ml of reagent grade acetone. The solution was heated in a sealed glass tube until equilibrium had been established (analysis by TLC or VPC). The excess acetone then was removed under reduced pressure and 30 ml of pentane added. The precipitate of acetone tosylhydrazone was removed by filtration and the remaining solution concentrated in vacuo. The carbonyl compound was isolated either by recrystallization or distillation from the residue.

α-Perdeuterated Ketones from Tosylhydrazones by Exchange with Acetone-d_6. The tosylhydrazone (150 mg) was dissolved in 0.6 ml of acetone-d_6 and heated in a sealed NMR tube until equilibrium was reached (analysis by NMR). The excess acetone-d_6 then was removed by distillation in vacuo and 5 ml of pentane was added to the residue. The solution was filtered from the precipitate and concentrated. The α-perdeuterated ketone was recovered by preparative VPC.

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Registry No.—Acetone, 67-64-1; acetone-d_6, 666-52-4.

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Solvent Effects in the Solvolysis of Aryldi-*tert*-butylcarbinyl *p*-Nitrobenzoates in Aqueous Acetic Acid. Substituent Effects on Transition State Charge Separation

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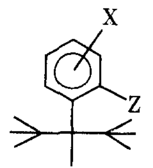
The Grunwald–Winstein equation,[1] log $k/k_0 = mY$, has proved invaluable in solvolysis studies because of the possibility of using m as an empirical criterion of reaction mechanism. However, recent data[2] on the solvolysis of phenyldi-*tert*-butylcarbinyl *p*-nitrobenzoate (**1d**) in aqueous acetone indicate an m value of 0.32 at 100°, substantially lower than is usual for limiting solvolysis without nucleophilic solvent assistance[3] or anchimeric assistance.[4,5]



1, Z = H
2, Z = Me

Table I
Grunwald–Winstein m Values for the Solvolysis of Aryldi-*tert*-butylcarbinyl *p*-Nitrobenzoates in Aqueous Acetic Acid at 85°

Compd	Substituent X	$10^4 k_{\mathrm{HOAc,\ 100\%}}$, sec^{-1}	m^a
1a	*p*-MeO	6.18	0.316
1b	*p*-Me	1.74	0.384
1c	*m*-Me	1.26	0.383
1d	H	0.805	0.370
1e	*p*-Cl	0.220	0.370
1f	*m*-Cl	0.100	0.402
1g	*m*-CF$_3$	0.0364	0.425
2b[b]	*p*-Me	393 (9.67)[c]	0.259
2c[b]	*m*-Me	332 (7.78)[c]	0.265
2d[b]	H	220 (4.93)[c]	0.274

[a] Standard deviation on k, 1–4%; standard deviation on m, less than 0.01 (**1**) or 0.02 (**2**). [b] Values at 85° were estimated from data at 30–60°; values in parentheses are at 50.5°. [c] Corresponding rate constants in 97.7% aqueous ethanol follow: **2b**, 2.74 × 10^{-4}; **2c**, 2.30 × 10^{-4}; **2d**, 1.56 × 10^{-4} sec^{-1}.

We have now determined the solvolysis rates of some aryldi-*tert*-butylcarbinyl *p*-nitrobenzoates **1** and **2** in aqueous acetic acid (0–8 M in water, 0.01 M in sodium acetate) by the uv spectroscopic method.[6] The m values range from 0.26 (**2b**) to 0.42 (**1g**) at 85° (Table I). The calculated value[7] for *tert*-butyl chloride under these conditions being 0.75, these values are indeed abnormally low. However, these molecules contain several features which are known to reduce m. Firstly, low solvent sensitivity is associated with leaving groups which are able to disperse the developing negative charge; m decreases in the order Cl > Br > OTs[8] and, more pertinently, Cl > *p*-NB > thionbenzoate.[9] Secondly, relief of steric strain in the solvolysis of congested tertiary derivatives leads to an early transition state with little charge separation.[3,10] The unusually small ρ value reported for **1** in 70% aqueous acetone at 100° (−1.79)[2a] is approximately confirmed in the present work[11] and is consistent with an early transition state. A further factor which could reduce m is steric inhibition of solvation of the incipient cation,[12] but its role has not yet been clearly demonstrated.

Notwithstanding some scatter, there is a well-defined trend in the relationship between solvent sensitivity and reactivity: as the reactivity (log k) of these aryldi-*tert*-butylcarbinyl *p*-nitrobenzoates increases, m tends to decrease linearly (Figure 1). The substituent dependence of m[13] raises an interesting point regarding the Hammett and

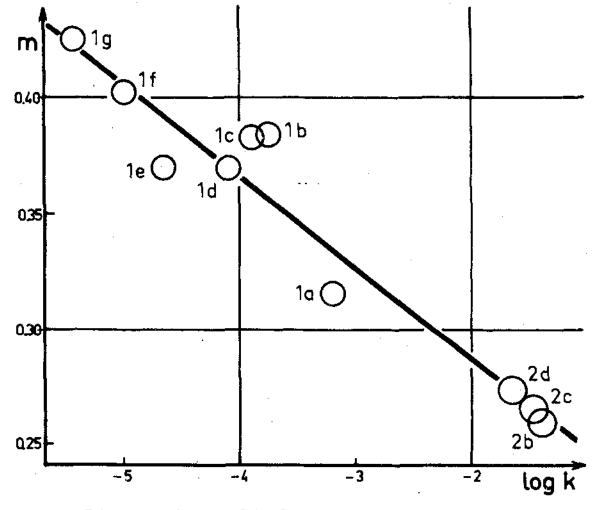


Figure 1. Linear relationship between reactivity (log k) and solvent effect (m) in the solvolysis of aryldi-*tert*-butylcarbinyl *p*-nitrobenzoates.

Grunwald–Winstein correlations. Both ρ and m are widely considered to indicate the extent of charge separation in the transition state, but both substituents and solvent must also modify the charge. We anticipate that ρ_2 would be smaller (less negative) than ρ_1 but the m values show that there is a *continuous* variation in the extent of charge separation. The value of ρ must be taken, therefore, as an *averaged* measure of the charge separation. The assumption that the charge separation is invariant within a reaction series[19] only leads to confusion.

The trend in the m–log k relationship observed here is in accord with the Hammond postulate[20] but not with Thornton's "push-pull" model of the SN1 mechanism.[21] This model, however, requires weak nucleophilic solvent participation which is scarcely conceivable, owing to the congestion of the reaction center, and which, moreover, is absent even in *tert*-butyl chloride solvolysis.[22] The values of $(k_{\text{aqEtOH}}/k_{\text{HOAc}})_Y$[23] determined at 50.5° for **2** (0.28–0.32) are similar to those of 1- and 2-adamantyl tosylates in which solvent is sterically excluded from the backside of the reaction center.[8,22,24] Values below unity are commonly encountered where hydrogen bonding to the leaving group occurs[4b,c] or where electrophilic catalysis by acetic acid is possible,[24] as in the present case. We have no direct evidence regarding the extent of ion-pair return in these systems. Nevertheless, it can be deduced from the low values of m and of $(k_{\text{aqEtOH}}/k_{\text{HOAc}})_Y$ that this is not an important process; the high values of $\Delta S^{\ddagger}$ (1.8, 2.1, and 2.4 eu for **2b**, **2c**, and **2d**, respectively) tend to confirm this conclusion.[22,24]

Registry No.—**1a**, 40601-70-5; **1b**, 40544-04-5; **1c**, 56437-67-3; **1d**, 40544-05-6; **1e**, 40544-06-7; **1f**, 56437-66-2; **1g**, 56437-65-1; **2b**, 56437-64-0; **2c**, 56437-63-9; **2d**, 56437-62-8.

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A New Approach to Triaminopyrimidine *N*-Oxides

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2,4-Diamino-6-(substituted amino)pyrimidine 3-oxides have useful hypotensive activity in man.[1] A general route to these compounds is reported below.

Generally, pyrimidine *N*-oxides are prepared (a) by modification of a preexisting pyrimidine *N*-oxide, (b) by direct N-oxidation, or (c) by cyclization reactions.[2] In the past, 6-aminopyrimidine *N*-oxides have been prepared in this laboratory by reaction of various amines with 2,4-diamino-6-chloropyrimidine 3-oxide.[3] The literature contains very few examples of the second general route, direct N-oxidation of triaminopyrimidines.[4] This paper describes a cyclization approach which uses hydroxylamine as a condensation agent in the synthesis of triaminopyrimidine *N*-oxides. Hydroxylamine[5-7] and its derivatives, benzyloxyamine,[8,9] hydroxyurea,[10,11] benzyloxyurea,[10,12,13] and amidooxime ethers[14] have been used to introduce the requisite N–O bond of pyrimidine *N*-oxides. However, the preparation of a triaminopyrimidine *N*-oxide by cyclization with hydroxylamine or its derivatives has not yet been reported.

Results and Discussion

Formally, triaminopyrimidine *N*-oxide **6** is an adduct of hydroxyguanidine and cyanoacetamide **2** or a suitable derivative such as **3**. In our hands, neither compounds **2** nor **3** gave pyrimidine **6** when reacted with hydroxyguanidine. Therefore, compound **5** was constructed from smaller molecular fragments (see Chart I).

Reactions of ethyl cyanoacetate with a variety of amines efficiently produced the corresponding cyanoacetamides **2** (see Chart I). Amide **2** was O-methylated with either methyl fluorosulfonate or trimethyloxonium fluoroborate (see Chart I). The resultant salt was treated with either potassium carbonate or sodium methoxide to give enol ether **3**. Compound **3** reacted with cyanamide in alcoholic solvent to give cyanoiminopropionitrile **4**. When NR^1R^2 was piperidine, the tautomeric structure **4** (3-cyanoimino-3-piperidinopropionitrile) was suggested by NMR (CH_2 singlet at δ 3.93) and by ir (lack of N–H stretch). In the normal application of this synthesis, compound **4** was not isolated, but was treated with hydroxylamine to form triaminopyrimidine *N*-oxide **6**, presumably via postulated intermediate **5**. Yields for the three-step process from amide **2** to crystalline pyrimidine *N*-oxide **6** range in most cases from 40 to