

## STUDIES ON HETEROCYCLIC QUATERNARY NITROGEN BASES

## Effect of Substituents on the Kinetics of Trans-Alkylation of Primary Amines by N-substituted 2,4,6-triphenylpyridinium Cations

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N-Substituents in 1-substituted 2,4,6-triphenylpyridinium cations are transferred to piperidine by unimolecular and/or bimolecular processes in chlorobenzene solution. The steric effects of the N-substituents was quite clear on the rate of the reaction constant.

## INTRODUCTION

Trans-alkylation of primary amines by quaternary pyridinium salts has received considerable attention recently.

Although this reaction has been used to affect several novel synthesis its exact mechanism is still not yet well understood.

In previous work we have reported unimolecular and bimolecular transfer of N-substituent from pyridinium cations; evidence for a clear mechanistic changeover [1, 2]. In the present paper we report the results of further studies in this area.

It is hoped that these results will shed further light on the mechanism of these reactions.

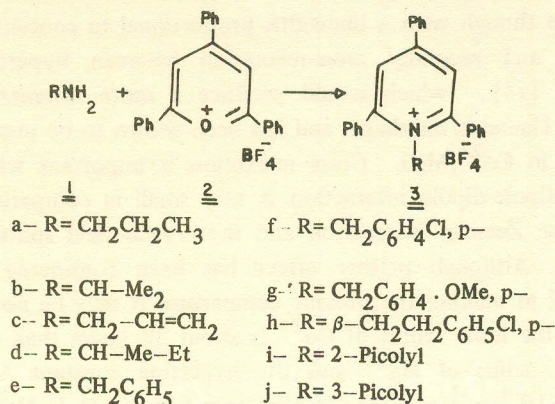
## EXPERIMENTAL

**Materials** — The N-alkyl, benzyl, substituted benzyl and heteroaryl 2,4,6-triphenylpyridinium tetrafluoroborate cations were prepared by the condensation of the corresponding pyrylium salts [3] (0.01 mol) with the desired amines (0.015 mol) in methanol (30 ml) at 25° for 1-3 hrs. [4].

Ether (100 ml) was added, and the solid obtained recrystallised from isopropyl alcohol in the form of white needles (Chart 1, Table 1, 3 a-j).

**Kinetic Method** — Kinetics were carried out in oil thermostate at temperature range 25-100° under pseudo-

first order conditions in chlorobenzene solution using piperidine as the nucleophilic reagent. Samples were taken periodically at short intervals and quenched by cooling in ice, then measured by UV Bechman spectrophotometer model 26, monitoring the decrease of absorbance of the pyridinium cation at analytical wave length 300 nm, (Table 2 & 3).



Pseudo-first order rate constants were calculated from the slope of conventional plots of:

$$\ln(a/a-x) = (E_1 - E_2)/(E - E_2) \quad \text{at } 300 \text{ nm versus time.}$$

Such plots were linear to at least 85% completion. In typical runs the initial concentration of pyridinium cations was  $0.324 \cdot 10^{-5}$  M solution while those of the nucleophile varied from  $160 \cdot 10^{-3}$  to  $0.324 \cdot 10^{-3}$  mole L<sup>-1</sup>.

The products obtained from N-alkyl, benzyl, substituted benzyl and heteroaryl piperidines were isolated and their structures were confirmed by identity with authentic specimens [4].



Table 1. Preparation of 1-substituted 2,4,6-triphenylpyridinium tetrafluoroborates (3 a-j).

Cpd.	Yield (%)	mp °C	Lit. mp °C	Elemental analysis			Ref.
				C	H	N	
3a	70	135	136	71.5 (71.4)	5.5 (5.5)	3.1 (3.2)	5
3b	46	172	173	71.3 (71.4)	5.7 (5.5)	3.3 (3.2)	5
3c	82	153		71.9 (71.8)	5.2 (5.1)	3.4 (3.2)	
3d	60	175		71.7 (71.9)	5.9 (5.8)	3.2 (3.1)	
3e	87	198	196	74.0 (74.2)	5.1 (5.0)	2.6 (2.8)	6
3f*	89	143	144	69.1 (69.3)	4.7 (4.5)	2.8 (2.7)	7
3g	63	148	148	72.2 (72.3)	5.3 (5.1)	2.5 (2.7)	7
3h**	67	144		69.9 (69.8)	4.4 (4.7)	2.6 (2.6)	
3i	61	220	219	71.8 (71.6)	4.9 (4.7)	5.9 (5.8)	7
3j	78	170	168	71.9 (71.6)	5.1 (4.7)	5.6 (5.8)	7

\* Found: Cl, 6.9; Calc.: 6.8%. \*\* Found: Cl, 6.5; Calc.: 6.7%.

## RESULTS AND DISCUSSION

Reactions in chlorobenzene solution, with piperidine as nucleophile, were followed spectrophotometrically under pseudo-first order conditions. Results are summarised in Tables 2 and 3.

In all cases, the observed rate constants was a linear function of the piperidine concentration. The observed rate variation can therefore be interpreted in terms of the  $S_N2$  mechanism, together with (*p*-methoxybenzyl, 2-butyl and isopropyl) a contribution from the  $S_N1$  mechanism; the  $S_N2$  rate, not the  $S_N1$ , rate depends on the nature and concentration of the nucleophile, also the nature of the N-substituent group. Calculated  $S_N2$  and  $S_N1$  rate constants are given in Table 2.

*Simultaneous  $S_N1$  and  $S_N2$  Reaction Mechanism.* — The mechanism of nucleophilic substitution has been controversial. Snee [8] proposed unification of the chemical duality of the  $S_N1$  and  $S_N2$  mechanism in which all nucleophilic substitution involved the formation of ion pairs. This approach was criticized particularly by McLennan [9], who favoured the traditional duality.

The evidence for and against each view point has been reviewed [10]. This work could rationalise the idea that there is a clear duality of mechanism for the reaction of 1-(*p*-methoxybenzyl), 1-(2-butyl) and 1-(isopropyl)-2,4,6-triphenylpyridinium cations with piperidine in chlorobenzene. The interpretation is further supported by the similar

Table 2. First- and second-order rate constants for reactions of N-substituted 2,4,6-triphenylpyridinium tetrafluoroborates with piperidine in chlorobenzene at 100°.

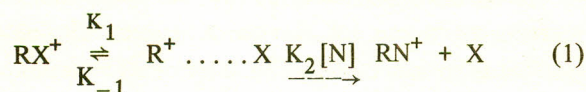
Cpd.	$\lambda_{\max}$ nm	$\epsilon_{\max}$ pyridinium	$10^5 k_1$	$T_{1/2}$	$10^3 k_2$
			( $S^{-1}$ )	min	( $1 \text{ mol}^{-1} \text{ S}^{-1}$ )
3a	307	30500	2.48	465.8	0.38
3b	305	34600	1.72	671.7	5.27
3c	306	38600	6.23	185.3	1.54
3d	306	39000	3.53	327.3	0.87
3e	312	34000	80.42	14.4	4.97
3f	313	30000	6.48	178.3	4.00
3g	312	31000	44.67*	25.9	139.15
3h	310	30500	1.23	939.2	0.54
3i	307	32200	0.56	2062.9	0.14
3j	315	23000	10.76	107.4	4.96

\* The reaction rate constant was measured at 60°.



results already reported for N-substituted 2,4,6-triphenylpyridinium cations with different leaving groups [2].

These results do not support the S<sub>N</sub>1 unified theory of nucleophilic substitution. Under pseudo-first-order conditions the unified mechanism for our reactions (Eq. 1) would require a kinetic dependence according to Eq. 2.



$$k_{\text{obsd}} = k_1 k_2 [\text{N}] (k_{-1} + k_2 [\text{N}]) \quad (2)$$

$$k_{\text{obsd}} = k_0 + k [\text{N}] \quad (3)$$

In place of kinetic dependence according to Eq. 2 we clearly find the kinetic dependence expected for the simultaneous occurrence of S<sub>N</sub>1 and S<sub>N</sub>2 reactions, i.e., as in Eq. 3.

The partial predominance of S<sub>N</sub>1 sequence with 3b, d, and g is readily understandable in terms of steric hindrance of the transition states (Eq. 1) needed for the S<sub>N</sub>2 pathway by bulky alkyl groups.

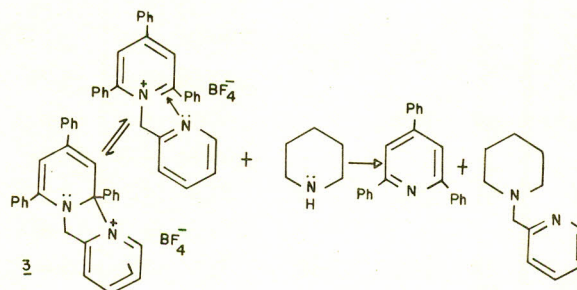
However, such rationalisation can not hold true for 3g (Table 2) as the effective bulk of the *p*-methoxyphenyl-methyl moiety would be almost the same as that of a benzyl or *p*-chlorobenzyl groups for which both reactions proceeded mainly by S<sub>N</sub>2 mechanism.

It may thus be assumed that 3g (*p*-methoxy) exists at least under reaction conditions, as an ion pair. This rationalisation for the unusual high rate constant of 3g as com-

pared to 3e (benzyl), that 3g exist as an ion pair can be readily interpreted by the ability of methoxy group to accommodate a positive charge. That the S<sub>N</sub>2 reaction rate constant increases in presence of aromatic substituents can be also readily understood by assuming participation of aromatic orbitals in stabilising the transition state. The reaction proceeds satisfactorily in all cases. However, it proceeds less satisfactorily with aralkyl pyridinium salts with strong electron donating substituents of highly branched and hence hindered, alkyl substituents.

The observation that the reaction is very slow in case of 3i (2-picoly) (Table 2) could be understandable by assuming that the latter may exhibit in the ring-chain tautomerism.

This finds parallelism with the reported ready addition of CN<sup>-</sup> to quaternary pyridinium salts (Reissert reaction [11, 12],



*Activation Parameters.* — The activation enthalpies for the S<sub>N</sub>2 reactions of these pyridinium cations of 13-78 KJ Mole<sup>-1</sup> (Table 3).

The relatively higher activation enthalpies (25-93 KJ

Table 3. Activation parameters for N-substituted pyridinium cations.\*

Cpd.	Order of reaction	E <sub>A</sub> KJ mole <sup>-1</sup>	ΔH <sub>373</sub> <sup>‡</sup> KJ mole <sup>-1</sup>	ΔS <sub>373</sub> <sup>‡</sup> e.u.
3a	2	47.69 ± 4.60	44.76 ± 4.60	-51.40 ± 5.50
3b	1	27.94 ± 0.79	24.85 ± 0.79	-64.87 ± 5.30
3c	2	44.30 ± 1.46	41.20 ± 1.46	-45.40 ± 3.90
3d	1	59.73 ± 0.13	56.64 ± 0.17	-43.04 ± 3.40
3e	2	76.38 ± 1.59	73.29 ± 1.72	-22.56 ± 1.65
3f	2	61.91 ± 0.84	58.56 ± 0.84	-32.34 ± 1.52
3g**	1	95.71 ± 0.13	92.95 ± 0.13	- 7.37 ± 0.36
3h	2	81.23 ± 2.68	78.14 ± 2.68	-23.85 ± 2.04
3i	2	16.23 ± 0.08	13.13 ± 0.04	-68.20 ± 3.80
3j	2	71.40 ± 0.84	68.31 ± 1.09	-25.75 ± 1.04

\* 90% confidence limits. \*\* Activation enthalpy was measured at 60°.



Mole<sup>-1</sup>) found for the unimolecular reaction of 3b, d, and g are to be compared with the activation energies reported for the solvolysis of benzyl chloride in Me<sub>2</sub>SO/water [13] and for the solvolysis of  $\alpha$ -methyl-*p*-methoxybenzyl chloride [14].

A consequence of the high  $\Delta H^\ddagger$  values for S<sub>N</sub>1 as compared to S<sub>N</sub>2 compounds is that the proportion of unimolecular reaction rises as temperature increases.

## REFERENCES

1. Alan R. Katritzky, Giuseppe Musumarra, Kumars Sakizadeh, Sayed M.M. El-Shafie and Bratislav Jovanovic, *Tetrahedron Letters*, **21**, 2701 (1980).
2. Sayed M.M. El-Shafie, *Gazz. Chim. Ital.*, **112**, 183 (1982).
3. Sayed M.M. El-Sahfie, *Indian Chem. J.*, **20**, 427 (1981).
4. Sayed M.M. El-Shafie, A'in Shams University Sciences Bulletin; (1981), in press.
5. A.R. Katritzky, Gaetano Liso *et al*, *J. Chem. Soc. Perkin*, **1**, 849 (1980).
6. R. Lombard and A. Kress, *Bull. Soc. Chim. France*, 1528 (1960).
7. A.R. Katritzky and Urban Gruntz, *J. Chem. Soc. Perkin*, **1**, 430, 436 and 439 (1979).
8. R.A. Sneen and J.W. Larsen, *J. Am. Chem. Soc.*, **91**, 6031 (1969).
9. D.J. McLennan, *Acc. Chem. Res.*, **9**, 281 (1976).
10. D.J. Raber, J.M. Harris and P.V.R. Schleyer, "Ions and Ion Pairs in Organic Reactions", (Wiley, New York, 1979), Vol. 2, M. Szwarc, Ed., T.W. Bentley and P.V.R. Schleyer, *Adv. Phys. Org. Chem.*, **14**, 1 (1977).
11. A. Reissert, *Ber.*, **38**, 1603, 3415 (1905).
12. W.E. McEwen and R.L. Cobb, *Chem. Reviews*, **55**, 511 (1955).
13. E. Tommila, *Acta Chem. Scand.*, **20**, 923 (1966).
14. Y. Tsuno, Y. Kusuyama, M. Sawada, T. Fujii and Y. Yukawa, *Bull. Chem. Soc. Jpn.*, **48**, 3337 (1975).