

Rapid scan spectrophotometric and kinetic studies in the reactions of 4-substituted-2,6-dinitro-*N-n*-butylanilines with *n*-butylamine in dimethyl sulfoxide



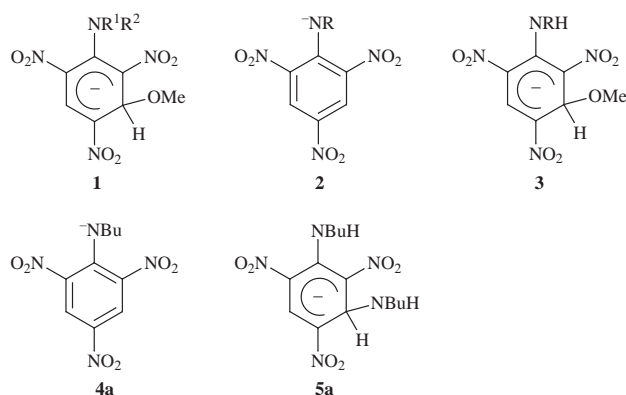
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The reactions of 2,4,6-trinitro-*N-n*-butylaniline **6a**, 4-cyano-2,6-dinitro-*N-n*-butylaniline **6b** and 4-methoxycarbonyl-2,6-dinitro-*N-n*-butylaniline **6c** with *n*-butylamine in dimethyl sulfoxide have been investigated by rapid scan spectrophotometry and a stopped-flow method. **6a** and **6b** react competitively with *n*-butylamine to give the conjugate bases due to fast proton transfer and anionic σ -adducts by the addition of amine at the 3-position, while **6c** reacts to give the conjugate base. The distinct spectra of only the conjugate bases have been observed. The effect of substituents on rate and equilibrium constants obtained for these competitive reactions is discussed.

Introduction

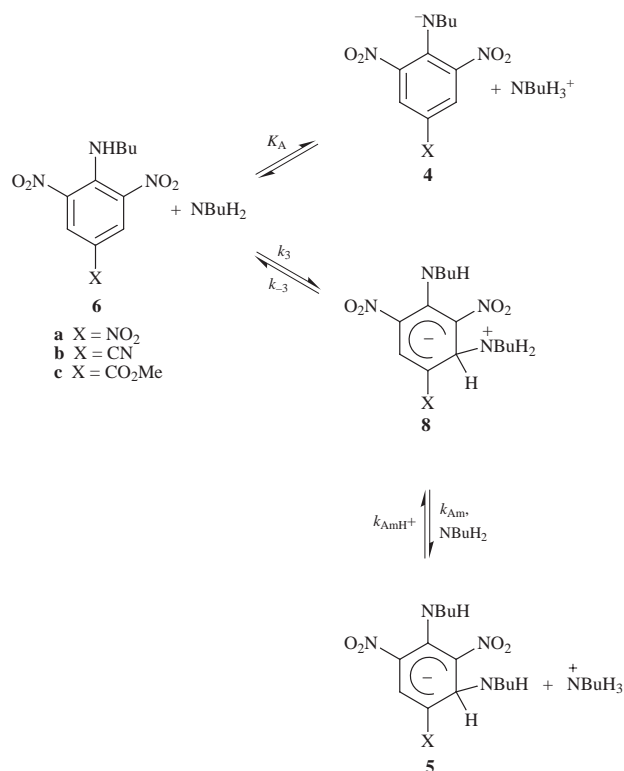
There have been several reports on the colour-forming interactions of 2,4,6-trinitro-*N*-substituted-anilines with methoxide ion in solution.¹⁻⁵ It has been revealed that, as for 1:1 interactions, methoxide addition at the 3-position to give anionic σ -adducts **1** occurs in the reactions of 2,4,6-trinitro-



N,N-dialkylanilines with methoxide ion in dimethyl sulfoxide (DMSO).¹⁻³ On the contrary, competitive proton transfer from the alkylamino-group to give anions **2** and methoxide addition to give **3** occur in the reactions of 2,4,6-trinitro-*N*-alkylanilines.¹⁻⁵ Previously we have reported that both an anion **4a** and an amine adduct **5a** are formed finally in the reaction of 2,4,6-trinitroanisole with *n*-butylamine in DMSO.⁶

Recently Chamberlin and Crampton have revealed by NMR measurements that **4a** and **5a** are formed competitively in the reaction of 2,4,6-trinitro-*N-n*-butylaniline with *n*-butylamine in DMSO and made kinetic and equilibrium studies relating to these interactions.⁷ However, it seems that competition between proton transfer and base addition has still remained obscure, since a distinct spectrum of only **4a** has never been observed.

We have made kinetic and equilibrium studies of the reactions of 4-substituted-2,6-dinitroanisoles with amines in DMSO.^{6,8-11} In this study we observed rapid scan spectra of anions **4** produced instantaneously after mixing of 2,4,6-trinitro-, 4-cyano-2,6-dinitro- and 4-methoxycarbonyl-2,6-dinitro-*N-n*-butylanilines with *n*-butylamine in DMSO. Kinetic and equilibrium studies on these interactions were made with rapid scan spectrophotometry and a stopped-flow method. The likely reaction mechanism is interpreted by Scheme 1.



Scheme 1

Results

Absorption spectra

UV absorption spectra relevant to the reaction of 4-methoxycarbonyl-2,6-dinitro-*N-n*-butylaniline **6c** with *n*-butylamine are shown in Fig. 1. The rapid scan spectrum measured immediately (2 ms) after mixing is curve (b), the spectral change of which was not observed with the elapse of time. Previously we have observed absorption bands similar to curve (b) in the reaction of 4-methoxycarbonyl-2,6-dinitroanisole with *n*-butylamine in DMSO.⁹ An absorption band at 540 nm is attributed to an anion **4c** (the conjugate base of **6c**) due to very fast proton transfer. This assignment was ascertained from the following UV absorption and NMR measurements for the reaction of **6c** with sodium methoxide in methanolic DMSO. The NMR

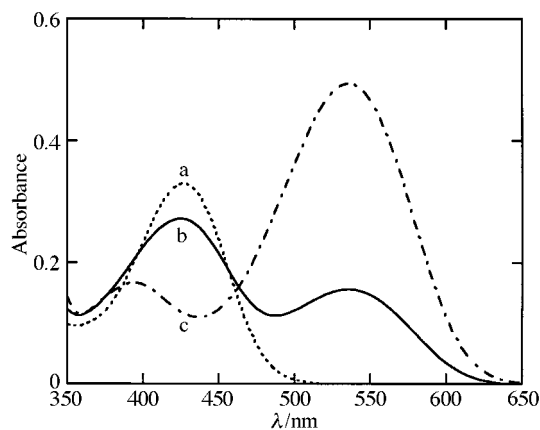


Fig. 1 Absorption spectra relevant to the reaction of **6c** 5.0×10^{-5} mol dm $^{-3}$ with *n*-butylamine (0.009 mol dm $^{-3}$) in DMSO at 25 °C: (a) **6c** in the absence of amine, (b) 2 ms (sweep time = 2 ms) after mixing and (c) spectrum of **6c** 5.0×10^{-5} mol dm $^{-3}$ in the presence of sodium methoxide 6×10^{-4} mol dm $^{-3}$ in DMSO–MeOH (0.8%)

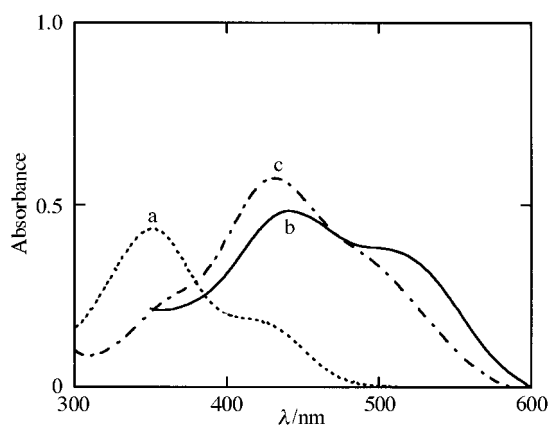
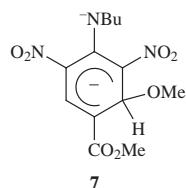


Fig. 2 Absorption spectra relevant to the reaction of **6a** 3.0×10^{-5} mol dm $^{-3}$ with *n*-butylamine (0.053 mol dm $^{-3}$) in DMSO at 25 °C: (a) **6a** in the absence of amine, (b) 2 ms and (c) 20 s after mixing (sweep time = 2 ms)

spectrum of **6c** has a single peak in the aromatic region at δ 8.62. The addition of 1 equivalent of sodium methoxide caused the appearance of two doublets (J , 2 Hz) at δ 7.92 and 8.33 attributed to **4c**. The non-equivalence of the ring-hydrogens is due to restricted rotation about the ring-carbon to nitrogen bond in the anion. In the presence of two equivalents of methoxide, two singlets were observed at δ 5.65 and 8.17, attributed to the dianion **7**. These changes are analogous



to those reported in the reactions of 2,4,6-trinitro-*N*-methylaniline with methoxide.³ The absorption spectrum of **6c** in the presence of low methoxide concentration in DMSO shows a band at 540 nm [see Fig. 1, curve (c)], assignable to **4c**. At a higher concentration of methoxide, bands at 325 and 422 nm appeared (not shown), which are attributed to **7**.

Absorption spectra relevant to the reaction of 2,4,6-trinitro-*N*-*n*-butylaniline, **6a**, with *n*-butylamine are shown in Fig. 2. Rapid scan spectrophotometry indicated the presence of two processes separated in time. Curves (b) and (c) are obtained 2 ms and 20 s after mixing respectively. The initial absorption

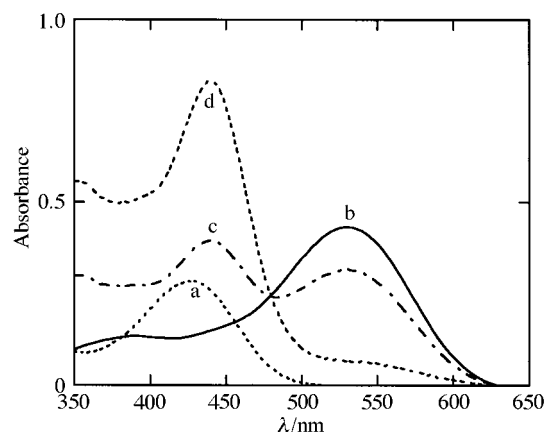


Fig. 3 Absorption spectra relevant to the reaction of **6b** 5.0×10^{-5} mol dm $^{-3}$ with *n*-butylamine (0.032 mol dm $^{-3}$) in DMSO at 25 °C: (a) **6b** in the absence of amine, (b) 0.12, (c) 0.84 and (d) 30 s after mixing (sweep time = 20 ms)

bands at 440 and 510 nm are attributed to **4a**, which was produced instantaneously after mixing. With a decrease in intensity of these bands, a new band at 430 nm developed for several seconds. Curve (c) is similar to the spectra observed finally in the reaction of 2,4,6-trinitroanisole with *n*-butylamine in DMSO⁶ and is attributed to the mixture of **4a** and **5a**.^{7,12}

Absorption spectra relevant to the reaction of 4-cyano-2,6-dinitro-*N*-*n*-butylaniline **6b** with *n*-butylamine are shown in Fig. 3. A band at 535 nm appeared instantaneously after mixing. At the expense of this band a band at 443 nm developed with an isosbestic point at 475 nm. The initial band is attributed to **4b** and the final band is ascribed to **5b**. In contrast to the case of **6a**, the band of **4b** did not overlap with that due to **5b** in the visible region.

Kinetic and equilibrium studies

Equilibrium data were obtained for **6a** and **6b** from rapid-scan spectra measured 2 ms after mixing, when the presence of amine adducts **5a** and **5b** was confirmed to be negligible under the buffer concentrations used. In contrast, data for reaction of **6c** were obtained using a convenient spectrophotometer, since there was no evidence for the formation of an amine adduct **5c**.

Equilibrium constant K_A is defined by eqn. (1), since the formation of **4** requires a single amine molecule. Values of K_A were obtained from Benesi–Hildebrand plots according to eqn. (1). Equilibrium data obtained are shown in Tables 1–3.

$$K_A = \frac{[4][\text{NBuH}_3^+]}{[6][\text{NBuH}_2]} \quad (1)$$

Table 1 Kinetic and equilibrium data for reaction of **6a** with *n*-butylamine in DMSO at 25 °C

[BuNH ₂]/10 ⁻³ mol dm ⁻³	[BuNH ₃ Cl]/10 ⁻³ mol dm ⁻³	Absorbance ^a	k_{obs}^b / s ⁻¹	k_{calc}^c / s ⁻¹
1.10	5.0	0.244		
1.47	5.0	0.283		
1.84	5.0	0.304		
2.2	5.0	0.309		
2.5	5.0	0.335		
51	5.0		27.3	26.8
76	5.0		23.7	23.1
102	5.0		21.2	21.4
127	5.0		20.4	20.0
142	5.0		19.8	19.6
152	5.0		19.8	19.4

^a Measured at 530 nm with [**6a**]₀ 3.0×10^{-5} mol dm $^{-3}$. ^b Measured at 430 nm with [**6a**]₀ 3.0×10^{-5} mol dm $^{-3}$. ^c Calculated from eqn. (3) with k_3 10 000 mol $^{-1}$ dm 3 s $^{-1}$, $k_{-3}k_{\text{AmH}^+}/k_{\text{Am}}$ 120 s $^{-1}$ and K_A 3.2.

Table 2 Kinetic and equilibrium data for reaction of **6b** with *n*-butylamine in DMSO at 25 °C

[BuNH ₂]/10 ⁻³ mol dm ⁻³	[BuNH ₃ Cl]/10 ⁻³ mol dm ⁻³	Absorbance ^a	<i>k</i> _{obs} ^b / s ⁻¹	<i>k</i> _{calc} ^c / s ⁻¹
10	4.0	0.068	22.3	24.6
15	4.0	0.092	22.8	21.7
20	4.0	0.113	21.6	21.2
25	4.0	0.132	22.2	21.6
32	4.0	0.155	22.8	22.5
53	4.0	0.211	25.6	25.6

^a Measured at 535 nm with [**6b**]₀ 5.0 × 10⁻⁵ mol dm⁻³. ^b Measured at 440 nm with [**6b**]₀ 5.0 × 10⁻⁵ mol dm⁻³. ^c Calculated from eqn. (3) with *k*₃ 900 mol⁻¹ dm³ s⁻¹, *k*₋₃*k*_{AmH⁺}/*k*_{Am} 43 s⁻¹ and *K*_A 0.085.

Table 3 Equilibrium data for reaction of **6c** with *n*-butylamine in DMSO at 25 °C

[BuNH ₂]/10 ⁻³ mol dm ⁻³	[BuNH ₃ Cl]/10 ⁻³ mol dm ⁻³	Absorbance ^a
27	4.0	0.049
39	4.0	0.073
60	4.0	0.097
78	4.0	0.115

^a Measured at 535 nm with [**6c**]₀ 5.0 × 10⁻⁵ mol dm⁻³.

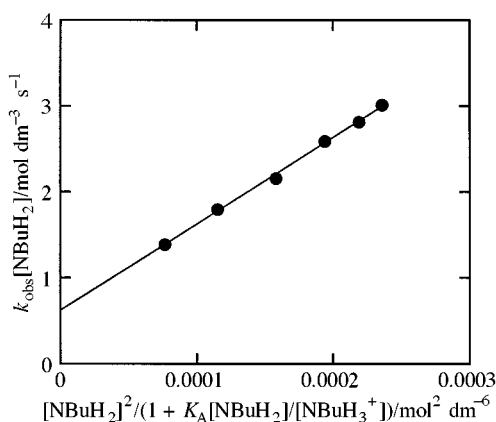


Fig. 4 Plot of *k*_{obs}[NBuH₂] vs. [NBuH₂]²/(1 + *K*_A[NBuH₂]/[NBuH₃⁺]) according to eqn. (4)

Reaction rates were measured by following the increase in the absorbance due to **5a** and **5b**. Rate constants were measured under first order conditions where buffer components were in large excess of the parent concentration.

The formation of **5** is likely to proceed *via* zwitterions **8**, which are assumed to be steady-state intermediates.⁶⁻¹⁰ Considering that the initial equilibrium is very fast, eqn. (2) applies.

$$k_{\text{obs}} = \frac{k_3 k_{\text{Am}} [\text{NBuH}_2]^2}{(k_{-3} + k_{\text{Am}} [\text{NBuH}_2]) \left(1 + K_{\text{A}} \frac{[\text{NBuH}_2]}{[\text{NBuH}_3^+]} \right)} + \frac{k_{-3} k_{\text{AmH}^+} [\text{NBuH}_3^+]}{(k_{-3} + k_{\text{Am}} [\text{NBuH}_2])} \quad (2)$$

Under the conditions *k*_{Am}[NBuH₂] ≫ *k*₋₃, where the deprotonation of **8** by NBuH₂ is rapid, eqn. (2) reduces to eqn. (3).

$$k_{\text{obs}} = \frac{k_3 [\text{NBuH}_2]}{1 + K_{\text{A}} \frac{[\text{NBuH}_2]}{[\text{NBuH}_3^+]}} + \frac{k_{-3} k_{\text{AmH}^+} [\text{NBuH}_3^+]}{k_{\text{Am}} [\text{NBuH}_2]} \quad (3)$$

Multiplying both sides of eqn. (3) by [NBuH₂] yields eqn. (4).

Table 4 Kinetic and equilibrium data for reaction of **6** with *n*-butylamine in DMSO at 25 °C

Parameter	Substrate	Value
<i>K</i> _A	6a	3.2
	6b	3.2 ^a
	6c	0.085
<i>K</i> _{c,3} /mol ⁻¹ dm ³	6a	83
	6b	58 ^a
	1-Pyrrolidin-1-yl-TNB	21
	1-Piperidino-TNB	0.47 ^b
<i>k</i> ₃ /mol ⁻¹ dm ³ s ⁻¹	1,3,5-TNB	6.3 ^b
	6a	1 000 ^c
	6b	10 000
	1-Pyrrolidin-1-yl-TNB	7 000 ^a
<i>k</i> ₋₃ <i>k</i> _{AmH⁺} / <i>k</i> _{Am}	6b	900
	1-Piperidino-TNB	690 ^b
	1,3,5-TNB	2 500 ^b
	6c	45 000 ^c

^a Data from ref. 7. ^b Data from ref. 16. ^c Data from ref. 15.

$$k_{\text{obs}} [\text{NBuH}_2] = \frac{k_3 [\text{NBuH}_2]^2}{1 + K_{\text{A}} \frac{[\text{NBuH}_2]}{[\text{NBuH}_3^+]}} + \frac{k_{-3} k_{\text{AmH}^+} [\text{NBuH}_3^+]}{k_{\text{Am}}} \quad (4)$$

Kinetic data obtained are listed in Tables 1–2. Fig. 4 shows a plot of *k*_{obs}[NBuH₂] vs. [NBuH₂]²/(1 + *K*_A[NBuH₂]/[NBuH₃⁺]) according to eqn. (4) for **6a**, when a value of *K*_A 3.2 was used. This plot is linear with a slope of 10 000 mol⁻¹ dm³ s⁻¹ and intercept of 0.62 mol dm⁻³ s⁻¹. Values of *k*₃ 10 000 mol⁻¹ dm³ s⁻¹ and of *k*₋₃*k*_{AmH⁺}/*k*_{Am} 120 s⁻¹ were derived, from which a value of *K*_{c,3} was calculated to be 83 mol⁻¹ dm³, using eqn. (5).

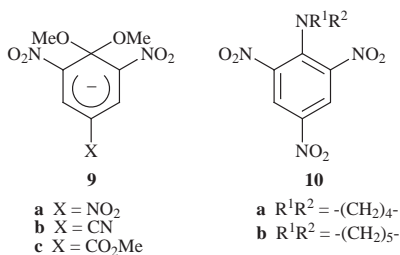
$$K_{\text{c},3} = \frac{k_3}{k_{-3}} \frac{k_{\text{Am}}}{k_{\text{AmH}^+}} \quad (5)$$

Values for *k*_{calc} estimated from eqn. (3) using the above kinetic parameters gave an excellent fit with those for observed rate constants *k*_{obs}. Similarly, kinetic parameters were obtained for **6b**. Equilibrium and rate constants are summarized in Table 4.

Discussion

Results of rapid scan spectrophotometry revealed that the reactions of **6a** and **6b** with *n*-butylamine consisted of two colour-forming processes separated in time. The first process was so rapid that the formation of coloured species was completed within 2 ms (the dead time of the apparatus), so that this fast process is attributed to proton transfer from the *n*-butylamino group to give the anions **4**. Distinct spectra of only the anions **4** were measured by rapid scan spectrophotometry, before the second process developed. The second process was slower, measurable and was ascribed to amine addition to yield **5a** and **5b**. The linear dependence of *k*_{obs}[NBuH₂] on [NBuH₂]²/(1 + *K*_A[NBuH₂]/[NBuH₃⁺]) indicates that the condition *k*_{Am}[Am] ≫ *k*₋₃ holds, so the deprotonation of **8** by *n*-butylamine is rapid.

Values of *K*_A decrease in the order **6a** (*K*_A 3.2) > **6b** (0.085) > **6c** (0.017) reflecting the order of electron-withdrawing ability of the 4-substituent groups, NO₂ > CN > COOMe. This order is the same as that of stability for methoxy-adducts **9** formed from 4-substituted-2,6-dinitroanisoles; values of equilibrium constant *K*₁ have been reported to be 17 000 for **9a**, 280 for **9b** and 6 mol⁻¹ dm³ for **9c**.^{13,14}



A value of K_A 3.2 for **6a** is identical with that (K_A 3.2) of the previous results,⁷ indicating that the previous equilibrium studies were carried out under appropriate buffer concentrations.

Values of $K_{c,3}$ decrease in the order **6a** ($K_{c,3}$ 83 mol⁻¹ dm³) > **6b** (21 mol⁻¹ dm³) > **6c** (not observed), also reflecting the order of electron-withdrawing ability of substituent groups at the *ortho* position to the sp³ carbon of the adducts **5**. The failure to observe **5c** is attributed to both less electron-withdrawing ability of the *ortho*-COOMe group and a steric effect between the bulky COOMe substituent and the added butylamino group.

As shown in Table 4, a value of k_3 10 000 mol⁻¹ dm³ s⁻¹ for **6a** is smaller than that (45 000 mol⁻¹ dm³ s⁻¹) for 1,3,5-trinitrobenzene (1,3,5-TNB)¹⁵ and greater than those for 1-pyrrolidin-1-yl-2,4,6-trinitrobenzene **10a** and 1-piperidino-2,4,6-trinitrobenzene **10b**.¹⁶ A composite effect consisting of conjugative stabilization of the 1-*n*-butylamino group and disruption in the coplanarity of the 2- and 6-nitro groups may deactivate the 3-position of **6a**, while less disruption in the coplanarity of the 2- and 6-nitro groups than in **10a** and **10b** will relatively activate the 3-position of the same reactant.

A value of $K_{c,3}$ 83 mol⁻¹ dm³ for **6a** is smaller than that (1000 mol⁻¹ dm³) for 1,3,5-TNB¹⁵ and greater than those for **10a** and **10b**.¹⁶ This tendency may be similarly attributable to the composite effect.

Experimental

The substrate **6a** synthesized previously⁶ was used as such. 4-Cyano-2,6-dinitro-*N-n*-butylaniline **6b** was prepared by reaction of 4-chloro-3,5-dinitrobenzotrile and *n*-butylamine in methanol and recrystallized from methanol. Found: C, 49.75; H, 4.47; N, 21.10. Calc. for C₁₁H₁₂O₄N₄: C, 50.00; H, 4.58; N, 21.20%.

4-Methoxycarbonyl-2,6-dinitro-*N-n*-butylaniline **6c** was prepared by esterification of 4-chloro-3,5-dinitrobenzoic acid followed by nucleophilic substitution of chlorine by *n*-butylamine. The product was recrystallized from methanol. Found: C,

48.65; H, 5.27; N, 13.89. Calc. for C₁₂H₁₅O₆N₃: C, 48.49; H, 5.09; N, 14.14%. DMSO was dried by refluxing over calcium hydride and fractionally distilled under reduced pressure before use. *n*-Butylamine, *n*-butylammonium hydrochloride and sodium methoxide were prepared as described previously.^{9,17}

UV spectra were recorded on a Hitachi U-3410 spectrophotometer. Rapid scan spectra were measured on an Otsuka Electronics rapid scan spectrophotometer. The apparatus was equipped with an automatically controlled mixing cell with a path length of 1 cm and controlled by a thermocirculator. Kinetic measurements were made with a RA-401 stopped-flow apparatus and a RA-451 data processor (Otsuka Electronics).

Kinetic traces were obtained after mixing at 25 °C. Rate constants obtained are ordinarily averages of several measurements and accurate to within ±3%. NMR spectra were recorded on a Hitachi R-22 Spectrometer (90 MHz).

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