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[2,3] Sigmatropic rearrangement: An Eco-friendly Expedient Avenue For The Synthesis Of 3-(aryloxyacetyl)-2,3-dihydrothieno[3,2-*c*][1]benzopyran-4-ones.

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***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-yne **4**(a-f). **5**(a-f) were subjected to [2,3] sigmatropic or sulfoxide rearrangement to give 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.*

***Keywords**: [2,3]sigmatropicrearrangement,4-mercaptocoumarin, 1-chloro-4-aryloxybut-2-yne ,Regioselective, Phase-transfer catalyst.*

I. Introduction

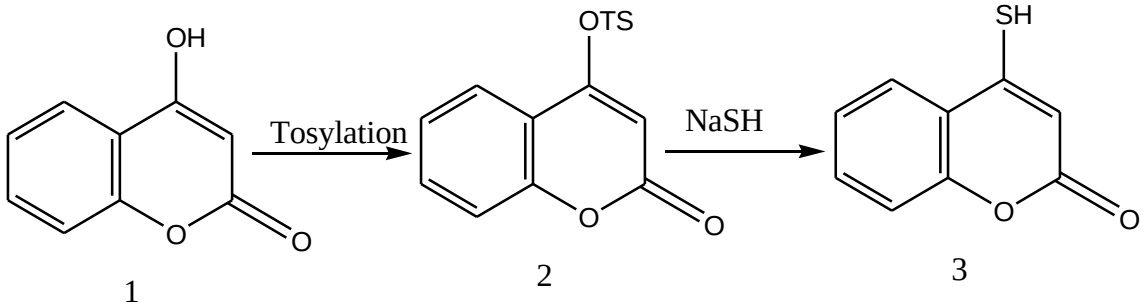
Thienocoumarins and other Coumarin derivatives are well known for their anti-inflammatory, antipyretic, antiallergic, antitermite, anticoagulant, antihelmintic and antioxidant properties.[1-6] The formation of five membered heterocyclic ring through [2,3] sigmatropic reaarangement was reported by Thyagarajan 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 **7**(a-f) starting from 4-[4-aryloxybut-2-ynylthio][1]benzopyran-2-ones, **5**(a-f).[7,8]

The tosyl derivative of 4-hydroxycoumarin was first prepared by dissolving 4-hydroxycoumarin in pyridine followed by addition of toluene-4-sulfonyl chloride with constant stirring under room temperature. Tosyl derivative, on treatment with NaSH in ethanol at 0-10^{0}C furnished 4-mercaptocoumarin. 4-mercaptocoumarin was used as starting material for the subsequent reactions of this study.

II. Result and Discussion.

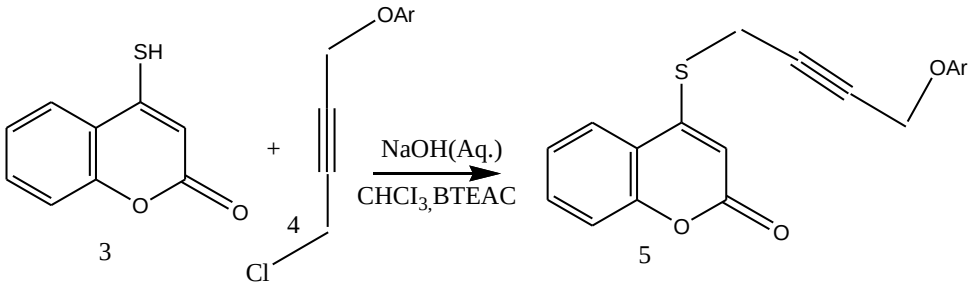
4-Hydroxycoumarin **1** was dissolved in pyridine and 4-toluenesulfonylchloride was added to it with constant stirring at room temperature to give a solid mass. The solid mass was poured into ice water. The crystalline solid was then filtered and dried. Thus tosyl derivative **2** of 4-hydroxycoumarin derivative was obtained.

The tosyl derivative was dissolved in ethanol and NaSH was added to it at 0-10^{0}C with constant stirring. The reaction mixture became a clear solution in ~2h. Then alcohol was evaporated and conc. HCI was added to it (PH ~ 2) when a white solid appeared. This was extracted with chloroform and the chloroform extract was washed with H_2O and dried (Na_2SO_4). Chloroform was evaporated and 4-mercaptocoumarin **3** was obtained. This was used in the subsequent reaction without further purification**. (Scheme1)**



1 2 3

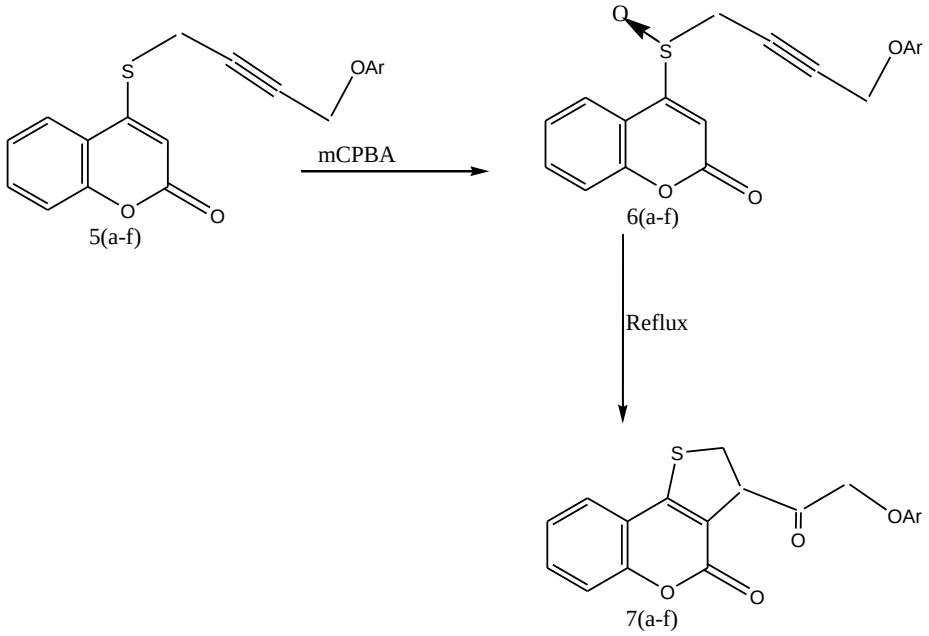
When a two phase mixture of 4-mercaptocoumarin **3**, 1-chloro-4-aryloxybut-2-yne **4**(a-f), chloroform and very dilute solution of aq. NaOH was stirred at r.t. in the presence of benzyltriethylammonium chloride(BTEAC) gave the single S-alkylated product **5(**a-f) in 75-87% yields**.(Scheme 2)**[9,10]



3 4 5

	Ar
a	C_6H_5
b	2-MeC_6H_4
c	4-MeC_6H_4
d	2-ClC_6H_4
e	4-ClC_6H_4
f	2,4-$Cl_2C_6H_3$

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^{0}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)**

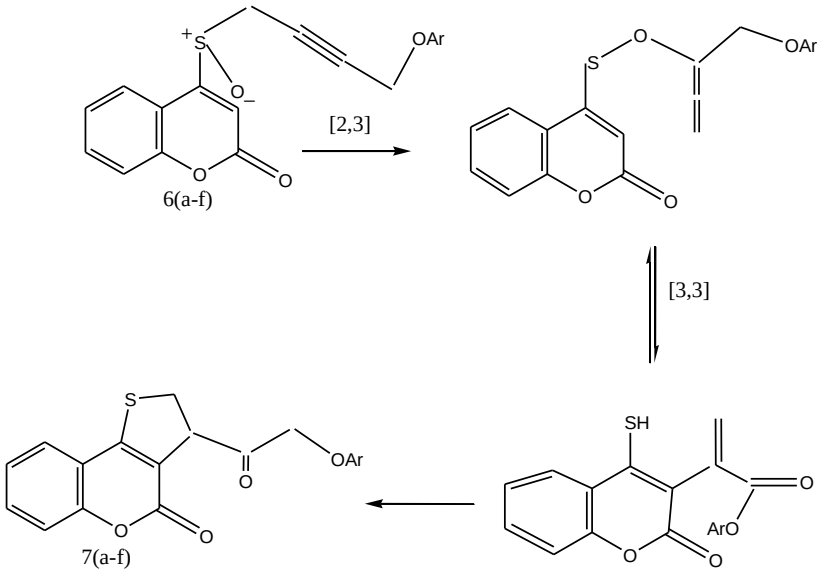


The characterisation of **7**(a-f) were done using the same principle of elemental analyses and spectroscopic data as our preceeding short communication paper.[11]

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.[12] 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 a –SH function for an internal Michael addition for the thiol to the enone moiety to give **7**(a-f).[11,12](**Scheme4)**



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 (v_{max} in cm^{-1}) using KBr as solvent. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer(wavelength in nm). ^1H NMR(300 MHz, 500 MHz) spectra were recorded on a Bruker DPX-300 and Bruker DPX-500 spectrometer in $CDCI_3$ with TMS as internal standard. Elemental analyses and mass spectra were recorded on a JEOL JMS600 instrument. ^1H 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 G[E-Merck(India)] was used for TLC. Petroleum ether refers to the fraction boiling between 60^0C and 80^0C.

General procedure for the preparation of 4-mercaptocoumarin:

4-Hydroxycoumarin 1 (25 mmol) was dissolved in pyridine (5 ml). Then 4-toluenesulfonylchloride (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^{o}C; yield 90%; UV(EtOH)λ_{max}:217, 274,314 nm; IR(KBr)Υ_{max} :1740, 1620, 1250 cm^{-1}; ^1H NMR(300MHz)δ: 2.47(s,3H), 6.31(s, 1H), 7.24-7.91 (m, 8H); m/z 316 (M+); Anal. Calcd. For $C_{16}H_{12}O_5S$: 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 $0\text{-}10^0$C with constant stirring. The reaction mixture became a clear solution in ~2h. The alcohol was evaporated and conc. HCI was added to it (PH ~ 2) when a white solid appeared. This was extracted with chloroform (2x 50 ml) and the chloroform extract was washed with H_2O (3X 25 ml) and dried (Na_2SO_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_2O (125 ml) and extracted with chloroform (2x50 ml). The chloroform extract was washed successively with 2(N) HCI (2x50ml), brine (2x50ml), H_2O (2x50ml) and dried (Na_2SO_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.

Compound 5a : m.p. 108°C; yield 75%; UV(EtOH)λ_{max}:218, 271 nm; IR(KBr)Υ_{max} : 1690, 1580, 1230 cm^{-1}; ^1H NMR(300MHz)δ: 3.82 (t, 2H, J= 2Hz), 4.71(t, 2H, J= 2Hz), 6.28(s, 1H), 6.92-7.73 (m, 9H); m/z 322 (M+); Anal. Calcd. For $C_{19}H_{14}O_3S$: C, 70.80; H, 4.35 found C, 70.67; H, 4.19%.

Compound 5b : m.p. 128°C; yield 87%; UV(EtOH) λ_{max}: :218, 272 nm; IR(KBr) Υ_{max} : 1700, 1590, 1220 cm^{-1}; ^1H NMR(300MHz) δ : 2.22(s, 3H), 3.82(t,2H, J= 2Hz), 4.72 (t, 2H, J= 2Hz), 6.28(s, 1H), 6.82-7.68 (m, 8H); m/z 336 (M+); Anal. Calcd. For $C_{20}H_{16}O_3S$: C, 71.43; H, 4.76 found C, 71.57; H, 4.61%.

Compound 5c : m.p. 116°C; yield 76%; UV(EtOH) λ_{max}: :218, 272 nm; IR(KBr) Υ_{max} : 1700, 1590, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 2.24(s, 3H), 3.84(t,2H, J= 2Hz), 4.68 (t, 2H, J= 2Hz), 6.30(s, 1H), 6.81-7.67 (m, 8H); m/z 336 (M+); Anal. Calcd. For $C_{20}H_{16}O_3S$: C, 71.43; H, 4.76 found C, 71.59; H, 4.81%.

Compound 5d : m.p. 142°C; yield 85%; UV(EtOH) λ_{max}: :218, 273 nm; IR(KBr) Υ_{max} : 1700, 1590, 1220 cm^{-1}; ^1H NMR(300MHz) δ : 3.82 (t, 2H, J= 2Hz), 4.80(t, 2H, J= 2Hz), 6.26(s, 1H), 6.87-7.67 (m, 8H); m/z 358, 356 (M+); Anal. Calcd. For $C_{19}H_{13}ClO_3S$: C, 64.04; H, 3.65 found C, 64.21; H, 3.53%.

Compound 5e : m.p. 106°C; yield 75%; UV(EtOH) λ_{max}: :218, 273 nm; IR(KBr) Υ_{max} : 1710, 1590, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 3.85 (t, 2H, J= 2Hz), 4.75(t, 2H, J= 2Hz), 6.30(s, 1H), 6.80-7.78 (m, 8H); m/z 358, 356 (M+); Anal. Calcd. For $C_{19}H_{13}ClO_3S$: C, 64.04; H, 3.65 found C, 64.27; H, 3.48%.

Compound 5f : m.p. 155°C; yield 82%; UV(EtOH) λ_{max}: :218, 273 nm; IR(KBr) Υ_{max} : 1700, 1590, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 3.81 (t, 2H, J= 2Hz), 4.78(t, 2H, J= 2Hz), 6.26(s, 1H), 6.91-7.66 (m, 7H); m/z 394, 392, 390 (M+); Anal. Calcd. For $C_{19}H_{12}Cl_2O_3S$: C, 58.46; H, 3.07 found C, 58.59; H, 3.27%.

VI. General procedure for the preparation of compounds 7(a-f):

M-Chloroperoxybenzoic acid (50%, 105mg, 0.61 mmol) in chloroform(20 ml) was slowly added to a well-stirred solution of the sulphides **5**(a-f) (0.3 mmol) in chloroform (20 ml) at 0-5^{0}C over a period of 30 min. The reaction mixture was stirred for additional 30 min. Then the chloform solution was washed with saturated sodium carbonate solution (3x20ml) to remove organic acid followed by brine (3x20 ml), H_2O (3x20 ml),and dried (Na_2SO_4). The solvent was removed and the residue was refluxed in carbon tetrachloride (25ml) 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)λ_{max}: 217, 270, 329 nm; IR(KBr)Υ_{max} : 1715, 1700, 1590 1250 cm^{-1}; ^1H NMR(300MHz)δ: 3.73(dd, 1H, J=9,12Hz), 3.82(dd, 1H, J= 6,12Hz), 4.86(dd, 1H, J= 6,9Hz), 4.95(d, 1H,J= 15Hz) 4.99(d, 1H, J= 15Hz), 6.93-7.58(m, 9H); m/z 338 (M+); Anal. Calcd. For $C_{19}H_{14}O_4S$: C, 67.45; H, 4.14 found C, 67.58; H, 4.23%.

Compound 7b : m.p. 144°C; yield 73%; UV(EtOH)λ_{max}: 218, 269, 330 nm; IR(KBr)Υ_{max} : 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 $C_{20}H_{16}O_4S$: C, 68.18; H, 4.54 found C, 68.31; H, 4.37%.

Compound 7c : m.p. 162°C; yield 75%; UV(EtOH)λ_{max}: 218, 269, 315 nm; IR(KBr)Υ_{max} : 1710, 1695, 1600, 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= 6,9 Hz), 4.93(brs, 2H), 6.78-7.58 (m, 8H); m/z 352 (M+); Anal. Calcd. For $C_{20}H_{16}O_4S$: C, 68.18; H, 4.54 found C, 68.031; H, 4.63%.

Compound 7d : m.p. 168°C; yield 70% UV(EtOH)λ_{max}: 217, 269, 315 nm; IR(KBr)Υ_{max} : 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 $C_{19}H_{13}ClO_4S$: C, 61.29; H, 3.49 found C, 61.18; H, 3.63%.

Compound 7e : : m.p. 139°C; yield 74% UV(EtOH)λ_{max}: 217, 270, 329 nm; IR(KBr)Υ_{max} : 1730, 1700, 1610, 1240 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 $C_{19}H_{13}ClO_4S$: C, 61.29; H, 3.49 found C, 61.43; H, 3.26%.

Compound 7f : : m.p. 164°C; yield 72% UV(EtOH)λ_{max}: 218, 273, 320 nm; IR(KBr)Υ_{max} : 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 $C_{19}H_{12}Cl_2O_4S$: C, 56.15; H, 2.95 found C, 56.37; H, 3.09%.

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