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Facile regioselective synthesis of 2*H*-thiopyrano[3,2-*c*]quinolin-5(6*H*)-ones by thio-Claisen rearrangement

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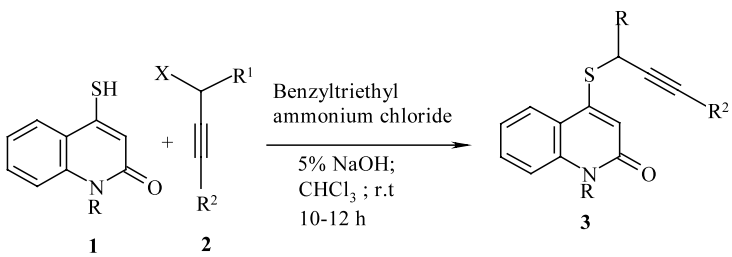
Abstract—A number of 1-alkyl-4-prop-2-ynylthioquinolin-2(1*H*)-one derivatives are synthesised by the phase transfer catalyzed reaction of 1-alkyl-4-marcaptoquinolin-2(1*H*)-ones with different prop-2-ynylic halides. These are then regioselectively cyclised in refluxing chlorobenzene to give hitherto unreported 2*H*-thiopyrano[3,2-*c*]quinolin-5(6*H*)-ones in 85–90% isolable yields.

Furo[3,2-*c*]quinolin-4(5*H*)-one and 2*H*-pyrano[3,2-*c*]quinolin-5(6*H*)one derivatives are abundantly distributed in nature[1,2] and a number of syntheses of these heterocycles have been reported,[3,4] which also includes our own work.[5,6] We have also reported[7–9] the regioselective synthesis of substituted furo[2,3-*c*]quinolin-4(5*H*)-ones and 2*H*-pyrano[2,3-*c*]quinolin-5(6*H*)-ones. However, there have been no reports on the synthesis of the corresponding 3,4-fused thieno- and 2*H*-thiopyrano[3,2-*c*]quinolones. Here we report the results of our efforts in this direction.

The starting materials for this study were easily obtained from the reactions of 1-alkyl-4-mercaptoquinolin-2(1*H*)-one (**1**) with the appropriate alkyl halides 2 viz. propargyl bromide, 4-chlorobut-2-yn-1-ol and 1-bromo-2-butyne under phase transfer catalyzed conditions (Scheme 1).



	X	R	R^1	R^2	Yield(%)
a)	Br	Me	H	H	80
b)	Br	Et	H	H	78
c)	Cl	Me	H	CH_2OH	80
d)	Cl	Et	H	CH_2OH	75
e)	Br	Me	H	Me	78
f)	Br	Et	H	Me	75

Scheme 1.

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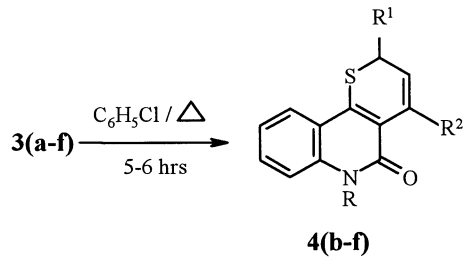
Hitherto unreported 1-alkyl-4-mercaptoquinolin-2(1*H*)-ones (**1**) in turn were synthesised by the reaction of 1-alkyl-4-chloroquinolin-2(1*H*)-ones with sodium hydrosulfide in ethanol at 0–10°C for 6 h.

Substrate **3a** was refluxed in chlorobenzene (bp 132°C) for 5 h to give a white crystalline solid, **4a**, mp 120°C in 90% yield. The products **3a** and **4a** were characterised by their elemental analyses and spectroscopic data. The ^{1}H NMR spectrum of **3a** showed signals at δ 3.8 (d, 2H, $J=2.5$ Hz), δ 3.7 (s, 3H) and δ 2.3 (t, 1H, $J=2.5$ Hz). The ^{1}H NMR spectrum of **4a** showed a two proton double doublet at δ 3.34 ($J=6$ Hz, 1.5 Hz); a one proton double triplet at δ 6.20 ($J=10$ Hz, $J=6$ Hz); and a one proton multiplet at δ 6.85 indicating the formation of the six-membered thiopyran ring. Encouraged by this result, other substrates **3b–f** were similarly subjected to thermal rearrangement to give the products **4b–f** in 82–90% yields (Scheme 2).

The formation of the products **4a–f** may be rationalised[10] by an initial [3,3] sigmatropic shift of the propynyl group to form the intermediate allene **5**, followed by enolisation to ene-thiol **6**, a 1,5-hydrogen shift to **7** and electrocyclic ring closure to give the cyclic products **4a–f** (Scheme 3).



Scheme 2.

Thio-Claisen rearrangement of aryl propargyl sulphide is known to give a mixture of products,[11] viz. 2-methylthionaphthene derivatives and 2*H*-thiochrom-3-ene derivatives. [1,3] Radical shifts[12] also occur in some cases when thio-Claisen rearrangements are attempted. It is interesting to note that in the present instance only 2*H*-thiopyrano derivatives are obtained so making this methodology a general regioselective synthesis.

Acknowledgements

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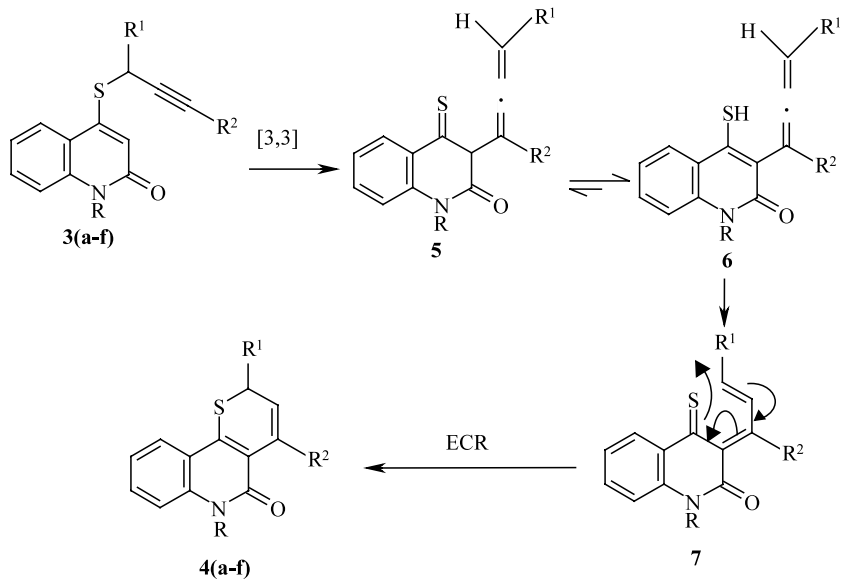

Scheme 3.

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