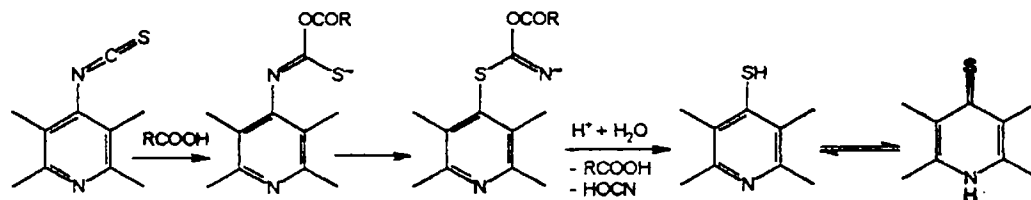


A NEW REARRANGEMENT OF HETEROCYCLIC ISOTHIOCYANATES

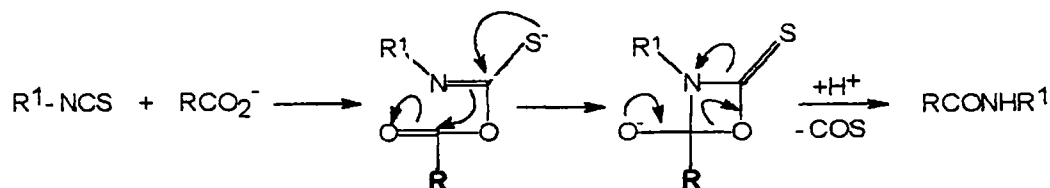
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ABSTRACT: A novel rearrangement of heterocyclic isothiocyanates in the presence of carboxylic acids is described.



INTRODUCTION

The condensation of mono- and di-carboxylic acids with aliphatic and aromatic isothiocyanates proceeds via addition-elimination to yield amides (1,2):



When the above mentioned reaction was carried out with carboxylic acids (acetic or salicylic acid) and heterocyclic isothiocyanates, another rearrangement was noticed, which leads finally to the corresponding thioderivatives.

EXPERIMENTAL

M.p. are uncorrected. The reactions were monitored by "MERCK" silicagel plates, eluting with 8:2 benzene-ether; the visualisation was done by iodine.

General synthetic procedure for thioacridones

The 9-isothiocyanate derivatives (1 mmol) and acetic acid (10 ml) were refluxed in a 25 ml flask for 1 hr. The reaction mixture was then cooled and diluted with water. The red precipitate was filtered, dried and recrystallized from an appropriate solvent (see the Table)

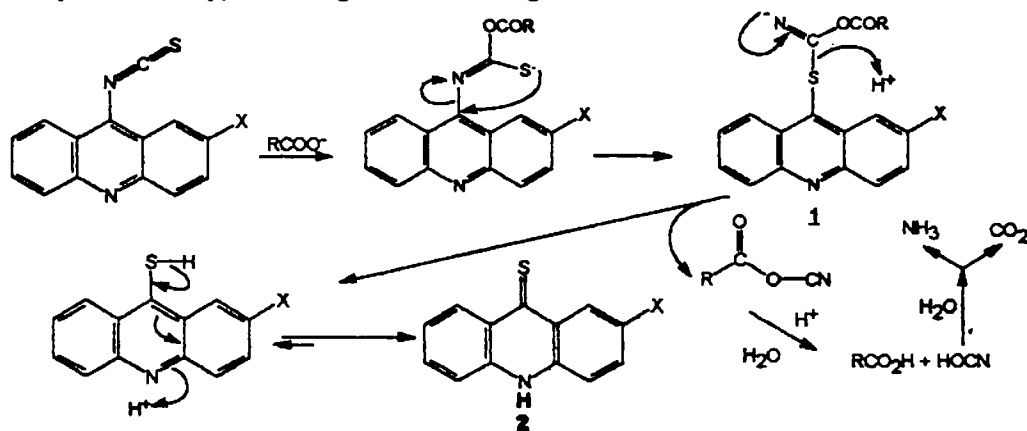
General synthetic procedure for disulphides

2- Or 4-pyridine isothiocyanate (1 mmol), acetic acid (2 ml) and toluene (15 ml) were refluxed for 14 hrs. The solvent was rotavapored and the residue extracted with petroleum ether (for di- α -pyridyl disulphide) or with 30% aqueous ammonia (for di- γ -pyridyl disulphide). Di- α -pyridyl disulphide was separated by concentration of the solvent and di- γ -pyridyl disulphide by cooling of the aqueous ammonia solution at -10°C (see Table). The 4-pyridine isothiocyanate prepared from 4-amino pyridine via dithiocarbamic acid triethylamine salt (3) is too unstable to undergo purification, so the yield given is based on the raw isothiocyanate (see Table).

DISCUSSION

In order to understand correctly the herewith reported rearrangement, which leads to new C-S bonds, it has to be recalled that the isothiocyanato structure of the compounds obtained from 9-chloroacridine derivatives and KSCN under PTC conditions was clearly demonstrated in the paper of Vlassa and co-workers (4); moreover, it is well known (5) that isothiocyanato derivatives are generally more stable from a thermodynamical point of view than the corresponding thiocyanato isomers. Methods for the preparation of isothiocyanato derivatives by isomerisation of thiocyanato compounds were recently reported (6,7). Thus thioacridone derivatives were obtained undoubtedly in our case by a rearrangement and not by a hydrolysis reaction of isomeric thiocyanato compounds.

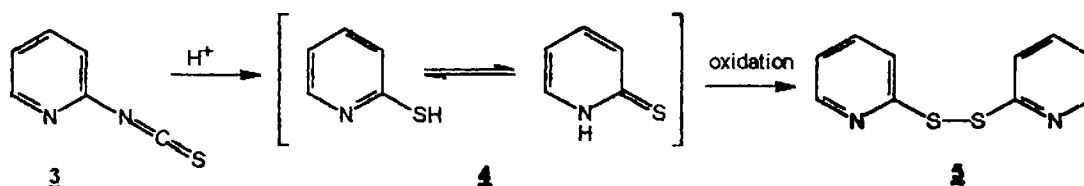
We assume that this rearrangement is possible due to the presence of nitrogen atom in the acridine ring which exhibits an electron-withdrawing effect, thus lowering the electron density at C-9, so that this position can be attacked by nucleophilic sulphur atom from the isothiocyanato moiety, according to the following scheme:



The rearranged compound **1** is not stable in acid medium and breaks up into thioacridone **2** and an unstable mixed anhydride, which is decomposed in its turn into

carboxylic acid and HOCN, further hydrolysed to NH_3 and CO_2 .

It is well known (6) that 2-pyridyl isothiocyanate at room temperature exists as a dimer, while at higher temperature a dissociation of the dimer into monomer takes place. In order to be sure that 2-pyridyl isothiocyanate 3 is in the monomeric form, the rearrangement was carried out by refluxing it in toluene, in the presence of a carboxylic acid. By extraction of the crude product with petroleum ether (after the toluene was rotavapored) di- α -pyridyl disulphide 5 was obtained in high yield by oxidation of the mercapto-pyridine 4 initially formed, under the action of air and light (9) :



Di- γ -pyridyl disulphide was obtained in a similar way from the corresponding 4-isothiocyanato derivative.

The highest reaction rates were observed when working with acetic acid alone or with acetic acid in toluene; with other acids e.g. salicylic acid in toluene or in dioxane as solvents a longer reaction time was necessary for obtaining the same yield.

The results of our experiments are shown in the table.

Table. Thione or disulphide obtained by rearrangement of the corresponding isothiocyanates.

-isothiocyanate	Yield of product(%)/ recrystallisation solvent	m.p.(lit.m.p.)(lit. quotation)
9-Acridine-	85/aq. pyridine	272-274 (272-274) (10)
2-Bromo-9-acridine-	70/aq. pyridine	256-268 (256) (11)
2-Chloro-9-acridine-	80/aq. pyridine	275-277 (273-275) (12)
2-Methyl-9-acridine-	75/aq. pyridine	258-260 (258-260) (10)
2-pyridyl-	90/pet.ether	55-57 (57-58) (13)
4-pyridyl-	50*/water	72-74 (74-75) (14)

*Yield based on unrecrystallized starting matter.

CONCLUSION

The above reported facts enable us to conclude that the hereby observed rearrangement is a rather general phenomenon, given the right structural conditions, and our future investigations will try to extend the application area of this reaction in the class of heterocyclic

isothiocyanates and aromatic isothiocyanates which contain electron withdrawing substituents.

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