Alternative Conditions for the Thio-Claisen Rearrangement

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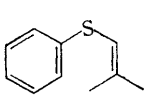
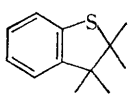
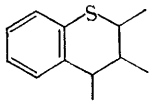
HITHERTO[1] the presence of high-boiling amine solvent was regarded as an indispensible condition for bringing about the thio-Claisen rearrangement. The role of this solvent has been attributed[2] (among other things) to its ability to prevent irreversible propenylization of the substrate. A recent review[3] has correlated the apparently exclusive need for an amine solvent with the occurrence of an unspecified base-catalysed step which was not accounted for by the suggested mechanism.

We report the use of a high-boiling carboxylic

TABLE

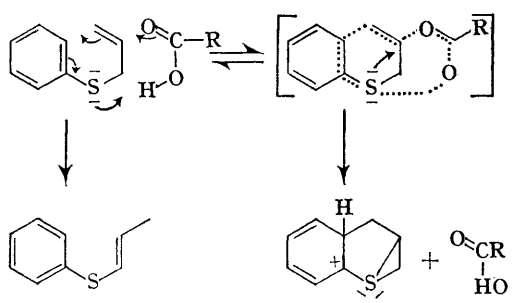
Thio-Claisen rearrangement products

Substrate	Conditions	Solvent	% Yield			
Allyl phenyl sulphide (I)	1·5 hr. at 300°	Octanoic	60	54[c]	29[a]	17[b]
		Quinoline	75	0	61·5	38·5[b]
β-Methylallyl phenyl sulphide (II)	1·5 hr. at 300°	Octanoic	66	51[d]	23·5[e]	25·5[f]
		Quinoline	72	6[d]	33[e]	61[f]
β-Chloroallyl phenyl sulphide (III)	1·5 hr. at 300°	Octanoic	22	0	100[g]	0
		Quinoline	41	0	100[g]	0
Crotyl phenyl sulphide (V)	2 hr. at 250°	Octanoic	60	81[i]	17·4[m]	2·6[p]
		Quinoline	88	0[i]	57·5[m] + 27[n]	10[p] + 5·5[q]
S-Crotylthiosalicylic acid (IV)	2 hr. at *ca.* 250°	neat	40·5	cleavage[h] 35	54[i] + 9·5[m]	1·5[p]
	2 hr. at *ca.* 260°	neat	44	25	38·5[i] + 36·5[m]	—

[a] 2-Methyl-1-thiacoumaran; [b] 1-Thiachroman; [c] Propenyl phenyl sulphide; [d] Isobutenyl phenyl sulphide; [e] 2,2-Dimethyl-1-thiacoumaran; [f] 3-Methyl-1-thiachroman; [g] 2-Methylthianaphthene; [h] Thiosalicyclic acid (not accounted for in computing yield); [i] 2-Ethyl-7-carboxy-1-thiacoumaran; [k] 2-Methyl-1-thiachroman; [l] Mixture of propenyl isomers; [m] 2-Ethyl-1-thiacoumaran; [n] 2,3-Dimethyl-1-thiacoumaran; [p] 2-Methyl-1-thiachroman; [q] 4-Methyl-1-thiachroman.

acid solvent in which the thio-Claisen rearrangement readily takes place. When solutions of various allyl phenyl sulphides (*ca.* 15%) in octanoic acid are heated at 300° for 1·5 hr., cyclic products are obtained whose compositions are compared in the accompanying Table with those observed for the corresponding reaction in an amine medium.

Evidently some form of complexation of the allyl phenyl sulphide with carboxylic acid at high temperature prevents all or part of the tendency to propenylization in similar fashion to (though somewhat less effectively than) the amine solvent. The data indicate that high-temperature isomerization of the double bond from the allylic position is also dependent on side-chain substitution, occurring to the largest extent in the case of the β-methylallyl sulphide (II) in the octanoic acid. Furthermore, the rearrangement products in both media are identical in nature. Reactions in the respective solvents differ only with regard to rate and product proportions. One case in point here is the rearrangement of β-chloroallyl phenyl sulphide (III) where apparently only a single product (see Table) arises *via* spontaneous dehydrochlorination of a thiacoumaran precursor. The yield of this thianaphthene is only *ca.* half as great in octanoic acid as in quinoline. These data suggest, therefore, that the complex between (I) and the solvent capable of bringing about reaction not only resists propenylization, but also possesses structural features which foster the cycle of bond-making and bond-breaking events characteristic of the thio-Claisen mechanism (possibly as shown below).



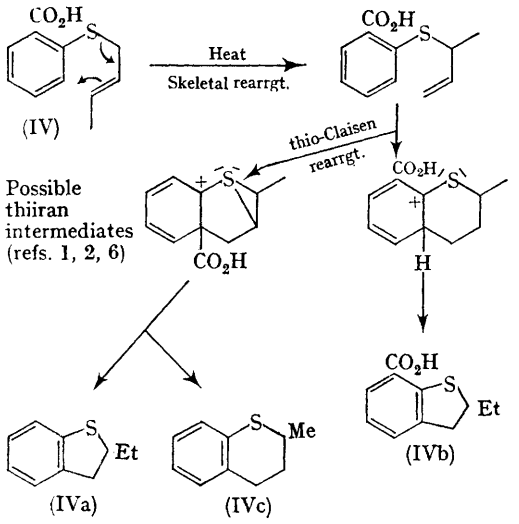
Reactant structure in carboxylic acid solution

Propenylization-resistant complex

The partitioning between thiachroman and thiacoumaran may also be regarded as a reflection of solvent complexation influencing the choice of product formation from common (complexed) intermediates. The evident disparity in product proportions (see Table) derived from reaction in the different media is consistent with this assumption.

It is now possible to understand the only instance reported[4] in which it would appear that the thio-Claisen rearrangement has been effected without benefit of an amine solvent, namely the

case of *S*-crotylthiosalicyclic acid (IV). In fact, we have found that an amine solvent actually inhibits product formation, and esterification of the carboxylic acid function completely suppresses the rearrangement reactions.[5] Clearly the rearrangement taking place on heating (IV) (neat) to high temperatures (*ca.* 250—260°) is dependent upon its own carboxylic acid medium, which has here been recognized as an alternative condition for effecting the thio-Claisen rearrangement. Furthermore, the thiachroman (IVc) we have now isolated in addition to the thiacoumaran (IVa and b), previously established by Tarbell and his co-workers[4] as products, serve to identify this unusual reaction of (IV) as a typical thio-Claisen rearrangement of the crotyl phenyl sulphide system. We have demonstrated[6] that the rearrangement of such substrates involves prior high-temperature conversion into an α-methylallyl phenyl sulphide, which then undergoes rapid and complete conversion into thiacoumaran and thiachroman as illustrated below for the course of rearrangement of (IV).



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[3] H. M. R. Hoffmann, *Ann. Reports*, 1966, **63**, 336.
[4] J. C. Petropoulos, M. A. McCall, and D. S. Tarbell, *J. Amer. Chem. Soc.*, 1953, **75**, 1130.
[5] Unpublished results, E. R. Evans, from these laboratories.
[6] Results from these laboratories to appear in a forthcoming article.