

ject to general acid catalysis in 50% ethanol.<sup>26</sup>

(26) M. D. Cohen and G. S. Hammond, *THIS JOURNAL*, **75**, 880 (1953). For the rearrangement of *p,p'*-dideuteriohydrazobenzene, see G. S. Hammond and W. Grundemeier, *ibid.*, **77**, 2444 (1955).

**Acknowledgment.**—We wish to express our gratitude to the "Universidad Nacional de Colombia" for a fellowship held by S. R. O. CAMBRIDGE 39, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF DEPAUL UNIVERSITY AND PURDUE UNIVERSITY]

## Kinetics of the Isomerization of Substituted 5-Amino-1,2,3-triazoles<sup>1</sup>

BY EUGENE LIEBER,<sup>2</sup> C. N. RAMACHANDRA RAO AND TAI SIANG CHAO

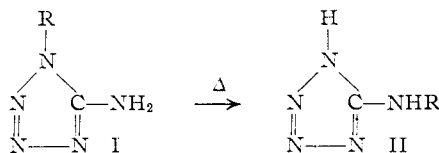
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A study of the kinetics of the equilibrium reaction involved in the independent thermal isomerization of 1-(substituted (R))-4-phenyl-5-amino-1,2,3-triazoles and 5-(substituted (R))-amino-4-phenyl-1,2,3-triazoles has demonstrated that the same electronic mechanism and electrical effects of groups applies to both the corresponding 1,2,3-triazole and tetrazole ring systems. The kinetics of the equilibrium where R is 4-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>, 3-ClC<sub>6</sub>H<sub>4</sub>, C<sub>6</sub>H<sub>5</sub>, 4-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 4-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub> and C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> were studied in the range of 133–159°. In the initial stages of the isomerization, the first-order rate law is obeyed. For the forward reaction, the rates (*k*<sub>1</sub>) decreased along the indicated series, the energies of activation increased from about 21,500 to 34,000 cal. per mole, and the heats of reaction varied from 11,840 cal. per mole (evolved) to about a value of 2200 cal. per mole (absorbed) extrapolated for the *p*-amino substituent. For the aryl substituted amino-1,2,3-triazoles, there was a good correlation between the logarithm of the rates of isomerization and Hammett's  $\sigma$ -value for groups.

### Introduction

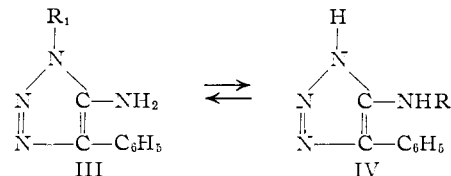
1-Substituted-5-amino-1,2,3-triazoles and 5-(substituted)-amino-1,2,3-triazoles are thermally unstable and can be isomerized without appreciable decomposition in solvents or undisturbed melts to equilibrium mixtures of both isomers.<sup>3</sup> The present work is concerned with the kinetics of this isomerization.

In 1953, Henry, Finnegan and Lieber<sup>4–7</sup> as well as Herbst and Garbrecht<sup>8</sup> reported the observation that 1-substituted-5-aminotetrazoles I undergo a facile thermal rearrangement to substituted-5-aminotetrazoles II



Subsequent studies<sup>6,7a</sup> demonstrated the equilibrium nature of  $I \rightleftharpoons II$  and determined the effect of the electrical properties of R on the position of equilibrium and the kinetics of the forward and reverse reactions. In particular the kinetics<sup>7a</sup> of the forward and reverse reactions were decisive in aiding in the selection of a reasonable mechanism among a number of possibilities.<sup>5–8</sup> In view of the isosteric relationship of the 1,2,3-triazole and tetrazole nuclei, it appeared fairly certain that the isomerization of their corresponding 5-amino derivatives involved the same electronic mechanism and that the electrical effects of groups could be extrapolated from the tetrazole system to the triazole system.<sup>6</sup> The determination<sup>5</sup> of the position of

equilibrium in homogeneous systems (undisturbed melts) for  $III \rightleftharpoons IV$  showed that  $K_{eq}$  (*i.e.*, the molar



ratio of [IV]/[III]) is dependent on the electrical nature of R<sub>1</sub> in a manner very nearly parallel to the effect observed in the substituted 5-aminotetrazole system. Accordingly, it has remained for kinetic information in order to conclusively demonstrate the parallelism between the 1,2,3-triazole and tetrazole systems. One essential difference between the 5-aminotetrazole and 5-amino-1,2,3-triazole system lies in the fact that in the latter the 4-position may be varied with groups of distinctly different electrical properties. However, in the present study the 4-position is maintained constant as a phenyl group. Further studies on the effect of substituents in the 4-position of the 1,2,3-triazole nucleus are in progress and will be reported in a separate communication.

### Experimental

**Materials.**—The 1-substituted-5-amino-1,2,3-triazoles and the 5-(substituted)-amino-1,2,3-triazoles were prepared as previously described.<sup>3</sup>

**Apparatus and Procedure.**—The apparatus used for the isomerizations consisted of a double walled flask. The reaction vessel consisted of a 25 mm., 7.6-cm. long tube sealed at one end, with the other end sealed to a 34/45 standard inner joint which in turn was sealed to a 24/40 standard outer joint. This was then fitted into the central neck (34/45 outer joint) of a 500-ml. 3-necked flask, a condenser being fitted to the outer end of the reaction vessel. Boiling *trans*-decalin, anisole, *n*-amyl alcohol, monoethanolamine and chlorobenzene enabled temperatures of 458, 432, 423, 406, and 401 °K. to be maintained. During any one experiment the temperature did not vary more than  $\pm 0.2^\circ$ .

A solvent boiling at the desired bath temperature was placed in the three-necked flask, and the reaction vessel was fitted to the central neck of the flask. Ethylene glycol was placed in the reaction vessel and a thermowell and condenser fitted to it. The three-necked flask was also fitted with a condenser and thermowell. As soon as the ethylene glycol

(1) Presented in part at the 128th National Meeting of the American Chemical Society, Minneapolis, Minn., September, 1955.

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(3) E. Lieber, T. S. Chao and C. N. R. Rao, *J. Org. Chem.*, **22**, 654 (1957).

(4) First reported at the 123rd Meeting of the American Chemical Society, Los Angeles, Calif., March, 1953.

(5) Henry, *et al.*, *THIS JOURNAL*, **75**, 2023 (1953).

(6) Henry, *et al.*, **76**, 88 (1954).

(7) (a) Henry, *et al.*, **77**, 2264 (1955); (b) *J. Org. Chem.*, **18**, 781 (1953).

(8) R. M. Herbst and W. L. Garbrecht, *ibid.*, **18**, 1260 (1953).

in the reaction vessel attained the temperature of the bath, a known quantity of it was transferred into a similar reaction vessel containing an accurately weighed amount of the triazole, and during transferring it was fitted into the central neck of another constant temperature bath set up just beside the one for the solvent. The loss of heat and time lag in attaining constant temperature were found to be a minimum with such a procedure. The reaction mixture was stirred immediately and some samples of the reaction mixture withdrawn by means of pre-heated pipets at various intervals of time into previously tared weighing bottles and chilled in an ice-water-bath. The amount of acid isomer in each case was estimated in non-aqueous media.<sup>9</sup> Correction was applied to the titers for the original acidity of the ethylene glycol.

The following  $R_1$  substituents in structures III and IV were selected for study: *p*-nitrophenyl, *m*-chlorophenyl, phenyl, *p*-tolyl, *p*-anisyl and benzyl. The concentrations of the substituted amino-1,2,3-triazoles varied between  $1.3$  to  $2.5 \times 10^{-4}$  mole per gram of solution. The data for the first 10 to 20% of reaction were used in each case and the effect of the reverse reaction was neglected. Both forward and backward reactions were found to be of first order; representative data are plotted in Fig. 1. The specific reaction rate constants were calculated using the plots of logarithm of concentration of reactant remaining, in moles/g. of solution, versus time in minutes. Figure 2 shows typical Arrhenius plots of  $\log k$  vs.  $1/T$ . The energies of activation were calculated from these Arrhenius plots of  $\log k$  vs.  $1/T$ . The results are summarized in Table I.

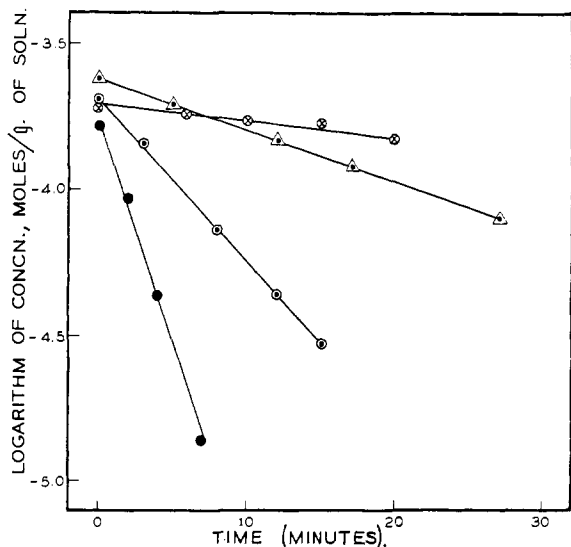


Fig. 1.—Rates of isomerization of substituted 5-amino-1,2,3-triazoles at 423°K.:  $\otimes$ , 5-(*p*-tolyl)-amino-4-phenyl-1,2,3-triazole;  $\Delta$ , 1-phenyl-4-phenyl-5-amino-1,2,3-triazole;  $\odot$ , 1-(*m*-chlorophenyl)-4-phenyl-5-amino-1,2,3-triazole;  $\bullet$ , 1-(*p*-nitrophenyl)-4-phenyl-5-amino-1,2,3-triazole.

**Determination of Equilibrium Constants.**—These constants were determined in the same apparatus used for the isomerization studies. Weighed samples of the substituted aminotriazoles were allowed to equilibrate in ethylene glycol at various temperatures. When the equilibrium was reached, the solution was chilled rapidly and estimated<sup>9</sup> for acid isomer. The equilibrium constant was the ratio of 5-(substituted phenyl)-aminotriazole to 1-(substituted phenyl)-5-aminotriazole. Figure 3 presents these data graphically. The heats of reaction were calculated from the plots of the logarithms of the equilibrium constant versus the reciprocals of absolute temperature. These results are summarized in Table II.

### Discussion

The isomerization of substituted 5-amino-1,2,3-triazoles follows the first-order rate law since a

(9) E. Lieber, C. N. R. Rao and T. S. Chao, *Anal. Chem.*, **29**, 932 (1957).

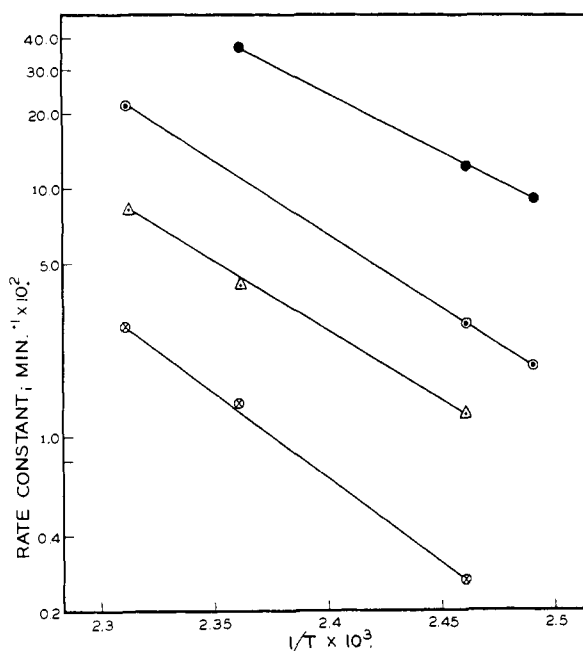


Fig. 2.—Effect of temperature on the rates of isomerization:  $\otimes$ , 5-(*p*-tolyl)-amino-4-phenyl-1,2,3-triazole;  $\Delta$ , 1-phenyl-4-phenyl-5-amino-1,2,3-triazole;  $\odot$ , 1-(*m*-chlorophenyl)-4-phenyl-5-amino-1,2,3-triazole;  $\bullet$ , 1-(*p*-nitrophenyl)-4-phenyl-5-amino-1,2,3-triazole.

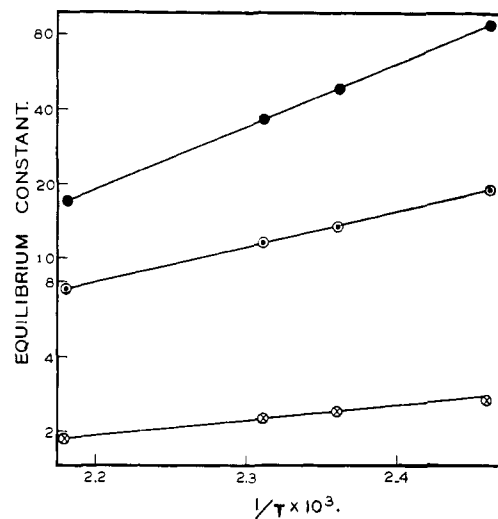


Fig. 3.—Effect of temperature on the equilibrium constants of the isomerization reaction in ethylene glycol:  $\bullet$ , 4-nitrophenyl;  $\odot$ , 3-chlorophenyl;  $\otimes$ , 4-tolyl.

straight line relationship is obtained in a plot of  $\log c$  against time for the examples studied (Fig. 1). Figures 4 and 5 show the correlations between Hammett's  $\sigma$ -values for groups and the logarithms of the rates of isomerization and the logarithms of the equilibrium constant for the aryl amino-1,2,3-triazoles.

Brown, Hammick and Heritage<sup>10</sup> made a fairly complete study of the acid-catalyzed (in ethanol as solvent) rates of isomerization of  $V \rightleftharpoons VI$ , in which  $R_2$  was maintained constant as the carboxy

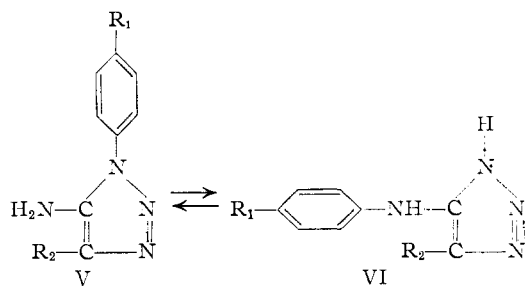
(10) B. R. Brown, D. L. Hammick and S. G. Heritage, *J. Chem. Soc.*, 3820 (1953).

TABLE I  
RATES OF ISOMERIZATION OF SUBSTITUTED  $\delta$ -AMINOTRIAZOLES

R	Forward reaction				Reverse reaction			
	Temp., °K.	$k_1$ , min. <sup>-1</sup> × 10 <sup>2</sup>	Energy of activation, cal./mole	Entropy of activation, cal./degree	$k_2$ , min. <sup>-1</sup> × 10 <sup>2</sup>	Energy of activation, cal./mole	Entropy of activation, cal./degree	
C <sub>6</sub> H <sub>5</sub>	406	1.25		-13.9	0.26			
	423	4.19		-14.1				
	432	8.41	25,220	-14.0				
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	406	0.71		-8.0	0.26		+0.3	
	423	3.25		-7.8		1.38	+ .4	
	432	6.21	28,070	-8.0		2.75	32,250	+ .3
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	406	0.52		-3.5	1.52			
	423	2.51		-3.4				
	432	4.8	30,150	-3.6			31,590 <sup>a</sup>	
3-ClC <sub>6</sub> H <sub>4</sub>	401	1.95		-12.4	0.92			
	406	2.88		-12.5				
	423	12.57		-12.1		1.84		+4.2
	432	21.49	25,130	-12.3			34,220	+3.0
4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	401	9.10		-18.4	0.65			
	406	12.30		-18.5				
	423	36.85	21,500	-18.5				
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	401				0.95		-8.4	
	406	0.04		+1.4			-8.5	
	423	.24		+1.5				
	432	.54	34,210	+1.4		7.79	27,640	-8.5

<sup>a</sup> Energy of activation calculated by taking values for  $k_2$  from  $k_1/K$ .

group (-CO<sub>2</sub>Et) and R<sub>1</sub> was varied over the range of electron-attracting to electron-repelling groups.<sup>11</sup> The present investigation differs from Brown, Hammick and Heritage<sup>10</sup> in two respects in that the



kinetics were obtained in ethylene glycol and in the absence of acid. In view of the fact that isomers of type V are weak bases, while those of VI are acids, the kinetics would undoubtedly be affected by the presence of the added strong acid. In addition

TABLE II  
EFFECT OF TEMPERATURE ON THE EQUILIBRIUM CONSTANTS

R	Temp., °K.	$K_{Eq.}^a$	$\Delta H_r$ , heat of reaction cal./mole
4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	458	16.8	
	432	36.5	
	423	48.0	
	406	88.3	-11,840

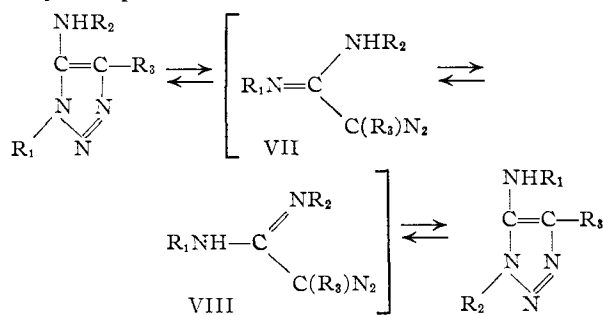
(11) R<sub>1</sub> = Me, NO<sub>2</sub>, Br, OMe, CO<sub>2</sub>Et. For R<sub>1</sub> = NO<sub>2</sub> only the acidic isomer II was studied, it being reported<sup>10</sup> that the rate of isomerization of the neutral isomer was too fast to measure.

3-ClC <sub>6</sub> H <sub>4</sub>	458	7.4		
	432	11.5(11.7) <sup>c</sup>		
	423	13.7(13.6) <sup>c</sup>		
	406	19.1		-6,699
C <sub>6</sub> H <sub>5</sub>	458	2.9		
	432	3.7		
	423	3.8		
	406	4.8(4.8) <sup>c</sup>		
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	458	1.85		
	432	2.25(2.26) <sup>c</sup>		
	423	2.40(2.36) <sup>c</sup>		
	406	2.70(2.7) <sup>c</sup>		-2,834
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	458	1.44		
	432	1.50		
	423	1.65(1.65) <sup>c</sup>		
	406	1.81		-1,638
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	458	0.076		
	432	.069(0.069) <sup>c</sup>		
	423	.065		
	406	.042(0.042) <sup>c</sup>		+2,210
4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> <sup>b</sup>	458	.58		
	423	.48		+2,200

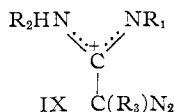
<sup>a</sup>  $K_{Eq.} = k_1/k_2 = [IV]/[III]$ . <sup>b</sup> The equilibrium constants for this were obtained by extrapolating the graph of  $\sigma$  vs.  $\log K$  to the  $\sigma$ -value of -0.66. <sup>c</sup> These values of the equilibrium constant are values obtained from experimental  $k_1/k_2$ .

Brown, Hammick and Heritage<sup>10</sup> do not measure  $k_1$  and  $k_2$  separately but compute them from  $(k_1 + k_2)$  and  $K_{Eq}$  values. In general, the results of Brown, Hammick and Heritage<sup>10</sup> and the present investigation are not contradictory in any way.

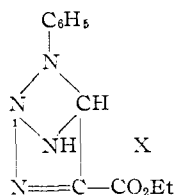
Dimroth and Michaelis<sup>12</sup> suggested an intuitive mechanism to account for the isomerization which may be represented as



Brown, Hammick and Heritage<sup>10</sup> extended this concept by the suggestion that the protonated open-chain guanyl diazo compound, IX, representing the



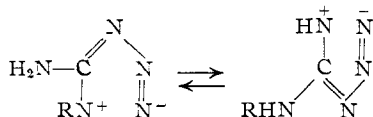
single canonical form of protonated VII and VIII, could account for a series of protonations and deprotonation intermediates lying between V and VI, the main feature of their theory being the open chain aliphatic diazo compounds VII or VIII. This is somewhat similar to the theory suggested by Henry, Finnegan and Lieber<sup>13</sup> for the substituted 5-aminotetrazole system. Brown, Hammick and Heritage<sup>10</sup> point out that while their theory could account for the kinetics of the forward reaction, the effect of substituents on the rate of the reverse reaction was not so easily inferred. It is interesting to note at this point that the structure of V ( $R_1 = H$ ;  $R_2 = CO_2Et$ ) was disputed by Dutt<sup>14</sup> who considered it to have the bicyclic structure X.



Attempts to answer this on chemical grounds were made by Dimroth and Michaelis.<sup>12</sup> While it can be stated that the chemical arguments on either side were not entirely convincing, the hypothesis of a bicyclic intermediate can be dismissed on the basis of its inability to account for the influence of substituents both on the position of equilibrium and the kinetics of the process. Further, the high degree of ring strain required by this type of intermediate would make its formation unlikely. Gar-

(12) O. Dimroth and W. Michaelis, *Ann.*, **459**, 44 (1927).

(13) R. A. Henry, W. G. Finnegan and E. Lieber<sup>8</sup> suggested an activated guanyl azide to account for the position of equilibrium en-



countered in the thermal isomerization of substituted 5-aminotetrazoles. This theory is unable to account for the observed kinetics.

(14) P. K. Dutt, *J. Chem. Soc.*, 265 (1923); 2476 (1924).

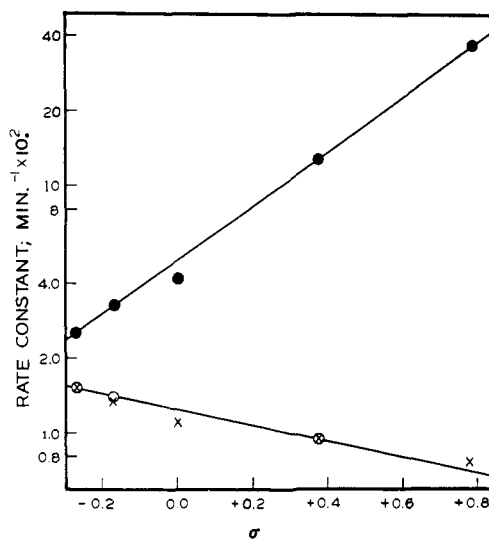


Fig. 4.—Correlation between the rates of isomerization at 423°K. with Hammett's  $\sigma$ -value for groups: ●, forward reaction ( $k_1$ ) of 1-substituted phenyl-4-phenyl-5-amino-1,2,3-triazoles. The rates are experimentally determined. ○, Reverse reaction ( $k_2$ ) of 5-(substituted phenyl)-amino-4-phenyl-1,2,3-triazoles. The rates are experimentally determined. ×, ( $k_2$ ) calculated from the experimentally determined equilibrium constants and  $k_1$ ;  $k_2 = k_1/K$ . The isomerizations were carried out in purified ethylene glycol as solvent.

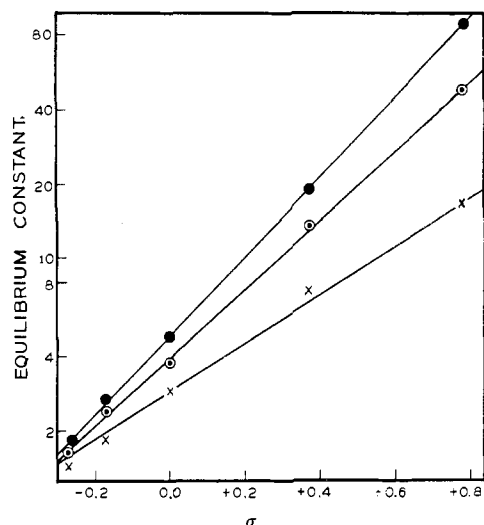
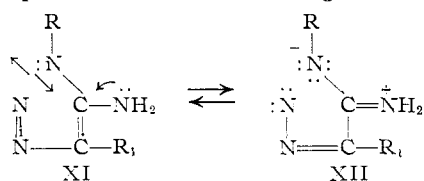


Fig. 5.—Correlation between equilibrium constants and Hammett's  $\sigma$ -values for groups for the isomerizations in purified ethylene glycol as solvent: ●, at 406°K.; ○, at 423°K.; ×, at 458°K.

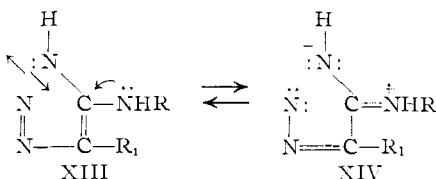
brecht and Herbst<sup>8</sup> have suggested a similar bicyclic intermediate to account for the isomerization of substituted aminotetrazoles which is open to the same objections.<sup>6</sup>

Figure 4 shows that experimentally the rate of the forward reaction increases with increasing electronegativity of a 1-substituent and that the rate of the reverse reaction decreases with increasing electronegativity of the substituent on the 5-amino group. Consequently, the heterolysis of the nitrogen-nitrogen bond in the ring (XI) must occur so as to

leave a negative charge on the substituted methyl diazo intermediate, XII, on the nitrogen originally in the 1-position of the triazole ring



a similar scheme applying to the isomeric partner, XIII



It will be apparent at once that numerous tautomeric (the proton shift could occur equally as well with ring opening or ring closure) and resonance structures for XII and XIV can be written including those with the substituted diazo methyl group. This heterolytic cleavage of the 1-2 nitrogen-nitrogen bond will be dependent on the shift of electrons on the 5-amino group into the ring and hence dependent on the electrical character of the R substituent in XI and XIII. In accordance with this hypothesis, an electronegative character for R should facilitate the heterolysis for the forward reaction (XI  $\rightarrow$  XIII) and retard it for the reverse reaction (XIII  $\rightarrow$  XI), the converse holding for an electropositive character for R, the rates of the forward and reverse reaction being dependent on the relative electrical character of R. The oscillation of the formal charges on the nitrogen atoms in XII and XIV, again dependent on the electron-attracting or electron-donating character of R, determines the ratio of XI and XIII present at equilibrium.<sup>3</sup>

The experimental data reported in this investigation are in agreement with these assumptions. The mechanism here proposed is exactly similar to that postulated for the isomerization of substituted 5-aminotetrazoles.<sup>7a</sup> This mechanism affords a satisfactory explanation for the formation of tetrazole derivatives by the reaction of hydrazoic acid with nitriles,<sup>15,16</sup> with ketones,<sup>17,18</sup> with carbodiimide<sup>19</sup> and by the diazotization of aminoguanidine derivatives,<sup>5,7a,20</sup> as well as offering an explanation for their acidic degradation.<sup>5,18,20</sup>

The rate of isomerization of the 1-substituted-4-phenyl-5-amino-1,2,3-triazoles (XI, R = substituted phenyl; R<sub>1</sub> = C<sub>6</sub>H<sub>5</sub>) increases 260% in the series 4-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub> to 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, whereas the rate of the isomeric 5-(substituted)-amino-4-phenyl-1,2,3-triazoles (XIII, R = substituted phenyl; R<sub>1</sub> = C<sub>6</sub>H<sub>5</sub>) decreases only 30%. The explanation offered for the corresponding substituted

5-aminotetrazole system<sup>7a</sup> can be used in the present situation, the effect being explained by the position of the substituent with respect to the nitrogen-nitrogen bond which breaks. It is interesting to note the comparative rates of isomerization for the forward reaction in the tetrazole and triazole systems, the change in rate of isomerization for the tetrazole being 600% for approximately the same gamut of Hammett's  $\sigma$ -values for groups. The fact that the relative influence of the substituents on the triazole system is less compared to the tetrazole system may be explained as due to the lesser electronegativity of the triazole ring.<sup>21</sup>

The entropies of activation ( $\Delta S^\ddagger$ ), summarized in Table I, which were calculated from the Eyring equation<sup>22</sup>

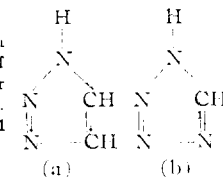
$$k = k_b T / h e^{-\Delta H^\ddagger / RT} e^{\Delta S^\ddagger / R}$$

are constant within experimental error for the isomerization of 1-substituted-5-amino-1,2,3-triazoles. If the activation of the molecule involves a rearrangement or a change in configuration, the entropy of activation can be considerable. In the case of a series of related compounds the influence of structure on the reaction rate is sometimes due to changes in the entropy of activation. If the spatial arrangements in the activated molecule are more probable than in the unactivated molecule,  $\Delta S^\ddagger$  will be positive, and negative, if less probable. The entropies of activation for the isomerization of the substituted 5-amino-1,2,3-triazoles are negative in most cases and slightly positive in a few cases. Negative entropies of activation have been observed in many such rearrangement or isomerization reactions.<sup>23,24</sup> The  $\Delta S^\ddagger$  values of the isomerization reaction are constant in each series and in agreement with previous observations<sup>25</sup> and necessarily follow from the correlation of the reaction rate constants and Hammett's  $\sigma$ -value for groups. The frequency factors calculated from the Arrhenius equation and summarized in Table III vary from 10<sup>13</sup> to 10<sup>15</sup> sec.<sup>-1</sup>. These entropies of ac-

TABLE III  
FREQUENCY FACTORS (IN SEC.<sup>-1</sup>) IN THE ARRHENIUS EQUATION

R	At temperatures in °K.		
	432°K.	423°K.	406°K.
4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	2.1 × 10 <sup>13</sup>	2.4 × 10 <sup>13</sup>	2.5 × 10 <sup>13</sup>
3-ClC <sub>6</sub> H <sub>4</sub>	5.5 × 10 <sup>13</sup>	6.3 × 10 <sup>13</sup>	4.7 × 10 <sup>13</sup>
C <sub>6</sub> H <sub>5</sub>	2.3 × 10 <sup>13</sup>	2.2 × 10 <sup>13</sup>	2.3 × 10 <sup>13</sup>
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	4.7 × 10 <sup>13</sup>	6 × 10 <sup>13</sup>	4.4 × 10 <sup>13</sup>
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	4.1 × 10 <sup>15</sup>	4.3 × 10 <sup>15</sup>	4.1 × 10 <sup>15</sup>

(21) For example, 1,2,3-triazole (a) is a weak base (Richter, "The Chemistry of Carbon Compounds," Vol. IV, Elsevier Publishing Co., New York, N. Y., 1947, p. 148); whereas tetrazole (b) is a weak acid of  $pK_a$  6.33.<sup>15</sup>



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tivation and the frequency factors are interpreted to mean that the isomerizations are not complicated by steric requirements or the necessity for oriented energetic collisions.

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[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

## The Nucleophilic Reactivity of Sodium Thiophenoxide with Aromatic Substrates<sup>1,2</sup>

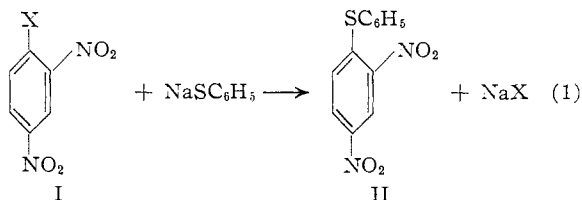
BY J. F. BUNNETT AND WILL D. MERRITT, JR.<sup>3</sup>

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Rates of reactions of sodium thiophenoxide with several 1-substituted-2,4-dinitrobenzenes have been measured. Four substituents, the nitro, phenylsulfonyl, phenylsulfinyl and pyridinio groups, were displaced too fast to measure by the technique used. Fluorine was displaced much faster than the other halogens, while chlorine, bromine, iodine and the *p*-nitrophenoxy group were all displaced at nearly the same rate. This sameness of rate shows the absence of an "element effect," and indicates that in the transition states of these displacements there is little or no breaking of the bond to the group being displaced. Thiophenoxide: methoxide rate ratios have been found to vary in a systematic fashion: the relative effectiveness of thiophenoxide increases with increasing polarizability of the halogen being displaced and with increasing activation by nitro groups.

In recent years the thiophenoxide ion has been recognized to be a very strong nucleophilic reagent in reactions with several aliphatic<sup>4</sup> and aromatic<sup>5</sup> substrates. For example, sodium thiophenoxide reacts (S<sub>N</sub>2 + S<sub>N</sub>2') with 3,3-dichloropropene-1 240 times faster than does sodium ethoxide.<sup>4c</sup> It was therefore something of a surprise when Bevan and Hirst<sup>6</sup> reported that thiophenoxide is no more reactive than methoxide ion toward the substrate *p*-fluoronitrobenzene. This discovery suggested that interesting relationships might be revealed by measuring the rates of reactions of sodium thiophenoxide with a group of appropriately chosen aromatic substrates. We now report a series of such measurements, and interesting relationships have indeed been found.

We have measured the rates of reactions (1) of sodium thiophenoxide with several 1-substituted-



2,4-dinitrobenzenes in methanol solution. These are fast reactions, and only at low concentrations were they slow enough for kinetic observation. Photometric analysis, depending on the color of the product, 2,4-dinitrodiphenyl sulfide (II), was used;

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(2) This paper is based on the Ph.D. thesis of Will D. Merritt, Jr., April, 1957.

(3) R. J. Reynolds Fellow, 1955-1956.

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this technique is especially satisfactory for reactions run at low concentrations.

Some preliminary observations on the rates of reactions of thiophenoxide with 1-substituted-4-nitrobenzenes also were made.

### Experimental

**Materials.**—*p*-Fluoronitrobenzene, *p*-chloronitrobenzene, *p*-bromonitrobenzene, *p*-iodonitrobenzene, 2,4-dinitrofluorobenzene, 2,4-dinitrochlorobenzene, 2,4-dinitrobromobenzene, 2,4-dinitrodiphenyl sulfone and thiophenol were prepared by standard methods or were commercial products re-purified. 1,2,4-Trinitrobenzene, 2,4,4'-trinitrodiphenyl ether, 2,4-dinitroiodobenzene and 2,4-dinitrodiphenyl sulfide were available from another investigation.<sup>7</sup> Reagent grade methanol was dried by the method of Hartley and Raikes.<sup>8</sup> Standard sodium thiophenoxide solutions were prepared from a weighed amount of thiophenol and an equivalent amount of a standard solution of methanolic sodium methoxide diluted to volume with methanol in a volumetric flask. The solutions were not kept more than eight hours, a new solution being prepared for each set of kinetics runs.

**Rate Measurements.**—A weighed portion of the substrate (in one series an aliquot of a standard solution) was placed in a flask in the thermostat and 100 cc. of methanol at thermostat temperature was added. After the substrate had dissolved, an exactly equivalent amount of a standard sodium thiophenoxide solution in methanol, at thermostat temperature, was added with swirling by means of a fast-delivery 9.88-cc. pipet. An accurate zero time was not necessary. Samples (8 or 9 per run) were taken with a fast-delivery pipet, precooled to thermostat temperature, and were discharged into a standard volume of dilute methanolic sulfuric or hydrochloric acid, the time of release being recorded. Thermostats were constant to  $\pm 0.03^\circ$  and their temperatures were determined with a thermometer certified by the National Bureau of Standards.

Upon completion of a run, the optical densities of the quenched samples were determined in a Beckman model B spectrophotometer at wave lengths in the vicinity of 410 m $\mu$ , the exact wave length for any run being chosen with regard to the absorption characteristics of the original substrates and the concentration of 2,4-dinitrodiphenyl sulfide in the quenched solutions. In the case of runs with 2,4-dinitroiodobenzene, it was necessary to add a few drops of aqueous sodium thiosulfate solution just prior to photometric measurements; otherwise, falsely high optical densities were read, no doubt owing to the presence of traces of iodine generated by air oxidation of iodide ion in acidic medium.

That the reactions had occurred quantitatively as repre-

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