4 and **6**. Benzaldehyde formation was monitored at 100 °C on a 12 ft × $\frac{1}{8}$ in. column containing 4% QF-1 and 1% Carbowax 20 M on 60/80 Chromosorb G. Formation of **6** was monitored on the same column at 150 °C. The formation of **4** and disappearance of ketones were monitored at 110–130 °C on a 3 ft × $\frac{1}{8}$ in. column containing 5% SE-30 on Chromosorb W.

All IR spectra were recorded on a Perkin-Elmer 237 B spectrometer with either neat samples or Nujol films and were calibrated against polystyrene. ^{1}H NMR spectra were recorded on a Varian T-60 spectrometer. Mass spectra were recorded on a Hitachi-Perkin-Elmer RMU-6 mass spectrometer, with 70 V ionizing voltage. UV spectra were recorded on a Unicam SP800 or Cary 14 instrument. ^{13}C NMR spectra were measured by Dr. R. C. Schoening on a Brucker HFX-10 spectrometer set at 22.6 MHz with the usual Fourier Transform and broad band proton decoupling methods. Freon 21 solutions containing 40% **1** by volume were held in a 10-mm diameter sample tube containing a thermometer.

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(1) This work was supported by National Science Foundation Grants MPS 70-01653 and CHE 76-11892.
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Mechanistic Aspects of the Wolff–Kishner Reaction. 7.[1] The W–K Reaction of Benzophenone Hydrazone in Dimethyl Sulfoxide

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Received June 21, 1976

Abstract: The kinetics and activation parameters of the W–K reaction of benzophenone hydrazone were determined in absolute Me_2SO in the presence of potassium *tert*-butoxide, sodium dimsyl, and other base catalysts. Results are presented concerning the solvation of hydrazones by Me_2SO, their ionization to hydrazone anions, and the roles of protic and basic solvents in the W–K reaction are elucidated. Also, the kinetics of the homogeneous W–K reaction in Me_2SO is compared with the heterogeneous reaction described in the literature[2] and with the conventional W–K reaction in hydroxylic solvents.

Introduction

The report of Cram, Sahyun, and Knox[2] concerning the room-temperature W–K reaction of benzophenone hydrazone (I) in a mixture of Me_2SO and potassium *tert*-butoxide (II) prompted a detailed study of the process under the reported and related experimental conditions. In the course of this study it became necessary to examine the role of protic and basic reagents that can be present in the reaction mixture.

Results and Discussion

Repetition of the experiments described by Cram and coworkers[2] revealed that one is dealing with a heterogeneous mixture of I, II, and Me_2SO, and this condition is obviously unsuitable for the determination of the kinetics and of the activation parameters of the W–K reaction. However, larger volumes of Me_2SO did give homogeneous solutions of I and II, but then it was found that the use of rigorously dried Me_2SO and of a large molar excess of freshly sublimed II converted I to its corresponding anion, and this process was accomplished by a very sluggish W–K reaction. Because of the very slow W–K reaction under these experimental conditions, it was possible to examine the spectrum of the anion of I and to demonstrate that it exhibited a characteristic maximum at 393 nm. The addition of solutions of sodium dimsyl to I gave identical results. The use of a 100-fold excess of II produced satisfactory Beer–Lambert plots for the hydrazone anion derived from I, as well as for those derived from the *p,p′*-dimethoxy- and *p,p′*-dichlorobenzophenone hydrazones (Figures 1 and 2). The maxima of the latter anions were located at 375 and 404 nm, respectively, in accord with the expected effect of these substituents on the excitation energies in delocalized anions. The molar absorptivities of the three hydrazone anions were found to be 24 000, 20 300, and 26 700, respectively, and were calculated on the assumption that the hydrazones were completely ionized in a 100-fold excess of base.

Attempts to determine the equilibrium constant for the ionization of I to its corresponding anion were only partially successful because of the sensitivity of the solutions to atmospheric oxygen and moisture. The latter caused a deterioration

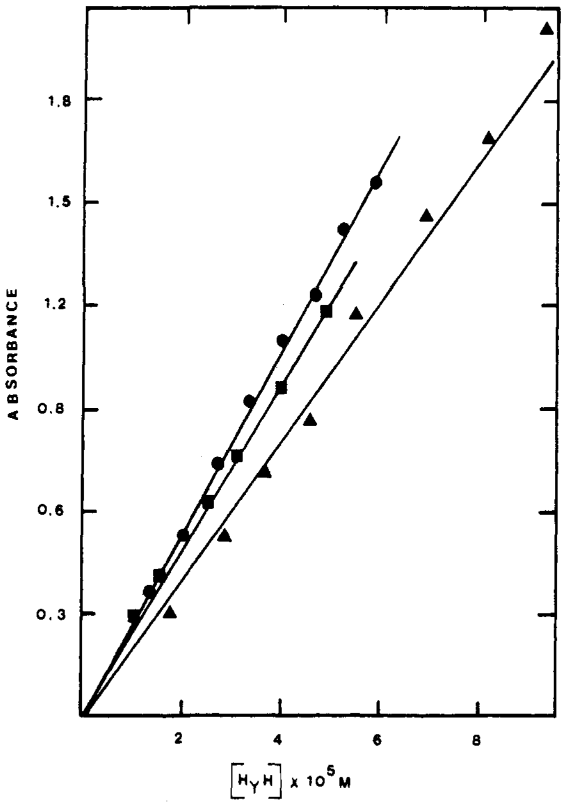


Figure 1. Beer-Lambert plot of diaryl ketone hydrazone anions produced in a dimethyl sulfoxide-potassium *tert*-butoxide system; the hydrazones (HyH) of benzophenone (■), *p,p'*-dimethoxybenzophenone (▲), and *p,p'*-dichlorobenzophenone (●).

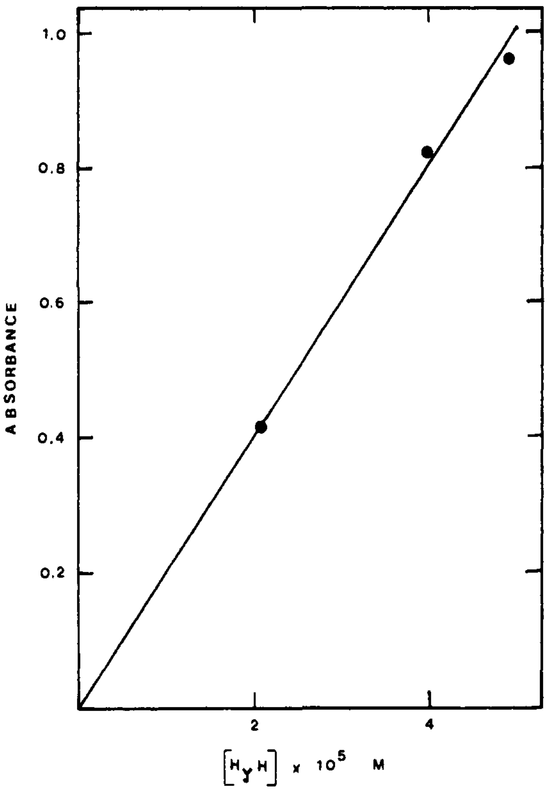


Figure 2. Beer-Lambert plot of benzophenone hydrazone anion produced in sodium methylsulfinyl carbanion.

Table I. Effect of *tert*-Butyl Alcohol on the Wolff-Kishner Reaction of Benzophenone Hydrazone ([I] = 0.195 M) in Dimethyl Sulfoxide in the Presence of Potassium *tert*-Butoxide ([II] = 0.081-0.083 M) at 37 °C

t-BuOH [molarity]$_0$	$\frac{[I]}{[II]}$	$k_1 \times 10^6$, s^{-1}
0.0826	2.41	8.19
0.0835	2.41	8.02
0.1239	2.41	8.56
0.1614	2.41	8.72
0.3453	2.36	10.3
0.6907	2.36	11.8
1.2278	2.35	9.60
2.4557	2.35	4.71
4.0593	2.40	1.62
6.0889	2.40	0.68

of the solutions with increasing dilutions[3] and produced decreasing values of the apparent equilibrium constants. However, the use of a solution 4 × 10^{-4} M in II, and varying volumes of a solution 8 × 10^{-4} M in I, gave rise to values for the dissociation constant that ranged from 3 down to 0.2 (at 23-24 °C). Assuming that the highest value is most reliable and that the pK_a value for *tert*-butyl alcohol[5] is 19, one can estimate a pK_a value of 18.5 for I.

The yellow color characteristic of the anion of I developed instantly in Me_2SO solutions ca. 0.2 m in I and ca. 0.4 m in sodium dimsyl, but these solutions failed to liberate significant volumes of nitrogen (maximum 3-4% of theory) when kept at room temperature for a period of 8 days. These experiments prove beyond any reasonable doubt that the formation of the hydrazone anion is not sufficient cause for the occurrence of the W-K reaction. Incidentally, these experiments also prove that the hydrazone anion does not undergo an intra- or intermolecular prototropic shift, since the anion of the diazene is

$$R_2C{=}N{-}NH^- \longrightarrow R_2CH{-}N{=}N^- \quad R, \text{phenyl}$$

known[6] to liberate nitrogen very readily ($k = 5 \times 10^{-2}\ M^{-1}\ s^{-1}$ in Me_2SO at 24°C).

The absence of a W-K reaction when the hydrazone anion was generated by means of sodium dimsyl proves that the reaction requires the presence of a more willing proton donor than Me_2SO itself (pK_a 31.3).[7] In the case of the formation of the hydrazone anion from II, it stands to reason that the process generates *tert*-buyl alcohol at or near the reaction site and that this hydroxylic solvent molecule becomes intimately involved in the W-K reaction. Under the latter reaction conditions it was of interest to determine the effect of the presence of additional *tert*-butyl alcohol on the rate of reaction. The results (Table I) are presented in Figure 3. At a constant concentration of II (ca. 0.082 M), the introduction of "external" *tert*-butyl alcohol is seen to give an almost proportional increase in the pseudo-second-order rate constant until the molarity of the alcohol reaches the value of 0.7-0.8 M. Above this concentration range, the presence of *tert*-butyl alcohol becomes detrimental to the W-K reaction. Possible reasons for the latter effect may be: (1) a decrease in the dielectric constant of the reaction mixture; (2) a decrease in the dissociation of the hydrazone anion contact ions; and (3) a deactivation of Me_2SO in the W-K reaction through competitive hydrogen bonding.

The last mentioned point seems of greatest interest since it fits the previously postulated hypothesis[8] that the rate-limiting step of the W-K reaction involves not only the hydrazone anion but also a protic and a basic solvent, and that the major reason for the ability of Me_2SO to promote the W-K reaction in the presence of a hydroxylic solvent is its superior basicity. In order to test this point further, a series of experiments was performed in which pyridine was added to a reaction mixture of I, II, and Me_2SO (Table II). Figure 4 shows that pyridine indeed causes an increase in the pseudo-second-order rate constants.

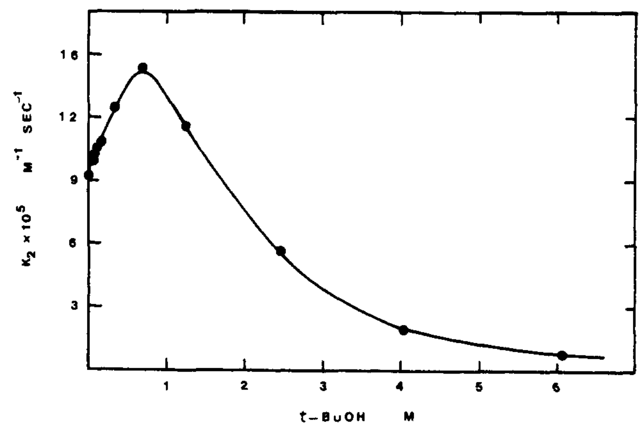


Figure 3. The effect of "external" *tert*-butyl alcohol on the rate of the Wolff-Kishner reaction of benzophenone hydrazone in absolute dimethyl sulfoxide in the presence of potassium *tert*-butoxide at 37 °C.

Table II. Effect of Pyridine on the Wolff-Kishner Reaction of Benzophenone Hydrazone ([I] = 0.195 M) (BPH) in Dimethyl Sulfoxide in the Presence of Potassium *tert*-Butoxide (II) as 37 °C

PTB, molarity	Pyridine, molarity	[I]/[II]	$k_1 \times 10^6$, s^{-1}	$k_2 \times 10^5$, $M^{-1} s^{-1}$
0.0836	1.5383	2.33	7.57	9.06
0.0836	3.0767	2.33	8.02	9.60
0.0836	5.5147	2.33	8.19	9.80
0.0836	8.1867	2.33	8.53	10.20
0.0000	6.1580[b]		0.34	0.0054[a]
0.0000	12.40[c]		0.18	0.0015[a]

[a] Calculated on the basis of pyridine concentration. [b] 50% pyridine, by volume. [c] 100% pyridine.

A series of relevant control experiments was carried out in which equimolar quantities of I and sodium dimsyl (ca. 0.1 M) were mixed in Me_2SO at 37 °C with the resulting instant development of the color characteristic of the hydrazone anion but without the liberation of nitrogen. Then, known amounts of *tert*-butyl alcohol were added, and the rate of evolution of nitrogen was followed. The pseudo-second-order rate constants were observed to drift from 2.7 (±0.2) × 10^{-5} M^{-1} s^{-1} to 3.3 (±0.2) × 10^{-5} M^{-1} s^{-1} as the concentration of the alcohol was increased from 0.0567 to 2.0193 M. These values are not thought to be significantly different from those listed in Table V (the four experiments in which the I/II molar ratios were ca. unity) when one takes into consideration minor differences attributable to the cation effect.[9] Kinetic differences because of the use of sodium or potassium salts are believed to be negligible when working in the leveling solvent Me_2SO at these relatively low temperatures, and this belief is supported by the failure of dicyclohexyl-18-crown-6 to produce an acceleration of the reaction carried out in Me_2SO. The conclusion derived from the above results is that the diffusion in Me_2SO of *tert*-butyl alcohol molecules (generated in the equilibrium between I and the alkoxide) to the reactive site of the hydrazone anion is not a rate-limiting phenomenon in the W-K reaction.

Next, the rate of the W-K reaction was examined under conditions in which I was added to a preformed equimolar solution of II and *tert*-butyl alcohol in Me_2SO. Since the rate of nitroger evolution was indistinguishable from that observed when the alcohol was the last reagent to be added, it must be concluded that the rate of hydrazone anion formation does not differ significantly (in Me_2SO, at 37 °C) when I reacts with either "free" or alcohol-solvated II.

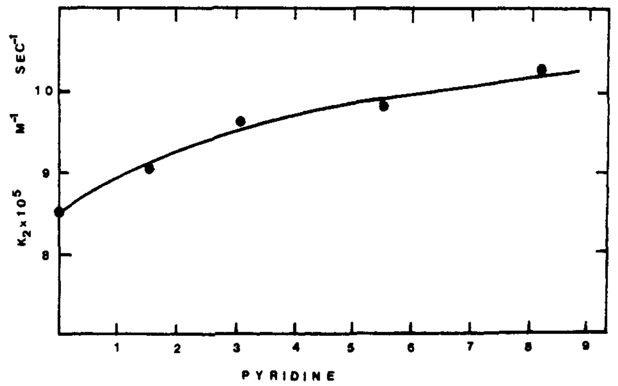


Figure 4. The effect of pyridine on the rate of the Wolff-Kishner reaction of benzophenone hydrazone in absolute dimethyl sulfoxide in the presence of potassium *tert*-butoxide at 37 °C.

Table III. Wolff-Kishner Reaction of Benzophenone Hydrazone ([I] = 0.194 M) in Absolute Dimethyl Sulfoxide in the Presence of Potassium *tert*-Butoxide (II) at 19 °C

II $[\text{molarity}]_0$	[I]/[II]	$k_1 \times 10^6$, s^{-1}
0.3665	0.53	1.99
0.2353	0.83	2.05
0.1832	1.06	1.60
0.1177	1.65	1.68
0.0794	2.45	1.51
0.0397	4.90	0.96
0.0202	9.63	0.82
0.0155	12.6	0.61
0.0101	19.3	0.53
0.0082	23.8	0.80
0.0077	25.1	0.61
0.0061	31.8	0.59
0.0040	48.7	0.25
0.0020	97.4	0.16

Table IV. Wolff-Kishner Reaction of Benzophenone Hydrazone ([I] = 0.184-0.194) in Absolute Dimethyl Sulfoxide in the Presence of Potassium *tert*-Butoxide (II) at 27 °C

I $[\text{molarity}]_0$	[I]/[II]	$k_1 \times 10^6$, s^{-1}
0.3465	0.56	3.14
0.332	0.55	2.59
0.322	0.57	2.59
0.322	0.58	2.63
0.2310	0.84	4.55
0.1642	1.18	4.05
0.1232	1.58	2.82
0.1095	1.78	2.92
0.0821	2.37	2.18
0.0617	3.15	2.51
0.0412	4.73	2.14
0.0191	10.2	1.43
0.0096	20.4	1.29
0.0058	33.4	0.77
0.0025	78.5	0.36

The pseudo-first-order rate constants for the evolution of nitrogen from Me_2SO solutions of I and catalytic amounts of II were determined at 19, 27, 37, and 49 °C (see Tables III-VI), and when the concentrations of II were relatively small, i.e., the molar ratio of I/II was greater than 2.5, the resulting pseudo-first-order rate constants gave a linear relationship when plotted against the concentration of base. The slopes of these graphs give pseudo-second-order rate constants of 7.5,

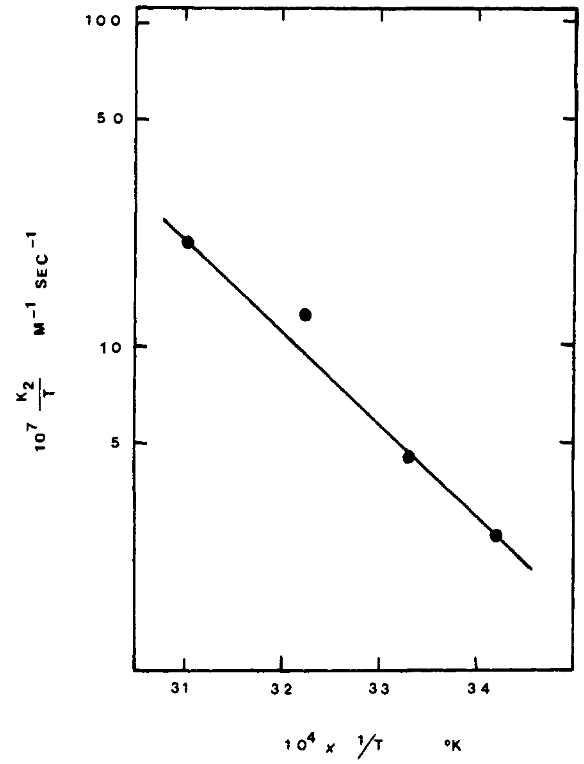


Figure 5. Temperature dependence of the second-order rate constants for the Wolff-Kishner reaction of benzophenone hydrazone in absolute dimethyl sulfoxide in the presence of low concentrations of potassium *tert*-butoxide.

Table V. Wolff-Kishner Reaction of Benzophenone Hydrazone (I) in Absolute Dimethyl Sulfoxide in the Presence of Potassium *tert*-Butoxide (II) at 37 °C

I [molarity]$_0$	II [molarity]$_0$	$\frac{[I]}{[II]}$	$k_1 \times 10^6$, s^{-1}
0.0750	0.3984	0.19	0.61
0.1919	0.3353	0.57	3.07
0.1746	0.3090	0.57	5.77
0.1938	0.2908	0.67	5.02
0.1913	0.2304	0.83	8.25
0.1944	0.1988	0.98	8.02
0.1965	0.1573	1.25	8.89
0.2288	0.1388	1.65	9.39
0.1943	0.0621	3.13	6.68
0.1936	0.0311	6.23	4.75
0.1895	0.0046	41.1	1.74
0.1945	0.0035	55.1	0.79
0.1945	0.0018	110	0.64

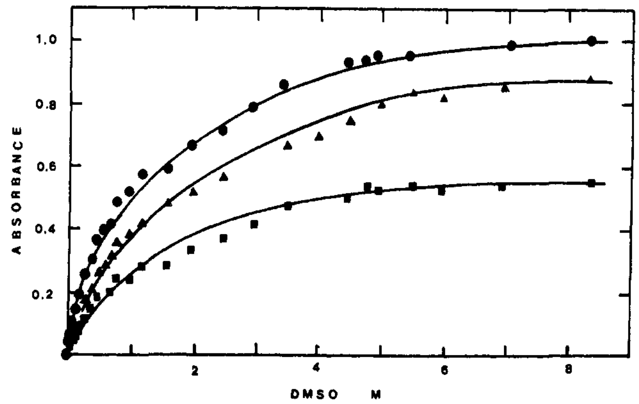


Figure 6. The effect of dimethyl sulfoxide on the absorbance of different infrared absorption peaks of benzophenone hydrazone in carbon tetrachloride; bands at 3390 cm^{-1} (●), at 330 cm^{-1} (■), and at 3210 cm^{-1} (▲).

Table VI. Wolff-Kishner Reaction of Benzophenone Hydrazone ([I] = 0.194 M) in Absolute Dimethyl Sulfoxide in Presence of Potassium *tert*-Butoxide (II) at 49 °C

II [molarity]$_0$	$\frac{[I]}{[II]}$	$k_1 \times 10^6$, s^{-1}
0.2864	0.68	13.36
0.1910	1.02	21.39
0.1566	1.24	22.00
0.1174	1.66	24.58
0.0558	3.48	13.75
0.0279	6.97	10.70
0.0205	9.51	8.43
0.0117	16.6	7.58
0.0048	39.5	2.77
0.0040	42.3	2.18
0.0024	79.0	1.86
0.0020	100	1.19
0.0010	200	0.87

14, 38, and 65 ($\times 10^{-5}$) M^{-1} s^{-1}, respectively, at the four temperatures cited above. The determination of the activation parameters based on these k_2 values (Figure 5) gave 14 kcal/mol and −30 eu for the activation enthalpy and entropy, respectively. These values differ significantly from the activation parameters determined[9] in butyl carbitol-potassium carbitolate ($\Delta H^{\ddagger} = 29.4 \pm 0.7$ kcal/mol, $\Delta S^{\ddagger} = -0.8 \pm 1.5$ eu). The lower enthalpy of activation observed in Me$_2$SO can be attributed to the greater basicity of this solvent, and hence its greater effectiveness in the N-H bond breaking process.[7] The difference between the two above mentioned solvent systems is not attributed to differences in cation solvation since the addition of "crown ether" to the butyl carbitol system did not produce[7] a significant change in the activation parameters. The distinctly more negative entropy of activation in Me$_2$SO can be reconciled with the tight solvation by Me$_2$SO of the hydroxylic cosolvent molecule (required in the formation of the C-H bond), as well as the tight solvation by Me$_2$SO of the hydrazone anion (vide infra) and cation. The decreased activity of the Me$_2$SO-solvated hydroxylic cosolvent is believed to produce, in turn, little, if any, development of the free nitrogen molecule in the transition state.[10] All of these effects could contribute to the relatively negative entropy of activation of the W-K reaction in the Me$_2$SO solvent system. The transition state under these conditions can thus be represented as shown in Scheme I.

Unlike the behavior observed previously when the W-K reaction was studied in hydroxylic solvents,[9,11,12] the use of relatively high concentrations of II, i.e., when [I]/[II] became smaller than 2.5, caused an unexpected *decrease* in the pseudo-first-order rate constant for the evolution of nitrogen (Figure 7). It is noteworthy that the concave nature of these plots was smaller at the lower temperatures.

One can rationalize the partial inhibition of the W-K reaction in the presence of relatively large concentrations of II by assuming that the *tert*-butyl alcohol molecules, shown to be necessary for the evolution of nitrogen, are deactivated by excessive amounts of II through the formation of strong alkoxide-alcohol complexes. Exner and Steiner[13] estimate the equilibrium constants for the competitive equilibria that occur at 25 °C in Me$_2$SO solution of *tert*-butyl alcohol and II to be as follows:

$$CH_3SOCH_2^- + ROH \rightleftharpoons Me_2SO + RO^- \qquad K \cong 800$$

$$RO^- + ROH \rightleftharpoons RO(HOR)^- \qquad K \cong 400$$

$$RO(HOR)^- + ROH \rightleftharpoons RO(HOR)_2^- \qquad K \cong 30$$

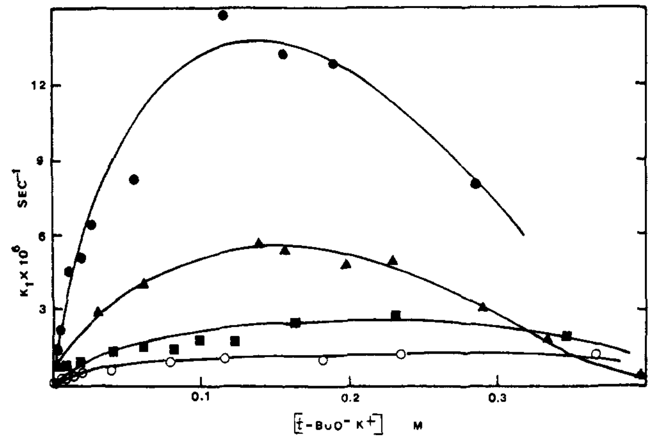
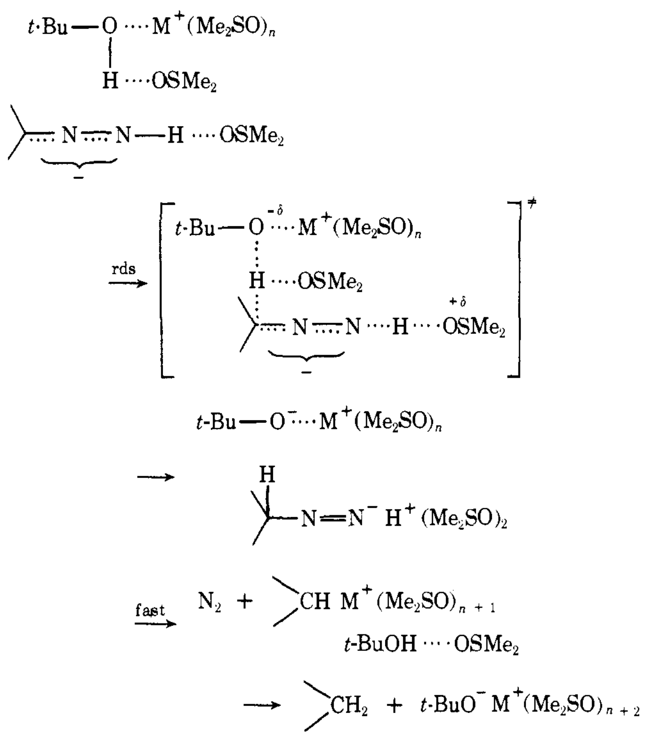


Figure 7. Dependence of the pseudo-first-order rate constant of the Wolff-Kishner reaction of benzophenone hydrazone on the concentration of potassium *tert*-butoxide over a large range of potassium *tert*-butoxide concentration; 19 °C (○); 27 °C (■); 37 °C (▲); 49 °C (●).

Scheme I



One of these authors has also attributed[7] the reduced acidity of alcohols complexed by alkoxide ions when proton-transfer reactions are carried out in Me_2SO.

If Δk, the difference between the observed pseudo-first-order rate constant at a relatively high [II] and the pseudo-first-order rate constant that one can extrapolate from the low to a high [II] range, is attributed to the detrimental effect of excessive II, then one can postulate the relationship

$$\Delta k[\mathrm{RO}^-]^n = k_1{}^{\mathrm{LB}} - k_1{}^{\mathrm{HB}}$$

where the superscripts LB and HB denote the low and high base concentrations, respectively, and n represents the kinetic order of the detrimental concentration of II. The log-log plots of the above relationship, $\log \Delta k + n \log [\mathrm{RO}^-] = \log k_1{}^{\mathrm{LB}} - k_1{}^{\mathrm{HB}}$, are shown in Figures 8-11 for the four temperatures employed in this work. It is noteworthy that the linear relationship is particularly satisfactory for the high concentrations of II, i.e., when the extrapolated $k_1{}^{\mathrm{LB}}$ values are quite remote from the initial linear portions of the plots shown in Figure 7. The slopes of the graphs in Figures 8-11 have the values 1.1-1.2 and thus support the assumption that essentially only one alkoxide ion is involved in causing the detrimental association with the hydroxylic component of the reaction mixture. The greater nonlinearity of the plots in Figure 7 at the higher temperatures could mean that the deactivation of alcohol

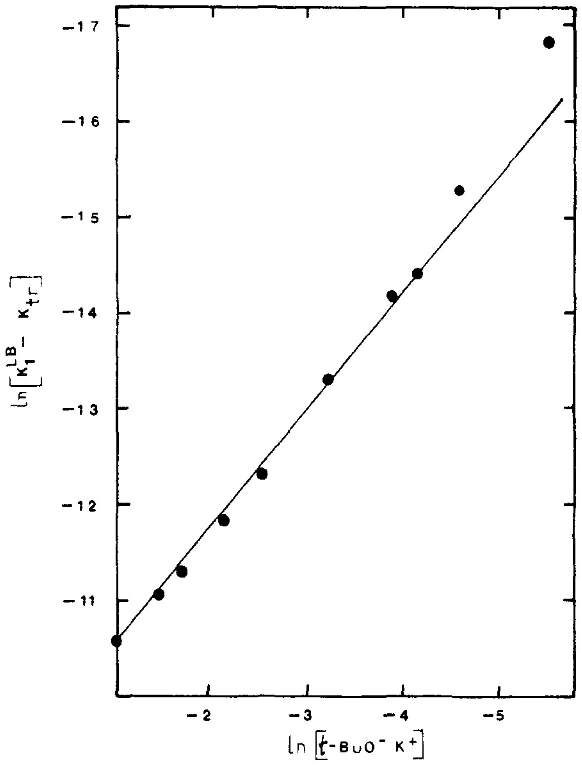


Figure 8. Plot of $\ln (k_1{}^{\mathrm{LB}} - k_1{}^{\mathrm{HB}})$ vs. $\ln [t\text{-BuO}^-\mathrm{K}^+]$ for the reaction of benzophenone hydrazone at 19 °C in Me_2SO.

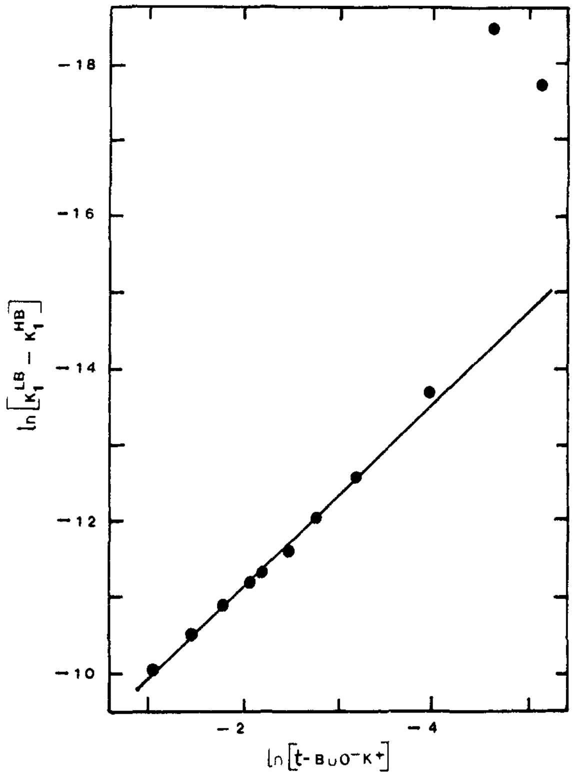


Figure 9. Plot of $\ln (k_1{}^{\mathrm{LB}} - k_1{}^{\mathrm{HB}})$ vs. $\ln [t\text{-BuO}^-\mathrm{K}^+]$ for the reaction of benzophenone hydrazone at 27 °C in Me_2SO.

Table VII. Nonhomogeneous Wolff-Kishner Reaction of Benzophenone Hydrazone (I) in Absolute Me_2SO in the Presence of Potassium *tert*-Butoxide (II)

Me_2SO, mL	I, g (mol × 10^3)	II, g (mol × 10^3)	Temp, °C (±1 °C)	% N_2 of theory	$k \times 10^5$, s^{-1}
2.0	0.7423 (3.78)	0.765 (6.82)	23	90	5.8
2.0	0.8125 (4.14)	0.765 (6.82)	24	94	5.9
1.0	0.3975 (2.03)	0.410 (3.65)	29	80	18
1.9	0.7464 (3.80)	0.800 (7.13)	58	34[a]	479[a]
1.8	0.7258 (3.70)	0.750 (6.68)	67	10[a]	683[a]
1.8	0.7239 (3.69)	0.725 (6.46)	103	39[a]	2452[a]

[a] Initial rates and percent of nitrogen evolution during the initial period.

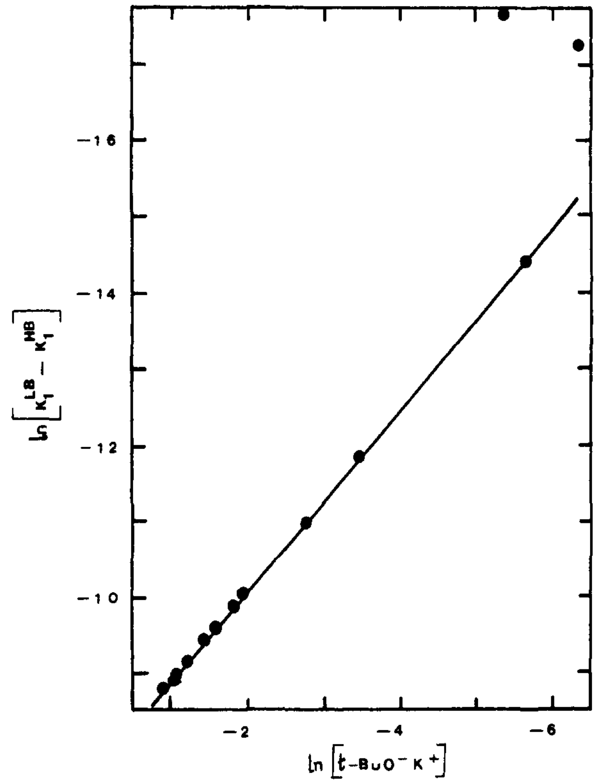


Figure 10. Plot of ln ($k_1^{LB} - k_1^{HB}$) vs. ln [t-BuO$^-$K$^+$] for the reaction of benzophenone hydrazone at 37 °C in Me_2SO.

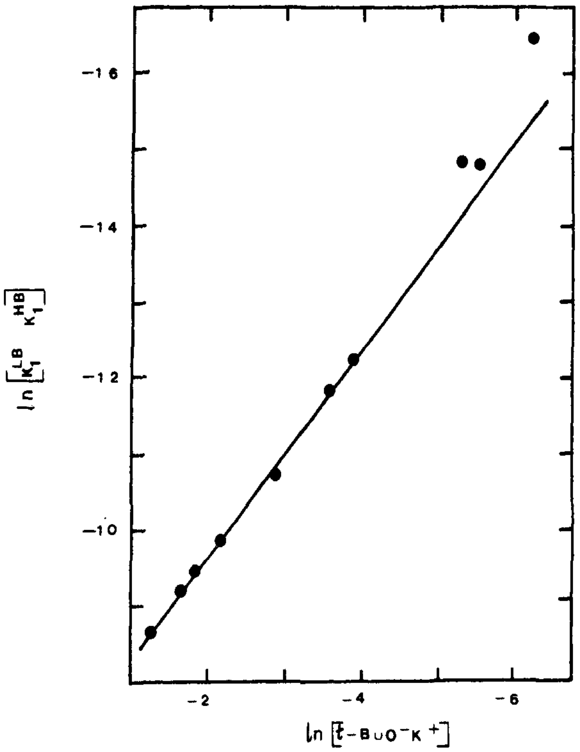


Figure 11. Plot of ln ($k_1^{LB} - k_1^{HB}$) vs. ln [t-BuO$^-$K$^+$] for the reaction of benzophenone hydrazone at 49 °C in Me_2SO.

molecules by alkoxide ions is more pronounced as the dissociation of ion pairs increases. Also, this result could be due to the temperature-induced dissociation of the alcohol-hydrazone anion complexes (formed in the course of the proton transfer when the alkoxide base reacts with the initial hydrazone) and the preferential complexing of these alcohol molecules by II.

A set of experiments was carried out in order to test the relatively low activity attributed above to the alcohol molecules that are complexed with the corresponding alkoxide ions. For this purpose, solutions of I and sodium dimsyl, i.e., solutions of performed hydrazone anion (ca. 0.2 M), were allowed to react with Me_2SO solutions containing varying concentrations (up to 0.7 M) of II and of *tert*-butyl alcohol present either in 0.2 or 0.4 M concentrations.

The results of these experiments are represented in Figure 12 which shows that the addition of increasing concentrations of II produces, first of all, an unmistakably downward trend in the pseudo-second-order rate constants (calculated on the basis of total base concentration, i.e., sodium dimsyl plus II), and secondly, that this effect is more pronounced at the lower initial level of *tert*-butyl alcohol.[14]

Next, we wish to comment with regard to the W-K reaction of I under the experimental conditions described by Cram and co-workers.[2] In spite of the heterogeneous nature of these reaction mixtures, it was found that at a relatively low reaction temperature the evolution of nitrogen obeyed a first-order rate law surprisingly well. At the higher temperatures (see Table VII), the evolution of nitrogen became erratic and only the initial rate constants could be estimated. In any case, it is surprising that the pseudo-first-order rate constants in the lower temperature range are of the same magnitude as the analogous rate constants determined for the homogeneous W-K reaction at 27 °C (Table IV). We can explain this by considering the possibility that the reaction of I occurs at the surface of particles of II, and that the *tert*-butyl alcohol formed in situ forms a complex with the hydrazone anion in a manner not greatly different from that in the homogeneous reaction mixture. Also, it is surprising that the pseudo-first-order rate constants give a reasonably satisfactory linear ln k_1/T vs. $1/T$ relationship when only the experiments at the lower temperatures are taken into account (A in Figure 13). The resulting enthalpy and entropy of activation estimated at 24 kcal/mol and −1 eu, respectively, differ significantly from the 14 kcal/mol and −30 eu values determined for the homogeneous W-K reaction in Me_2SO. The apparent difference in the activation

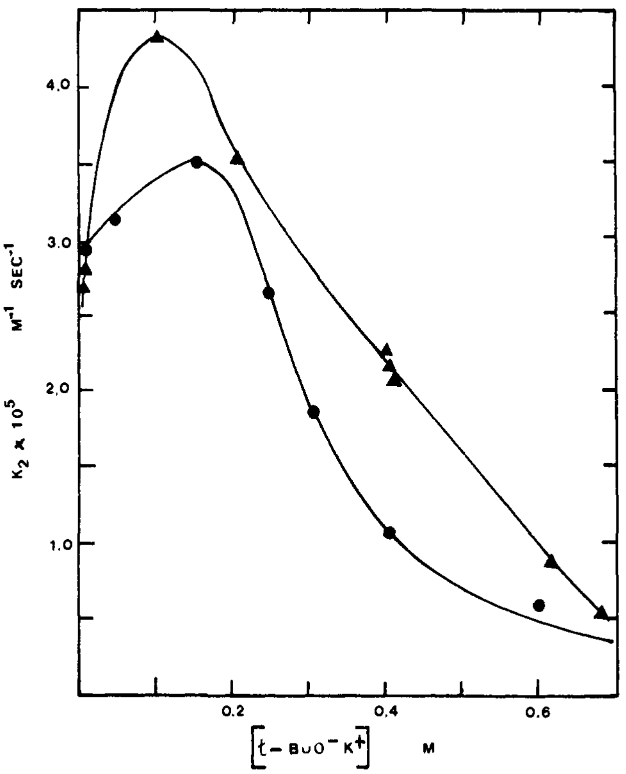


Figure 12. Effect of potassium *tert*-butoxide on rate of the Wolff-Kishner reaction when added to an equimolar solution of benzophenone hydrazone and sodium dimsyl at 37 °C in the presence of *tert*-butyl alcohol [0.2 M (●); 0.4 M (▲)].

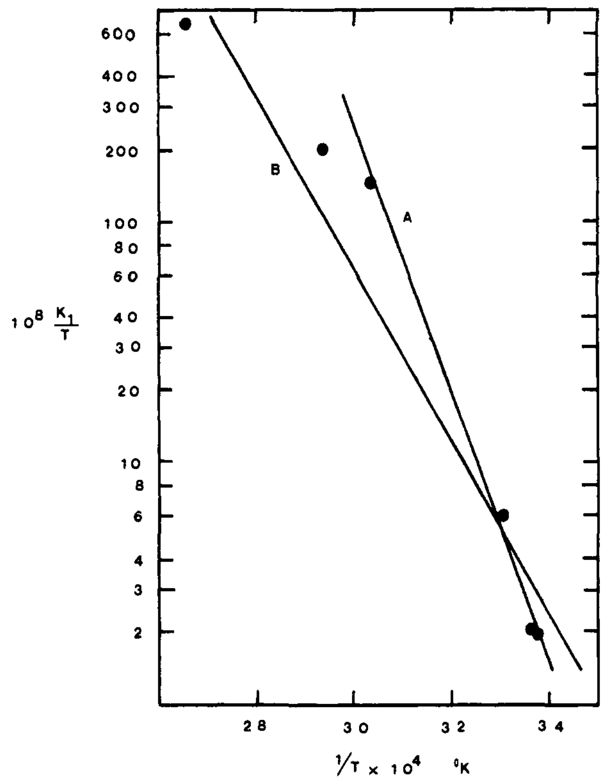


Figure 13. Temperature dependence of the pseudo-first-order rate constants for nonhomogeneous Wolff-Kishner reaction in absolute dimethyl sulfoxide in the presence of potassium *tert*-butoxide; (A) lower temperatures considered; (B) all temperatures considered.

parameters is consistent with the idea that the heterogeneous reaction probably occurs with a hydrazone molecule adsorbed on II and that the rate-limiting step involves the release of the products from the surface.

Finally, we wish to report the attempts to determine the constants for the association of Me_2SO and I and its *p,p'*-dichloro- and *p,p'*-dimethoxy derivatives. The formation of these complexes is of interest in connection with the solvation of hydrazone anions by Me_2SO invoked above in the discussion of the W-K reaction mechanism. The asymmetric and symmetric N-H stretching frequencies of the above mentioned hydrazones were found at 3440, 3442, 3437 and 3298, 3303, 3291 cm^{-1}, respectively, in a carbon tetrachloride solution at 23-24 °C. The presence of Me_2SO gave rise to a new band at 3210-3215 cm^{-1}, and the asymmetric band at ca. 3440 decreased but overlapped with a developing band at ca. 3380 cm^{-1}. The intensity of the symmetric stretching frequency at ca. 3300 cm^{-1} actually showed a tendency to increase in the presence of Me_2SO. Figure 6 represents the changes in the absorbance of the stretching frequencies of I upon addition of Me_2SO, and it is noted that these changes tend to level off when the concentration of Me_2SO reaches ca. 4 M. A parallel behavior was observed in the case of the *p,p'*-dichloro and *p,p'*-dimethoxy derivatives of I. From the plateau of the absorbance, and by assuming the formation of a 1:1 complex[15] as well as the constancy of the molar absorptivity throughout the changing composition of the medium, one can calculate the apparent association constants using any one of the three frequencies mentioned in the case of each hydrazone. Actually, the use of the nonoverlapping new absorption band at ca. 3210 cm^{-1} gave the most consistent results for the association constants, and these were found to be 0.9, 1.3, and 0.7 M^{-1} for I and its *p,p'*-dichloro and *p,p'*-dimethoxy derivatives, respectively. These values are believed to be accurate within ±10% and are consistent with the relative order expected from the electronic nature of the substituents present in the hydrazones.

Experimental Section

A. Materials. The hydrazones of benzophenone and its *p,p'*-dimethoxy and *p,p'*-dichloro derivatives were prepared as described previously.[8,16]

Dimethyl sulfoxide, purchased from Crown Zellerbach, was dried over calcium hydride for several days and redistilled in vacuo, and the fraction, bp 64 °C at 4 Torr, or bp 30 °C at 0.015 Torr, was collected and stored under purified nitrogen over Linde molecular sieves type 4A.

Potassium *tert*-butoxide, MSA Research Corporation, was freshly sublimed in vacuo at 150 °C (0.010 Torr) for each individual experiment.

Sodium methylsulfinyl carbanion (dimsyl) was prepared according to Corey and Chaykovsky[17] by heating dry redistilled dimethyl sulfoxide with sodium hydride (Alfa Inorganics) under nitrogen atmosphere. The solution was transferred to a special anaerobic buret similar to that described by Baumgarten and Hauser[18] but with some modifications that permitted the storage and standardization of sodium methylsulfinyl carbanion in dimethyl sulfoxide under an inert atmosphere and its transfer to the reaction vessels.

Commercially available, pure nitrogen was further purified in order to remove traces of oxygen and water. It was passed through a train consisting of the following parts: (a) a solution of 12.6 g (0.10 mol) of pyrogallol and 4.8 g (0.12 mol) of sodium hydroxide in 150 mL of distilled water; (b) concentrated sulfuric acid; (c) granulated anhydrous calcium chloride; and (d) a solution of ketyl radical anion prepared from 5 g of benzophenone and 5 g of a 1:1 sodium-potassium alloy dissolved in 100 mL of dry xylene.

B. Kinetics of the Wolff-Kishner Reaction. The kinetic experiments were carried out in a reaction vessel connected to a gas buret and immersed in a constant temperature bath described previously.[9] The apparatus was carefully flushed with purified nitrogen, and all the reagents and solvents were stored under purified nitrogen.

Two fundamentally different experimental conditions were employed in this work for the determination of reaction rates. The first

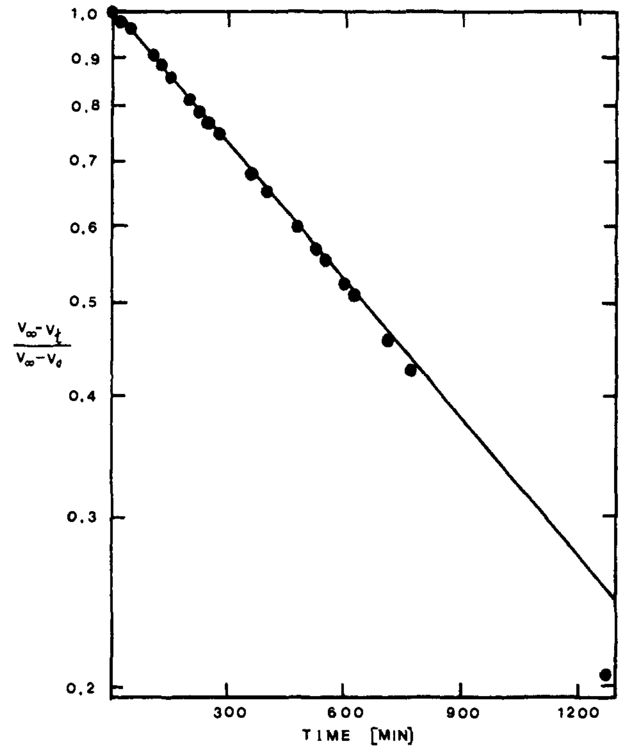


Figure 14. Pseudo-first-order kinetics of the Wolff-Kishner reaction of benzophenone hydrazone in absolute dimethyl sulfoxide in the presence of potassium *tert*-butoxide at 49 °C (I/II = 3.48, Table VI).

was meant to reproduce the conditions of Cram and co-workers[2] and consisted of the addition of hydrazone to a mixture of potassium *tert*-butoxide and dimethyl sulfoxide in the proportions listed in Table VII. Magnetic stirring was employed in order to homogenize the pasty reaction mixture. The second experimental condition employed a homogeneous solution of the base catalyst in dimethyl sulfoxide, and the hydrazone solution was introduced at zero time.

Those kinetic experiments in which the presence of traces of oxygen was apparent because of a discoloration of the hydrazone anion to give a blood red solution of diphenyldiazomethane[4] were discarded. In the valid kinetic experiments, the reaction mixture developed only a yellow color characteristic of the hydrazone anion (vide infra).

The occurrence of the Wolff-Kishner reaction of benzophenone hydrazone was followed principally by the evolution of nitrogen. Diphenylmethane was also determined in some of the final reaction mixtures. For this purpose the final reaction mixture was quenched with water, neutralized with dilute hydrochloric acid, and extracted with hexane during a minimum of 24 h in a continuous extractor. The hexane extracts were dried over calcium chloride and then analyzed by means of a Perkin-Elmer Model 881 gas chromatograph equipped with a 15-ft silicone (GESF-96)-chromosorb (W, AW-DMCS) column at a temperature of 220 °C, and with a helium flow of approximately 30 mL per minute. A calibration curve was prepared using solutions of known concentrations of diphenylmethane in *n*-hexane. The agreement between the extent of the Wolff-Kishner reaction deduced from the nitrogen evolution and from the analysis for diphenylmethane was excellent, and yields in the case of homogeneous reactions carried out in the presence of ca. equimolar amounts of *tert*-butyl alcohol were 90% or better.

The experiments in which the reaction mixture also contained pyridine or *tert*-butyl alcohol were carried out by preparing the solution of the hydrazone and of all the other components except potassium *tert*-butoxide, allowing this solution to reach thermal equilibrium, and then, at zero time, rapidly injecting the solution of potassium *tert*-butoxide by means of a calibrated syringe.

Under certain experimental conditions that were of interest, such as the experiments in which the concentration of potassium *tert*-butoxide was either very low or very high, the reaction was followed during a period of 3-4 days even though only 10-15% of the theoretical nitrogen had evolved during this period. It was impractical to follow the reaction for a longer period in view of the well-known[19] decomposition of the methylsulfinyl carbanion which is generated to some extent in a dimethyl sulfoxide solution of potassium *tert*-butoxide.[20] The rate constants of these experiments are referred to as "initial rates". Normally, the kinetic experiments were allowed to continue over 1 to 2 half-lives (approximately 2 to 3 days), but several experiments were run to completion of the reaction, and it was shown that the nitrogen evolution indeed corresponds to the values calculated on the basis of the initial hydrazone concentration. Thus, all pseudo-first-order rate constants were calculated on the basis of the theoretical nitrogen volumes by constructing log $(V_t - V_0/V_\infty - V_0)$ vs. time plots such a representative one shown in Figure 14.

The second-order rate constants were calculated by considering the concentration of the base that was present in a given experiment.

C. Formation of Hydrazone Anions. Solutions of sodium dimsyl prepared and stored in a special buret as described above were titrated with a standard solution of 2-naphthol in Me_2SO using triphenylmethane as indicator.[21] Under conditions of careful exclusion of oxygen, 5-10 mL of the standard solution of base were mixed with variable volumes (0.1-1.0 mL) of a Me_2SO solution of I of known concentration (8.5×10^{-4} M), and the solutions of the hydrazone anion were then transferred by means of a syringe into rubber-capped spectrophotometric cells. A Cary 14 spectrophotometer was used, and the absorbance was determined against an equivalent solution of the base.

Potassium *tert*-butoxide was quickly transferred from a sublimation apparatus into a 10- or 25-mL volumetric flask previously flushed with purified nitrogen, and the rubber-capped flask was again flushed with nitrogen and weighed. Me_2SO was then added, and known amounts of the resulting solution were placed in a small flask. The hydrazone solutions were added to these flasks, and the spectrometric measurements were carried out as described above.

The Beer-Lambert plots of the typical absorption bands of the three hydrazone anions are shown in Figures 1 and 2.

An attempt to follow the formation of benzophenone hydrazone anion in solutions of *tert*-butyl alcohol using potassium *tert*-butoxide was unsuccessful because of the absence of a visible color change. Similarly, the hydrazone failed to give the coloration of the anion in a solution of *n*-hexane in the presence of *n*-butyllithium.

D. Association between Hydrazones and Dimethyl Sulfoxide in Carbon Tetrachloride at 23-24 °C. Solutions of known concentrations of the desired ketone hydrazones in reagent grade carbon tetrachloride were examined by means of a Beckman IR-12 spectrophotometer. The solutions were freshly prepared immediately before each determination because they were found to change from colorless to slightly yellow over a period of 2 to 3 h probably due to oxidation by atmospheric oxygen. A Beer-Lambert plot was constructed for each hydrazone in order to determine the range of concentrations in which the spectrum was essentially free of absorption bands characteristic of intramolecular associations. A convenient hydrazone concentration was then chosen, and solutions were prepared in which Me_2SO replaced a portion of the carbon tetrachloride and the absorbance of both the "free" and "bonded" N-H stretching frequencies was thus determined. A correction for the background absorption by carbon tetrachloride is included in the reported values. Representative results for I are summarized in Figure 6.

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(15) The formation of a 2:1 complex would be expected to give two plateaus as the concentration of Me_2SO is increased. Calculations based on the assumption of a 2:1 complex gave very inconsistent values for the association constants. On the assumption that the formation of a 1:1 complex is indeed the limit of hydrogen bonding between a diaryl hydrazone and Me_2SO, one is tempted to speculate that the preferred planar conformation of the hydrazone impedes sterically the association of Me_2SO with one of the N–H bonds (the "endo" N–H).

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Intramolecular Dipolar Cycloaddition Reactions of Unsaturated 2*H*-Azirines[1]

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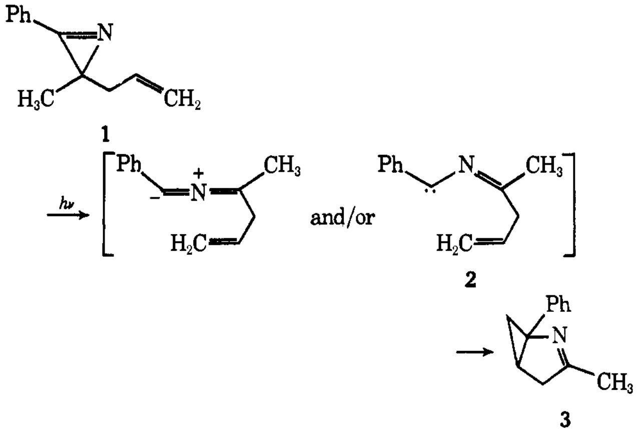
Abstract: The intramolecular dipolar cycloaddition reaction of 2-(4-pentenyl)-2*H*-azirines has been examined in mechanistic detail. Upon irradiation with ultraviolet light, this system undergoes rearrangement to cyclopenta[*b*]pyrroles via a transient nitrile ylide. This reactive 1,3-dipole can be intercepted with added dipolarophiles to give Δ^1-pyrroline derivatives. Although frontier molecular orbital theory correctly rationalizes the regioselectivity of all known bimolecular nitrile ylide cycloadditions, it fails completely when applied to these intramolecular cycloadditions. The inversion of regiospecificity can be attributed to steric factors which destabilize the transition states for formation of the expected regioisomers. A kinetic investigation, involving Stern–Volmer plots and relative reactivity studies, shows that there is a marked leveling of the rate profile associated with these internal cycloadditions. The photochemistry and thermal chemistry of the homologous 2-(3-butenyl)-2*H*-azirine system was also studied. Evidence was obtained which indicates that the spatial relationship of the nitrile ylide and dipolarophile π orbitals plays an extremely important role in controlling the mode of intramolecular cycloaddition. The thermolysis of but-3-enyl substituted 2*H*-azirines was found to give substituted pyridines and biphenyl derivatives via a novel 1,4-hydrogen transfer from the methylene group of an initially formed vinylnitrene intermediate.

1,3-Dipolar cycloadditions have been shown to be an astonishingly fruitful synthetic method for the preparation of five-ring heterocycles.[2-6] Numerous possibilities for variation are available by changing the structure of both the dipolarophile and dipole. In spite of the copious literature dealing with bimolecular cycloaddition reactions, intramolecular examples have received only a minimum of attention.[7] 1,3-Dipoles bearing a functional group able to behave as a dipolarophile are extremely interesting substrates. In fact, the intramolecular cycloaddition of a properly functionalized 1,3-dipole represents a general scheme for the synthesis of novel fused ring heterocycles. Intramolecular dipolar cycloadditions have been carried out with nitrones,[8-14] diazoalkanes,[15-19] azides,[20-24] azomethine imines,[25,26] carbonyl oxides,[27] and nitrile imines.[28,29]



Our research group has recently investigated the intramolecular cycloaddition reactions of nitrile ylides[30,31] generated by photolysis of 2*H*-azirines.[32] Nitrile ylides may be classified as nitrilium betaines, a class of 1,3-dipoles containing a central nitrogen atom and a π bond orthogonal to the 4π-allyl system. Among the possible forms of a nitrile ylide, a carbene structure (i.e., **2**) can be envisaged which makes conceivable a 1,1-cycloaddition of this 1,3-dipole.[33] We uncovered the first example of such a process during a investigation of the photochemistry of 3-phenyl-2-methyl-2-allyl-2*H*-azirine (**1**).[30] The formation of a 1,1-cycloadduct (i.e., **3**) from the photolysis of **1** clearly indicates that the spatial relationship of the dipole and dipolarophile plays an important role in controlling the intramolecular dipolar cycloaddition reactions of nitrile ylides. The primary spatial requirement for intramolecular 1,3-dipolar cycloaddition is that the distance between the two reacting centers should be sufficiently short so that effective three-center overlap of the 1,3-dipole with the dipolarophile occurs. For concerted 1,3-dipolar cycloaddition to take place, the atoms of the dipolarophile should be arranged in such a way as to allow their p orbitals to lie in a plane parallel to the plane of the nitrile ylide.[2] Inspection of molecular models of the allyl-substituted nitrile ylides indicates that the normal "two-plane" orientation approach of the ylide and allyl π system is impossible as a result of the geometric restrictions imposed on the system. Consequently, the normal mode of 1,3-dipolar addition does not occur here. With this system, attack by the double bond is constrained to occur perpendicular to the plane of the nitrile ylide. The second LUMO of the dipole, which is perpendicular to the ylide plane, is low lying and presents a large vacancy at C-1 for attack by the more nucleophilic terminus of the neighboring double bond, without the possibility of simultaneous bonding at the C-3 carbon. In