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Studies on thio-Claisen Rearrangement of propargyl vinyl sulphide moiety in presence of aryl propargyl ether segment to give 4-aryloxymethyl-2*H*- thiopyrano[3,2-*c*][1]benzopyran-5(2*H*)-ones.

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***Abstract**: The substrates 4-[4-aryloxybut-2-ynylthio][1]benzopyran-2-ones **5**(a-f) for this purpose were prepared in 70-87% 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 heated in chlorobenzene to furnish 4-aryloxymethyl-2H- thiopyrano[3,2-c][1]benzopyran-5(2H)-ones with high yield and atom economy.*

***Keywords**: 4- mercaptocoumarin, 1-chloro-4-aryloxybut-2-yne ,Regioselectivity, Phase-transfer catalyst, [3,3] sigmatropic rearrangement.*

I. Introduction

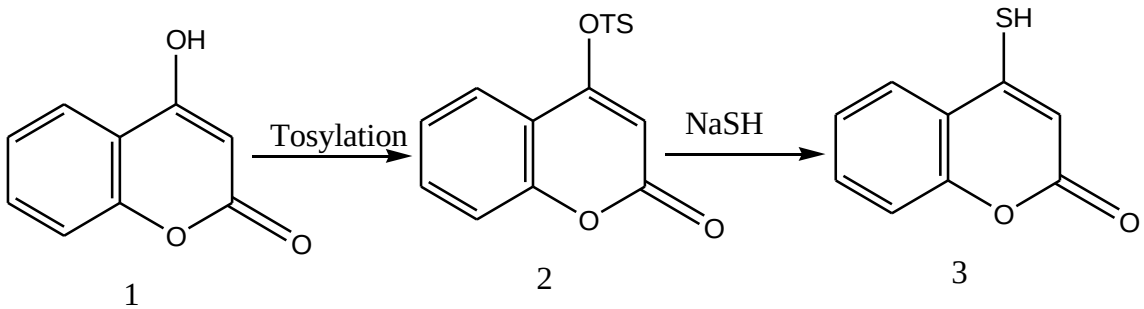
Coumarin and their derivatives are well known for their biological activities. They have antitermite, anticoagulant, antihelmintic and antioxidant properties.[1-3] Different physiological activity of coumarin and their derivatives created our interest to take part in the studies on thio-Claisen Rearrangement of Propargyl vinyl sulphide moiety in presence of aryl propargyl ether segment in **5**(a-f) to give 4-aryloxymethyl-2*H*-thiopyrano[3,2-*c*][1]benzopyran-5(2*H*)-ones **6**(a-f) starting from 4-[4-aryloxybut-2-ynylthio][1]benzopyran-2-ones, **5**(a-f).[4-7]We have also studied here the effect catalyst during the course of [3,3] sigmatropic rearrangement.

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.

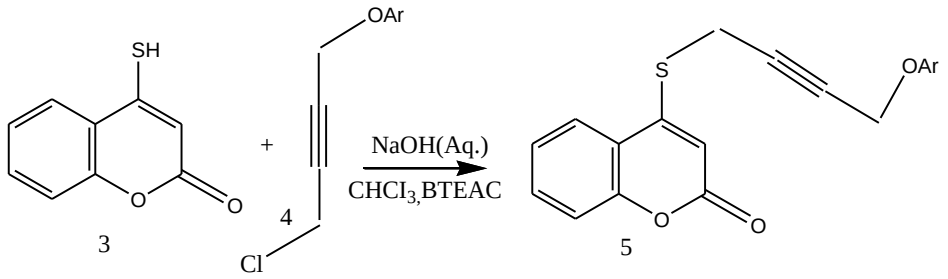
4-Hydroxycoumarin **1** was dissolved in pyridine and 4-toluenesulfonylchloride was added to it with constant stirring at room temperature to give a solid mass. The solid mass was poured into ice water. The crystalline solid was then filtered and dried. Thus tosyl derivative **2** of 4-hydroxycoumarin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

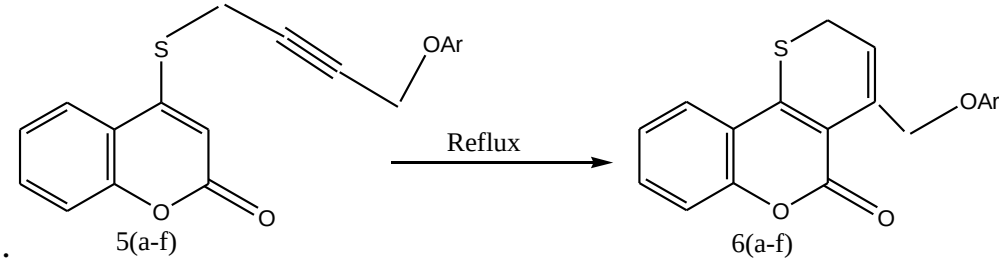
When a two phase mixture of 4-mercaptocoumarin **3**, 1-chloro-4-aryloxybut-2-yne **4**(a-f), chloroform and very dilute solution of aq. NaOH was stirred at r.t. in the presence of benzyltriethylammonium chloride(BTEAC) gave the single S-alkylated product **5(**a-f) in 75-87% yields**.(Scheme 2)**[7,9]



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 refluxe in chlorobenzene for 4 h to give solid compounds **6**(a-f) in 75-87 % yields**.(Scheme 3)**



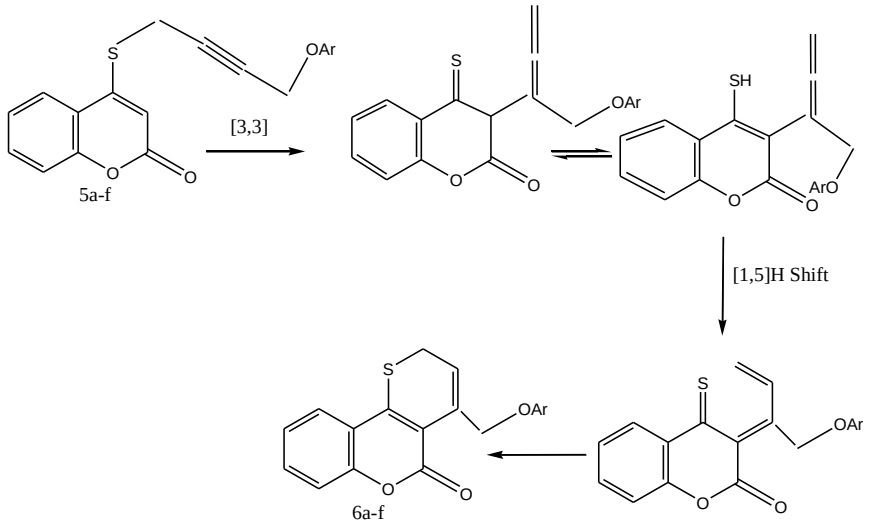
5(a-f) 6(a-f)

The characterisation of **6**(a-f)were done using the same principle of elemental analyses and spectroscopic data as our preceeding short communication paper.[11,12]

To test the generality of the rearrangement, the thermal rearrangement of six sulphides **5**(a-f) were studied and similar result was obtained in every cases like previous observations.[8,10] As our expectation, in every cases sulphur heterocycle was obtained without affecting the aryl propargylether segment. The aryloxypropargyl ether may undergo oxygen Claisen rearrangement while the propargylvinyl sulphide may undergo thio-Claisen rearrangement. Hence these substrates provide excellent scope for studying the competition between oxygen Claisen and thio-claisen rearrangements as well as synthesis of sulphur heterocycles. However, the activation enegy required for the arylpropargyl ether rearrangement is much higher than that of propargylvinyl sulphide rearrangement.[13] Every sulphide shows perfect regioselectivity with high yield and atom economy. Thus this is very eco-friendly synthesis of sulphur heterocycles.

To test the effect of catalyst on this rearrangement, every sulphide, **5**(a-f) was heated in presence of acid(p-toluene sulfonic acid) and base (pyridine) but no product other than **6**(a-f) was obtained.

The formation of **6** from **5** involves a [3,3] sigmatropic rearrangement at the propargylvinyl sulphide segment of **5** leading to an allenyl-ene-thiol 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 six sulphides **5**(a-f) exhibits excellent regioselective ring closure. Therefore, this is a general eco-friendly regioselective method for the synthesis of 4-aryloxymethyl- 2*H*-thiopyrano[3,2-**c**][1]benzopyran-5(2*H*)-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 (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°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 (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 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. Rearrangement of sulphides 3a-d in chlorobenzene:

The sulphides **5**(a-f)(1 mmol) were refluxed in chlorobenzene(3 ml) for 4h . 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-f) were obtained by eluting the column with 20% ethylacetate in pet-ether solution.

Compound 6a : m.p. 120°C; yield 75%; UV(EtOH)λ_{max}:220, 360 nm; IR(KBr)Υ_{max} : 1700, 1600, 1230 cm^{-1}; ^1H NMR(300MHz) δ: 3.44(d, 2H, J= 6Hz), 5.14(d, 2H, J= 1Hz), 6.18(tt, 1H, J=1,6Hz), 6.92-7.82 (m, 9H); m/z 322 (M+); Anal. Calcd. For $C_{19}H_{14}O_3S$: C, 70.80; H, 4.35 found C, 70.92; H, 4.47%.

Compound 6b : m.p. 104°C; yield 85%; UV(EtOH) λ_{max}: :222, 360 nm; IR(KBr) Υ_{max} : 1700, 1600, 1240 cm^{-1}; ^1H NMR(300MHz) δ : 2.23(s, 3H), 3.46(d,2H, J= 6Hz), 5.14 (d, 2H, J= 1Hz), 6.21(tt, 1H, J=1, 6Hz), 6.85-7.85 (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, 4.62%.

Compound 6c : m.p. 102°C; yield 87%; UV(EtOH) λ_{max}: :221, 360 nm; IR(KBr) Υ_{max} : 1710, 1610, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 2.27(s, 3H), 3.44(d,2H, J= 6Hz), 5.11(d, 2H, J= 1Hz), 6.17(tt, 1H, J=1, 6Hz), 6.82-7.84 (m, 8H); m/z 336 (M+); Anal. Calcd. For $C_{20}H_{16}O_3S$: C, 71.43; H, 4.76 found C, 71.38; H, 4.61%.

Compound 6d : m.p. 138°C; yield 85%; UV(EtOH) λ_{max}: :220, 360 nm; IR(KBr) Υ_{max} : 1700, 1580, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 3.47 (d, 2H, J= 6Hz), 5.20(d, 2H, J= 1Hz), 6.33(tt, 1H, J=1, 6Hz), 6.89-7.82 (m, 8H); m/z 358, 356 (M+); Anal. Calcd. For $C_{19}H_{13}ClO_3S$: C, 64.04; H, 3.65 found C, 64.24; H, 3.57%.

Compound 6e : m.p. 132°C; yield 77%; UV(EtOH) λ_{max}: :223, 360 nm; IR(KBr) Υ_{max} : 1010, 1580, 1230 cm^{-1}; ^1H NMR(300MHz) δ : 3.48 (d, 2H, J= 6Hz), 5.16(d, 2H, J= 1Hz), 6.20(tt, 1H, J=1, 6Hz), 6.80-7.81 (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, 3.53%.

Compound 6f : m.p. 186°C; yield 82%; UV(EtOH) λ_{max}: :220, 360 nm; IR(KBr) Υ_{max} : 1690, 1580, 1240 cm^{-1}; ^1H NMR(300MHz) δ : 3.47 (d, 2H, J= 6Hz), 5.18(d, 2H, J= 1Hz), 6.26(tt, 1H, J=1, 6Hz), 6.91-7.85 (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, 58.31; H, 3.17%.

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