room temperature overnight, the ethanol was concentrated *in vacuo* and the residue recrystallized from ethanol, m.p. 175-178°.

Anal. Caled. for C<sub>11</sub>H<sub>17</sub>ClN<sub>2</sub>: C, 62.12; H, 8.00; N, 13.13. Found: C, 61.57; H, 8.08; N, 13.23.

That the reaction of a 1,1-dialkylhydrazine with an alkyl halide gives the quaternary compound rather than a 1,1,2trialkylhydrazine has been amply demonstrated before. For a review of hydrazonium compounds see Sisler, *et al.*<sup>17</sup>

1,2,3,4-Tetrahydro-1-naphthylhydrazine.—A mixture of 10 g. of 3,4-dihydro-1(2H)-naphthalenone and 10 g. of hydrazine hydrochloride in 100 ml. of ethanol was hydrogenated over Raney nickel and worked up as described for IXa. However, the *p*-toluenesulfonic acid salt of the hydrazine was prepared. It was recrystallized from ethanolethyl acetate, m.p. 154–156° dec.

*Anal.* Calcd. for C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>·C<sub>7</sub>H<sub>5</sub>O<sub>3</sub>S: C, 61.06; H, 6.63; N, 8.38. Found: C, 60.72; H, 6.70; N, 8.83.

1,1-Dimethyl-1-(1-phenylethyl)hydrazonium Bromide.—A solution of 3.3 g. of 1-phenylethyl bromide and 6 ml. of dimethylhydrazine in 15 ml. of ethanol was allowed to stand overnight at room temperature. The alcohol was evapo-

(17) H. H. Sisler, G. M. Omietanski, and B. Rudner, Chem. Rev., 57, 1021 (1957).

rated in vacuo and the residue recrystallized from ethanolether, m.p. 140-143°.

Anal. Caled. for C<sub>10</sub>H<sub>17</sub>BrN<sub>2</sub>: C, 48.98; H, 6.94; N, 11.43. Found: C, 49.37; H, 7.00; N, 11.29.

Comparative Study of the Stability of Benzylhydrazines.— An approximate measure of the ease of fragmentation of these compounds into the hydrazine and the olefin was obtained as follows: To 1 ml. of an aqueous solution of IXa (10 min.), X (0.5 min.), 1,2,3,4-tetrahydro-1-aphthylhydrazine (10 min)., 1,1-dimethyl-1-(1-phenylethyl)hydrazonium bromide (20 min.), 1-indaneamine (stable), and IIId (stable) was added 1 ml. of concentrated hydrochloric acid. The times were noted when separation of the insoluble hydrocarbons became readily noticeable. These are included in parentheses after the appropriate compound. The characteristic odor of indene was noted after acid treatment of IXa and X, of 1,2-dihydronaphthalene from 1,2,3,4tetrahydro-1-naphthylhydrazine and of styrene from 1,1dimethyl-1-(1-phenylethyl)hydrazonium bromide.

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# Structural Effects and Reactivity in Guanylhydrazone Formation: Temperature Coefficients of Rate of Formation of Several Guanylhydrazones

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Rates of reaction of seven carbonyl compounds, of a variety of structural types, with aminoguanidine,  $NH_2NHC(NH)NH_2$ , have been determined at 25° and 50° in aqueous phosphate buffer of pH 7, using an iodometric method of analysis. Guanylhydrazone formation for all the compounds investigated is a second order reaction and reversible, except for furfural, under the experimental conditions of the investigation. Relative thermodynamic activation quantities were calculated from experimentally determined temperature coefficients of rate. A previously proposed correlation between the presumed rigidities of carbonyl compounds and corresponding entropies of activation was not observed. This agrees essentially with previous data for oxime formation and thiosemicarbazone formation but diverges from results established for semicarbazone formation and at least six other reaction systems. However, an excellent linear free energy relationship exists between the logarithms of specific rates of guanylhydrazone formation and the logarithms of specific rates of semicarbazone formation. This linear relationship strongly suggests the fundamental similarity of the two reaction systems.

In 1941 Price and Hammett<sup>2</sup> measured the temperature coefficients of rate of semicarbazone formation and found a parallelism between a presumed order of molecular rigidity, derived from logical structural considerations, and entropies of activation, which is demonstrated by the data in columns one and two of Table I. They suggest that the observed parallelism was general in nature and would apply with high probability to other carbonyl reaction systems. The parallelism found subsequent confirmation in the aldol condensation,<sup>3</sup> the acid-catalyzed hydration of olefins,<sup>4</sup> the heterogenously catalyzed hydrolysis of esters,<sup>5</sup> the reaction of methyl iodide with certain amines in nitrobenzene<sup>6,7</sup> and in thiosemicarbazone formation of several alkyl butyrophenones.<sup>8</sup> Fitzpatrick and Gettler<sup>9</sup> and Fiarman and Gettler<sup>10</sup> studied oxime formation and thiosemicarbazone formation, respectively, in an attempt to secure additional support for the Hammett parallelism and to determine its validity

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<sup>(2)</sup> F. P. Price, Jr., and L. P. Hammett, J. Am. Chem. Soc., 63, 2387 (1941).

<sup>(3)</sup> J. D. Gettler and L. P. Hammett, ibid., 65, 1824 (1943).

 <sup>(4) (</sup>a) R. W. Taft, Jr., J. B. Levy, D. Aaron, and L. P. Hammett, *ibid.*, **74**, 4735 (1952); **75**, 3955 (1953); (b) E. L. Parlee, R. W. Taft, Jr., and C. A. Defazio, *ibid.*, **77**, 837 (1955).

<sup>(5) (</sup>a) V. C. Haskell and L. P. Hammett, *ibid.*, **71**, 1284 (1949);
(b) S. A. Bernhard and L. P. Hammett, *ibid.*, **75**, 1798 (1953). (c)
S. A. Bernhard, E. Garfield, and L. P. Hammett, *ibid.*, **76**, 991 (1954).
(d) P. Riesz and L. P. Hammett, *ibid.*, **76**, 992 (1954). (e) M. Samelson and L. P. Hammett, *ibid.*, **78**, 524 (1956).

<sup>(6)</sup> H. C. Brown and A. Cahn, ibid., 77, 1717 (1955).

<sup>(7)</sup> H. C. Brown and N. R. Eldred, ibid., 71, 445 (1949).

<sup>(8)</sup> J. L. Maxwell, M. Joanne Brownlee, and Paretta P. Holden, *ibid.*, **83**, 589 (1961).

<sup>(9)</sup> F. W. Fitzpatrick and J. D. Gettler, ibid., 78, 530 (1956).

<sup>(10)</sup> I. S. Fiarman and J. D. Gettler, ibid., 84, 961 (1962).

# BROOKS AND GETTLER

## TABLE I

Relative Entropies of	ACTIVATION FOR SI	EMICARBAZ	zone Foi	rmation, <sup>2</sup> O3	KIME FORMATION, <sup>9</sup>	THIOSEMICARBAZONE
	FORMATION, 10 ANI	GUANYL	HYDRAZO	NE FORMATI	on at pH 7.0	
		1.04		1 (0.0		

$(\Delta S^* - \Delta S_0^*), \text{ cal.}/{}^\circ C.$				
	Semicarbazone formation 12.5°	Oxime formation 12.5°	Thiosemicarbazone formation 37.5°	Guanylhydrazone formation 37.5°
Cyclopentanone	3.30	0.20	4.20	16.50
Furfural	3.20	15.00	8.80	13.00
Cyclohexanone	0.40	-5.30	2.70	16.80
Acetophenone	-1.90	3.00		
Acetone	(0.00)	(0.00)	(0.00)	(0.00)
Methyl ethyl ketone		4.50	6.40	1.40
Diethyl ketone	-6.50	-4.50	4.80	4.00
Di-n-propyl ketone		-15.10		
Methyl isopropyl ketone		6.30		
Methyl isobutyl ketone		7.10		
Pinacolone	-9.70	7.10	-0.40	0.90

TABLE II

SAMPLE DATA: METHYL ETHYL KETONE GUANYLHYDRAZONE FORMATION

(Medium: 0.0571 M Na<sub>2</sub>HPO<sub>4</sub>, 0.0286 M NaH<sub>2</sub>PO<sub>4</sub>; temperature 25.00°; initial concn., methyl ethyl ketone 0.01331 M; aminoguanidine 0.007661 M; time in seconds; k, in l./mole-sec.)

		1 $x + x_e + c + K$	
Time	[Reagent]	$\frac{1}{2x_e+c+K}$ If $\frac{1}{x-x_e}$	$k   imes  10^8$
0	0.007661	$79.81^{a}$	
982	0.007514	81.36	1.57
1868	0.007410	82.46	1.42
3350	0.007259	84.17	1.30
5622	0.007040	86.61	1.25
7038	0.006984	88.88	1.29
9023	0.006719	91.22	1.26
10483	0.006533	94.13	1.37
12312	0.006405	96.28	1.34
14109	0.006294	98.27	1.31
			Av. $1.35 \pm 0.07$

<sup>a</sup> For the significance of the heading of this column see ref. 2, page 2389.

range. Derived relative entropies of activation for these two latter reactions are listed in Table I, columns 3 and 4. An examination of these data reveals little or no internal parallelism between molecular rigidities and relative activation entropies for either oxime formation or thiosemicarbazone formation, and certainly no great amount of discernable concordance among the entropy of activation values for any particular carbonyl compound across the three reaction systems.

To obtain additional information respecting this divergence, temperature coefficients of reaction for guanylhydrazone formation were measured. The stoichiometry of guanylhydrazone formation is represented by the equation

$$C = 0 + NH_2 NHC(NH)NH_2 \implies C = N - NHC(NH)NH_2 + H_2 O$$

## Experimental

Materials.—Aminoguanidine hydrochloride which is commercially unavailable was prepared by dissolving aminoguanidine bicarbonate (Eastman Kodak Co.) in a 10% molar excess of concentrated hydrochloric acid and evaporating the resulting solution to dryness on a steam bath. The resultant solid residue was recrystallized twice from 50% ethyl alcohol, and the purified crystals were dried in vacuo and stored in a vacuum desiccator over sodium hydroxide and calcium chloride. Two such crystallizations sufficed to yield white crystals with a constant melting range of  $161-163^\circ$  and possessing an acidimetric titer within 2 parts per 1000 of its iodometric titer. The above conditions of preparation and storage made for a product which was stable for at least eight months.

Carbonyl compounds were distilled in all-glass apparatus before use. Eastman Kodak Company products: Acetone was redistilled; b.p., 56.0°. Diethyl ketone was redistilled; b.p. 101.5°. Methyl ethyl ketone was redistilled; b.p., 79-80°. Cyclohexanone was redistilled; b.p., 154-155°. Furfural was first redistilled at atmospheric pressure, then further purified by vacuum distillation; b.p., 60-61° at 15 mm., stored under nitrogen at -15°, and used the following day. Matheson, Coleman and Bell, Inc. products: Cyclopentanone was redistilled; b.p., 131°. Pinacolone was redistilled; b.p., 105-106°.

Baker and Adamson sodium phosphates were used to prepare buffer solution.

**Preparation of Solutions.**—Buffer solutions were prepared and their pH values confirmed, and aminoguanidine solutions and solutions of carbonyl compounds were prepared as previously described.<sup>2</sup>

Apparatus.—Thermostats were of conventional design. Constant temperatures of  $25.00 \pm 0.001^{\circ}$  and  $50.00 \pm 0.02^{\circ}$  were maintained without difficulty.

The timing of the kinetic experiments was done with a precision, aeronautical, split-second chronometer manufactured by the Waltham Precision Instrument Company, Waltham, Mass.

#### TABLE III

RATE CONSTANTS FOR GUANYLHYDRAZONE FORMATION (Medium: 0.0571 M Na<sub>2</sub>HPO<sub>4</sub>, 0.0286 M NaH<sub>2</sub>PO<sub>4</sub>;  $k \times 10^3$ , in 1 / mole-sec.)

			/	
Compound	Town	[Com-	(Bearont)	k × 108
Actono	25 AA	0.007025	0 008608	2 20
Acetone	20.00	0.007925	0.007758	3.52
		0.007201	0.007758	2.97
		0.007201	0.001100	Av. 2 15
				Av. 5.15
	50.00	0.007729	0.009292	3.47
		0.007729	0.007941	3.47
		0.007392	0.007941	3.45
				Av. 3.46
Diethyl ketone	25 00	0.01933	0.008823	0 393
201001191 12000110	-0.00	0.01933	0.007323	0.340
		0.01804	0.007323	0.324
				Av 0 352
				1100 0.002
	50.00	0.01869	0.008937	0.528
		0.01869	0.007506	0.528
•		0.01814	0.007506	0.553
				Av. 0.536
Dimensions	95 00	0.05026	0.000067	0 0959
Pinacoione	20.00	0.05920	0.009007	0.0202
		0.05920	0.000438	0.0208
		0.00800	0.009408	0.0201
				Av. 0.0220
	50.00	0.05949	0.008741	0.0326
		0.05949	0.009528	0.0372
		0.05291	0.009528	0.0405
				Av. 0.0368
<b>A 1</b>	a= 00	0.00000	0.000044	
Cyclopentanone	25.00	0.02296	0.008944	0.542
		0.02296	0.007555	0.510
		0.02082	0.007555	0.558
				Av. 0.537
	50.00	0.02246	0.008965	1.31
		0.02246	0.007781	1.27
		0.02069	0.007781	1.27
				Av. 1.28
Cyclohexanone	25.00	0.008304	0.009009	15.2
		0.008304	0.007487	16.0
		0.007290	0.007487	15.4
			1	Av. 15.6
	50 00	0 009112	0.009108	32.6
	00.00	0.009112	0.007468	26.8
		0.007082	0.007468	27.9
				Av 20 1
			1	14. 20.1
Furfural	25.00	0.02483	0.009106	0.706
		0.02483	0.007546	0.656
		0.02349	0.008981	0.653
				Av. 0.671
	50.00	0 02385	0.008047	1 49
	00.00	0.02385	0.003547	1.42
		0.02330 0.02432	0.007506	1.40
		0.02102	0.001000	Av 1 38
				ATA0 1.00
Methyl ethyl	25.00	0.01311	0.008885	1.38
ketone		0.01311	0.007660	1.33
		0.01164	0.007661	1.29
				Av. 1.34
	50 00	0.01251	0 008709	1 74
	50.00	0.01251	0.007857	1 46
		0.01125	0.007857	1.79
		20		Av. 1.66

Calibrated thermometers used in the thermostats were graduated in such a manner that temperature changes of  $\pm 0.001^{\circ}$  were readily discernable.

Volumetric equipment and weights met customary standards for precision work.

The reaction flasks were 250-ml. Pyrex flasks fitted with 50-ml. side bulbs, standard taper ground glass joints and ground glass stoppers.

Analytical Method.—The iodometric method used so effectly by previous investigators<sup>2,9,11</sup> proved to be accurate for the quantitative determination of aminoguanidine.

Kinetic Procedure.—The kinetic procedure was essentially that described previously.<sup>2,9</sup>

#### Results

The specific rate data presented in Tables II and III were calculated from an equation previously derived by Conant and Bartlett<sup>11</sup> for semicarbazone formation and subsequently employed by other investigators.<sup>2,10</sup> The value of k for any single kinetic experiment was determined by the application of least squares methods to values of an appropriate concentration function and values of time.

Table II lists detailed data for the kinetics of methyl ethyl ketone guanylhydrazone formation, while Table III contains a summary of all rate data for guanylhydrazone formation obtained during the course of the present research. Equilibrium and rate constants for the hydrolysis of several guanylhydrazones are listed in Table IV.

	Table	> IV				
Equilibrium Constants, $K$ , and Rate Constants, $k_h$ , for Hydrolysis of Several Guanylhydrazones <sup>a</sup>						
Compound	Temp.	K	$kh \times 10^{5}$ sec. <sup>-1</sup>			
Acetone	50.00	0.01353	4.67			
	25.00	0.007493	2.36			
Diethyl ketone	50.00	0.1213	6.50			
	25.00	0.07948	2.80			
$\operatorname{Cyclopentanone}$	50.00	0.009573	1.23			
	25.00	0.003666	0.197			
Cyclohexanone	50.00	0.01616	47.0			
	25.00	0.00541	8.44			
Methyl ethyl ketone	50.00	0.03425	5.69			
	25.00	0.01520	2.04			
Pinacolone	50.00	0.09615	0.354			
	25.00	0.06283	0.138			

<sup>a</sup> Same reaction medium as in Table III.

For all compounds investigated, the validity of the rate equation and the accuracy of the results were so satisfactory that least squares analysis showed no trend in the values of the specific rate constants for the entire duration of any one kinetic experiment. Most experiments involved the plotting of a minimum of ten experimental points. The deviation of the mean of the rate constants was taken as the precision of the average since reproducibility was considered a better measure of the accuracy of the rate constant than the probable error in the least squares slope of any individual measurement. This error ranged from 1 to 2%.

(11) J. B. Conant and P. D. Bartlett, J. Am. Chem. Soc., 54, 2881 (1932).

Since the problem under consideration is one involving the effect of structural change upon reactivity,<sup>2</sup> the pertinent thermodynamic quantities are not the absolute values of the free energy,  $\Delta G^*$ , entropy,  $\Delta S^*$ , and heat,  $\Delta H^*$  of activation for a single reaction, but rather the values of these quantities relative to that of a standard reactant, for which acetone has been selected. Such relative quantities were calculated from equations previously reported<sup>2</sup> and the results are presented in Table V.

### TABLE V

Relative Entropies, Heats and Free Energies of Activation for Guanylhydrazone Formation at  $37.5^\circ$ 

$\sim \Delta H_0^* = 800 \text{ cal}$			
( <i>\(\Delta\)S*</i>	$(\Delta H^* -$	(Δ <b>G*</b> —	
$\Delta S_0^*$ ),	ΔH0*),	$\Delta G_0^*$ ),	
cal./°C.	cal.	cal.	
0.00	0.00	0.00	
4.00	2500	1200	
0.90	3200	2900	
16.50	5900	800	
16.80	4100	-1200	
13.00	4800	700	
1.40	900	500	
	$(\Delta S^* - \Delta S_0^*),$ cal./°C. 0.00 4.00 0.90 16.50 16.80 13.00 1.40	$\begin{array}{c c} \Delta H_0^* = 800 \text{ cal.} \\ (\Delta S^* - (\Delta H^* - \Delta S_0^*), & \Delta H_0^*), \\ \text{cal./°C.} & \text{cal.} \\ 0.00 & 0.00 \\ 4.00 & 2500 \\ 0.90 & 3200 \\ 16.50 & 5900 \\ 16.80 & 4100 \\ 13.00 & 4800 \\ \hline 1.40 & 900 \end{array}$	

## Discussion

The use of an accurate analytical method, the careful experimental design, the care applied in obtaining kinetic data and the failure to fit such data to any kinetic equation, save that of a reversible second order type, all lead to the inescapable conclusion that guanylhydrazone formation for all compounds studied in unequivocally second order and, save for furfural, reversible, under the experimental conditions employed. It was further observed that for the carbonyl compounds investigated, there was an absence of any appreciable variation in specific rate with change in the initial reactant concentrations or with time for any one particular kinetic experiment. This suggests the essential soundness of the analytical technique and the absence of any environmental factors of appreciable magnitude.

Factors of both similarity and dissimilarity are evident among semicarbazone formation,<sup>2</sup> oxime formation,<sup>9</sup> thiosemicarbazone formation,<sup>10</sup> and guanylhydrazone formation. As one case in point, all these four reaction systems are kinetically second order. Secondly, all compounds investigated in semicarbazone formation exhibit reversible characteristics. However, furfural and acetophenone possess equilibria so far toward completion that there was no evidence of a trend in the rate constants during the course of the reaction. Oxime formation is irreversible in all cases, while in thiosemicarbazone formation and guanylhydrazone formation, furfural is the only compound which exhibits an appreciable degree of irreversibility.

An examination of rate data for semicarbazone

formation,<sup>2</sup> oxime formation,<sup>9</sup> thiosemicarbazone formation,<sup>10</sup> and guanylhydrazone formation indicates that for carbonyl compounds, where comparable data exist, rates of oxime formation relative to semicarbazone formation are appreciably greater than unity, while the averages of correspondingly derived relative rates for thiosemicarbazone formation and guanylhydrazone formation are 0.101 and 0.0366, respectively.

Moreover, it is evident from an examination of pertinent data<sup>29,10</sup> that temperature coefficients of rate of the four reaction systems decrease in the sequence oximation > semicarbazone formation >thiosemicarbazone formation > guanylhydrazone formation for the compounds acetone, diethyl ketone, and pinacolone. For the compounds cyclopentanone, cyclohexanone, furfural, and methyl ethyl ketone an inversion is noted and the decreasing sequence is guanylhydrazone formation > oximation > semicarbazone formation > thiosemicarbazone formation. Available data reveal that the decreasing rate sequence cyclohexanone >acetone > methyl ethyl ketone > cyclopentanone >furfural > diethyl ketone > pinacolone > acetophenone holds, generally, for semicarbazone formation, oxime formation, thiosemicarbazone formation and guanylhydrazone formation. The only outstanding exception occurs in oxime formation where the partially anomalous sequence diethyl ketone > cyclopentenone > furfural is observed. Any one carbonyl compound shows, without exception the rate sequence oxime formation >semicarbazone formation > thiosemicarbazone formation > guanylhydrazone formation. These factors indicate that failure to observe a parallelism between molecular rigidity and entropy of activation is neither a function of any particular rate magnitude nor of any particular temperature coefficient of rate magnitude.

The cardinal objective of the present research was to probe further the validity of the Hammett parallelism<sup>2</sup> which has been challenged by data on oxime formation<sup>9</sup> and thiosemicarbazone formation.<sup>10</sup> In Table I are reproduced values of relative activation entropies for the four pertinent reaction systems. An examination of the four sets of relative entropies shows striking differences. In the case of semicarbazone formation, there is, with the exception of acetophenone, a parallelism between presumed molecular rigidities and corresponding relative entropies of activation. Oxime formation fails to yield the parallelism which is so evident for semicarbazone formation. In the former reaction dialkyl ketones exhibit both positive and negative relative entropy values, while only negative entropy values are theoretically admissible and only negative values are found in semicarbazone formation for dialkyl ketones. No such parallelism is evident for thiosemicarbazone formation, although there are

several points of similarity between this reaction system and semicarbazone formation. The compounds cyclopentanone, furfural, cyclohexanone, and pinacolone occupy approximately comparable positions in the two series. The numerical values of the relative activation entropies for these four compounds differ in each reaction series, but this is somewhat inconsequential since there is no apparent theoretical reason to expect identity of magnitudes for compounds in different reaction series. In semicarbazone formation the entropy values of cyclopentanone, furfural, and cyclohexanone form a graded series, while in thiosemicarbazone formation the corresponding three entropy values pass through a maximum.

A comparison of oxime formation<sup>9</sup> with thiosemicarbazone formation<sup>10</sup> also reveals significant differences. The compounds cyclopentanone, furfural, and methyl ethyl ketone occupy comparable positions in both series while diethyl ketone, cyclohexanone and pinacolone occupy divergent positions with respect to the sign of relative entropy values.

In guanylhydrazone formation a distinctly new pattern of behavior appears in which there is found a complete lack of any parallelism in the original sense of positive and negative relative entropies of activation, for all the relative entropies of activation are positive in character. This completely positive character of the entropy values does not of itself preclude the existence of a parallelism. One might conceive of a parallelism consisting of entropy values where less rigid compounds would exhibit small positive entropies and more rigid substances large positive entropies. However, even this extreme type of parallelism is not realized for guanylhydrazone behavior.

It is readily evident that significant deviations from the parallelism observed in semicarbazone formation exist for oxime formation, thiosemicarbazone formation, and guanylhydrazone formation. The nature and magnitude of these deviations lead overwhelmingly to the conclusion that the correspondence of activation entropies with structural rigidity is, in the four reaction systems studied, entirely random in nature.

The relative entropies of activation for guanylhydrazone formation in the case of the compounds listed in Table I vary over some seventeen entropy units which is equivalent to approximately four orders of magnitude in the reaction rate. It is safe to assume that the variations are many times greater than the probable error in the measurement of the relative activation entropy. This variation of approximately seventeen entropy units is approximately 30% greater than the corresponding variation for semicarbazone formation.

Hammett<sup>2</sup> reported that both activation entropies and activation enthalpies are important in determining specific rates in semicarbazone formation. A comparison of data in Table V for guanylhydrazone formation reveals a similar situation. In some cases under consideration entropy effects on rate are more important, in other instances, enthalpy factors exert a predominant role. while in still other situations both entropy and enthalpy factors are equally significant and may act either in concert or opposition. For instance, it is patently obvious that the rate difference between cyclohexanone and cyclopentanone stems almost entirely from the enthalpy factor. For diethyl ketone and furfural the activation entropy difference exerts a greater effect in determining the rate difference although the enthalpy difference is of the same magnitude as in the immediately preceding case. A comparison of cyclopentanone and methyl ethyl ketone indicates entropy and enthalpy contributions approximately equal but opposite in effect on the rate quantity. For the two cases of furfural and cyclohexanone and pinacolone and diethyl ketone entropy and enthalpy factors act in concert. For the former pair the entropy effect on rate is twice the enthalpy effect while in the latter pair both effects are of approximately equal magnitude.

In Fig. 1 is illustrated plots of the logarithms of rate constants for semicarbazone formation versus the logarithms of rate constants for guanylhydrazone formation (line A), the logarithms of rate constants for thiosemicarbazone formation (line B), the logarithms of rate constants for oxime formation (line C), taken at 25°. The three plots, which represent typical free energy relationships,<sup>12-16</sup> exhibit a marked parallelism in that line A possesses a slope of 0.96, line B possesses a slope of 0.93, while the slope of line C is 1.1. An exceedingly high degree of linearity is reflected by correlation coefficients of 0.96, 0.98, and 0.99, respectively.

The high degree of linearity in the free energy plots for the reaction series under consideration is significant in view of the variation in structure of the carbonyl compounds examined. Furthermore, the linearity is striking in that the data of the four systems were obtained by different sets of investigators employing two fundamentally different techniques. The satisfying degree of linearity can be ascribed to some combination of the following three factors. Firstly, it arises, in part, from an implied similarity of the transition states of semicarbazone formation, oxime formation, thiosemicarbazone formation, and guanylhydrazone

(13) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, chap. VII.

<sup>(12)</sup> J. N. Brønsted and K. Pederson, Z. physik. Chem., Series A, 108-185 (1923).

<sup>(14)</sup> H. L. Pfluger, J. Am. Chem. Soc., 60, 1513 (1938).

<sup>(15)</sup> R. L. Bell and T. I. Crowell, abstracts of papers, 127th National Meeting of the American Chemical Society, Cincinnati, Ohio, April, 1955, p. 36 N.

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Fig. 1.—Plot of log k for semicarbazone formation vs.log k for guanylhydrazone formation (A), log k for thiosemicarbazone formation (B), and log k for oxime formation (C). Reading from the uppermost end of the plots downward the points correspond to cyclohexanone, acetone, cyclopentanone, furfural, diethyl ketone, pinacolone, and acetophenone.



Fig. 2.—Plot of the logarithm of relative rate against the sum of Taft sigma values for (A) guanylhydrazone formation, (B) thiosemicarbazone formation, (C) semicarbazone formation, and (D) oxime formation. The numbered points in increasing order correspond to acetone, methyl ethyl ketone, methyl isobutyl ketone, methyl isopropyl ketone, diethyl ketone, di-*n*-propyl ketone, and pinacolone. The position of the scale of ordinates is arbitrary.

formation; secondly, from the inherent compressive features of the logarizing process, generally; thirdly, from the essential soundness of the four series of experimental data under consideration. The almost perfect, linear free energy relationships that are illustrated in Fig. 1 demand equally good linear free energy relationships between guanylhydrazone and thiosemicarbazone formation and guanylhydrazone and oxime formation. It is doubtful that this mutuality of relationship is merely a mathematical oddity. It is highly probable that the mutuality arises from some inherent similarity in the fundamental nature of the four reactions.

Numerous correlations between structure and reactivity have been realized through the agency of Hammett's sigma-rho function<sup>17a,b</sup> and Taft<sup>18</sup> has extended the use of this relationship to aliphatic compounds by calculating sigma values from the rates of hydrolysis of esters. In many cases,<sup>19</sup> a wide variety of reaction types fit with relatively good precision an equation, analogous to that of Hammett with respect to the proportionality of polar effects, namely

$$\log\left(k/k_{\rm s}\right) = \sigma^* \rho^* \tag{1}$$

where  $\sigma^*$  is the polar substituent constant for the group R relative to the standard CH<sub>3</sub> group:  $\rho^*$ is a constant giving the susceptibility of a given reaction series to polar substitution. Fig. 2 demonstrates the result of plotting Taft  $\sigma^*$  values against corresponding log  $(k/k_0)$  values for guanylhydrazone formation (curve A), thiosemicarbazone formation (curve B), semicarbazone formation (curve C), and oxime formation (curve D). The resultant plots are definitely curvilinear in character. The realization of these curvilinear relationships does not necessarily contraindicate the proportional nature of polar effects, but shows that in these cases rates are probably determined by other factors. The curves in Fig. 2 exhibit approximately mutual parallelism indicating some common, internal factor of resemblance.

Jencks<sup>20-22</sup> and others have recently demonstrated that the mechanism of both semicarbazone and oxime formation under the experimental conditions of the present research proceed through a rapid acid-catalyzed carbinolamine formation followed by a slow acid-catalyzed dehydration. In view of the formal similarity of the reactions compared in this report, it is highly probable that thiosemicarbazone formation and guanylhydrazone formation proceed by the same type of mechanism; nevertheless, the data of these reaction systems deviate from the original parallelism of Hammett. To further elucidate the significance of the thermodynamic activation quantities of these over-all reactions within the scope of the Hammett parallelism, measurements of the thermodynamic activation quantities of carbinolamine formation and subsequent dehydration are being initiated in these laboratories.

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# Aromatic Nuclei by the Sulfur Extrusion Reaction. I. Phenanthridizinium Derivatives

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The action of an excess of hydrogen peroxide on pyrido [2,1-b] benzo [f] [1,3] thiazepinium salts (I) at 56° followed by heating at 100° has been found to cause extrusion of the sulfur atom, yielding phenanthridizinium salts (II). The consumption of hydrogen peroxide at 56°, and analogy to related reactions suggest that a sulfoxide may be the intermediate.

Recently the first synthesis of pyrido[2,1-b]benzo[f][1,3]thiazepinium salts (I) was described.<sup>2</sup> When these salts were treated with 30% hydrogen peroxide and acetic acid, under essentially the condition reported<sup>3</sup> to effect the oxidation of diaryl sulfides to sulfones, crystalline sulfur-free products were obtained. The analytical results obtained for these products suggested that they might be substituted phenanthridizinium<sup>4</sup> perchlorates (II). The correctness of the postulate was confirmed by direct comparison of the product IIa with a sample of 7-methylphenanthridizinium perchlorate prepared from an authentic sample<sup>5</sup> of the bromide. The results of the sulfur-extrusion reaction are summarized in Table I.

The procedure for carrying out the ring-contraction reaction involved an initial period of three to ten hours during which the thiazepinium compound (I) was heated at about 50° with acetic acid and an excess of hydrogen peroxide, followed by a period of about equal length during which a temperature of  $100^{\circ}$  was maintained.

Since it is known that certain dibenzo [b, f] thiepins (III)<sup>6</sup> and dibenzo [b, f]-1,4-thiazepines (IV)<sup>7,8</sup> on heating in the presence (or absence)<sup>9</sup> of copper

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yield phenanthrenes (V) or phenanthridines (VI), respectively, it seemed important to determine first whether the extrusion of sulfur from phenanthridizinium (I) salts was not also purely thermal.

Since 7-methylphenanthridizinium perchlorate (IIa) showed an absorption maximum at 3548 Å.,



and the absorption of solutions obeyed Beer's law, it was possible to follow the thermal reaction spectrophotometrically. A solution of the thiazepinium salt (Ia) in acetic acid, with no hydrogen peroxide added, was heated for twenty-two hours at 100°. Under these extreme conditions there was definite indication of the formation of the