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SPECIFIC DEAMINATION OF 4-AMINO-1,2,4-TRIAZIN-5(4H)-ONES BY CATALYTIC OXIDATION WITH t-BUTYLHYDROPEROXIDE. A CHEMICAL MODEL FOR METABOLISM OF 1,2,4-TRIAZINE HERBICIDES

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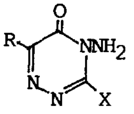
The oxidation of 4-amino-1,2,4-triazine herbicides (1) with t-butylhydroperoxide catalyzed by Co(Salen) resulted in the specific deamination of the 4-amino group, providing a chemical model for the metabolism of the herbicides.

4-Amino-1,2,4-triazin-5(4H)-ones (1) are important herbicides, which act as inhibitors of the photosynthetic electron flow.[1] Recent works on the metabolism of the herbicides 1, implying significantly detoxification in herbicide-tolerant plants, have revealed that three metabolites, 6-t-butyl-3-methylthio-1,2,4-triazin-5(4H)-one (2a), 4-amino-6-t-butyl-3,5(2H, 4H)-dione (3), and 6-t-butyl-1,2,4-triazin-3,5(2H, 4H)-dione (4), are obtained *in vivo* from 1a,[2a] and 3-methyl-6-phenyl-1,2,4-triazin-5(4H)-one (2b) from 1b.[2b] A chemically important metabolite is the deamination product 2. Little has been known about artificial formation of 2 from 1, except for the irradiation of 1a with UV-light in an aqueous solution to give 2a.[1,3] However, in contrast to the photochemical deamination, the enzymatic reaction does not require light.[1]



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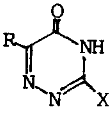

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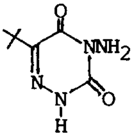

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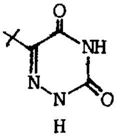

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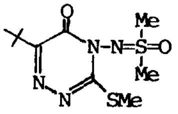

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a; R = t-Bu, X = SMe
b; R = Ph, X = Me

We now wish to report that the oxidation of the herbicides 1 with t-butylhydroperoxide catalyzed by M(Salen) [M = Co(II), Mn(II); Salen = N,N'-disalicylideneethylenediamine] under dark conditions resulted in the exclusive deamination giving rise to 2. This provides a chemical model for the metabolism of the herbicides.

Compounds 1 were quite stable against t-butylhydroperoxide without catalyst, contrary to 1,1-diphenylhydrazine.[4] When a catalytic amount (0.2 mmol) of Co(Salen) was added to a solution of 1a (1 mmol) and t-BuOOH (2.3 mmol, a commercial material) in CH_2Cl_2 (20 ml), the reaction took place smoothly at room temperature to give 2a quantitatively (80% conversion in 7 h). When the reaction mixture was allowed to stand at room temperature for 2 days, hydrolyzed prodct 4 was obtained in 24% yield. The oxidation took place also in methanol, where the reaction became slower than that in CH_2Cl_2 and gave a mixture of 2a, 3, and 4[5] as obtained in the enzymatic reaction. It is noted that no product due to oxidation of the methylthio group was obtained, whereas thioethers normally act as good reducing agents toward hydroperoxides. Application of the same oxidation conditions to compound 1b resulted also in the quantitative formation of 2b,[5] while the reaction was slower (15% conversion in 5 h) than that of 1a. Mn(Salen) was found to be more effective catalyst than Co(Salen): **2b** was formed quantitatively from **1b** with 90% conversion in 6 h.[6] The oxidation of 1a with $Pb(OAc)_4$ in CH_2Cl_2 also gave 2a quantitatively. When this oxidation was carried out in the presence of Me_2SO (2 equiv.), sulfoximide 5[7] was obtained in 61% yield. On the other hand, the catalytic oxidation of 1a with t-BuOOH in the presence of Me_2SO did not give 5 but only **2a**. It is therefore evident that the present catalytic oxidation of 1 with t-BuOOH does not involve an N-nitrene intermediate.[7] Since an 4-(N, N-dimethyl)amino derivative of 1a was quite stable under the catalytic oxidation conditions, hydrogen abstraction by t-butylperoxyl and/or t-butoxyl radical from the 4-amino group in 1 should be the initiation reaction. The interaction between the resulting amino radical and t-BuOOH may cause an oxidative cleavage of the N-N bond.[4] In view of obtaining further informations on mechanism of the present catalytic oxidation, the catalytic oxidation of 4-(4-chlorobenzyl)amino and 4-(4-methoxybenzyl)amino derivatives of 1a was examined. However, the reaction was extremely slow and no significantly informative products ascribable to the benzylic substituent were obtained at present. Hydrogen peroxide was also found to oxidize 1 in the presence of Co(Salen) to give 2. Interestingly, the use of Mo and V complexes in place of the redox catalysts M(Salen) for the catalytic oxidation of 1a resulted in the quantitative formation of 3.[8]

The present results suggest that hydroperoxidic species may play an important role in the metabolism of the herbicides 1.

References and Notes

1) W. Draber and C. Fedtke, "Advances in Pesticide Science", H. Geissbühler, Ed., Part 3, Pergamon Press, Oxford, 1978, p. 475.
2) (a) R. R. Schmidt and C. Fedtke, Pestic. Sci., 8, 611 (1977). (b) B. L. Mangeot, F. E. Slife, and C. Rieck, Weed Science, 27, 267 (1979).
3) H. Parlar and F. Korte, Chemosphere, 10, 797 (1979).
4) K. Maruyama, T. Otsuki, and T. Iwao, J. Org. Chem., 32, 82 (1967).
5) Products 2, 3, and 4 were identified with authentic samples readily available by the reported methods: H. Neunhoeffer, "The Chemistry of Heterocyclic Compounds", Vol. 33, A. Weissberger and E. C. Taylor, Ed., John Wiley and Sons, Inc., New York, N. Y., 1969.
6) Complexes such as M(Pc) [M = Fe(II), Co(II), Cu(II); Pc = phthalocyanin]and Co(TPP) are also found to catalyze the oxidative deamination of 1 but less active than Mn(Salen).
7) The structure 5, isolated as pale yellow needles, m.p. 212-213 °C, was determined by its spectral and analytical data. The formation of an N-nitrene intermediate trapped by DMSO was demonstrated by the $Pb(OAc)_4$ oxidation of 1-aminoquinoxalines: B. Adger, C. W. Rees, A. A. Sale and R. C. Storr, J. Chem. Soc. Chem. Commun., 695 (1971).
8) $MoO_2(acac)_2$ or $VO(acac)_2$ (0.2 mmol) was used for the oxidation of 1a (1 mmol) with t-BuOOH (2.3 mmol) in CH_2Cl_2 (20 ml) at room temperature. The reaction was complete in 1 h.

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