112 °C, identical to an authentic sample.<sup>6</sup>

# 4-Chloro-3-(4-chlorophenyl)sydnone (3i)

3-(4-Chlorophenyl)sydnone (**1i**) [0.201 g, 1.02 mmol] for 0.5 h by the general procedure gave **3i** as colorless crystals (0.167 g, 0.723 mmol, 71%), mp. 108–109 °C, identical to an authentic sample.<sup>10</sup>

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62

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