Short Communication

Kinetics of aromatic nucleophilic substitution reactions of 2-chloroquinoxaline with anilines

RAVJI D. PATEL* AND SHANTI R. PATEL

Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar 388 120, India

Abstract

Rate constants for the reactions of 2-chloroquinoxaline with various aniline derivatives in methanol have been measured at four different temperatures. The reactions are accelerated by electron-releasing, and retarded by electron-withdrawing, substituents on aniline. A second-order kinetics, first order with respect to both substrate and reagent is observed with all the anilines. The rate data are correlated with both Hammett and Bronsted relations. The activation parameters supported SN2Ar mechanism

Key words: 2-Chloroquinoxaline, nucleophilic substitution, substituent effect, kinetics.

1. Introduction

The course of aromatic nucleophilic substitution (SNAr) reactions in aromatic[1-3] and heterocyclic compounds[4-6] has been studied extensively both for anionic and neutral reagents. Even though there are a few reports on the kinetic study of N-heteroaromatic compounds[5-8], no systematic investigation has been made on the kinetics of 2-chloroquinoxaline (2CQ) with various nucleophiles of a homologus series. With a view to extending the scope of linear-free energy relationship, kinetics of the reactions of 2CQ with anilines is described in the present paper.

2. Experimental

2-Chloroquinoxaline was prepared and purified by the method of Castle and Onda[9]. Methanol was purified by the method of Bjerrum and Lund[10]. Laboratory-grade reagents and anilines were used after recrystallization from suitable solvents or distillation over pure zinc powder.

2.1. *Method*

Rates were measured conductometrically up to about 30% conversion under thermostated ($\pm 0.1°C$) conditions. The rate constants were calculated[7] with a

---

* For correspondence.
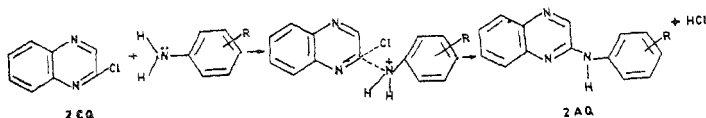
reproducibility within 3% error. Order of the reaction was determined by applying the differential method on the rate data obtained on varying four different initial concentrations of the reactants[11].

2.2. Product analysis

Standard solutions of a particular aniline and 2CQ in methanol were mixed in glass-stoppered bottles and kept at the kinetic temperature until the completion of the reaction. After concentrating the alcoholic solution to small volume ($\sim$ 25 ml), a little water ($\sim$ 10 ml) was added to remove aniline hydrochloride. The solid obtained was washed with small amount of methanol ($\sim$ 10 ml), dried and recrystallized from petroleum ether (60-80°C). The products obtained, in almost quantitative yields, were corresponding to 2-anilinoquinoxalines (2AQ). Analytical data and some spectral features of the products are similar to those reported in an earlier communication[12].

3. Results and discussion

The solutions of 0·02M 2CQ in methanol did not show any change in conductance when left at 40°C for a period of about 8 hours indicating the absence of solvolysis reaction under experimental conditions. The rates of reactions of 2CQ with all the anilines were independent of autocatalysis as revealed by good linear plots of conductance *versus* time. On applying the differential method to rate data, the kinetics was observed to be of second order; first order with respect to both 2CQ and anilines.

Table 1
Rate constants and activation parameters for the reactions of 2CQ with anilines in methanol

| Aniline	$k \times 10^5 \ dm^3 \ mol^{-1} \ s^{-1}$				$\Delta H^* \pm 4$ $kJ \ mol^{-1}$	$\Delta S^* \pm 6$ $J \ mol^{-1} \ k^{-1}$
	25°	30°	35°	40°		
Aniline	1·0	2·7	4·1	7·9	84·8	173·9
o-Toluidine	0·5	2·3	3·5	7·2	87·8	164·7
m-Toluidine	1·1	3·3	4·2	9·6	76·5	179·3
p-Toluidine	1·4	3·7	4·4	9·9	73·1	182·2
o-Cl-Aniline	0·5	2·0	2·8	4·9	113·3	160·5
m-Cl-Aniline	0·8	2·1	3·3	6·3	102·0	165·1
p-Cl-Aniline	0·9	2·7	4·0	7·3	89·0	172·2
m-Anisidine	1·3	3·2	4·4	6·9	81·5	170·5
p-Anisidine	1·9	3·9	4·8	10·7	70·6	167·2
2,4-Xylidine	0·8	3·1	4·3	9·1	85·3	155·6
2,6-Xylidine	0·4	2·4	2·7	7·0	129·2	161·8
4-Cl-o-Toluidine	0·4	1·5	3·2	6·5	147·1	182·2
6-Cl-o-Toluidine	1·3	2·9	4·5	8·2	149·2	190·2
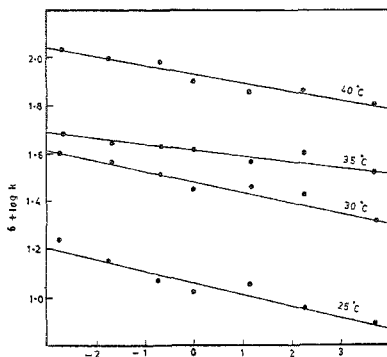
Fig 1. Hammett plots for the reactions of 2-chloroquinoxaline with *m*- and *p*-substituted anilines at different temperatures

The rate constants for the reactions of 2CQ with various aniline derivatives at four different temperatures (Table I) reveal that electron-donating substituents at *meta* or *para* positions accelerate while electron-withdrawing substituents retard the reaction. The substituents at *ortho* position in aniline retard the reaction due to stearic hindrance.

The rate data for the *meta*- and *para*-substituted aniline derivatives fit well with the Hammett equation at all the four temperatures (Fig. 1). The reaction constants (ρ) obtained by linear regression analysis on log k and the substituent constants $(\sigma)^{13}$ are −0·55, −0·39, −0·29 and −0·13 at 25, 30, 35 and 40°C, respectively. The negative values of σ signify that the reaction is facilitated by electron-releasing group on aniline.

A more direct correlation would be between the rate of the reaction and the basicity of the anilines[14]. This correlation might be useful even for *ortho* substituents where simple Hammett equation is not applicable. A linear correlation (correlation coefficient, $\gamma = 0.95$) was found between log k at 30°C and pKa of corresponding protonated anilinium ions[15] in water at 30°C. The value of the Bronsted coefficient (β) was observed to be 0·19. Here the value of β has very little significance as log k and pKa are in two different media; however, the positive sign of Bronsted coefficient is expected for nucleophilic substitution reactions.

The energies of activation were calculated from the linear regression of ln k *versus* reciprocal temperature and the values of enthalpy and entropy of activation were determined by the standard formulae based on absolute theory of reaction rates. The data in Table I indicate that these reactions are of isoentropic type and the

reactions are controlled by ΔH^*. Thus, the activation parameters agree well with the proposed SN2Ar-type addition-elimination mechanism[16] for the present reactions. A similar type of mechanism for the reactions of 2CQ with all the anilines is revealed from the very good linear Exner's plots[17] of log k_{40} versus log k_{30} (correlation coefficient, $\gamma = 0.97$).

Acknowledgements

References

1. BUNETT, J F.   Mechanism' and reactivity in aromatic nucleophilic substitution reactions, *Q. Rev*, 1958, **2**, 1–16.

2. MILLER, J.   *Aromatic nucleophilic substitution*, 1968, Elsevier.

3. BANJOKO, O. AND OTIONO, P.   Kinetics of aryl halides, *J Chem. Soc., Perkin Trans. II*, 1981, 399–402

4. ILLUMINATI, G.   Nucleophilic heteroaromatic substitution, *Adv. Heterocyclic Chem.*, 1964, **3**, 285–311

5. BROWER, K.R., WAY, J W ,   Kinetics study of displacement reactions of heterocyclic chlorides
   SAMUEL, W.P. AND AMATUTZ, A.D   with piperidine, *J Org. Chem.*, 1954, **19**, 1830–1835.

6. BREWIS, D.M., CHAPMAN,   Nucleophilic displacement reactions in aromatic systems, Part X,
   N.B , PAINE, J.S. AND   *J. Chem. Soc , Perkin Trans II*, 1974, 1802–1805.
   SHORTER, J.

7 NAIK, N.R. AND PATEL, S.R,   Kinetics of the reactions of 2-methyl-6,7-methylenedioxy-4-chloroquinoline with morpholine, piperidine and diethylamine, *Indian J Chem* B, 1978, **16**, 82–84

8 ,PATEL, R.D. AND PATEL, S.R.   Kinetics of nucleophilic substitution reactions of 2-chloroquinoxaline with aniline, piperidine and triethylamine in pure alkanols. *Gazz Chim. It.*, 1985, **115**, 659–661.

9. CASTLE, R.N AND ONDA, M   Quinoxalines-II, Basic ethers from 2-chloroquinoxaline, *J Org. Chem.*, 1961, **26**, 954–956

10. LUND, H AND BJERRUM, J   Eine einfache methode zur darstellung wasser-freir alkohole, *Ber. Chem Ges.* B, 1931, **64**, 210–213

11. LAIDLER, K J.   *Chemical kinetics*, 1965, McGraw-Hill.

12 PATEL, R.D   A convenient synthesis of 2-anilino-quinoxalines as potential antifungal and antibacterial agents, *J Indian Council Chemists* (in press)

13. HAMMETT, L.P.   *Physical organic chemistry*, 1954, McGraw-Hill

14 BRONELLI, E.C.S., MORAN, P.J.S. The reactivity of some primary amines in SN2Ar reactions with
   AND RODRIGUES, J.A.R.   2-chloro-3, 5-dinitropyridine, *J. Chem. Res.* (Synop.), 1989, **12**, 369–372; *Chem. Abstr.*, 1990, **112**, 215885j.

15. ALBERT, A. AND SERJEANT, E.P. *Ionization constants of acids and bases*, 1962, Wiley.

16. RYAN, J.J. AND HUMFFRAY, A.A. Rate correlations involving the linear combinations of substituent parameters, Part III, *J. Chem. Soc.*, B, 1967, 1300–1305.

17. EXNER, O.   Enthalpy-entropy relations, *Colln Czech. Chim. Commun.*, 1964, **29**, 1094–1113, *Chem. Abstr.*, 1964, **61**, 1324d.