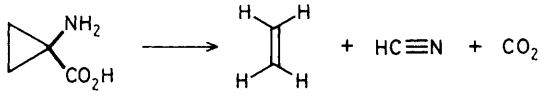
The Stereochemistry of Oxidation of 1-Amino-cyclopropanecarboxylic Acid

Jack E. Baldwin,* David A. Jackson, and in part Robert M. Adlington and Bernard J. Rawlings

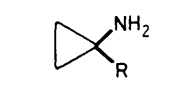
The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford OX1 3QY, U.K.

Whereas hypochlorite oxidation of 1-amino-*cis*-[2,3-$^2H_2$]cyclopropane carboxylic acid yields ethylene with retention of stereochemistry the use of transition metal oxidants, such as copper(II), permanganate, and ferrate ions gives completely scrambled *cis*- and *trans*-[1,2-$^2H_2$]ethylene as is found in the biosynthetic process.

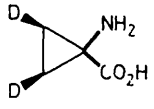
The formation of ethylene in plants involves the oxidative conversion of 1-aminocyclopropanecarboxylic acid (ACC) (**1a**) into ethylene,[1] cyanide,[2] and presumably carbon dioxide, Scheme 1. We were the first to show that this process unexpectedly proceeded with complete loss of stereochemistry since *cis*-[2,3-$^2H_2$]ACC (**2**) gave an equal mixture of *cis*- and *trans*-[1,2-$^2H_2$]ethylene,[3] a result which was subsequently found also in mung beans.[4] In contrast, the efficient chemical oxidation of (**2**) with sodium hypochlorite gave *cis*-[1,2-$^2H_2$]ethylene with retention of configuration.[3] We have now found that the biosynthetic stereochemical result can be duplicated by oxidation of ACC with various transition metal ions, such as Cu^{2+}, MnO_4^-, and FeO_4^{2-}, Table 1. That the amino group is the site of reaction in these processes was indicated by the absence of reaction of ACC in acidic media and further by the observation that whereas cyclopropylamine (**1b**) gave ethylene (9%) with $CuSO_4$, neither the *N*-ethoxycarbonyl-ACC (**4**) nor cyclopropanecarboxylic acid produced ethylene when oxidized under the same conditions. Oxygen was not required for these reactions. That nitriles are, like the biosynthetic process, found in these reactions was shown by the oxidation of 1-methylcyclopropylamine (**1c**) in 3.5% aq. NH_3 with $CuSO_4$ (40 °C, 6 days) or $KMnO_4$ (20 °C, 20 h) to ethylene and acetonitrile (3% and 15% respectively, ^1H n.m.r. and i.r. spectroscopy). The clear stereochemical difference between the biological and the metal ion oxidations and that seen with hypochlorite can be explained on the basis that the former involve a cation radical (**5**) with rapid ring opening and rotation in the acyclic intermediate (**6**) whereas the latter involves a nitrene (**7**) followed by simultaneous breakage of both carbon–carbon bonds, resulting in stereochemical retention, Scheme 2. Although we have not been able to observe the *N*-chloro compounds suggested to be involved in the hypochlorite oxidation we have been able to observe a similar species. Thus oxidation of imine (**8a**) (*m*-chloroperbenzoic acid or CF_3CO_3H, CD_2Cl_2, −70 °C) monitored by ^1H n.m.r. spectroscopy gave the oxaziridine (**9a**) [40%, ^1H n.m.r. δ 4.4 (1H, s)], which decomposed at



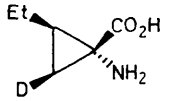
Scheme 1



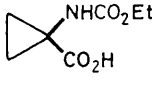
(1); **a**, R = CO_2H
b, R = H
c, R = Me



(2)



(3)

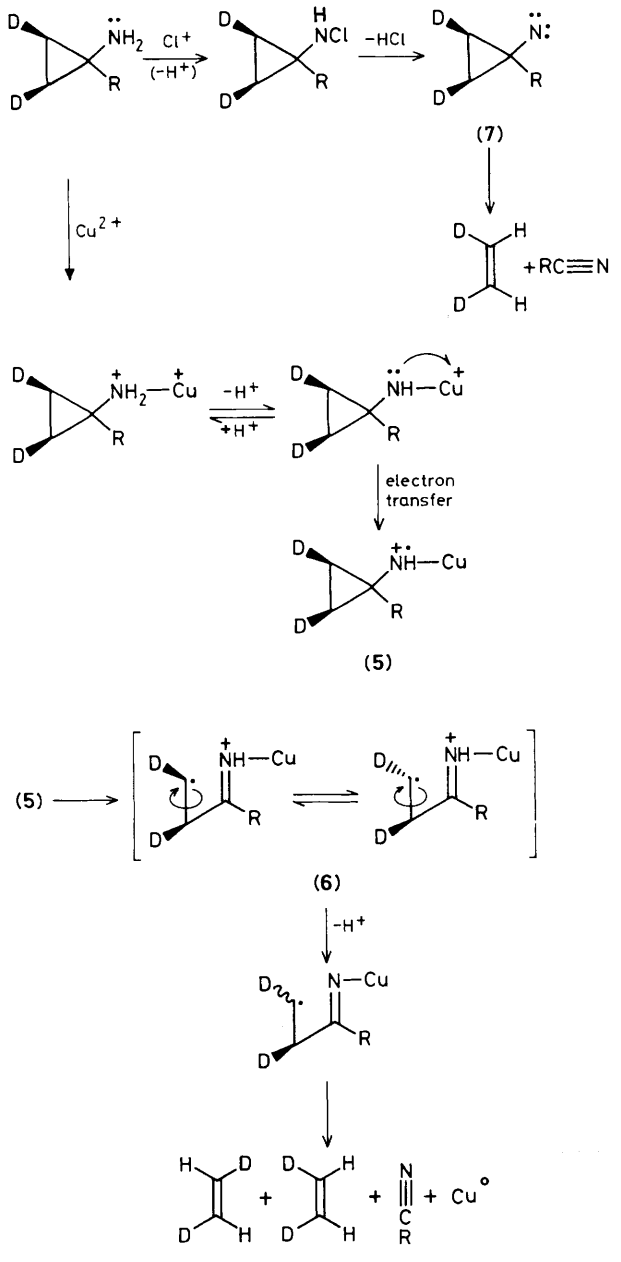


(4)

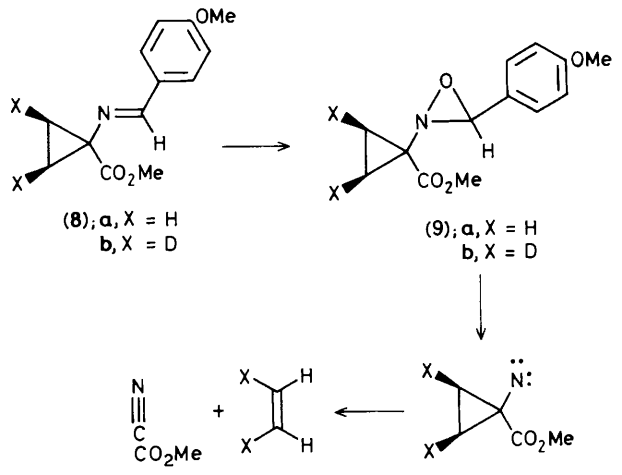
Table 1. Production of olefins from ACC and derivatives.

Precursor		$CuSO_4$[a]	$KMnO_4$[b]	K_2FeO_4[c]
(**1a**)	Yield/%[d]	20	25	30
(**2**)	Stereochem.[e]	1:1	1:1	1:1
(**3**)	Yield/%	4	7	12
(**3**)	Stereochem.[f]	1:1	1:1	1:1

[a] In 3.5% aq. NH_3, 1 equiv. $CuSO_4$, 40 °C, 4.5 days. [b] In 3.5% aq. NH_3, 2 equiv. $KMnO_4$, 20 °C, 18 h. [c] In 0.15 M NaOH, 2 equiv. K_2FeO_4, 20 °C, 2 h. [d] Determined by g.l.c. [e] Ratio of *cis*- and *trans*-[1,2-$^2H_2$]ethylene, determined as in ref. 3. [f] Ratio of *cis*- and *trans*-[1-^2H]but-1-ene, determined by ^2H n.m.r. spectroscopy on the products of *trans*-bromination by comparison with authentic standards.



Scheme 2



Scheme 3

−40 °C to ethylene, *p*-methoxybenzaldehyde, and methyl-cyanoformate. When this reaction was conducted on the imine (**8b**), derived from *cis*-[2,3-$^2H_2$]ACC there was obtained only *cis*-[1,2-$^2H_2$]ethylene. These results may be rationalised by the decomposition of the oxaziridine intermediate to the nitrene, followed by stereospecific collapse to ethylene with retention of stereochemistry, Scheme 3.

In summary, oxidation of ACC and derivatives with transition metal ions provides ethylene and nitrile products in a manner reminiscent of the biosynthetic pathway, whereas hypochlorite oxidation or the oxaziridine derived from ACC ester collapses to ethylene with retention of configuration. These two stereochemically distinct pathways may arise from the operation of cation radical and nitrene intermediates, respectively.

Received, 30th October 1984; Com. 1545

References

1 M. Lieberman, *Annu. Rev. Plant Physiol.*, 1979, **30**, 533; D. O. Adams and S. F. Yang, *Trends Biochem. Sci.*, 1981, 161; N. E. Hoffman, J-R. Fu, and S. F. Yang, *Plant Physiol.*, 1983, **71**, 197; M. Guy and H. Kende, *Planta*, 1984, **160**, 281 and references therein.
2 G. D. Peiser, T-T. Wang, N. E. Hoffman, S. F. Yang, H-W. Liu, and C. T. Walsh, *Proc. Natl. Acad. Sci. USA*, 1984, **81**, 3059.
3 R. M. Adlington, J. E. Baldwin, and B. J. Rawlings, *J. Chem. Soc., Chem. Commun.*, 1983, 290.
4 M. C. Pirrung, *J. Am. Chem. Soc.*, 1983, **105**, 7207.