

Charge Density—Activation Energy Correlations in Bromination of Thiophenes by N-Bromosuccinimide in Solution

LALITHA RAJARAMAN & M J NANJAN

Physical Chemistry Department, University of Madras, Madras 600 025

and

V KANNAPPAN*

Chemistry Department, Presidency College, Madras 600 005

Received 5 August 1986; revised and accepted 4 August 1987

The activation energies for N-bromosuccinimide bromination of several thiophene derivatives in 80% (v/v) aqueous acetic acid have been determined and discussed in the light of electron densities at the reaction site. The effect of substituents at different positions of thiophene ring has been investigated quantitatively by the actual calculation of total ($\pi + \sigma$) charge densities at various positions of the substituted thiophenes.

Earlier work from this laboratory reported on the charge-density distributions in several benzene and thiophene derivatives using Hückel LCAO MO and Del Re methods and their correlation with the experimental activation energy (E_a) values in the bromination of these compounds by molecular bromine in 100% acetic acid and acetic acid-water mixtures¹⁻³. As an extension, charge densities of eleven thiophene derivatives have now been correlated with activation energies of their bromination by N-bromosuccinimide (NBS) in order to generalise the effect of substituents in thiophene ring towards electrophiles from quantum mechanical data.

Fluka (purum) samples of thiophene, 2-chlorothiophene and ethyl thiophene-2 carboxylate were used as such. 2-Bromothiophene (Fluka), 3-bromothiophene and 2-acetylthiophene were distilled before use. 2-Iodothiophene (b.p. 90°/30 mm) was prepared by iodination of thiophene⁴. 2-Fluorothiophene (b.p. 83°) was prepared by *ipso* fluorination of 2-iodothiophene⁵. Acetic acid (LR, BDH) was purified before use⁶. N-Bromosuccinimide (Riedel, m.p. 176°) was recrystallised and used. The procedure for the rate measurements has been described earlier⁶.

The method of separation of bromination products under kinetic conditions has been described elsewhere⁷. The analysis of bromination product of thiophene was done at 220°C using a Varian GC dual column chromatograph model 3700 fitted with a 10%. OV-101 stainless steel column-chrom WHP 80/100 (2m × 1/8 inch) with nitrogen as the carrier

gas. The GLC results showed the formation of only 2-bromothiophene. NBS bromination of 2-bromothiophene in 80% (v/v) aqueous acetic acid led to 2,5-dibromothiophene as confirmed by its PMR spectra. 3-Bromothiophene was brominated at position-2. Ethyl thiophene 2-carboxylate, 2-acetylthiophene and 3-acetylthiophene underwent bromination exclusively at 5-position⁸⁻¹⁰. Benzothiophene on bromination gave 3-bromobenzothiophene.

Charge-density calculations

The calculation of σ - and π -charges for 2-acetyl- and 3-acetyl-thiophenes was programmed in FORTRAN for the computer IBM 1130. The π -charges were calculated by the Hückel LCAO MO method. Del Re method was used for σ -charge calculations. Veillard and Pullman¹¹ have shown that with the correct choice of parameters, this method gives satisfactory charge density distributions comparable with those obtained by SCF calculations, even in large molecules of biological importance. Berthod-Pullman atom and bond parameters were used in these calculations. The π - and σ -systems have been treated separately and the total ($\pi + \sigma$) charge density (Table 1) on an atom was obtained as usual by adding the π - and σ -charge densities on that atom. The data used for other molecules have already been reported by us².

The kinetic data obtained for the bromination of thiophenes in aqueous acetic acid using NBS as the brominating agent are given in Table 2. On simple electrostatic considerations, the strong electrophile,

Table 1— π -Charges, σ -Charges and Total ($\pi + \sigma$) Charge Densities at Various Ring Positions in 2-Acetyl- and 3-Acetyl-thiophenes

Position	Charge Densities × 10 ³		
	ΔQ_π	ΔQ_σ	ΔQ_t
2-Acetylthiophene			
S ₁	+ 799	+ 040	+ 839
C ₂	- 177	+ 003	- 174
C ₃	- 134	- 051	- 185
C ₄	- 148	- 042	- 190
C ₅	- 151	- 081	- 232
3-Acetylthiophene			
S ₁	+ 785	+ 048	+ 833
C ₂	- 141	- 089	- 230
C ₃	- 169	+ 043	- 126
C ₄	- 138	- 045	- 183
C ₅	- 156	- 086	- 242

Table 2—Rate Constants and E_a Values for NBS Bromination of Thiophenes and Charge Densities at Reaction Sites

([Substrate]=[NBS] = 2×10^{-3} mol dm $^{-3}$; solvent: 80% (v/v) aq. acetic acid)

Compound	$k_1 \times 10^3$ s $^{-1}$ (20°C)	E_a (kJ mol $^{-1}$)	$\Delta Q_t \times 10^3$
Thiophene	17.77	52.3	-256
2-Fluorothiophene	11.51	48.5	-258
2-Chlorothiophene	4.08	58.6	-249
2-Bromothiophene	4.08	51.5	-249
2-Iodothiophene	6.67	43.9	-254
3-Bromothiophene	27.29	55.2	-242
2,5-Dibromothiophene	5.33	63.2	-189
3-Acetylthiophene	1.92	55.2	-242
Benzothiophene	40.30	57.3	-254
Ethylthiophene-2 carboxylate	1.25†	55.2	-216
2-Acetylthiophene	1.38†	59.4	-232

† $k_2 \times 10^5$ (dm 3 mol $^{-1}$ s $^{-1}$) values at 20°C.

Br $^+$ is expected to undergo electrophilic attack more easily than the dipolar bromine molecule. This should lead to smaller E_a values in NBS bromination. Contrary to expectations NBS bromination of thiophenes involves higher E_a value as compared to that by molecular bromine. This may be due to the fact that in NBS bromination the approaching electrophile Br $^+$ is not a bare cation but it is highly solvated in aqueous acetic acid and the extent of solvation should be more than that in the case of bromine molecule.

The experimental activation energy (E_a) value decreases as the total ($\pi + \sigma$) charge density at the reaction centre increases. There is a satisfactory linear correlation between the calculated charge densities and the experimental activation energies. This supports our earlier proposal that Arrhenius activation energy values can be explained on the basis of

electron density at the reaction site for bromination of aromatic compounds^{12,13}. The linear equations (1) and (2) can be obtained for the E_a values of bromination by molecular bromine and NBS respectively in terms of total charge density (ΔQ_t) at the reaction centre.

$$38.6 - 120 \times \Delta Q_t \quad \dots (1)$$

$$(n = 10; r = 0.99)$$

$$33.6 - 82 \times \Delta Q_t \quad \dots (2)$$

$$(n = 11; r = 0.98)$$

It is clear from the slopes that in the case of bromination by NBS the effect of total charge density in the E_a values is less than that in bromination by molecular bromine. Thus, the susceptibility of Br $^+$ to approach reaction centres of different total charge densities is less than that of molecular bromine, which is anticipated on the basis of their relative electrophilicities. Similar observation has also been made in the case of homocyclic aromatic compounds⁶.

References

- 1 Nanjan M J, Kannappan V & Ganesan R, *Mh Chem*, **112** (1981) 581.
- 2 Nanjan M J, Kannappan V & Ganesan R, *Z Physik Chem, Frankfurt*, **127** (1981) 13.
- 3 Kannappan V, *Ph.D Thesis, University of Madras*, 1980.
- 4 Lew H Y & Noller C R, *Org Synth*, **30** (1950) 53.
- 5 Van Vleck R T, *J Am Chem Soc*, **71** (1949) 3256.
- 6 Sivakamasundari A S & Ganesan R, *Int J Chem Kinet*, **XII** (1980) 837.
- 7 Kannappan V, Nanjan M J & Ganesan R, *Indian J Chem*, **19A** (1980) 1183.
- 8 Marino G, *Prac Nauk Inst Chem Tech Naft Wegla. Polit Wrocla*, **15** (1973) 89; *Chem Abstr*, **79**, 77565a.
- 9 Marino G, *Acad Naz Lineei Rend, Series VIII*, **38** (1965) 700.
- 10 Hartough H D, *The chemistry of heterocyclic compounds* (Interscience, New York) 1952.
- 11 Veillard A & Pullman B, *J theor Biol*, **4** (1963) 37.
- 12 Ganesan R, *Z physik Chem, Frankfurt*, **90** (1974) 82.
- 13 Nanjan M J & Ganesan R, *Mh Chem*, **110** (1979) 647.