# RING-CHAIN TAUTOMERISM OF OXAZOLIDINES

Joseph V. Paukstelis (1) and Larry L. Lambing

Department of Chemistry, Kansas State University, Manhattan, Kansas   66502

It has been established that the condensation products of β-amino alcohols and aldehydes and ketones are in mobile equilibrium, I⇌II, between a closed form (I) and an open form (II) (2).   The equilibrium is largely dependent on the ability of solvent to hydrogen bond with the free hydroxyl group of (II).   It is also quite clear that the equilibrium is highly
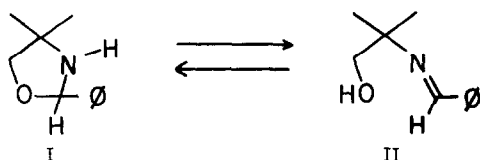
dependent on the structure of the aminoalcohol and the ketone or aldehyde (3).

To test the effect of electron demand in the aldehyde portion of the molecule, we synthesized a series of oxazolidines from β-aminoalcohols and substituted benzaldehydes.   The simplest choice of an β-aminoalcohol for our method of analysis (n.m.r.) was 2-amino-2-methyl-1-propanol.   The benzaldehydes and 2-amino-2-methyl-1-propanol were condensed by reaction in refluxing benzene from which water was removed by means of a'Dean-Stark trap (4).   The products (5) were recrystallized or distilled until no extraneous signals (those of
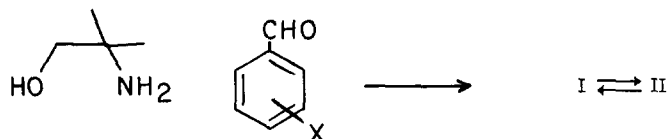
starting materials) were detected by n.m.r. and i.r.   The compounds were dissolved in carbon tetrachloride (5 mole %) and the equilibria were measured by integration of the signals due to each form.   The results are summarized in TABLE 1.

A Hammett plot of log K/K_0 versus σ yielded a correlation in which the electron donating substituents p-dimethylamino and p-methoxy were far from a line determined by the remaining substituents.   When the data was reduced by means of a standard multiple regression program, a correlation r = -0.973 was found.   The slope and its standard deviation

TABLE 1

SUBSTITUENT	K(II/ I)	log K/ K_O	σ (6)	σ^+ (6)
p-dimethylamino	4.78	0.930	-0.83	-1.7
p-methoxy	1.526	0.435	-0.268	-0.778
p-methyl	0.851	0.180	-0.170	-0.311
H	0.584	0	0	0
m-methoxy	0.509	-.042	0.115	0.047
p-chloro	0.464	-.084	0.227	0.114
m-chloro	0.368	-.184	0.373	0.399
m-nitro	0.250	-.352	0.710	0.674

were determined to be ρ = -0.86 $\pm$ 0.09, with a standard error for each point (log K/ K_o) of 0.11. Our results were in qualitative agreement with those reported for oxazines (7). Because of the large deviations of the p-dimethylamino and p-methoxy substituents, a Hammett plot versus σ^+ was made. The improvement was remarkable as can be seen in Figures 1 and 2. Reexamination of the data for oxazines (7) indicated an improvement in the correlation, though not as large because data for p-dimethylamino and p-methoxy was not available.
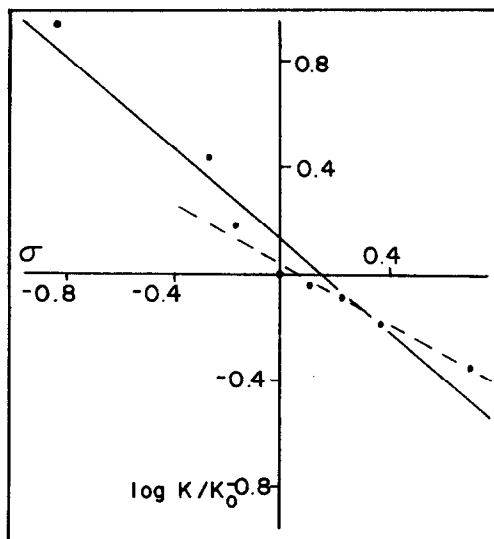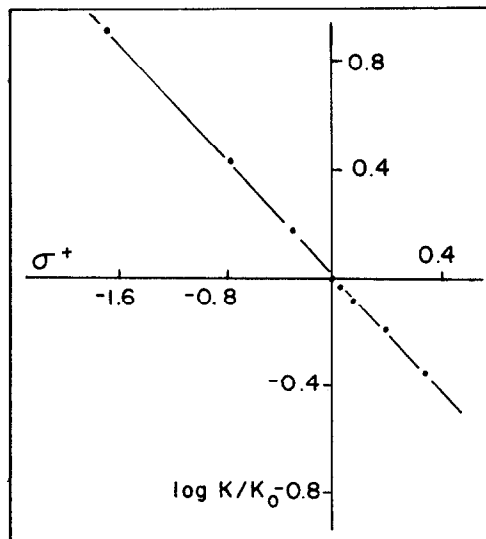
FIGURE 1

FIGURE 2

A careful analysis of the variance for the regressions indicated that correlations with σ^+ are significantly better than those with σ for the oxazolidines and oxazines (7) so far studied. Since the correlation coefficients r are so close to unity, they do not provide any information concerning the significance of a correlation. Thus from correlation coefficients alone, one cannot say that a correlation coefficient of 0.999 is significantly better than one of 0.97. One must use some other criterion such as the magnitude of the standard error of the estimate or the ratio, F, of the mean squares of the regression and the mean squares of the deviation from the regression. A large value of F corresponds to a small value for the mean squares of the deviation from the regression and is equivalent to the omega test for choice of a functional relationship (8). The details of the statistical analysis are summarized in TABLE 2.

TABLE 2

	OXAZOLIDINES		OXAZINES [7]	
	σ	σ^+	σ	σ^+
No. of points	8	8	5	5
Correlation r =	-.973	-.999	-.993	-.999
Slope =	-.856	-.543	-.738	-.680
Standard Error in the Slope	$\pm$.083	$\pm$.010	$\pm$.047	$\pm$.022
Standard Error of the Estimate of log K/K_H	$\pm$.102	$\pm$.019	$\pm$.040	$\pm$.021
Intercept	$\pm$.127	$\pm$.005	$\pm$.054	$\pm$.004
F	108	3200	243	916

It is clear that for oxazines and oxazolidines correlate with σ^+ and not σ. It is also clear that the small ρ value of -0.54 $\pm$ .01 for oxazolidines and -0.68 $\pm$ .02 for oxazines implies that this equilibrium of I $\rightleftharpoons$ II does not involve direct resonance of a positive charge with an aromatic ring. This apparent contradiction can be understood in terms of a loss of resonance of the aromatic ring with the imino group as being responsible for the σ^+ correlation. The only other similar observation has been the Diels-Alder reaction of 1-phenyl-1,3-butadiene with maleic anhydride (9). This example, (10) which had a correlation coefficient of r = 0.997 and a ρ = -.62 is similar to our oxazolidine-imine equilibrium in that the reaction consists of formation of a ring and a loss of resonance for the phenyl group. Thus, one might conclude from these examples that σ^+ correlations do not always require a positive charge to be involved but that direct resonance of the phenyl ring must be lost in the reaction. In this equilibrium one can assume that the substituents do not interact with the oxazolidine but

interact by resonance only with the imine $\;>C = N.$ That the reaction of II to I is a nucleophilic addition has no importance.

The oxazolidine-imine tautomerization provides a unique cyclic system for the study of substituent effects. The initial results showing a σ^+ correlation with a near zero ρ confirms the novelty of the system and suggests that additional experiments are needed. Furthermore, when crystalline solids were dissolved in methylene chloride at low temperature (-78°) only signals attributable to the imine form were observed. As the temperature was raised the signals from the oxazolidine were observed to increase. Kinetic measurements for the conversion of II to I are now in progress.

REFERENCES

1. To whom all inquiries should be sent.

2. J. V. Paukstelis and R. M. Hammaker, Tetrahedron Letters, 3557 (1968).

3. E. D. Bergmann, Chem. Rev., 53, 309 (1953).

4. M. Senkus, J. Am. Chem. Soc., 67, 1515 (1945).

5. All new products gave satisfactory analyses.

6. J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, New York, 1963, p. 204.

7. A. F. McDonagh and H. E. Smith, J. Org. Chem., 33, 1 (1968).

8. L. G. Parratt, "Probability and Experimental Errors in Science," John Wiley and Sons, Inc., New York, New York, 1961, p. 133-5.

9. E. J. DeWitt, C. T. Lester and G. A. Ropp, J. Am. Chem. Soc., 78, 2101 (1956).

10. Reference 6, p. 209.