# Novel Cyclization of *S*-(*o*-Acetylaryl) Dimethylthiocarbamates. A New Synthesis of 3-Hydroxybenzothiophenes and 2-Hydroxythiochromones

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*Received September 19, 1986*

The rearrangement of *O*-(*o*-acetylaryl) dimethylthiocarbamates to their corresponding *S*-aryl dimethylthiocarbamates, previously reported to be a very low yielding reaction, have been achieved in acceptable yields. The versatility of these intermediates is demonstrated by their transformation into different heterocyclic systems. Thus, when the resulting *S*-(*o*-acetylaryl) dimethylthiocarbamates are treated with base in the presence of air, they cyclize in a novel fashion to yield substituted *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamides and substituted 2-hydroxythiochromones. In the absence of air, only the latter was formed.

## Introduction

The thermal rearrangement of *O*-aryl dimethylthiocarbamates **1** to *S*-aryl dimethylthiocarbamates **2**, which is known as the Newman-Kwart rearrangement, is in general a high yielding reaction.[1] The rearrangement has been considered to be the best general route for the conversion of phenols to thiophenols. However, one of the limitations of this general reaction according to Newman[1] is that *O*-(*o*-acetyl-substituted aryl) dimethylthiocarbamates (**1**; X = *o*-$COCH_3$) do not yield the corresponding *S*-aryl dimethylthiocarbamates (**2**; X = *o*-$COCH_3$) when subjected to the normal rearrangement conditions. Decomposition usually occurred before the desired rearrangement took place (Scheme I).

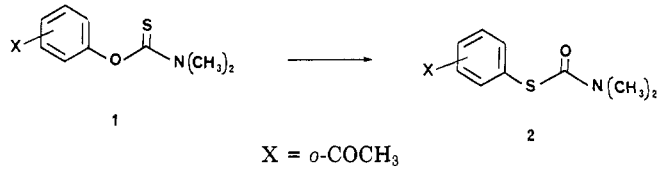
Since then, it appears that there have been no other attempts to rearrange substrates having an *o*-acetyl substituent. Recently, Scrowston et al.[2] reported the first successful rearrangement of *O*-(*o*-formyl-substituted aryl) dimethylthiocarbamates (**1**; X = *o*-CHO) to the corresponding S-aryl products (**2**; X = *o*-CHO).

We have reinvestigated the Newman-Kwart rearrangement and we would like to report here that *O*-(*o*-acetyl-substituted aryl) dimethylthiocarbamates (**1**; X = *o*-$COCH_3$) can be readily rearranged to their corresponding *S*-aryl dimethylthiocarbamates (**2**; X = *o*-$COCH_3$) in reasonable yields.

We have also found that the *S*-(*o*-acetylaryl) dimethylthiocarbamates **2** obtained from this thermal rearrangement are very versatile intermediates. They can be hydrolyzed readily to the corresponding *o*-acetylthiophenols but more interestingly they can be cyclized in a novel fashion to *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamides **3** and to the 2-hydroxythiochromones **4** (Scheme II).

Substituted *O*-(*o*-acetylaryl) dimethylthiocarbamates **1** were prepared as described by Newman.[1] Using *O*-(2-acetyl-3-hydroxyphenyl) dimethylthiocarbamate (**1c**) as substrate, we have investigated the rearrangement reaction with or without solvent, under normal atmosphere and within a bomb. The optimum condition found for obtaining the *S*-phenyl dimethylthiocarbamate (**2c**) was to reflux the substrate in *o*-dichlorobenzene for 18 h. The same condition was then used for other substrate and the results are summarized in Table I. Most of the substrates listed in Table I required 18 h of reflux except **1e**, which took only 8 h to complete. The products were isolated by chromatography and characterized by NMR, mass spectroscopy, and elemental analysis. With no other substituent on the ring, *O*-(2-acetylphenyl) dimethylthiocarbamate (**1a**) rearranged to give a 55% isolated yield of *S*-(2-acetylphenyl) dimethylthiocarbamate (**2a**) together with 4% of the corresponding 2-(dimethylamino)thiochromone (**5a**). With an electron-donating methoxy substituent on the ring (**1b**, **1d**), the overall yield was slightly lower. In the case of hydroxyl substituents (**1c**), the desired *S*-aryl dimethylthiocarbamate **2c** was obtained in 25% yield. These results are in accordance with the mechanism of the reaction.[1,3] With a less strongly electron-releasing group such as acetoxy (**1f**) or [(trifluoromethyl)sulfonyl]oxy group (**1e**), the yields of the corresponding rearranged products (**2f**, 66%; **2e**, 91%) are higher. In most of the cases studied, 2-(dimethylamino)thiochromone derivatives (**5**) were formed in small amounts. The possible utility of this transformation as a novel approach to the synthesis of the thiochromone ring

**Scheme I**




**Scheme II**

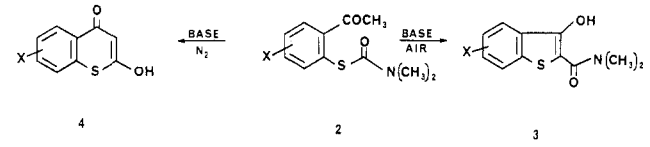



**Table I. Thermal Rearrangement of *O*-(*o*-Acetylphenyl) Dimethylthiocarbamates 1**

| substrate | X | products (yield, %) |
|---|---|---|
| **1a** | H | **2a** (55), **5a** (4) |
| **1b** | 5-MeO | **2b** (41), **5b** (7) |
| **1c** | 3-OH | **2c** (25), **5c** (5)[a] (0), (50)[b] |
| **1d** | 3-MeO | **2d** (45) |
| **1e** | 3-$CF_3SO_2O$ | **2e** (91) |
| **1f** | 3-OAc | **2f** (66) |

[a] Pyrolyzed in refluxing *o*-dichlorobenzene. [b] Pyrolyzed neat without solvent.

(1) (a) Newman, M. S.; Karnes, H. K. *J. Org. Chem.* **1966**, *31*, 3980. (b) Kwart, H.; Evans, E. R. *J. Org. Chem.* **1966**, *31*, 410.

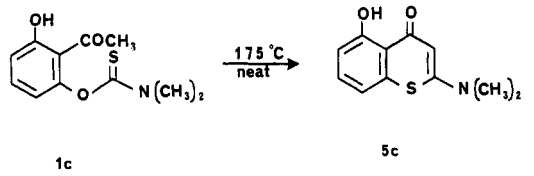
(2) Rahman, L. K. A.; Scrowston, R. M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2973.

(3) (a) Kaji, A.; Araki, Y.; Miyazaki, K. *Bull Chem. Soc. Jpn.* **1971**, *44*, 1393. (b) Miyazaki, K. *Tetrahedron Lett.* **1968**, 2793.

(4) (a) Rath, P. C.; Rajagopal, K. *Indian J. Chem.* **1969**, *7*, 1273. (b) Schank, K.; Lich, C. *Synthesis* **1983**, *5*, 392.

0022-3263/87/1952-1670$01.50/0 

**Scheme III**




1c 5c

**Table II. Base-Catalyzed Cyclization of S-(o-Acetylphenyl) Dimethylthiocarbamate under Normal Atmosphere**

| substrate | X | products (yield, %) |
|---|---|---|
| **2a** | H | **3a** (39), **4a** (23) |
| **2b** | 5-MeO | **3b** (33), **4b** (10) |
| **2c** | 3-OH | **3c** (7) |
| **2d** | 3-MeO | **3d** (22) |

system was investigated. Thus, *O*-(3-hydroxy-2-acetylphenyl) dimethylthiocarbamate (**1c**) was found to rearrange and cyclize exclusively to 5-hydroxy-2-(dimethylamino)thiochromone (**5c**) in 50% yield when heated neat at 175 °C for 18 h. This result differs considerably from those obtained when the rearrangement is carried out in refluxing *o*-dichlorobenzene, which gives a mixture of 25% of **2c** and of 5% of **5c**. **1c** was the only substrate that gave an appreciable amount of the 2-(dimethylamino)thiochromone derivative (**5**) when pyrolyzed neat or otherwise. (Scheme III).

Other substrates when subjected to various pyrolysis conditions, including sealed tube with or without solvents, do not give any significant amounts of substituted 2-(dimethylamino)thiochromones (**5**). Therefore, it is possible that *O*-(3-hydroxy-2-acetylphenyl) dimethylthiocarbamate (**1c**) having an *o*-hydroxy substituent next to the acetyl group provides the internal protonation needed for the enolization to take place and then effect the cyclization to 5-hydroxy-2-(dimethylamino)thiochromone. In order to determine if cyclization can be catalyzed by other proton sources, *O*-(*o*-acetylphenyl) dimethylthiocarbamate was pyrolyzed in *o*-dichlorobenzene in the presence of various proton sources that included phenol, polyphosphoric acid, and *p*-toluenesulfonic acid. No substituted 2-(dimethylamino)thiochromones (**5**) were obtained. Attempts to cyclize *S*-(*o*-acetylphenyl) dimethylthiocarbamate (**2a**) under various acidic conditions also failed to give the corresponding 2-(dimethylamino)thiochromone (**5**).

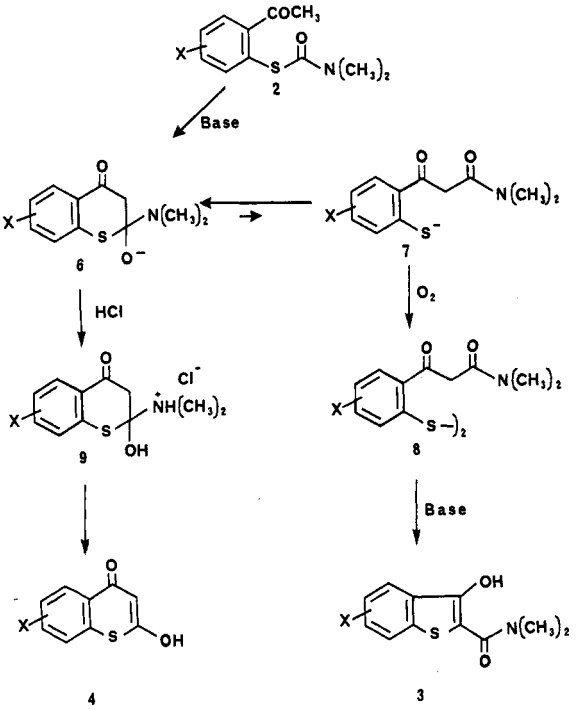
When the *S*-(*o*-acetylphenyl) dimethylthiocarbamate (**2a**) was treated with sodium hydride in dimethylformamide (DMF) under normal atmospheric conditions, an unexpected *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamide (**3a**) was obtained in 39% yield together with 23% of 2-hydroxythiochromone (**4a**). No traces of 2-(dimethylamino)thiochromone (**5a**) were detected.

Other substituted *S*-(*o*-acetylphenyl) dimethylthiocarbamates (**2**) also gave the corresponding *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamide derivatives (**3**) in variable yields. The results are summarized in Table II. Hydroxy-substituted derivative (**2c**) gave only 7% of the corresponding 3-hydroxybenzothiophene derivative (**3c**). The [(trifluoromethyl)sulfonyl]oxy (**2e**) or the acetoxy (**2f**) derivatives likewise gave very low yields. However, the methoxy derivatives (**2b**, **2d**) gave 33% and 22% of the corresponding benzothiophene derivatives, respectively. When the *S*-(*o*-acetylphenyl) dimethylthiocarbamate (**2a**) was treated with sodium hydride in DMF under nitrogen, only the corresponding 2-hydroxythiochromone (**4a**) was isolated. There was no trace of the corresponding *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamide (**3a**). Similar results were obtained when **2b** and **2d** were subjected to the same conditions. Table III summarizes the results of the formation of the 2-hydroxythiochromones (**4**).

**Table III. Base-Catalyzed Cyclization of S-(o-Acetylphenyl) Dimethylthiocarbamate under Nitrogen Atmosphere**

| substrate | X | products (yield, %) |
|---|---|---|
| **2a** | H | **4a** (43) |
| **2b** | 5-MeO | **4b** (79) |
| **2d** | 3-MeO | **4d** (72) |

**Scheme IV**




The formation of *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamides (**3**) from *S*-(*o*-acetylphenyl) dimethylthiocarbamates (**2**) only in the presence of air indicates that an oxidative process involving oxygen must have taken place. In an attempt to increase the yield of the benzothiophene derivative, pure oxygen was bubbled throught the reaction mixture during the entire span of the reaction. However, more decomposition products resulted. To rationalize the formation of *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamide (**3a**) in the presence of air and the exclusive formation of 2-hydroxythiochromone (**4**) in the absence of air, the following mechanism is proposed (Scheme IV).

When the *S*-(*o*-acetylphenyl) dimethylthiocarbamate (**2**) was treated with base, the enolate of the acetyl group is formed and attacks the carbonyl of the thiocarbamate to give the cyclic intermediate (**6**), which may be in equilibrium with **7**. In the presence of air, intermediate **7** is oxidized to form the disulfide **8**. In the presence of more base, disulfide **8** is cyclized to give the 3-hydroxybenzothiophene-2-carboxamide (**3**), the thiolate anion acting as a leaving group. In the absence of air, dimer **8** is not formed. When the reaction mixture is quenched with aqueous HCl, intermediate **9** becomes the first formed product. The protonated dimethylamino group now being a better leaving group than water is eliminated to give 2-hydroxythiochromone.

The novel rearrangement of *S*-(*o*-acetylphenyl) dimethylthiocarbamate (**2**) thus provides an interesting alternative to prepare substituted *N,N*-dimethyl-3-

hydroxybenzothiophene-2-carboxamides (**3**) and substituted 2-hydroxythiochromones (**4**).

## Experimental Section

Proton nuclear magnetic resonance spectra were obtained on a Varian EM390 spectrometer and proton chemical shifts are relative to tetramet ylsilane ($Me_4Si$) as internal standard. The infrared spectra were measured on a Perkin-Elmer 681 spectrophotometer. Melting points were measured on a Buchi 510 melting point apparatus in open capillary tubes and are uncorrected. Low resolution mass spectral analyses were performed by the Morgan-Schaffer Corporation, Montreal, and elemental analyses were performed by Guelph Chemical Laboratories Ltd., Guelph, Ontario. All reactions as well as column chromatography were monitered routinely with the aid of thin layer chromatography using precoated silica gel GF plates (Analtech).

***O*-(2-Acetylphenyl) Dimethylthiocarbamate (1a).** To a stirring mixture of 99% sodium hydride (2.6 g, 0.11 mole) in dimethylformamide (150 mL) at room temperature and under nitrogen atmosphere was added dropwise a solution of 2-hydroxyacetophenone (13.6 g, 0.1 mol) in DMF (10 mL), followed by the dropwise addition of a solution of dimethylthiocarbamoyl chloride (13.5 g, 0.11 mol) in DMF (15 mL). After being stirred for 18 h, the mixture was diluted to 500 mL with ether, filtered through Celite and the filtrate was washed with water (3 × 200 mL). The organic layer was dried ($Na_2SO_4$) and filtered, and the filtrate was concentrated in vacuo to yield an oil, which was purified by chromatography on silica gel, eluting with 30% ethyl acetate in hexane to give *O*-(2-acetylphenyl) dimethylthiocarbamate (13.1 g, 57%): mp 69–71 °C; $^1$H NMR ($CDCl_3$, $\delta$) 2.53 (s, 3 H, $CH_3$), 3.37 (s, 3 H, $CH_3$), 3.43 (s, 3 H, $CH_3$), 7.07 (dd, $J$ = 9 Hz, 2 Hz, 1 H, $H_6$), 7.40 (m, 2 H, $H_4$, $H_5$), 7.78 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_3$). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.16; H, 5.86; N, 6.27; S, 14.35. Found: C, 59.07; H, 6.00; N, 6.28; S, 14.40.

The *O*-(2-acetylphenyl) dimethylthiocarbamates (**1b–d**) listed in Table I were prepared by using this procedure.

For **1b** (48% yield): $^1$H NMR ($CDCl_3$, $\delta$) 2.63 (s, 3 H, $CH_3$), 3.40 (s, 3 H, $CH_3$), 3.47 (s, 3 H, $CH_3$), 3.90 (s, 3 H, $CH_3$), 6.57 (dd, $J$ = 9 Hz, 2 Hz, 1 H, $H_6$), 6.83 (dd, $J$ = 9 Hz, 2 Hz, 1 H, $H_4$), 7.80 (d, $J$ = 9 Hz, 1 H, $H_3$). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.89; H, 5.96; N, 5.52; S, 12.65. Found: C, 56.77; H, 6.16; N, 5.55; S, 12.78.

For **1c** (52% yield): mp 149–151 °C; $^1$H NMR ($CDCl_3$, $\delta$) 2.63 (s, 3 H, $CH_3$), 3.40 (s, 3 H, $CH_3$), 3.50 (s, 3 H, $CH_3$), 6.53 (d, $J$ = 9 Hz, 1 H, $H_4$), 6.93 (d, $J$ = 9 Hz, 1 H, $H_6$), 7.43 (t, $J$ = 9 Hz, 1 H, $H_5$). Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.47; N, 5.85; S, 13.39. Found: C, 55.06; H, 5.53; N, 5.54; S, 13.02.

For **1d** (61% yield): mp 88–89 °C; $^1$NMR ($CDCl_3$, $\delta$) 2.53 (s, 3 H, $CH_3$), 3.27 (s, 3 H, $CH_3$), 3.37 (s, 3 H, $CH_3$), 3.83 (s, 3 H, $CH_3$), 6.73 (d, $J$ = 9 Hz, 1 H, $H_4$), 6.83 (d, $J$ = 9 Hz, 1 H, $H_5$), 7.37 (t, $J$ = 9 Hz, 1 H, $H_6$). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.89; H, 5.96; N, 5.52; S, 12.65. Found: C, 56.82; H, 6.11; N, 5.53; S, 12.39.

***O*-[2-Acetyl-3-[[(trifluoromethyl)sulfonyl]oxy]phenyl] Dimethylthiocarbamate (1e).** Trifluoromethanesulfonyl chloride (3.2 g, 19.5 mmoles) was added dropwise to a stirring mixture of *O*-(2-acetyl-3-hydroxyphenyl) dimethylthiocarbamate (**1c**) (3.9 g, 16.3 mmol), triethylamine (2.3 g, 22 mmol), and tetrahydrofuran (65 mL) at 5 °C. After being stirred for 1 h, the mixture was diluted with ether and poured into water. The organic layer was separated, dried ($Na_2SO_4$), and filtered, and the filtrate was concentrated in vacuo to give a residue that was purified by chromatography on silica gel, eluting with 20% ethyl acetate in toluene to yield *O*-[2-acetyl-3-[[(trifluoromethyl)-sulfonyl]oxy]phenyl] dimethylthiocarbamate (1.90 g, 31%), as an oil: $^1$H NMR 2.53 (s, 3 H, $CH_3$), 3.07 (s, 6 H, $CH_3$), 7.40 (m, 3 H, aromatic protons). Anal. Calcd for $C_{12}H_{12}F_3NO_5S_2$: C, 38.81; H, 3.25; N, 3.77; F, 15.34; S, 17.26. Found: C, 38.92; H, 3.44; N, 3.52; F, 15.48; S, 17.40.

***O*-(2-Acetyl-3-acetoxyphenyl) Dimethylcarbamate (1f).** Acetyl chloride (942 mg, 12 mmol) was added dropwise to a stirring mixture of *O*-(2-acetyl-3-hydroxyphenyl) dimethylthiocarbamate (**1c**) (2.4 g, 10 mmol), triethylamine (1.4 g, 14 mmol), and tetrahydrofuran (50 mL) at 5 °C. After being stirred for 1 h, the mixture was diluted with ether and poured into water. The organic layer was separated, dried ($Na_2SO_4$), and filtered, and the filtrate was concentrated in vacuo to give a residue that was purified by chromatography on silica gel, eluting with 20% ethyl acetate in toluene, to yield *O*-(2-acetyl-3-acetoxyphenyl) dimethylthiocarbamate (2.6 g, 95%), as an oil: $^1$H NMR 2.30 (s, 3 H, $CH_3$), 2.53 (s, 3 H, $CH_3$), 3.17 (s, 6 H, $CH_3$), 7.30 (m, 3 H, aromatic protons). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.97; S, 11.39. Found: C, 55.33, H, 5.57; N, 5.03; S, 11.56.

**Thermal Rearrangement of *O*-(2-Acetylphenyl) Dimethylthiocarbamate (1a).** A solution of *O*-(2-acetylphenyl) dimethylthiocarbamate (**1a**) (12.0 g, 52.8 mmol) in *o*-dichlorobenzene (60 mL) was refluxed under a nitrogen atmosphere for 12 h. The mixture was chromatographed on silica gel, eluting with 30% ethyl acetate in hexane, to yield successively *S*-(2-acetylphenyl) dimethylthiocarbamate (**2a**) (6.6 g, 55%), bp 250 °C/0.5 mm, and 2-(dimethylamino)thiochromone (**5a**) (400 mg, 3.6%) as an oil, $m/e$ 205 ($M^+$, 16.6%).

***S*-(2-Acetylphenyl) dimethylthiocarbamate (2a):** $^1$H NMR 2.53 (s, 3 H, $CH_3$), 3.07 (s, 6 H, $CH_3$), 7.40 (m, 4 H, aromatic protons). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.16; H, 5.86; N, 6.27; S, 14.35. Found: C, 59.14; H, 5.95; N, 6.31; S, 14.10.

**2-(Dimethylamino)thiochromone (5a):** $^1$H NMR 2.97 (s, 6 H, $CH_3$), 6.10 (s, 1 H, $H_3$), 7.40 (m, 3 H, $H_6$, $H_7$, $H_8$), 7.88 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_5$). Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82; S, 15.61. Found: C, 64.09; H, 5.88; N, 7.21; S, 15.20.

The *S*-(*o*-acetylphenyl) dimethylthiocarbamates **2b–f** and the (dimethylamino)thiochromones **5a–c** listed in Table I were prepared according to this procedure.

For **2b** (41% yield): $^1$H NMR ($CDCl_3$, $\delta$) 2.57 (s, 3 H, $CH_3$), 3.10 (s, 6 H, $CH_3$), 6.88 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_4$), 7.13 (d, $J$ = 2 Hz, $H_6$), 7.67 (d, $J$ = 9 Hz, 1 H, $H_3$). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.89; H, 5.96; N, 5.52; S, 12.65. Found: C, 56.79; H, 6.36; N, 5.47; S, 12.52.

For **5b** (7% yield): mp 87–89 °C; $^1$H NMR ($CDCl_3$, $\delta$) 2.97 (s, 6 H, $CH_3$), 3.90 (s, 3 H, $CH_3$), 5.97 (s, 1 H, $H_3$), 6.90 (m, 3 H, $H_6$, $H_7$, $H_8$), 7.80 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_5$). Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 57.35; H, 5.21; N, 5.57; S, 12.75. Found: C, 56.99; H, 5.34; N, 5.35; S, 12.80.

For **2c** (25% yield): mp 127–130 °C; $^1$H NMR ($CDCl_3$, $\delta$) 2.77 (s, 3 H, $CH_3$), 3.10 (s, 6 H, $CH_3$), 7.00 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_5$), 7.13 (d, $J$ = 2 Hz, 1 H, $H_6$), 7.30 (d, $J$ = 9 Hz, 1 H, $H_4$). Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.47; N, 5.85; S, 13.39. Found: C, 55.59; H, 5.48; N, 5.71; S, 12.66.

For **5c** (5% yield): mp 147–149 °C; $^1$H NMR ($CDCl_3$, $\delta$) 3.07 (s, 6 H, $CH_3$), 6.20 (s, 1 H, $H_3$), 6.60 (d, 1 H, $H_6$), 6.72 (t, $J$ = 9 Hz, 1 H, $H_8$), 7.23 (t, $J$ = 9 Hz, 1 H, $H_7$). Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90; S, 13.51. Found: C, 55.16; H, 4.90; N, 5.79; S, 12.20.

For **2d** (45% yield): mp 59–61 °C; $^1$H NMR ($CDCl_3$, $\delta$) 2.47 (s, 3 H, $CH_3$), 3.03 (s, 6 H, $CH_3$), 3.80 (s, 3 H, $CH_3$), 6.98 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_4$), 7.13 (dd, $J$ = 2 Hz, 9 Hz, 1 H, $H_6$), 7.30 (t, $J$ = 9 Hz, 1 H, $H_5$). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.89; H, 5.96; N, 5.52; S, 12.65. Found: C, 56.68; H, 6.07; N, 5.63; S, 12.43.

For **2e** (91% yield): $^1$H NMR ($CDCl_3$, $\delta$) 2.57 (s, 3 H, $CH_3$), 3.03 (s, 6 H, $CH_3$), 7.50 (s, 3 H, $H_4$, $H_5$, $H_6$). Anal. Calcd for $C_{12}H_{12}F_3NO_5S_2$: C, 38.31; H, 3.25; N, 3.77; S, 17.26; F, 15.34. Found: C, 39.16; H, 3.34; N, 3.63; S, 17.29; F, 15.35.

For **2f** (66% yield): $^1$H NMR ($CDCl_3$, $\delta$) 2.30 (s, 3 H, $CH_3$), 2.50 (s, 3 H, $CH_3$), 3.00 (s, 6 H, $CH_3$), 7.30 (s, 3 H, $H_4$, $H_5$, $H_6$). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.97; S, 11.39. Found: C, 55.84; H, 5.63; N, 5.17; S, 11.21.

Base-catalyzed cyclization of *S*-(2-acetylphenyl) dimethylthiocarbamates (**2a**) under normal atmosphere.

To a solution of *S*-(2-acetylphenyl) dimethylthiocarbamate (**2a**) (2.66 g, 11.7 mmol) in DMF (50 mL) was added 99% sodium hydride (337 mg, 14 mmol). The mixture was stirred for 18 h in the presence of dry air (the reaction mixture was protected by drying tube only) and then acidified with 1 N HCl (50 mL). The mixture was extracted with ether (300 mL), and the organic layer was washed with water (2 × 50 mL), dried ($Na_2SO_4$), filtered, and concentrated in vacuo. The residue was chromatographed by using 30% ethyl acetate in hexane as eluent to yield 550 mg (39%) of *N,N*-dimethyl-3-hydroxybenzothiophene-2-carboxamide (**3a**): mp 109–110 °C; $^1$H NMR 3.17 (s, 6 H, $CH_3$), 7.50 (m, 3 H, $H_5$, $H_6$, $H_7$), 7.93 (m, 1 H, $H_4$), 13.30 (s, 1 H, OH). Anal. Calcd for

$C_{11}H_{11}NO_2S$: C, 64.36; H, 5.40; N, 6.82; S, 15.61. Found: C, 64.09; H, 5.88; N, 7.21; S, 15.21.

Further elution gave also 490 mg (23%) of the more polar 2-hydroxythiochromone (**4a**): mp 206–208 °C; MS, *m/e* 178 ($M^+$, 61%); $^1H$ NMR 6.18 (s, 1 H, CH), 7.40 (m, 3 H, $H_6$, $H_7$, $H_8$), 8.17 (m, 1 H, $H_5$). Anal. Calcd for $C_9H_6O_2S$: C, 60.65; H, 3.39; S, 17.99. Found: C, 60.81; H, 3.61; S, 18.20.

The 3-hydroxybenzothiophene-2-carboxamides (**3b–d**) and the 2-hydroxythiochromone **4b** listed in Table II were prepared according to this procedure.

For **3b** (33% yield): mp 146–149 °C; $^1H$ NMR ($CDCl_3$, δ) 3.28 (s, 6 H, $CH_3$), 3.90 (s, 3 H, $CH_3$), 7.03 (dd, *J* = 2 Hz, 9 Hz, 1 H, $H_5$), 7.13 (d, *J* = 2 Hz, $H_7$), 7.90 (d, *J* = 9 Hz, 1 H, $H_4$), 13.45 (s, 1 H, OH). Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 61.25; H, 5.56; N, 5.95; S, 13.62. Found: C, 59.33; H, 5.76; N, 5.94; S, 14.33.

For **3c** (7% yield): mp, 141–143 °C; $^1H$ NMR ($CDCl_3$, δ) 3.27 (s, 6 H, $CH_3$), 6.77 (d, *J* = 9 Hz, 1 H, $H_5$), 7.17 (d, *J* = 2 Hz, $H_7$), 7.33 (t, *J* = 9 Hz, 1 H, $H_6$), 7.90 (s, 1 H, OH). Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 59.70; H, 5.01; N, 6.33; S, 14.49. Found: C, 59.77; H, 5.18; N, 6.05; S, 14.75.

**2-Hydroxy-5-methoxythiochromone (4d).** A mixture of *S*-(2-acetyl-3-methoxyphenyl) dimethylthiocarbamate (0.253 g, 1.0 mmol) and sodium hydride (57.6 mg, 1.2 mmol, 50% dispersion in mineral oil) in DMF (10 mL) was stirred for 18 h at room temperature under an atmosphere of nitrogen. Dilute HCl (1 N) was added and the mixture was extracted with ethyl acetate. The organic layer was washed with water, dried ($Na_2SO_4$), filtered, and concentrated in vacuo. The residue was chromatographed by using 50% ethyl acetate in hexane as eluent to yield 150 mg (72%) of 2-hydroxy-5-methoxythiochromone (**4d**): mp 158–160 °C; $^1H$ NMR 4.05 (s, 3 H, $CH_3$), 6.10 (s, 1 H, CH), 6.80–7.50 (m, 3 H, $H_6$, $H_7$, $H_8$), 10.3 (s, 1 H, OH).

The compounds listed in Table III were prepared according to this procedure.

For **4b** (79% yield): mp 146–149 °C; $^1H$ NMR ($CDCl_3$, δ) 3.28 (s, 6 H, $CH_3$), 3.90 (s, 3 H, $CH_3$), 7.03 (dd, *J* = 2 Hz, 9 Hz, 1 H, $H_5$), 7.13 (d, *J* = 2 Hz, $H_7$), 7.90 (d, *J* = 9 Hz, 1 H, $H_4$), 13.45 (s, 1 H, OH). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 61.25; H, 5.56; N, 5.95; S, 13.62. Found: C, 59.33; H, 5.76; N, 5.94; S, 14.33.

**2-Hydroxy-4-methoxyacetophenone.** A mixture of 2,4-dihydroxyacetophenone (15.2 g, 0.1 mol), potassium carbonate (13.8 g, 0.1 mol), and methyl iodide (14.2 g, 0.1 mol) in acetone (250 mL) was refluxed for 22 h. The mixture was filtered and the filtrate was concentrated in vacuo to a residue that was chromatographed on silica gel, eluting with 15% ethyl acetate in hexane to yield 2-hydroxy-4-methoxyacetophenone (15.3 g, 92%): mp 49–50 °C; $^1H$ NMR 2.58 (s, 3 H, $CH_3$), 3.88 (s, 3 H, $CH_3O$), 6.40 (m, 2 H, $H_3$, $H_5$), 7.63 (d, *J* = 9 Hz, 1 H, $H_6$). Anal. Calcd for $C_9H_{10}O_3$: C, 65.04; H, 6.06. Found: C, 64.94; H, 6.22.

**2-Hydroxy-6-methoxyacetophenone.** A mixture of 2,6-dihydroxyacetophenone (15.2 g, 0.1 mol), potassium carbonate (13.8 g, 0.1 mol), and methyl iodide (14.2 g, 0.1 mol) in acetone (250 mL) was refluxed for 22 h. The mixture was filtered and the filtrate was concentrated in vacuo to a residue that was chromatographed on silica gel, eluting with 15% ethyl acetate in hexane to yield 2-hydroxy-6-methoxyacetophenone (14.0 g, 84%): mp 57–58 °C; $^1H$ NMR 2.70 (s, 3 H, $CH_3$), 3.88 (s, 3 H, $CH_3O$), 6.40 (d, *J* = 9 Hz, 1 H, $H_3$), 6.58 (d, *J* = 9 Hz, 1 H, $H_5$), 7.38 (t, *J* = 9 Hz, 1 H, $H_4$). Anal. Calcd for $C_9H_{10}O_3$: C, 65.04; H, 6.06. Found: C, 64.74; H, 6.24.

**Acknowledgment.** We thank Dr. Joseph G. Atkinson for useful comments and Dr. Yvan Guindon, Merck Frosst Canada Inc., Montreal, for his support of this work.

# Ruthenium Complex Catalyzed N-Heterocyclization. Syntheses of Quinolines and Indole Derivatives from Aminoarenes and 1,3-Propanediol of Glycols

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*Received September 2, 1986*

Aniline reacts with 1,3-propanediol under reflux in diglyme with spontaneous hydrogen evolution in the presence of a catalytic amount of ruthenium trichloride hydrate ($RuCl_3 \cdot nH_2O$)–tributylphosphine ($PBu_3$) to give quinoline in good yield. The yield of quinoline was markedly affected by the molar ratios of aniline to 1,3-propanediol and $PBu_3$ to $RuCl_3 \cdot nH_2O$. The best yield (76%) was achieved at the molar ratios of 2.5 of aniline/1,3-propanediol and 2.0 of $PBu_3/RuCl_3 \cdot nH_2O$. Also, N-substituted anilines react with ethylene glycol in the presence of a catalytic amount of dichlorotris(triphenylphosphine)ruthenium ($RuCl_2(PPh_3)_3$) to give N-substituted indole derivatives. The reactions were carried out at 180 °C in dioxane with spontaneous hydrogen evolution. Aminoarenes also react with 2,3-butanediol and 1,2-cyclohexanediol (mixture of cis and trans) in the presence of $RuCl_2(PPh_3)_3$ to give the corresponding 2,3-dimethylindoles and 1,2,3,4-tetrahydrocarbazoles in good to excellent yields. As the key intermediates of the reactions, *N,N'*-diarylpropylenediamine (**5a**) and *N,N'*-diarylethylenediamine (**5b**) and their dehydrogenated imine derivatives are postulated.

The Skraup and related syntheses[1] are well-known as the method for the preparation of quinoline derivatives. This method, however, requires a large amount of sulfuric acid at temperatures above 150 °C, and the reaction is often violent.

Recently, transition-metal-catalyzed synthesis of quinoline derivatives under nonacidic conditions has been developed.[2-5] However, these methods are sucessful only with substituents on the heterocyclic ring.[6]

On the other hand, the Fischer indole synthesis is by far the most widely used route to substituted indoles and has been extensively reviewed.[7] It involves the rearrangement

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