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ACID CATALYSED CYCLODEHYDRATION VERSUS SULPHUR EXTRUSION OF 2-(4-QUINAZOLINYLTHIO)KETONES

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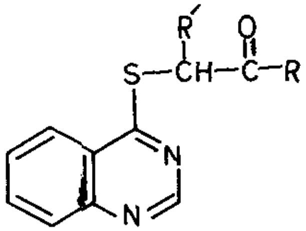
2-(4-Quinazolinylthio)ketones on keeping in minimum amount of sulphuric acid provide only 2-(4(3H)-quinazolinylidene)ketones but in an excess of the acid, thiazolo[3,2-c]quinazolin-4-ium cations are also formed.

Carbothioamide derivatives, 2-(4-quinazolinylthio)ketones, 1, with sodium ethoxide/DMF lost sulphur to form 2-(4(3H)-quinazolinylidene)ketones, 2, in synthetically useful yields.[1] Sulphur extrusion of similar carbothioamide derivatives has also been performed with triphenylphosphine[2] and Zn/acetic acid.[3] Heterocyclic carbothioamides bearing an α-ketosulphide chain undergo acid catalysed cyclodehydration to thiazolo heterocycles.[4] In order to procure thiazolo[3,2-c]quinazolin-4-ium perchlorates, 3, needed for another project, we performed the already reported cyclodehydration of 2-(4-quinazolinylthio) ketones, 1, with conc. sulphuric acid[5] and found that sulphur extrusion was the major mode of reaction.



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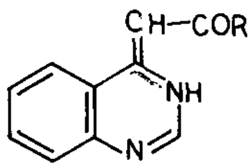

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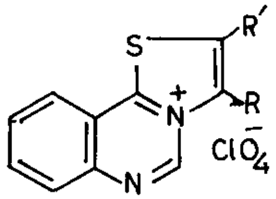

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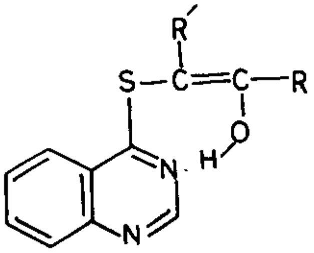
On keeping the solutions of 2-(4-quinazolinylthio)acetophenones, 1, in minimum amount of conc. sulphuric acid for 3-4 h followed by work up and treatment with perchloric acid (60%),[5] the products formed were found to be devoid of sulphur. These products were assigned the structure, perchlorates of 2-(4(3H)-quinazolinylidene)acetophenone, 2, on the basis of analytical, spectral data and conversion to 2,[1] on basification. The structure, 3(R=aryl, R'=H), had earlier been assigned to these products[5] merely on the basis of their analysis for nitrogen which is of limited distinctive significance amongst 3 and perchlorates of 2. Moreover, the m.p.s of the perchlorates of 2 are the same as those reported for the perchlorates of corresponding 3 (table).[5] The reaction mixtures, on basification, directly formed 2 in equally good yields. Evidently, here, 1, did not undergo cyclodehydration due to weaker nucleophilicity of the diazine nitrogen[6] and alternately its enol form 4 formed the thiirane intermediate 5 which lost sulphur to form 2.



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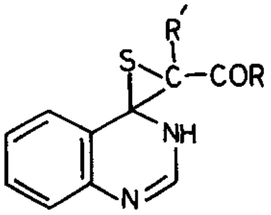

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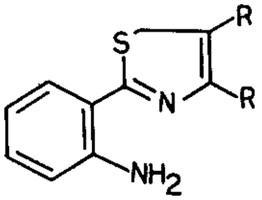

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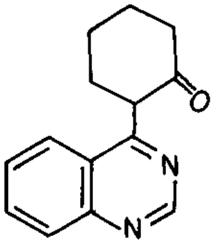

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On repeating the cyclodehydration of 2-(4-quinazolinylthio)cyclohexanone 1(R,R'=-$(CH_2)_4$-), to procure 3(R,R'=-$(CH_2)_4$-),[7] we had often noticed anamolous results depending upon the amount of sulphuric acid used. Hence, we kept the solutions of 1 in an excess of conc. sulphuric acid at room temperature. The products were obtained as mixtures which could not be separated by fractional crystallisation. Evidently, the mixtures formed could be of the perchlorates of 2 and 3. Earlier, we had seen that 3(R,R'=-$(CH_2)_4$-) on treatment with aqueous sodium hydroxide formed 6(R,R'=-$(CH_2)_4$-) almost quantitatively.[8] Hence, these mixtures of products, obtained after work up in each case, were treated with aqueous sodium hydroxide and 2 and 6 formed were isolated by chromatography. The percentage yields of the perchlorates of 2 and 3 (table) have been calculated from the amounts of 2 or 7 and 6, thus isolated. An alternate synthesis of 6 has been developed[9] and these 6 have been found to be identical with the ones obtained from the reaction mixtures.

TABLE

1 R	R'	Reaction condition	m.p. of perchlorates of 2	Yields of perchlorates of 2	3
C_6H_5	H	a	168-69° (264°)^c	85	-
		b		65	20
C_6H_4-CH_3-p	H	a	271-72° (270°)^c	90	-
		b		70	15
C_6H_4-OCH_3-p	H	a	270-71° (268°)^c	80	-
		b		65	20
C_6H_4-Cl-p	H	a	254-55° (251°)^c	87	-
		b		75	15
			7	7	3
R,R'=-$(CH_2)_4$-		a	172-73°	70	10
		b		60	20

(a) For one gm. of 1, only 2 ml of conc. sulphuric acid was used.

(b) For one gm. of 1, 10 ml of conc. sulphuric acid was used.

(c) The m.p.s in parentheses are those reported in ref. (5) for perchlorates of corresponding 3.

From these results, it is evident that cyclodehydration of 1 does take place to some extent but whether the product isolated alongwith the perchlorate of 2 or 7 is 3 or the perchlorate of 6, formed by the reaction of 3 with aqueous perchloric acid, could not be ascertained because analytically pure samples of these compounds could not be procured from the mixtures.

Hence **1** on treatment with conc. sulphuric acid mainly cause sulphur extrusion and cyclodehydration constitutes only a minor reaction.

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