that the methoxyl group was present. This material was not characterized.

cis-1-(2-**Methoxycyclohexyl**)-2-**methylpropan-2-ol** (**X**).—To 0.0675 mole of methylmagnesium bromide in ether was added 6.4 g. (0.038 mole) of cis-1-(2-methoxycyclohexyl)propan-2-one (E) in 50 ml. of ether. The ketone solution was added cautiously and the ether was allowed to reflux gently. The reaction mixture was refluxed for 0.5 hr., cooled, and treated with 13 ml. of a saturated solution of ammonium chloride. The ether was removed and the residue was distilled to yield 5.75 g. (82%) of a colorless liquid, b.p. 67–68° (0.8 mm.), $n^{27}D$ 1.4612. The infrared spectrum showed hydroxyl absorption at 3398 cm.$^{-1}$; v.p.c. analysis failed to detect the tertiary alcohol because it underwent elimination on the acid-washed column.

Anal. Calcd. for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.67; H, 11.80.

cis-2,2-**Dimethylperhydrobenzofuran** (**Y**) *via* **Methoxyl Cleavage**.—The tertiary alcohol X (3.8 g.) in 15 ml. of anhydrous pyridine was added to 4.34 g. of p-toluenesulfonyl chloride in 15 ml. of anhydrous pyridine. The solution remained at room temperature for 2 days. After the usual work-up procedure, an infrared spectrum of the crude residue indicated that the alcohol function had disappeared. There was also evidence of double bond absorption. Distillation of the liquid residue gave two products; the first was the desired cis-2,2-dimethylperhydrobenzofuran (Y) (30%), b.p. 63–65° (19 mm.), $n^{24}D$ 1.4528, as was shown by comparison with an authentic sample. The infrared spectrum contained bands at 1177, 1149, 1099, and 998 cm.$^{-1}$ indicative of the cyclic ether. The v.p.c. results indicated that the material was very pure (98%), and it had an identical retention time with the authentic sample of cis-2,2-dimethylperhydrobenzofuran.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 78.29; H, 11.97.

The second fraction, b.p. 67–72° (19 mm.), $n^{23}D$ 1.4577, was homogeneous as shown by v.p.c. analysis. The infrared spectrum of this material contained a strong band at 1640, and bands at 926 and 878 cm.$^{-1}$ indicative of a trisubstituted double bond. This unsaturated compound represented 60–63% of the material.

cis-3-(2-**Methoxycyclohexyl**)-2-**methyl-2-propene** (**Z**).—The tertiary alcohol X (1.8 g.) was heated under reflux for 3 hr. and then distilled to yield 1.4 g. of a colorless material, b.p. 68–70° (18 mm.), $n^{25}D$ 1.4570. The infrared spectrum contained strong bands at 1640, 926, and 878 cm.$^{-1}$; v.p.c. analysis indicated that the material was at least 98% pure.

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.04; H, 11.67.

cis-2,2-**Dimethylperhydrobenzofuran** from **Z**.—The unsaturated compound Z (1 g.) was refluxed in a mixture of 5 ml. of 48% hydrobromic acid and 20 ml. of acetic acid for 0.5 hr. The hot solution was poured onto ice and extracted with three 20-ml. portions of ether. The ether extracts were combined, washed with five 20-ml. portions of cold water, and dried. The ether was filtered and removed to yield a pink residue, which was distilled to yield 0.41 g. (44%) of a colorless liquid, b.p. 67–68° (19 mm.), $n^{25}D$ 1.4524. This material had an identical infrared spectrum and v.p.c. retention time with the cis-2,2-dimethylperhydrobenzofuran prepared by the methoxyl cleavage of the tertiary alcohol X.

Preparation of 2,2-**Dimethyl-2,3-dihydrobenzofuran** (**AA**).—β-Methylallylphenol (15 g.), $n^{24}D$ 1.5512 (lit. $n^{20}D$ 1.5534)^{12} was refluxed in 60 ml. of glacial acetic acid and 30 ml. of 48% hydrobromic acid. The standard work-up procedure was employed to yield, after distillation, 8 g. (54%), b.p. 68–70° (12 mm.), $n^{24}D$ 1.5160 (lit.^{12} $n^{20}D$ 1.5190).

2,2-**Dimethylperhydrobenzofuran** (**Y**).—The aromatic material AA (5 g.) was hydrogenated in the presence of 2 g. of 5% rhodium-on-alumina. After 4 hr. the absorption of hydrogen ceased and the catalyst was filtered off. The acetic acid solution was extracted with three 20-ml. portions of petroleum ether, washed with five 25-ml. portions of cold water, and dried. The ether was filtered and removed to yield 3.5 g. of the desired cis-2,2-dimethylperhydrobenzofuran, b.p. 67° (20 mm.); $n^{24}D$ 1.4528. V.p.c. analysis on a 30% Apiezon L column at 136° (He flow 82 cc./min.) gave three peaks: two minor ones (less than 1%) and a large peak which corresponded to the retention time of the cis-2,2-dimethylperhydrobenzofuran produced by the cyclization of the tertiary cis-alcohol X. The infrared spectra of the two materials were identical.

The Wolff–Kishner Reaction of Hydrazones[1]

By H. Harry Szmant and Charles M. Harmuth

Received February 13, 1964

Kinetic and thermodynamic data for the base-catalyzed, homogeneous Wolff–Kishner reaction of negatively substituted hydrazones are presented. The nonlinearity of the Hammett plot is interpreted in terms of solvation effects in the transition state.

Introduction

Previously obtained[2] kinetic results for the base-catalyzed, homogeneous Wolff–Kishner reaction of diaryl ketone hydrazones were shown[3] to obey the Hammett equation. However, that study was limited to positively or mildly negatively substituted hydrazones, and it was of interest, therefore, to extend the series to include strongly negatively substituted compounds. It was immediately apparent that the kinetic results obtained with the latter type hydrazones were not in agreement with those predicted on the basis of the Hammett relationship. In this paper we wish to report the more recent results and to offer an explanation for the nonlinearity of the Hammett plot.

(1) Experimental data from the Ph.D. Thesis of C. M. H., Duquesne University, 1956. All inquiries should be directed to H. H. S. at PRNC, San Juan, Puerto Rico.

(2) H. H. Szmant, H. F. Harnsberger, T. J. Butler, and W. P. Barie, *J. Am. Chem. Soc.*, **74**, 2724 (1952).

(3) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

Experimental and Results

The apparatus and experimental procedure in carrying out the kinetic study were essentially identical with those described in the preceding publication[2] in this series. Special precautions were observed to exclude atmospheric oxygen from the base and the reaction mixture, and the apparatus was flushed thoroughly with nitrogen before each kinetic run. The base concentration was determined at the end of each kinetic experiment and the run was discarded when a serious loss of base was found to have taken place. The temperatures were recorded on a thermometer which was calibrated against a National Bureau of Standards calibrated set of Anschütz thermometers. The kinetic results are summarized in Table I and representative, linear $\ln k/T$ vs. $1/T$ plots are shown in Fig. 1–2. The enthalpies and entropies of activation were calculated by means of the Eyring equation and are listed in Table II.

Table I

Summary of Kinetic Experiments

o-Nitrobenzaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00269	0.3681	0.3620	96.9	15.3	15.2 ± 0.2
	.00620	.1243	.1236	95.2	15.7	
206.2	.00240	.4125	.4102	95.3	21.5	21.3 ± 0.3
	.00366	.4210	.4184	98	21.0	
	.00324	.4034	.4001	96.2	21.3	
217	.00315	.1010	.1000	97.5	30.0	30.1 ± 0.1
	.00800	.1337	.1329	97.8	30.1	
221	.00311	.1210	.1201	96.1	32.5	32.7 ± 0.3
	.00298	.1862	.1786	94.3	33.0	
	.00340	.1325	.1315	94.8	32.7	

m-Nitrobenzaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00163	0.2700	0.2674	94.0	4.9	5.1 ± 0.3
	.00145	.2680	.2632	93.6	5.4	
	.00158	.2655	.2610	94.5	5.1	
206.2	.00236	.1557	.1547	86.0	8.0	8.9 ± 0.1
	.00228	.1620	.1586	96.2	8.0	
	.00201	.1498	.1472	95.7	8.8	
217	.00504	.0219	.0214	92.6	16.0	16.0
	.00127	.3330	.3321	93.5	16.0	

p-Nitrobenzaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
221	0.00320	0.3201	0.3186	94.7	19.0	19.1 ± 0.1
	.00489	0.3298	0.3210	96.8	19.1	
195	.00539	2.259	2.250	97.0	3.4	3.5 ± 0.1
	.00620	2.246	2.228	96.3	3.5	
206.2	.00521	1.795	1.788	89.0	6.3	6.2 ± 0.1
	.01620	1.462	1.451	94.2	6.2	
217	.00569	0.0671	0.0665	94.7	11.6	11.7 ± 0.2
	.00467	.3930	.3926	95.7	11.9	
	.00513	.3263	.3228	90.0	11.7	
221	.00489	.2186	.2142	98.2	14.8	14.8
	.00462	.1925	.1925	97.8	14.8	

2-Benzoylpyridine

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00895	0.0373	0.0368	93.9	8.6	8.4 ± 0.2
	.00553	.0773	.0752	95.6	8.3	
	.00621	.0689	.0682	94.7	8.3	
206.2	.00900	.0386	.0362	92.0	12.5	12.9 ± 0.4
	.00543	.0608	.0601	97.5	13.2	
	.00786	.0492	.0479	96.4	12.9	
217	.00818	.0341	.0308	95.0	16.7	16.7 ± 0.1
	.00846	.0378	.0359	93.0	16.6	
221	.00720	.0365	.0358	93.4	18.3	18.2 ± 0.1
	.00821	.0342	.0337	97.6	18.1	

3-Benzoylpyridine

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00150	0.0842	0.0801	97.3	3.3	3.5 ± 0.2
	.00437	.2638	.2625	95.9	3.6	
206.2	.00247	.0663	.0631	91.8	7.9	7.8 ± 0.3
	.00199	.0598	.0585	93.8	7.9	
	.00212	.0625	.0619	93.6	7.5	
217	.00200	.0221	.0202	96.0	14.5	14.5 ± 0.1
	.01110	.0274	.0269	93.0	14.4	
221	.00215	.0417	.0401	97.2	18.0	18.2 ± 0.2
	.00234	.0501	.0493	98.7	18.3	

4-Benzoylpyridine

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00692	0.1844	0.1829	90.0	2.1	2.3 ± 0.2
	.00507	.1150	.1139	91.6	2.4	
	.00594	.1282	.1274	93.2	2.2	
206.2	.00661	.2555	.2537	86.3	3.6	3.6 ± 0.1
	.00621	.0628	.0619	94.6	3.7	
217	.00500	.2066	.2016	90.0	5.4	5.4
	.00538	.2120	.2114	95.7	5.4	
221	.00628	.1982	.1974	97.6	6.1	6.1 ± 0.1
	.00514	.2057	.2049	98.1	6.2	

2-Pyridaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00196	0.1628	0.1614	94.6	12.2	12.1 ± 0.1
	.00224	.1591	.1586	93.2	11.8	
	.00215	.1643	.1633	94.2	12.0	
206.2	.00262	.1828	.1819	95.2	19.1	19.1 ± 0.1
	.00239	.2012	.2001	94.7	19.2	
217	.00129	.2572	.2564	97.2	25.7	25.8 ± 0.1
	.00284	.2100	.2088	98.1	25.9	
221	.00210	.2278	.2267	97.3	29.4	29.5 ± 0.1
	.00261	.1928	.1915	98.6	29.5	

3-Pyridaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00210	0.3301	0.3292	93.1	3.4	3.4
	.00184	.2840	.2828	32.8	3.4	
206.2	.00162	.2102	.2097	91.4	7.7	7.6 ± 0.1
	.00216	.1249	.1234	94.6	7.6	
217	.00310	.3012	.3001	94.0	11.4	11.4 ± 0.1
	.00140	.1666	.1658	97.2	11.5	
221	.00321	.2016	.2009	97.6	14.5	14.4 ± 0.1
	.00210	.1631	.1623	98.3	14.3	

4-Pyridaldehyde

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00222	0.2290	0.2281	91.3	4.7	4.7 ± 0.1
	.00682	.2102	.2092	92.7	4.2	
	.00543	.3450	.3443	90.6	4.6	
206.2	.00601	.1563	.1551	95.0	8.9	8.8 ± 0.2
	.00482	.1563	.1551	94.3	8.6	
	.00302	.2301	.2289	94.9	8.9	
217	.00406	.1393	.1385	96.1	14.1	14.2 ± 0.1
	.00497	.2216	.2207	97.6	14.3	
221	.00612	.1356	.1348	98.3	17.7	17.7 ± 0.2
	.00592	.2108	.2100	97.8	17.6	
	.00824	.2812	.2803	98.7	17.9	

m-Nitrobenzophenone

T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00340	0.0781	0.0772	91.6	3.8	3.7 ± 0.1
	.00328	.0728	.0718	92.0	3.7	
206.2	.00429	.0844	.0832	97.3	7.9	7.7 ± 0.2
	.00324	.0643	.0639	94.0	7.5	
217	.00338	.0613	.0610	94.4	12.0	12.2 ± 0.2
	.00665	.0246	.0238	97.0	12.4	
221	.00416	.0862	.0851	98.8	16.3	16.4 ± 0.1
	.00422	.0757	.0729	97.6	16.5	

p-Nitrobenzophenone

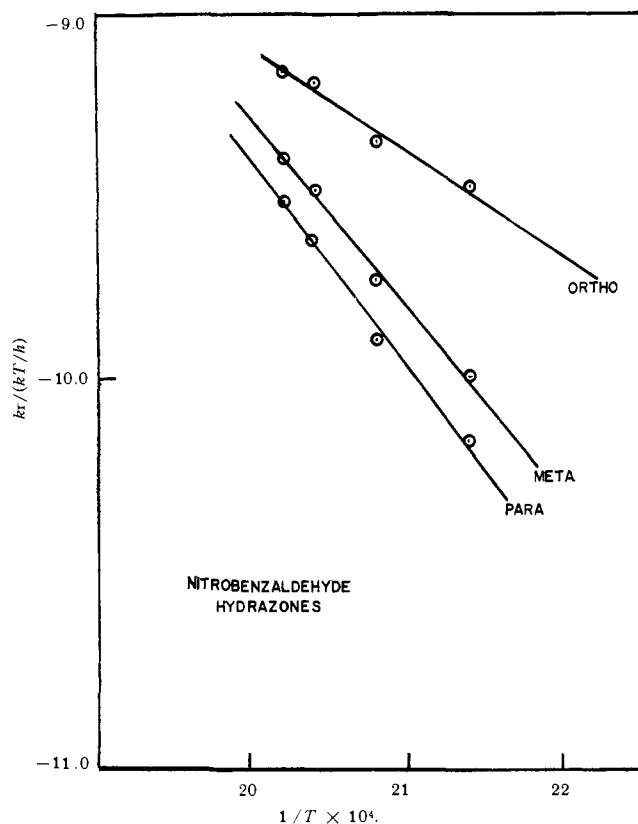| T, °C.	Initial hydrazone, mole/l.	Concn. base, mole/l.	Final base, mole/l.	Final % of theor. N₂	$k \times 10^2$, l./mole-sec.	$k \times 10^2$ av., l./mole-sec.
195	0.00178	0.1880	0.1877	95.4	2.1	2.3 ± 0.3
	.00546	.1043	.1022	92.8	2.6	
206.2	.00223	.4357	.4349	93.0	3.8	3.7 ± 0.1
	.00253	.1511	.1500	94.8	3.7	
217	.00232	.1048	.1040	92.0	6.8	7.0 ± 0.2
	.00348	.1308	.1300	96.4	7.2	
	.00891	.1817	.1809	97.8	7.0	
221	.00267	.1562	.1551	97.8	7.5	7.5 ± 0.1
	.00284	.1428	.1409	98.3	7.6	

Fig. 1.—Heats and entropies of activation plots for the Wolff–Kishner reaction of the hydrazones of the isomeric nitro-benzaldehydes.
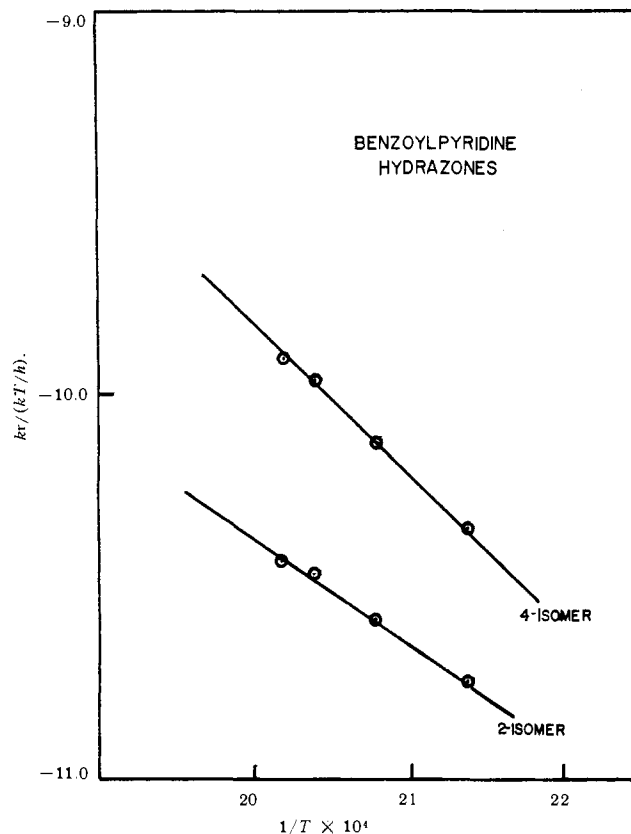
TABLE II

ENTHALPIES AND ENTROPIES OF ACTIVATION

Hydrazone	$\Delta H^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, cal./deg. mole
Aldehydes		
o-Nitrobenzaldehyde	12.4	−36.1
m-Nitrobenzaldehyde	22.5	−16.3
p-Nitrobenzaldehyde	24.1	−22.4
2-Pyridinecarboxaldehyde	14.3	−32.0
3-Pyridinecarboxaldehyde	23.0	−16.7
4-Pyridinecarboxaldehyde	20.7	−21.1
Diaryl ketones		
m-Nitrobenzophenone	19.7	−22.8
p-Nitrobenzophenone	21.6	−20.8
2-Benzoylpyridine	14.4	−33.0
3-Benzoylpyridine	17.3	−27.5
4-Benzoylpyridine	20.1	−23.3
2-Benzoylthiophene[a]	15.7	−31.0
p-Chlorobenzophenone[a]	18.2	−26.6
2,4,2′,4′-Tetrachlorobenzophenone[a]	23.3	−16.8
Benzophenone[a]	23.6	−17.0
p,p′-Dimethoxybenzophenone[a]	24.5	−16.4
p-Phenylbenzophenone[a]	26.7	−10.1
p-Phenoxybenzophenone[a]	29.3	− 4.4
p,p′-Dichlorobenzophenone[a]	37.4	+13.8
Methyl aryl ketones		
Acetophenone[b]	22.9	−19.3
p-Methoxyacetophenone[b]	21.8	−22.8
p-Chloroacetophenone[b]	31.0	− 2.0

[a] Values from ref. 2. [b] Values from ref. 4.

For sake of comparison, Table II includes enthalpy and entropy of activation values from the preceding publication[2] and from unpublished work.[4]

(4) W. P. Barie, M.S. Thesis, Duquesne University, 1951.

Fig. 2.—Heats and entropies of activation plots for the Wolff–Kishner reaction of the hydrazones of the isomeric benzoyl-pyridines.
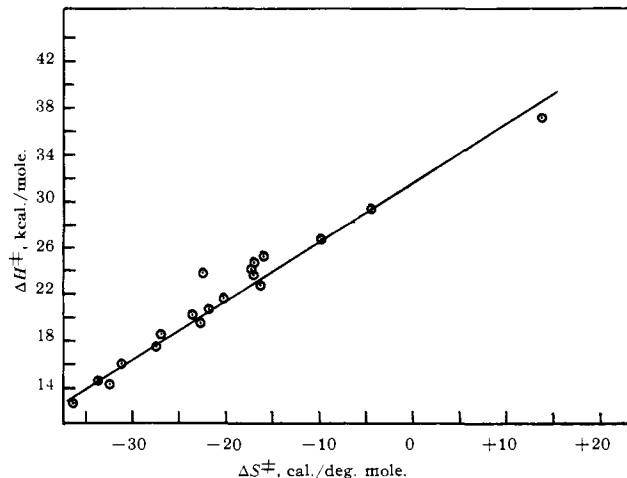
Fig. 3.—Enthalpy–entropy plot for the Wolff–Kishner reaction of hydrazones.

The preparation of the new hydrazones was described elsewhere.[5]

Discussion

The wide range of the observed enthalpy and entropy of activation values (Table II) raises the question if the reaction of all of the hydrazones follows the same mechanism, and hence if there is any *a priori* reason for the Hammett relationship to be obeyed. An accepted criterium of the validity of the Hammett equation under conditions of varying entropies of activation is the linearity of the enthalpy–entropy relationship,[6] and Fig. 3 demonstrates that all of the com-

(5) H. H. Szmant and C. M. Harmuth, J. Am. Chem. Soc., 81, 962 (1959).
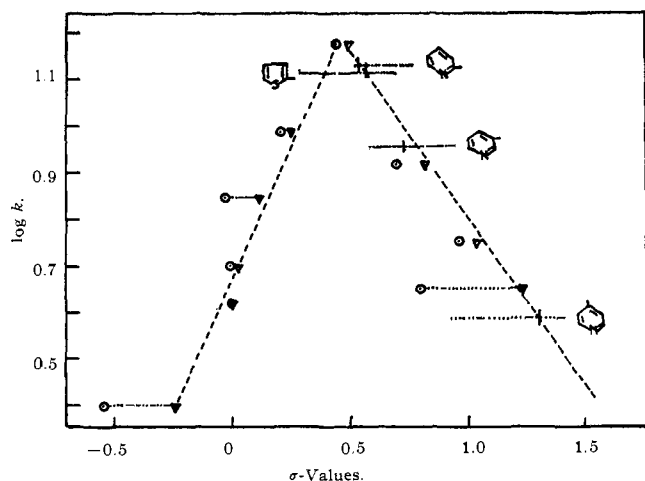(6) J. E. Leffler, J. Org. Chem., 20, 1202 (1955).

Fig. 4.—Hammett plot for the Wolff–Kishner reaction of diaryl ketone hydrazones. σ and σ⁻ values are represented by circles and triangles, respectively.

Fig. 5.—Hammett plot for the Wolff–Kishner reaction of the hydrazones of aryl aldehydes (triangles) and methyl aryl ketones (circles).

pounds listed in Table II (except the hydrazone of *p*-nitrobenzaldehyde) give a satisfactory fit of the linear graph. One is therefore encouraged to proceed with the examination of the Hammett relationship.

The largest available series of compounds is that of the diaryl ketone hydrazones, and here we must distinguish between the nine compounds for which σ-values are known with some certainty, and the remaining four heterocyclic systems, the σ-values of which are scarcely known. Considering the fact that the rate-determining step in the Wolff–Kishner reaction is believed to involve the hydrazone anion, one is tempted to compare the Hammett relationship using both "normal" σ-values and σ⁻-values.[7] Figure 4 shows that the Hammett plot of the log *K* values (all at 210.5°) for the diaryl ketone hydrazones is definitely nonlinear, and that the use of σ⁻-values decreases the scatter of the points. Accepting the validity of the Hammett curve drawn through the well or better known σ⁻-values, we can estimate the values for the lesser known heterocycles. Such estimates produce values of 0.58, 0.76, and 1.26 for the 2-, 3-, and 4-pyridyl groups, respectively, and 0.58 for the 2-thienyl group. The 2- and 3-pyridyl values are in general agreement with those reported previously, but one would expect the 2-pyridyl value to be higher. Such difference in the σ⁻-value for the 2-pyridyl system is the result of an abnormally high log *k*-value and this, in turn, is probable due to some type of *ortho acceleration effect*[8] *produced by the hetero atom*. The estimated σ⁻-value for the 2-thienyl system is reasonable in view of the value 0.36 which was reported[9] for the reactions of 2-carboxythiophene and its derivatives. One would expect the 2-thienyl system to possess a greater electron-
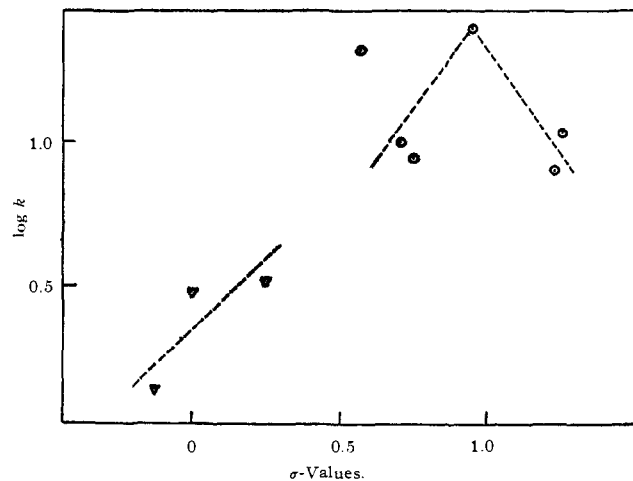
withdrawing character under circumstances when it is called upon to stabilize a negative charge since then the valence shell expansion of the sulfur atom can enter into the picture[10] in addition to its electronegativity.[11]

The Hammett plot for the smaller series of aldehyde and acetophenone hydrazones[12] is shown in Fig. 5. The scarcity of data, on one hand, and the fact that two somewhat different parent compounds are employed make it difficult to draw any conclusions. Nevertheless, the sketched lines indicate the same general trend as observed in Fig. 4, and the only point which seriously deviates from the graph is that for the hydrazone of pyridine-2-carboxaldehyde in which the above-mentioned *ortho*-acceleration effect must be even greater than in the diaryl ketone system.

The σ⁻-value of the *o*-nitro group was estimated by adding 0.46 unit (the difference between the "normal" and σ⁻-value for the *p*-nitro substituent) to 0.50, an average "normal" *o*-nitro σ-value reported by Solomon and Filler.[7]

Some time ago it was shown[13] by one of us that the basicity constants of hydrazones derived from methyl aryl and diaryl ketones could be fitted onto the same Hammett plot by considering the hypothetical hydrazone of formaldehyde as the parent compound of both series. In other words, the imine system is assumed to transmit the effect of the substituents (R, R′) in $\frac{R}{R'}$C=N—NH₂, and one employs the sum of the σ-values of R and R′. A similar extension of the Hammett equation was reported later by Charton and collaborators[14] in connection with acrylic acids, and acetylenic and vinylidene systems. The application of this treatment to the Wolff–Kishner data permits construction of a Hammett plot for the hydrazones of thirteen

(7) Most of the σ⁻-values employed here are those cited by L. A. Cohen and W. M. Jones, *J. Am. Chem. Soc.*, **85**, 3397 (1963). The value for the *p*-chloro substituent was assumed to be +0.25, and that for the *o*-chloro group was taken as 0.26 in accord with the work of J. J. Solomon and R. Filler, *ibid.*, **85**, 3492 (1963). Since the change from "normal" "negative" σ-values for the *p*-methoxy group involves an increase of 0.13 unit, the same increase was assumed to hold for the *p*-phenoxy group. Thus, the σ-value for the latter group becomes −0.03 + 0.13 = +0.10, which falls within the range of previously reported values (see Table VIII in ref. 3).

(8) (a) R. O. C. Norman and G. K. Radda, *J. Chem. Soc.*, 3030 (1961); (b) R. G. Shepard, W. E. Taft, and H. M. Krazinski, *J. Org. Chem.*, **26**, 2764 (1961).

(9) S. Oae and C. C. Price, *J. Am. Chem. Soc.*, **79**, 2547 (1957).

(10) R. R. Beishline, *J. Org. Chem.*, **26**, 2533 (1961).

(11) The relative electronegativity values for trigonal carbon and sulfur atoms are calculated by J. Hinze and H. H. Jaffé, *J. Am. Chem. Soc.*, **84**, 540 (1962), to be 2.75 and 3.46, respectively.

(12) The log *k* values (at 210.5°) for the hydrazones of acetophenone and its *p*-methoxy and *p*-chloro derivatives are reported (ref. 4) to be 0.474, 0.143, and 0.505, respectively.

(13) H. F. Harnsberger, E. L. Cochran, and H. H. Szmant, *J. Am. Chem. Soc.*, **77**, 5048 (1955).

(14) M. Charton, *et al.*, *ibid.*, **80**, 5940 (1958); *J. Org. Chem.*, **26**, 735 (1961); Abstracts, 141st National Meeting of the American Chemical Society, Chicago, Ill., 1961, p. 91Q.

diaryl ketones, six aldehydes, and three acetophenones using, in each case, the sum of the σ^--values. In the case of complex substituents, such as p-methoxyphenyl, for example, one must add the σ^--value of the p-methoxy group to a σ^--value for the benzene ring. Even though the phenyl group is usually given[3,15] a σ-value of nearly zero, the consideration of its electronegative character and its capacity to stabilize a negative charge by resonance leads us to suggest a σ^--value of 0.30. The Hammett plot that results from this treatment is shown in Fig. 6. Considering the many uncertainties involved in its construction, one is forced to conclude that, in spite of the obvious imperfections, there is demonstrated a nonlinear Hammett relationship rather than a random scatter of points. Two points are seriously out of order in the plot, but these correspond to the hydrazones of the 2-pyridyl and o-nitro-substituted aldehydes. In these compounds the previously mentioned *ortho*-acceleration effect is apparently extremely strong, more so than in the diaryl ketone system in which the pyridyl ring can be coplanar with the side chain only part of the time. The slopes of the left- and right-handed portions of the plots in Fig. 4 and 6 are essentially identical (ρ +1.0 and −0.8, respectively) and this supports the correctness of the assumptions employed in constructing Fig. 6.

The best known system that produces a nonlinear concave upward or U-shape Hammett plot is the reaction of benzyl halides with nucleophiles.[16] Also recognized, but not as well understood, are nonlinear concave downward Hammett plots observed in the formation of reactions of imine derivatives of carbonyl compounds,[17] and in the reactions of diazonium salts.[18]

The nonlinearity of the Hammett plot of the benzyl halide reactions has been rationalized in terms of relatively minor changes of the transition state induced by the presence of electron-donating or withdrawing substituents, and Swain and Langsdorf[19] discussed the situation in terms of a "loose" or "tight" transition state. We must reconcile our case also with the proven great variations of the enthalpies and entropies of activation. Variations such as those observed here, where the enthalpy and entropy compensate each other, and thus the linear free energy relationship is maintained, are believed[20] to result mainly from solvent effects. Since the rate-determining step of the Wolff–Kishner reaction is most probably[2] the transfer of a hydrogen from the nitrogen to the carbon terminal in the hydrazone anion

$$R_2C{=}\ddot{N}{-}\ddot{N}{-}H \xrightarrow{\text{r.d.s.}} R_2CH{-}\ddot{N}{=}\ddot{N}{:}^{\ominus}$$
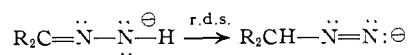
one can visualize the transition state to involve a minimum of one molecule of the hydroxylic solvent

(15) M. Rapoport, C. K. Hancock, and E. A. Meyers, *J. Am. Chem. Soc.*, **83**, 3489 (1961).

(16) R. Fuchs and D. M. Carlton, *ibid.*, **85**, 104 (1963), in which references to older studies are given.

(17) (a) G. M. Santerre, C. J. Hansrote, Jr., and T. I. Crowell, *ibid.*, **80**, 1254 (1958); (b) D. S. Noyce, A. T. Bottini, and S. C. Smith, *J. Org. Chem.*, **23**, 752 (1958); (c) A. V. Willi, *Helv. Chim. Acta*, **39**, 1193 (1958); (d) A. V. Willi and R. E. Robertson, *Can. J. Chem.*, **31**, 361 (1953).

(18) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 294 (1951).

(19) C. G. Swain and W. P. Langsdorf, *J. Am. Chem. Soc.*, **73**, 2813 (1951).

(20) L. L. Schaleger and F. A. Long in "Advances in Physical Organic Chemistry," Vol. 1, V. Gold, Ed., Academic Press, Inc., New York, N. Y., p. 21.
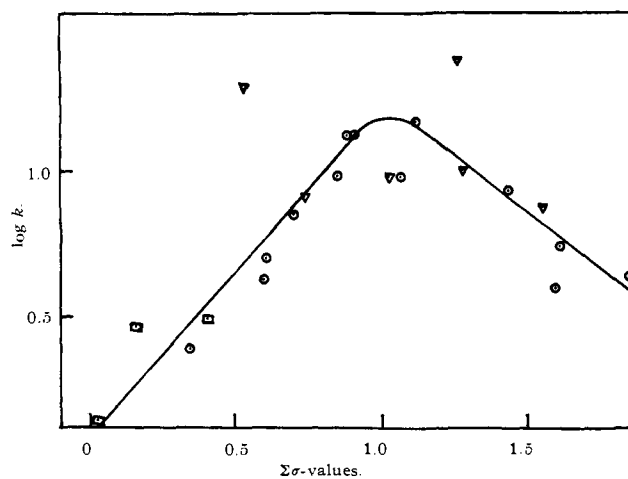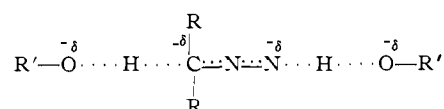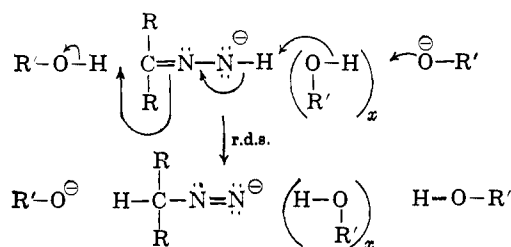
Fig. 6.—Hammett plot for the Wolff–Kishner reaction of hydrazones of aldehydes (triangles), diaryl ketones (circles), and methyl aryl ketones (squares).

(R'OH), in order to permit a concerted hydrogen transfer.

$$R'{-}\overset{-\delta}{O}\cdots H\cdots \overset{-\delta}{\underset{|}{\overset{|}{C}}}{:}{=}N{:}{=}\overset{-\delta}{N}\cdots H\cdots \overset{-\delta}{O}{-}R'$$

In favor of such a postulate is the high temperature requirement of the traditional Wolff–Kishner reaction (the high activation energy being a consequence of the required approach of two negatively charged species), and the amazingly low temperature requirement of the Wolff–Kishner reaction carried out in dimethyl sulfoxide[21] in which the hydrogen is abstracted from the hydrazone anion by the neutral sulfoxide molecule.[22] However, the many recent studies proving the involvement of solvent molecules in separating ions[23] make us conscious of at least one additional solvent molecule that is most likely forming a part of the transition state, and this is a hydroxylic solvent molecule weakly hydrogen bonded at the N–H terminal. As a matter of fact, this hypothesis is very attractive because it explains how the base R'–O$^-$ can cause the N–H bond breaking without having to overcome all of the Coulombic repulsion, since the proton removal may take place by relay involving one, or more, solvent molecules

We can now offer an explanation of the concave downward Hammett plot and of the observed large range of enthalpy–entropy of activation values in the Wolff–Kishner reaction. Mildly electron-attracting

(21) D. J. Cram, M. V. R. Sahyun, and G. R. Knox, *J. Am. Chem. Soc.*, **84**, 1734 (1962).

(22) Extensive research is in progress to substantiate this point and to determine other solvent effects.

(23) See, for example, D. J. Cram, *et al.*, *J. Am. Chem. Soc.*, **83**, 3696 (1961); S. Winstein, *et al.*, *ibid.*, **83**, 885 (1961); and A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).
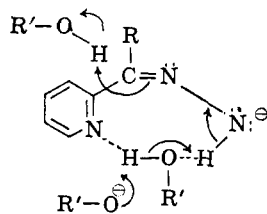
Figure 7.

substituents (left-handed portion of the Hammett plot) are favoring the reaction (ρ approximately $+1.0$) by balancing somewhat the electronegativity of the two nitrogen atoms of the hydrazone anion, increasing the fractional negative charge at the carbon terminal, and thus favoring the C–H bond formation. As the electron-attracting character of the substituents increases further, however, a second, unfavorable factor comes into play (ρ approximately -0.8). The smaller the negative charge that remains at the N–H terminal, the stronger is the hydrogen bond which binds the first hydroxylic solvent molecule to the hydrazone anion, and the "harder" and bigger the solvation shell which is built up at the N–H terminal. Hence the base R'–O⁻ becomes less effective in the N–H bond breaking process. Since the observed $\Delta S^{\ddagger}$ values take into account the highly complex over-all change in the degrees of freedom of the hydrazone anion, solvent molecules, and base, it is not surprising that one fails to note a relationship between the enthalpy and entropy values and substituent constants. On the other hand, it seems hardly accidental that structural features which were at first thought[2] capable of promoting an intramolecular hydrogen transfer are present in compounds exhibiting the lowest enthalpies and the highest negative entropies of activation (see Table II). The behavior of the 2-pyridyl system, for example, can be rationalized in the light of the proposed mechanism by visualizing a hydroxylic solvent molecule "frozen" between the "ortho substituent" and the N–H terminal, with the double consequence of making it relatively easy for another hydroxylic solvent molecule to approach the carbon terminal (thus promoting the displacement of the negative charge in that direction), and also relatively easy for the base R'–O⁻ to approach the N–H terminal. The high degree of organization which this mechanism implies (Fig. 7) explains the exceptionally negative entropy values which are observed. Similar explanations can be postulated in all cases in which an ortho-acceleration effect seems to operate. In accord with this mechanism, the "ortho substituent" simply aids in the fixation of a hydroxylic solvent molecule at the N–H terminal, while the previously implied[2] intramolecular hydrogen transfer mechanism should be sufficiently different from the more general intermolecular hydrogen transfer mechanism to cause scattering of the points corresponding to the two mechanisms on the enthalpy–entropy graph.

Phosphate Esters. I. Catalytic Hydrolysis of p-Nitrophenyl Dihydrogen Phosphate by Ceric Ion Precipitates in the pH Range 2-7[1]

By Frank Millich[2] and Elbert L. Hayes, Jr.[3]

No catalytic influence could be observed upon the hydrolysis of the monoanion of p-nitrophenyl dihydrogen phosphate by hydronium, calcium, ferric, or ceric ions in monophasic aqueous solution. However, catalysis is found upon the occurrence of precipitate formation when $Ce(NH_4SO_4)_4$ is solvolyzed. Catalysis takes place in the solid phase as substrate becomes associated. The catalyst is partly defined, and two maxima, at pH 4.5 and 6.0, are revealed in a pH–rate profile of the catalyzed hydrolysis at 49°. Relation of this catalysis to enzymic acid–phosphorylase activity is briefly discussed.

Introduction

Kinetic studies have revealed that the following facts seem to be fairly general for acid hydrolysis of simple monoesters of phosphoric acid: (a) the monoanion is more susceptible to hydrolysis than the corresponding neutral or dianionic conjugate species; (b) hydrolysis of the monoanion proceeds by P–O bond cleavage; and (c) its kinetic rate depends upon the concentration of the monoanion, but the transition state does not specifically involve catalysis by hydronium ion. A brief report in the literature[4] has indicated that these three facts obtain in the acid hydrolysis of p-nitrophenyl dihydrogen phosphate (PNPP) monoanion. The details of hydrolysis of dianions of simple phosphate monoesters h... been studied extensively because of the very ... ver relative reactivity of these species. This p... scribes results of a study undertaken to evaluate whether fact c remains unaltered in the presence of polyvalent metal ions, but which has progressed further to a study of heterophasic catalysis with ceric ion.

The catalytic activity of substrate-associated metal ions in phosphate ester hydrolysis and several other heterophasic reactions has been the subject of study by E. Bamann and his collaborators for a quarter century.[5] They have shown these catalysts to mimic very many of the properties characteristic of enzymes. Much of the catalytic activity of metal ions and of enzymes must depend on common physical and chemical phenomena. Elucidation of the mechanism of action of the latter may profitably be approached through a study of the former without the narrow

(1) This project was partly supported by a National Science Foundation grant, NSF-G 21590, of the Undergraduate Science Education program.

(2) To whom correspondence should be directed.

(3) Participant in National Science Foundation Undergraduate Research Program, 1962–1963.

(4) See C. A. Vernon in "Phosphoric Esters and Related Compounds," Special Publication No. 8, The Chemical Society, London, 1957, pp. 19–22.

(5) For a review, see H. Trapmann, Arzneimittel-Forsch., **9**, 341, 403 (1959).