Electronic structure and reactivity of 3-acetyl-2-methylbenzo[*b*]thiophene: a quantum chemical study*

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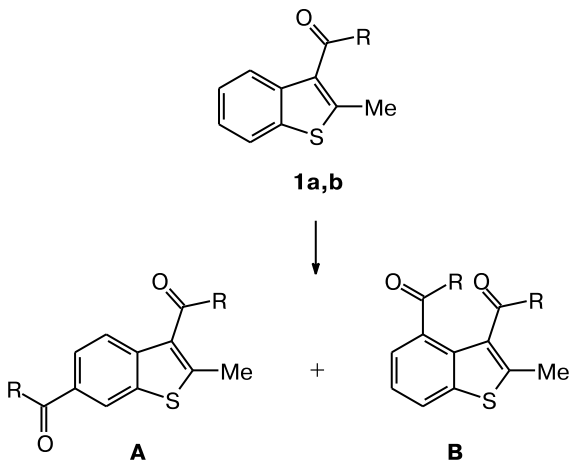
The electronic structures of 3-acetyl-2-methylbenzothiophene, the cations resulting from its C-protonation at positions 4—7 and O-protonation, and the dications formed upon protonation at positions 4—7 of the O-protonation product were studied by the MNDO, HF/3-21G, and B3LYP/3-21G methods. Analysis of the relative energies of these cations and dications is in line with the earlier authors´ data on the predominant reactivity of positions 4 and 6 of the 3-acetyl-2-methylbenzothiophene molecule toward acylation.

Key words: quantum chemical calculations, MNDO, Hartree—Fock method, density functional theory (DFT), B3LYP functional, electrophilic substitution.

Previously,[1] we studied the acylation of 3-acyl-2-methylbenzo[*b*]thiophene and determined the position of the electrophilic substitution in its benzene ring. It was shown that this reaction gives mixtures of two isomers in which products **A** predominated (Scheme 1).

Scheme 1



Reagents: RC(O)Cl, 2 equiv. $AlCl_3$.

The structures of the products were mainly established by analysis of 1D and 2D NMR spectra.[1]

This communication presents the results of a quantum chemical study of the electrophilic substitution in molecule **1**. The results of semiempirical MNDO calculations and HF/3-21G and B3LYP/3-21G calculations were compared with the published results[1] in order to elucidate the applicability of these methods for predicting the position of electrophilic substitution in type **1** benzothiophenes. On the basis of earlier experience,[2—6] when choosing the calculation methods, we considered the results for similar heteroaromatic compounds obtained in previous works[2—4] where the MNDO, HF, and B3LYP methods were used. In particular, we demonstrated that inclusion of polarization functions did not affect qualitatively the drawn conclusions.

Previously,[7,8] it was demonstrated that the geometric and energy parameters of heterocyclic compounds can be reliably calculated within the density functional theory (DFT) using the B3LYP hybrid functional. In order to evaluate the ability of thiophene, pyrrole, furan, and corresponding benzoannelated systems to function as Diels—Alder dienes, B3LYP/6-311+G(2d,p) calculations were performed to study the structures and to determine the NICS (Nuclear Independent Chemical Shift) indexes,[8] which serve as an aromaticity criterion and thus provide knowledge about the aromatic stabilization and reactivity of these compounds.

The same method was used to obtain characteristics of the aromatic stabilization, structure, and magnetic properties (NICS) for benzo[*b*]- and benzo[*c*]furans, -thiophenes, and -pyrroles. The reactivity was estimated only for positions 2 and 3 of the five-membered heterocycles.[9]

The electrophilic substitution constants were determined[10] for all six positions of benzo[*b*]thiophene by titrimetric measurements of solvolysis of six isomeric

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1-(benzo[*b*]thienyl)ethyl chlorides in a 80% ethanol—water solution. The negative σ_{Ar}^{+} values indicate that in electrophilic reactions, all of the positions in the benzo[*b*]-thiophene system are more reactive than in the benzene ring. According to calculations, the position reactivity decreases in the series 3 > 2 > 6 > 5 > 4 > 7 (see Ref. 10). The earlier studies of the reactivity of benzo[*b*]thiophene in electrophilic reactions were restricted to positions 2 and 3 (see Refs 11—13).

In compound **1a** studied here, these positions are occupied, and it may be pertinent to compare the relative reactivities of vacant positions in the benzene system. To this end, we performed quantum chemical calculations for the molecule of 3-acetyl-2-methylbenzo[*b*]thiophene (**1a**) and its monoprotonated (**2—6**) and diprotonated (**7—10**) forms, *i.e.*, a proton, which is used most often in qualitative analysis of the selectivity of electrophilic substitution, served as the model electrophile.[2—4]

Calculation Procedure

All calculations were carried out using the GAUSSIAN-98 program package: in the semiempirical MNDO approximation, by the Hartree—Fock *ab initio* method with the 3-21G basis set, and by the DFT (B3LYP/3-21G) method (see Ref. 14).

Results and Discussion

The chemically most significant geometric parameters of structures **1—10** optimized by these three methods are summarized in Tables 1—3. A comparison of the corresponding values shows that almost all lengths of same-type chemical bonds (except for S(1)—C(2) and S(1)—C(9)) do not differ much from one another, *i.e.*, they are almost insensitive to any of the three computational approximations used. For each structure **1—10**, both S—C bond lengths determined by the HF/3-21G and B3LYP/3-31G methods are quite similar (~1.8 Å) and differ considerably from those found in the MNDO approximation (~1.7 Å).

It is noteworthy that for the benzo[*b*]thiophene molecule, which is related to **1a**, higher-level calculations by the HF/6-31G**, B3LYP/6-31G*, and MP2/6-311G** methods predict[15] the lengths of both S—C bonds to be in the range from 1.730 Å to 1.758 Å. The lengths of other chemical bonds in the molecular cage are close to those presented in Tables 1—3. The experimental values for the S—C bond lengths (see Ref. 15) in benzo[*b*]thiophene and dibenzothiophene are ~1.75 Å.

From this it can be concluded that the S—C chemical bond lengths in molecule **1** calculated by the HF/3-21G

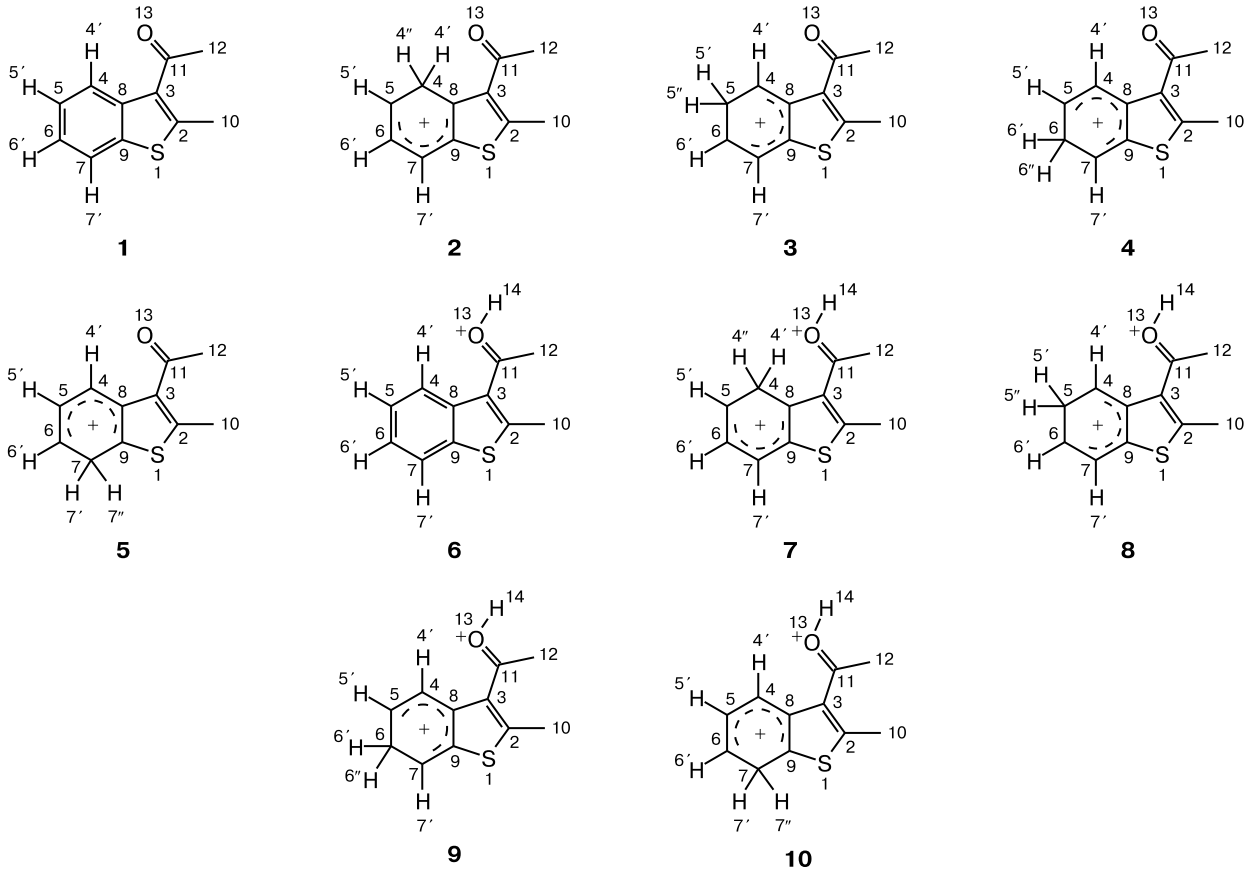

Table 1. Bond lengths (d) in molecules **1**—**10** calculated by the MNDO method

Bond	d/Å									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
S(1)—C(2)	1.69	1.66	1.70	1.67	1.69	1.65	1.65	1.70	1.65	1.68
C(2)—C(3)	1.38	1.42	1.38	1.41	1.38	1.42	1.43	1.39	1.43	1.40
C(3)—C(8)	1.47	1.42	1.48	1.43	1.47	1.48	1.45	1.48	1.45	1.47
C(8)—C(4)	1.41	1.50	1.38	1.44	1.41	1.41	1.50	1.38	1.43	1.43
C(4)—C(5)	1.40	1.50	1.50	1.37	1.43	1.40	1.51	1.50	1.38	1.41
C(5)—C(6)	1.41	1.37	1.50	1.50	1.37	1.41	1.38	1.50	1.50	1.39
C(6)—C(7)	1.40	1.44	1.37	1.50	1.50	1.40	1.42	1.38	1.50	1.50
C(7)—C(9)	1.41	1.40	1.43	1.37	1.49	1.41	1.42	1.42	1.38	1.50
C(9)—C(8)	1.43	1.44	1.46	1.47	1.43	1.43	1.42	1.46	1.46	1.42
S(1)—C(9)	1.70	1.68	1.64	1.69	1.64	1.68	1.68	1.66	1.69	1.66
C(2)—C(10)	1.49	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
C(3)—C(11)	1.50	1.51	1.51	1.51	1.51	1.44	1.47	1.48	1.47	1.48
C(11)—C(12)	1.53	1.52	1.52	1.52	1.52	1.52	1.52	1.52	1.52	1.52
C(11)—O(13)	1.23	1.22	1.22	1.22	1.22	1.32	1.30	1.30	1.30	1.30
O(13)—H(14)	—	—	—	—	—	0.95	0.96	0.96	0.96	0.96
C(4)—H(4′)	1.10	1.12	1.09	1.09	1.09	1.09	1.12	1.09	1.09	1.09
C(4)—H(4″)	—	1.12	—	—	—	—	1.12	—	—	—
C(5)—H(5′)	1.09	1.09	1.12	1.09	1.09	1.09	1.09	1.12	1.09	1.09
C(5)—H(5″)	—	—	1.12	—	—	—	—	1.12	—	—
C(6)—H(6′)	1.09	1.09	1.09	1.12	1.09	1.09	1.09	1.09	1.12	1.09
C(6)—H(6″)	—	—	—	1.12	—	—	—	—	1.12	—
C(7)—H(7′)	1.09	1.09	1.09	1.09	1.12	1.09	1.10	1.09	1.09	1.12
C(7)—H(7″)	—	—	—	—	1.12	—	—	—	—	1.12

Table 2. Bond lengths (d) in molecules **1**—**10** calculated by the HF/3-21G method

Bond	d/Å									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
S(1)—C(2)	1.80	1.77	1.83	1.78	1.82	1.75	1.74	1.79	1.74	1.78
C(2)—C(3)	1.34	1.37	1.33	1.37	1.34	1.39	1.40	1.37	1.41	1.38
C(3)—C(8)	1.48	1.42	1.48	1.43	1.47	1.48	1.45	1.49	1.45	1.48
C(8)—C(4)	1.40	1.49	1.36	1.43	1.40	1.39	1.49	1.36	1.42	1.41
C(4)—C(5)	1.38	1.48	1.48	1.34	1.42	1.38	1.48	1.48	1.35	1.40
C(5)—C(6)	1.39	1.34	1.48	1.48	1.34	1.39	1.35	1.48	1.48	1.35
C(6)—C(7)	1.38	1.42	1.34	1.48	1.49	1.38	1.40	1.35	1.48	1.48
C(7)—C(9)	1.38	1.67	1.41	1.33	1.48	1.37	1.39	1.40	1.34	1.47
C(9)—C(8)	1.39	1.39	1.42	1.43	1.37	1.39	1.37	1.42	1.42	1.36
S(1)—C(9)	1.80	1.79	1.74	1.80	1.75	1.80	1.80	1.77	1.80	1.77
C(2)—C(10)	1.51	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
C(3)—C(11)	1.49	1.50	1.50	1.50	1.50	1.39	1.41	1.42	1.42	1.42
C(11)—C(12)	1.51	1.50	1.50	1.51	1.50	1.50	1.49	1.49	1.50	1.49
C(11)—O(13)	1.22	1.22	1.21	1.21	1.22	1.31	1.30	1.30	1.29	1.30
O(13)—H(14)	—	—	—	—	—	0.97	0.97	0.97	0.97	0.97
C(4)—H(4′)	1.06	1.09	1.07	1.06	1.07	1.06	1.09	1.07	1.06	1.07
C(4)—H(4″)	—	1.09	—	—	—	—	1.09	—	—	—
C(5)—H(5′)	1.07	1.07	1.09	1.07	1.07	1.07	1.07	1.10	1.07	1.07
C(5)—H(5″)	—	—	1.09	—	—	—	—	1.10	—	—
C(6)—H(6′)	1.07	1.07	1.07	1.09	1.07	1.07	1.07	1.07	1.10	1.07
C(6)—H(6″)	—	—	—	1.09	—	—	—	—	1.10	—
C(7)—H(7′)	1.07	1.09	1.07	1.07	1.09	1.07	1.07	1.07	1.07	1.10
C(7)—H(7″)	—	—	—	—	1.09	—	—	—	—	1.10

Table 3. Bond lengths (*d*) in molecules **1**—**10** calculated by the B3LYP/3-21G method

Bond	*d*/Å									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
S(1)—C(2)	1.82	1.79	1.86	1.79	1.85	1.76	1.76	1.80	1.76	1.81
C(2)—C(3)	1.37	1.40	1.36	1.40	1.36	1.42	1.43	1.40	1.42	1.39
C(3)—C(8)	1.47	1.42	1.47	1.43	1.47	1.48	1.45	1.49	1.46	1.48
C(8)—C(4)	1.41	1.49	1.37	1.43	1.40	1.41	1.49	1.37	1.42	1.41
C(4)—C(5)	1.39	1.48	1.48	1.36	1.42	1.39	1.48	1.48	1.37	1.41
C(5)—C(6)	1.40	1.36	1.49	1.49	1.36	1.40	1.37	1.48	1.48	1.37
C(6)—C(7)	1.39	1.42	1.36	1.49	1.49	1.39	1.41	1.37	1.48	1.48
C(7)—C(9)	1.39	1.38	1.42	1.35	1.48	1.39	1.40	1.41	1.36	1.48
C(9)—C(8)	1.41	1.41	1.44	1.44	1.40	1.41	1.39	1.43	1.44	1.40
S(1)—C(9)	1.81	1.81	1.76	1.81	1.76	1.82	1.82	1.78	1.82	1.78
C(2)—C(10)	1.50	1.49	1.50	1.50	1.50	1.50	1.49	1.49	1.49	1.49
C(3)—C(11)	1.49	1.50	1.51	1.52	1.51	1.40	1.42	1.42	1.43	1.43
C(11)—C(12)	1.52	1.51	1.51	1.50	1.51	1.50	1.49	1.49	1.49	1.48
C(11)—O(13)	1.24	1.24	1.24	1.24	1.24	1.34	1.32	1.32	1.32	1.32
O(13)—H(14)	—	—	—	—	—	1.00	1.00	1.00	1.00	1.00
C(4)—H(4′)	1.08	1.11	1.08	1.08	1.08	1.08	1.11	1.08	1.08	1.08
C(4)—H(4″)	—	1.11	—	—	—	—	1.11	—	—	—
C(5)—H(5′)	1.08	1.08	1.11	1.08	1.08	1.08	1.09	1.11	1.08	1.08
C(5)—H(5″)	—	—	1.11	—	—	—	—	1.11	—	—
C(6)—H(6′)	1.08	1.08	1.08	1.11	1.08	1.08	1.08	1.08	1.11	1.08
C(6)—H(6″)	—	—	—	1.11	—	—	—	—	1.11	—
C(7)—H(7′)	1.08	1.08	1.08	1.08	1.11	1.08	1.09	1.08	1.08	1.11
C(7)—H(7″)	—	—	—	—	1.11	—	—	—	—	1.11

or B3LYP/3-21G methods are overestimated by ~0.05 Å, while these values determined in the MNDO approximation are underestimated by ~0.05 Å. However, these deviations are approximately constant for compounds **1**—**10** and, hence, they cannot significantly affect their relative energy characteristics.

The energy characteristics obtained by each of the three methods for the model intermediates of electrophilic substitution (protonated compounds (**2**—**6**) and compounds doubly protonated at different positions of the benzene ring (**7**—**10**), *i.e.*, cationic σ-complexes) are close to one another and attest to higher reactivity of positions 4 and 6 (Table 4), which coincides with the experimental data on acylation.[1] The protonation energies at positions 4 and 6 of molecule **1a** (structures **2** and **4**) calculated by the MNDO method differ by 0.48 eV; for σ-complex **6** with the protonated carbonyl group, this difference is 0.02 eV. Qualitatively similar, although smaller differences (0.02 and 0.08, 0.01 and 0.07 eV, respectively) were found by the HF/3-21G and B3LYP/3-21G methods. This provides grounds for using simpler quantum chemical methods in the studies of electrophilic substitution involving a real electrophile, namely, the complex polyatomic system AcCl—$AlCl_3$.

As could be expected, the results of higher-level calculations of structures **1**—**10** by the B3LYP/6-31G(d) method were in qualitative agreement with the results of the B3LYP/3-21G and HF/3-21G calculations, *i.e.*, the sequence of isomer energies did not change (see Table 4).* The bond lengths were also close to those determined by the above-mentioned DFT and *ab initio* methods. Note

Table 4. Calculated energies (eV) of molecule **1**, cation **6**, and products **2**—**5** and **7**—**10** protonated at positions 4—7

Structure	*N**	MNDO	HF/3-21G	B3LYP/3-21G	B3LYP/6-31G(d)
1	—	0	0	0	0
2	4	−6.34	−8.82	−8.97	−9.13
3	5	−6.19	−8.66	−8.84	−8.98
4	6	−6.82	−8.74	−8.90	−9.04
5	7	−6.29	−8.61	−8.76	−8.91
6	**	−6.87	−9.44	−9.54	−9.69
7	4	−2.98	−5.27	−5.21	−5.31
8	5	−2.83	−5.16	−5.17	−5.26
9	6	−3.00	−5.25	−5.20	−5.29
10	7	−2.91	−5.14	−4.64	−5.23

* *N* is the protonation position.
** O atom.

* The B3LYP/6-31G(d) calculations were performed by the E. G. Baskir (N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences), the authors are sincerely grateful to her for useful discussion and help.

very close coincidence of the bond lengths with the published[15] values determined by the B3LYP/6-31G(d) method for unsubstituted benzo[*b*]thiophene. However, the MNDO method gives the opposite relationship between the energies of protonated structures **2** and **4** as compared with other methods and also evidently underestimated C—S bond lengths (see Tables 1—4). However, this underestimation is systematic and should not markedly affect the conclusions concerning the site of electrophilic substitution for ketone **1a**.

Thus, the structural and energy characteristics of the 3-acetyl-2-methylbenzothiophene molecule and the model intermediates of electrophilic substitution at various positions of the benzene ring (cationic σ-complexes) calculated by the MNDO, HF/3-21G, B3LYP/3-21G, and B3LYP/6-31G(d) methods are in qualitative agreement with one another, and in the case of the two last-mentioned methods, the results nearly coincide. The conclusions drawn from the results of our quantum chemical calculations for the 3-acetyl-2-methylbenzothiophene molecule and the σ-complexes formed from it generally coincide with the experimental data, and the computational methods we used are applicable, in our opinion, for evaluating the selectivity of electrophilic substitution reactions.

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