Elimination Reactions of Hydrazonium Salts: Experimental and Theoretical Evidence for a Large Stereoelectronic Effect of Nitrogen

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Elimination of trimethylamine from hydrazonium salts (**8**, R = Me) is promoted by base (methoxide ion in methanol). The mechanism is characterized as E2 as shown by substituent effects (ρ = +2.57), Brønsted coefficients, a primary kinetic isotope effect (k_H/k_D = 2.10), and solvent effects. Variation in the leaving group (**8**, R = arylmethyl) shows that N–N bond cleavage is less well advanced in the transition state than C–H bond breaking. The elimination to give the nitrile is syn-periplanar and, using the phthalazinium salt **4** as a model for the anti elimination, an anti/syn ratio of ca. 10^2 is found. The reactions have been modelled using ab initio methods with the transition structures located at the HF/3-21G level and relative energies computed using the MP2/6-31G* method. Using both H_2O and NH_3 as model bases to induce elimination on $[H_2C=NNH_3]^+$, the calculated energy for anti elimination is lower (in the range 11–13 kcal mol^{-1}) than that for syn elimination. The implications of the results for the ease of formation of nitriles from aldehydes via the hydrazonium salt route are discussed.
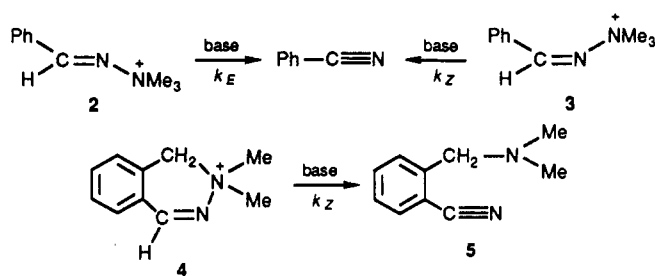
Introduction

The importance of the carbon–nitrogen triple bond as a functional group resides in its ease of introduction and its exceptional reactivity due to a unique combination of unsaturation, polarity, and steric demand. A survey of the literature available on the syntheses of nitriles[3] reveals that the methodologies may be broadly categorized as follows: (i) the introduction of the cyano group by the use of reagents possessing that moiety and (ii) synthetic procedures which involve the formation of the cyano group by elimination, rearrangement, or oxidation reactions.

In the eliminative processes, several nitrogen-containing derivatives of aldehydes can serve as intermediates en route to nitriles (Scheme I). Among these, the base-initiated 1,2-elimination reaction of hydrazonium salts **1** is not well studied, but this route, reported first by Smith and Walker[4] in 1962, is facile and high yielding in all three steps. The overall conversion may, if desired, be accomplished in one pot by coupling the aldehyde and *N,N*-dimethylhydrazone with CH_3I (or CH_3OTs) followed by elimination of a Me_3NHX molecule in CH_3O^-/CH_3OH to yield the desired nitrile.

In this work, we have investigated the mechanism of the conversion of hydrazonium salts **1** to nitriles on the basis of structural variations, the nature of the base and solvents used, as well as ab initio molecular orbital calculations on model species. An objective was also to establish the effect of the stereochemistry about the C=N double bond on the reaction rate. Although this could in theory be accomplished by determining the rate ratio, k_Z/k_E for (*E*)- and (*Z*)-benzaldehyde trimethylhydrazonium iodide **2** and **3**, extensive attempts to photoisomerize **2** to a mixture of **2** and **3** have so far been unsuccessful.[5]
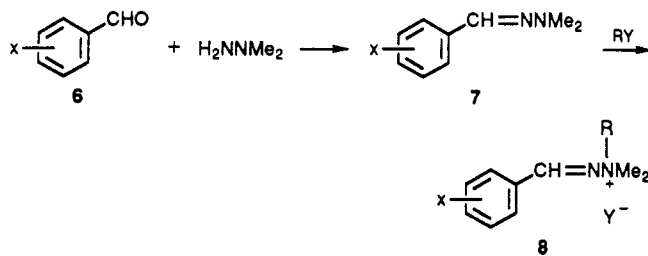
On the other hand, the formation of the nitrile **5** from **4** (an amino nitrile rearrangement[6]) provides a model for

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(3) For leading references, see: (a) *The Chemistry of the Cyano Group*; Rappoport, Z., Ed.; Wiley Interscience: New York, 1970. (b) *The Chemistry of the Triple-bond Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley Interscience: New York, 1983. (c) *Comprehensive Organic Chemistry*; Barton, D., Ollis W. D., Eds.; Pergamon Press: New York, 1979; Vol. 2, Part 8.2, pp 528–590.

(4) (a) Smith, R. F.; Otremba, E. D. *J. Org. Chem.* 1962, *27*, 879. (b) Smith, R. F.; Walker, L. *J. Org. Chem.* 1962, *27*, 4372.

(5) Clarke, L. F., Ph.D. Thesis, National University of Ireland, 1987, Chapter 2.

the reaction of **3**. Overall, this combined experimental and theoretical study has enabled us to establish a large stereoelectronic effect of nitrogen in the elimination of hydrazonium salts.

Results and Discussion

Syntheses and Structures of Substrates. A range of substituted (*E*)-benzaldehyde *N,N,N*-trimethylhydrazonium salts (**8**, X = *p*-CH$_3$, H, *p*-Cl, *m*-Br, *m*-NO$_2$, and *p*-NO$_2$) were prepared from the condensation of *as*-dimethylhydrazine with the appropriate aldehyde followed by alkylation of the product dimethylhydrazone **7** in refluxing methanol.

	X	R	Y$^-$
a	*p*-Me	Me	I$^-$
b	H	Me	I$^-$
c	*p*-Cl	Me	I$^-$
d	*m*-Br	Me	I$^-$
e	*m*-NO$_2$	Me	I$^-$
f	*p*-NO$_2$	Me	I$^-$
g	H	Ph	Br$^-$
h	H	*p*-BrC$_6$H$_4$	Br$^-$
i	H	*p*-NO$_2$	Br$^-$

NMR data (Table I) and sharp melting points indicate a single geometrical isomer for each quaternary salt. The

(6) Ioffe, B. V.; Zelemin, K. N. *Dolk. Akad. Nauk SSSR* 1960, *134*, 1094; 1962, *144*, 1303; *Tetrahedron Lett.* 1964, 1081.

Scheme I

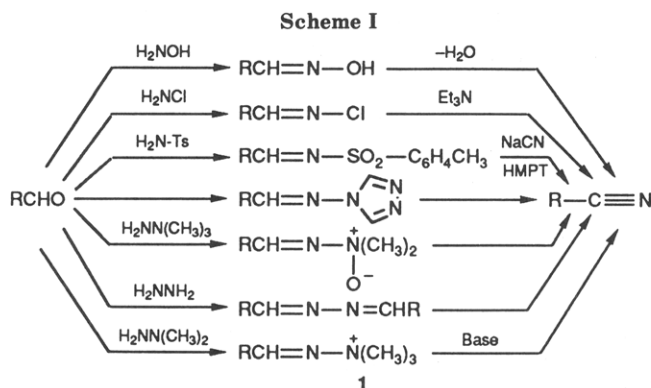**Table I. ¹H NMR Data for Substituted Benzaldehyde N,N,N-Trimethylhydrazonium Iodides 8 in CD₃OD**

compd	substituent X	chemical shift, δ (ppm)		
		$^{+}N(CH_3)_3{}^{a}$	$H_1{}^{b}$	Ar^{c}
8a	p-CH₃	3.56	9.02	7.37 (2 H, d, J = 8.06), 7.81 (2 H, d, J = 8.06)
8b	H	3.58	9.07	7.52–7.66 (3 H, m), 7.93 (2 H, d, J = 8.06)
8c	p-Cl	3.58	9.08	7.59 (2 H, d, J = 8.61), 7.92 (2 H, d, J = 8.61)
8d	m-Br	3.59	9.08	7.49 (1 H, t, J = 8.06), 7.82 (1 H, d, J = 8.06), 7.91 (1 H, d, J = 8.06), 8.12 (1 H, s)
8e	m-NO₂	3.62	9.24	7.80–8.80 (4 H, m)
8f	p-NO₂	3.62	9.24	8.19 (2 H, d, J = 2.02), 8.40 (2 H, d, J = 2.20)

^{a}Integration 9 H, multiplicity singlet in all cases. ^{b}Integration 1 H, multiplicity singlet in all cases. ^{c}Coupling constant, J given in units of hertz.

Table II. Second-Order Rate Constants ($M^{-1} s^{-1}$) for the Elimination Reaction of Substituted Trimethylhydrazonium Iodides 8a in Dry Methanol at 25 °C with Bases (a) NEt₃ and (b) NaOMe

compd	substituent	$\log k_2$		σ
		(a)	(b)	
8a	p-CH₃	−2.353	0.243	−0.17
8b	H	−1.761	0.663	0.00
8c	p-Cl	−1.067	1.297	0.23
8d	m-Br	−0.704	1.727	0.39
8e	m-NO₂	−0.018	2.402	0.71
8f	p-NO₂	−0.361	–	0.78

products were assigned the E configuration on the basis that dimethylhydrazones, their precursor, exist exclusively in this configuration and do not appear to isomerize either in the presence of acid or base or by the application of heat.[7]

[1-²H]Benzaldehyde N,N,N-trimethylhydrazonium iodide was prepared from benzil (and D₂O) in an overall yield of 56% with deuterium incorporation of 99.7% as shown by high-resolution NMR.[8]   2,2-Dimethyl-1,2-dihydrophthalazinium iodide was synthesized by a combination of two literature procedures,[4,9] the first of which involved the condensation of o-phthalaldehyde 9 with an excess of hydrazine hydrate in ethanol to form phthalazine 10. This azine was methylated to yield 2-methylphthalazinium iodide 11, which was then reduced in aqueous sodium borohydride to give 2-methyl-1,2-dihydrophthalazine 12,

(7) (a) Karabatros, G. J.; Krumel, K. L. *Tetrahedron* **1986**, *23*, 1097. (b) Karabatros, G. J.; Taller, R. A.; Vane, F. M. *Tetrahedron Lett.* **1964**, 1081.
(8) Burgstahler, A. W.; Walker, D. E.; Kuebrich, D. P.; Schowen, R. L. *J. Org. Chem.* **1972**, *37*, 1272.
(9) Hirsch, A.; Orphanos, D. *J. Heterocycl. Chem.* **1965**, *2*, 206.

Table III. Second-Order Rate Constants ($M^{-1} s^{-1}$) for the Elimination Reaction of N-(Substituted benzyl)-N,N-dimethylhydrazonium Bromides 8g–i in Dry Methanolic NEt₃ at 25 °C

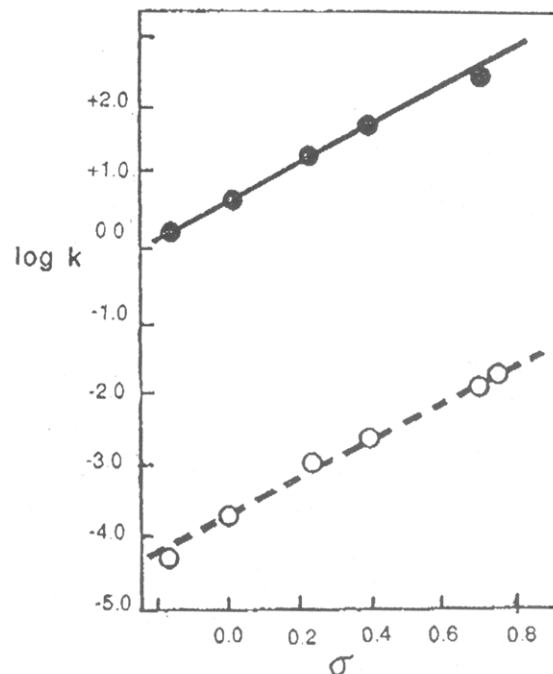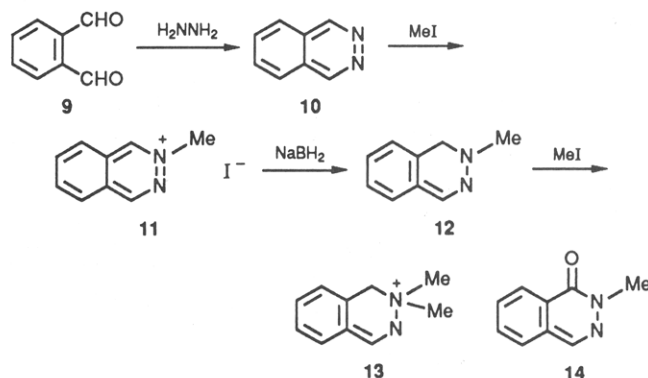| compd	substituent	$\log k_2$	σ	pK_{BH^+} (50% aqueous CH₃OH)
8g	H	−1.916	0.00	8.20
8h	p-Br	−1.809	0.23	7.76
8i	p-NO₂	−1.412	0.78	7.07

Figure 1. Hammet Plots for substituted (E)-benzaldehyde N,N,N-trimethylhydrazonium iodides in methanol at 25 °C; (—) NaOMe as base, (- -) NEt₃ as base. (Graph points from left to right: p-CH₃, H, p-Cl, m-Br, m-NO₂, p-NO₂.)

which was methylated in situ to 13 (avoiding oxidation to 14).

Substituent Effects. The 1,2-elimination reactions of the trimethyl- and benzyldimethylhydrazonium salts 8 were examined in dry methanol at 25 °C. Rates of reaction which were base-initiated by triethylamine or sodium methoxide were monitored spectrophotometrically at an appropriate wavelength. The reactions were monitored under pseudo-first-order conditions and the second-order rate constants, k_2, obtained are tabulated in Tables II and III.

Correlation with Hammett σ values gave $\rho = 2.59$. A similar correlation between k_{obs} and $\sigma(\rho = 2.57)$, which included the p-NO₂ compound, was obtained on using triethylamine as base (see Figure 1). Previously, Hegarty
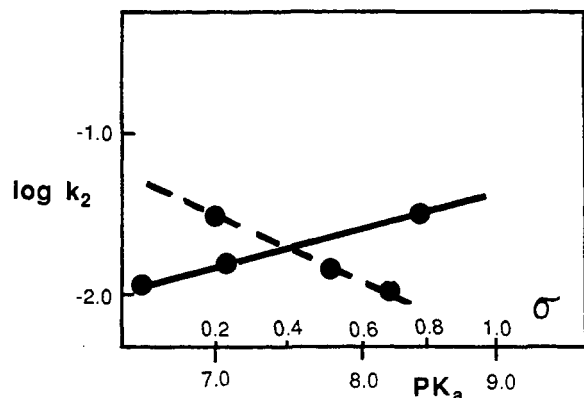
Figure 2. Hammett plot (—) and Brønsted plot (- -) for the elimination reaction of (*E*)-benzaldehyde *N*-(substituted benzyl)-*N*,*N*-dimethylhydrazonium bromide in methanolic NEt₃.

Table IV. Rate Constants for the Elimination Reaction of (a) Trimethylhydrazonium Iodide 2 and (b) Its Deuterium Analogue 16 in Methanolic NaOMe at 25 °C

	$10^3 k_{obs}$, s^{-1}		
[MeO⁻]	(a)	(b)	$k_{obs}{}^H/k_{obs}{}^D$
2.50×10^{-1}	455.5	212.0	2.1
1.25×10^{-1}	264.0	129.0	2.0
5.00×10^{-2}	144.3	70.8	2.0
3.75×10^{-2}	117.3	55.3	2.1
2.50×10^{-2}	88.5	41.2	2.0
1.25×10^{-2}	53.1	26.4	2.0
5.00×10	25.7	12.3	2.1

and Tuohey[10] have reported the nitrile-forming elimination of oxime ethers, where ρ is 2.07 for the hydroxide-initiated reaction of substituted (*E*)-*O*-(*p*-nitrophenyl)benzaldoxime in water–dioxane (4:1) at 25 °C, interpreted in terms of a central E2 elimination reaction. The equivalent value for the E2 reaction of (2-phenylethyl)trimethylammonium iodide [ArCH₂CH₂N⁺(CH₃)₃·I⁻] in ethoxide/ethanol at 30 °C[11] is 3.77. This indicates a larger build up of negative charge on the β-carbon in the transition state in the C—C—N⁺ than in the C=N—N⁺ and C=N—O systems.

The second-order rate constants k_2 (Table III) for the three (*E*)-benzaldehyde *N*-(substituted benzyl)-*N*,*N*-dimethylhydrazonium bromides (**8g–i**) were found to satisfy both the Hammett (ρ = 0.65) and Brønsted (β_{1g} = −0.44) equations (Figure 2). The pK_a values[17] used are for 50% aqueous methanolic solutions. The ρ = 0.65 reflects modest sensitivity to the nature of the benzyl substituents (bearing in mind that the electronic effect must be transmitted through the α-carbon atom of the benzyl group). Accepting a value of 2.3 as the attenuation factor[13] for the α-carbon atom, then, ρ for **15** would be predicted to be 1.50.
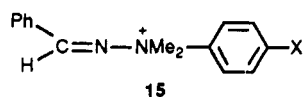
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(10) Hegarty, A. F.; Tuohey, P. J. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1313.

(11) Saunders, W. H.; Cockerill, A. F. In *Mechanism of Elimination Reactions*; John Wiley: New York, 1973; p 61.

(12) Reference deleted in press.

(13) Jones, R. A. Y. In *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press: Cambridge, UK, 1984; p 42.

(14) Keeffe, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 265.

(15) Cristol, S. J.; Norris, W. P. *J. Am. Chem. Soc.* **1954**, *76*, 3005.

(16) Reference deleted in press.

(17) *Handbook of Biochemical Selected Data for Molecular Biology*; Sober, H. A., Harte, R. A., Eds.; The Chemical Rubber Co.: Cleveland, OH, 1970; p J203.
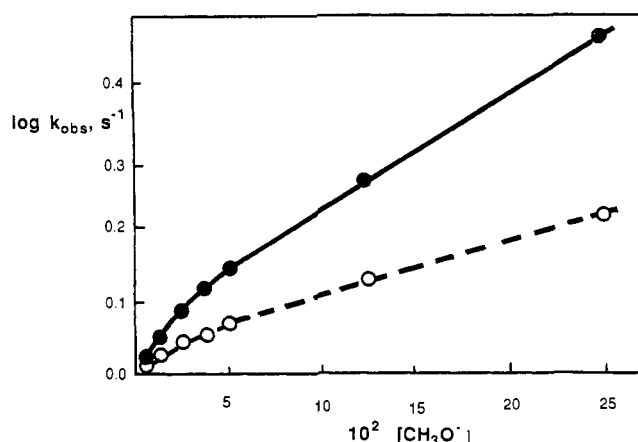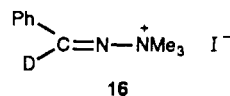
Figure 3. Pseudo-first-order rate constant versus methoxide ion concentration for benzaldehyde trimethylhydrazonium iodide **2** (—) and its deuterated analogue **16** (- -) in methanol at 25 °C.

Primary Isotope Effect. Benzaldehyde trimethylhydrazonium iodide **8b** and its isotopomer **16** were studied

16

in methanol/sodium methoxide within the concentration range 5×10^{-4} to 5×10^{-2} M at 25 °C (Table IV).

Plots of k_{obs} versus base concentration gave excellent linear fits up to 1×10^{-2} M NaOMe for both compounds and from these data k_H = 4.16 M^{-1} s^{-1} and k_D = 2.00 M^{-1} s^{-1} were calculated for **8b** and **16**. Therefore the primary kinetic isotope effect, k_H/k_D, for the reaction is 2.1.

In an effort to establish if there was a change in mechanism with base concentration, substrates **8** and **16** were examined up to 2.5×10^{-1} M NaOMe using a stopped-flow spectrometer. No plateau or saturation point was observed in the k_{obs} versus [NaOMe] plots for either substrate (Figure 3). In fact it was evident that there was also a linear relationship between the rate of elimination and methoxide ion concentration beyond 5×10^{-2} M, but $k_{obs}{}^H/k_{obs}{}^D$ remained equal to 2.1 over the entire concentration range (see Table IV). Keeffe and Jencks[14] observed similar behavior during a study of the hydroxide-catalyzed 1,2-elimination of [2-(*p*-nitrophenyl)ethyl]trimethylammonium perchlorate as buffer concentration was increased. They interpreted their results as a change in the rate-determining step from (E1cB)ᵢ to an (E1cB)ᴿ mechanism.

A change in mechanism from rate-determining elimination to methanolysis of the resulting nitrile is unlikely since the latter process, studied independently, occurs much more slowly (>10⁵-fold). Taking into account (i) that k_H/k_D remains constant throughout the entire concentration range and (ii) curvature was not observed when the neutral base triethylamine was used as base at least up to 5×10^{-2} M, we conclude that the observed deviation from linearity is due to a salt effect when ion pairing and competition for solvent molecules predominates at high methoxide concentration.

Base and Configuration Effects. The effects of different bases on the reactivity of (*E*)-benzaldehyde trimethylhydrazonium iodide **2** and 2,2-dimethyl-1,1-dihydrophthalazinium iodide **4** in methanol at 25 °C was considered in order (i) to determine the extent of C–H bond breaking in the transition state of the reaction and (ii) to estimate the difference between syn- and anti-periplanar elimination (using **4** as a model for the acyclic *Z* isomer **3**) with the amine bases morpholine, *N*-methyl-

Table V. Data for Brønsted Plots Obtained in Anhydrous Methanolic Solution at 25 °C for (a) Substrate 2 and (b) Substrate 4

base[a]	pK_a	log k_2, M⁻¹ s⁻¹	
		2	4
pyrrolidine	11.27	−1.33	0.65
triethylamine	10.65	−1.84	−0.04
N-methylpiperidine	10.08	−2.07	−0.26
morpholine	8.36	−2.74	−0.75
N-ethylmorpholine	7.70	−3.78	−1.67
N-methylmorpholine	7.41	−	−1.80

[a] pK_a values taken from ref 17.

piperidine, triethylamine, and pyrrolidine (pK_a values ranging between 7.41 and 11.27).

The linear Brønsted plots defined by the data given in Table V for the 1,2-elimination reaction give an estimate of the extent of the C–H bond breaking in the transition state; for (E)-benzaldehyde N,N,N-trimethylhydrazonium iodide **2**, β = 0.69, while for 2,2-dimethyl-1,2-dihydrophthalazinium iodide **4**, β = 0.57 (Figure 4). From these values it can be estimated that the C–H bond is about 70% broken for **2** and it is less advanced in the case of the cyclic **4**. The rate of 1,2-elimination for **4** is about 60 times faster than the E isomer **2** (although this ratio varies somewhat with the nature of the base).

From kinetic data for **2** measured at six temperatures in the range 25–50 °C and at six base (MeO⁻) concentrations, $\Delta H^{\ddagger}$ = 20.6 kcal mol⁻¹ and $\Delta S^{\ddagger}$ = 3.0 cal mol⁻¹ K⁻¹ were estimated. These may be compared with the values for the acetylene-forming reactions which also show near zero as $\Delta S^{\ddagger}$ values of trans-β-bromostyrene (**17**, E_a = 31.8 kcal/mol; $\Delta S^{\ddagger}$ = 4.0 cal mol⁻¹ K⁻¹) and cis-β-bromostyrene (**18**, E_a = 21.1 kcal/mol; $\Delta S^{\ddagger}$ = −5.8 cal mol⁻¹ K⁻¹). Interestingly the very large rate ratio of 21 × 10⁴ for **18** to **17** was explained in terms of a multistep carbanion intermediate process for syn elimination and a concerted process for anti elimination.[15]

Ph   H   Ph   Br
  \ C=C /   \ C=C /
  /   \   /   \
H   Br   H   H
     17   **18**
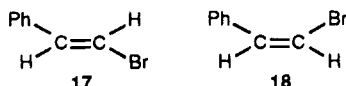
Taken together the kinetic data for the elimination of trimethylamine from the hydrazonium salts **2** indicates that it occurs via an E2 transition state (see **19**) in which C–H bond breaking has proceeded to a marked extent and N–N bond cleavage is less well advanced.

Ar
  \
   C≡N
  .'' ''.
 H   NMe₃
δ⁻   δ⁺
 B'

19
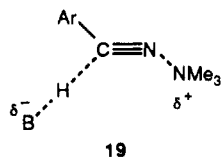
Solvent Effect and Product Analysis. The overall reactivity of **2** was found to decrease nonlinearly as the water content of aqueous methanolic solutions, of constant base concentrations, increased from 0 to 80%. Since base-catalyzed elimination and hydrolysis were both taking
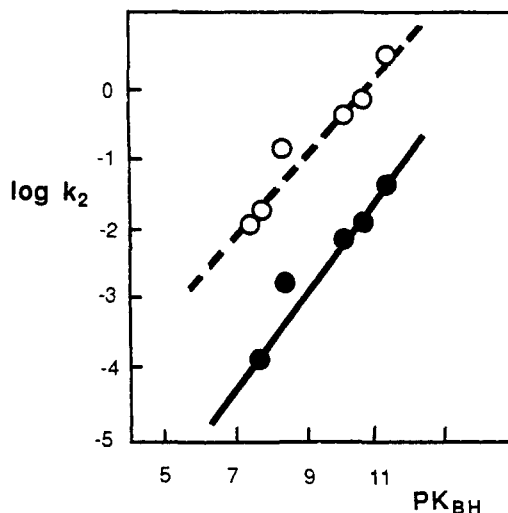

Figure 4. Brønsted plots for benzaldehyde trimethylhydrazonium iodide **2** (—) and 2,2-dimethyl-1,2-dihydrophthalazinium iodide **4** (⁻⁻) in methanolic solution at 25 °C.

place when water was present the product ratio (benzonitrile versus benzaldehyde) as a function of percent H_2O was determined by analyzing the UV absorption of the mixture when the reaction had gone to completion. This analysis was made possible by (i) the quantitative decomposition of the quaternary salt under the experimental conditions and (ii) the very significant difference in optical densities between benzaldehyde (ϵ = 11 942) and benzonitrile (ϵ = 658) at 245 nm in aqueous methanolic solutions of similar concentration.

From these results (Table VI) it can be seen that the hydrolytic reaction becomes significant only when the water concentration of the methanolic solutions exceeds 7% (v/v) and that its rate steadily increases until in 100% water it is predicted to be 4.7 × 10⁻¹ M⁻¹ s⁻¹ (concentration of HO⁻ + $CH_3O^−$ = 0.870 × 10⁻² M). The rate of elimination (k_{elim}) on the other hand rapidly decreases as the polarity of the solvent system increases.

From the slope of a Grunwald–Winstein plot[20] of log k_{elim} versus Y (Figure 5) a value of −0.255 was calculated for m. The parameter m can also be considered as an index of the degree of charge separation at the transition state. In the related elimination of trimethylsulphonium salt for example the index m = −0.778 (0–100% $EtOH/H_2O$).[16]

Reversible addition of MeO⁻ to the (E)-hydrazonium salt **2** could in theory lead to the formation of the (more rapidly eliminating) isomer **3**. While we cannot rigorously exclude this possibility, it is unlikely that this is the main reaction pathway since (a) rate-determining methoxide-induced isomerization is unlikely to show such a large kinetic isotope effect and (b) attempts to induce isomerization using low concentrations of MeO⁻ showed no NMR evidence for the presence of the less stable **3**.

Ab Initio Calculations on Model Species. In order to gain further information about the eliminative processes, we have also considered the model reactions involving the

Table VI. Pseudo-First-Order Rate Constants for Decomposition of 2 in Aqueous Methanolic Solution (25 °C, 255 nm) and Percentage Product Composition

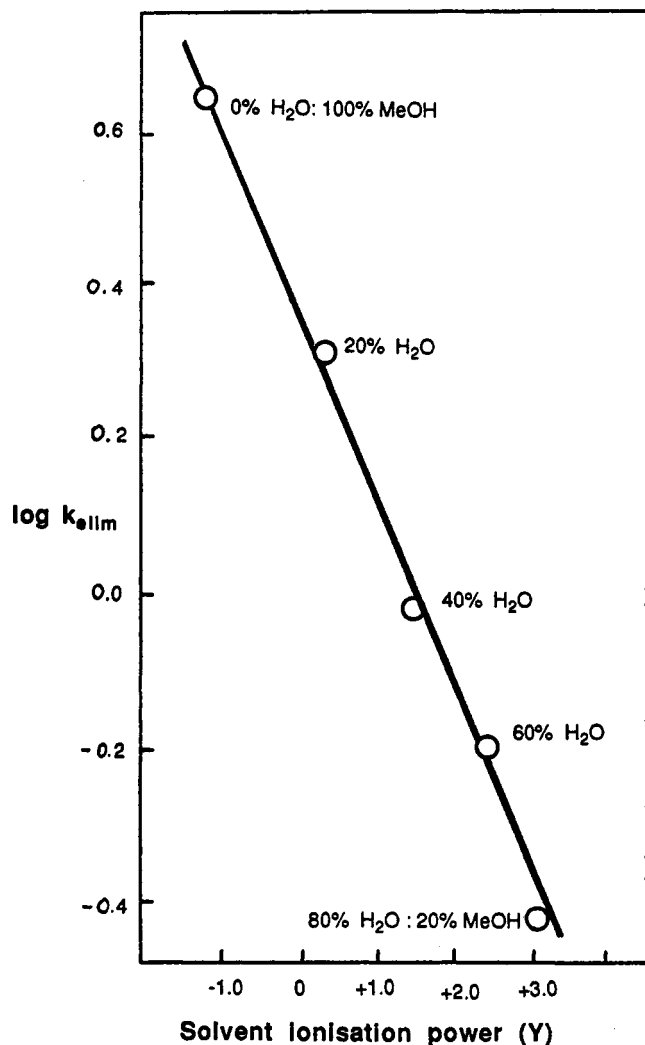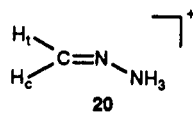| % H_2O (v/v)	$10^2[CH_3O^− + HO^−]$, M	$10^3 k_{obs}$, s⁻¹	% PhCHO[a]	% PhCN[a]	k_{hydr}, M⁻¹ s⁻¹	k_{elim}, M⁻¹ s⁻¹
0	0.810	37.78	−	100	−	4.66
20	0.817	17.28	3.4	96.6	0.072	2.04
40	0.920	10.18	13.9	86.1	0.15	0.95
60	0.875	7.75	28.8	71.2	0.26	0.63
80	0.930	6.74	48.0	52.0	0.35	0.38

[a] Using mean value $[CH_3O^− = OH^−]$ = 0.87 × 10⁻² M.

Figure 5. The elimination reaction of the unsubstituted hydrazonium iodide **8b** in aqueous methanolic HO^-/CH_3O^- (0.870 × 10^{-2} M) at 25 °C satisfies the Grunwald–Winstein equation.

Table VII. Total (Hartrees) and Relative (kcal/mol) Energies for the Anti- and Syn-Periplanar Elimination of the (H_2O, CH_2=NNH_3^+) System

	anti elimination[a]		syn elimination[a]	
	21a	**21b**	**21c**	**21d**
Total Energies[d]				
HF/3-21G	−224.15617	−224.11144	−224.17985	−224.09656
HF/6-31G*	−225.39165	−225.32323	−225.40793	−225.31137
MP2/6-31G*	−226.02962	−225.97590	−225.04938	−225.95507
ZPE[b]	56.7	51.1	58.0	50.9
S[c]	83	79	76	82
Relative Energies				
HF/3-21G	0.0	28.1	0.0	52.3
HF/6-31G*	0.0	42.9	0.0	60.6
MP2/6-31G*	0.0	33.7	0.0	59.2
MP2/6-31G* + ZPE	0.0	28.1	0.0	52.1

[a] Using HF/3-21G geometries given in Figure 6. [b] Zero-point vibrational energies at HF/3-21G and scaled by 0.9. [c] Entropies in cal/mol K. [d] The MP2/6-31G* energy of the isolated (H_2O + H_2C=NNH_3)$^+$ system is −226.01020 Hartrees.

Table VIII. Barrier Heights ($\Delta E^{\ddagger}$, kcal/mol)[a] and Entropy Variations ($\Delta S^{\ddagger}$, cal/mol K)[b] in the Concerted Eliminations of Hydrazonium Ion 20 Using H_2O and NH_3 as Bases

	anti elimination		syn elimination	
base	$\Delta E^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta E^{\ddagger}$	$\Delta S^{\ddagger}$
H_2O	28	−4	52	6
NH_3	13	−2	38	5

[a] Values at MP2/6-31G* + ZPEs. [b] Using HF/3-21G geometries and frequencies.

simplest hydrazonium cation **20** with water and ammonia molecules as bases.

20

Because of the computational difficulties encountered in treating zwitterionic systems, the neutral molecules (H_2O and NH_3) represent, for this reaction, better theoretical models for bases than their corresponding anions.

Ab initio calculations were carried out with the GAUSSIAN-82 program system.[19] Molecular geometries of stationary points on the potential energy surfaces were optimized at the Hartree–Fock level of theory using the split-valence 3-221G basis set.[20] Harmonic vibrational frequencies were calculated at this level in order to characterize stationary points as minima or transition structures and to estimate the zero-point vibrational contributions to relative energies. The latter have been estimated at the second-order Møller–Plesset perturbation theory[21]

making use of the polarized 6-31G* basis set[22] and the optimized HF/3-21G geometries (MP2/6-31G*//HF/3-21G). To simplify the presentation of data, only geometrical parameters for the (H_2O·H_2C=NNH_3)$^+$ system are displayed in Figure 6.

Firstly, we note that the NH_2-site proton affinity of hydrazone (giving rise to the ion **20**) amounts to 210 kcal/mol at MP2/6-31G*. This value is somewhat smaller than that of 238 kcal/mol previously computed (at a similar level of theory) for amidine.[23]

The hydrazonium ion **20** is also found to be quite stable conformationally. At the HF/3-21G level, the barrier to inversion at nitrogen in **20** is calculated to be 51 kcal/mol whereas the corresponding values in the neutral hydrazone (CH_2=NNH_2) and methanimine (H_2C=NH) amount only to 34 and 26 kcal/mol, respectively. Such a reluctance to undergo isomerization is consistent with the observed difficulty in forming the (Z)-hydrazonium ion either thermally or photochemically, employing E isomers as starting materials.[5]

Removal of the H_t and H_c atoms in **20** by water are preceded by the formation of molecular complexes **21a** and **21c**, respectively (Figure 6). Owing to an extra hydrogen bond, the syn complex **21c** is markedly more stabilized than the anti **21a** (Table VII). In contrast, the transition structure for the anti-periplanar elimination **21b** is calculated to be significantly lower in energy (12.9 kcal/mol at MP2/6-31G* + ZPEs) than that for the syn elimination **21d**. In both cases, the eliminative process is concerted and highly synchronous. In both **21b** and **21d**, the C–H and N–N distances are lengthened appreciably with respect to those in the starting ion **20** (namely, 1.07 and 1.55 Å, respectively) and the ratio of C–H_t distances in **21a** and

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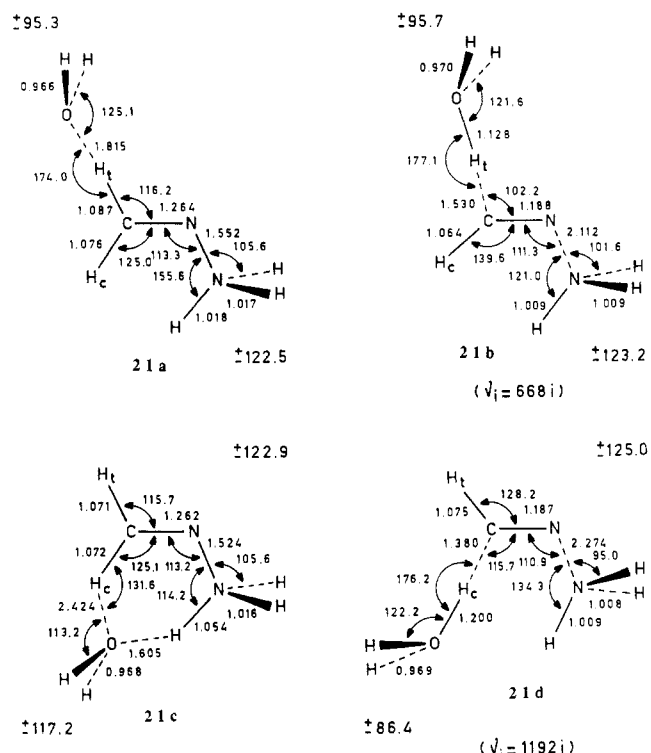(23) Del Bene, J. E. *J. Comput. Chem.* **1984**, *5*, 381.

Figure 6. HF/3-21G optimized geometries of the complex **21a** and transition structure **21b** for anti elimination and the complex **21c** and transition structure **21d** for syn elimination. Bond lengths given in angstroms and bond angles in degrees. ν_i are imaginary frequencies in cm^{-1}. Values with "±" are dihedral angles of symmetrical hydrogen atoms.

21b and N–N are in fact similar to each other (0.70 Å for C–H$_t$ and 0.73 Å for N–N).

The entropy variations given in Table VIII show that the anti elimination bears a negative $\Delta S^{\ddagger}$ while the syn elimination is associated with a positive $\Delta S^{\ddagger}$. The computed value of $\Delta S^{\ddagger} = 6$ cal mol^{-1} K^{-1} for the syn elimination can be compared with the value of 3 cal mol^{-1} K^{-1} determined experimentally for the syn elimination of **2**. Thus, it is tempting to suggest that a "preassociation mechanism" through the complex formation also occurs in the reactions in solution.

Similar calculations have also been carried out for reactions between the ion **20** and NH$_3$. Structure **22a** represents the initial H-bonded complex (which is an energy minimum). The transition structure for an anti-periplanar elimination **22b** lies 11.2 kcal/mol (at MP2/6-31G* + ZPEs) *lower* in energy than that for the syn process. The transition structure **22b** is also product-like with extensive C–H bond fission but only modest extension in its N–N bond, the reaction being more asynchronous than in the water case.
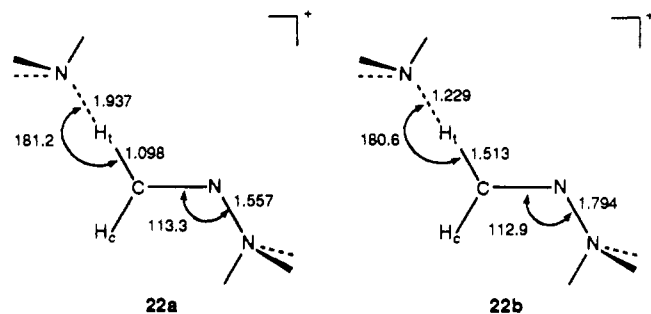
It is clear from data given in Table VIII that the eliminative process involving NH$_3$ as the attacking base is far

more favored over that involving H$_2$O.

Overall, calculated results for the model elimination reactions are consistent with kinetic data showing clearly that the anti elimination of hydrazonium salts is, under the same experimental conditions, much easier to achieve than the syn process. The high stereospecificity of these reactions was previously discussed in detail in MO calculations of the energy pathway for decomposition of cis and trans (HCNH)$^-$ anions.[24] The *anti elimination is stereoelectronically allowed* simply because the two engaging electron pairs migrate in the same sense. In contrast, the *syn elimination is stereoelectronically forbidden* because the two responsible electron pairs migrate in opposite senses.[24] Alkyne-forming eliminations from haloalkenes show a similar preference for anti elimination with the calculated barrier for loss of halide from the corresponding anions being 4.1 kcal/mol lower than from the syn anion.[25]

Concluding Remarks

Many chemists associate 1,2-elimination reactions solely with olefin- and acetylene-forming processes. This is quite understandable as there are comparatively few mechanistic studies of 1,2-eliminations that yield imines or nitriles as product. It has now become clear that anti-periplanar eliminations leading to nitriles proceed with greater ease than syn elimination (the ratio k_{anti}/k_{syn} is typically 60–70). Together with previous studies,[10,24,26] it can be generalized that the stereoelectronic effect of nitrogen in elimination reactions (or in nucleophilic additions) is always large (where other electronic or steric factors are not involved to a marked sense). Such an effect is due to the localization of the lone pair on nitrogen to well-defined areas of space in contrast to the case of oxygen.

This study has also shown the synthetic advantages of converting an aldehyde group to a nitrile in the base-initiated elimination of a quaternary hydrazone. The method represents a one-pot synthesis which is facile, rapid, and high yeilding (>75%) in the case of aromatic derivatives.

Experimental Section

General. Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1710 IR Fourier transform spectrometer. Proton NMR spectra of approximately 10% (v/v) in stated deuterated solvents were obtained on a JEOL JNM-GX 270 Spectrometer. Tetramethylsilane was used as internal standard, and chemical shifts were reported in parts per million.

Aryl Aldehyde *N,N*-Dimethylhydrazones. A mixture of the aldehyde (0.025 moles) and as-dimethylhydrazine (1.5 g, 0.025 mol) in 50 mL of benzene was refluxed in a Dean–Stark apparatus until the theoretical quantity of water (0.9 mL) was collected. Removal of the solvent under reduced pressure gave the desired product in high enough purity to be used directly in the next synthetic step.

Aryl Aldehyde *N,N,N*-Trimethylhydrazonium Iodides. Two equivalents of methyl iodide (3.55 g, 0.025 mol) were added to the appropriate dimethylhydrazone (0.0125 mol) in methanol (25 mL), and the resulting solution was refluxed for 4 h. In many cases the hydrazonium iodide precipitated; however, if this did not occur it was induced by concentrating the solution and adding dry diethyl ether. The crude product thus obtained was recrystallized from methanol (see Table I for ^{1}H NMR data). (a) X = H: white crystals of mp 217–218 °C (lit.[27] mp 233–235 °C

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ex methanol). Anal. Found: C, 41.44; H, 5.19; N, 9.37. $C_{10}H_5N_2I$ requires: C, 41.39; H, 5.21; N, 9.66. (b) X = *p*-CH₃: white crystals of mp 206–207 °C. Anal. Found: C, 43.16; H, 5.47; N, 8.93. $C_{11}H_{17}H_2I$ requires: C, 43.43; H, 5.63; N, 9.21. (c) X = *m*-Br: white crystals of mp 201–202 °C. Anal. Found: C, 32.61; H, 3.64; N, 7.29. $C_{10}H_{14}N_2BrI$ requires: C, 32.54; H, 3.82; N, 7.59. (d) X = *p*-Cl: yellow crystals of mp 197 °C. Anal. Found: C, 36.93; H, 4.20; N, 8.42. $C_{10}H_{14}N_2ClI$ requires: C, 37.00; H, 4.35; N, 8.63. (e) X = *p*-NO₂: yellow crystals of mp 210–214 °C (sublimes and decomposes) (lit.[28] mp 197 °C). Anal. Found: C, 35.71; H, 4.14; N, 12.68. $C_{10}H_{14}N_3O_2I$ requires: C, 35.84; H, 4.21; N, 12.54. (f) X = *m*-NO₂: orange crystals of mp 204–205 °C (lit.[27] mp 212–214 °C ex DMF). Anal. Found: C, 36.71; H, 4.32; N, 12.31. $C_{10}H_{14}N_3O_2I$ requires: C, 35.84; H, 4.21; N, 12.54.

Benzaldehyde-*formyl*-²H. By means of a syringe, 20 mL (10 equiv) of D₂O (99.8% atom % D; Aldrich, Gold Label) was added to a magnetically stirred solution of 21 g (0.1 mol) of benzil (recrystallized from carbon tetrachloride) in 50 mL of 1,4-dioxane (freshly distilled form sodium sand) under a dry atmosphere of nitrogen at 20–25 °C. To the resulting fine suspension of benzil were added, with rapid stirring at 2-min intervals, four 2-g portions of potassium cyanide (dried overnight at 125 °C). After the second addition the mixture became homogeneous and the yellow color disappeared shortly after the last addition of cyanide. Stirring was continued for 1 h as potassium benzoate gradually precipitated. The mixture was then diluted with 200 mL of distilled water and extracted with two 100-mL portions of diethyl ether. The combined ether extracts were then washed with 5% sodium carbonate solution, 200 mL of water, and finally with 100 mL of saturated sodium chloride solution. The yellow organic layer was finally dried with anhydrous magnesium sulfate. After removal of the solvent the residue was distilled under water-pump pressure to yield 6.04 g (56% yield) of a colorless liquid of bp 70 °C (18 mmHg). By NMR analysis the product contained 0.997 atom of deuterium per molecule. IR (thin film): 2100, 2075 (C–D stretching), 1690 (C=O) cm⁻¹.

[1-²H]Benzaldehyde *N,N*-dimethylhydrazone: colorless liquid (54% yield), 99.7% deuterium incorporation; bp 72 °C (0.4 mmHg); ¹H NMR (CDCl₃) δ 2.96 (6 H, s), 7.17–7.38 (3 H, m), 7.52–7.6 (2 H, m).

[1-²H]Benzaldehyde *N,N,N*-trimethylhydrazonium iodide: white platelike crystals (85% yield), 99.7% deuterium incorporation (vide infra); mp 233–234 °C (ex methanol). Anal. Found: C, 41.44; H, 5.19; N, 9.37. $C_{10}H_{15}N_2I$ requires: C, 41.39; H, 5.21; N, 9.66.

Benzaldehyde *N,N*-Dimethyl-*N*-benzylhydrazonium Bromide. Benzaldehyde *N,N*-dimethylhydrazone (2.96 g, 0.02 mol) and benzyl bromide (3.42 g, 0.02 mol) were stirred overnight in 25 mL of dry benzene while it was maintained at 40–45 °C. The resulting white precipitate was filtered under suction, washed with *n*-pentane, and finally recrystallized from dioxane/hexane to afford 3.71 g (58% yield) of product, mp 120–121 °C. Anal. Found: C, 60.00; H, 6.07; N, 8.76; Br, 25.33. $C_{16}H_{19}N_2Br$ requires: C, 60.19; H, 6.00; N, 8.78; Br, 25.03. Similarly prepared was **benzaldehyde *N,N*-dimethyl-*N*-(*p*-bromobenzyl)-hydrazomium bromide:** long needlelike white crystals (33% yield); mp 156–157 °C (ex acetonitrile). Anal. Found: C, 48.01; H, 4.48; N, 6.84; Br, 40.55. $C_{16}H_{18}N_2Br_2$ requires: C, 48.26; H, 4.56; N, 7.04; Br, 40.14.

Benzaldehyde *N,N*-Dimethyl-*N*-(*p*-nitrobenzyl)-hydrazonium Bromide. A mixture of *p*-nitrobenzyl bromide (4.32 g, 0.02 mol) and benzaldehyde *N,N*-dimethylhydrazone (2.96 g, 0.02 mol) in 40 mL of acetonitrile was refluxed for 1 h. Within the first 10–15 min the product began to precipitate. The reaction vessel was cooled, and the isolated product was washed with dry diethyl ether and recrystallized from ethanol (4.95 g, 68% yield): mp 158–161 °C. Anal. Found: C, 52.97; H, 5.01; N, 11.66; Br, 21.78. $C_{16}H_{18}N_3O_2Br$ requires: C, 52.76; H, 4.98; N, 11.54; Br, 21.94.

2-Methylphthalazinium Iodide. Phthalazine (5.67 g, 0.0435 mol) and methyl iodide (14.2 g, 0.1 mol) were boiled under reflux in methanol (100 mL) for 3 h. When the reaction solvent was removed under reduced pressure, precipitation of the product ensued rapidly. The bright yellow crystalline material (11.65 g, 98%) was collected by filtration, washed well with diethyl ether, and left overnight in an oven at 55–60 °C: mp 243–244 (lit.[4a] mp 240–243 °C dec).

2,2-Dimethyl-1,2-dihydrophthalazinium Iodide. 1-Methylphthalazinium iodide (6 g, 0.022 mol) was added to a stirred solution of 18 g of sodium borohydride in 600 mL of water. Over the following 3 h the reaction mixture became mildly exothermic. Workup involved extraction of the intermediate product with two 200-mL aliquots of diethyl ether followed by a further two aliquots after the aqueous layer had been saturated with sodium chloride. The combined ethereal extracts were dried with anhydrous magnesium sulfate, and the solvent was removed to yield 2-methyl-1,2-dihydrophthalazine as a cloudy yellow oil. This was rapidly dissolved in 50 mL of methanol, and methyl iodide (9.36 g, 0.066 mol) was added. The resulting mixture was refluxed for 3 h during which time it became yellow in color and translucent. On cooling overnight pale yellow crystals precipitated. Then the filtrate was reduced to half volume and cooled; further product was recovered. After washing the combined crystalline product with diethyl ether it was recrystallized from methanol to yield 3.89 g (61% yield) of 2,2-dimethyl-1,2-dihydrophthalazinium iodide: mp 181–182 °C (lit.[4a] mp 175–176 °C). Anal. Found: C, 41.71; H, 4.58; N, 9.82; I, 43.91. $C_{10}H_{13}N_2I$ requires: C, 41.68; H. 4.55; N, 9.72; I, 44.05.

Kinetic Measurements. Methanol (Merck) was dried prior to being used by refluxing overnight and distilling from magnesium methoxide which was prepared in situ from magnesium turnings and iodine as catalyst. Methanolic solutions of sodium methoxide, standardized by volumetric analysis, were obtained by diluting an approximately 0.5 M solution which in turn was prepared by adding a fractured glass vial of pure sodium (Sodium Ampoules, Ventron (D 7500 Karlsruhe 1)) to the solvent under nitrogen. This primary solution was standardized prior to use by titrating against a methanolic HCl solution (concentrated aqueous HCl vial; B.D.H. "Convol" ampoule) using phenolphthalein as indicator and was otherwise stored under an atmosphere of dry nitrogen. Methanolic solutions of other bases used in the kinetic study were freshly prepared as outlined above, following purification of the bases by distillation in the presence of a dehydrating agent (indicated in parenthesis): triethylamine and morpholine (KOH), *N*-methyl- and *N*-ethylmorpholine, *N*-methylpiperidine, and pyrrolidine (BaO).

The kinetics of all reactions were studied in anhydrous methanol or aqueous methanol by following the change in optical density with time at suitable wavelengths using a Cary Model 210 spectrometer or a Durrum stopped-flow spectrometer. Initial repetitive scans of the reaction mixture established a suitable wavelength at which an appreciable optical density change occurred during the course of the reaction. For 2,2-dimethyl-1,2-dihydrophthalazinium iodide this wavelength was 260 nm. Kinetic runs were initiated by injecting a known aliquot, usually 25 μL, of stock solution (1 × 10⁻² M) into a quartz cell containing the reaction solvent which had been previously equilibrated at the appropriate temperature for at least 15 min. The change in optical density with time was then followed at a fixed wavelength. Pseudo-first-order rate constants were calculated from plots of log (A_t – A_∞) versus time where A_t is the absorbance of the solution at any time t and A_∞ is the absorbance of the solution at time equal to infinity. All stock solutions were made of methanol with the following exceptions: *m*-NO₂- and *p*-NO₂-benzaldehyde *N,N,N*-trimethylhydrazonium iodide and 2,2-dimethyl-1,2-dihydrophthalazinium iodide, which were prepared in anhydrous acetonitrile.

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