
S. K. Ghosh

Department of Chemistry, Krishnath College, Berhampore, Marshallabad 742101, West Bengal, India.

Abstract: The starting materials 4-[4-aryloxybut-2-ynylthio][1]benzopyran-2-ones 5(a-f) for this purpose were synthesised in 75-87% yield by the phase transfer-catalysed alkylation of 4-mercaptocoumarin 3 with 1-chloro-4-aryloxybut-2-ynyl chloride (BTEAC) gave the single S-alkylated product 5(a-f) in 75-87% yield.

Keywords: [2,3] sigmatropic rearrangement, 4-mercaptocoumarin, 1-chloro-4-aryloxybut-2-ynyl chloride, Regioselective, Phase-transfer catalyst.

I. Introduction

Thienocoumarins and other Coumarin derivatives are well known for their anti-inflammatory, antipyretic, antiallergic, antitermite, anticoagulant, antihelmintic and antioxidant properties. The formation of five membered heterocyclic ring through [2,3] sigmatropic rearrangement was reported by Thyagarajan and majumdar. This simple and exceedingly facile reaction for the creation of five membered heterocyclic ring with sulphur atom prompted us to synthesise 3-(aryloxyacetyl)-2,3-dihydrothieno[3,2-c][1]benzopyran-4-ones with high yield and atom economy under very mild condition through treatment with metachloroperoxybenzoic acid followed by refluxing in carbon tetrachloride.

II. Result and Discussion.

4-Hydroxycoumarin 1 was dissolved in pyridine and 4-toluene sulfonyl chloride was added to it with constant stirring at room temperature to give a solid mass. This solid mass was filtered and dried. Thus tosyl derivative 2 of 4-hydroxycoumarin derivative was obtained.

The tosyl derivative was dissolved in ethanol and NaSH was added to it at 0-10°C with constant stirring. The reaction mixture became a clear solution in ~2 h. Then alcohol was evaporated and conc. HCl was added to it (PH ~ 2) when a white solid appeared. This was extracted with chloroform and the chloroform extract was washed with H₂O and dried (Na₂SO₄). Chloroform was evaporated and 4-mercaptocoumarin 3 was obtained. This was used in the subsequent reaction without further purification. (Scheme 1)

When a two phase mixture of 4-mercaptocoumarin 3, 1-chloro-4-aryloxybut-2-ynyl chloride (BTEAC) gave the single S-alkylated product 5(a-f) in 75-87% yields. (Scheme 2)

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Compound 5(a-f) were characterised from their elemental analyses and spectroscopic data. Substrates 5(a-f) were oxidised to the corresponding sulfoxides 6(a-f) by slow addition of m-chloroperoxybenzoic acid in chloroform at 0-5°C over 30 minutes. Formation of a new product was indicated by a single spot (TLC monitoring) and disappearance of the starting sulphide. The sulfoxides 6(a-f) are quite unstable. They seem to rearrange even during work up of the reaction mixture. Therefore, no attempt was made to characterise them. They were directly subjected to thermal rearrangement without further purification. The sulfoxides 6(a-f) were refluxed in carbon tetrachloride to get the compounds 7(a-f) in 70-75% yield. (Scheme 3)

The characterisation of 7(a-f) were done using the same principle of elemental analyses and spectroscopic data as our preceeding short communication paper. To test the generality of the rearrangement, the thermal rearrangement of six sulfoxides 6(a-f) were studied and similar result was obtained in every cases like previous observation. Every sulfoxide shows perfect regioselectivity with high yield and atom economy. Thus this is very efficient eco-friendly synthesis of sulphur heterocycles.

The formation of products 7(a-f) from the sulfoxides 6(a-f) may be rationalised by the initial [2,3] sigmatropic rearrangement of the sulfoxides to give the intermediate allenylsulphenates followed by [3,3] sigmatropic rearrangement and enolisation leading to the intermediate having an enone moiety favourably.
juxtaposed to an –SH function for an internal Michael addition for the thiol to the enone moiety to give 7(a-f).\(^{11,12}\) (Scheme 4)

III. Conclusion

It is important to note that thermal rearrangement of six sulfoxides 6(a-f) exhibits excellent regioselective ring closure. Therefore, this is a general eco-friendly regioselective method for the synthesis of 3-(aryloxyacetyl)-2,3-dihydrothieno[3,2-c][1]benzopyran-4-ones in excellent yields. This is also an example of the application of sulfoxide rearrangement in heterocyclic substrates to yield polyheterocycles.

IV. Experimental Section:

General Procedures: Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer (\(\nu_{\text{max}}\) in \(\text{cm}^{-1}\)) using KBr as solvent. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer (wavelength in nm). \(^1\)H NMR(300 MHz, 500 MHz) spectra were recorded on a Bruker DPX-300 and Bruker DPX-500 spectrometer in CDCl\(_3\) with TMS as internal standard. Elemental analyses and mass spectra were recorded on a JEOL JMS600 instrument. \(^1\)H spectra were recorded at Indian Institute of Chemical Biology, Kolkata and Bose Institute, Kolkata. Silica gel (60-120 mesh), Spectrochem, India was used for chromatographic separation. Silica gel GE-Merck(India) was used for TLC. Petroleum ether refers to the fraction boiling between 60\(^\circ\)C and 80\(^\circ\)C.

General procedure for the preparation of 4-mercaptocoumarin:

4-Hydroxycoumarin 1 (25 mmol) was dissolved in pyridine (5 ml). Then 4-toluenesulfonyl chloride (5 g, 26.3 mmol) was added to it with constant stirring (30 min.) at room temperature to give a solid mass. It was poured into ice water. The crystalline solid was then filtered and dried. Thus tosyl derivative 2 of 4-hydroxycoumarin derivative was obtained.

**Compound 2**: m.p. 114\(^\circ\)C; yield 90%; UV(\(\text{EtOH}\))\(\nu_{\text{max}}\): 217, 274, 314 nm; IR(KBr)\(\nu_{\text{max}}\): 1740, 1620, 1250 cm\(^{-1}\); \(^1\)H NMR(300MHz)\(\delta\): 2.47(s,3H), 6.31(s, 1H), 7.24-7.91 (m, 8H); m/z 316 (M+); Anal. Calcd. For C\(_{16}\)H\(_{12}\)O\(_5\)S: C, 60.76; H, 3.80 found C, 60.86; H, 3.72%.

The tosyl derivative 2 (13 mmol) was dissolved in ethanol (100 ml). Then NaSH (1.5 g, 27 mmol) was added to it at 0-10\(^\circ\)C with constant stirring. The reaction mixture became a clear solution in ~2h. The alcohol was evaporated and conc. HCl was added to it (PH ~ 2) when a white solid appeared. This was extracted with chloroform (2x50 ml) and the chloroform extract was washed with H\(_2\)O (2x50ml) and dried (Na\(_2\)SO\(_4\)). Chloroform was evaporated and 4-mercaptocoumarin 3 was obtained. This was used in the subsequent reaction without further purification.

V. General procedure for the preparation of sulphides 5(a-f):

To a mixture of 4-mercaptocoumarin 3 (6.2 mmol) and 4(a-f) (9 mmol) in chloroform (50 ml) was added a solution of BTEAC (0.25g, 0.9 mmol) in 1% NaOH (50 ml) and the mixture was stirred for a period of 4h. It was then diluted with H\(_2\)O (125 ml) and extracted with chloroform (2x50 ml). The chloroform extract was washed successively with 2(N) HCl (2x50ml), brine (2x50ml), H\(_2\)O (2x50ml) and dried (Na\(_2\)SO\(_4\)). The solvent was removed and the residual mass was chromatographed over silicagel. All the compounds 5(a-f) were obtained when the column was eluted with 40% ethylacetate in pet-ether solution.
**VI. General procedure for the preparation of compounds 7(a-f):**

M-Chloroperbenzoic acid (50%, 105mg, 0.61 mmol) in chloroform (20 ml) at 0°C over a period of 30 min. The reaction mixture was stirred for additional 30 min. Then the chloroform solution was washed with saturated sodium carbonate solution (3x20ml) to remove organic acid followed by brine (3x20 ml), and dried (Na₂SO₄). The solvent was removed and the residue was refluxed in carbon tetrachloride (25 ml) for 4h. Then carbon tetrachloride was removed and a viscous liquid was obtained. It was then chromatographed over silicagel using 30% ethylacetate in pet-ether solution as eluent to give the solid compounds 7(a-f).

**Compound 7a:** m.p. 138°C; yield 70%; UV(EtOH)λmax: 217, 270, 329 nm; IR(KBr): C=O; yield 82%; UV(EtOH)λmax: 1715, 1700, 1590 1250 cm⁻¹; ¹H NMR(300MHz) δ: 3.37(dd, 1H, J=9,12Hz), 3.82(dd, 1H, J=6,12Hz), 4.91(dd, 1H, J=6,9Hz), 4.99(d, 1H, J=15Hz), 4.99(d, 1H, J=15Hz), 6.93-7.58 (m, 9H); m/z 338 (M⁺); Anal. Calcd. For C₁₉H₁₈ClO₂S: C, 67.45; H, 4.14 found C, 67.58; H, 4.23%.

**Compound 7b:** m.p. 144°C; yield 73%; UV(EtOH)λmax: 218, 269, 330 nm; IR(KBr): C=O; yield 79%; UV(EtOH)λmax: 1710, 1695, 1585, 1240 cm⁻¹; ¹H NMR(300MHz) δ: 2.29(s, 3H), 3.43(dd, 1H, J=9,12Hz), 3.81(dd, 1H, J=6,12Hz), 4.91(dd, 1H, J=6,9Hz), 4.45(d, 1H, J=15Hz), 4.98(d, 1H, J=15Hz), 6.93-7.58 (m, 8H); m/z 352 (M⁺); Anal. Calcd. For C₂₀H₂₀ClO₂S: C, 68.18; H, 4.54 found C, 68.31; H, 4.37%.

**Compound 7c:** m.p. 162°C; yield 75%; UV(EtOH)λmax: 218, 269, 315 nm; IR(KBr): C=O; yield 85%; UV(EtOH)λmax: 1710, 1695, 1590, 1250 cm⁻¹; ¹H NMR(300MHz) δ: 2.26(s, 3H), 3.71(dd, 1H, J=9,12Hz), 3.80(dd, 1H, J=6,12Hz), 4.86(dd, 1H, J=6,9Hz), 4.93(brs, 2H), 6.78-7.58 (m, 8H); m/z 352 (M⁺); Anal. Calcd. For C₂₀H₂₀ClO₂S: C, 68.18; H, 4.54 found C, 68.31; H, 4.63%.

**Compound 7d:** m.p. 168°C; yield 70% UV(EtOH)λmax: 218, 269, 315 nm; IR(KBr): C=O; yield 76%; UV(EtOH)λmax: 1730, 1700, 1610, 1260 cm⁻¹; ¹H NMR(300MHz) δ: 3.67(dd, 1H, J=9,12Hz), 3.98(dd, 1H, J=6,12Hz), 5.08(dd, 1H, J=6,9Hz), 4.86(d, 1H, J=15Hz); 4.98(d, 1H, J=15Hz), 6.91-8.04; (m, 8H); m/z 374, 372 (M⁺); Anal. Calcd. For C₂₁H₂₁ClO₂S: C, 61.29; H, 3.49 found C, 61.18; H, 3.63%.

**Compound 7e:** m.p. 139°C; yield 74% UV(EtOH)λmax: 217, 270, 329 nm; IR(KBr): C=O; yield 75%; UV(EtOH)λmax: 1730, 1700, 1610, 1260 cm⁻¹; ¹H NMR(300MHz) δ: 3.73(dd, 1H, J=9,12Hz), 3.85(dd, 1H, J=6,12Hz), 4.80(dd, 1H, J=6,9Hz), 4.93(d, 1H, J=15Hz), 5.02(d, 1H, J=15Hz), 6.86-7.62; (m, 8H); m/z 374, 372 (M⁺); Anal. Calcd. For C₂₁H₂₁ClO₂S: C, 61.29; H, 3.49 found C, 61.43; H, 3.26%.

**Compound 7f:** m.p. 164°C; yield 72% UV(EtOH)λmax: 218, 273, 320 nm; IR(KBr): C=O; yield 77%; UV(EtOH)λmax: 1725, 1710, 1605, 1250 cm⁻¹; ¹H NMR(300MHz) δ: 3.82(dd, 1H, J=9,12Hz), 3.86(dd, 1H, J=6,12Hz), 4.92(dd, 1H, J=6,9Hz), 4.98(d, 1H, J=15Hz), 5.04(d, 1H, J=15Hz), 6.87-7.59; (m, 7H); m/z 410, 408, 406 (M⁺); Anal. Calcd. For C₂⁰H₂₂Cl₂O₃S: C, 56.15; H, 2.95 found C, 56.37; H, 3.09%.

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