

# Studies in Sigmatropic Rearrangement: Synthesis of a [6,6]Pyranothiopyran Ring System by Sequential Claisen Rearrangement and Pyridine Hydrotribromide Mediated Regioselective “6-Endo” Cyclization†

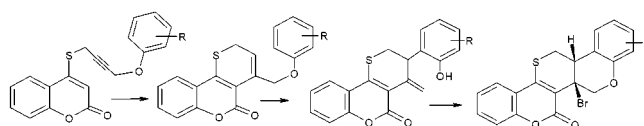
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## ABSTRACT



4-(4'-Aryloxybut-2'-ynylthio)[1]benzopyran-2-ones are refluxed in chlorobenzene to afford 4-aryloxymethylthiopyrano[3,2-c][1]benzopyran-5(2*H*)-ones which are subsequently subjected to heating in *o*-dichlorobenzene in the presence of *N,N*-diethylaniline and then treated with pyridine hydrotribromide to give [6,6]pyranothiopyrans in almost quantitative yield.

We have recently reported<sup>1–5</sup> the regioselective synthesis of pyrano- and furocoumarins and pyrido- and pyrrolocoumarins fused at the 3,4-position of the coumarin nucleus by the application of sigmatropic rearrangements. In continuation we have also successfully synthesized<sup>6,7</sup> thiopyrano and thieno [3,2-*c*] coumarins. In the case of studying the sigmatropic rearrangement of 4-(4'-aryloxybut-2'-ynyloxy)coumarins and 3-(4'-aryloxybut-2'-ynyloxy)coumarins, it was observed that the products of the first Claisen rearrangement contained an aryloxyallyl moiety for a further Claisen rearrangement and the second Claisen rearrangement did afford interesting

results.<sup>8,9</sup> This has created our interest in undertaking a study on the sequential Claisen rearrangement of 4-(4'-aryloxybut-2'-ynylthio)coumarin. The substrate 4-(4'-aryloxybut-2'-ynylthio)coumarins **3a–d** for this purpose were synthesized in 70–80% yield by the phase transfer-catalyzed alkylation of 4-mercaptocoumarin with 1-chloro-4-aryloxybut-2-yne. Compounds **3a–d** are all solids and were characterized from their elemental analyses and spectral data<sup>10</sup> (Scheme 1).

Substrate **3a** was refluxed in chlorobenzene (132 °C) for 4 h to give a crystalline solid, **4a** (mp 186 °C), in 75% yield. This was characterized from its elemental analysis and spectral data.<sup>11</sup> The other substrates **3b–d** were also similarly treated to give products **4b–d**. Substrates **3a–d** possess two

† This paper is dedicated to Professor B. S. Thyagarajan of the University of Texas at San Antonio, Texas, on the occasion of his 75th birthday.

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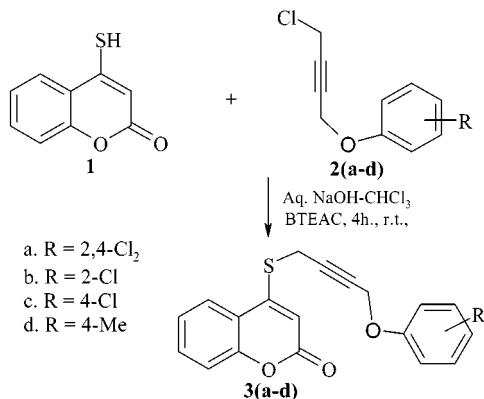
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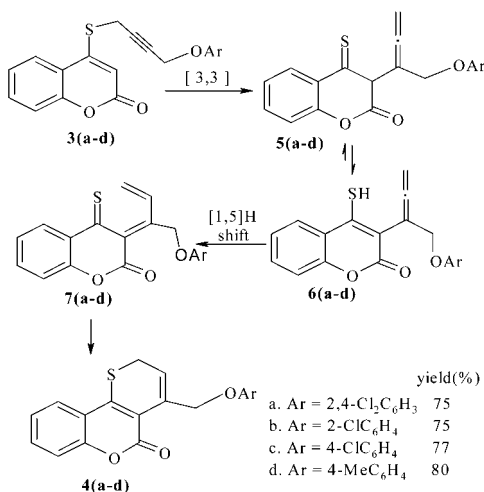
(10) **Compound 3a**: mp 155 °C; yield 72%; UV (EtOH)  $\lambda_{\text{max}}$  218, 273 nm; IR (KBr)  $\nu_{\text{max}}$  1700, 1590, 1230  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz):  $\delta$  3.81 (t, 2H,  $J = 2$  Hz), 4.78 (t, 2H,  $J = 2$  Hz), 6.26 (s, 1H), 6.91–7.66 (m, 7H);  $m/z$  394, 392, 390 ( $\text{M}^+$ ). Anal. Calcd for  $\text{C}_{19}\text{H}_{12}\text{Cl}_2\text{O}_5\text{S}$ : C, 58.46; H, 3.07. Found: C, 58.59; H, 3.27.

Scheme 1



potential sites for [3,3] sigmatropic rearrangement: an aryl propargyl ether moiety and a vinyl propargyl sulfide moiety. All the substrates underwent [3,3] sigmatropic rearrangement at the vinyl propargyl sulfide moiety to give thiopyrano-[3,2-*c*][1]benzopyran-5(2*H*)-ones. The formation of products **4a–d** from substrates **3a–d** may be easily explained by the [3,3] sigmatropic rearrangement of **3a–d** and rapid enolization to form the intermediate allenylene-thiols **6a–d** followed by [1,5] hydrogen shift and 6*π*-electrocyclic ring closure to give the products **4a–d** (Scheme 2).

Scheme 2



Substrates **3a–d** on thermal rearrangement by heating in chlorobenzene (132 °C) could have yielded other types of products, e.g. 3-aryloxymethyl-2-methylthieno[3,2-*c*]coumarin<sup>12</sup> or 4'-aryloxybut-2'-ynyl-4-mercaptocoumarin<sup>13</sup> (by 1,3-radical shift) as a consequence of the usual course of

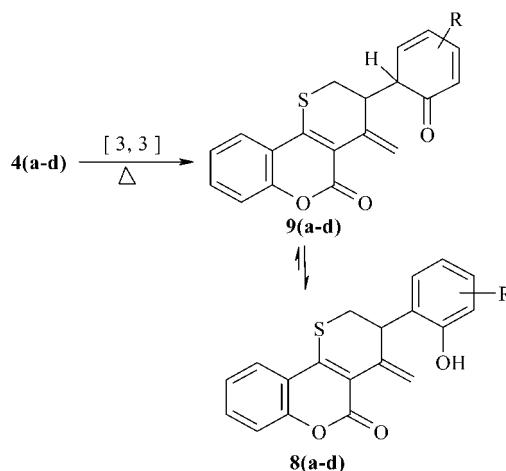
(11) **Compound 4a**: mp 186 °C; yield 75%; UV (EtOH)  $\lambda_{\text{max}}$  220, 360 nm; IR (KBr)  $\nu_{\text{max}}$  1690, 1580, 1240 cm<sup>-1</sup>; <sup>1</sup>H NMR (300MHz)  $\delta$  3.47 (d, 2H, *J* = 6Hz), 5.18 (d, 2H, *J* = 1.0 Hz), 6.26 (tt, 1H, *J* = 1, 6 Hz), 6.91–7.85 (m, 7H); *m/z* 394, 392, 390 (M<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>3</sub>S: C, 58.46; H, 3.07. Found: C, 58.31; H, 3.17.

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rearrangement. It is remarkable to note that all the substrates **3a–d** studied in this instance regioselectively afforded exclusively products **4a–d**.

As products **4a–d** possess the aryl allyl ether moiety, these were subjected to heating in refluxing 1,2-dichlorobenzene in the presence of *N,N*-diethylaniline for 12–14 h to give phenolic products **8a–d**. These were characterized from their elemental analyses and spectral data.<sup>14</sup> Here again the isolation of phenolic product is quite unusual. In all other previous instances either the formation of cyclic products or the rearranged endo cyclic phenolic products were reported.<sup>9,15</sup> The formation of products **8a–d** from **4a–d** is easily explained by a [3,3] sigmatropic rearrangement followed by enolization (Scheme 3).

Scheme 3



Our target was to synthesize polyheterocyclic compounds. We had earlier used pyridine hydrotribromide<sup>16</sup> and hexamethylenetetramine hydrotribromide<sup>17</sup> for regioselective cyclization of *o*-cyclohex-2-enyl phenols. We therefore treated products **8a–d** with 1 equiv of pyridine hydrotribromide in chloroform at 0–5 °C for 0.5 h to afford [6,6]pyranothio-pyrans<sup>18</sup> **10a–d** in almost quantitative yield. The formation of products **10a–d** from **8a–d** is easily explained by the formation of a cyclic bromonium ion **11a–d** followed by a “6-endo” cyclization (Scheme 4).

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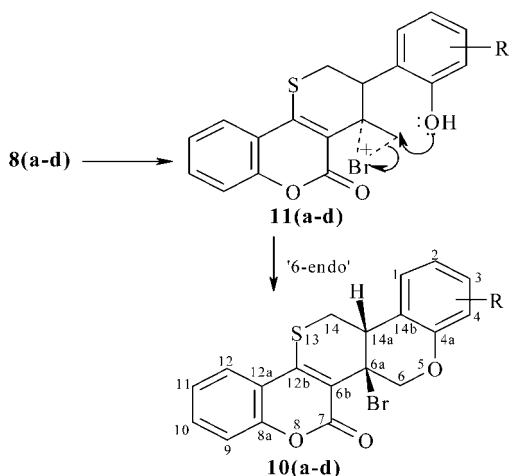
(14) **Compound 8a**: mp 198 °C; yield 75%; UV (EtOH)  $\lambda_{\text{max}}$  220, 274, 334 nm; IR (KBr)  $\nu_{\text{max}}$  3390, 2910, 1670, 1600, 1210 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  3.33 (dd, *J* = 3.3, 12.6 Hz, 1H, SCH<sub>2</sub>), 3.62 (dd, *J* = 7.1, 12.6 Hz, 1H, SCH<sub>2</sub>), 4.40 (dd, *J* = 3.3, 7.1 Hz, 1H), 5.38 (s, 1H, =CH<sub>2</sub>), 5.79 (s, 1H, =CH<sub>2</sub>), 6.75–6.86 (m, 2H, ArH) 7.28–7.33 (m, 2H, ArH), 7.50–7.55 (m, 1H, ArH), 7.72–7.75 (m, 1H, ArH); MS *m/z* 394, 392, 390 (M<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>3</sub>S: C, 58.46; H, 3.07. Found: C, 58.32; H, 3.19.

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**Scheme 4**



The stereochemistry of the ring fusion of the cyclic system can only be surmised from molecular models (Dreiding Model) which show a strain free *cis*-arrangement.

In conclusion, all four substrates gave single products in each of the three steps used for the regioselective synthesis of the [6,6]pyranothiopyrans. This presents a simple synthesis of this type of ring system.

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**Supporting Information Available:** Experimental results for **3b-d**, **4b-d**, **8b-d**, and **10b-d**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(18) **Compound 10a**: mp 168 °C; yield 93%; UV (EtOH)  $\lambda_{\text{max}}$  219, 280 nm; IR (KBr)  $\nu_{\text{max}}$  2910, 1700, 1190  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  2.87 (dd,  $J = 11.5, 13.1$  Hz, 1H,  $\text{SCH}_2$ ), 3.27 (dd,  $J = 4.2, 13.1$  Hz, 1H,  $\text{SCH}_2$ ), 3.65 (d,  $J = 9.9$  Hz, 1H,  $-\text{OCH}_2$ ), 4.12 (dd,  $J = 4.2, 11.5$  Hz, 1H), 4.80 (d,  $J = 9.9$  Hz, 1H,  $-\text{OCH}_2$ ), 7.12–7.36 (m, 4H, ArH), 7.58–7.81 (m, 2H, ArH);  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  29.05 ( $\text{C}_{14}$ ), 34.78 ( $\text{C}_6$ ), 48.15 ( $\text{C}_{14a}$ ), 88.06 ( $\text{C}_{6a}$ ), 116.18 ( $\text{C}_{14b}$ ), 117.33 ( $\text{C}_9$ ), 117.74 ( $\text{C}_{6b}$ ), 118.08 ( $\text{C}_{12a}$ ), 123.46 ( $\text{C}_{12}$ ), 124.69 ( $\text{C}_{11}$ ), 125.38 ( $\text{C}_1$ ), 127.23 ( $\text{C}_4$ ), 130.23 ( $\text{C}_3$ ), 130.64 ( $\text{C}_2$ ), 133.38 ( $\text{C}_{10}$ ), 151.79 ( $\text{C}_{12b}$ ), 152.56 ( $\text{C}_{8a}$ ), 156.04 ( $\text{C}_{4a}$ ), 157.22 ( $\text{C}_7$ ); MS  $m/z$  468, 470, 472, 474 ( $\text{M}^+$ ). Anal. Calcd for  $\text{C}_{19}\text{H}_{11}\text{BrCl}_2\text{O}_3\text{S}$ : C, 48.71; H, 2.35. Found: C, 48.52; H, 2.29.