The Ring-opening Addition Reactions of Exo-imino Cyclic Compounds with Carboxylic Acids

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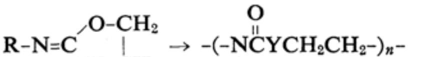
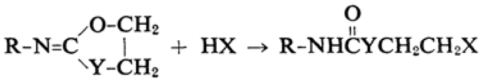
Preceding papers[1-5] have reported that the 1,4-addition type ring-opening polymerization of exo-imino cyclic compounds, such as ethylene iminocarbonates, 2-iminooxazolidines and 2-iminotetrahydrofurans, in the presence of cationic catalysts, such as Lewis acids or protonic acids, affords polyurethanes, polyureas and polyamides respectively, as is shown in the following equation:



$$\mathrm{R{-}N{=}C}\begin{matrix}\mathrm{O{-}CH_2}\\ |\\ \mathrm{Y{-}CH_2}\end{matrix} \rightarrow -(-\underset{\mathrm{R}}{\mathrm{N}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{YCH_2CH_2}-)_n-$$

where Y is an oxygen atom, a substituted imino or a methylene group.

Further, it has been shown there that the exo-imino cyclic compounds react with acidic substances, such as carboxylic acids or phenols, to give the corresponding addition compounds by a ring-opening 1,4-addition reaction:



$$\mathrm{R{-}N{=}C}\begin{matrix}\mathrm{O{-}CH_2}\\ |\\ \mathrm{Y{-}CH_2}\end{matrix} + \mathrm{HX} \rightarrow \mathrm{R{-}NH}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{YCH_2CH_2X}$$

In the present investigation, the rate constants, the activation energies and the entropies of the activation of the reactions of the exo-imino cyclic compounds with carboxylic acids in various solvents were determined in order to study the mechanism of the reactions.

The results lead to the conclusion that the ring-opening addition reactions involve two stages, namely, the initial formation of the salt from the exo-imino cyclic compound and the acid, followed by the reaction of the salt with another molecule of the acid to yield the addition compounds.

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[1] T. Mukaiyama, T. Fujisawa and T. Hyugaji, This Bulletin, 35, 687 (1962).

[2] T. Mukaiyama, T. Fujisawa, H. Nohira and T. Hyugaji, *J. Org. Chem.*, 27, 3337 (1962).

[3] T. Mukaiyama and K. Sato, This Bulletin, 36, 99 (1963).

[4] T. Fujisawa, Y. Tamura and T. Mukaiyama, ibid., in press.

[5] H. Nohira, Y. Nishikawa and T. Mukaiyama, ibid., in press.

Experimental

Materials. — Ethylene *N*-phenyliminocarbonate was prepared from phenylimidophosgene and sodium ethylene glycolate.[1]

2-Phenylimino-3-methyloxazolidine was prepared by the treatment of 1-(2-chloroethyl)-1-methyl-3-phenylurea with hot water.[5]

The *N*-substituted 2-iminotetrahydrofurans were prepared from 2,2-diethoxytetrahydrofuran and the corresponding amines.[8]

The carboxylic acids were obtained from a commercial source and were purified by recrystallization. The melting points and the pK_a values for these carboxylic acids are listed in Table I.

TABLE I. THE MELTING POINTS AND pK_a VALUES OF CARBOXYLIC ACIDS USED

Acid	M. p., °C	p$K_a^{25°C}$
C_6H_5-	121.7	4.17
o-CH_3O-C_6H_4-	101.5	4.09
p-CH_3O-C_6H_4-	184.0	4.49
o-Cl-C_6H_4-	141.0	2.89
m-Cl-C_6H_4-	154.5	3.82
p-Cl-C_6H_4-	234.0	3.98
m-CN-C_6H_4-	139.0	3.50
p-CN-C_6H_4-	219.0	3.51
o-NO_2-C_6H_4-	148.0	2.21
p-NO_2-C_6H_4-	240.0	3.40
o-Br-C_6H_4-	149.0	2.82
3, 5-$(NO_2)_2C_6H_3$-	205.0	2.80
$ClCH_2$-	63.0	2.81

Solvent.—Dioxane (b. p. 101.0°C), toluene (b. p. 111°C), xylene (b. p. 138∼140°C) and benzene (b. p. 78°C) were distilled and dried over metallic sodium wire, and chlorobenzene (b. p. 132°C) was purified by distillation.

General Kinetic Method. — An equimolar solution of ethylene *N*-phenyliminocarbonate and carboxylic acid in various solvents in a 50 ml. reaction tube was maintained at a desired, constant temperature by immersion into a thermostat. The temperature control of the thermostat was accurate to ±0.03∼0.07°C within the temperature ranges between 20∼90°C. Five milliliter aliquots of this solution were withdrawn from time to time by means of a pipet and were put into 15 ml. of dioxane in a 50 ml. Erlenmeyer flask in order to make the titration mixture homogeneous. The unreacted carboxylic acid was titrated with a standard 0.5 N sodium hydroxide solution, using phenolphthalein as an indicator. In the case of the reaction with *m*-cyano-, *p*-cyano- and 3,5-dinitro-benzoic acids, thymolcresolgreen was used as an indicator.

Similarly, the percentage reaction of 2-phenylimino-3-methyloxazolidine or *N*-substituted 2-iminotetrahydrofurans with carboxylic acids was measured by this method.

Results and Discussion

The Reaction of Ethylene *N*-Phenyliminocarbonate with Carboxylic Acids.

— Figure 1

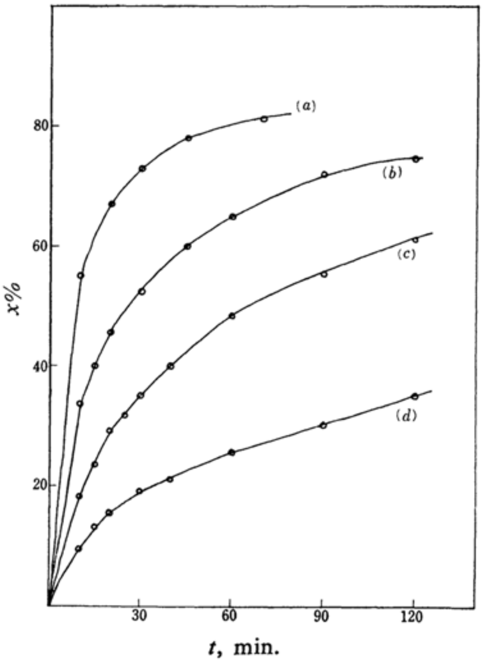


Fig. 1. The reactions of ethylene *N*-phenyliminocarbonate with benzoic acid in xylene. The plots of percentage reaction against time at various temperatures.
a) 60°C (0.50 mol./l.) b) 52°C (0.33 mol./l.) c) 43.5°C (0.33 mol./l.) d) 30°C (0.33 mol./l.)

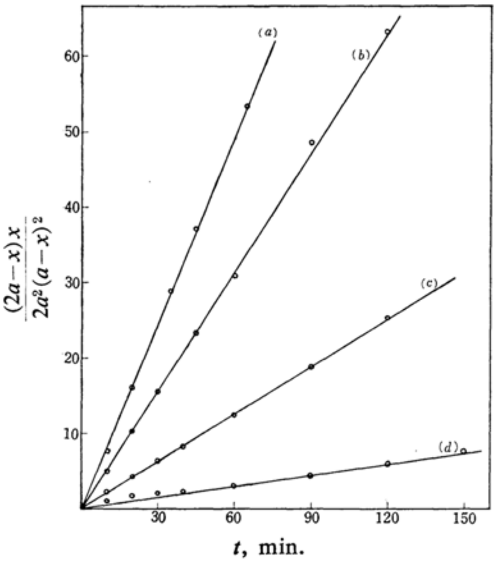
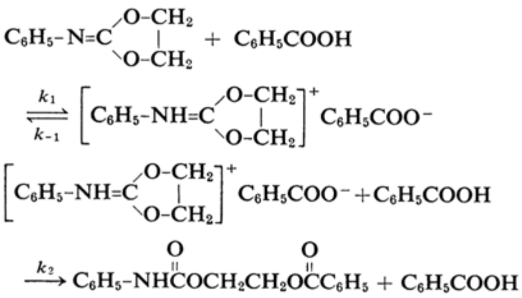


Fig. 2. The reactions of ethylene *N*-phenyliminocarbonate with benzoic acid in xylene at various temperatures.
The plots of the third order function against time.
a) 60°C b) 52°C c) 43.5°C d) 30°C
a: Initial concentration
x: Concentration of addition compound

shows plots of the percentage reaction against time (min.) for the reaction of ethylene *N*-phenyliminocarbonate (0.33 mol./l.) and benzoic acid (0.33 mol./l.) in xylene at various temperatures. As Fig. 2 shows, the third-order plots show sufficiently straight lines, from which the overall reaction order of ethylene *N*-phenyliminocarbonate with benzoic acid is shown to be third from a 20% to 90% completion of the reaction, without any noticeable side reaction.

On the basis of the experimental results mentioned above, the mechanism of the reaction can be considered to proceed via two stages, namely, the initial formation of the salt from the iminocarbonate and the acid, followed by the reaction of the salt with the other acid to yield β-benzoyloxyethyl *N*-phenylcarbamate.



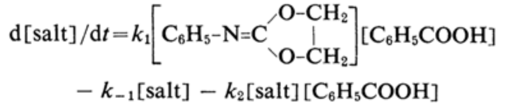
$$C_6H_5\text{-}N{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right. + C_6H_5COOH$$

$$\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \left[C_6H_5\text{-}NH{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right.\right]^+ C_6H_5COO^-$$

$$\left[C_6H_5\text{-}NH{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right.\right]^+ C_6H_5COO^- + C_6H_5COOH$$

$$\xrightarrow{k_2} C_6H_5\text{-}NH\overset{O}{\overset{\|}{C}}OCH_2CH_2O\overset{O}{\overset{\|}{C}}C_6H_5 + C_6H_5COOH$$

For the first stage, the rate of the formation of the salt may be expressed as:



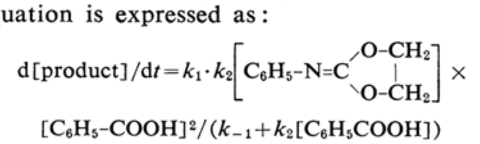
$$d[\text{salt}]/dt = k_1\left[C_6H_5\text{-}N{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right.\right][C_6H_5COOH] - k_{-1}[\text{salt}] - k_2[\text{salt}][C_6H_5COOH]$$

For the second stage, the rate of formation of the product may be given by:

$$d[\text{product}]/dt = k_2[\text{salt}][C_6H_5COOH]$$

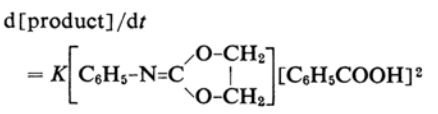
where k_1, k_{-1} and k_2 are the rate constants of these stages.

When the rate of the formation of the salt is zero at the steady state, the overall kinetic equation is expressed as:



$$d[\text{product}]/dt = k_1\cdot k_2\left[C_6H_5\text{-}N{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right.\right] \times [C_6H_5\text{-}COOH]^2/(k_{-1}+k_2[C_6H_5COOH])$$

If k_{-1} is much larger than $k_2[C_6H_5COOH]$, when, namely, the second stage is the rate-determining step, the rate of the reaction can be expressed as follows:



$$d[\text{product}]/dt = K\left[C_6H_5\text{-}N{=}C\left\langle\begin{array}{l}O\text{-}CH_2\\ \;|\\ O\text{-}CH_2\end{array}\right.\right][C_6H_5COOH]^2$$

The plots of the logarithm of the rate constants vs. the reciprocal absolute temperatures gave a satisfactorily straight line (Fig. 3); the activation energy of the reaction was thus found to be 20.4 kcal./mol.

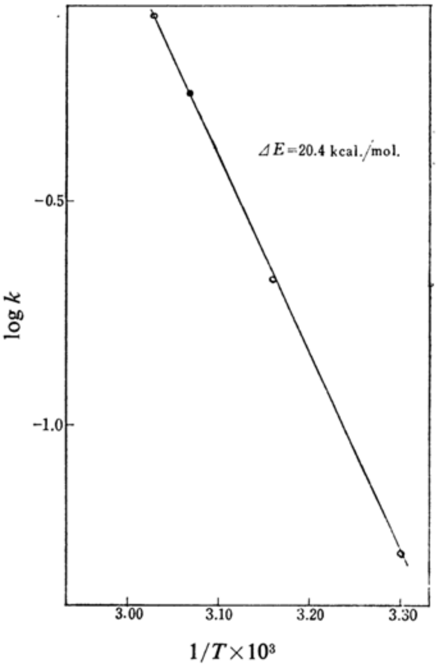


Fig. 3. The reactions of ethylene *N*-phenyliminocarbonate with benzoic acid in xylene. The plots of the rogarithm of the rate constants against the reciprocal absolute temperature.

Moreover, the reaction order changes to the second from the third, when the equimolar reaction of ethylene *N*-phenyliminocarbonate with benzoic acid ($pK_a=4.17$) was carried out in the presence of a stronger acid, e. g., diphenyl phosphate (pK_a=ca. 1.9), in xylene, as is shown in Fig. 4. The rates of the second-order reaction increase as the concentration of diphenyl phosphate increases. These results show that the reaction is a general acid-catalyzed reaction.

Furthermore, the reactions of ethylene *N*-phenyliminocarbonate with various substituted benzoic acids or chloroacetic acid in dioxane show that the rate increases as the acidity of carboxylic acid increases, as Table II shows. The effect of substituents in meta- and para-substituted benzoic acids follows the Hammett equation. As is shown in Fig. 5, $\log(k/k_0)$ is a linear function of the substituent constant σ given by Hammett,⁶⁾ and the gradient of the plots gave a value for the reaction constant ρ of $+1.74$ for the reaction. In ortho-substituted benzoic acids, the reactions are

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6) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York (1941), p. 188.

Table II. The rate constants, the activation energies and the entropies of activation of the reactions of ethylene *N*-phenyliminocarbonate with carboxylic acids in dioxane

Carboxylic acid	k, $l^2\,mol^{-2}\,min^{-1}$							ΔE kcal.	$-\Delta S^{\ne}$ e. u.
	80°C	70°C	60°C	50°C	40°C	30°C	20°C		
C_6H_5-	0.709	0.245	0.111	0.0875	0.0225			19.6	3.34
p-CH_3O-C_6H_4-	0.241	0.113	0.0466	0.0267				15.7	13.90
o-CH_3O-C_6H_4-	0.247	0.112	0.0516	0.0400				15.7	17.30
p-CN-C_6H_4-		4.36	1.97	0.600	0.376			17.5	5.94
m-CN-C_6H_4-		4.42	2.00	0.700	0.379			17.8	3.77
o-Cl-C_6H_4-		2.54	1.25	0.750	0.271			16.6	7.13
p-Cl-C_6H_4-	1.65	0.680	0.367	0.194	0.0866			16.7	10.20
m-Cl-C_6H_4-	3.71	0.985	0.447	0.250	0.139			16.4	11.10
o-NO_2-C_6H_4-				11.5	3.50	2.04	0.710	17.7	3.24
p-NO_2-C_6H_4-			2.56	1.42	0.486	0.145		21.2	−7.40
3,5-$(NO_2)_2C_6H_3$-				21.5	10.0	3.88	1.08	16.7	0.75
o-Br-C_6H_4-				0.955					
$ClCH_2$-							1.30		

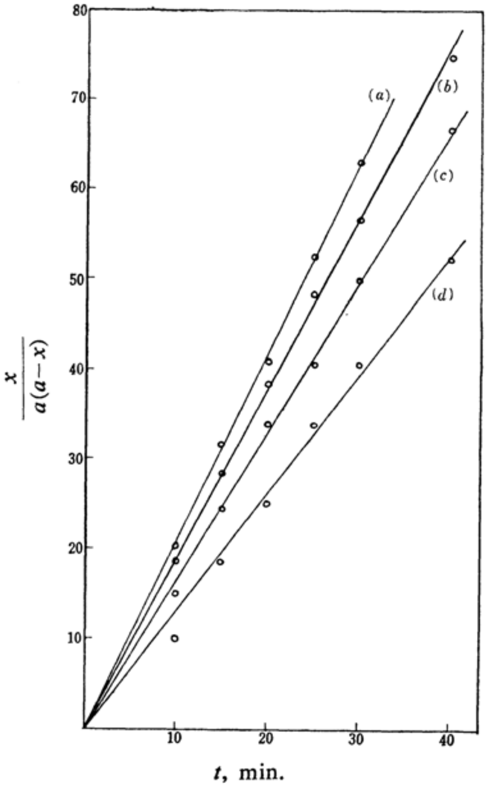


Fig. 4. The reactions of ethylene *N*-phenyliminocarbonate with benzoic acid in the presence of a catalytic amount of diphenyl phosphate in xylene at 70°C.
The plots of the second order function against time.
Concentration of diphenyl phosphate.
a) 5.75×10^{-3} b) 3.84×10^{-3} c) 1.92×10^{-3}
d) 3.20×10^{-4} (mol./benzoic acid mol.)

not so fast as might be expected from their acidities; this may be attributed to the steric hindrance of the ortho substituents.

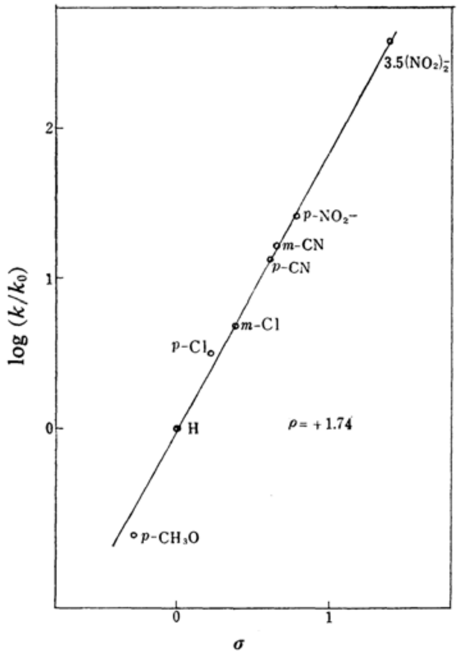


Fig. 5. The reactions of ethylene *N*-phenyliminocarbonate with meta and para substituted benzoic acids in dioxane at 50°C.
The plots of $\log(k/k_0)$ against the Hammett σ-values.

In addition, the rates of this reaction are slightly influenced by the polarity of the solvents used. The results listed in Table III show that the reactions in xylene are about 8∼9 faster times than those in dioxane. The slower rate in dioxane than in xylene may result from the possible formation of a complex from a carboxylic acid and dioxane, a complex which prevents the formation of the above-mentioned salt of ethylene *N*-phenyliminocarbonate by the carboxylic acid. It

TABLE III. THE RATE CONSTANTS, THE ACTIVATION ENERGIES AND THE ENTROPIES OF ACTIVATION OF THE REACTIONS OF ETHYLENE *N*-PHENYLIMINOCARBONATE WITH BENZOIC ACID IN VARIOUS SOLVENTS

Solvent	k, $1^2\,\mathrm{mol}^{-2}\,\mathrm{min}^{-1}$ 80°C	70°C	60°C	50°C	40°C	30°C	ΔE kcal.	$-\Delta S^{\neq}$ e. u.
Xylene			0.833	0.533	0.211	0.0522	20.4	−2.81
Toluene		2.17	0.790	0.303	0.150		19.2	0.11
Benzene		1.50	0.644	0.255	0.110		19.0	1.92
Chlorobenzene	4.90	2.25	1.03				19.0	2.10
Dioxane	0.709	0.245	0.111	0.0875	0.0225		19.6	3.34
Dioxane 1 : Xylene 1	1.07	0.430	0.198	0.094			17.8	7.87
Dioxane 1 : Xylene 3		0.797	0.408	0.156	0.072		17.5	8.17

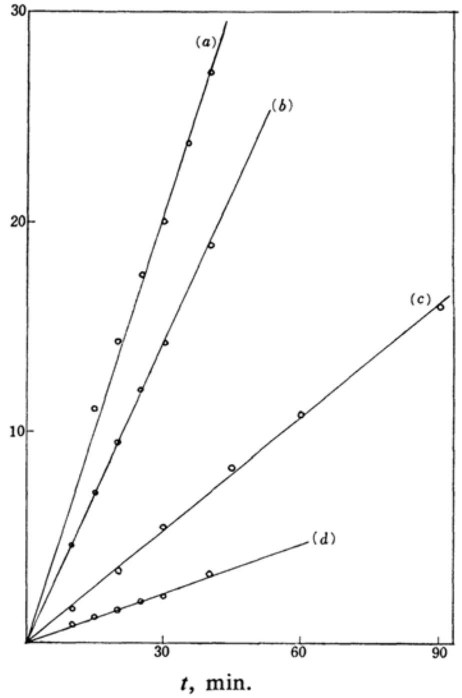


Fig. 6. The reaction of 2-phenylimino-3-methyloxazolidine with benzoic acid in xylene at various temperatures.
The plots of the third order function against time.
a) 90°C (0.25 mol./l.) b) 80°C (0.125 mol./l.)
c) 70°C (0.25 mol./l.) d) 60°C (0.50 mol./l.)

was also observed that the addition of dioxane to a toluene solution retards the reaction considerably.

The Reaction of 2-Phenylimino-3-methyloxazolidine with Carboxylic Acids. — Figure 6 shows that the reaction of 2-phenylimino-3-methyloxazolidine with benzoic acid in xylene satisfied the requirement for the third-order reaction kinetics. Analogous to the case of ethylene *N*-phenyliminocarbonate, the reaction can also be considered to proceed via two stages to give 1-(2-benzoyloxyethyl)-1-methyl-3-phenylurea.

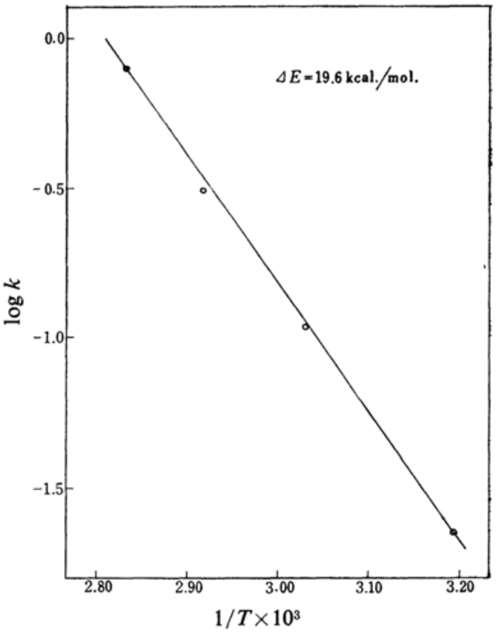
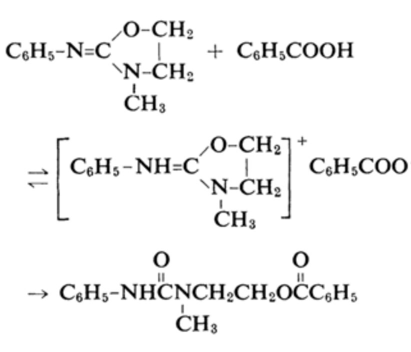


Fig. 7. The reactions of 2-phenylimino-3-methyloxazolidine with benzoic acid in xylene.
The plots of the logarithm of the rate constants against the reciprocal absolute temperature.



The activation energy of this reaction was determined to be 19.6 kcal./mol. (see Fig. 7).

It was also confirmed that the rates of the reactions of 2-phenylimino-3-methyloxazolidine

TABLE IV. THE RATE CONSTANTS OF THE REACTIONS OF 2-PHENYLIMINO-3-METHYLOXAZOLIDINE WITH CARBOXYLIC ACIDS IN DIOXANE

Carboxylic acid	k, $1^2\,mol^{-2}\,min^{-1}$			
	90°C	80°C	70°C	60°C
C_6H_5-	0.0814	0.0373		
p-Cl-C_6H_4-	0.179	0.0925	0.0614	
p-NO_2-C_6H_4-	1.17	0.785	0.323	
p-CN-C_6H_4-		0.416		
m-CN-C_6H_4-	1.05	0.415		
3,5-$(NO_2)_2C_6H_3$-		9.70	5.65	

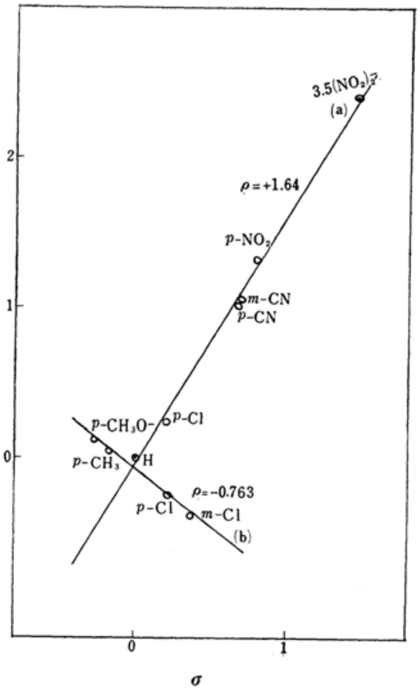


Fig. 8. a) The reactions of 2-phenylimino-3-methyloxazolidine with meta and para substituted benzoic acids in dioxane at 80°C.
b) The reactions of N-substituted phenyliminotetrahydrofurans with chloroacetic acid in xylene at 80°C.
The plots of $\log(k/k_0)$ against the Hammett σ-values.

with various substituted benzoic acids in dioxane increase as the acidities of the acids increase (see Table IV). The gradient of the plot $\log(k/k_0)$ against the substituent constant σ shown in Fig. 8 gave a value for the reaction constant ρ of $+1.64$, which was nearly equal to the case of ethylene N-phenyliminocarbonate mentioned above.

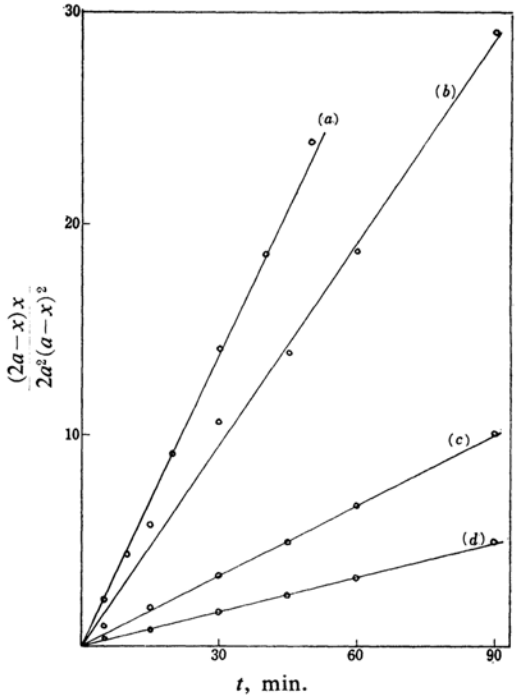
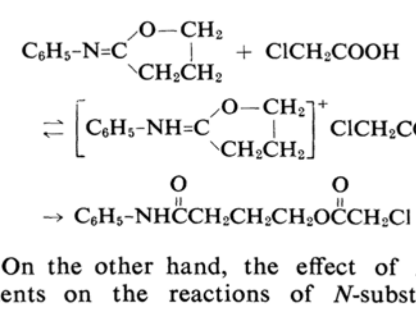


Fig. 9. The reactions of 2-phenyliminotetrahydrofuran with chloroacetic acid in xylene at various temperatures.
The plots of the third order function against time.
a) 90°C (0.25 mol./l.) b) 80°C (0.25 mol./l.)
c) 70°C (0.25 mol./l.) d) 60°C (0.50 mol./l.)

The Reaction of *N*-Substituted 2-Iminotetrahydrofurans with Chloroacetic Acid.—2-Phenyliminotetrahydrofuran reacts so very slowly with benzoic acid in xylene that the rate of the reaction cannot be measured. Since it was found by the above experiment that the rate increases as the acidity of carboxylic acid increases, the rates of the reaction of 2-phenyliminotetrahydrofuran were determined by using chloroacetic acid. As Fig. 9 shows, the third-order plots have sufficiently straight lines, suggesting that the reaction also proceeds via two stages to give γ-chloroacetoxybutyranilide, as in the case of ethylene N-phenyliminocarbonate.



$$C_6H_5\text{-}N{=}C\langle^{O-CH_2}_{CH_2CH_2}\rangle + ClCH_2COOH \rightleftarrows \left[C_6H_5\text{-}NH{=}C\langle^{O-CH_2}_{CH_2CH_2}\rangle\right]^+ ClCH_2COO^- \rightarrow C_6H_5\text{-}NH\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2O\overset{O}{\overset{\|}{C}}CH_2Cl$$

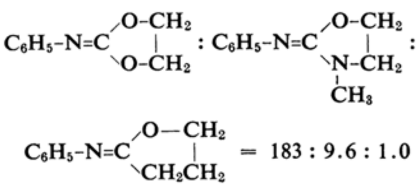
On the other hand, the effect of N-substituents on the reactions of N-substituted 2-iminotetrahydrofurans with chloroacetic acid indicated that the N-aliphatic derivatives react faster than N-aromatic ones and that the rates

TABLE V. THE RATE CONSTANTS OF THE REACTIONS OF *N*-SUBSTITUTED 2-IMINOTETRAHYDROFURANS WITH CHLOROACETIC ACID IN XYLENE

R-	k, $l^2\,mol^{-2}\,min^{-1}$			
	90°C	80°C	70°C	60°C
C_6H_5-	0.695	0.472	0.181	0.0796
o-CH_3-C_6H_4-		0.311		
p-CH_3-C_6H_4-		0.519		
p-CH_3O-C_6H_4-		0.605		
o-CH_3O-C_6H_4-		0.700		
p-Cl-C_6H_4-		0.282		
o-Cl-C_6H_4-		0.150		
m-Cl-C_6H_4-		0.190		
n-C_6H_{13}-		0.445		
		1.75		

of the reactions of *N*-substituted phenyliminotetrahydrofurans decrease when the electron-attractive groups, such as *o*-chloro, *p*-chloro- or *m*-chlorophenyl groups, are introduced, as is shown in Table V. The gradient of the Hammett plots in Fig. 8 gave a value for the reaction constant ρ of -0.763. This evidence shows that the rate of the reaction increases as the electron density of the imino group increases.

Finally, the relative rate of the reactions of the three exo-imino cyclic compounds, e. g., ethylene *N*-phenyliminocarbonate, 2-phenylimino-3-methyloxazolidine and 2-phenyliminotetrahydrofuran, with carboxylic acids has been determined as:



$$C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O\text{-}CH_2\\ \quad\ \ |\\ \diagdown O\text{-}CH_2\end{array} : C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O\text{-}CH_2\\ \quad\ \ |\\ \diagdown N\text{-}CH_2\\ \quad |\\ \quad CH_3\end{array} : C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O-CH_2\\ \qquad\ |\\ \diagdown CH_2CH_2\end{array} = 183 : 9.6 : 1.0$$

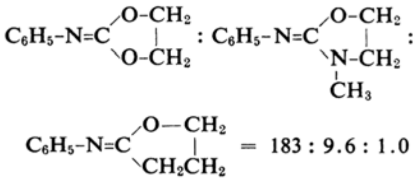
In conclusion, it can be said that the rates of the reactions of the exo-imino cyclic compounds with carboxylic acids depend both on the basicity of the cyclic compounds, which affects the initial formation of the neccessary intermediate salt, and on the number of the oxygen-carbon bond to be cleaved in the ring opening.

Summary

The rate constants, the activation energies and the entropies of the activation of the ring-opening addition reactions of exo-imino cyclic compounds, such as ethylene *N*-phenyliminocarbonate, 2-phenylimino-3-methyloxazolidine and *N*-substituted 2-iminotetrahydrofurans, with carboxylic acids in various solvents have been determined in order to study the mechanism of these reactions.

The rate of the reactions increases as the acidity of carboxylic acids increases, and the linear Hammett relation is observed in the reactions of ethylene *N*-phenyliminocarbonate or 2-phenylimino-3-methyloxazolidine with meta- and para-substituted benzoic acids.

The relative rate of the reactions of the three exo-imino cyclic compounds, ethylene *N*-phenyliminocarbonate, 2-phenylimino-3-methyloxazolidine and 2-phenyliminotetrahydrofuran, with carboxylic acids is as follows:



$$C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O\text{-}CH_2\\ \quad\ \ |\\ \diagdown O\text{-}CH_2\end{array} : C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O\text{-}CH_2\\ \quad\ \ |\\ \diagdown N\text{-}CH_2\\ \quad |\\ \quad CH_3\end{array} : C_6H_5\text{-}N{=}C\begin{array}{l}\diagup O-CH_2\\ \qquad\ |\\ \diagdown CH_2CH_2\end{array} = 183 : 9.6 : 1.0$$

These results show that the ring-opening addition reaction involves two stages, namely, the initial formation of the intermediate salt from the exo-imino cyclic compound with carboxylic acid, followed by the reaction of the salt with the other acid to give the ring-opening addition compound.

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