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LUMAZINESULFENATES - A NEW CLASS OF STABLE SULFENIC ACIDS

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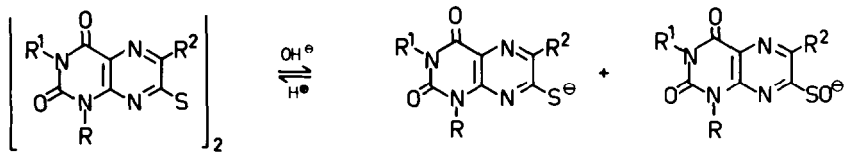
Hydrolysis of the S-S bond in some heterocyclic disulfides leads to stable sulfenic acids. 1,3,6-Trimethyllumazine-7-sulfenic acid (5) was prepared in pure form as a crystalline solid to study its physical properties and chemical reactivity.

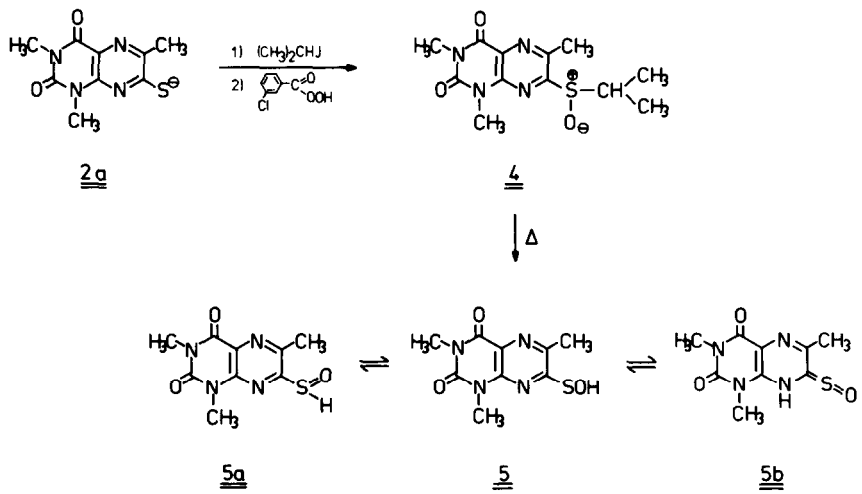
The chemistry of sulfenic acids is not well developed due to the fact that so far only very few stable compounds of this series [1] have been isolated and characterized. Since the synthesis of 1-anthraquinone-sulfenic acid by Fries [2] in 1912 there is permanent interest in these compounds which have been proposed as intermediates in various types of reactions.
During investigations of dilumazin-7-yl disulfides (1a-d) we noticed that these compounds are nucleophilically cleaved at the disulfide bond on dissolution in alkaline medium to form equimolar mixtures of lumazine-7-thionates (2a-d) and lumazine-7-sulfenates (3a-d). These latter anions are surprisingly stable under these conditions and do not disproportionate as most other sulfenates [3]. Acidification of the solutions after hydrolysis produces in the reverse reaction the disulfides 1a-d again in almost quantitative yield.



1a-d 2a-d 3a-d

	R	R^1	R^2
a	CH_3	CH_3	CH_3
b	CH_3	CH_3	H
c	CH_3	H	H
d	H	CH_3	H

Structurally similar heterocyclic disulfides such as the 7,7'-di-(6-chloro-1,3-dimethyllumazinyl)-disulfide, 6,6'-di-(1,3-dimethyllumazinyl)-disulfide, 5,5'-di-(2-methylamino-3-N-methylcarbamoylpyrazinyl)-disulfide, and 2,2'-dipyridinyl-disulfide respectively are, however, not able to form stable sulfenate anions on hydrolysis but only products of disproportionation.
More detailed investigations have been carried out with 1,3,6-trimethyllumazine-7-sulfenic acid (5). This compound can be isolated as a silver salt (3a) analogously to the procedure of Pal et al. [4] from the alkaline hydrolysate of 1a. Addition of silver ion forms first silver 1,3,6-trimethyllumazine-7-thionate (2a) as an almost insoluble material, which is filtered off before further addition of silver ions and careful neutralization of the filtrate by acetic acid leads to the separation of a deeply red-coloured powder of silver 1,3,6-trimethyllumazine-7-sulfenate (3a).
A second synthesis of 3a and its isolation as a silver salt could be performed by mild oxidation of 2a with one equivalent of hydrogen peroxide in slightly alkaline solution.



2a 4

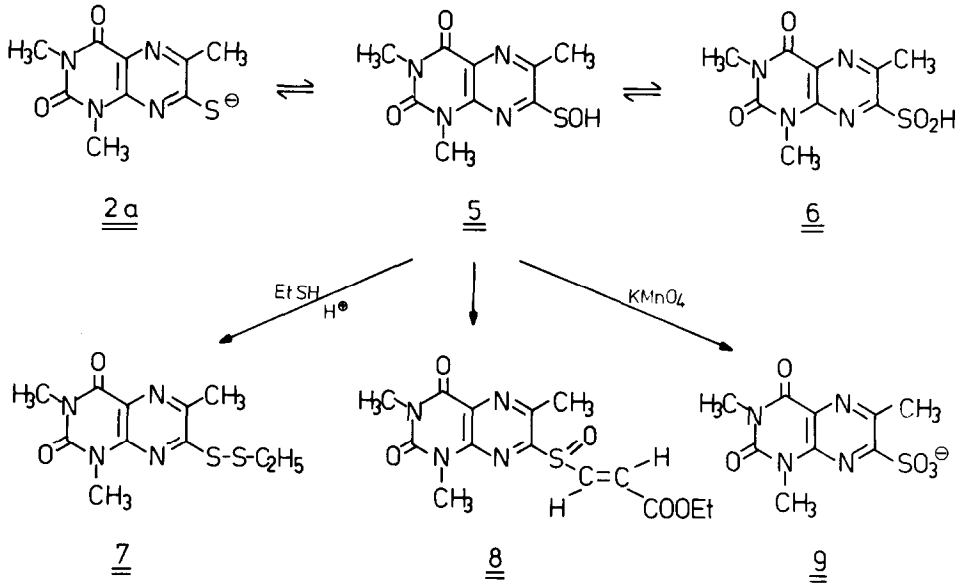
5a 5 5b

Since the free 1,3,6-trimethyllumazine-7-sulfenic acid (5) could not be obtained from its silver salt a new approach starting from 2a has been achieved. Alkylation by isopropyl iodide led to 7-isopropylthio-1,3,6-trimethyllumazine which could be oxidized by m-chloroperbenzoic acid to the corresponding sulfoxide 4 [UV(MeOH): λ max = 245, 353 nm; lgε = 4.16, 4.00. NMR ($CDCl_3$): 1.32 (2d, 6H, $CH(C\underline{H}_3)_2$; 2.88 (s, 3H, $C\text{-}CH_3$); 3.52 (m, 1H, $C\underline{H}(CH_3)_2$; 3.54 (s, 3H, $N\text{-}CH_3$); 3.72 (s, 3H, $N\text{-}CH_3$)].
Its thermal cleavage in boiling absolute toluene proceeded in an S-type-Cope elimination to the free and analytically pure 1,3,6-trimethyllumazine-

7-sulfenic acid (5) [UV (pH 2): λmax = 224, 262, 360 nm; lgε = 4.27, 3.75, 4.10; (pH 9): λ max = 226, 294, 416 nm; lgε = 4.19, 3.16, 4.10. NMR (TFA): 2.76 (s, 3H, C-CH_3); 3.68 (s, 3H, N-CH_3); 3.95 (s, 3H, N-CH_3)] which recrystallized out of the solution on cooling.

This compound may exist in principle in three tautomeric forms 5, 5a and 5b. We propose from IR-spectroscopic studies that in the crystals the 1,3,6-trimethyllumazine-7-sulfenic acid prefers to form 5a because the IR spectrum shows S=O (1050 cm^{-1}) as well as S-H (2500 cm^{-1}) vibrations. On the other hand lead comparisons of the UV spectra of 5 with its methyl-blocked derivatives of the three tautomeric forms to the conclusion that in aqueous solution the "normal" from 5 predominates.

The pK_a of 5 was found at 4.84 whereas that of 2a was much lower at 2.5. The latter compound can be considered as a vinylogous acid [5] whereas the former substance should be looked at as a vinylogous peracid. According to pK_a-values reported in literature peracides show an acidity 2-3 orders of magnitude less than the corresponding acids [6].
5 is rather stable in alkaline solution, whereas an acidic medium initiates disproportionation to 2a and 1,3,6-trimethyllumazine-7-sulfinic acid (6). However, 2a could not clearly been detected under these conditions due to its immediate reaction with the unchanged starting material to yield the symmetrical di-(1,3,6-trimethyllumazin-7-yl)-disulfide (1a). [UV (CH_2Cl_2): λmax = 252, 352, 369 nm; lgε = 4.42, 4.43, 4.48. NMR ($CDCl_3$): 2.90 (s, 3H, C-CH_3); 3.60 (s, 3H, N-CH_3); 3.62 (s, 3H, N-CH_3)].
Analogously form other sulfur compounds such as ethylmercaptane unsymmetrical disulfides (7). [UV (MeOH): λ max = 210, 254, 357 nm; lgε = 4.29, 4.03, 4.24. NMR ($CDCl_3$): 1.46 (t, 3H, CH_2-CH_3); 2.94 (q, 2H, CH_2CH_3); 2.68 (3, 3H, C-CH_3); 3.52 (s, 3H, N-CH_3); 3.78 (s, 3H, N-CH_3)].
1,3,6-Trimethyllumazine-7-sulfenic acid (5)adds also stereospecifically to ethyl propiolate to form the trans-substituted ethyl acrylate 8. [UV (CH_2Cl_2): λ max = 245, 353 nm; lgε = 4.31, 4.02. NMR ($CDCl_3$): 2.96 (s, 3H, C-CH_3); 3.66 (s, 3H, OCH_3); 3.80 (s, 3H, N-CH_3); 3.92 (s, 3H, N-CH_3); 7.04 (d, 1H); 7.82 (d, 1H)].
Reduction of 3a by sodium borohydride leads to 7-mercapto-1,3,6-trimethyllumazine (2a), whereas the formation of the oxidation products depends upon the chemical nature of the oxidizing agent. 1,3,6-Trimethyllumazine-7-sulfenic acid (5) reacts with the "electrophilic" hydrogen peroxide to 1,3,6-trimethyllumazine-7-sulfinic acid (6) and from the "nucleophilic" oxidation [7] by potassium permanganate results 1,3,6-trimethyllumazine-7-sulfonic acid (9). [UV (pH 7): λmax = 242, 345 nm; lgε = 4.24; 3.96. NMR (D_6-DMSO): 2.78 (s, 3H, C-CH_3); 3.30 (s, 3H, N-CH_3); 3.50 (s, 3H, N-CH_3)].



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