Tetrahedron Letters No. 19, pp 1937 - 1940, 1972. Pergamon Press. Printed in Great Britain.

THE OXIDATION OF AMINOCYCLOPROPYL SULFIDES

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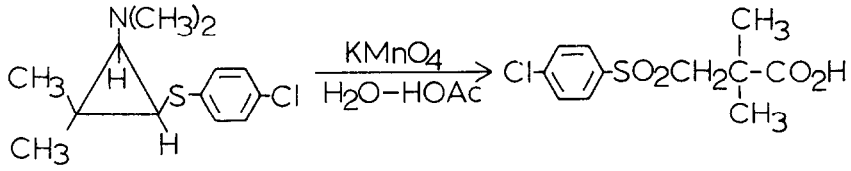
(Received in USA 7 March 1972; received in UK for publication 5 April,1972)

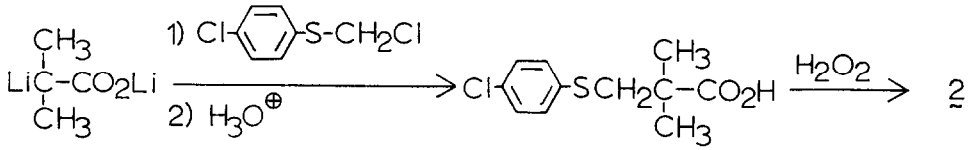
There has been recent interest in the ring-opening of cyclopropanes via zwitterionic intermediates.[1-5] This report describes the oxidation of aminocyclopropyl sulfides[6] to afford ring-opened products, presumably via zwitterionic intermediates.

Treatment of 1[6] with $KMnO_4$ in aqueous acetic acid at 25-30° afforded the sulfone acid 2[7] in 52% yield, mp, 134-135.5°.



1 2

Compound 2 was independently synthesized by the oxidation of sulfide 3, mp 84.5-86°, which was obtained from the alkylation of the dilithium salt of isobutyric acid[8] with chloromethyl p-chlorophenyl sulfide.



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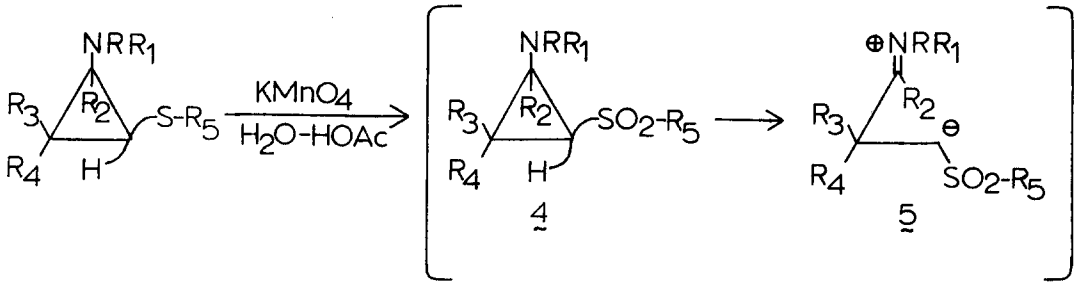
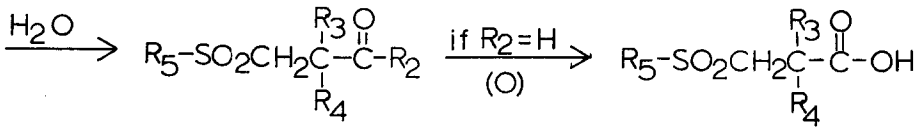
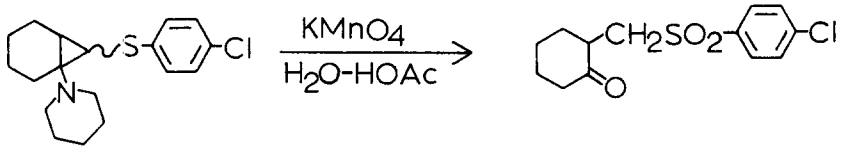
The conversion of 1 into 2 can be best rationalized by initial formation of the aminocyclopropyl sulfone intermediate of type 4 which subsequently opened to a zwitterionic intermediate

of type 5. Reaction of the zwitterion with water afforded the ring-opened aldehyde which was then oxidized to the acid (2). This mechanistic sequence is summarized by the following generalized schematic representation:

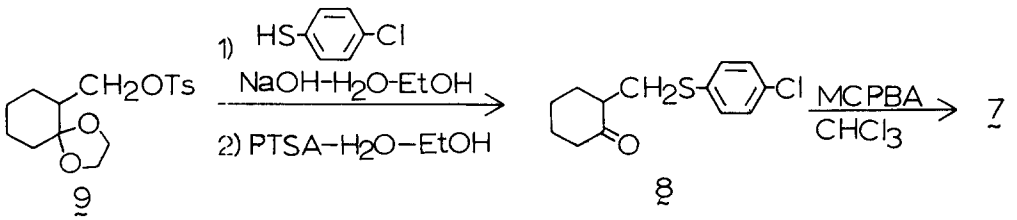




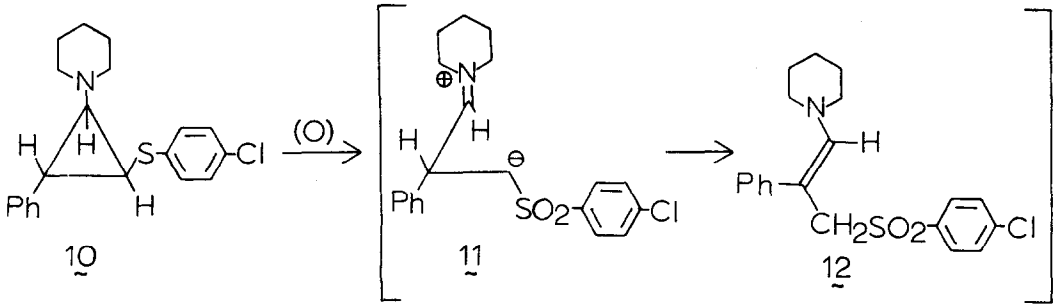
Application of this oxidative ring-opening reaction to the aminocyclopropyl sulfide 6[9] afforded the ketosulfone 7, mp 65-66°, in 62% yield. Compound 7 was independently prepared by the



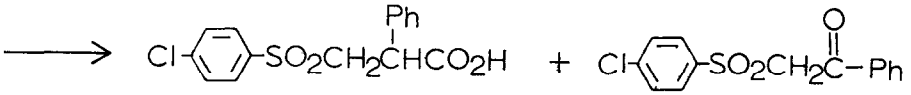
oxidation of ketosulfide 8, bp 160-164°/0.2 mm, which was obtained from tosylate 9[10].



Treatment of 10 under similar conditions afforded a mixture of acid 13, mp 145-147° (18% yield),

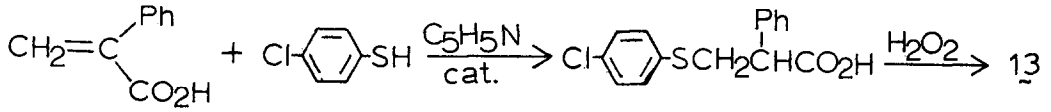


10 11 12



13 14

and ketone 14[11] (58% yield). Compound 13 was independently synthesized by oxidation of sulfide 15, mp 84.5-86.5°, which was obtained from the addition of p-chlorothiophenol to atropic acid.



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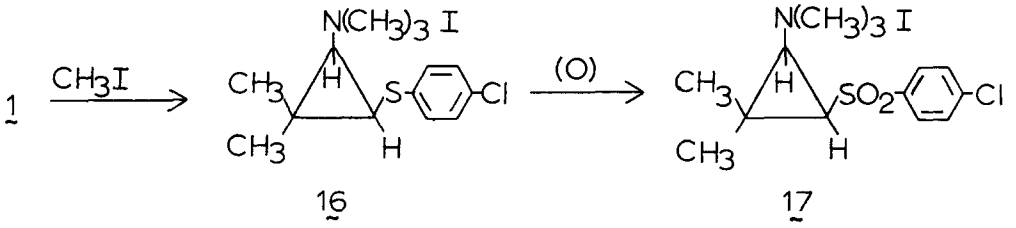
Acid 13 presumably arose from intermediate 11 in a manner analogous to the formation of 2. The formation of ketone 14 can be rationalized by the oxidative cleavage of the enamine intermediate 12[12].

A major driving force for these ring opening reactions is the formation of well stabilized zwitterionic intermediates. Evidence for zwitterion involvement was obtained when a compound (16, mp 96-98°), in which the electron pair of the nitrogen atom is not available for zwitterion stabilization, was submitted to similar oxidizing conditions.[13] The product obtained was the unopened sulfone 17, mp 186°d (66% yield).



16 17

REFERENCES AND FOOTNOTES

1. I. G. Bolesov, S. A. Gladyr, A. S. Kozmin and R. Y. Levina, Zh. Org. Khim., 6, 2431 (1970).

2. E. W. Yankee and D. J. Cram, J. Amer. Chem. Soc., 92, 6328 (1970).

3. ibid., 92, 6329 (1970).

4. ibid., 92, 6331 (1970).

5. D. J. Cram and A. Ratajczak, J. Amer. Chem. Soc., 90, 2198 (1968).

6. The preparations of the aminocyclopropyl sulfides used in this work are described in the accompanying communication.

7. The ir, nmr, and mass spectra are in accord with the proposed structures for all new compounds. Satisfactory elemental analyses were also obtained for all new compounds.

8. P. L. Creger, J. Amer. Chem. Soc., 89, 2500 (1967).

9. Mixture of endo and exo isomers.

10. W. Kirmse and S. Schneider, Chem. Ber., 102, 2440 (1969).

11. H. Martin and R. Hirt, U. S. Patent No. 2,207,021.

12. The oxidative decarboxylation of 13 into 14 is not the major pathway for the formation of 14 since treatment of 13 under identical reaction conditions ($KMnO_4$-HOAc-H_2O) afforded only a 14% yield of 14 with a 60% recovery of 13.

13. The periodate generated in this oxidation was back-reduced to iodide by sodium bisulfite.