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The Synthesis of Arylsulfonylphthalimides and Their Reactions with Several Amines in Acetonitrile

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Abstract

In this study, several N-(p-substituted-arylsulfonyl)phthalimides (**1a-e**) were synthesized. The synthesized compounds were then examined with respect to their substitution reactions with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane in acetonitrile. In order to determine the mechanism, substituent effect, activation entropy, and nucleophile effect were used as criteria.

Keywords: Arylsulfonyl Phthalimides, Mechanism, Substituent Effect, Activation Entropy

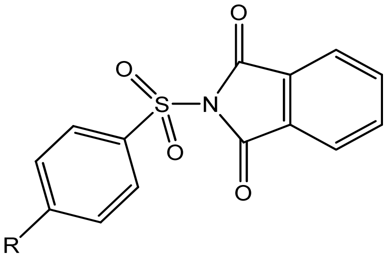
1. Introduction

N-Alkyl and N-arylsulfonyl phthalimides were prepared by Heller [1] from the reaction of potassium phthalimide and sulfonyl chlorides. Earlier attempts by Evans and Dehn to prepare several N-aryl derivatives [2-3] and later by Scott and Lutz to prepare some N-alkyl derivatives by this reaction had been unsuccessful [4]. Later, potassium phthalimide was reported to interact with p-toluenesulfonyl chloride at 140˚C or in dimethylformamide at 5˚C to 40˚C to yield N-(p-tolylsulfonyl)phthalimide [5]. The mechanism of acid-catalyzed hydrolysis of N-(p-substituted-arylsulfonyl)phthalimides was studied in detail in our laboratory [6]. We now report a complementary study of the nucleophilic substitution reactions of a series of N-(p-substituted-arylsulfonyl)phthalimides (**1a-e**) in acetonitrile (**Scheme 1**).

2. Results and Discussions

In this study, N-(p-methoxyphenylsulfonyl)phthalimide **(1a)**, N-(p-toluenesulfonyl)phthalimide **(1b)**, N-(phenylsulfonyl)phthalimide **(1c)**, N-(p-bromophenylsulfonyl) phthalimide **(1d)** and N-(p-nitrophenylsulfonyl)phtha- limide **(1e)** were synthesized. The synthesized compounds were examined with respect to their substitution reactions with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane. In order to determine the mechanism, substituent effect, activation entropy and nucleophile effect were used as criteria.

The substituent effect was investigated at 30.0˚C ± 0.1˚C in acetonitrile. Positive ρ values were obtained for the substitution of N-(p-substituted-arylsulfonyl)phthalimides with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane. Electron withdrawing substituents (-Br, -NO_2) increased the reaction rate, while electron donating substituents (-CH_3, -OCH_3) led to a decrease (**Figures 1-4**). A positive ρ value indicates the S_N2 mechanism or an addition-elimination mechanism. The ρ values for the reaction of N-(p-substituted-arylsulfonyl) phthalimides in acetonitrile with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane were 1.18, 1.12, 1.05 and 1.14 respectively. A similar behavior was observed for the alkaline hydrolysis of sulfonimidic esters and reactions of sulfinylphthalimides with several nucleophiles [7,8].



1a R=OCH_3
1b R=CH_3
1c R=H
1d R=Br
1e R= NO_2

Scheme 1. N-(p-Substitued-arylsulfonyl)phthalimides.

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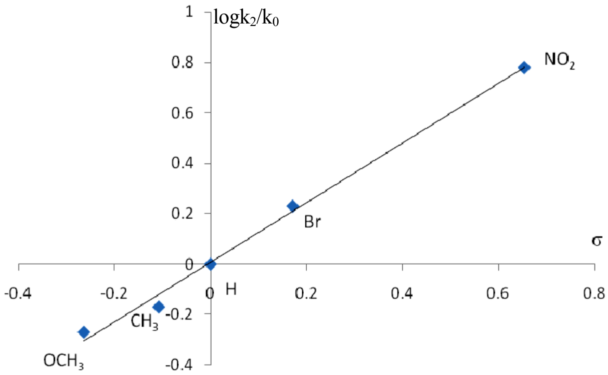

Figure 1. Hammett Plots of $\log k_2/k_0$ versus σ for the reactions of 1a-e with t-butylamine at 30.0˚C ± 0.1˚C in acetonitrile.

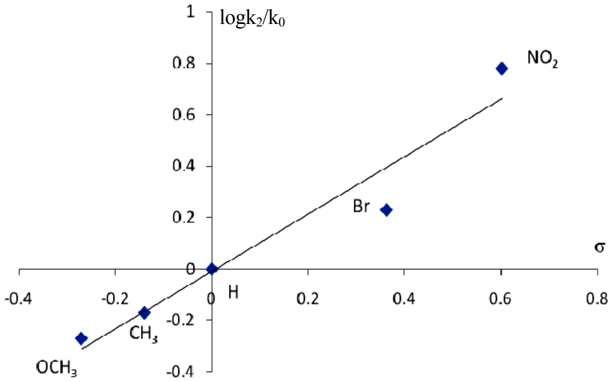

Figure 2. Hammett Plots of $\log k_2/k_0$ versus σ for the reactions of 1a-e with diethylamine at 30.0˚C ± 0.1˚C in acetonitrile.

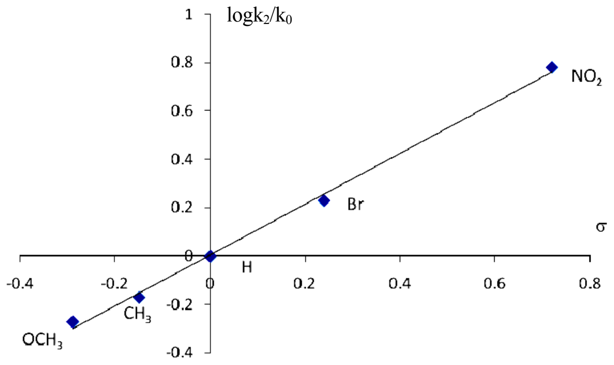

Figure 3. Hammett Plots of $\log k_2/k_0$ versus σ for the reactions of 1a-e with cyclohexylamine at 30.0˚C ± 0.1˚C in acetonitrile.

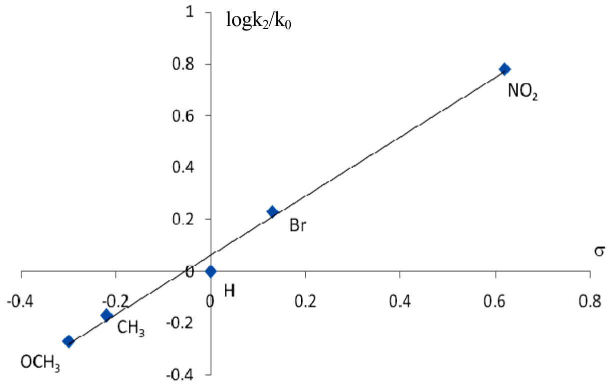

Figure 4. Hammett Plots of $\log k_2/k_0$ versus σ for the reactions of 1a-e with trans-1,2-diaminocyclohexane at 30.0˚C ± 0.1˚C in acetonitrile.

The activation entropy was also studied, and negative $\Delta S^{\neq}$ values were obtained. The $\Delta S^{\neq}$ values for the reaction of N-(phenylsulfonyl)phthalimides in acetonitrile with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane were –148.94, –106.55, –132.02 and –48.78 J/mol·K respectively. The negative $\Delta S^{\neq}$ values indicate that the reaction followed the S_N2 mechanism or an addition-elimination mechanism. Similar behavior was observed for the aminolysis of 1-tosyl-3-methyl imidazolium chloride as well [9]. Arrhenius parameters for the reaction of N-(phenylsulfonyl)phth- alimides in acetonitrile with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane are shown in **Table 1**.

Second order kinetics, showing dependence both on the nucleophile and on the substrate, are widely observed in nucleophilic substitutions [10]. It was also observed that the reactions with cyclohexylamine, and trans-1,2-diaminocyclohexane nucleophiles took place much faster than those with t-butylamine and diethylamine nucleophiles as shown in **Table 2**.

In the light of the overall evidence, we propose that the substitution reactions of a series of N-(p-substituted-arylsulfonyl)phthalimides with t-butylamine, diethylamine, cyclohexylamine and trans-1,2-diaminocyclohexane occur with S_N2 mechanism or an addition-elimination mechanism, as shown in **Schemes 2** and **3** respectively.

3. Experimental

3.1. Materials and Methods

N-(p-Substituted-arylsulfonyl)phthalimides **1a-e** were prepared from the corresponding p-substituted-arylsulfonyl

Table 1. Activation parameters for the reaction of N-(phenylsulfonyl) phthalimide in acetonitrile with t-butylamine, diethylamine, cyclohexylamine, and trans-1,2-diaminocyclohexane.

Nucleophile	$\Delta H^{\neq}$ (kJ/mol)	$\Delta S^{\neq}$ (J/mol·K)	R^2
t-Butylamine	29.75	–148.94	0.9981
Diethylamine	39.60	–106.55	0.9978
Cyclohexylamine	20.66	–132.02	0.9928
trans-1,2-Diaminocyclohexane	46.18	–48.78	0.9829

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Table 2. Values of k_2 ($M^{-1}s^{-1}$) for the substitution of N-(*p*-substitutedarylsulfonyl) phthalimides with nucleophiles at 30.0˚C ± 0.1˚C in acetonitrile.

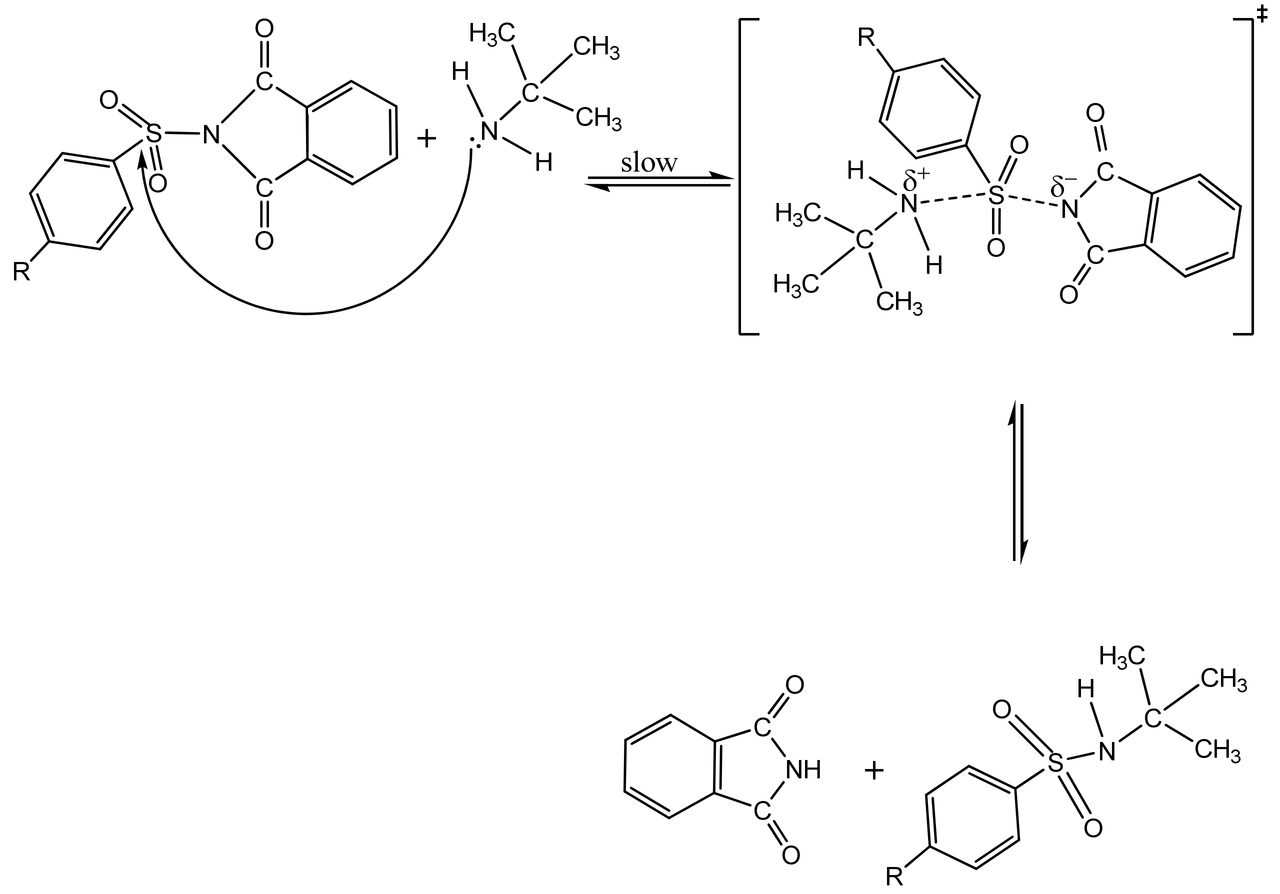
Nucleophile	Substituent	k_2 ($M^{-1}s^{-1}$)
t-Butylamine	**1a**	0.47
	1b	0.68
	1c	0.87
	1d	1.29
	1e	3.91
Diethylamine	**1a**	1.41
	1b	1.91
	1c	2.63
	1d	6.06
	1e	10.51
Cyclohexylamine	**1a**	108.63
	1b	147.78
	1c	210.64
	1d	363.74
	1e	1093.56
trans-1,2-Diaminocyclohexane	**1a**	102.07
	1b	123.40
	1c	204.84
	1d	276.86
	1e	856.09

chlorides with potassium phthalimides in acetonitrile as described by Heller [1]. All melting points were determined using an electrothermal digital melting point apparatus.

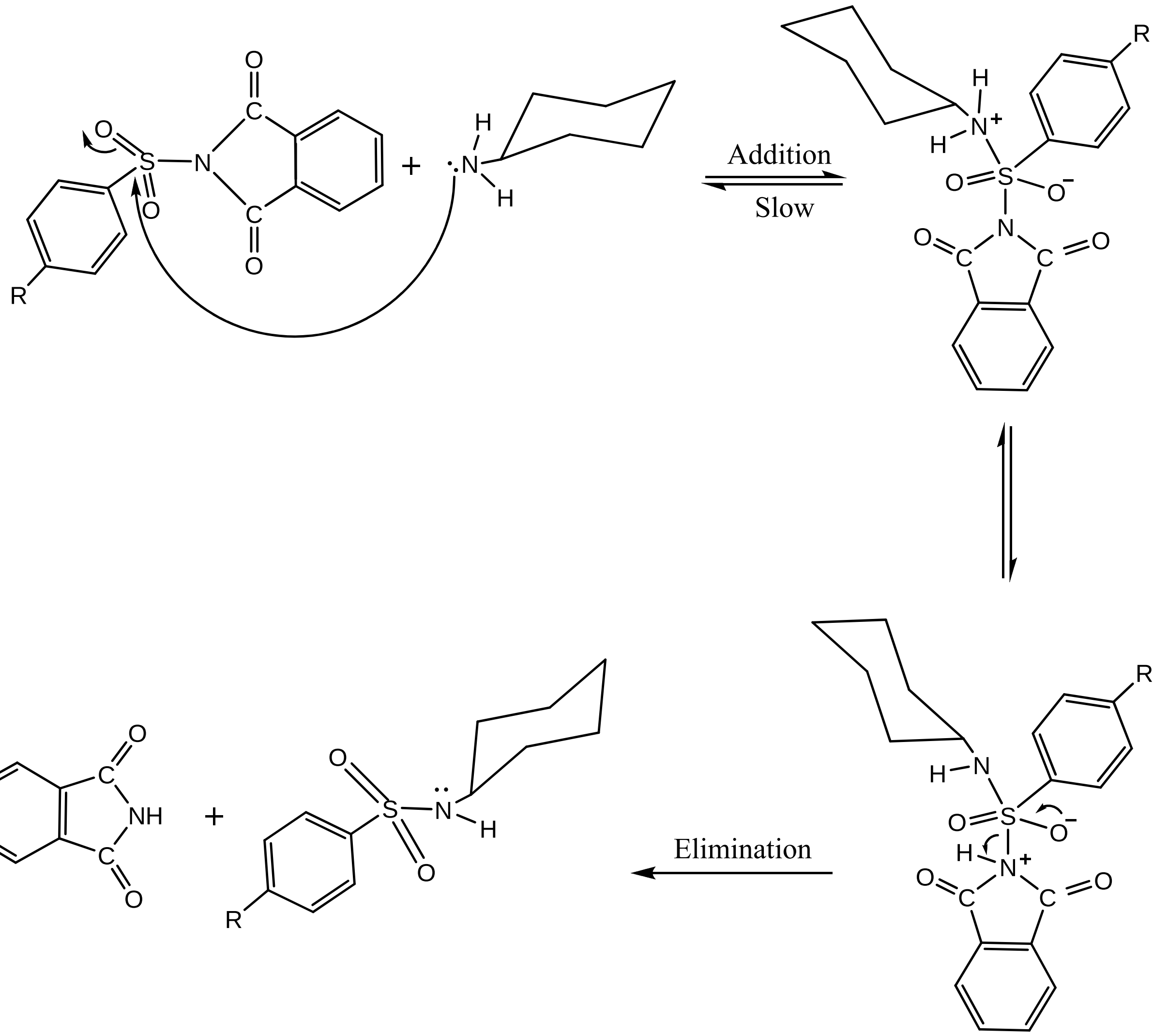
1a: m.p. 218˚C - 219˚C (Lit.[11] 218˚C - 219˚C). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.90 - 8.10 (d, 2H), 7.80 - 8.00 (s, 2H), 7.1 - 7.3 (d, 2H), 3.8 (s, 3H); ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 164.61, 163.43, 136.27, 131.04, 130.92, 129.65, 124.70, 115.19, 56.40; IR (ATR, cm^{-1}) 3067, 1739, 1593 - 1417, 1252 - 975, 1165, 1143, 1089, 866 - 663, 663.

1b: m.p. 240˚C - 241˚C (Lit.[1] 239˚C - 240˚C). ^{1}H NMR (200 MHz, DMSO-d$_6$): δ 8.40 - 7.60 (d, 4H), 7.50 - 7.00 (dd, J = 7.6 Hz, 4H), 2.34 (s, 3H); ^{13}C NMR (200 MHz, DMSO-d$_6$): δ 146.04, 135.43, 134.29, 130.97, 129.92, 128.44, 124.54, 123.59, 21.30; IR (KBr disk, cm^{-1}) 3066, 2988, 1747, 1593 - 1466, 1256 - 965, 1178, 1088, 865 - 632, 657.

1c: m.p. 202˚C - 203˚C (Lit.[1] 202.5˚C - 203.5˚C). ^{1}H NMR (200 MHz, DMSO-d$_6$): δ 8.09 - 8.07 (d, 2H), 8.07 - 8.02 (dd, J = 3.4 Hz, 2H), 7.94 - 7.90 (d, 2H), 7.77 - 7.73 (d, 2H), 7.70 - 7.60 (d, 1H); ^{13}C NMR (200 MHz, DMSO-d$_6$): δ 162.60, 137.94, 135.82, 134.90, 130.54, 129.53, 127.75, 124.28; IR (KBr disk, cm^{-1}) 3069, 1748, 1604 - 1448, 1255 - 999, 1138, 1087, 864 - 682, 682.



Scheme 2. **S_N2 mechanism for N-(*p*-Substitued-arylsulfonyl)phthalimides with t-butylamine.**



Scheme 3. An addition-elimination mechanism for N-(p-Substitued-arylsulfonyl)phthalimides with cyclohexylamine.

1d: m.p. 249°C - 250°C (Lit.[1] 247°C - 248°C). ^{1}H NMR (200 MHz, DMSO-d$_6$): δ 8.00 - 7.80 (d, 2H), 7.70 - 7.50 (dd, J = 4.0 Hz, 2H), 7.50 - 7.30 (dd, J = 4.2 Hz, 2H); ^{13}C NMR (200 MHz, DMSO-d$_6$): δ 167.34, 135.97, 131.96, 131.84, 130.59, 129.52, 129.43, 127.40; IR (KBr disk, cm^{-1}) 3101, 1752, 1608 - 1466, 1258 - 969, 1140, 1086, 864 - 669, 707, 600.

1e: m.p. 239°C - 240°C (Lit.[12] 238°C - 240°C) ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 8.40 - 8.60 (d, 2H), 8.20 - 8.40 (d, 2H), 7.80 - 8.10 (dd, J = 4.8 Hz, 4H), ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 163.13, 151.41, 143.23, 136.35, 131.24, 130.34, 125.19, 124.85; IR (ATR, cm^{-1}) 3107, 1754, 1602 - 1466, 1528, 1252 - 964, 1138, 1084, 854 - 690, 602.

3.2. Kinetic Studies

The rates of substitution reactions of N-(*p*-substituted-arylsulfonyl)phthalimides were followed spectrophotometrically using a GBC Cintra 20 Model UV-VIS spectrophotometer with a thermostatted cell compartment (±0.05°C). Values of k_1 were calculated from the standard equation using a least-squares procedure. All kinetic mea- surements were duplicated, and the average deviation from the mean was <3%. Second-order rate constants (k_2) were calculated from the slope of the plots of pseudo-first-order rate constants versus nucleophile concentrations (at least three different concentrations).

$$k_2 = \frac{kT}{h}\exp\frac{\Delta H^{\neq}}{RT}\exp\frac{\Delta S^{\neq}}{R} \tag{1}$$

where *k*, is Boltzman's constant, *h*, Planck's constant and the other symbols have their usual meanings. Expressing Equation (1) in logarithmic form, Equation (2) is obtained. From a plot of Ink_2 versus $1/T$, $\Delta S^{\neq}$ and $\Delta H^{\neq}$ can be obtained from the intercept and slope respectively.

$$\ln k_2 = \frac{kT}{h} - \frac{\Delta H^{\neq}}{RT} + \frac{\Delta S^{\neq}}{R} \quad (2)$$

3.3. Product Analysis

N-t-Butyltoluenesulfonamide was prepared from t-butylamine with p-toluenesulfonyl chloride and cupric oxide in acetonitrile at room temperature [13]. m.p. 112˚C - 113˚C [14].

Analysis of the products was also determined by comparing the UV spectrum obtained after completion of the kinetic experiment with the spectrum of the expected products at the same concentration and under the same conditions. Thus, for the reaction of N-(p-toluenesulfonyl)phthalimide with t-butylamine, the UV spectrum recorded at the end of the reaction was identical with that of a 1:1 mixture of phthalimide and N-t-butyltoluenesulfonamide.

4. Acknowledgements

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5. References

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