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THE THIO-CLAISEN REARRANGEMENT OF ALLYL 4-QUINOLYL SULFIDES

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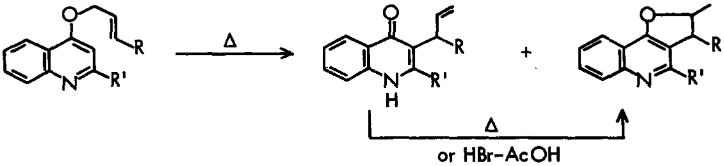
It was reported in our previous papers (1) that, on heating at 200°, allyl 4-quinolyl ethers were readily converted into the Claisen products, 3-allyl-4(1H)-quinolones, in good yields accompanying small amounts of ring closure products, 2,3-dihydrofuro-[3,2-c]quinolines.



Several previous attempts to bring about the Claisen Rearrangement in the allyl phenyl sulfide system (thio-Claisen rearrangement*) have failed (2, 3). It was recently reported, however, that heating of allyl phenyl sulfide with quinoline or N,N-dimethylaniline afforded 2-methylthiacoumaran (4) and thiachroman (5) and the formation of these products was interpreted as the results of cyclization of the initially formed normal Claisen product, 2-allylthiophenol, although an intermediacy of this compound was not confirmed. We wish to report a new example of the thio-Claisen rearrangement in allyl 4-quinolyl sulfide and its derivatives.

Allyl 4-quinolyl sulfides (Ia and Ib) were prepared in good yields by alkylation of

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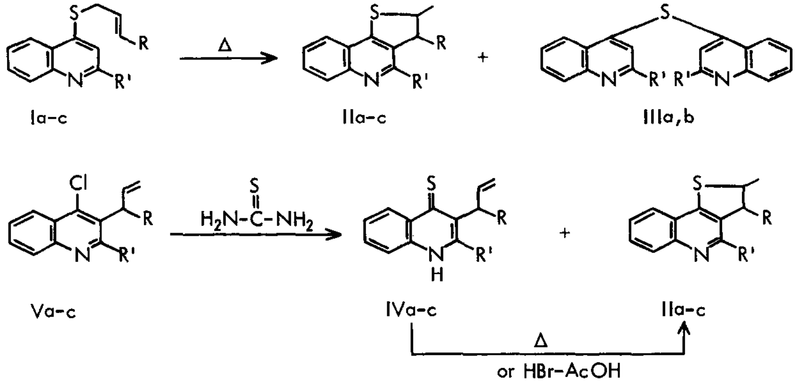
* This name has been designated by Prof. Kwart (see ref. 8).

4(1H)-quinolinthione and its 2-methyl derivative with allyl bromide in the presence of sodium ethoxide. Heating of 4-allylthioquinoline (Ia), b.p$_{0.3}$ 130°, at 200° for 1 hr. without solvent (an ordinary Claisen condition) resulted in the formation of 2-methyl-2,3-dihydrothieno[3,2-c]quinoline (IIa), b.p$_{0.07}$ 142-143°; NMR, τ 8.56 (3H, doublet, J=6.6 c.p.s.), in 73% yield and bis-(4-quinolyl)sulfide (IIIa), m.p. 145-146°, in 2% yield. Similarly, rearrangement of 4-allylthioquinaldine (Ib), m.p. 44-46°, gave a 69% yield of 2,4-dimethyl-2,3-dihydrothieno[3,2-c]quinoline (IIb), m.p. 88-89°; NMR, τ 8.56 (3H, doublet, J=6.6 c.p.s.) and 7.47 (3H, singlet) along with a 4.5% yield of bis-(2-methyl-4-quinolyl)sulfide (IIIb), m.p. 159-160° [ref. (6), m.p. 154°]. Although careful examination of the above reaction mixtures could not detect the expected normal Claisen products, 3-allyl-4(1H)-quinolinthiones (IVa and IVb), it was assumed that 2,3-dihydrothieno[3,2-c]quinolines (IIa and IIb) were formed by a subsequent cyclization of the initially formed Claisen products, IVa and IVb, and that a facility of IVa and IVb for cyclization into IIa and IIb, probably due to the participation of thiocarbonyl group, made their isolation difficult. Then, in order to verify an intermediacy of the normal Claisen products, 3-allyl-4(1H)-quinolinthiones (IVa and IVb) were synthesized and their thermal behavior was tested.

Reaction of 3-allyl-4-chloroquinoline (Va) (1) with thiourea in boiling ethanol for 1 hr. afforded a 58% yield of 3-allyl-4(1H)-quinolinthione (IVa), m.p. 170-171°; ν_{max}^{Nujol} 3198 (NH), 1154 (C=S), and 1641, 994, and 924 (-CH=CH$_2$) cm^{-1}, and a 32% yield of an oil, identical with IIa. Similar reaction of 3-allyl-4-chloroquinaldine (Vb) (7) with thiourea gave a 66% yield of 3-allyl-2-methyl-4(1H)-quinolinthione (IVb), m.p. 174-175°; ν_{max}^{Nujol} 3190 (NH), 1137 (C=S), and 1635, 1004, and 900 (-CH=CH$_2$) cm^{-1}, and a 25% yield of ring closure product, identical with IIb. The structures of the thio-Claisen product, IIa and IIb, were also synthetically confirmed

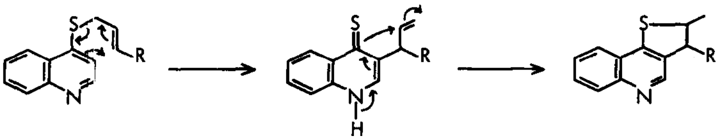


a: R=R'=H, b: R=H, R'=CH_3, c: R=CH_3, R'=H

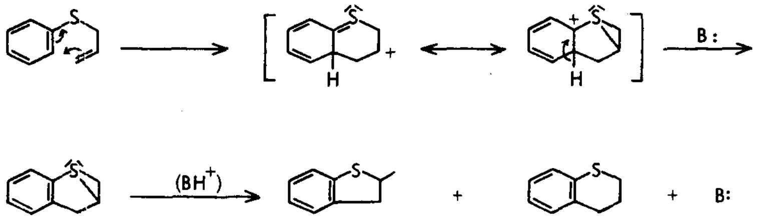
by identification with the cyclization products, obtained quantitatively from IVa and IVb, respectively, by treatments with HBr-AcOH. The compounds IVa and IVb quantitatively isomerized into IIa and IIb, respectively, even under a relatively mild conditions (at 180° for a few minutes). These results suggest that the normal Claisen products, 3-allyl-4(1H)-quinolinthiones, may be a possible intermediates of the thio-Claisen rearrangement of allyl 4-quinolyl sulfides.

Furthermore, in order to confirm that allyl 4-quinolyl sulfides follow the path of the Claisen rearrangement, 4-crotylthioquinoline (Ic), m.p. 53-54°, was prepared from 4(1H)-quinolinthione and crotyl chloride and treated under the same conditions as above. Thus, Ic was transformed into a mixture consisting of 75% of 2,3-dimethyl-2,3-dihydrothieno[3,2-c]quinoline (IIc), b.p$_{0.3}$ 146-147°, and 3% of IIIa. The structure of IIc was confirmed by the IR and NMR spectral analyses and by the following chemical method. Reaction of 4-chloro-3-(1-methylallyl)quinoline (Vc)(1) with thiourea afforded a 66% yield of 3-(1-methylallyl)-4(1H)-quinolinthione (IVc), m.p. 157-158°; ν_{max}^{Nujol} 3181 (NH), 1136 (C=S), and 1636, 993, and 916 (-CH=CH_2) cm^{-1}

and a 25.4% yield of IIc. The ring closure product obtained by treatment of IVc with HBr-AcOH was identical with IIc. A cyclization of IVc to IIc was also easily accomplished by heating of IVc at 180° for 5 min. Thus, the formation of IIc in pyrolysis of the crotyl sulfide Ic and the facile cyclization of IVc to IIc provide evidence that the normal Claisen product, 3-allyl-4(1H)-quinolinthione, derived from I with inversion of a migrating allylic group, is an intermediate in the thio-Claisen rearrangement of allyl 4-quinolyl sulfides.



Only recently, Kwart and Evans (8) proposed against the previously assumed mechanism (4,5) a new special mechanism involving a thiirane intermediate for the thio-Claisen rearrangement of allyl phenyl sulfides, on the basis of the fact that the cyclization of 2-allylthiophenol and the thio-Claisen rearrangement of allyl phenyl sulfide under an identical condition yielded the same, but in quite different proportions, two products (2-methylthiacoumaran and thiachroman). Then, we reinvestigated the



cyclization of 3-allyl-4(1H)-quinolinthione (IVa) and the thio-Claisen rearrangement of allyl 4-quinolyl sulfide (Ia) under the Kwart condition. Both the reactions gave a sole product, IIa, in more than 90% yield and any other products (e.g. dihydrothiapyrano[3,2-c]quinoline corresponding to thiachroman in the case of allyl phenyl sulfide) were not detectable. Thus, any evidence supporting the mechanism proposed by Kwart was not obtainable in our study. We assume that the initial electron flow in the Kwart mechanism is obstructed by the electron attracting property of the ring nitrogen in allyl 4-quinolyl sulfides.

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