

chloride and the resulting solution was passed over a 2×5 cm. column of silica gel. The column was washed with a little solvent and the combined eluates were evaporated. There was obtained 12.8 g. of 2-nitro-*p*-cymene, b.p. 94° (2.0 mm.), n_D^{20} 1.5288. The infrared spectrum of this product was identical in all respects to that of an authentic sample.

Oxidation of Ethyl *p*-Aminobenzoate to Ethyl *p*-Nitrobenzoate.—The reaction when carried out in the usual way gave 14.7 g. of crude product which after recrystallization from ethanol weighed 12.8 g. (66%) and melted at 53 – 55° . It showed no depression in melting point when mixed with an authentic specimen of ethyl *p*-nitrobenzoate.

Oxidation of *sec*-Butylamine to 2-Nitrobutane.—Hydrogen peroxide (65.2 ml., 2.4 moles) was added dropwise fairly rapidly to 300 ml. of ice-cooled ethylene chloride with vigorous stirring. After addition of four drops of sulfuric acid catalyst 292 g. (2.88 moles) of acetic anhydride was added to the cooled solution over a 90-minute period. The mixture so obtained was stirred 30 minutes at 0° and 30 minutes at room temperature. It was diluted with 200 ml. of ethylene chloride and heated rapidly to reflux. At this temperature a solution of 43.8 g. (0.6 mole) of *sec*-butylamine in 50 ml. of ethylene chloride was added dropwise over a one-hour period. The reaction was very exothermic during this addition and rapidly developed a blue color. After the amine addition was complete the mixture was heated under reflux one hour. It was then cooled, washed with 2×500 ml. of cold 1:1 ammonia, and finally with 500 ml. of water. The organic extract was dried over magnesium sulfate, and the major portion of solvent removed by frac-

tionation in a Todd column packed with glass helices. The residue, still containing some solvent, was fractionated in a spinning band column, and 40.2 g. (65%) of 2-nitrobutane, b.p. 64 – 66° (60 mm.), n_D^{20} 1.4043, obtained. The infrared spectrum of this product was identical in all respects to that of an authentic sample.

Reaction of Trifluoroacetic Acid with *n*-Hexylamine.—A solution of trifluoroacetic acid was prepared by dropwise addition of 60.5 ml. (0.36 mole) of trifluoroacetic anhydride to a cooled suspension of 8.2 ml. (0.3 mole) of 90% hydrogen peroxide in 50 ml. of methylene chloride. This solution was then added over a 30-minute period to a well-stirred suspension of 85 g. (0.8 mole) of anhydrous sodium carbonate in 400 ml. of methylene chloride at -25° to -35° . At this temperature a solution of 5.0 g. (0.05 mole) of *n*-hexylamine in 10 ml. of solvent was added dropwise, and the resulting mixture was stirred at -30° for one hour. It was then poured into 500 ml. of water. The organic layer was dried over magnesium sulfate and the volatile solvent evaporated. There was obtained 7.9 g. (80%) of *n*-hexyl trifluoroacetamide, b.p. 80° (1.0 mm.). The infrared spectrum was typical of an *N*-substituted amide and showed carbonyl bands at 1710 and 1550 cm^{-1} .

Anal. Calcd. for $\text{C}_8\text{H}_{17}\text{NOF}_3$: C, 48.72; H, 7.16; N, 7.10. Found: C, 48.76; H, 7.48; N, 7.62.

Acknowledgment.—We are indebted to Mr. A. S. Pagano for certain preliminary experiments in connection with this work.

HUNTSVILLE, ALABAMA

[CONTRIBUTION FROM THE INSTITUTE OF SCIENTIFIC AND INDUSTRIAL RESEARCH, OSAKA UNIVERSITY]

The Curtius Rearrangement. I. The Decomposition of *m*- and *p*-Substituted Benzazides in Toluene

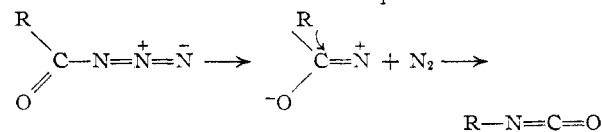
BY YASUhide YUKAWA AND YUHO TSUNO

RECEIVED FEBRUARY 15, 1957

The rates of the Curtius rearrangement of various substituted benzazides in toluene were measured by collecting the nitrogen evolved; the activation energies and log *PZ* were calculated. The rate differences attributable to substitution were small but the activation and log *PZ* varied over a wide range. The rate changes were, however, found to depend on the changes in activation energy. Electron-releasing groups in the *m*-position of benzazide increased the reaction rate and electron-attracting groups decreased it. On the other hand, all substituents in the *p*-position decreased the rate. These results, which differ from those reported for the Lossen, Hofmann and Schmidt rearrangements, are discussed in terms of the polar effects of the substituents and the effect of conjugation of the carbonyl group with the benzene ring on the breaking bond.

Although the Curtius rearrangement,¹ the decomposition of acyl azide into an isocyanate and nitrogen, is an important procedure for replacing a carboxyl group by an amino group or amino derivatives, few kinetic studies^{2,3} have been reported.

The Curtius rearrangement has been thought to proceed through a mechanism⁴ analogous to those of similar rearrangements such as the Lossen, Hofmann and Schmidt rearrangements. Of the various mechanisms^{5,6} proposed, the following expression has been considered to be a probable one.



(1) For a comprehensive review see, P. A. S. Smith, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 337.

(2) C. W. Porter and L. Young, *THIS JOURNAL*, **60**, 1497 (1938); E. W. Barrett and C. W. Porter, *ibid.*, **63**, 3434 (1941).

(3) M. S. Newman, S. H. Lee, Jr., and A. B. Garrett, *ibid.*, **69**, 113 (1947).

(4) F. C. Whitmore, *ibid.*, **54**, 3274 (1932).

(5) C. R. Hauser and S. W. Kantor, *ibid.*, **72**, 4284 (1950).

(6) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, pp. 319–320.

An azide decomposes to give a molecule of nitrogen and an intermediate which contains a nitrogen atom with an incomplete octet, followed by intramolecular migration of R. In other words, the reaction in which loss of nitrogen occurs is the rate-determining step.

Newman and co-workers,³ in their kinetic study of this rearrangement, demonstrated that the kinetics in various solvents was first order and that no salt effect was present. However, kinetic effects of structural changes in the azide, and effects of substituents on the migration of the phenyl group in benzazide have not been investigated. The study made by Hauser and others^{7,8} on the Lossen and Hofmann rearrangements indicated that electron-releasing substituents in the migrating phenyl group increase and electron-attracting groups decrease the rate, the sequence being in accord with the polar effects of the respective substituents, and the experimental results were found to follow Hammett's equation. In the

(7) T. F. Bright and C. R. Hauser, *THIS JOURNAL*, **61**, 618 (1939); W. B. Renfrow, Jr., and C. R. Hauser, *ibid.*, **59**, 2308 (1937).

(8) C. R. Hauser and W. B. Renfrow, Jr., *ibid.*, **59**, 121 (1937).

Schmidt reaction of benzoic acids⁹ the effect of *m*-substituents was found to give a rate sequence¹⁰ similar to that of the Lossen and Hofmann rearrangements. This reaction is a close variant of the Curtius rearrangement, the only difference being the presence of sulfuric acid as a strong acid catalyst. Newman has predicted and verified the fact that the Curtius reaction is controlled by an acid catalyst.^{6,11,12} It seemed possible then that the effect of substituents in a migrating phenyl group in the Curtius rearrangement would give a similar rate sequence, therefore, kinetic studies on the decomposition of *m*- and *p*-substituted benzazides in toluene were undertaken.

Experimental

Materials.—Various substituted benzazides were prepared from hydrazides by the method of Curtius,¹³ and by the Naegeli method.^{13,14} The Barrett and Porter modification² of the latter method was adopted for the preparation of benzazide. An attempt to prepare *p*-nitrobenzazide by this method in either acetone-water or chloroform was unsuccessful, due to difficulty involved in separating and purifying the product. The method was, however, applicable to the preparation of *m*-nitrobenzazide.¹⁵ All other azides were prepared from hydrazides according to the usual method¹⁶ by the action of sodium nitrite on the hydrazide in aqueous hydrochloric acid, followed by extraction with ether. The solvent was removed under vacuum

at room temperature. The residue was taken up in alcohol and water was added to the alcoholic solution until it became cloudy.¹⁷ When the mixture was cooled, the product separated; it was recrystallized several times from ether and aqueous alcohol.

As the *m*-substituted benzazides are liquids, the ether solution obtained as described above was dried over calcium chloride, the solvent was removed under vacuum and the residue dried again over anhydrous sodium sulfate. The filtrate obtained after removing the drying agent was used for the rate measurement without further purification. The treatment of *m*-methoxy and *m*-bromo-compounds with active charcoal or potassium carbonate should be avoided because vigorous and sometimes explosive evolution of a gas occurs. The melting points of the compounds obtained are listed in Table I.

Solvent.—Anhydrous toluene, which was prepared by the usual method,¹⁸ was washed successively with concentrated sulfuric acid, a 20% aqueous sodium hydroxide solution and water. It was dried over calcium chloride, fractionally distilled in the presence of sodium, and stored over sodium, b.p. 110.5°.

Kinetic Runs.—The rate was determined by measuring the volume of nitrogen evolved. The apparatus and procedure used were essentially the same as that described in several recent papers.¹⁹ The reaction mixture was not stirred. The temperature of the constant temperature bath was adjusted to within 0.01°.

Seventy-five milliliters of toluene was placed in the reaction flask, which had been connected through a stopcock to the azotometer containing a 50% aqueous solution of potassium hydroxide. The flask was immersed in the thermostat, and the reaction mixture allowed to reach an equilibrium temperature. A 5-mmole sample of an azide which had been weighed to the nearest mg. was transferred to the flask, the stopcock closed and the contents of the flask shaken vigorously to obtain the complete dissolution of the azide. After thermal equilibrium was again attained, the stopcock was opened to the gas buret and the nitrogen evolved was collected. The volume of nitrogen was measured at definite intervals as frequently as possible over the period necessary for the evolution of 80–90% of the theoretical amount. The volume at infinite time was determined when the reaction had progressed to 9–10 times its half-time. The measurements were made at least three different temperatures, each being repeated several times. Stirring of the solution and slight changes in the temperature of the solution in the gas buret did not significantly affect the results.

When the reaction was complete, the reaction mixture was treated with a small amount of water and allowed to stand for several days. The product was then separated quantitatively as the corresponding substituted *sym*-diphenylurea, the melting points of which are shown in Table I.

Results and Discussion

It has been shown that the rate of the decomposition of benzazide in various solvents follows the first order,³ and rate constant k_1 was calculated from equation

$$k_1 t = 2.303 \log (V_{\infty} / (V_{\infty} - V))$$

where V is the volume of nitrogen at time t and V_{∞} is the total volume of nitrogen collected. The substituted benzazides decomposed quantitatively in toluene (usually close to the theoretical amount) and first-order kinetics were obtained. A plot of the $\log (V_{\infty} - V)$ against time, t , gave a straight line, covering over 70% of the reaction in every

(17) This treatment is important to obtain a colorless substance and to remove nitrogen oxides.

(18) A. Weissberger, "Technique of Organic Chemistry," Vol. VII, "Organic Solvents," 2nd edition, Interscience Publishers, Inc., New York, N. Y., 1955, p. 318.

(19) C. G. Overberger, M. T. O'Shaughnessy and H. Shalit, *THIS JOURNAL*, **71**, 2661 (1949).

TABLE I

MELTING POINTS^a OF SUBSTITUTED BENZAZIDES, BENZ-HYDRAZIDES AND DIPHENYLUREAS

Substituents	Azides	Melting points, °C. <i>sym</i> -Diphenyl- Hydrazides ureas	
H ^a	27		237
<i>p</i> -HO ^b	132	255–256	Decomp.
<i>p</i> -CH ₃ O ^{c,d}	70–71	136	233–234
<i>p</i> -C ₂ H ₅ O ^d	31	128	224
<i>p</i> - <i>t</i> -C ₄ H ₉ ^e	63–65	134	281
<i>p</i> -CH ₃ ^{c,f}	35	117	263
<i>p</i> -Br ^g	47	164	244–246
<i>p</i> -Cl ^h	43	163	305
<i>p</i> -NO ₂ ^{b,i}	65	209–211	308–311
<i>m</i> -CH ₃ ^j	Liquid	97	210–211
<i>m</i> -CH ₃ O ^c	Liquid	109	
<i>m</i> -Br ^g	Liquid	153	260
<i>m</i> -NO ₂ ^{b,i}	68	154	242

^a All melting points are uncorrected. ^b T. Curtius, A. Straube and R. Radenhausen, *J. prakt. Chem.*, [2] **52**, 227 (1895). ^c C. Naegeli, A. Tyabji and L. Conrad, *Helv. Chim. Acta*, **21**, 1127 (1938). ^d P. P. T. Sah and Kwang-Shih Chang, *Ber.*, **69**, 2762 (1936); R. Robinson and M. L. Tomlinson, *J. Chem. Soc.*, 1524 (1934). ^e H. Yale, K. Losee, J. Martins, M. Holsing, F. M. Perry and J. Bernstein, *THIS JOURNAL*, **75**, 1933 (1953). ^f T. Curtius and H. Franzen, *Ber.*, **35**, 3239 (1902). ^g T. Curtius and E. Portner, *J. prakt. Chem.*, [2] **58**, 190 (1898). ^h C. H. Kao, H. Y. Fang and P. P. T. Sah, *J. Chinese Chem. Soc.*, **3**, 137 (1935); *C.A.*, **29**, 6172 (1935). ⁱ T. Curtius and O. Trachmann, *J. prakt. Chem.*, [2] **51**, 165 (1895). ^j R. Stolle and H. P. Stevens, *ibid.*, [2] **69**, 366 (1904).

(9) L. H. Briggs and J. W. Lyttleton, *J. Chem. Soc.*, 421 (1943).

(10) Only two *p*-substituted compounds were examined.

(11) M. S. Newman and H. L. Gildenhorn, *THIS JOURNAL*, **70**, 317 (1948).

(12) R. A. Coleman, M. S. Newman and A. B. Garrett, *ibid.*, **76**, 4534 (1954).

(13) See the references in Table I and ref. 1, pp. 382–385.

(14) Houben-Weyl, "Methoden der Organischen Chemie," Band VIII, Georg Thieme Verlag, Stuttgart, 1952, pp. 676–684.

(15) C. Naegeli, *Helv. Chim. Acta*, **16**, 349 (1933).

(16) L. Gattermann, "Die Praxis des Organischen Chemikers," 26. auf., Walter De Gruyter & Co., Berlin, 1939, pp. 160–161.

case²⁰; see Fig. 1. The precision of these rate constants is revealed by their excellent reproducibility (Fig. 1). The logarithms of the rate con-

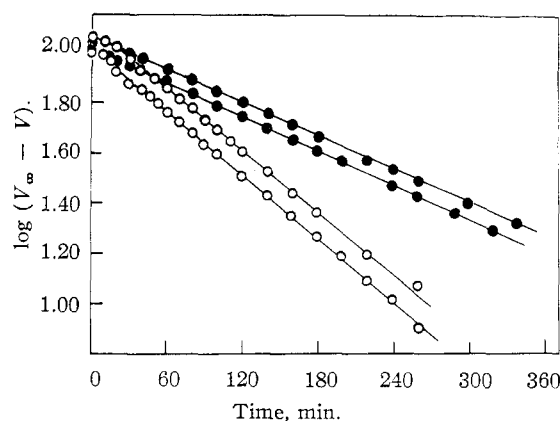


Fig. 1.—Typical first-order plots for the decomposition of *p*-nitrobenzazide in toluene: open circles at 70.10° ($k_1 = 3.42 \times 10^{-3}$); closed circles at 75.20° ($k_1 = 6.17 \times 10^{-3}$).

stants plotted against the reciprocal of the temperatures (data given in Table II) give a straight line. From the rate constants Arrhenius parameters were calculated by the method of least squares; they are given in Table II.

In the Curtius rearrangement of the substituted benzazides in toluene, the rate constant varied little with respect to the substituents as shown in Table II, at most by a factor of about two, whereas the energy and entropy of activation varied over a wide range. The rate changes were, however, found to depend on the changes of activation energy.

The substitution of electron-releasing groups in the *m*-position of benzazide accelerated the reaction, while the *m*-substitution of electron-attracting groups retarded it; these effects can be correlated with the Hammett equation, as shown in Fig. 2. On the other hand, all substituents in the *p*-position, except the *t*-butyl group, reduced the rate of decomposition of benzazides, regardless of whether a substituent was electron releasing or attracting; the strongly electron-attracting *p*-nitro group which would be expected to decelerate the reaction was found to retard it to a small extent, while the strongly electron-releasing *p*-methoxy and *p*-hydroxy groups unexpectedly reduced the rate of the reaction.

This reaction sequence is very different from that reported for the Lossen, Hofmann and Schmidt rearrangements,⁷⁻⁹ in which, as previously mentioned, the reactivities can be correlated with the polarity of substituents in either the *m*- or *p*-position.

In the decomposition of benzenediazonium salts in an acidic medium²¹ and the thermal decomposi-

(20) During the first few minutes the amount of nitrogen evolved was sometimes less than that predicted; this appears to be due mainly to the slow dissolution of some azides, as the liquid azides did not show this phenomenon. This discrepancy tended to persist for a longer time with the less soluble azides.

(21) (a) M. L. Crossley, R. H. Kienle and C. H. Benbrook, *THIS JOURNAL*, **62**, 1400 (1940); (b) C. K. Ingold, "Structure and Mechanism of Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 800-802; (c) E. S. Lewis and E. B. Miller, *THIS JOURNAL*, **75**, 429 (1953).

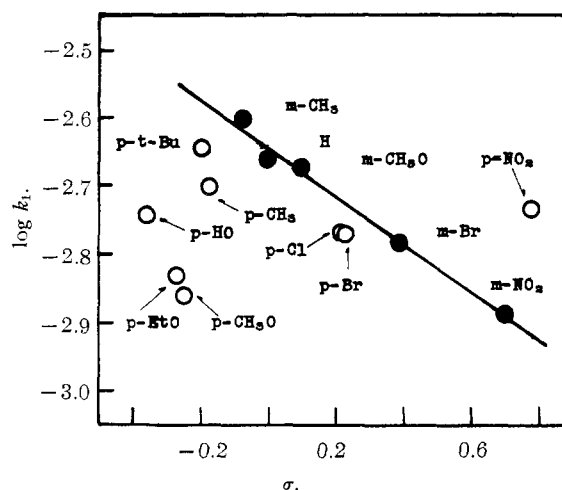


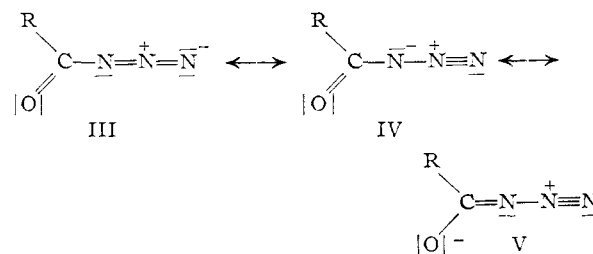
Fig. 2.—Correlation of rate constants with Hammett σ -values.

tion of phenylazotriphenylmethanes,²² all substituents, both electron releasing and attracting, in the *p*-position decrease the rate, and the rate sequence is in close agreement with that of the Curtius rearrangement (see Table III). The rate of decomposition of benzenediazonium salts is influenced by the polar effect of substituents in the *m*-position, but not by that of substituents in the *p*-position. When for a given substituent, $\log k$ for this reaction is plotted against $\log k$ for the Curtius rearrangement (values given in Table III), an almost linear relationship is obtained. This indicates clearly that the effect of a given substituent on both reactions is due to the same electronic factor. This reaction is strongly influenced by conjugation between the benzene ring and the azo group.²¹ The mesomeric electron-releasing *p*-substituent, for example the *p*-methoxy group, increases the resonance contribution of structure II and therefore increases the bond energy of the carbon-nitrogen bond, which would lead to retardation of the bond fission.



The same explanation may be equally applicable to the decomposition of phenylazotriphenylmethanes.²²

The structural characteristic present in an acyl azide, but absent in hydroxamic acid and a *N*-bromobenzamide, is the conjugation between the carbonyl and the triazo group, which would give resonance stabilization to this compound.



(22) S. G. Cohen and C. H. Wang, *ibid.*, **75**, 5504 (1953).

TABLE II
KINETIC RESULTS OF THE CURTIUS REARRANGEMENT

Subst.	Temp., °C.	Rate constant 10 ³ , min. ⁻¹	$\Delta E \pm$, kcal. mole ⁻¹	log <i>PZ</i> , min. ⁻¹
<i>p</i> - <i>t</i> -C ₄ H ₉	59.90	1.22 \pm 0.004	26.2	14.26
	65.20	2.28 \pm .006		
	70.10	3.95 \pm .002		
	75.20	7.04 \pm .02		
H	59.90	1.15 \pm .001	27.1	14.88
	65.20	2.19 \pm .007		
	70.10	3.97 \pm .01		
	75.20	6.98 \pm .04		
<i>p</i> -CH ₃	65.20	1.984 \pm .004	28.4	15.62
	70.10	3.64 \pm .002		
	75.20	6.60 \pm .08		
	80.17	12.1 \pm .03		
<i>p</i> -HO	65.20	1.81 \pm .006	28.9	15.90
	70.10	3.23 \pm .001		
	75.20	6.18 \pm .15		
	80.17	11.1 \pm .2		
<i>p</i> -CH ₃ O	65.20	1.48 \pm .003	28.6	15.65
	70.10	2.69 \pm .02		
	75.20	4.81 \pm .01		
	80.17	9.13 \pm .1		
<i>p</i> -C ₂ H ₅ O	65.20	1.39 \pm .006	28.6	15.6
	70.10	2.55 \pm .01		
	75.20	4.71 \pm .05		
	80.17	8.45 \pm .03		
<i>p</i> -Cl	65.20	1.69 \pm .005	27.7	15.09
	70.10	2.92 \pm .01		
	75.20	5.44 \pm .05		
	80.17	9.58 \pm .07		
<i>p</i> -Br	59.90	0.879 \pm .009	27.4	14.95
	65.20	1.685 \pm .003		
	70.10	3.01 \pm .025		
	75.20	5.44 \pm .035		
<i>p</i> -NO ₂	65.20	1.88 \pm .004	28.0	15.38
	70.10	3.42 \pm .016		
	75.20	6.17 \pm .015		
	80.17	10.9 \pm .1		
<i>m</i> -CH ₃	59.90	1.49 \pm .003	24.5	13.25
	65.20	2.54 \pm .008		
	70.10	4.39 \pm .05		
	75.20	7.49 \pm .05		
<i>m</i> -CH ₃ O	59.90	1.12 \pm .013	27.7	15.16
	65.20	2.18 \pm .04		
	70.10	3.96 \pm .04		
<i>m</i> -Br	59.90	0.95 \pm .005	27.7	15.13
	65.20	1.66 \pm .002		
	70.10	3.32 \pm .009		
	75.20	5.78 \pm .05		
<i>m</i> -NO ₂	65.20	1.303 \pm .002	29.2	16.01
	70.10	2.46 \pm .005		
	75.20	4.44 \pm .09		
	80.17	8.22 \pm .10		

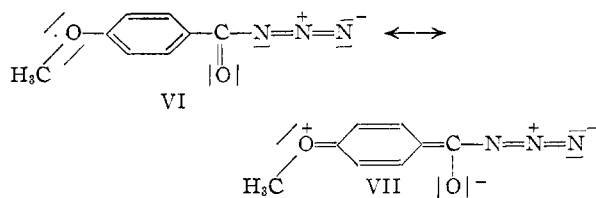
If R is an aryl group, the resonance stabilization is increased further by additional resonance of the benzene ring. The cross conjugation of the carbonyl group with the benzene ring leads to an increase in the double bond character of the nitrogen-nitrogen bond, owing to the contribution of structure VII to the initial state. This is particularly significant in the case of benzazide contain-

TABLE III
THE EFFECT OF *p*-SUBSTITUENTS ON THE RATE

Substituent	XC ₆ H ₄ CON ₃ ^a	Reaction XC ₆ H ₄ N ₂ ^b	XC ₆ H ₄ N ₂ CPh ₃ ^c
CH ₃ O	148	0.11	210
HO	181	0.93	170
CH ₃	198	37	220
H	219	740	230
Br	169		105
Cl	169	1.4	
NO ₂	188	3.1	57

^a $10^5 \times k_1$ (min.⁻¹) at 65.20°. ^b $10^7 \times k_1$ (sec.⁻¹) at 28.8°; from Ingold, ref. 21b. ^c $10^6 \times k_1$ (sec.⁻¹) at 53.35°; ref. 22.

ing a *para* electron-releasing group. For instance, the *p*-methoxy group strengthens the conjugation of the carbonyl group with the benzene ring, but weakens the conjugation with the triazo group with an increase in the double bond character of the



nitrogen-nitrogen bond in the initial state; as a result, the molecule is stabilized toward the bond fission. Therefore, mesomeric electron-releasing groups in *p*-position lead to a decrease in the reaction rate.

The effect of resonance²³ is not the only important factor. That polar effects are also important, is shown by the rate sequence for the *meta* series. In the Lossen and Hofmann rearrangements, the degree of double bond character of the breaking bond, N-halogen and N-acyloxy, is small; therefore, the influence of cross conjugation with the carbonyl group would be negligible and the polar effect of the substituents appears to play a significant role.

The difference between the reaction under consideration and the Schmidt rearrangement of benzoic acids remains obscure. It is of interest to ascertain whether the rate sequence of the Curtius rearrangement in toluene prevails also in hydroxylic solvents and under acid-catalyzed conditions, as in the case of the acid-catalyzed Schmidt reaction. Actually, the Curtius rearrangement in acetic acid containing sulfuric acid (20% vol.) gave the regular rate sequence²⁴ *p*-OH > *p*-CH₃O > *p*-*t*-C₄H₉ > H > *p*-Cl > *p*-NO₂. These results will be reported and discussed in detail in a succeeding paper.

(23) The decomposition of a diazonium salt results in the cleavage of one bond, but in the Curtius rearrangement two bonds must be broken. In the intramolecular concerted type mechanism, the participation of the aryl group must be accompanied by partial breaking of the aryl-carbonyl bond, and the anomalous rate sequence may be due to the bond energy possessed by the C-C bond. Accordingly, the consideration described above seems to be applicable to the case of C-C bond instead of the N-N bond. However, the effect of the bond breaking of this type has not usually been considered and the dissociation of the nitrogen molecule has been accepted as the rate-determining step of this reaction. No intrinsic evidence is available to support reasonably the effect of the C-C bond strength.

(24) Y. Yukawa and Y. Tsuno, unpublished.

It is a characteristic of this reaction that the energy of activation varies greatly with the substituents and that this change is accompanied by a large and parallel change in $\log PZ$. The change in entropy of activation parallels that of $\log PZ$; thus, a large entropy is associated with a large energy of activation and a small entropy with a small energy.

The energies of activation plotted against $\log PZ$ (values in Table II) gives a straight line; the relationship is given by the equations

$$\log PZ = 0.60\Delta E^\ddagger - 1.4$$

$$\Delta E^\ddagger = 1.7 \log PZ + 2.4$$

$$= 0.37 \Delta S^\ddagger_{66-20^\circ} + 23.9$$

The existence of this relationship is evidence that the decomposition reactions of the substituted benzazides proceed through the same mechanism, in spite of the considerable differences in energy and entropy of activation. Although such a functional relationship between energies and entropies of activation, a linear relation, has been observed

in various rate processes²⁵ and has been widely discussed,^{25,26} no clear-cut explanation has been given for it. It usually has been explained on the basis of change in solvation,^{3,25b,26a} but unfortunately the effect of structural changes on the solvation in the transition state has not yet been investigated in detail. Further investigations, now in progress, on the effect of structural change and solvation may provide a key to this problem.

Acknowledgment.—The authors wish to express their sincere appreciation to Professor M. Murakami and Dr. I. Moritani for their numerous and invaluable suggestions in this work, and also to the Ministry of Education for the partial financial support of this research.

(25) (a) C. N. Hinshelwood, "Kinetics of Chemical Change," The Clarendon Press, Oxford, 1940, pp. 257–261; (b) J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955); (c) A. T. Blomquist and J. A. Berstein, *THIS JOURNAL*, **73**, 5546 (1951); (d) W. K. Wilmarth and N. Schwartz, *ibid.*, **77**, 4543 (1955).

(26) (a) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1333 (1936); (b) A. Wassermann, *J. Chem. Soc.*, 621, 623 (1942); (c) R. W. Taft, Jr., *THIS JOURNAL*, **75**, 4534 (1953); (d) A. Shepp and S. H. Bauer, *ibid.*, **76**, 265 (1954); L. Slutsky and S. H. Bauer, *ibid.*, **76**, 270 (1954).

OSAKA, JAPAN

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, RESEARCH DIVISION, AMERICAN CYANAMID COMPANY, LEDERLE LABORATORIES]

The Synthesis of Certain 5-Deoxy-D-ribofuranosylpurines¹

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1,2,3-Tri-*O*-acetyl-5-deoxy-D-ribofuranose (II), obtained in three steps from methyl 2,3-*O*-isopropylidene-5-*O*-mesyl-D-ribofuranoside (IV), was converted to the 1-chloro sugar (I). Condensation of I with chloromercuri-6-dimethylaminopurine, followed by deblocking, afforded 6-dimethylamino-9-(5-deoxy-β-D-ribofuranosyl)-purine (VII). Condensation of I with chloromercuri-6-benzamidopurine afforded, after deblocking, 5'-deoxyadenosine (VIII) mixed with some α-anomer. The use of chloromercuri-6-chloropurine in condensation with I followed by ammonolysis yielded VIII free of anomeric contamination. Ammonolysis of the same condensation product in the cold afforded 6-chloro-9-(5-deoxy-β-D-ribofuranosyl)-purine (XII). Reductive dehalogenation of XII yielded 9-(5-deoxy-β-D-ribofuranosyl)-purine (5'-deoxynebularine, XI).

As part of a general synthetic program in the field of nucleoside analogs,² which originated with work on the antibiotic puromycin,³ it was of interest to determine whether the replacement of the 5'-hydroxyl group of a normal purine riboside with a hydrogen atom would confer any new biological properties to the molecule. The preparation of several 5'-deoxy-D-ribofuranosylpurine nucleosides is the subject of this paper.

The synthesis of these nucleosides was carried out by the method which Davoll and Lowy⁴ had developed for the preparation of purine nucleosides and which consisted in the condensation of a purine mercuric chloride derivative with an *O*-acetyl blocked 1-chloro sugar. For the synthesis of the 5'-deoxy-D-ribofuranosyl nucleosides it was neces-

sary to have available 1,2,3-tri-*O*-acetyl-5-deoxy-D-ribofuranose (II) and 5-deoxy-D-ribose (III). After the investigation described in this paper had been completed, Shunk, Lavigne and Folkers⁵ reported a synthesis of 5-deoxy-D-ribose (III).⁶ Their method for the preparation of III is similar to ours but there are enough experimental differences to warrant a short discussion of our procedure. Methyl 2,3-*O*-isopropylidene-D-ribofuranoside⁷ was converted to the crystalline methyl 2,3-*O*-isopropylidene-5-*O*-mesyl-D-ribofuranoside (IV) with methanesulfonyl chloride in pyridine in 63% yield. Transformation of IV to methyl 2,3-*O*-isopropylidene-5-deoxy-5-iodo-D-ribofuranoside (V)⁸ was brought about with sodium iodide in refluxing dimethylformamide. Reduc-

(1) Presented in part at the Meeting-in-Miniature, Metropolitan Long Island Subsection, American Chemical Society's New York Section in Brooklyn, New York, on February 15, 1957. Correspondence regarding this communication should be addressed to H. M. K.

(2) For a recent paper in this program, cf. H. M. Kissman and M. J. Weiss, *J. Org. Chem.*, **21**, 1053 (1956).

(3) See, for example, paper XI of the puromycin series; H. M. Kissman, C. Pidacks and B. R. Baker, *THIS JOURNAL*, **77**, 18 (1955).

(4) J. Davoll and B. A. Lowy, *ibid.*, **73**, 1650 (1951).

(5) C. H. Shunk, J. E. Lavigne and K. Folkers, *ibid.*, **77**, 2210 (1955).

(6) The phenyl- and *p*-bromophenylosazones of III were obtained from a degradation product of digitoxose by F. Mischeel, *Ber.*, **63**, 347 (1930).

(7) P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, **104**, 299 (1934).

(8) P. A. Levene and E. T. Stiller, *ibid.*, **106**, 421 (1934), prepared V by reaction of the less readily obtainable methyl 2,3-*O*-isopropylidene-5-*O*-tosyl-D-ribofuranoside with sodium iodide in acetone in a sealed tube. Shunk, *et al.*,⁵ used the Levene and Stiller procedure.