[Contribution from the Department of Chemistry, Duquesne University]

Kinetics of the Wolff–Kishner Reaction of Diaryl Ketone Hydrazones

By H. Harry Szmant, Hugh F. Harnsberger, Thomas J. Butler and Walter P. Barie[1]

Received August 8, 1951

The Wolff–Kishner reaction of the diaryl ketone hydrazones is shown to be first order with respect to the base catalyst and the hydrazone. The mechanism of this reaction appears to involve the formation of an anion of the hydrazone, and the rate-determining step is thought to be a shift of a hydrogen in the intermediate hydrazone anion. From the large range of the observed heats and entropies of activation encountered in this study it is concluded that the rate-determining hydrogen shift can occur in more than one way.

In spite of the wide applicability of the Wolff–Kishner reaction in organic synthesis little is known about its mechanism.[2,3] The only kinetic study reported in the literature appears to be that of Balandin and Vaskevich[4] who found the decomposition of cyclohexanone hydrazone over platinum and solid potassium hydroxide to follow a first-order rate law. Several possible mechanisms were recently suggested by Seibert.[5] He proposes the formation of the hydrazone anion as the initial step and the subsequent decomposition of this anion or a diimine ($R_2CHN{=}NH$). Todd[6] studied the thermal decomposition of several substituted hydrazones over solid sodium or potassium hydroxide and platinum at 250° and concluded that this reaction occurred by a free radical mechanism and *via* the diimine. Unlike the studies of Balandin and Todd the present work was carried out in a homogeneous reaction system, no platinum catalyst being employed.

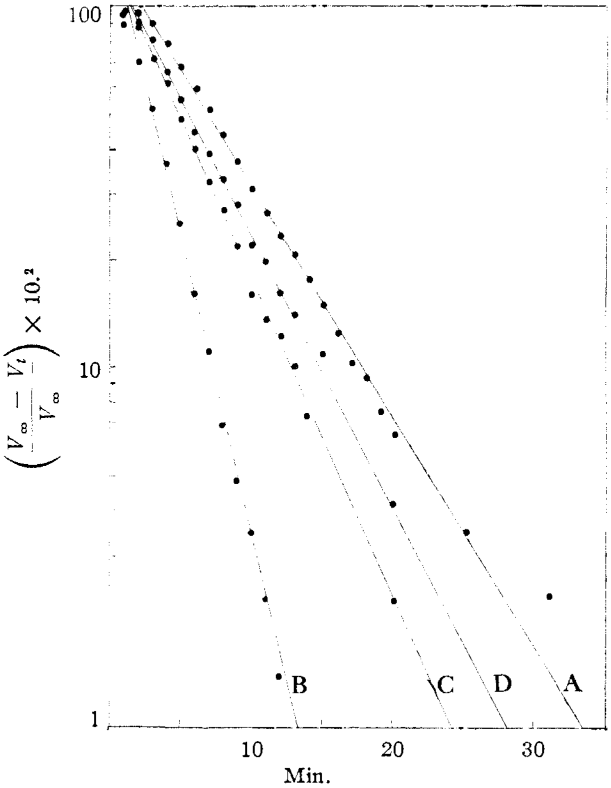


Fig. 1.—Evolution of nitrogen in the Wolff–Kishner reaction of benzophenone hydrazone at: A, 190.5°; B, 199.5°; C, 210.5°; D, 221.5°.

Experimental and Results

The apparatus used for the kinetic studies consisted of a reaction flask immersed in a constant temperature oil-bath and connected through a vertical condenser to a gas buret and manometer.[7] A glass capsule containing the hydrazone sample was held above the reaction flask by an iron rod which could be moved by a magnet. The flask was charged with 100 cc. of an alkoxide solution prepared by dissolving metallic sodium in purified butyl carbitol. The basicity of the reaction mixture was determined by titration with standard hydrochloric acid. When the apparatus had come to thermal equilibrium it was closed to the atmosphere and the hydrazone was released into the basic butyl carbitol medium. The dissolution of the sample was found to occur almost immediately upon contact with the hot solution. The barometric pressure, the temperature of the water in the gas buret and of the room were noted during the experiments; any abnormal changes in these conditions for which no corrections could be made were sufficient cause to discard the given run.

In Table I there are listed representative kinetic experiments carried out with eight hydrazones of diaryl ketones in the range of 190–221.5°. The rate constants listed in Table I are the bimolecular rate constants obtained from the slopes of the log $((V_\infty - V_t)/V_\infty)$ *vs.* time plots. The linearity of these plots illustrated in Fig. 1 demonstrates the fact that the reaction follows the rate law $-d(V_\infty - V_t)/dt = k[V_\infty - V_t][B^-]$, where V_∞ and V_t are the volumes of nitrogen evolved at completion of the reaction and at time t, respectively, and $[B^-]$ represents the concentration of the base catalyst. It is noted that the volumes of gas evolved correspond closely to the theoretical volume of nitrogen in the temperature range of this study. Below 190° there was noted a progressive decrease in the final volume of the gas evolved during the reaction. The non-quantitative nitrogen evolution, the formation of more highly colored reaction products and the non-linearity of the log k *vs.* $1/T$ plot, all point to the presence of reactions other than the Wolff–Kishner that occur competitively in the temperature range of 130–190°. Since this phase of the Wolff–Kishner reaction is still under investigation the results will appear in a future publication from these laboratories. In Fig. 2 there is demonstrated the first-order base dependence of the reac-

---

[1] This material was presented in part at the Cleveland Meeting of the A. C. S., April, 1951, and is taken from the M.S. theses of T. J. B. and W. P. B.

[2] D. Todd, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 378–422.

[3] E. R. Alexander, "Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 275.

[4] A. A. Balandin and D. N. Vaskevich, *J. Gen. Chem.* (*U.S.S.R.*), **6**, 1878 (1936).

[5] W. Seibert, *Chem. Ber.*, **80**, 494 (1947); **81**, 266 (1948).

[6] D. Todd, This Journal, **71**, 1356 (1949).

[7] The apparatus was similar to that described recently by M. Schubert (*ibid.*, **71**, 2640 (1949)).

TABLE I

REPRESENTATIVE EXPERIMENTAL RESULTS

Ketone hydrazone	Temp., °C.	Initial hydrazone mole/l.	Initial base mole/l.	Final, % theoretical "nitrogen"	k_r × 10² l./mole-sec.
Phenyl 2-thienyl	221.5	0.01485	0.0392	100.0	20.41
	210.5	.01485	.0360	100.0	13.25
	199.5	.01485	.0497	99.0	9.50
	190.5	.01716	.0602	97.0	6.43
Phenyl *p*-chlorophenyl	221.5	0.00867	0.0395	100.0	13.32
	210.5	.01518	.0626	100.0	9.54
	199.5	.01520	.0497	99.0	5.81
	190.5	.01460	.0800	97.0	3.75
Di-(2,4-dichlorophenyl)	221.5	0.00940	0.0531	100.0	11.23
	210.5	.01132	.0626	100.0	5.53
	199.5	.01392	.1055	93.0	3.28
	190.5	.03102	.1324	97.0	2.14
Diphenyl	221.5	0.01534	0.0383	100.0	7.55
	210.5	.00869	.0800	100.0	4.25
		.01532	.0320	100.0	4.32
		.01532	.0100	100.0	4.42
	199.5	.01831	.2688	100.0	2.36
	190.5	.01770	.1400	84.0	1.68
Di-(*p*-methoxy phenyl)	221.5	0.00860	0.0544	100.0	3.51
	210.5	.01100	.0140	92.0	2.51
	199.5	.00924	.2300	94.0	1.17
	190.5	.01172	.2210	75.0	0.67
Phenyl *p*-xenyl	221.5	0.00445	0.0420	100.0	10.21
	210.5	.01103	.0316	100.0	5.03
	199.5	.01088	.1055	100.0	2.70
	190.5	.00396	.1400	100.0	1.57
Phenyl *p*-phenoxyphenyl	221.5	0.00738	0.0420	100.0	10.47
	210.5	.01215	.0647	98.0	7.12
	199.5	.01271	.0720	100.0	2.47
	190.5	.00920	.1330	88.0	1.55
Di-(*p*-chlorophenyl)	221.5	0.00870	0.0132	100.0	26.75
	210.5	.00943	.0380	100.0	14.83
	199.5	.01310	.0392	92.0	5.43
	190.5	.01710	.0428	83.0	2.10

tion rate in the case of benzophenone hydrazone, and identical relationships were observed with the remaining hydrazones. In Figs. 3–5 there are shown the log $k_r/kT/h$ *vs.* $1/T$ plots from which the heats and entropies of activation listed in Table II were obtained. Although the experimental errors were, in general, very small, the slopes of the log $((V_\infty - V_t)/V_\infty)$ *vs.* time plots were drawn by the least squares method, and the mean deviation of the slope measurements is estimated to be less than two per cent.

TABLE II

HEATS AND ENTROPIES OF ACTIVATION

Ketone hydrazone	$\Delta H^{\ddagger}$, kcal. mole⁻¹	$\Delta S^{\ddagger}$, cal. deg.⁻¹ mole⁻¹
Phenyl 2-thienyl	15.7	−31.0
Phenyl *p*-chlorophenyl	18.2	−26.6
Di-(2,4-dichlorophenyl)	23.3	−16.8
Diphenyl	23.6	−17.0
Di-(*p*-methoxyphenyl)	24.5	−16.4
Phenyl *p*-xenyl	26.7	−10.1
Phenyl *p*-phenoxyphenyl	29.3	− 4.4
Di-(*p*-chlorophenyl)	37.4	13.8

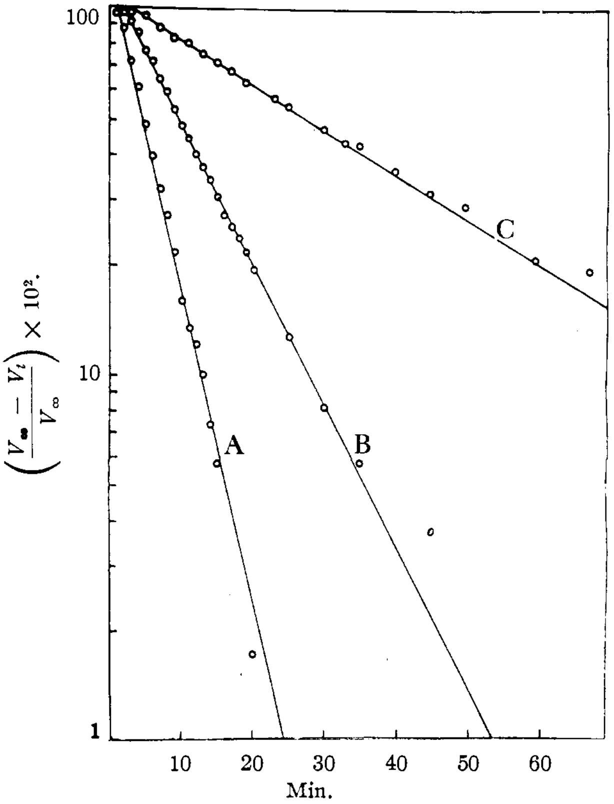


Fig. 2.—The base dependence of the Wolff–Kishner reduction of benzophenone hydrazone at 210.5°; [BPH] = benzophenone hydrazone concn.; [B:⁻] = base catalyst concn.: A, [BPH] = 0.00869 mole/l., [B:⁻] = 0.0800 mole/l., k_r = 4.25 × 10⁻² l. mole⁻¹ sec.⁻¹; B, [BPH] = 0.01532 mole/l., [B:⁻] = 0.0320 mole/l., k_r = 4.32 × 10⁻² l. mole⁻¹ sec.⁻¹; C, [BPH] = 0.01532 mole/l., [B:⁻] = 0.0100 mole/l., k_r = 4.42 × 10⁻² l. mole⁻¹ sec.⁻¹.

The hydrazones were prepared in the course of another study[8] from the corresponding ketones and 85% hydrazine hydrate.

Discussion

Since the rate of the Wolff–Kishner reaction is directly dependent on the concentration of the base catalyst it is assumed that the first step of the mechanism involves an acid–base equilibrium

$$R_2C{=}\ddot{N}\ddot{N}H_2 + B{:}^{(-)} \rightleftarrows R_2C{=}\ddot{N}\underset{\cdot\cdot}{\ddot{N}}H^{(-)} + BH\ (K_1) \qquad (1)$$

The acid ionization constants of hydrazones have, as far as we know, not been reported in the literature. On the basis of a recently completed study of the basicity of various hydrazones[9] the value of K_1 is estimated[10] to be of the magnitude of 10^{-6}.

---

(8) H. H. Szmant and C. McGinnis, THIS JOURNAL, **72**, 2890 (1950); **74**, 240 (1952).

(9) H. F. Harnsberger, H. H. Szmant and E. Cochran, manuscript in preparation.

(10) Since $K_1 = ((R^-)(BH)/(RH)(B^-)) = K_{a(RH)}/K_{a(BH)}$, where RH = hydrazone, and BH = carbitol, a value for K_1 may be estimated by assuming that $K_{a(RH)} \cong 10^{-26}$ and $K_{a(BH)} \cong 10^{-20}$. The estimate of $K_{a(RH)}$ is made by considering a parallelism between anilines and hydrazones: If $pK_{R'NH_2} - pK_{R'NH_3^+} = 18.5 - (-3.6) \cong 22$ (where R′ = 2.4-dinitrophenyl) then $pK_{a(RH)} - pK_{a(RH_2^+)} \cong 22$ (where RH = hydrazone). The $pK_{a(RH_2^+)}$ as measured in ethanol[9] has a typical value of about 5, and $pK_{a(BH)}$ is assumed to be ≅ 20 (slightly larger than the pK_a of ethanol which is 19.1). The value of $pK_{a(R'NH_2)}$ is taken from the work of Stearns and Wheland (THIS JOURNAL, **69**, 2025 (1947)).

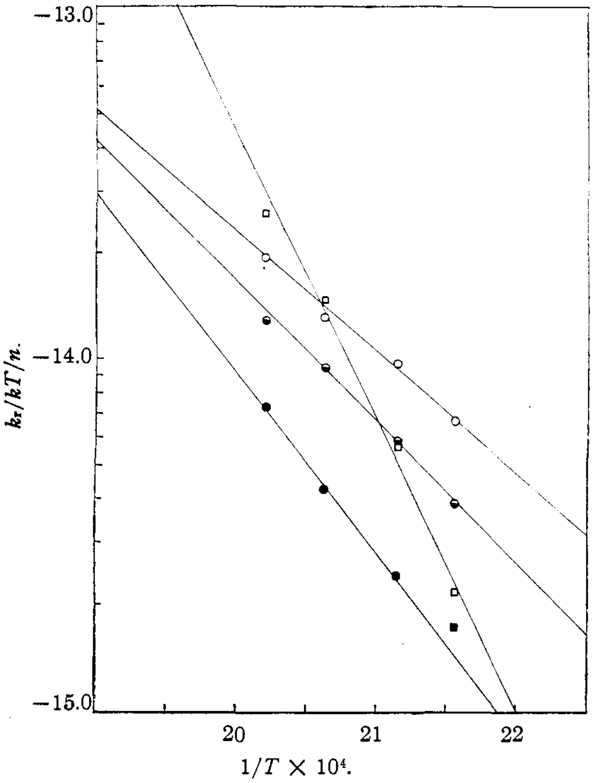
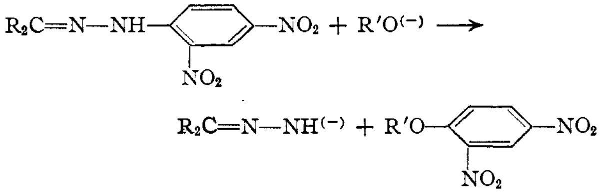


Fig. 3.—Heats and entropies of activation plots for the Wolff–Kishner reductions of the hydrazones of benzophenone, ●; *p*-chlorobenzophenone, ◒; *p,p'*-dichlorobenzophenone, □; 2-thienyl phenyl ketone, ○.

The value of K_1 will be smaller when a weaker base (than sodium carbitolate) is employed as catalyst; still the value of K_1 cannot be prohibitively small since in some procedures an excess of hydrazine is used as the base catalyst.[2] In this connection it should be pointed out that the hydrazones of diaryl ketones are expected to be stronger acids than the hydrazones of dialkyl ketones because of the resonance stabilization of the anions of the former. This expectation is substantiated by the observed differences in basicities of the hydrazones of diaryl and alkaryl ketones.[9]

It has been recently shown[10a] that 2,4-dinitrophenylhydrazones can give typical Wolff–Kishner reduction products on treatment with base. The mechanism of this reaction as well as that of the Wolff–Kishner reduction of semicarbazones under anhydrous conditions[10b] would be expected to involve the formation of the same hydrazone anion discussed above.



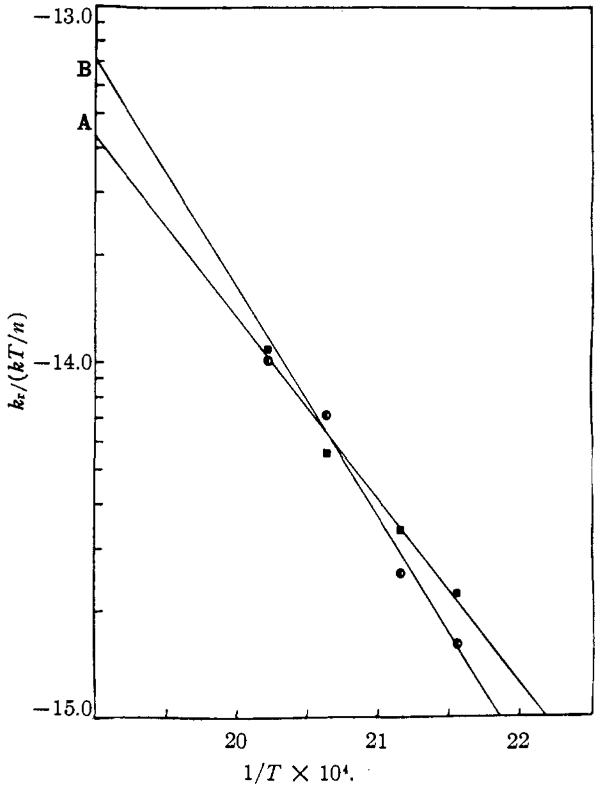
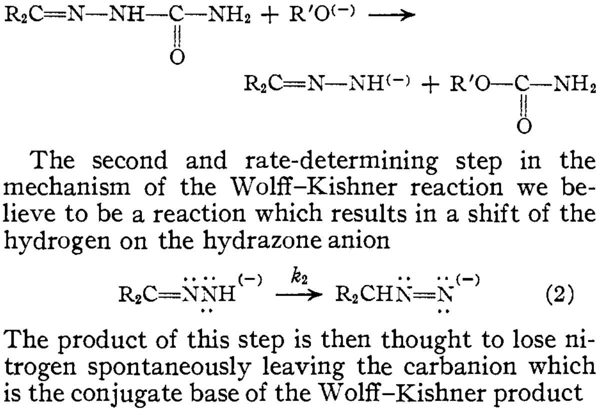


Fig. 4.—Heats and entropies of activation plots for the Wolff–Kishner reductions of the hydrazones of di-(2,4-dichlorophenyl) ketone, ■ (A); phenyl *p*-phenoxyphenyl ketone, ◐ (B).



$$R_2C{=}N{-}NH{-}\underset{\underset{O}{\|}}{C}{-}NH_2 + R'O^{(-)} \longrightarrow R_2C{=}N{-}NH^{(-)} + R'O{-}\underset{\underset{O}{\|}}{C}{-}NH_2$$

The second and rate-determining step in the mechanism of the Wolff–Kishner reaction we believe to be a reaction which results in a shift of the hydrogen on the hydrazone anion

$$R_2C{=}\ddot{N}\ddot{N}H^{(-)} \xrightarrow{k_2} R_2CH\ddot{N}{=}\ddot{N}^{(-)} \quad (2)$$

The product of this step is then thought to lose nitrogen spontaneously leaving the carbanion which is the conjugate base of the Wolff–Kishner product

$$R_2CH{-}\ddot{N}{=}\ddot{N}^{\cdot(-)} \xrightarrow{\text{(very fast)}} R_2CH\!:^{(-)} + N_2 \quad (3)$$

Since the diarylmethanes obtained in this work are very weak acids as compared to the hydroxylated solvent,[11] the carbanion produced in (3) reacts with the solvent to restore the base used up in equilibrium (1)

$$R_2CH\!:^{(-)} + BH \longrightarrow R_2CH_2 + B\!:^{(-)} \quad (4)$$

The formation of the carbanion in (3), for the reason mentioned above, could not be proved under the conditions of the experiments described here. However, in another series of experiments in which benzophenone hydrazone was allowed to react with

---

[10a] N. O. V. Sonntag, E. I. Becker and P. E. Spoerri, Abstracts of Chicago meeting of the A. C. S., September, 1950. Also private communication from Dr. E. I. Becker.

[10b] Eisenlohr and Polenske, *Ber.*, **57**, 1639 (1924).

[11] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 50.

sodamide in xylene, it was possible to prove the presence of the diphenylmethane carbanion by carbonation of the reaction mixture and the isolation of diphenylacetic acid.[12]

An alternative mechanism of the Wolff–Kishner reaction assumes the formation and subsequent decomposition of a diimine[5,6] from the hydrazone. There is actually very little experimental evidence to suggest that the diimine intermediate is essential, and furthermore, it is impossible at this time to distinguish between the above and the diimine mechanisms on kinetic grounds.

$$R_2C{=}N{-}NH_2 \rightleftarrows R_2CH{-}N{=}NH \text{ (base catalyzed)} \quad (1a)$$

$$R_2CH{-}N{=}NH + \overset{(-)}{B}: \longrightarrow R_2CH{-}\ddot{N}{=}\ddot{N}:^{(-)} + BH \quad (2a)$$

$$R_2CH{-}\ddot{N}{=}\ddot{N}:^{(-)} \longrightarrow R_2\overset{(-)}{CH}: + N_2 \quad (3)$$

It is known the equilibrium (1a) favors the hydrazone (particularly in non-substituted hydrazones), and in the process of obtaining the diimine there is obtained the resonating anion $R_2C{=}\ddot{N}{-}\ddot{N}H^{(-)} \leftrightarrow R_2\underset{(-)}{\ddot{C}}{-}\ddot{N}{=}\ddot{N}H$ which, in our opinion, undergoes the rate-determining formation of $R_2CH{-}\ddot{N}{=}\ddot{N}:^{(-)}$. Since statement (2) does not imply the exact mechanism by which the $R_2CH{-}N{=}\ddot{N}:^{(-)}$ is formed, equations (1a) and (2a) represent one of the possible paths. Step (2) leads to the following rate law for the Wolff–Kishner reaction

$$\frac{d(N_2)}{dt} = k_2K_1\frac{[R_2C{=}NNH_2][B:^{(-)}]}{[BH]} = k_r\frac{[R_2C{=}NNH_2][B:^{(-)}]}{[BH]} \quad (5)$$

It can be seen from (5) that the observed rate constants are proportional to the product of the equilibrium constant K_1 and of the specific rate constant k_2 in each given case. From this it follows that the heats and entropies of activation which were obtained from the temperature dependence of k_r are the sums of the heats and entropies of activation of the rate-determining step (2) and the heats and entropies of the equilibrium (1). Even a tenfold variation in the equilibrium values of the various hydrazones studied here, however, does not justify the observed range in the heats and entropies of activation (Table II) unless one assumes that step (2) can occur by paths having different heats and entropies of activation. It is seen that the heats of activation are by no means the chief determining factor on the magnitude of the rates of this series of homologous reactions. Although insufficient information is available at this time to explain quantitatively the variation of the values listed in Table II with the structural changes in the hydrazones, it is possible to offer the following thoughts.

The exceptionally low heat of activation of the thiophene compound agrees with the observation of the remarkable ease of Wolff–Kishner reactions of α-thienyl carbonyl compounds by King and Nord,[13] and is probably related to the ease with which the hydrazones of 1,2-diketones[5] or of *o*-nitrophenylcarbonyl compounds[5] react. The unusually high negative entropy of activation of 2-thienyl phenyl ketone hydrazone (−31 e.u.) suggests that the hydrogen transfer in this type of hydrazone occurs intramolecularly by a cyclic transition state. The rigidity of this transition state would explain the large negative entropy, and the intramolecular transfer of hydrogen would justify the low heat of activation. The similarity of the situations in the Wolff–Kishner reaction of the compounds mentioned above is obvious from the inspection of the equations

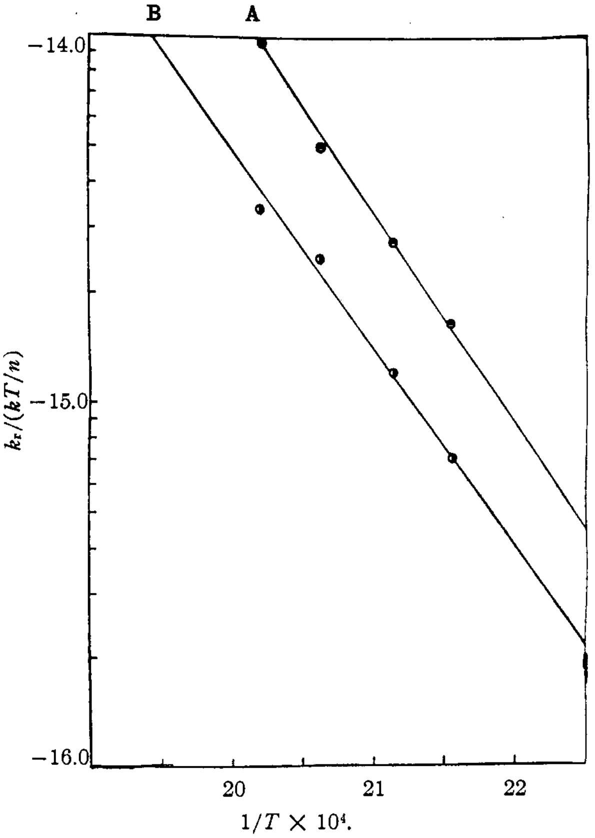
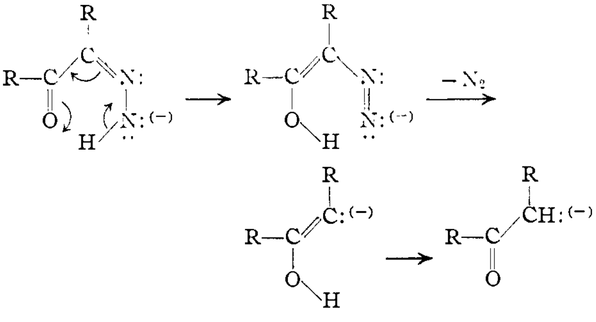
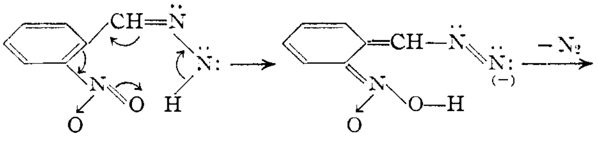


Fig. 5.—Heats and entropies of activation plots for the Wolff–Kishner reductions of the hydrazones of phenyl *p*-xenyl ketone, ◓ (A); di-(*p*-methoxyphenyl) ketone, ◑ (B).

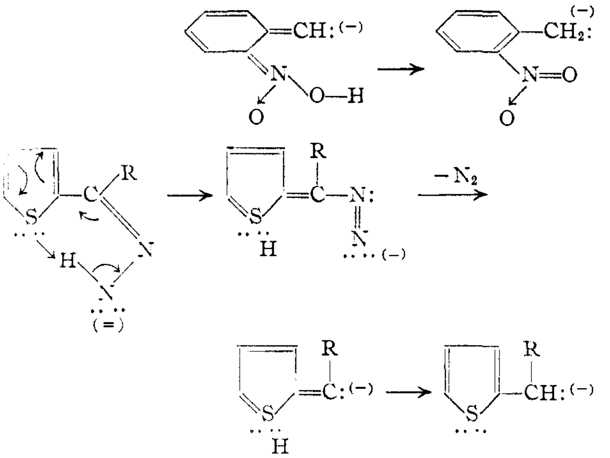




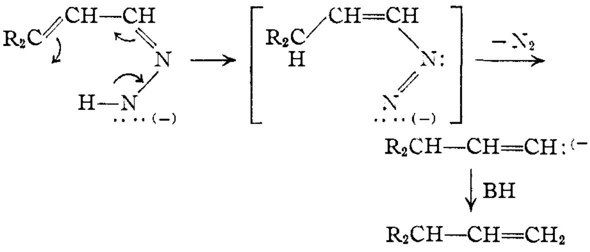
---

[12] H. H. Szmant and C. McGinnis, unpublished work.

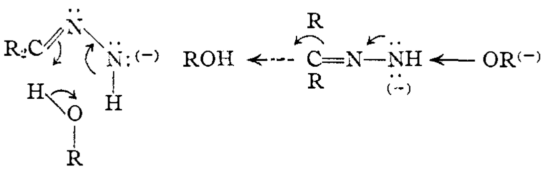
[13] W. J. King and F. F. Nord, *J. Org. Chem.*, **14**, 638 (1949).



An additional argument in favor of the cyclic transition state is offered by the results of Wolff–Kishner reactions in α,β-unsaturated systems.[14,15]



Whenever the intramolecular hydrogen transfer is inhibited by the structural characteristics of the hydrazone anion, the hydrogen shift probably involves additional solvent molecules and may be represented by (A) or (B). Of these two, the latter concerted mechanism is more probable since the hydrazones of sterically hindered ketones are known to resist the Wolff–Kishner reaction and to require more drastic conditions. Thus, camphor hydrazone shows an exceptional resistance to the reduction,[2,16] and recently it has been shown that 11-ketosteroids are reduced by the Wolff–Kishner procedure only under vigorous conditions.[17] The inspection of Table II shows that it is difficult to correlate quantitatively the changes in the heats and entropies of activation with the electronic nature of the substituents when the intramolecular hydrogen transfer mechanism is excluded. There appears to be a trend toward higher heats of activation and more positive entropies as the electron-withdrawing character of the substituents is increased. Thus, the p,p'-dichloro compound represents the extreme, and the *p*-phenyl and *p*-phenoxy compounds are nearby. However, the position of the monochlorobenzophenone hydrazone is unexpected, while the position of the 2,2′,4,4′-tetrachlorobenzophenone hydrazone may be justified by assuming an intramolecular hydrogen transfer mechanism. It is hoped that the additional work now in progress will elucidate the dependence of the heats and entropies of activation on the electronic nature of the substituents.[18]



(A) (B)

The existence of a homogeneous, base-catalyzed Wolff–Kishner reaction mechanism does not exclude the possibility of mechanisms by heterogeneous catalysis. It has been already pointed out by Todd[2] that the use of platinum catalyst was introduced by Kishner when certain cyclic ketone hydrazones failed to react in the presence of base alone. In sterically hindered ketone derivatives where the hydrogen transfer discussed above occurs with difficulty, it is very likely that a heterogeneous catalyst facilitates the Wolff–Kishner reduction.

Pittsburgh 19, Penna.

---

(14) G. Lardelli and O. Jeger, *Helv. Chim. Acta*, **32**, 1817 (1947).

(15) D. H. R. Barton, *et al.*, *J. Chem. Soc.*, 2456 (1949).

(16) This fact is substantiated by preliminary kinetic data obtained in this Laboratory.

(17) R. B. Moffett and J. H. Hunter, This Journal, **73**, 1973 (1951).

(18) It has been found that in the acetophenone hydrazone series the *p*-methoxy group does not cause drastic changes, while the *p*-chloro group gives a large increase in the heat of activation and a much less negative entropy of activation.