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# Thio-Claisen Rearrangement: An expedient avenue for the synthesis of 2*H*-thiopyrano [3,2-*c*][1]benzopyran-5-ones.

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***Abstract**: 4-Propargylthio[1]benzopyran-5-ones **5**(a-d) were heated in chlorobenzene to furnish 2H-thiopyrano[3,2-c][1]benzopyran-5-ones **6**(a-d) with high yield and atom economy. In all cases regioselectivity was maintained. Substrates **5**(a-d) were prepared using phase-trasfer catalysed alkylation process rather than classical alkylation to get higher yield under mild condition.*

***Keywords**: Thio-Claisen rearrangement, Coumarin derivatives, Propargyl halides,Regioselective, Phase-transfer catalyst*

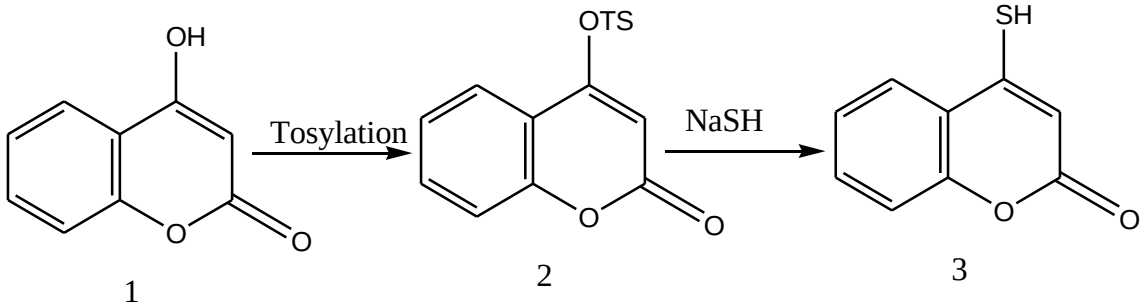
## I. Introduction

Biological activity of Coumarin and coumarin derivatives are quite well known to us. They contain various physiological activities like antitermite activity and antioxidant properties etc. Coumarin derivatives along with their antithelmintic, hypnotic,anticoagulant properties are very important.[1-3] The biological activity of coumarin derivatives prompted us to undertake the study of thio-Claisen rearrangement of 4-Propargylthio[ 1 ]benzopyran-5-ones **5**(a-d). The tosyl derivative of 4-hydroxycoumarin was prepared by dissolving 4-hydroxycoumarin in pyridine followed by addition of toluene-4-sulfonyl chloride with constant stirring under ordinary condition. 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.

## II. Result and Discussion.

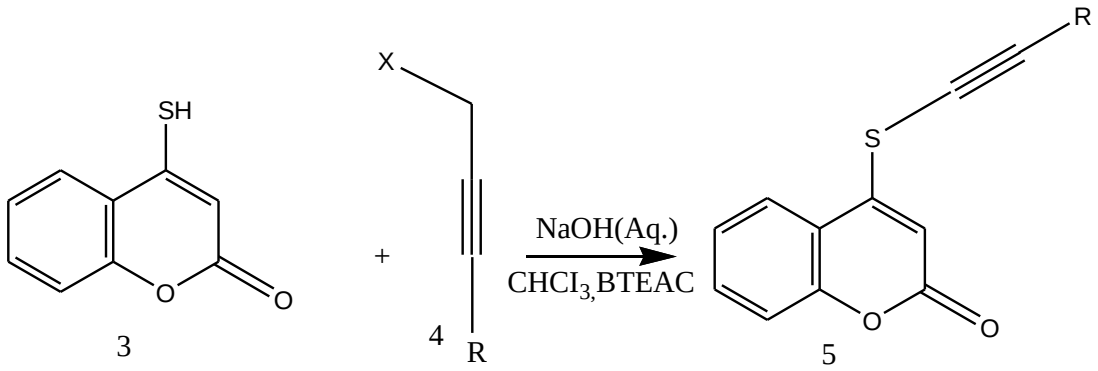
4-Hydroxycoumarin **1** was dissolved in pyridine and 4-toluenesulfonylchloride was added to it with constant stirring at room temperature to give a solid mass. It was poured into ice water. The crystalline solid was then filtered and dried. Thus tosyl derivative **2** of 4-hydroxycoumarin derivative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



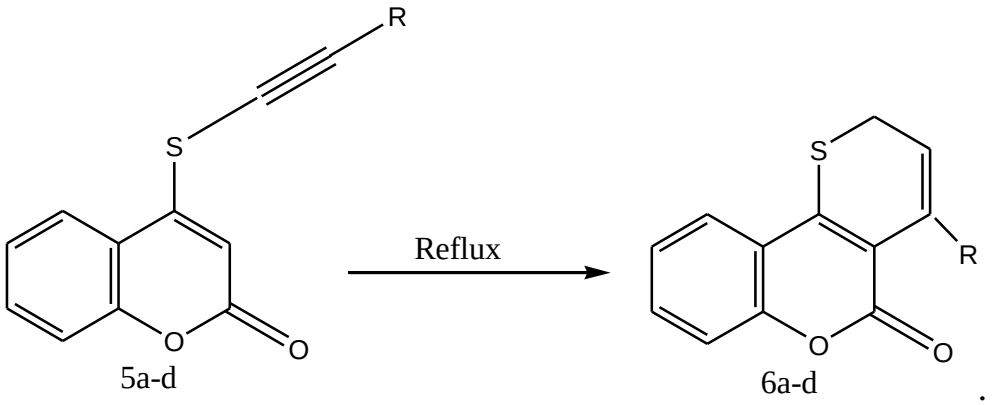

1 2 3

When a two phase mixture of 4-mercaptocoumarin **3**, propargyl halides **4**(a-d), 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-d) in 75-85% yields**.(Scheme 2)**[4,6]




| | X | R |
|---|---|---|
| a | Br | H |
| b | CI | $CH_2CI$ |
| c | Cl | $CH_2OH$ |
| d | CI | $CH_2OAC$ |

Compound **5**(a-d) were characterised from their elemental analyses and spectroscopic data as our previous short communicated paper[8]. Substrates **5**(a-d) were refluxe in chlorobenzene for ½-4 h to give solid compounds **6**(a-d) in 75-85 % yields**.(Scheme 3)**

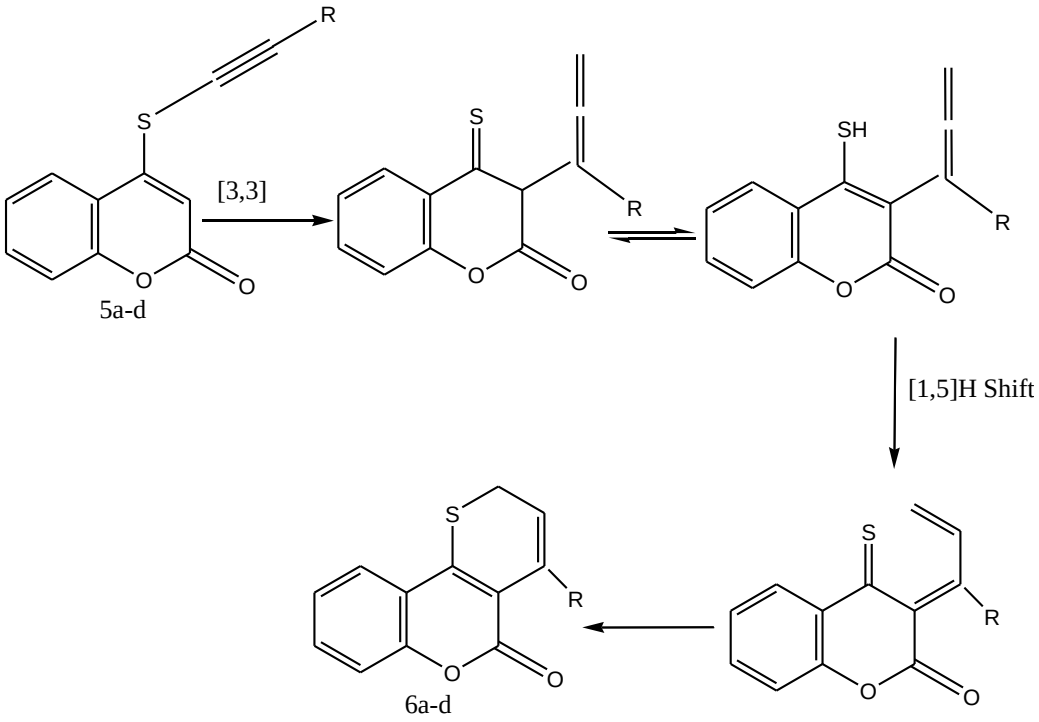



The characterisation of **6**a have been done in our preceeding paper.[8]The characterisation of **6**(b-d )were done using the same principle of elemental analyses and spectroscopic data as our preceeding short communication paper.[8,9]

To test the generality of the rearrangement, the thermal rearrangement of four sulphides **5**(a-d) were studied and similar result was obtained in every cases like previous observation.[5,7] Every sulphide shows perfect regioselectivity with high yield and atom economy. Thus, this is a very eco-friendly synthesis of sulphur heterocycles.

To test the effect of catalyst on this rearrangement, every sulphide was heated in presence of acid(p-toluene sulfonic acid) and base ( pyridine ) but no product other than **6(**a-d) was obtained.

Mechanistic rationalisation of formation of **6** from **5** involves a [3,3] sigmatropic rearrangement at the vinyl propargyl sulphide segment of **5** leading to an allenyl intermediate. This intermediate undergoes tautomerisation, [1,5]H shift followed by electrocyclic ring closure to give **6.(Scheme4)**




## III. Conclusion

It is important to note that thermal rearrangement of four sufides **5**(a-d) exhibits excellent regioselective ring closure. Therefore, this is a general eco-friendly regioselective method for the synthesis of 2*H*-thiopyrano[3,2-*c*][1]benzopyran-5-ones in excellent yields.

## 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 ($\nu_{max}$ in $cm^{-1}$ ) 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 $CDCI_3$ 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 G[E-Merck(India)] was used for TLC.

**General procedure for the preparation of 4-mercaptocoumarin:**

4-Hydroxycoumarin (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)$\lambda_{max}$:217, 274,314 nm; IR(KBr)$\Upsilon_{max}$ :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 $C_{16}H_{12}O_5S$: C, 60.76; H, 3.80 found C, 60.86; H, 3.72%.

The tosyl derivative ( 13 mmol ) was dissolved in ethanol (100 ml ). Then NaSH (1.5 g, 27 mmol ) was added to it at 0-10$^0$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 was obtained. This was used in the subsequent reaction without further purification.

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

To a mixture of 4-mercaptocoumarin **3** ( 6 mmol ) and propargyl halides **4**(a-d) ( 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) HCl ( 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-d) were obtained when the column was eluted with 10% ethylacetate in benzene solution.

**Compound 5a :** m.p. 142$^o$C; yield 75%; UV(EtOH)$\lambda_{max}$:213, 273,295 nm; IR(KBr)$\Upsilon_{max}$ : 3240,1690, 1590, 1270 cm$^{-1}$; $^1$H NMR( 300MHz )$\delta$: 2.35(t,1H, J= 2Hz), 3.82 (d, 2H, J= 2Hz), 6.35(s, 1H), 7.15-7.70 (m, 4H); m/z 216 (M+); Anal. Calcd. For $C_{12}H_8O_2S$: C, 66.67; H, 3.70 found C, 66.45; H, 3.83%.

**Compound 5b :** m.p. 108$^o$C; yield 82%; UV(EtOH) $\lambda_{max}$: :212, 275,295 nm; IR(KBr) $\Upsilon_{max}$ : 1700, 1590, 1250 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 3.86(t,2H, J= 2Hz), 4.15 (t, 2H, J= 2Hz), 6.30(s, 1H), 7.26-7.69 (m, 4H); m/z 266, 264 (M+); Anal. Calcd. For $C_{13}H_9ClO_2S$: C, 59.09; H, 3.41 found C, 58.95; H, 3.57%.

**Compound 5c :** m.p. 118$^o$C; yield 75%; UV(EtOH) $\lambda_{max}$: :213, 273,296 nm; IR(KBr) $\Upsilon_{max}$ : 3400,1690, 1600, 1270 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 3.26(brs, 1H, $D_2O$ Exchangeable), 3.84(t,2H, J= 2Hz), 4.29 (t, 2H, J= 2Hz), 6.33(s, 1H), 7.26-7.69 (m, 4H); m/z 246 (M+); Anal. Calcd. For $C_{13}H_{10}O_3S$: C, 63.41; H, 4.06 found C, 63.57; H, 4.16%.

**Compound 5d :** m.p. 92$^o$C; yield 85%; UV(EtOH) $\lambda_{max}$: :213, 273,295 nm; IR(KBr) $\Upsilon_{max}$ : 1740, 1705, 1600, 1240 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 2.09(s, 3H), 3.83 (t, 2H, J= 2Hz), 4.68(t, 2H, J= 2Hz), 6.30(s, 1H), 7.26-7.69 (m, 4H); m/z 288 (M+); Anal. Calcd. For $C_{15}H_{12}O_4S$: C, 62.50; H, 4.17 found C, 62.33; H, 4.31%.

## VI. Rearrangement of sulphides 3(a-d) in chlorobenzene:

The sulphides **5**(a-d)( 1 mmol ) were refluxed in chlorobenzene( 3 ml ) for 4h except **5**a which was refluxed only for 30 min. It was then chromatographed over silicagel. Elution of the column with petroleum ether(60-80$^0$C) removed the chlorobenzene and the compounds **6**(a-d) were obtained by eluting the column with benzene

**Compound 6a** : m.p. 92$^o$C; yield 85%; UV(EtOH) $\lambda_{max}$: :214, 243,371 nm; IR(KBr) $\Upsilon_{max}$ : 1690, 1600, 1260 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 3.55(dd,2H, J= 1,6 Hz), 5.78 (dt, 1H, J= 6,9Hz), 6.80(dt, 1H,J= 1,9 Hz), 7.19-7.75 (m, 4H); m/z 216 (M+); Anal. Calcd. For $C_{12}H_8O_2S$: C, 66.67; H, 3.70 found C, 66.81; H, 3.57%.

**Compound 6b :** m.p. 138$^o$C; yield 79%; UV(EtOH) $\lambda_{max}$: :209, 246,355 nm; IR(KBr) $\Upsilon_{max}$ : 1690, 1600, 1270 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 3.42(d,2H, J= 6Hz), 4.81 (s, 2H), 6.10(t, 1H, J= 6Hz), 7.26-7.82 (m, 4H); m/z 266, 264 (M+); Anal. Calcd. For $C_{13}H_9ClO_2S$: C, 59.09; H, 3.41 found C, 59.25; H, 3.31%.

**Compound 6c :** m.p. 119$^o$C; yield 85%; UV(EtOH) $\lambda_{max}$: :216, 245,259 nm; IR(KBr) $\Upsilon_{max}$ : 3300,1680, 1590, 1250 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 3.45(d, 2H, J= 6Hz), 3.98(brs, 1H, $D_2O$ Exchangeable), 4.39(s,2H), 6.01(t, 1H, J= 6Hz), 7.26-7.85 (m, 4H); m/z 246 (M+); Anal. Calcd. For $C_{13}H_{10}O_3S$: C, 63.41; H, 4.06 found C, 63.29; H, 4.21%.

**Compound 6d :** m.p. 114$^o$C; yield 83%; UV(EtOH) $\lambda_{max}$: :212, 240,326 nm; IR(KBr) $\Upsilon_{max}$ : 1720, 1700, 1230 cm$^{-1}$; $^1$H NMR( 300MHz ) $\delta$ : 2.04(s, 3H), 3.42 (d, 2H, J= 6Hz), 5.20(s, 2H), 6.01(t, 1H, J= 6Hz), 7.26-7.83 (m, 4H); m/z 288 (M+); Anal. Calcd. For $C_{15}H_{12}O_4S$: C, 62.50; H, 4.17 found C, 62.31; H, 4.06%.

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