DECOMPOSITION OF 7-NITRO-2,4-DIHYDROXY-1,4-BENZOXAZIN-3-ONE IN AQUEOUS SOLUTIONS

Héctor R. Bravo and Hermann M. Niemeyer

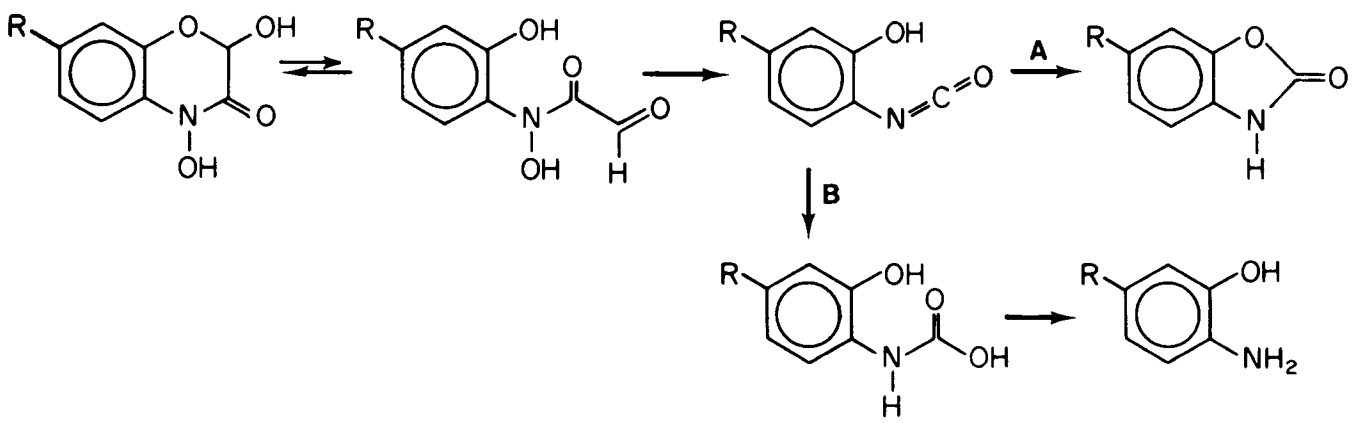
Departamento de Química, Facultad de Ciencias, Universidad de Chile, Casilla 653, Santiago, Chile

Abstract - Kinetic and product studies indicate that the title compound decomposes in aqueous solutions to give 5-nitro-2-aminophenol with the intermediacy of N-(2-hydroxy-4-nitrophenyl)carbamic acid.

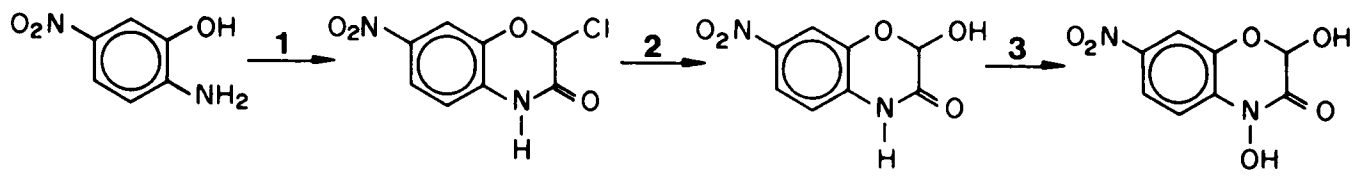
Cyclic hydroxamic acids (HX) derived from 2,4-dihydroxy-1,4-benzoxazin-3-one (DIBOA) present in cereal extracts,[1] show antibiotic and antifeedant effects towards cereal aphids,[2-4] toxicity against several plant pathogenic fungi[5] and bacteria,[6] allelopathic effects towards weeds,[7-8] and possess considerable anti-inflammatory activity.[9]

The decomposition of DIBOA and its 7-methoxy derivative to the corresponding benzoxazolin-2-ones has been studied in detail.[10-14] The mechanism involving an isocyanate intermediate depicted in Scheme 1 path A accounts for the observations reported. When a series of 7-substituted DIBOAs was studied, the reactions followed a common kinetic pattern and gave rise to a Hammett plot consistent with the mechanism above.[15] The 7-nitro compound (NDIBOA) constituted an exception. We report herein the characterization of the decomposition of NDIBOA.

Scheme 1



NDIBOA was synthesized by oxidation of the corresponding lactam, which was obtained by reaction of 5-nitro-2-aminophenol with dichloroacetylchloride and further hydrolysis of the product with aqueous $NaHCO_3$.[16]



1 : $Cl_2CHCOCl$ / $(C_2H_5)_3N$, anhydrous ether
2 : 10 % aq. $NaHCO_3$
3 : i) BSA , ii) $MoO_5(DMF)_2$ / CH_2Cl_2 , iii) $Na_4(EDTA)$

The main product isolated from ethereal extracts of the decomposition reaction mixture at every pH studied was 5-nitro-2-aminophenol, identified by comparison of its spectroscopic and chromatographic properties with those of a commercial standard.

Kinetics of decomposition was followed at 50°C between pH 3 and 10 for a least 3 half-lives by taking spectra between 300 and 460 nm after different time intervals. Data were fitted to a first-order kinetic model. Standard errors of the rate constants were lower than 3%.

The spectra of reactants, intermediates and products were pH-dependent. In the pH range 3 to 7, kinetics was monophasic with disappearance of the band in the region 335-380 nm concomitant with the appearance of a band at 395 nm. Runs at pH higher than 8 showed biphasic behaviour. The first phase consisted of the decrease of the absorption in the region 390-410 nm and concomittant increase in the region 320-355 nm and showed an isosbestic point in the region 360-375 nm. During the second phase, the band in the region 320-355 nm disappeared and another one was formed in the region 360-420 nm. Kinetic plots for these processes are shown in Figure 1.

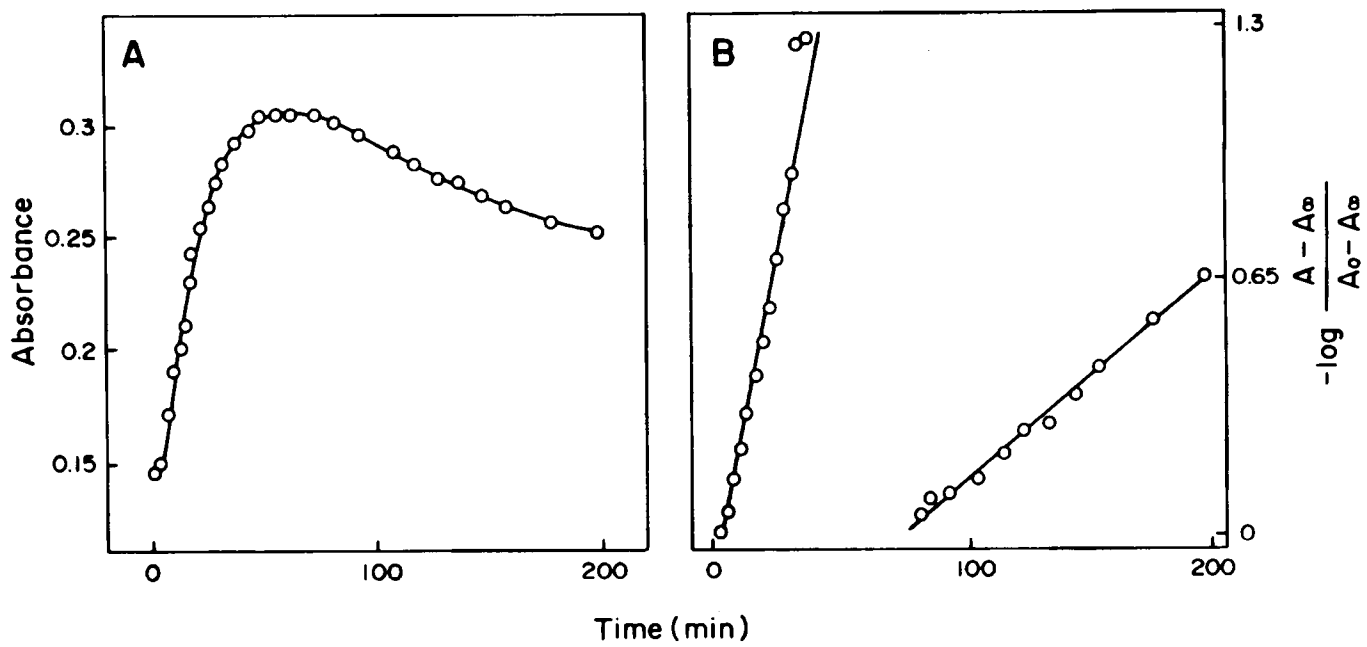


Figure 1. Decomposition of NDIBOA at pH 10, 50°C followed at 320 nm: direct plot (A), semilog plots for the two phases (B).

Table 1 shows the rate constants obtained for the decomposition of NDIBOA at different pH. The rates for the first process (k_I) were pH-dependent. The rate-pH profile (Figure 2) suggests the independent decomposition of NDIBOA and its monoanion. The solid line in the graph corresponds to the least-squares fit of the data to equation 1 arising from the model in Scheme 2. The fit generates values for k_1 = 0.94 x 10^{-3} min^{-1}, k_2 = 11.68 x 10^{-3} min^{-1} and pK = 5.3. A value of 6.14 has been determined at 30°C from thermodynamic spectral data.[15] The second process (k_{II}) does not show a clear cut dependence on pH.

Table 1. pH dependence of the pseudo first order rate constants for the decomposition of NDIBOA at 50°C

pH	k_I . 10^{-3} (min^{-1})	k_{II} . 10^{-3} (min^{-1})
3.0	0.94	
4.0	0.90	
4.5	1.52	
5.0	1.77	
5.5	3.15	
6.0	5.68	
7.0	10.7	
8.0	11.3	2.20
9.0	11.5	2.74
10.0	11.7	2.53

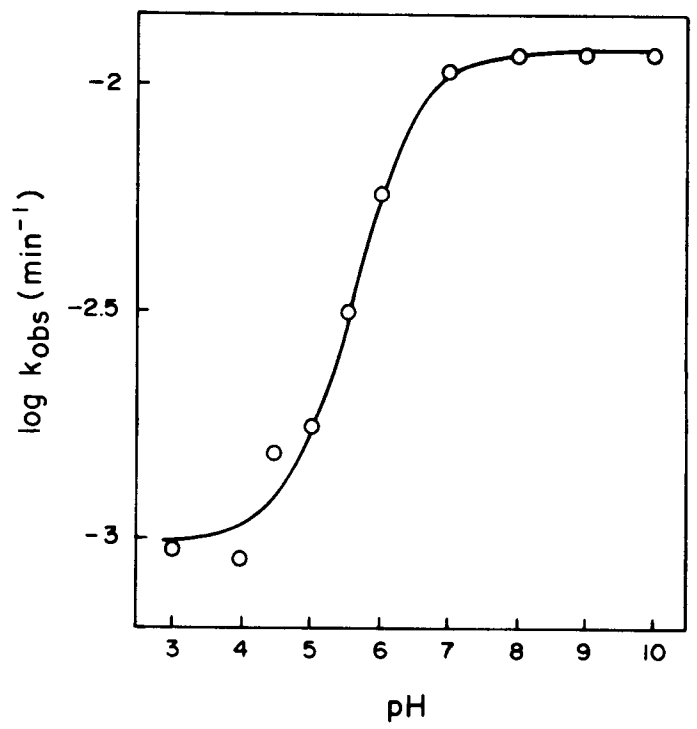
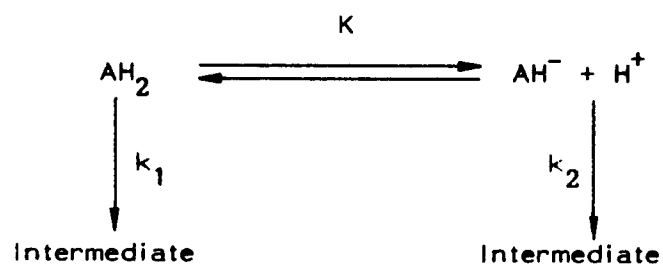


Figure 2. pH-rate profile for the decomposition of NDIBOA in aqueous solutions at 50°C.

Scheme 2



$$k_{obs} = \frac{K_1 (H^+) + k_2 K}{(H^+) + K}$$

Two likely possibilities for the structure of the intermediate that accumulates between pH 7 and 10 are an isocyanate and a carbamic acid. The following evidence indicates that this latter possibility prevails: i) the uv spectrum of the intermediate is similar to that expected for a carbamic acid;[17] ii) addition of amines to the reaction medium failed to produce any measurable amount of substituted urea; iii) the spectrophotometric changes and the rates observed for the second phase of the reaction were comparable to those reported for the conversion of N-(p-nitrophenyl)carbamate into p-nitroaniline;[17] iv) control runs subjecting 6-nitrobenzoxazolin-2-one to similar reaction conditions failed to produce the corresponding aminophenol. In the reaction of 2,4-dihydroxy-1,4-benzoxazin-3-ones with substituents in position 7 less electron-accepting than the nitro group, internal nucleophilic attack by the phenolic oxygen in the isocyanate prevents the formation of a carbamic acid and leads directly to a 1,3-benzoxazin-2-one. When the 7-nitro group is present, its electron-attracting properties decrease the nucleophilicity of the phenolic oxygen. In this case, nucleophilic attack by solvent brings the rapid formation and accumulation of the corresponding carbamic acid, as has been reported earlier (Scheme 1, path B).[17,18]

At pH lower than ca. 7, the spectral changes do not evidence the accumulation of an intermediate. In this case formation of the intermediate is slower than its further reaction with solvent since this latter reaction is acid catalyzed.[19] However, since the product of the reaction is the same at every pH studied, it is safe to assume that the reaction follows the mechanism described throughout the pH range considered.

ACKNOWLEDGEMENTS

Financial support by International Foundation for Science, Agency for International Development, International Program in the Chemical Sciences and Universidad de Chile is gratefully acknowledged.

REFERENCES

1. H.M. Niemeyer, Phytochemistry, 1988, 27, 3349.
2. V.H. Argandoña, J.G. Luza, H.M. Niemeyer, and L.J. Corcuera, Phytochemistry, 1980, 19, 1665.
3. H.M. Niemeyer, E. Pesel, S. Franke, and W. Francke, Phytochemistry, 1989, 28, 2307.
4. A. Givovich and H.M. Niemeyer, Entomol. Exp. Appl., 1991, **59**, 79.
5. T.E. Toth, Novenytermeles, 1983, **33**, 213.
6. L.J. Corcuera, M.D. Woodward, J.P. Helgeson, A. Kelman, and C.D. Upper, Plant Physiol., 1978, **61**, 803.
7. R.B. Wolf, G.F. Spencer, and R.D. Plattner, J. Nat. Prod., 1985, 48, 59.
8. F.J. Pérez, Phytochemistry, 1990, **29**, 773.
9. H. Otsuka, Y. Hirai, T. Nagao, and K. Yamasaki, J. Nat. Prod., 1988, 51, 74.
10. J.B. Brendenberg, E. Honkanen, and A.I. Virtanen, Acta Chem. Scand., 1962, 10, 135.
11. E.E. Smissman, M.D. Corbett, N.A. Jenny, and O. Kristiansen, J. Org. Chem., 1972, **37**, 1700.
12. H.J. Grambow, J. Lückge, A. Klausener, and E. Müller, Z. Naturforsch., 1986, 41, 684.
13. M.D. Woodward, L.J. Corcuera, J.P. Helgeson, and C.D. Upper, Plant Physiol., 1978, 61, 796.
14. H.R. Bravo and H.M. Niemeyer, Tetrahedron, 1985, 41, 4883.
15. J. Atkinson, P. Morand, J.T. Arnason, H.M. Niemeyer, and H.R. Bravo, J. Org. Chem., 1991, 56, 1788.
16. S.A. Matlin, P.G. Sammes, and R.M. Upton, J. Chem. Soc., Perkin I, 1979, 2481.
17. S.L. Johnson and D.L. Morrison, J. Am. Chem. Soc., 1972, **94**, 1323.
18. M. Caplow, J. Chem. Soc., Perkin II, 1968, 6795.
19. A.F. Hegarty and L.N. Frost, J. Chem. Soc., Perkin II, 1973, 1719.

Received, 21st May, 1991