Research Article

Quantification of the Nucleophilicities of 3-X-Thiophenes: Highlighting the Hyperortho Correlation

W. Gabsi [ID],[1,2] T. Boubaker,[2] and R. Goumont[3]

[1]*Chemistry Department, College of Sciences and Arts, Jouf University, Algrayat, Saudi Arabia*
[2]*Laboratory CHPNR, Faculty of Sciences of Monastir, University of Monastir, Avenue of the Environment,*
5019 Monastir, Tunisia
[3]*Lavoisier Institute of Versailles, UMR 8180, University of Versailles, 45, United States Avenue, 78035 Versailles Cedex, France*

Correspondence should be addressed to W. Gabsi; wgabsi@ju.edu.sa

Kinetics studies for the coupling reactions of the 3-X-thiophene **1a-c** (X = CH$_3$, H and Br) with the electrophiles **2a** and **3a-c** have been investigated in acetonitrile at 20°C The second-order rate constants have been employed to determine the nucleophilicity parameters N and s of the thiophene **1** according the Mayr equation log k (20°C) = s (E + N). The nucleophilic-specific parameters N and s quantified in this work have been derived and compared with the reactivity of other C nucleophiles. Based on the linear correlations log $k_1 = f(E)$ and log $k_1 = f(\sigma_p^+)$, we have shown that the mechanism of interactions occurs by a unique process: electrophilic heteroaromatic substitution of an α-carbon position of substituted 3-X-thiophenes **1** known hyperortho correlation.

1. Introduction

Nowadays, it has been shown that five-membered rings are very useful for various applications such as phosphor materials [1] and semiconductors [2–4]. As an example, the use of thiophene dicarboxylic acids has made it possible to prepare organometallic nanoarchitectures having very interesting optoelectronic properties [5].

The study of the reactivity of some mono- and bis-substituted thiophenes has attracted the attention of researchers because of their ability to react according to different processes and largely dependent on the substituent [6–8]. Indeed, Mayr and coworkers [6] showed that benzhydrylium ions react very easily with 3-methoxythiophene to form C-substituted derivatives in acetonitrile, which further confuses the idea that the position of α-carbon of aminothiophenes has a high potential for nucleophilic carbon reactivity [9]. In this regard, to provide more information concerning the behavior of these types of heterocycles, we report, in this paper, on the results of a kinetic investigation of the α-carbon reactivity of the 3-X-thiophenes **1a-c** with a series of superelectrophiles **2a** and **3a-c** in acetonitrile.

## 2. Experimental Section

2.1. Materials. 3-X-thiophene **1** used in this study (Aldrich products) was of the highest quality commercially available. The electrophiles **2** and **3** have been synthesized by the team of Professor Régis GOUONT at the Versailles laboratory. Acetonitrile (for HPLC, ≥99.9%) was available of the highest quality and used without further purification.

2.2. Rate Measurements. Kinetic measurements were performed using a conventional spectrophotometer (Shimadzu UV-visible model 1650) equipped with a thermoelectrically temperature controlled cell holder (model TCC-240 A) which was maintained at 20 ± 0.1°C.

All the reactions were carried out at 20°C under pseudo-first-order conditions with a thiophene concentration of approximately 5×10^{-3} mol·dm^{-3} and oxygen-nucleophile concentrations in the range 1×10^{-1}–1 mol·dm^{-3}. The pseudo-first-order rate constants, k_{obsd}, measured were found to be reproducible to ±3–5%. Concentrations and the measured rate constants, k_{obsd}, for the individual kinetic experiments values, are given in Tables S1–S3 in Supplementary Material.
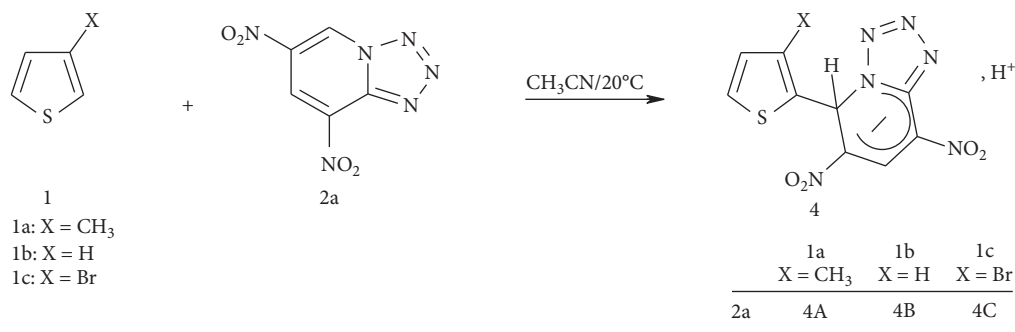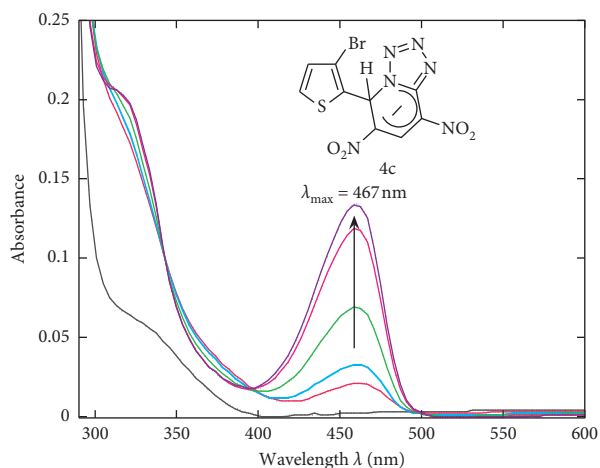
SCHEME 1
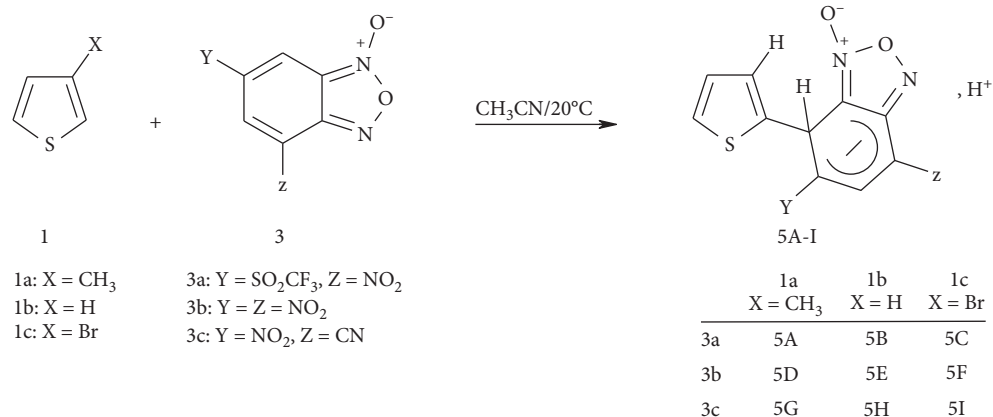
SCHEME 2

FIGURE 1: UV-visible spectrum of thiophene **1c** and the progressive evolution of the formation of the product **4C** in acetonitrile at 20°C with $[\mathbf{1c}] = 1\,mol{\cdot}L^{-1}$ and $[\mathbf{2a}] = 5.10^{-5}\,mol{\cdot}L^{-1}$.

2.3. Supporting Information Available. Tables S1–S3: kinetic data for reactions of thiophenes **1** with 4,6-dinitrote-trazolopyridine **2a** and benzofuroxane **3a-c** in an aqueous solution at 20°C.

Table S4: physical data for the formation of σ-adducts **4A-C** and **5A-I** derived from the reaction of 3-X-substituted thiophenes **1a-c** with the electrophiles **2a** and **3a-c**.
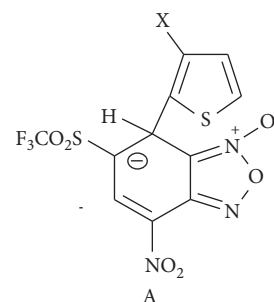

FIGURE 2

Figures S1-S2: UV-visible spectrum of thiophenes **1a** and **1b** and the progressive evolution of the formation of the product **4A** and **4B**.
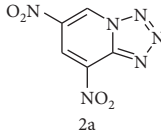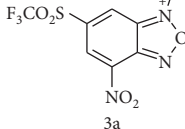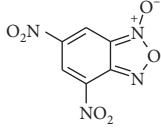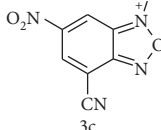
3. Results and Discussion

3.1. Kinetic Investigation. The evolution of the kinetic constants of the coupling reaction between 3-X-thiophene **1a-c** and the various electrophiles **2a** (Scheme 1) and **3a-c** (Scheme 2) requires a preliminary study by UV-visible spectrophotometry to determine the wavelengths of these reagents and their σ-adducts **4** and **5**. The addition of a solution of 3-X-substituted thiophene **1a-c** on electrophiles **2a** and **3a-c** in acetonitrile gives rise to absorbents **4A-C** and
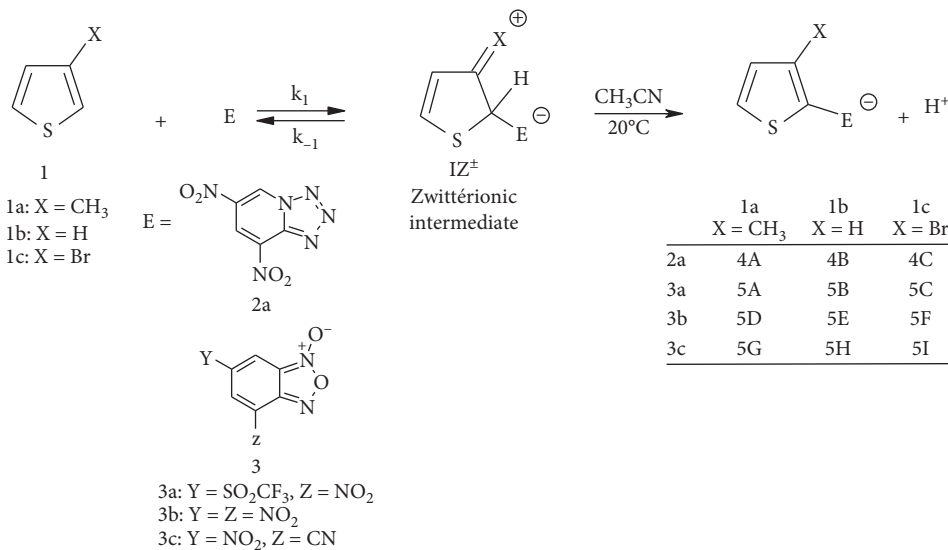
SCHEME 3

TABLE 1: Second-order rate constants (k_1/M^{-1}·s^{-1}) and electrophilicity parameters (E) of the reactions of 3-X-thiophene **1** with the electrophiles **2a** and **3a-c** in acetonitrile at 20°C.

Electrophile	E[a]	Nucleophile	k_1 (M^{-1}s^{-1})
2a	−4.58	**1a**	4.08×10^{-3}
		1b	1.28×10^{-3}
		1c	3.41×10^{-4}
3a	−4.74	**1a**	2.67×10^{-3}
		1b	7.18×10^{-4}
		1c	2.22×10^{-4}
3b	−5.06	**1a**	1.23×10^{-3}
		1b	3.39×10^{-4}
		1c	1.08×10^{-4}
3c	−6.41	**1a**	4.10×10^{-5}
		1b	1.35×10^{-5}
		1c	4.36×10^{-6}

[a]Ref [7].

FIGURE 3: Plots of log k_1 versus E for the reactivity of thiophenes **1a-c** with the reference electrophiles **2a** and **3a-c** in acetonitrile at 20°C (the identity of points is given in Table 1).

5A-I adducts at wavelengths between 405 and 487 nm. A typical experiment is illustrated in Figure 1. The spectral data for the σ-adducts **4** and **5** considered in this work (the absorption maxima and the corresponding molar extinction coefficients in acetonitrile) are collated in Table S4.

A comparison of these values of λ_{max} makes it possible to obtain information on the structure of the various adducts. Indeed, the spectra of all the adducts **4 A-C** and **5 D-I** have a very high absorption maximum up to 465–487 nm. These high wavelengths translate a strong delocalization of the
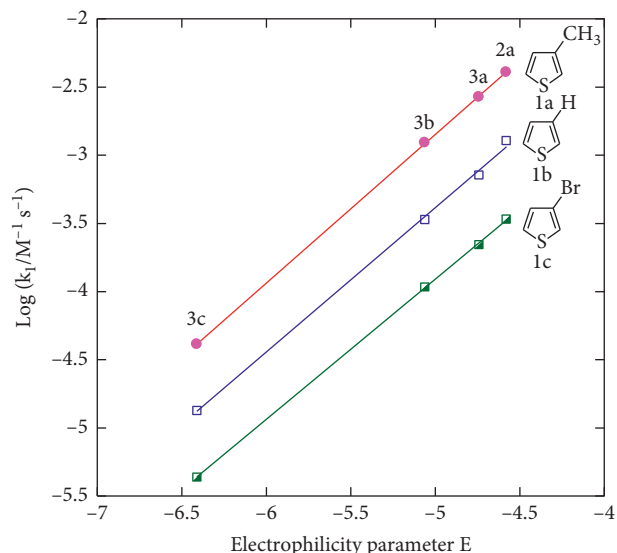
negative charge on the Z group (NO$_2$ or CN) of the carbocyclic. In this respect, it should also be noted that the strong electro-deficient character of the carbocycles of electrophiles **2a**, **3b**, and **3c** is known to promote the formation of the σ−anionic complexes [10–14].

The analysis in Table S4 reveals that the σ-adducts **5A-C** show an absorption maximum around 410 nm. This hypochromic effect observed with respect to the σ-complexes resulting from the coupling reaction between the electrophiles **2a**, **3b**, and **3c** with thiophenes **1a-c** suggests that a very high negative charge density is preferentially localized on the carbon bearing the SO$_2$CF$_3$ group (Figure 2).

It is interesting to note that electrophiles **2a** and **3a-c** showed negligible absorption at the absorbance wavelengths λ_{max} of the σ-adducts considered in this work (Figures 1, S1,

TABLE 2: Second-order rate constants k_1 ($M^{-1} \cdot s^{-1}$) and selectivity parameters (ρ and pK_a) of the reactions of 3-X-thiophene **1** with the electrophiles **2a** and **3a-c**.

Thiophene	N/s	σ^{+b}	k_1 ($M^{-1}s^{-1}$)			
			2a	**3a**	**3b**	**3c**
CH₃ thiophene **1a**	2.38/1.09	−0.31	4.08×10^{-3}	2.76×10^{-3}	1.23×10^{-3}	4.10×10^{-5}
H thiophene **1b**	1.79/1.06	0.00	1.28×10^{-3}	7.18×10^{-4}	3.39×10^{-4}	1.35×10^{-5}
Br thiophene **1c**	1.20/1.03	0.15	3.41×10^{-4}	2.22×10^{-4}	1.08×10^{-4}	4.36×10^{-6}
ρ			−2.23	−2.27	−2.22	−2.03
pK_a			0.30	2.95	3.75	5.86

[b]Ref [18].

and S2). This observation made possible the kinetic study of the coupling reaction of thiophenes **1a-c** with the various electrophiles **2a** and **3a-c** in acetonitrile.

Theoretically, the reactions proceed according to Scheme 3 and the bimolecular rate constant k_1 is related to the formation of the zwitterionic intermediate $\mathbf{IZ}^{\pm}$ while the monomolecular rate constants k_{-1} and k_2 are associated with the decomposition processes of the intermediate $\mathbf{IZ}^{\pm}$ with, respectively, a return to the starting reagents or rearomatization of the thiophenic entity. So, as can be seen, the proposed mechanism is the result of an electrophilic aromatic substitution of the α-carbon position of the thiophenes **1a-c** with formation of a zwitterionic intermediate $\mathbf{IZ}^{\pm}$. The various add adducts are the result of a two-step S_EAr process of the addition-elimination type.

The graphs Ln $(A_e - A)$ as a function of time measured for a given interaction are linear ($R^2 > 0.9998$). From the slope of these lines, the constants k_{obsd} were easily determined as follows:

$$\text{Ln}\,(A_e - A) = -k_{obs}t + \text{Ln}\,(A_e - A_o). \tag{1}$$

The straight lines k_{obsd} as a function of the concentration of thiophenes **1a-c** have proved to be linear and are characterized by a zero origin ordinate.

It follows that the nucleophilic attack of the various thiophenes **1a-c** on the position 7 of the electrophiles **2a** and **3a-c** studied is then the determining step of the coupling reaction, which implies

$$k_{obsd} = k_1\,[3 - X - \text{thiophene}]. \tag{2}$$

The values of the relative bimolecular rate constants k_1 for each electrophile studied are grouped in Table 1.

3.2. Nucleophilicities of Thiophenes 1a-C.
Based on the values measured in acetonitrile at 20°C of the bimolecular rate constants k_1 associated with the coupling reaction between thiophenes **1a-c** and electrophiles **2a** and **3a-c** which are grouped in Table 1 with the values of the

parameters E of the various electrophiles **2a** and **3a-c** reported in the literature [7], the plots $\log k_1/s$ as a function of the parameter E could be constructed. The situation is illustrated in Figure 3.

As can be seen, satisfactory lines of equal slope or near unity have been obtained in accordance with Mayr's rearranged equation (equation (3) [15–17]). The values of the parameters N and s relative to each 3-X-substituted thiophene **1a-c** could thus be determined graphically.

$$\frac{\log k_1}{s} = E + N. \tag{3}$$

In light of the values of N grouped in Table 2, we have undertaken to compare the reactivity of our thiophenes **1a-c** with that of other nucleophiles. Figure 4 reveals that the N parameters for 3-X-substituted thiophenes **1a-c** are located on over a reactivity range of nearly 3 orders of magnitude. As can be seen, the reactivity of the most reactive thiophene **1d** (N = 3.96) [19] is approximately 13 units above the reactivity of tetraethylsilane **6** (N = −6.50) [20] and tris-p-tolylmethane **7** (N = −8.80) [20], but it remains significantly lower (25 units) than that of the 2-phenylpropionitrile anion **8** (N = 28.95) [21] considered to be the nucleophile more reactive encrypted to date. Another important observation is that the nucleophilic reactivity of the pyrroles **9a** and **9b** [22] and the furans **10a** and **10b** [6] is higher than that of the thiophene series **1a-c**. Moreover, the nucleophilicity of the thiophenes **1e** and **1d** is at the level of that of the indoles **11b** and **11c** [23]. Regarding the nucleophilicity of the three less-reactive thiophenes **1a-c**, we find that their ranking on the universal scale N of Mayr is about 4 units higher than that of naphthalenes **12** and **13** [20].

3.3. Effect of Substituents on Reactivity.
The analysis of Table 2 clearly shows that the bimolecular rate constant k_1 associated with the coupling reaction of thiophenes **1a-c** with the superelectrophiles **2a** and **3a-c** is very sensitive to the nature of the substituent X located in position
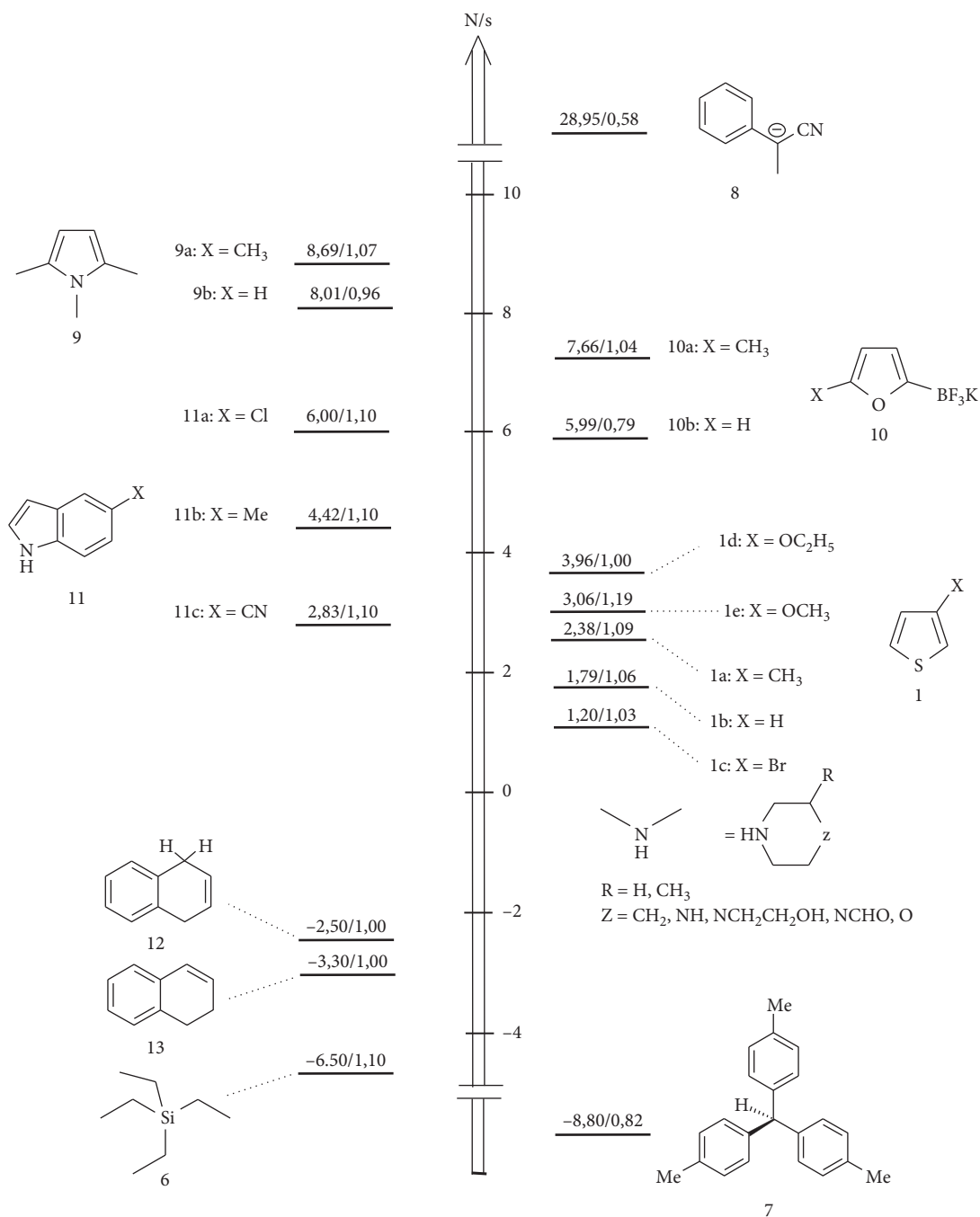
FIGURE 4: Ranking the carbon reactivity of the 3-X-substituted thiophene **1** on the Mayr N universal N scale.

C-3 of the thiophenes **1a-c**. Indeed, the constant k_1 decreases regularly when $X = CH_3$, the most electro-donor substituent, and changes to $X = Br$, the most electro-attracting substituent.

This behavior is well illustrated in Figure 5, where the logarithm of the rate constant k_1 is a function of the Hammett constant σ^+, reported in the literature, of the various X substituents [24].

It is interesting to note that obtaining such correlations means the same reaction mechanism despite the variation of the substituent and confirms that the addition step of

thiophenes **1a-c** on electrophiles **2a** and **3a-c** is the decisive stage of the reaction.

The negative values of the reaction constants ρ deduced from the slopes of the lines $\log k_1 = f(\sigma^+)$, as shown in Table 2, indicate a development of a positive charge on the thiophenic entity in the transition state that means a decrease in electron density on the C-2 carbon atom of thiophene (Figure 6). It is noted that the more the substituent X is an electron donor, the more this charge is positive, and therefore the corresponding transition state is stabilized, which confirms the decrease in k_1 observed
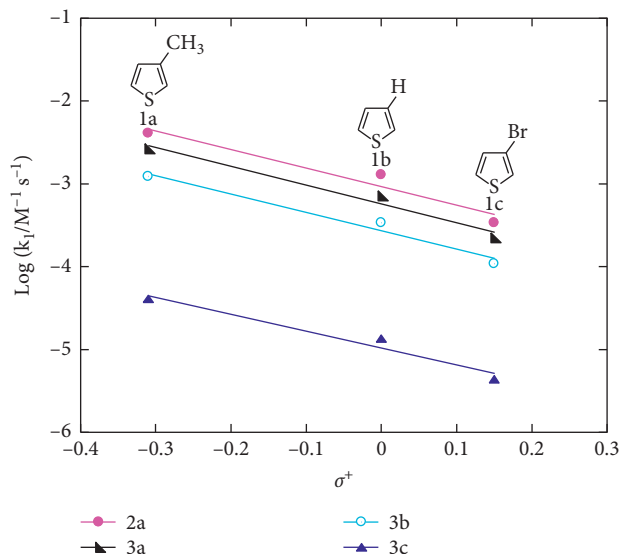
FIGURE 5: Hammett correlations: influence of the nature of the substituent X on the constant k_1 relating to the coupling reaction of thiophenes **1a-c** with electrophiles **2a** and **3a-c** in acetonitrile at 20°C.
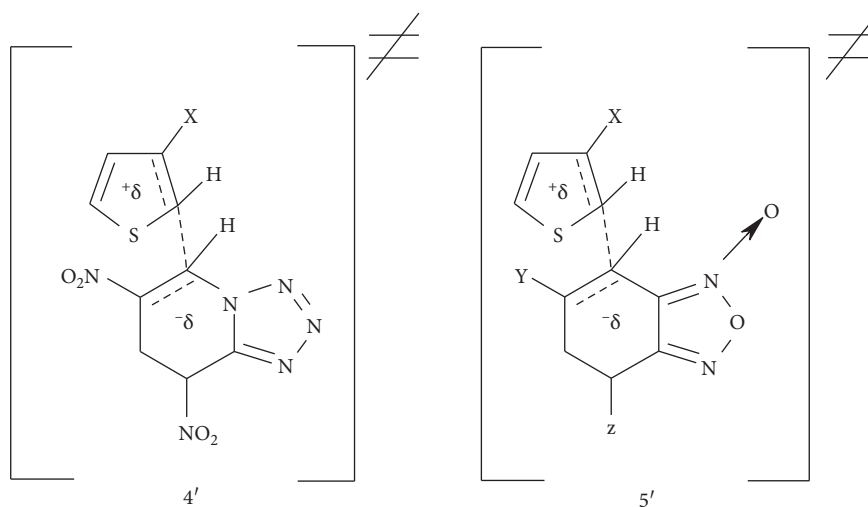

FIGURE 6: Proposed transitional state structures for σ-adducts **4** and **5** in acetonitrile.

when passing from 3-methylthiophene **1a** to 3-bromo-thiophene **1c**.

It is interesting to note that the low values of ρ obtained can also be interpreted in terms of a large delocalization of the negative charge in the carbocyclic of electrophiles **2a** and **3a-c**. In addition, our values ($-2.23 < \rho < -2.03$) are similar to the values measured by several authors [18, 25–29]. El Guesmi and coworkers have shown that the aromatic nucleophilic substitution reactivity of triflone 2,4,6-tris (trifluoromethanesulfonyl) anisole with various anilines in acetonitrile at 15°C is characterized by a value of ρ equal to -1.80 [25].

Moreover, the existence of linear correlations $\log k_1 = f(\sigma_p^+)$ and result of the study of the variation of the reactivity according to the structural variations of the nucleophilic pattern (thiophene) exhibits the phenomenon known as "Hyper-Ortho Correlation" [10, 30]. Currently, such a

situation has never been encountered in the context of five-membered heterocycles.

However, $\log k = f(\sigma_p)$ correlations were obtained in thiophenic series, but in these cases, the reactivity variations were made from structural variations in the electrophilic motif [18, 30]. In this regard, we note that Spinelli and coworkers were the first to identify a hyperortho effect in the case of the coupling reaction of various thiophenes such as 2-bromo-3-X-5-nitrothiophene with piperidine in methanol [31].

3.4. Reactivity-Acidity Relationship.

A comparison of electrophilic reactivity can be made using the linear free-energy relation similar to that proposed by Brönsted [32, 33]. The relation 4 relates the reactivity k to the thermodynamic acidity of the electrophile pK_a. The
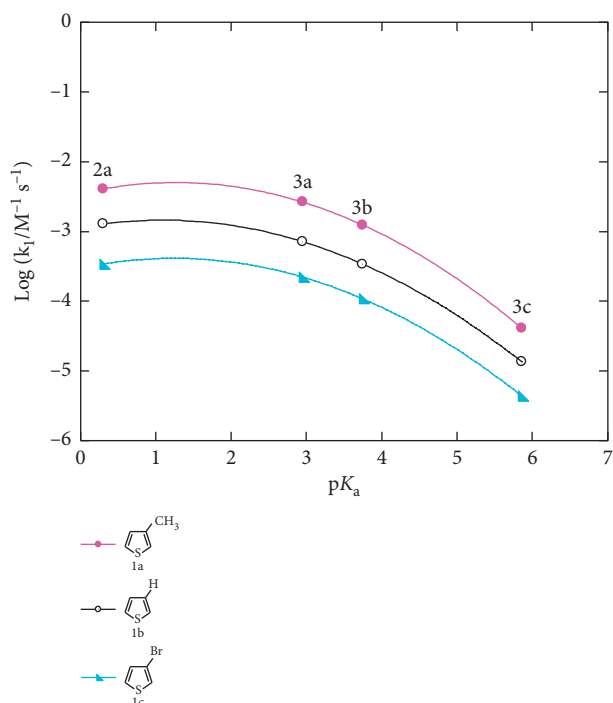
FIGURE 7: Bronsted nonlinear correlations: influence of electrophilic acidity **2a** and **3a-c** on bimolecular rate constants, k_1, related to the coupling reaction of the thiophene **1a-c** with the electrophiles **2a** and **3a-c** in acetonitrile at 20°C.

constants A measure the reactivity of the family of electrophiles, and α_{El} is the sensitivity of the reaction to the variations of acidity of the electrophile. As can be seen, an
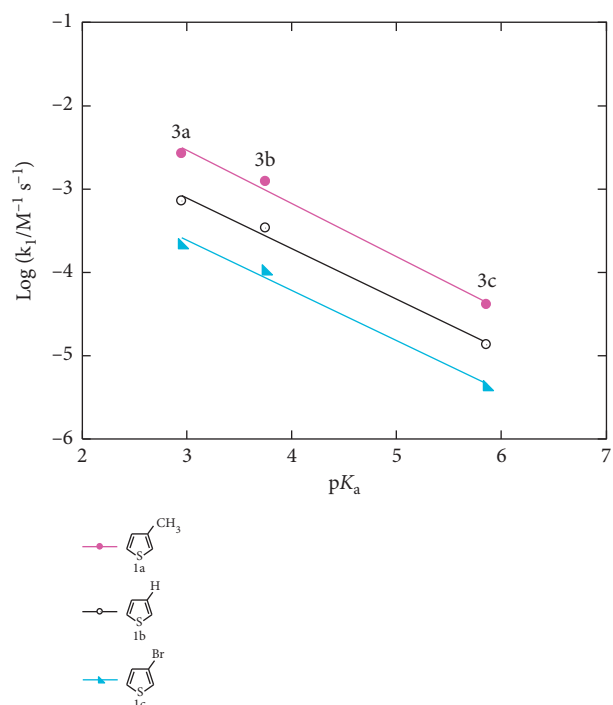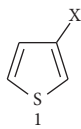

FIGURE 8: Bronsted linear correlations for the coupling reaction of the thiophenes **1a-c** with the electrophiles **3a-c** in acetonitrile at 20°C.

TABLE 3: Nucleophilicity parameters N of 3-X-substituted thiophenes in acetonitrile at 20°C.

	σ^+	N	Reference
OCH$_3$	−0.78	3.06	[6]
OC$_2$H$_5$	−0.81	3.69	[16]
CH$_3$	−0.31	2.38	This work
H	0.00	1.79	This work
Br	0.15	1.20	This work
NH$_2$	−1.30	4.62	Estimated
CF$_3$	0.61	0.23	Estimated
CN	0.66	0.13	Estimated
NO$_2$	0.79	−0.17	Estimated

examination of Figure 7 leaves no doubt that the Brönsted type graphs for the three thiophenes **1a-c** have a curvilinear appearance:

$$\log k = A + \alpha_{El}pK_a. \tag{4}$$

However, at $pK_a > 3$, the three electrophiles **3a-c** define a linear Brönsted correlation according to equation (4). The slope values deduced from the linear straight lines in Figure 8 ($\alpha_{El}^{1a} = -0.64$, $\alpha_{El}^{1b} = -0.61$, $\alpha_{El}^{1c} = -0.60$) suggest that the formation of the carbon-carbon and thus the transfer of the charge of the nucleophile (thiophene) to the electrophile (benzofuraxanes **3a-c**) is almost 60% carried out in the state of transition.

Numerous electrophilic substitution studies exist in the literature in which the variations in reactivity have been studied from structural variations in the nucleophilic motif [34, 35]. Challis and coworkers, for example, investigated the reaction of 4,6-dinitrobenzofuraxane **3b** with 5-X substituted indoles **11** [34]. In these systems, the Brönsted-type straight lines associated with the reactivity changes are characterized by a slope of β_{nuc}-type since these changes are the structural variations of the nucleophile. However, in the present work, the α_{El} values reveal the structural variations of the electrophile and we have not found in the literature values of the same type that we could compare to our system.

On the other hand, it remains that our values of α_{El} obtained are in good agreement with a polar heteroaromatic electrophile substitution mechanism [36, 37].

3.5. Effect of Substituant X on the Nucleophilicity N. The aim of this part is to verify if the C-2 carbon nucleophilicity of the 3-X-substituted thiophenes measured by the parameter N is dependent on the electronic effect of the substituent X in position 3. In this context, we have grouped in Table 3 the values of the parameter N of the thiophenes **1a-c** quantified in this work as well as that of 3-methoxythiophene **1d** reported by Berionni and coworkers [6] and the constants of Hammett σ of various groups used in this study [24].

As can be seen, Figure 9 shows that a satisfactory linear line is obtained by carrying the values of N as a function of
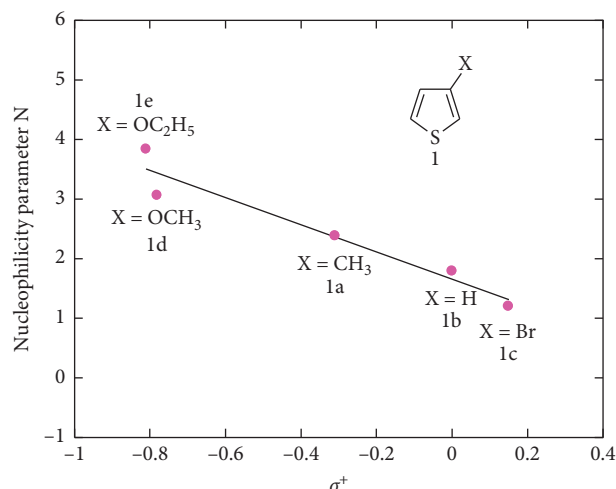
Figure 9: Correlation $N = f(\sigma^+)$ of a series of 3-X-substituted thiophenes in acetonitrile at 20°C.

Hammett constants σ. Equation (5) describes this linear dependence:

$$N = 1.65 - 2.28 \cdot \sigma^+,$$
$$R^2 = 0.9663. \tag{5}$$

We note that obtaining the correlation (5) informs us about the exceptional α-carbon nucleophilic reactivity of 3-X-substituted thiophenes. Also, it can be used for a direct estimation of N values that are not easily measurable.

4. Conclusion

According to the free-energy relationship $\log k = s\,(N + E)$, the nucleophile-specific parameters N and s of 3-X-thiophenes **1** have been evaluated and compared with the reactivity of other C-nucleophiles in acetonitrile. On the other hand, the satisfactory Hammett correlations ($\log k_1$ vs. σ^-) obtained confirms that a 3-X substituent exerts an effect on the 2-position of the same type as that exerted from the 5-position: hyperortho correlations.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors confirm that this article content has no conflicts of interest.

Acknowledgments

Supplementary Materials

This is the UV-visible spectrum and the kinetics data of each thiophene **1a-c**. Tables S1–S3: kinetics data for reactions of thiophene **1** with 4,6-dinitrotetrazolopyridine **2a** and benzofuroxane **3a-c** in aqueous solution at 20°C. Table S4: physical data for the formation of σ-adducts **4A-C** and **5A-I** derived from the reaction of 3-X-substituted thiophenes **1a-c** with the electrophiles **2a** and **3a-c**. Figures S1-S2: UV-visible spectrum of thiophenes **1a** and **1b** and the progressive evolution of the formation of the products **4A** and **4B**. (*Supplementary Materials*)

References

[1] L. D. Earl, B. O. Patrick, and M. O. Wolf, "Synthesis, structure, and magnetic properties of bithiophene- and terthiophene-linked manganese metal-organic frameworks," *Inorganic Chemistry*, vol. 52, no. 17, pp. 10021–10030, 2013.

[2] D. M. Vriezema, J. Hoogboom, K. Velonia et al., "Vesicles and polymerized vesicles from thiophene-containing rod-coil block copolymers," *Angewandte Chemie International Edition*, vol. 42, no. 7, pp. 772–776, 2003.

[3] H.-h. Yu, A. E. Pullen, M. G. Büschel, and T. M. Swager, "Charge-specific interactions in segmented conducting polymers: an approach to selective ionoresistive responses," *Angewandte Chemie International Edition*, vol. 43, no. 28, pp. 3700–3703, 2004.

[4] I. F. Perepichka and D. F. Perepichka, *Handbook of Thiophene-Based Materials: Applications in Organic Electronics and Photonics*, Eds. Wiley, Hoboken, NJ, USA, 2009.

[5] N. B. Vinh, S. M. Devine, L. Munoz et al., "Design, synthesis, and biological evaluation of tetra-substituted thiophenes as inhibitors of p38α MAPK," *ChemistryOpen*, vol. 4, no. 1, pp. 56–64, 2015.

[6] G. Scammells, V. Morozova, M. Heininger, P. Mayer, P. Knochel, and H. Mayr, "Electrophilic aromatic substitutions of aryltrifluoroborates with retention of the BF3-group: quantification of the activating and directing effects of the trifluoroborate group," *Journal of the American Chemical Society*, vol. 135, no. 16, pp. 6317–6324, 2013.

[7] F. Terrier, S. Lakhdar, T. Boubaker, and R. Goumont, "Ranking the reactivity of superelectrophilic heteroaromatics on the electrophilicity scale," *The Journal of Organic Chemistry*, vol. 70, no. 16, pp. 6242–6253, 2005.

[8] F. Terrier, *Modern Nucleophilic Aromatic Substitution*, Wiley, Hoboken, NJ, USA, 2013.

[9] D. Brugier, F. Outurquin, and C. Paulmier, "Studies on the reactivity of N-(3-thienyl) carbamates," *Journal of the Chemical Society, Perkin Transactions 1*, vol. 1, no. 1, pp. 37–43, 2001.

[10] F. Terrier, *Modern Nucleophilic Aromatic Substitution*, John Wiley & Sons, Hoboken, NJ, USA, 2013.

[11] T. Boubaker, R. Goumont, E. Jan, and F. Terrier, "An extremely highly electrophilic heteroaromatic structure: 4,6-dinitrotetrazolo[1,5-a]pyridine," *Organic and Biomolecular Chemistry*, vol. 1, p. 2764, 2003.

[12] T. Boubaker, A. P. Chatrousse, F. Terrier, B. Tangour, J. M. Dust, and E. Buncel, "Water and hydroxide ion pathways in the σ-complexation of superelectrophilic 2-aryl-4,6-dinitrobenzotriazole 1-oxides in aqueous solution. A kinetic and thermodynamic study," *Journal of the Chemical Society, Perkin Transactions 2*, vol. 2, no. 9, pp. 1627–1633, 2002.

[13] D. Vichard, T. Boubaker, F. Terrier, M.-J. Pouet, J. M. Dust, and E. Buncel, "The versatile reactivity of 2-aryl-4,6-dinitrobenzotriazole 1-oxides in Diels-Alder type condensations and in σ-complexation—a relationship between super-electrophilicity and pericyclic reactivity," *Canadian Journal of Chemistry*, vol. 79, no. 11, pp. 1617–1623, 2001.

[14] F. Terrier, M. Mokhtari, R. Goumont, J.-C. Hallé, and E. Buncel, "High Brønsted β_{nuc} values in S_NAr displacement. An indicator of the SET pathway?" *Organic and Biomolecular Chemistry*, vol. 1, no. 10, pp. 1757–1763, 2003.

[15] H. Mayr and M. Patz, "Scales of nucleophilicity and electrophilicity: a system for ordering polar organic and organometallic reactions," *Angewandte Chemie International Edition in English*, vol. 33, no. 9, pp. 938–957, 1994.

[16] H. Mayr and M. Patz, "Nucleophilie- und Elektrophilieskalen als Ordnungsprinzipien polarer organischer und metallorganischer Reaktionen," *Angewandte Chemie*, vol. 106, no. 9, pp. 990–1010, 1994.

[17] H. Mayr, M. Patz, M. F. Gotta, and A. R. Ofial, "Reactivities and selectivities of free and metal-coordinated carbocations," *Pure and Applied Chemistry*, vol. 70, no. 10, pp. 1993–2000, 1998.

[18] A. Echaieb, W. Gabsi, and T. Boubaker, "Nucleophilic substitution reactions of 2-Methoxy-3-X-5-nitrothiophenes: effect of substituents and structure-reactivity correlations," *International Journal of Chemical Kinetics*, vol. 46, no. 8, pp. 470–476, 2014.

[19] W. Gabsi, T. Boubaker, and R. Goumont, "Azo-coupling reactions of para-X-benzenediazonium cations with 3-ethoxythiophene in acetonitrile," *International Journal of Chemical Kinetics*, vol. 48, no. 5, pp. 266–273, 2016.

[20] M. Horn, L. H. Schappele, G. Lang-Wittkowski, H. Mayr, and A. R. Ofial, "Towards a comprehensive hydride donor ability scale," *Chemistry—A European Journal*, vol. 19, no. 1, pp. 249–263, 2013.

[21] O. Kaumanns, R. Appel, T. Lemek, F. Seeliger, and H. Mayr, "Nucleophilicities of the anions of arylacetonitriles and arylpropionitriles in dimethyl sulfoxide," *The Journal of Organic Chemistry*, vol. 74, no. 1, pp. 75–81, 2009.

[22] T. A. Nigst, M. Westermaier, A. R. Ofial, and H. Mayr, "Nucleophilic reactivities of pyrroles," *European Journal of Organic Chemistry*, vol. 2008, no. 14, pp. 2369–2374, 2008.

[23] S. Lakhdar, M. Westermaier, F. Terrier et al., "Nucleophilic reactivities of indoles," *The Journal of Organic Chemistry*, vol. 71, no. 24, pp. 9088–9095, 2006.

[24] L. P. Hammett, *Physical Organic Chemistry, Reaction Rates Equilibria, and Mechanisms*, McGraw-Hill, NewYork, NY, USA, 1970.

[25] N. El Guesmi and T. Boubaker, "Substituent effects on the reactions of aromatic triflones with para-X-anilines in methanol: low intrinsic reactivity and transition state imbalances," *International Journal of Chemical Kinetics*, vol. 43, no. 5, pp. 255–262, 2011.

[26] N. E. Guesmi, T. Boubaker, and R. Goumont, "Activation of the aromatic system by the SO_2CF_3 group: kinetics study and structure-reactivity relationships," *International Journal of Chemical Kinetics*, vol. 42, no. 4, pp. 203–210, 2010.

[27] Résultats Non Publiés.

[28] I. Jamaoui, T. Boubaker, and R. Goumont, "Reactivity of 4-phenoxy-7-nitrobenzofurazane: mechanism and correlations structure-reactivity," *Journal of the Tunisian Chemical Society*, vol. 15, pp. 191–200, 2014.

[29] E. A. Hamed, A. A. El-Bardan, E. F. Saad, G. A. Gohar, and G. M. Hassan, "Nucleophilic substitutions at the pyridine ring. Conformational preference of the products and kinetics of the reactions of 2-chloro-3-nitro- and 2-chloro-5-nitro-pyridines with arenethiolates," *Journal of the Chemical Society, Perkin Transactions 2*, vol. 2, no. 11, pp. 2415–2422, 1997.

[30] S. B. Salah, T. Boubaker, and R. Goumont, "Kinetic studies on nucleophilic addition reactions of 4-X-substituted anilines to N1-methyl-4-nitro-2,1,3 benzothiadiazolium terafluoroborate in acetonitrile: reaction mechanism and Mayr' approach," *International Journal of Chemical Kinetics*, vol. 47, no. 8, pp. 461–470, 2015.

[31] D. Spinelli, G. Consiglio, and R. Noto, "Linear free energy ortho-correlations in the thiophen series. Part III. The kinetics of piperidino-substitution of some 3-X-5-nitro-2-thienyl phenyl sulphones in methanol," *Journal of the Chemical Society, Perkin Transactions 2*, vol. 2, no. 13, p. 1495, 1976.

[32] J. N. Bronsted and K. Pederson, "The catalytic decomposition of the nitramide and its physico-chemical meaning," *The Journal of Physical Chemistry*, pp. 108–185, 1924.

[33] T. C. Bruice and R. Lapinski, "Imidazole catalysis. IV.1 The reaction of general bases with p-nitrophenyl acetate in aqueous solution," *Journal of the American Chemical Society*, vol. 80, no. 9, pp. 2265–2267, 1958.

[34] B. C. Challis and E. M. Millar, "Heteroaromatic hydrogen exchange reactions. Part IV. Base-catalysed protodetritiation of 3-3H1-indoles in aqueous sodium hydroxide," *Journal of the Chemical Society, Perkin Transactions 2*, vol. 2, no. 9, pp. 1111–1116, 1972.

[35] F. Terier, M. J. Pouet, J. C. Hallé, S. Hunt, J. R. Jones, and E. Buncel, "Electrophilic heteroaromatic substitutions: reactions of 5-X-substituted indoles with 4,6-dinitrobenzofuroxan," *Journal of the Chemical Society, Perkin Transactions 2*, p. 1665, 1993.

[36] F. G. Bordwell, A. H. Clemens, D. E. Smith, and J. Begemann, "Reactions of carbanions with electron acceptors," *The Journal of Organic Chemistry*, vol. 50, no. 8, pp. 1151–1156, 1985.

[37] F. G. Bordwell and D. L. Hughes, "Nucleophilic aromatic substitution reactions with carbanions and nitranions in dimethyl sulfoxide solution," *Journal of the American Chemical Society*, vol. 108, no. 19, pp. 5991–5997, 1986.