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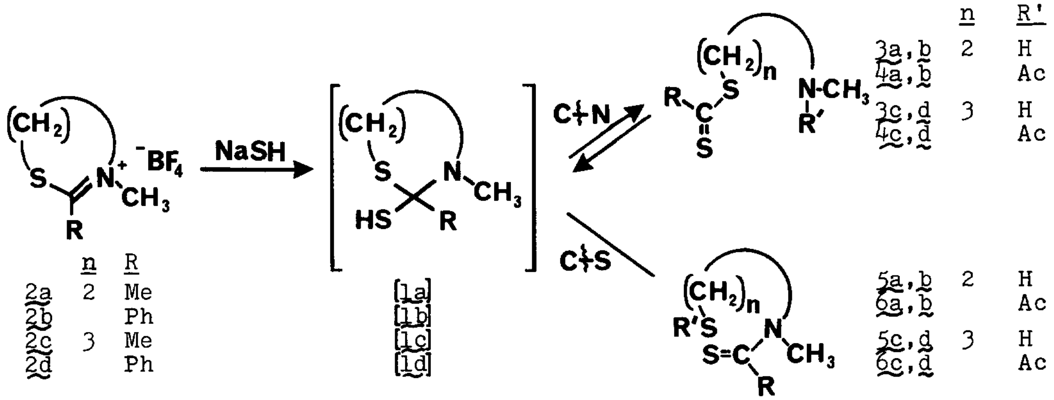
BREAKDOWN OF CYCLIC DITHIOHEMIORTHOAMIDE TETRAHEDRAL INTERMEDIATES - RC(SR')(NR$''_2$)SH - AT SUB-ZERO TEMPERATURES[1,2]

Moses K. Kaloustian* and Liliane Khouri

Department of Chemistry, Fordham University, Bronx, N.Y. 10458

ABSTRACT: The sulfhydrolyses of thioimidate salts 2a-2d, in the presence of anh. NaSH in dry 2-butanone at -82°C, proceed by the preferential cleavage of the C-N bond rather than the C-S bond.

Several reports have appeared on the generation and breakdown of short-lived tetrahedral intermediates of the following types: RC(OR')(OH)$_2$, RC(OR')$_2$OH, RC(OR')(NR$''_2$)OH,[3] RC(OR')(NR$''_2$)SH, RC(OR')$_2$SH, and RC(SR')(NR$''_2$)OH.[4] We herein present the first report on the generation and kinetic breakdown of four cyclic intermediates of the type RC(SR')(NR$''_2$)SH, *viz*. [1a] - [1d].



These short-lived intermediates, generated *in situ* by the reaction of the respective parent thioimidate salt, 2a-2d, with hydrosulfide ion, under a dry nitrogen atmosphere, fall apart through competing C-N and C-S cleavage pathways to give an amino-dithioester 3 (C‡N) and/or a mercapto-thioamide 5 (C‡S). To assess the kinetic breakdown of [1a] - [1d], we performed our studies in aprotic solvents (principally 2-butanone) at low temperatures (down to -82°C)

Table I. Sulfhydrolysis of 2-Methyl- and 2-Phenyl-N-methyl-1,3-thiazolinium, and 2-Methyl- and 2-Phenyl-N-methyl-5,6-dihydro-1,3-thiazinium Tetrafluoroborates (2a - 2d)

Thioimidate Salt	Entry	Solvent	Trapping Agent (equiv.)	T(°C)	% C-N Cleavage[a]	% C-S Cleavage[a]	% Overall Yield
2a	1	MeCN	-	0	0	100	96
	2	MeCN	AcCl/py (10)[b]	-42	0[c]	100[c]	-[d]
	3	MeC(=O)Et	Ac_2O (5)[e]	-82	76	24	83
2b	4	MeCN	-	0	0	100	-[d]
	5	$Me_2C{=}O$	AcCl/py (10)[b]	-78	5	95	35
	6	MeC(=O)Et	Ac_2O (5)[e]	-82	77	23	66
2c	7	MeCN	-	0	0	100	84
	8	MeC(=O)Et	Ac_2O/py (5)[f]	-82	100	0	95
	9	MeC(=O)Et	Ac_2O (5)[e]	-82	100[c]	0[c]	-[d]
	10	MeC(=O)Et	C_6H_5COCl (5)[e]	-82	100[c]	0[c]	-[d]
2d	11	MeCN	-	0	0	100	99
	12	MeC(=O)Et	AcBr/py (10)[b]	-82	67	33	42
	13	$Me_2C{=}O$	AcCl/py (10)[b]	-78	69	31	63
	14	MeC(=O)Et	Ac_2O/py (10)[b]	-82	77	23	77
	15	MeC(=O)Et	Ac_2O/py (5)[f]	-82	99	1	97

[a] Product ratio (expressed as % molar ratio) was determined by isolation and weighing of C-N and C-S cleavage products, except where noted. [b] NaSH was added to the substrate; trapping agent was added subsequently. [c] Determined by TLC. [d] Not determined. [e] NaSH is introduced immediately after trapping agent is added. [f] Substrate is mixed with Ac_2O; NaSH is added next, followed by pyridine.

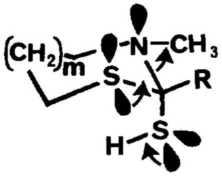
in the presence of trapping agents.[5] The results of our experiments are summarized in Table I.

The C∤N/C∤S ratios are at their lowest (0:100), as expected, when the reaction is allowed to proceed at relatively high temperatures (0°C), and in the absence of trapping agent (Table I, entries 1, 4, 7, 11); that is, in these cases exclusive C-S scission occurs (thermodynamic control). Once formed, 5 does not rearrange to 3; under these conditions, any of 3 that might be formed, as the result of kinetically-controlled C-N cleavage, cannot be assessed. Indeed, attempts at trapping any C∤N product, immediately *after* its presumed formation, were ineffective for the 5-membered ring systems (entries 2, 5) or inefficient for the 6-membered cases (entries 12, 13, 14).[6]

However, the C∤N products were efficiently trapped when one added trapping agent (Ac_2O, Ac_2O/py, C_6H_5COCl) to the thioimidate salt (2a-2d) *prior* to the addition of NaSH. Optimum conditions for these trappings were attained for all four systems (entries 3, 6, 8, 9, 10, 15). For the 6-membered ring systems, maximal %C∤N/%C∤S ratios of 100:0 were obtained with three trapping agents - Ac_2O, Ac_2O/pyridine, C_6H_5COCl (entries 8, 9, 10, 15). The optimum ratios for the 5-membered cases were 76:24 and 77:23 (entries 3, 6). The latter values represent, in all likelihood, lower limits since the *intramolecular* S→N thionacyl transfer may be in strong competition with the *intermolecular* trapping.

The proclivity to dominant (5-membered systems) or exclusive (6-membered rings) scission of the C-N bond, instead of the C-S bond, in intermediates [1a] - [1d] is yet another manifestation of the Deslongchamps effect. Despite a large difference in pK_a's of the two potential leaving groups (in favor of RS^-)[7] the overriding stereoelectronic factor assists in the preferential cleavage of the C-N bond, *vis-a-vis* an "acetyl sink."

m = 0,1



These results demonstrate that the kinetically-preferred route for the breakdown of cyclic $RC(SR')(NR''_2)SH$ in aprotic media and in the presence of an "acetyl sink" entails the cleavage of the C-N bond. Furthermore, these studies underscore the necessity of carrying out such stereochemical investigations in aprotic solvents and at sufficiently low temperatures.

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2. (a) Presented at the New York Academy of Sciences, New York, N.Y., June 10, 1980; (b) Taken in part from the M.S. Thesis of Liliane Khouri, Fordham University, 1979.
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5. For kinetic control, the %C⌇N/%C⌇S ratio equals the molar ratio of either **3**/**5** (when no trapping agent is used) or *4*/*6* (when trapping agent is used); in both instances, the ratios are derived from the weights of isolated products.
6. The *improved* efficiency of the kinetic trapping manifests itself in *higher* %C⌇N/%C⌇S ratios.
7. The potential leaving groups may be looked at as "RS^-" and "R_2N^-". Since the pK_a's of the corresponding conjugate acids are 12 (for RSH) and ~28 (for R_2NH), RS^- is the weaker base and ought to be a "better leaving group" than R_2N^-.

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