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ANCHIMERICALLY ASSISTED REDOX REACTIONS

COMPARISONS OF THE EFFECT OF TRANSANNULAR – OH AND $-NH_2$ GROUPS ON THE RATE OF THE AQUEOUS I_2 OXIDATION OF THIOETHERS STRUCTURES OF THE HETEROATOM BRIDGED 1-THIONIABICYCLO[3.3.1]NONANE INTERMEDIATES

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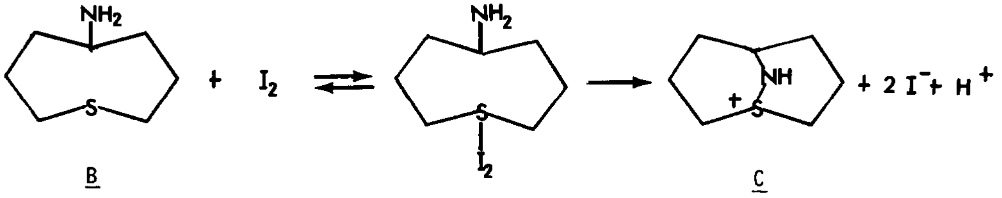
Summary· The rate law for the aqueous I_2 oxidation of 5-amino-1-thiacyclooctane has been determined and compared with 5-hydroxy-1-thiacyclooctane The crystal structures of the 9-aza- and 9-oxa-1-thioniabicyclo[3.3.1]nonanes formed on oxidative cyclization are compared

We recently reported the first X-ray crystal structure determination of an alkoxysulfonium salt, 9-oxa-1-thioniabicyclo[3.3.1]nonane triiodide [1] This salt is formed by oxidative cyclization of 5-hydroxy-1-thiacyclooctane, A, using buffered aqueous I_2 We have now confirmed that the analogous amine derivative, 5-amino-1-thiacyclooctane, B,[2] undergoes rapid oxidative cyclization to give the azasulfonium salt, 9-aza-1-thioniabicyclo[3.3 1]nonane triiodide, C.[4] Crystals of C formed on standing and were suitable for X-ray analysis. Thus, we can compare for the first time, both the relative rates of the oxidation (at a given pH and iodide concentration) and the structures of the initial products formed when thioethers undergo oxidative cyclization with amines and alcohols

The rate law for the oxidation of B by I_2 is identical to that of 5-methyl-1-thia-5-azacyclooctane (TACO).[5] $\frac{dB}{dt} = -k[\underline{B}H^+][I_2][H^+]^{-1} = -k'[\underline{B}][I_2]$. Since the rate is first order in B and first order in iodine, the rate-limiting step can be viewed as proceeding via attack of the transannular amine group on the iodine complex Consistent with this observation is the fact that the reaction is independent of the nature and concentration of buffer used to maintain the pH. Thus the reaction can be written as follows

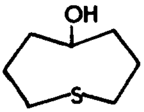
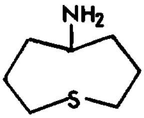
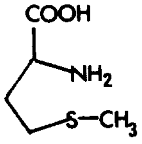
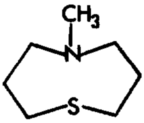


B

C

$$I^- + I_2 \longrightarrow I_3^-$$

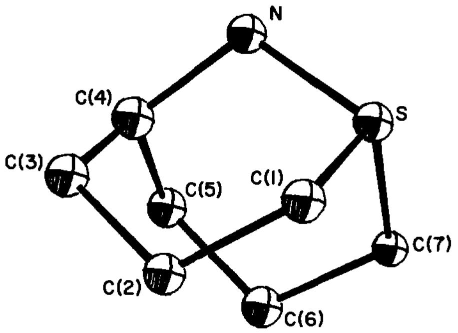
This contrasts with the behavior of A where a two-term rate law is found. One term is buffer independent whereas the other term is buffer dependent.[6] Since the rate laws for B and A are different, the only way to compare the rates is at an arbitrary pH and iodide concentration. We haven chosen pH = 6.0 and an iodide concentration of 0 060M for convenience. The buffer independent rate for A was calculated by extrapolation of observed values to zero buffer concentration. We have also found it informative to compare the relative rate of oxidation of A and B with that of methionine (met)[7] and TACO[5] under the same conditions.

	A	B	met	TACO
Relative Rate	1	10	10	4×10^3

At this pH A reacts at a rate which is only 10 times slower than the two primary amines. This result is surprising since hydroxyl group participation in thioether oxidations has not been observed in acyclic systems. The two primary amines react at similar rates even though different ring systems are formed on cyclization All previous kinetic studies of the oxidation of amine-thioethers were carried out on systems which would give five-membered rings on cyclization. Traditionally, methionine is considered to be the prime example of a system which undergoes facile oxidative cyclization, but methionine is actually quite slow when compared with the tertiary amine, TACO.

The crystal selected for data collection was a purple brown prism of dimensions 0 43 x 0.30 x 0.38 mm. The determination of cell dimensions and data collection were carried out with the crystal cooled to 140 K on a Syntex $P2_1$ diffractometer using MoKα radiation and a graphite monochromator. Crystal data are· space group, $P2_1/c$, a = 11 640(2), b = 8 452(1), c = 13.542(3) Å. β = 104.39(2)°, Z = 4; ρ exptl (298K) > 2.4 g cm^{-3} (the crystals dissolve slowly in the mixture of $C_2H_4Br_2$ and CCl_4 used for density determination) A total of 1688 unique reflections with $2\Theta_{max}$ = 45° were measured using a variable speed ω scan technique The data were corrected for Lorentz, polarization, and absorption effects. There were 1492 reflections with I > 3 σ(I) that were used in the subsequent solution and refinement of the structure. The structure was solved by direct methods. The three iodine atoms were located on an E map and refined to an R of 0.19. The remaining nonhydrogen atoms were located on a Fourier map. Full-matrix least-squares refinement of these atoms yielded R of 0.082 using isotropic thermal parameters. The scattering factors used were those for the neutral atoms Corrections for the real and imaginary parts of anomalous dispersion were applied to iodine and sulfur Tables of positional and thermal parameters and structure factors are available [8]



The overall structure (Figure 1) of the azasulfonium salt is similar to that found for the alkoxysulfonium salt,[1] the major difference being the replacement of O by NH in the bridge position. In both structures the bicyclo[3.3 1]nonane ring system adopts the common chair-chair conformation.[9] The crystal structure determinations clearly establish the gross structural identity of these two unusual species. Unfortunately, there is a loss of geometric detail due to the dominating influence of triiodide on the X-ray scattering. The results (Table I) for the azasulfonium salt can be compared with those found for dehydromethionine, the only strictly comparable structure to date.[10] In the latter compound, the N—S and C—N distances are 1.679(3) and 1.475(4)A, respectively. Both the aza- and alkoxysulfonium cations interact weakly with the triiodide anion. The distance between sulfur and one end of a triiodide anion is slightly less than the sum of the S(1.80 ± .05 Å) and I(2.15 Å) van der Waals radii. For the aza- cation this distance is 3.71 Å, and for the alkoxy- cation it is 3.91 Å The approach of the iodine atom to the sulfur atom is along the line of the sulfur-C(7) bond in the aza- salt, forming a 163° angle, for the alkoxy- salt it approaches along S—O, forming a 164° angle.

From these results it is apparent that the thioether group can undergo rapid oxidative coupling with a variety of neighboring groups in aqueous solution to give stable products Similar coupling reactions could occur under biological conditions.

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TABLE I. Table of Bond Distances (Å) and Angles for $(SNC_7H_{14})(I_3)$.

I(1)-I(2)	2.935(3)	C(4)-C(5)	1.53(4)	S-C(1)-C(2)	112.(2)
I(2)-I(3)	2.903(3)	C(5)-C(6)	1.53(5)	S-C(7)-C(6)	116.(2)
S-N	1.67(3)	C(6)-C(7)	1.60(4)	C(1)-C(2)-C(3)	113.(3)
C(4)-N	1.52(4)	S···C(4)	2.64(3)	C(2)-C(3)-C(4)	113.(3)
S-C(1)	1.82(3)	I(1)-I(2)-I(3)	178.6(1)	C(3)-C(4)-N	110.(2)
S-C(7)	1.77(3)	C(4)-N-S	112(2)	C(5)-C(4)-N	113(2)
C(1)-C(2)	1.55(4)	N-S-C(1)	100 (1)	C(3)-C(4)-C(5)	117.(3)
C(2)-C(3)	1.59(4)	N-S-C(7)	108(1)	C(4)-C(5)-C(6)	114.(2)
C(3)-C(4)	1.50(4)	C(1)-S-C(7)	105(1)	C(5)-C(6)-C(7)	112.(3)

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Thermal parameters deposited with the British Lending Library at Boston Spa, Wetherby, W.Yorkshire as SUP.45,071
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