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Synthesis of Furan Derivatives. LXXXIV.[1a] Kinetic Studies of the Curtius Rearrangement of 5-Substituted 2-Furoyl Azides and Related Compounds[2]

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Kinetic studies of the thermolytic Curtius rearrangement of set A of 5-substituted 2-furoyl azides (**1**—**6**), 5-substituted 2-thenoyl azides (**7**, **8** and **9**) and 2-pyrroyl azide (**10**), and set B of *p*-substituted benzoyl azides (**11**, **12** and **13**) and 2-, 3- and 4-pyridinemonocarbonyl azides (**14**, **15** and **16**) in toluene were executed by means of IR (infrared) spectrophotometric method. It was found through the relationship between log k and $1/T$ that the isokinetic temperature (Q) of the set A and B are Q=371° and 353 °K, respectivery.

Based on $\Delta E^{\ast}$ and $\Delta S^{\ast}$, it seems to be reasonable that the reactivity of the each of unsubstituted acyl azides (**2**, **7**, **9** and **12**) is very nearly parallel to that the each resonance energy of the parent rings of the above four acyl azides. Additionally, it was found that the substituent dependence on $\Delta S^{\ast}$ in the rearrangement of the 5-substituted 2-furoyl azides (**2**—**6**) and also the 5-substituted 2-thenoyl azides (**9** and **10**) is indifferent to whether the substituents are electron releasing or attracting groups, and on the other hand, the rearrangement of *p*-substituted benzoyl azides (**12** and **13**) has $\Delta S^{\ast}$ decreased, respectively.

Keywords——acyl azide; thermolytic Curtius rearrangement; isokinetic temperature; compensation effect; activated three-membered intermediacy; structure-reactivity relationship; IR spectrophotometric method; substituent effect; concerted reaction; resonance energy

In our previous publications[1] concerned with the synthesis of versatile 5-substituted 2-furoyl isocyanates and also the rate studies on the reaction of the furoic acids with diphenyl phosphorazide (DPPA),[4] we have reported that the formation of isocyanate was determined by virtue of a characteristic IR (infrared spectrum) band (ν_{NCO}: 2275 cm^{-1}) because of being too unstable to isolate it from the reaction mixture, and also a conceivable reaction mechanism on the basis of the kinetic data in the DPPA reaction was discussed.[1a]

In connection with the previous work,[1a] the synthetic and kinetic interests in this area promoted us to elaborate the thermolytic Curtius rearrangement of 5-substituted 2-furoyl azides[substituent: H-, (**1**); CH_3-, (**2**); O_2N-, (**3**); Br-, (**4**); OHC-, (**5**) and MeOOC-, (**6**)]and some related acyl azides, *i.e.*, 2-pyrroyl azide (**7**), 5-substituted 2-thenoyl azides[substituent: H-, (**8**); CH_3-, (**9**) and O_2N-, (**10**)], *p*-substituted benzoyl azides[substituent: H-, (**11**); CH_3-, (**12**) and O_2N-, (**13**)], 2-pyridinecarbonyl azide (**14**), 3-pyridinecarbonyl azide (**15**) and 4-pyridinecarbonyl azide (**16**) by using a quantitative measurement of IR band of ν_{N_3} in the region of 2130—2180 cm^{-1}. Emphatically, this measurement is convenient, accurate and quantitative rather than the azotometric method[5] as used before.

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[1] *a*) Part LXXXIII: H. Saikachi and T. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **25**, 1651 (1977); *b*) H. Saikachi and K. Takai, *Yakugaku Zasshi*, **89**, 34 (1969); *c*) *Idem, ibid.*, **89**, 304 (1969).

[2] Some parts of this work presented at the 95th Annual Meeting of the Pharmaceutical Society of Japan at Nishinomiya, April 1975.

[3] Location: *Ikawadani-cho, Tarumi-ku, Kobe, 673, Japan.*

[4] T. Shioiri and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **22**, 849 (1974).

[5] *a*) M.S. Newman, S.H. Lee, Jr. and A.B. Garrett, *J. Am. Chem. Soc.*, **69**, 113 (1947); *b*) Y. Yukawa and Y. Tsuno, *J. Am. Chem. Soc.*, **79**, 5530 (1957); *c*) Y. Othuji, M. Yoshikawa, and E. Imoto, *Nippon Kagaku Zasshi*, **80**, 1307 (1959); *d*) Y. Yukawa and Y. Tsuno, *J. Am. Chem. Soc.*, **81**, 2007 (1959); *e*) D.C. Berndt, M. Zuika, and M.S. Clark, Jr., *Chem. Ind.* (London), **1965**, 139.

Therefore, in comparing with some kinetic respects of 5-substituted 2-furoyl azides (**1**—**6**), the rate studies were also made on the Curtius rearrangement of 2-pyrroyl azide (**7**), 5-substituted 2-thenoyl azides (**8**, **9** and **10**), *p*-substituted benzoyl azides (**11**, **12** and **13**) and 2-, 3- or 4-pyridinemonocarbonyl azides (**14**, **15** and **16**) in toluene, respectively.

As listed in Table 1, the pseudo first order rate constants, the activation energies ($\Delta E^{\ast}$), the activation entropies ($\Delta S^{\ast}$) and the frequency factores (log PZ) were respectively calculated from the experimental results. Additionally, two almost straight lines, which are pointed out to be both corresponding compensation effects derived from the propotional relation between $\Delta E^{\ast}$ and log PZ related to the five-membered heterocyclic acyl azides (**1**—**10**) and the other six-membered cyclic and heterocyclic acyl azides (**11**—**16**), are drawn almost in parallel, respectively (Fig. 5).

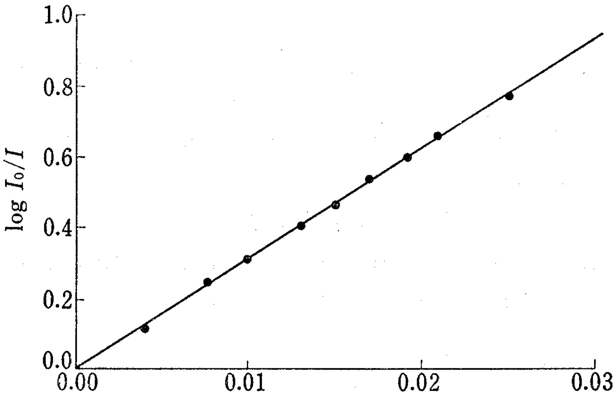

Fig. 1. Plot of log I_0/I *vs.* the Concn. of 2-Furoyl Azide (**1**) in Toluene at Room Temperature.

In addition, it is of interest to note that the both isokinetic temperatures[6] (Q), 371 °K and 353 °K (367 °K),[5c] were incidentally found by plotting log *k*(axis of ordinate) *vs.* $1/T$(axis of abscissa) in 5-

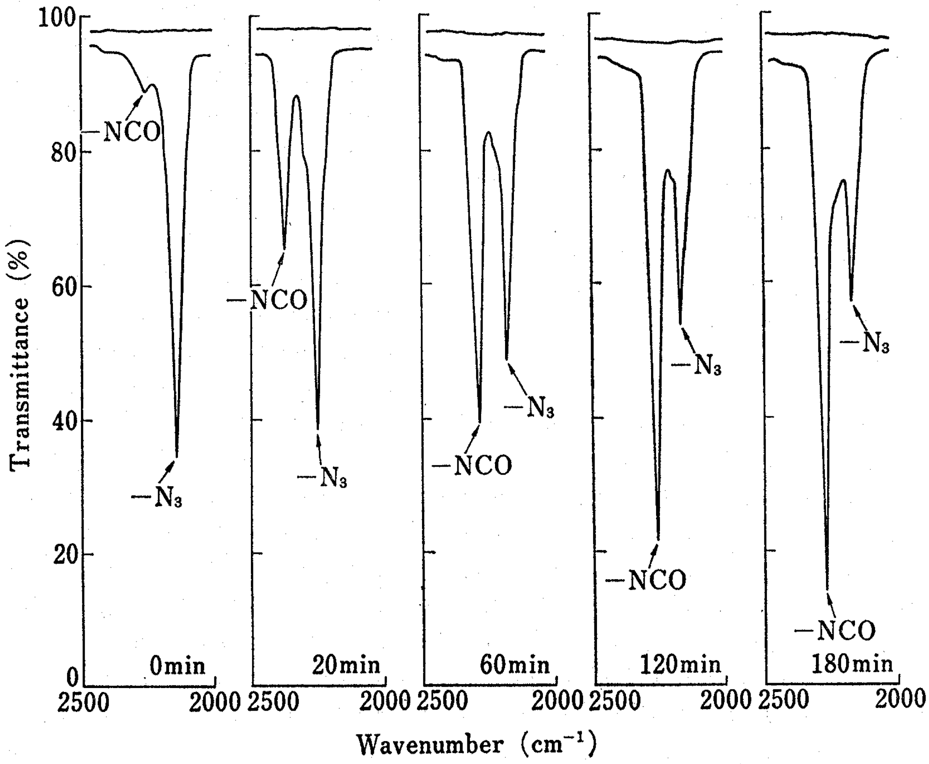

Fig. 2. IR Spectra of the Reaction Mixture of 2-Furoyl Azide (**1**) and 2-Furyl Isocyanate in Toluene

The reaction temperature is 80° ±0.03°.

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6) *a*) M. Boudart, "Kinetics of Chemical Processes," Prentice-Hall, Inc., Englewood, Cliffs, N.J., U.S.A., 1968, p. 179; *b*) K.J. Laidler, "Chemical Kinetics," McGraw-Hill, London, 1965, p. 251; *c*) L.P. Hammett, "Physical Organic Chemistry," 2 ed., McGraw-Hill, London, 1970, p. 391.

substituted 2-furoyl azides (**1**, **2** and **3**) and also *p*-substituted benzoyl azides (**11**, **12** and **13**) (Fig. 4).

In the course of the rearrangement, the increase in absorbance of ν_{NCO} at 2275 cm^{-1} with time has been found to obey pseudo first order kinetics at 70°, 80°, 90°, 100° and 110° (±0.03°). Hence, the rate constants (k) from this method are in satisfactory agreement with the rate constants from the decrease in absorbance of each $\nu_{\mathrm{N_3}}$ of the azido groups in the region of 2130—2180 cm^{-1} at the above five temperatures (Fig. 2 and Table 1).

Results and Discussion

These rate constants (k) were calculated from the customary first order rate expression as follows;

$$k = 2.303/t \cdot \log a/x \qquad (1)$$

where a is equal to the each initial concentration of the acyl azides (**1**, **16**) (mol/l), and x is the each mole number of the unchanged acyl azides at a measured period of time t(min).

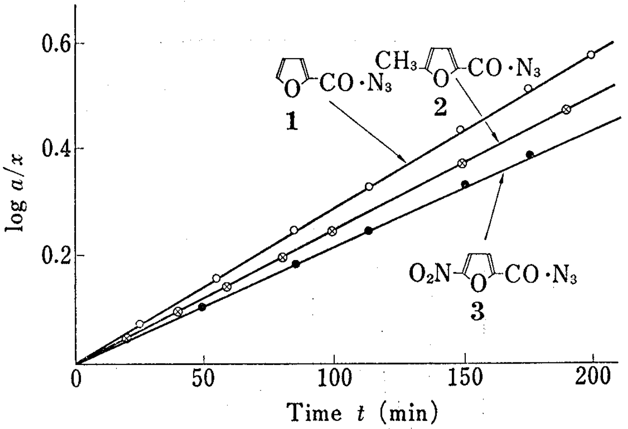

Fig. 3. First Order Rate Plot for 2-Furoyl Azide (1), 5-Methyl-2-furoyl Azide (2) and 5-Nitro-2-furoyl Azide (3) in Toluene at 80°±0.03°

As ahown in Fig. 3, the each of three plotting lines obtained from kinetic measurement of the rearrangement of three furoyl azides (**1**, **2** and **3**) follows a linear relation near to about 75% of completion of the reaction. Further, the activation energies ($\Delta E^{\neq}$) and the frequency factors ($\log PZ$) were obtained from the Arrhenius' equation in terms of the method of least squars, and also the activation entropies ($\Delta S^{\neq}$) were calculated from the following equation[5a)];

$$\Delta S^{\neq} = 2.303 (\log PZ - 1 - \log Kb \cdot T/h) \qquad (2)$$

where Kb is Boltzmann's constant and h is Planck's constant. Detailed empirical data relative to all the acyl azides (**1**—**16**) are displayed in Table I.

The fact that the each $\Delta E^{\neq}$ of the acyl azides (**1**—**16**) ranges from 26 kcal/mol to 32 kcal/mol can be found. To the contrary, the every activation entropy ($\Delta S^{\neq}$) presents positive value ranging from 1.3 e.u. to 18 e.u.. Considering the above evidences, it is suggestible that the positive $\Delta S^{\neq}$ as one of the thermodynamical functions may predominantly be responsible for promoting the thermolytic rearrangement. As compared with the magnitudes of $\Delta S^{\neq}$ of the four unsubstituted acyl azides (**2**, **7**, **9** and **12**), we found an interesting relationship among them, increasing $\Delta S^{\neq}$ to be 2-furoyl azide(**2**)[1.3 e.u.]$<$2-pyrroyl azide(**7**)[4.7 e.u.]$<$2-thenoyl azide(**9**)[9.3 e.u.]$<$benzoyl azide(**12**)[13 e.u.]. In addition, the sequence in the reactivity of the acyl azides (**2**, **7**, **9** and **12**) in the rearrangement is very nearly parallel to that in the resonance energies[7)] of the aromatic and heteromatic parent rings of the acyl azides, increasing to be furan(23 kcal/mol)[7b)]$<$pyrrole(31 kcal/mol)[7b)]$\leqq$thiophene(31 kcal/mol)[7b)]$<$benzene(37 kcal/mol).[7b)] Incidentally, we may remark that the reaction mechanism concerned with the

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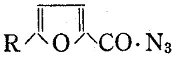
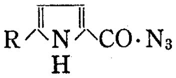
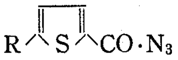
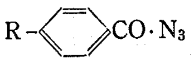
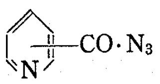
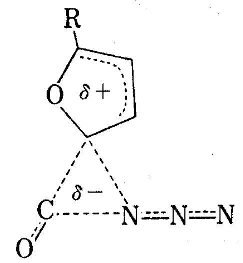
[7)] *a*) N.D. Epiotis, W.R. Cherry, F. Bernardi, and W.J. Hehre, *J. Am. Chem. Soc.*, **98**, 4361 (1976); *b*) L. Pauling, "The Nature of the Chemical Bond," 3rd. ed., Cornell University Press, Ithaca, New York, 1960, p. 197; *c*) G.W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, New York, 1955, p. 75; *d*) F. Klagan, *Chem. Ber.*, **82**, 358 (1949).

Table I. Kinetic Results for the Curtius Rearrangement of Aroyl or Heteroaroyl Azides

Compounds	No.	Substituent R	Rate constant, $k \times 10^4$ (min^{-1}) At 70°	At 80°	At 90°	At 100°	At 110°	$\Delta E^{\neq}$ kcal/mol	log PZ	$\Delta S^{\neq}$ at 80° e.u.
	**1**	H–		0.692	1.95	5.33	14.6	26.4 (29.2)[a]	14.2 (15.8)[a]	1.3_4
	2	CH_3–		0.549	1.86	5.86	15.8	30.3	16.5	$12._2$
	3	O_2N–		0.570	1.65	5.53	16.7	30.6	16.7	$12._8$
	4	Br–	0.148	0.551	1.89	4.92		31.3	17.1	$14._9$
	5	OHC–	0.182	0.667	1.80	5.45		29.1	15.9	9.1_5
	6	MeOOC–	0.166	0.561	2.07	5.60		29.1	15.8	8.8_5
	**7**	H–		0.174	0.579	1.66	4.15	27.0	14.0	4.7_8
	**8**	H–		0.481	1.73	5.44	13.8	29.3 (31.5)[a]	15.9 (17.4)[a]	9.3_0
	9	CH_3–		0.526	1.80	5.56		29.9	16.3	$10._9$
	10	O_2N–		0.354	1.25	3.39	10.4	32.6	17.9	$18._3$
	**11**	H–		1.07	3.53	10.1	30.4	30.3 (27.2)[a] (27.1)[b]	16.8 (15.0)[a] (14.9)[b]	$13._4$
	12	CH_3–		1.07	3.22	10.0	26.5	28.2 (28.4)[b]	15.5 (15.6)[b]	7.3_8
	13	O_2N–		1.02	3.28	10.1	28.3	29.7 (28.0)[b]	16.4 (15.4)[b]	$11._5$
	**14**	2–		4.78	15.5	40.3	106	27.8 (19.6)[a]	15.9 (10.2)[a]	9.2_1
	15	3–		1.08	3.51	10.2	30.8	29.9 (27.7)[a]	16.6 (15.3)[a]	$12._4$
	16	4–		1.04	3.51	11.0	35.2	31.5 (25.4)[a]	17.5 (13.7)[a]	$16._7$

a) Data of Othuji, lit. 5*c*), *b*) Data of Yukawa, lit. 5*d*).



R=H–, CH_3–, O_2N–, Br–, OHC– and MeOOC–

Chart 1

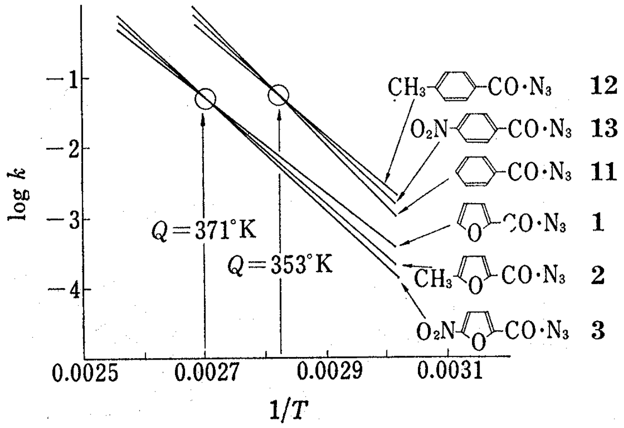


Fig. 4. The Isokinetic Temperatures (Q) of 5-Substituted 2-Furoyl Azides (**1**, **2** and **3**) and *p*-Substituted Benzoyl Azides (**11**, **12** and **13**)

Curtius rearrangement has plausibly been discussed on the nitrene[8] and also the concerted theory.[9] Assuming that the thermolytic Curtius rearrangement may belong to the concerted reaction in this work, the formation of an activated three-membered complex as an inter-

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[8] *a*) M. Imoto, *Kagaku* (Kyoto), **30**, 556 (1975); *b*) R. Breslow, "Organic Reaction Mechanisms," W.A. Benjamin, Inc., New York, 1966, p. 91; *c*) P. Smith, "Organic Reactions," Vol. 3, ed. R. Adams, John Wiley and Sons, New York, 1946, p. 337.

[9] *a*) W. Lwowski, R.A. deMauriac, and M. Thompson, *J. Org. Chem.*, **40**, 2608 (1975); *b*) A. Fry and J.C. Wright, *Chem. Eng. News*, **1968**, 28.

mediacy (Chart 1) designed to be a transition state in the course of this reaction appears to be acceptable in propotional to the increase of the resonance energy of the each parent ring itself with the acyl azido group.

It is noteworthy that the substituent dependence on the activation entropy ($\Delta S^{\neq}$) in the rearrangement of the 5-substituted 2-furoyl azides (**2**—**6**), and also the 5-substituted 2-thenoyl azides (**9** and **10**) are indifferent to whether the substituents are electron releasing or attracting groups. On the contrary, however, it resulted in that the rearrangement of *p*-substituted benzoyl azides (**12** and **13**) has $\Delta S^{\neq}$ decreased. Consequently, we puzzle to assert a definite conclusion of why these two diverse results concerned with the change of $\Delta S^{\neq}$ can be found in the number of the above nine substituted acyl azides. However, a major attribution to the increased $\Delta S^{\neq}$ of the 5-substituted 2-furoyl azides (**2**—**6**) may almost be conformed to the stability of the furan ring influenced, to some extent, by each electronic effect of the five substituents (CH_3-, O_2N-, Br-, OHC- and MeOOC-). Considering the above evidence in the concerted reaction assumed to be reasonable, this suggests us that the 5-substituted 2-furoyl azides (**2**—**6**) may have more greater possibility to form an activated three-membered cyclic intermediacy than the unsubstituted 2-furoyl azide (**1**) (Chart 1).

Next, plotting the logarithm of the rate constants (k) as ordinate and $1/T$ of the reaction temperature as abscissa, both isokinetic temperatures involving Q=371 °K and Q=353 °K were found from a set of the three furoyl azides (**1**, **2** and **3**) and the three benzoyl azides (**14**, **15** and **16**), respectively (Fig. 4), and separately an isokinetic temperature (Q) can be obtained from the following empirical formula[6a];

$$Q = 1/2.303\,\boldsymbol{R}C \qquad (3)$$

where Q is an isokinetic temperature, ***R*** gas constant and C the slope for the plotted straight line of $\Delta E^{\neq}$ *vs.* log PZ(compensation effect) (Fig. 5). Practically, the both straight lines

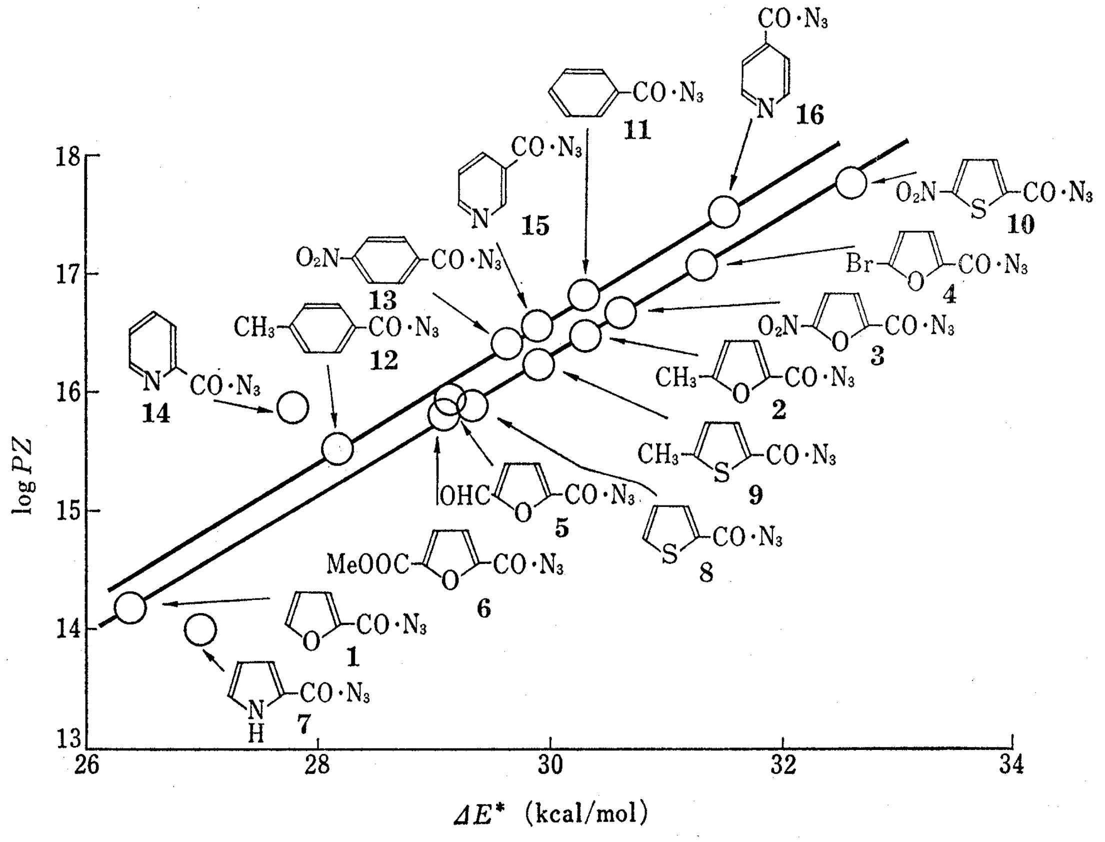

Fig. 5. The Compensation Effects for the Curtius Rearrangement of Aroyl or Heteroaroyl Azides (**1**—**16**)

plotted gave 0.589 to the slope of set A for the five-membered heterocyclic acyl azides (**1**—**10**) and 0.619 to that of set B for the six-membered cyclic and heterocyclic acyl azides (**11**—**16**), respectively. It is very of interest that the pattern on the set A(**1**—**10**) is analogous to that on the set B(**11**—**16**) in the linear relationship between $\Delta E^{\neq}$ and $\log PZ$.

However, no theoretical reasons have unambiguously been found for such an occurrence of the compensation effects in connection with the isokinetic temperatures. From the almost parallel straight lines (Fig. 5) related to the compensation effects, it seems to be suggestible that there are some delicate differences in a possibility of the formation of the activated three-membered cyclic intermediacy (Chart 1) between a reaction pathway of the set A(**1**—**10**) and the set B(**11**—**16**) in the presence of toluene as a solvent. Therefore, the solvent effects must play, to some extent, a delicate role in controlling the reactivity of the acyl azides for this work. Our work concerned with this paper will be continued to study in the future.

Experimental[10]

Materials[11]——The acyl azides (**1**—**16**) for the measurement were prepared from the reaction of the corresponding carboxylic acids with DPPA[4] in the presence of equal amount of triethylamine, and were purified by recrystallization from the solvent described previously:[1a] 2-furoyl azide (**1**),[12a] mp 62—63°; 5-methyl-2-furoyl azide (**2**),[12a] mp 35—36°; 5-nitro-2-furoyl azide (**3**),[1b] mp 67—68°; 5-bromo-2-furoyl azide (**4**),[12a] mp 59—60°; 2-pyrroyl azide (**7**),[12c] mp 101—102°; 2-thenoyl azide (**8**),[5c] mp 32—33°; 5-methyl-2-thenoyl azide (**9**),[1a] mp 54—55°; 5-nitro-2-thenoyl azide (**10**),[1a] mp 61—62°; benzoyl azide (**11**),[5b] mp 27—28°; *p*-toluoyl azide (**12**),[5c] mp 35—36°; *p*-nitrobenzoyl azide (**13**),[5b] mp 65—67°; 2-pyridinecarbonyl azide (**14**),[5c] mp 49—50°; 3-pyridinecarbonyl azide (**15**),[5c] mp 47—48°; 4-pyridinecarbonyl azide (**16**),[5c] mp 50—51°.

5-Methoxycarbonyl-2-furoic Acid[13]——This acid was prepared by a method similar to that described by Baba[14] for 2-furoic acid. To a pyridine solution (5 ml) of methyl 5-formyl-2-furoate[15a] (3 g, 0.019 mol) was added 10% hydrogen peroxide solution (8 ml) with stirring and cooling. After all H_2O_2 solution had been added, the reaction mixture was stirred for 6 hr at room temperature, and then acidified to Congo red with 10% hydrochloric acid. The precipitated acid was filtered off, washed on the filter with three 5 ml portions of cold water, recrystallized from water; colorless needless, yield, 2.8 g (84.8%), mp 201—202°, IR cm^{-1}: ν_{CO} 1680 and 1720 (KBr).

5-Formyl-2-furoyl Azide (5)——To a dimethyl sulfoxide (DMF) solution (10 ml) of 5-formyl-2-furoic acid[15] (1.4 g, 0.01 mol) and triethylamine (1.0 g, 0.01 mol), was added a DMF solution (3 ml) of DPPA (2.75 g, 0.01 mol) with stirring and cooling. After all DPPA had been added (10 min), the reaction mixture was stirred for 6 hr at room temperature, and immediately poured into a mixture of ether and ice. The requisite product (**5**) is extracted with ether, and the organic layers were washed with 10% sodium bicarbonate solution and water, and the dried over anhydrous sodium sulfate. The ether layer was removed under reduced pressure at room temperature. The residue was recrystallized from benzene–cyclohexane (1: 1); colorless needless, yield, 1.5 g (80.2%), mp 70—72°, IR cm^{-1}: ν_{N_3} 2150 (KBr).

5-Methoxycarbonyl-2-furoyl Azide (6)——(**6**) was also prepared according to the method as mentioned above using 5-methoxycarbonyl-2-furoic acid[13] (1.7 g, 0.01 mol) and recrystallized from pet. ether (bp 45-50°)–cyclohexane (1: 1); colorless needless, yield, 1.6 g (82.1%), mp 79—80°, IR cm^{-1}: ν_{N_3} 2150 (KBr).

5 and **6** were sufficiently pure for the rate measurement and before use, drying in a desiccator over phosphorus pentoxide. Solvent. Toluene was spectroscopic grade[16] and stored over Linde Molecular Sives (obtained from the Nakarai Pure Chemicals Co., Ltd., type 4A 1/16) to prevent it from moisture.

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[10] All melting points were determining using the Yanagimoto melting point test apparatus, and have not been corrected; IR spectra were measured on a Hitachi 215 spectrophotometer.

[11] These samples were ensured to be authentic by measuring melting point and IR spectrum, respectively.

[12] *a*) A.T. Blomquist and H.B. Stevenson, *J. Am. Chem. Soc.*, **56**, 146 (1934); *b*) H.M. Singleton and W.R. Edwards, Jr., *J. Am. Chem. Soc.*, **60**, 540 (1938); *c*) A.N. Howard and F. Wild, *Brit. J. Exptl. Pathol.*, **38**, 640 (1957) [*C.A.*, **52**, 10261 (1958)].

[13] I.K. Phelps and W.J. Hale, *Am. Chem. J.*, **25**, 445 (1901).

[14] H. Baba, *Kagaku Kenkyusho Hokoku*, **33**, 168 (1957) [*C.A.*, **52**, 7267*g* (1958)].

[15] *a*) A.A. Aroian, V.G. Afrikian, N.A. Babiian, O.L. Mndzhoian, and G.T. Tatevosian, "Syntheses of Heterocyclic Compounds," Vol. 3, ed. A.L. Mndzhoian, translated from Russian by A.E. Stubbs, Consultants Bureau, Inc., New York, 1959, p. 39; *b*) H.B. Hill and H.E. Sowyer, *Am. Chem. J.*, **20**, 169 (1898).

[16] J.A. Riddick and W.B. Bunger, "Techniques of Chemistry, Vol. II, Organic Solvents," ed. A. Weissberger, Wiley-Interscience, A Division of John Wiley and Sons, Inc., New York, 1970, p. 611.

Kinetic Procedure——IR measurements were made in a 0.5 mm sodium chloride micro cell using the Shimazu Model IR-400 double-beam recording spectrophotometer.

In a 50 ml four-necked round-bottomed flask equipped with a mechanical stirre, a reflux condenser which was fitted a calcium chloride drying tube and a thermometer, was placed toluene (25 ml). The flask and its content were placed in a constant temperature oil-bath[17] (70°, 80°, 90°, 100° and 110° ± 0.03°) and the temperature in the solvent (toluene) was equilibrated at the prescribed temperature. The time of addition of each acyl azides (**1**—**16**) (0.025 mol) into the reaction flask at the above prescribed temperature was taken as zero time. About 0.3 ml of sample from the reaction mixture was quickly withdrawn at regular intervals, and quenched in a mixture of acetone and dry ice. The samples were immediately examined in the IR spectrum from 2500 to 2000 cm^{-1} *vs.* pure solvent (toluene). The amount of unchanged acyl azide at time t (min) was determined from the intensity of the $-N_3$ asymmetric stretching frequency of the above acyl azide at 2130—2180 cm^{-1}. The molar absorptivity for each acyl azides (**1**—**16**) was obtained from the solpe of the straight line by plotting log I_0/I against concentration (mol/l) of (**1**—**16**). A typical plot of 2-furoyl azide (**1**) is shown in Fig. 1. There was no interference of this band with that of the corresponding isocyanate. The typical IR spectra of the rearrangement of 2-furoyl azide (**1**) with time at 80° were shown in Fig. 2.

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[17] The temperature was controlled by the Tabai Universal Power Controller (model UPC-PR) and Thermoregulator.