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MECHANISM OF THE CYCLIZATION REACTION OF THE INTERMEDIATE, 3-MERCAPTO-4-METHALLYLQUINOLINE, IN THE THIO-CLAISEN REARRANGEMENT

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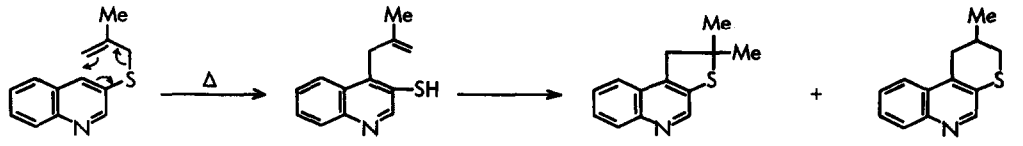
We have reported, in the preceding communication (1), that the thermal rearrangement of methallyl 3-quinolyl sulfide (I) affords 2,2-dimethyl-1,2-dihydrothieno[2,3-c]quinoline (II) and 2-methyl-2,3-dihydro-1H-thiopyrano[2,3-c]quinoline (III) in total yield over 85% and that these thio-Claisen products are formed by the cyclization of the intermediate, 3-mercapto-4-methallylquinoline (IV) produced from I by the [3,3] sigmatropic rearrangement of aromatic allyl sulfides (2-4). We now wish to report on the details and mechanism of the cyclization of IV to the thio-Claisen products II and III.



I IV II III

When the thiol IV was heated at various temperatures in the atmosphere of oxygen-free argon and in dark, the thio-Claisen products II and III were obtained in total yields over 95%. Reinvestigation of the thermal rearrangement of the sulfide I under the same conditions yielded the same, and in identical proportions, two products in total yields of about 90%. Heating of the thio-Claisen product II or III under the same conditions gave no evidence of their interconvertibility. Table I represents a comparison of product composition data (5) obtained from runs at 100°, 150°, and 200° and the identity of the product ratios in both the reactions substantiates the intermediacy of the thiol IV in the thio-Claisen rearrangement of I. However, the great sensitivity of product composition to temperature is consonant with the existence of competitive two product forming paths from the intermediate IV.

It has been known that ionic additions of thiols to olefins generally give products resulting from

normal (Markownikoff) addition, whereas radical additions are characteristically abnormal (anti-Markownikoff addition) (6,7). Acid-catalyzed additions of thiols to olefins are familiar and the usual free radical initiators, such as oxygen, peroxides, and ultraviolet radiation, are effective in initiating the free radical additions of thiols to olefins.

To verify mechanism of the cyclization of the thiol IV, influence of these catalysts on the cyclization of IV was examined. As shown in Table II, the results prove that the acid (pyridine hydrochloride) catalyzes the cyclization of IV to the Markownikoff product II and the free radical initiators (oxygen and benzoyl peroxide) promotes the cyclization of IV to the anti-Markownikoff product III. The ESR spectrum exhibited a broad singlet signal ($g = 2.0037$, $\Delta H_{msl} \fallingdotseq 13$ gauss) in the reaction of IV in air at 150°, suggesting the generation of free radical species.

TABLE I
Comparison of the Product Composition in the Cyclization of the Thiol IV and the Rearrangement of the Sulfide I at Several Temperatures (in O_2-free Ar and dark)

Starting material	Reaction conditions		Product ratio II	Product ratio III
IV	100°	100 hr	1.0	0.4
	150°	20 hr	1.0	1.2
	200°	2 hr	1.0	2.1
I	100°	100 hr	1.0	0.5
	150°	20 hr	1.0	1.1
	200°	2 hr	1.0	2.5
	200°	2 hr[a]	1.0	2.6

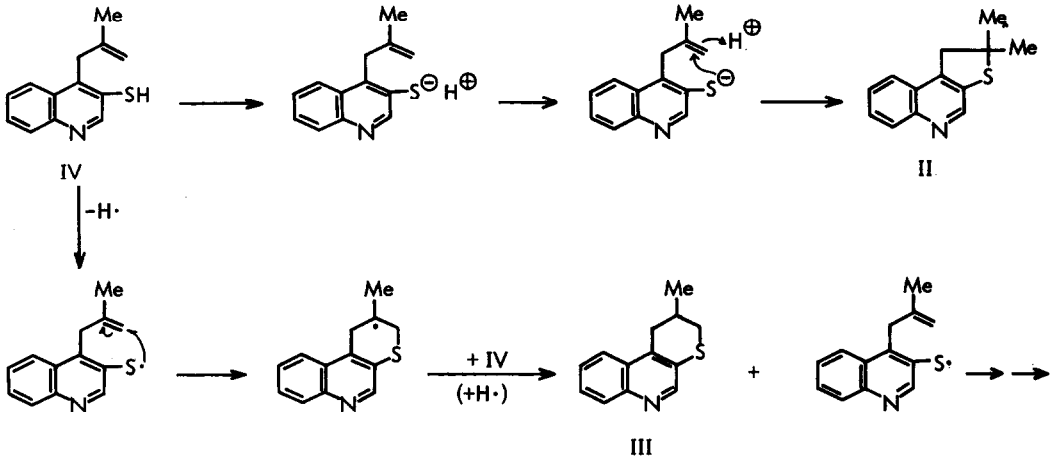
a in dimethylaniline

TABLE II
Influence of the Catalysts on Product Proportions in the Thermal Cyclization of the Thiol IV at 150° (in dark)

Reaction conditions		Catalyst	Product ratio II	Product ratio III
in O_2-free Ar	20 hr	———	1.0	1.2
in O_2-free Ar	3 hr	$(C_6H_5COO)_2$	1.0	5.0
in air	2 hr	O_2	1.0	10.0
in O_2-free Ar	5 hr	pyridine-HCl	15.0	1.0

Since competition of the two product forming paths was observed in these reactions at 150°, properties of IV at room temperature were carefully investigated. Although the thiol IV was stored almost unchanged for 1 week under the condition of oxygen-free argon atmosphere and in dark, the NMR spectral analysis

showed that IV changed to II in the extend of about 15% after 5 months. The exclusive formation of II in the absence of the free radical initiators demonstrates that the cyclization of IV by the ionic mechanism affords only II. The easiness of this cyclization reaction is reasonably explanable on the basis of the large acidity of the thiol and great assistance through participation of the neighboring thiol anion with great nucleophilicity in attack of the proton at the allyl double bond. On the other hand, the thiol IV was readily transformed into III in air and dark or under the conditions of oxygen-free argon atmosphere and exposure to sunlight (in quartz tube). The exclusive formation of III in the presence of the free radical initiator (oxygen or hν) demonstrates that the cyclization of IV by the free radical mechanism gives only III. Addition of a thiyl radical generated through hydrogen abstraction by the free radical initiators to the allyl double bond is considered to proceed via a multistep chain mechanism (8).



It was thus verified that the thio-Claisen rearrangement (1) of allyl 3-quinolyl sulfides proceeds through the [3,3] sigmatropic rearrangement to 4-allyl-3-mercaptoquinolines followed by their competitive cyclization to 1,2-dihydrothieno[2,3-c]quinolines and 2,3-dihydro-1H-thiopyrano[2,3-c]quinolines due to the thermally induced heterolytic and homolytic fissions of the thiol S-H bond.

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