Tetrahedron Vol. 32, pp. 1395 to 1398. Pergamon Press 1976. Printed in Great Britain

HYDROLYSIS OF 1-METHYL-2-METHYLTHIO-Δ^2-IMIDAZOLINE

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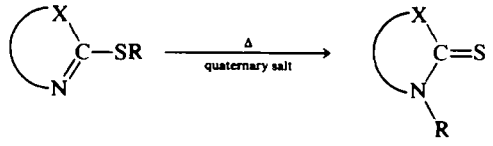
(*Received in the UK 27 October 1975; Accepted for publication 12 January 1976*)

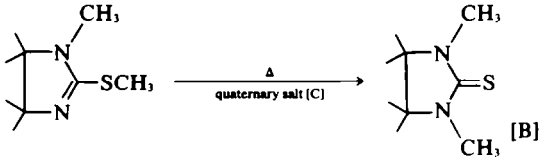
Abstract—New results in S–N methyl transfer reaction in the series of Δ_2-imidazoline with and without quaternary salt catalyst are reported. The hydrolysis of monocyclic compounds containing the 2-alkyl thio, uronium group leads to the formation of a salt. Rearrangement reactions observed in the "uncatalysed reaction" may be due to a true catalytic reaction.

The rearrangement concerned in the present paper is essentially intermolecular. The general scheme is as follows:



Scheme 1.

Several authors have studied particular aspects of these reactions.[2-4] The rearrangement of 1-methyl-2-methylthio-Δ^2-imidazoline [A][5,6] is discussed in this paper.

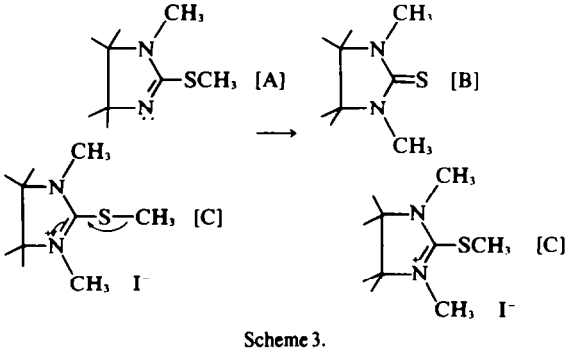


Scheme 2.

Reaction with catalyst

When [A] is heated for 30 min at 100° with 3% M of 1,3-dimethyl-2-methylthio-imidazolinium iodide [C] 35% of rearrangement occurs. This rearrangement can be followed by NMR. We have studied this S–N methyl transfer reaction at 100, 120 and 140°.

The most efficient catalyst of the rearrangement is the iodide quaternary salt [C][1,5,6] (see Scheme 3). Related kinetic processes have been studied on heterocyclic series.[7] In our case, the reactions were conducted without solvent, and the mechanism of the rearrangement with quaternary salt catalyst is described by Chambonnet.[4] The following scheme may be proposed:



Scheme 3.

Reactions without catalyst

Carefully purified 1-methyl-2-methylthio-Δ^2-imidazoline, is rearranged only to a 10% extent when heated for 30 min at 100° to give 1,3-dimethyl-imidazolidine-2-thione [B].

We have studied this reaction without catalyst at 100, 120 and 140° without solvent.

In order to explain this result, it is necessary to choose between radical and ionic mechanism.[1,8,9] A radical mechanism has been suggested for this reaction without catalyst.[1] The results of studies with radical initiators and inhibitors, and ESR, do not give evidence for the radical mechanism.[5] But, an ionic mechanism may account for the rearrangement.[1,5,6] We observed, nevertheless, that the so called "uncatalysed reaction" is catalysed by "a parasite salt". This was partly confirmed by the isolation of a compound [D] resulting from the hydrolysis of [A]. Such a product was in fact isolated for the first time in this type of reactions (Scheme 4).

The formation of this intermediate [D] is followed by NMR, IR and UV.[5,6] This intermediate [D] then induces a catalytic or degradation reaction.

Potential radicals were quenched by t-butylnitroso- and nitroso-benzene and o-nitrosotoluene. The results were in all cases negative (ESR). We have also attempted to observe the presence of radicals at the time of the rearrangement by CIDNP did not provide any evidence for their existence in our system.[5]

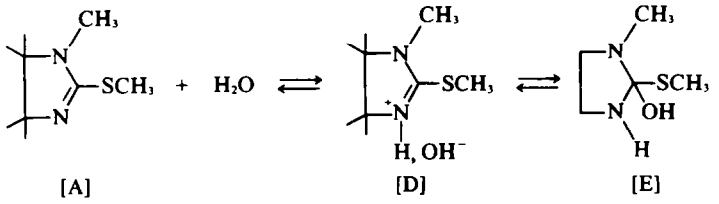
The structure [D] has been assigned to this compound

Table 1.

	100°		120°		140°	
Time (min)	B%	A%	B%	A%	B%	A%
0	0	100	0	100	0	100
5	13.5	86.5	45	55	87.5	12.5
10	20	80	56	44	90	10
15	28	72	65	35	91	9
30	35	65	75	25	92.5	7.5

Table 2.

	100°		120°		140°	
Time (min)	B%	A%	B%	A%	B%	A%
0	0	100	0	100	0	100
5	2.7	97.3	10	90	73.5	26.5
10	3.5	96.5	26	74	84	16
15	4.5	95.5	38	62	89	11
30	10	90	52.5	47.5	90	10

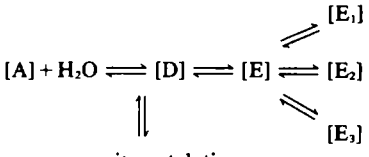


Scheme 4.

because the wavelength absorption (UV) varied with temperature. Moreover, in NMR the chemical shift of the N-methyl group in [D] (2.96 ppm; $CDCl_3$; TMS) appears at lower field than in compound A (2.83 ppm).

Mechanism of degradation

The thioether [A] reacts with water (present in small amount) to give [D] which either catalyses a parasite rearrangement or undergoes degradation reaction according to the following (Scheme 5):



Scheme 5.

The degradation compound [E_1] was identified by NMR, IR and MS and methyl mercaptan was isolated. This is not the case for the products resulting from the ring opening [E_2] and [E_3].

In mol Δ^2-thiazoline and Δ^2-oxazoline series, the hydrolysis did not give cyclic degradation products and ring-chain equilibrium was observed.[11,12] The cyclic degradation reaction confirms the existence of the reaction intermediate [E].[13]

Mechanism of parasite rearrangement

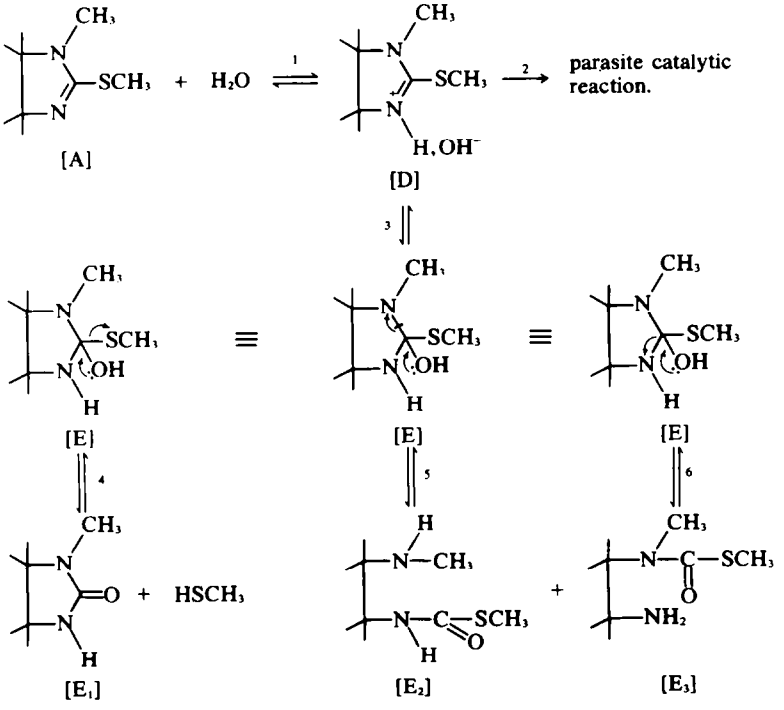
Independently of the degradation reaction, we can explain the rearrangement without iodide quaternary salt by an auto-catalytic mechanism (Scheme 7). We observed a competition between degradation (Scheme 6, steps 1, 3 and 5) and parasite catalysis (Scheme 6, steps 1 and 2). The parasite catalysis may be explained by the following Scheme 7:

In step 1, the intermediate [D] resulting from the hydrolysis of the 1-methyl-2-methylthio-Δ^2-imidazoline [A] give with [A] the true quaternary salt catalyst C' and 1-methyl-imidazolidine-2-thione [F] D'Amico[13] and Chanon[1] have shown that compounds such as [F] are efficient quenchers for the catalysed rearrangement.

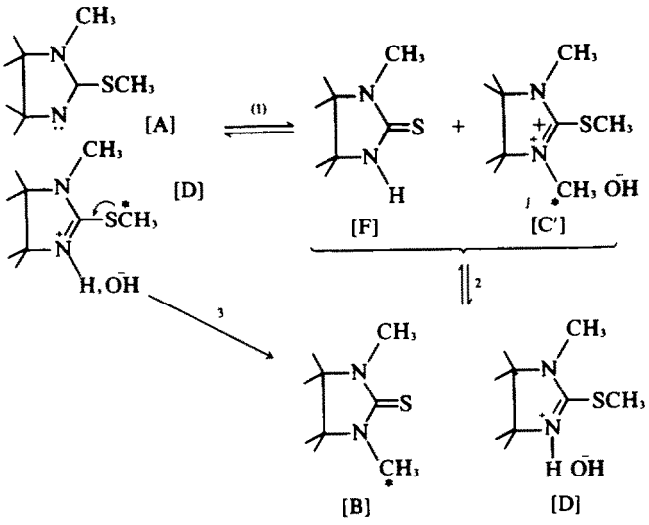
In step 2, the thione [F] an efficient quencher for the catalyst [C'] gives the salt [D] and 1,3-dimethyl-imidazolidine-2-thione [B], the product of the classical rearrangement.

The global mechanism of reaction 3 is a classic catalysed rearrangement.[4]

This competition between parasite rearrangement and degradation reaction is verified with other compounds of the diazole series and the generalisation of the reaction is presently under study in our laboratory.



Scheme 6.



Scheme 7.

Action of water on the purified thioether

When we performed the rearrangement with quaternary salt [C], we obtained simultaneous parasite rearrangement due to the intermediate [D] which was formed by water.

After a purification of the thioether [A] by distillation over potassium hydroxide and storage over it, the thioether is no longer coloured in yellow and is odourless. Without purification, a strong odour of methyl mercaptan evolves. A sample of this pure product heated 3 h at 100° gave no rearrangement and after 1 h at 140° only 2.30% of rearrangement occurred.

We then studied the reaction of the thioether [A] in the presence of 8% of water. After stirring for 5 min at room temperature we heated the mixture at 140° and we noticed the liberation of methylmercaptan (tested with lead acetate paper), which shown that the degradation well occurred. Results are indicated in Table 3.

The proposed mechanism illustrated in Scheme 7 is certainly debatable, considering the complexity of the implicated reactions. Nevertheless, we have established the intervention of a reaction intermediate to explain the competition between parasite catalytic reaction and the degradation process. The proof of the catalytic nature of the rearrangement called "without catalyst" is demonstrated and similar reaction may well have been due to traces of water in the starting material.

Table 3.

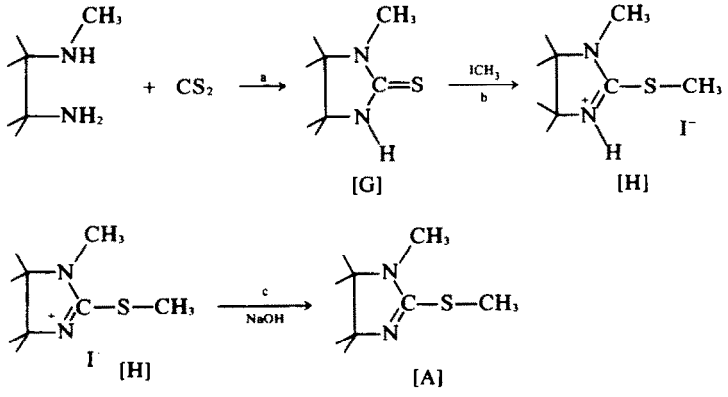
Time (min)	0	5	15	30	60
B%	0	4.2	5.85	6.5	8.8
A%	100	95.8	94.15	93.5	91.2

EXPERIMENTAL

1-Methyl-2-methylthio-Δ^2-imidazoline

(a) To a solution of 22.94 g (0.31 mole) of 2-aminoethyl methylamine in 90 cm³ 50% ethanol at 60° was added dropwise with stirring 24.9 g (0.315 mole) of carbon disulfide. The mixture was stirred for a further 3 h and then 10 cm³ of hydrochloric acid were added. The reaction was heated at 80° for 6 h and kept overnight. The solid [G] was filtered off; (66%), m.p. 128° from H_2O. $C_4H_8N_2S$ requires C, 41.06; H, 7.0; N, 23.89; S, 27.72; found: C, 41.3; H, 6.9; N, 24.1; S, 27.6%. NMR ($CDCl_3$): N–CH_3, 3.10 ppm (s), NH, 6.86 ppm (s), (CH_2), 3.60 ppm (m). TLC SiO_2, $CHCl_3$/MeOH (11/2), R_f: 0.76.

(b) To a solution of 46.4 g (0.40 mole) of [G] in a minimum of acetone, was added dropwise 59.64 g (0.42 mole) of methyliodide. The mixture was stirred for 3 h at room temperature, and the solid [H] filtered off. Yield 85%, m.p. 100°. $C_5H_{11}N_2SI$ requires C, 23.26; H, 4.26; N, 10.85; S, 12.7; found C, 23.32; H, 4.35; N, 10.80; S, 12.30%. NMR ($CDCl_3$) SCH_3, 2.99 ppm (s), NCH_3, 3.20 ppm (s), NH, 9 ppm (s), (CH_2), 4.1 ppm (m). UV (Ethanol) λ_{max} 220 nm.



Scheme 8.

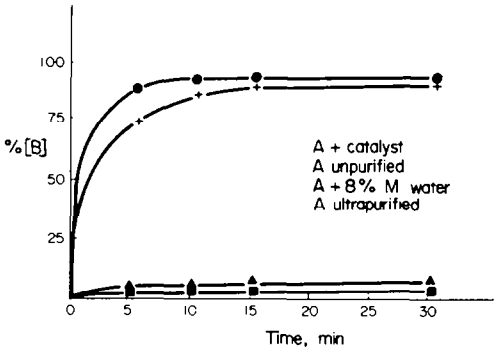


Fig. 1. A plot of percentage of [B] at 140° vs time (min) for the rearrangement of 1-methyl-2-methylthio-Δ^2-imidazoline.

(c) To a suspension of 77.4 g (0.3 mole) of [H] in anhydrous chloroform, was added 12.0 g (0.3 mole) of pulverized sodium hydroxide. The mixture was refluxed for 6 h and allowed to stand overnight at room temperature. The solution was filtered off to eliminate the sodium iodide, the solvent was evaporated and the product distilled off under vacuum. Yield 95%, b.p. 61° (3 mm Hg). $C_5H_{10}N_2S$ requires C, 46.1; H, 7.7; N, 21,50; found C, 46.22; H, 7.75; N, 21.10%. NMR ($CDCl_3$) SCH_3, 2.53 ppm (s), NCH_3, 2.83 ppm (s), $(CH_2)2$, 3.60 ppm (m). UV (Ethanol) λ_{max} 243 nm. TLC SiO_2, $CHCl_3$/MeOH (11/2) R_f: 0.68.

1,3-*Dimethyl imidazolidine 2-thione B*

As (a) in the synthesis of G. Yield 78%, m.p. 110°. $C_5H_{10}N_2S$ requires C, 46.1; H, 7.70; N, 21.50; found C, 46.35; H, 7.82; N, 21.0%. NMR ($CDCl_3$) NCH_3, 3.06 ppm (s), $(CH_2)2$, 3.55 ppm (s). UV (Ethanol) λ_{max} 241 nm. TLC SiO_2, $CHCl_3$/MeOH (11/2), R_f: 0.79.

1,3-*Dimethyl 2-methylthio imidazolinium iodic C*

13 g (0.1 mole) of 1-methyl-2-methylthio-Δ^2-imidazoline was mixed with 15.6 g (0.11 mole) of methyl iodide. The mixture was heated at 140° (fusion). Acetone was a good solvent for recrystallization. Yield 85%, m.p. 145°. $C_6H_{13}N_2SI$ requires C, 26.47; H, 4.79; N, 10.29; found C, 26.13; H, 4.92; N, 10.41%. NMR ($CDCl_3$) NCH_3, 3.3 ppm (s), SCH_3, 2.75 ppm (s), $(CH_2)2$, 4.1 ppm (s). UV (Ethanol) λ_{max} 218, 255 nm. TLC SiO_2, $CHCl_3$/MeOH (11/2), R_f: 0.36.

Analytical characteristics of the hydrolysis products

1-methyl-2-methylthio-imidazolinium hydrate D: NMR ($CDCl_3$) SCH_3, 2.73 ppm (s), NCH_3, 2.96 ppm (s), $(CH_2)2$, 3.83 ppm (t), NH, 6.20 ppm (s). UV. The UV spectrum of the quaternary salts show a particular feature in ethanol and methylene dichloride; we observed a shift towards lower wavelength and a decrease of the optical density when the temperature of the UV solvent (during the recording time) increased.[14,15] 20°, λ_{max} 220 nm (O.D. = 0.65); 10°, λ_{max} 220 nm (O.D. = 0.68); 5°, λ_{max} 221 nm (O.D. = 0.70). TLC SiO_2, $CHCl_3$/MeOH (11/2), R_f: 0.31. 1-Methyl imidazolidone E_1: NMR ($CDCl_3$) NCH_3, 2.80 (s), $(CH_2)2$, 3.43 (t), NH, 5.70 (s). IR (KBr) NH: 3380, 3250, CH: 2950–2850 (s), 1160 (s), 1280–670 (s).

Rearrangement

The rearrangement is followed by NMR (a) directly in the NMR tube if the spectrometer is equiped with temperature regulation (Jeol); (b) in the reaction vessel with samples taken at different reaction times.

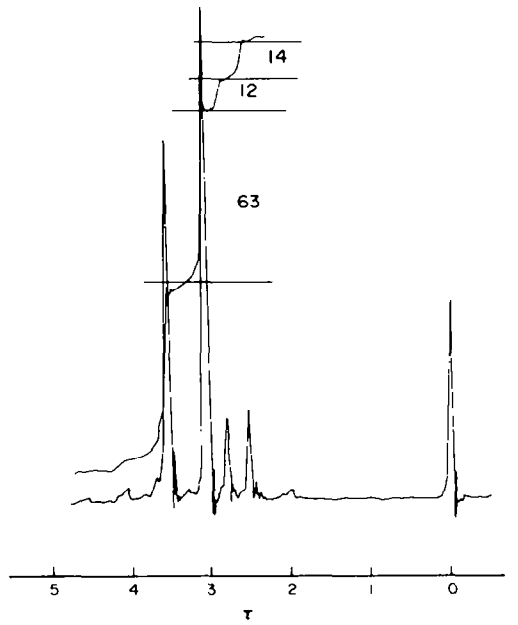


Fig. 2. Thione present to extent $\frac{63 \times 100}{63 + 12 + 14} = 71\%$.

On the NMR spectrum we observed the disappearance of the SCH_3 signal (2.5 ppm (s)) and the appearance of the NCH_3 signal (3.46 ppm (s)) of the thione, the NCH_3 signal of the thiol being at 3.58 ppm (Fig. 2).

The thione per cent is given by the ratio: integration of the NCH_3 (thione)/(integration of the $NCH_{3thione} + NCH_{3thiol} + SCH_{3thiol}$)

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