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^{1}H NMR Chemical Shift Correlations and Thermodynamic Functions of Methyl-4-acetoxybenzothiophene-6-carboxylate and 4-Hydroxybenzothiophene-6-carboxylic acid

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The gross atomic charges at various position in methyl-4-acetoxybenzothiophene-6-carboxylate and 4-hydroxybenzothiophene-6-carboxylic acid were calculated by the parametric quantum mechanical molecular model AM1 and PM3, based on neglect of diatomic differential overlap approximations. These data were correlated with ^{1}H NMR chemical shifts of the present molecules. Thermodynamic functions, namely, heats of formation, enthalpy and entropy of these molecules also calculated in the temperature range 100–1000 K were reported.

Key Words: ^{1}H NMR, Methyl-4-acetoxybenzothiophene-6-carboxylate, 4-Hydroxybenzothiophene-6-carboxylic acid.

INTRODUCTION

Various derivatives of benzothiophenes and some compounds with glycolic acid moiety exhibiting analgesic and anti-inflammatory activities were reported by earlier workers[1–5]. Attimarad and Bagavant[6] recently synthesized the title compounds possessing benzothiophene ring, acidic sites and hydroxamic acid group to evaluate their anti-inflammatory and analgesic activities. However, there is no literature available for study of NMR chemical shifts correlation and thermodynamic properties data for these compounds. In the present study, quantum mechanical molecular model AM1 (Austin model) and PM3 (parametric model) methods were used to study the charge density and thermodynamic functions of these compounds.

EXPERIMENTAL

The initial geometry for the title molecules was constructed with Chemsketch and Babel free software packages. The obtained data were used as an input for the Gamess program[7] to get optimized equilibrium geometry. Using this finalized geometry input data, semi-empirical Hamiltonians AM1 and PM3 calculations were performed using MOPAC software packages[8].

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RESULTS AND DISCUSSION

Charge density analysis: Computations were performed with a view to calculate charge density at various positions in the title molecules to correlate proton NMR chemical shifts and thermodynamic functions at various temperatures ranging from 100–1000 K. The geometry and atom numbering for methyl 4-acetoxybenzothiophene-6-carboxylate and 4-hydroxybenzothiophene-6-carboxylic acid were shown in Figs. 1 and 2 respectively.

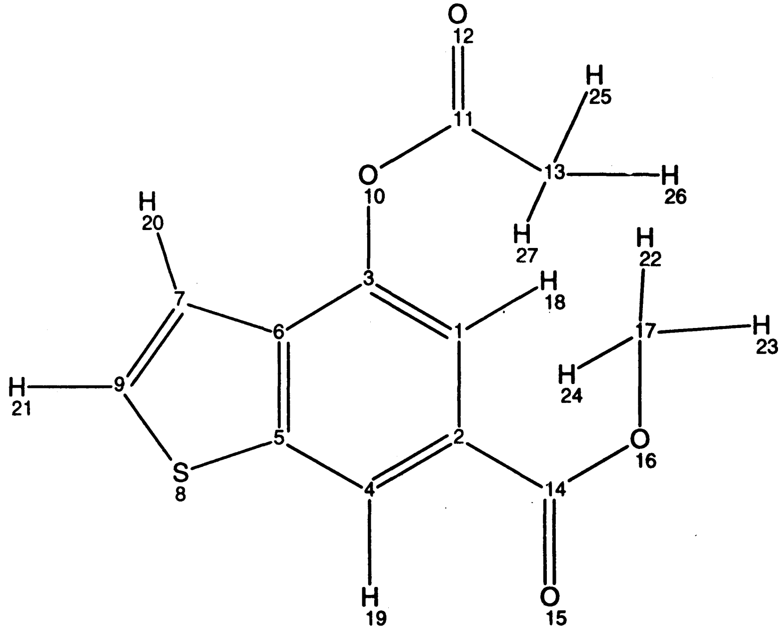

Fig. 1. The molecular structure of methyl-4-acetoxybenzothiophene-6-carboxylate

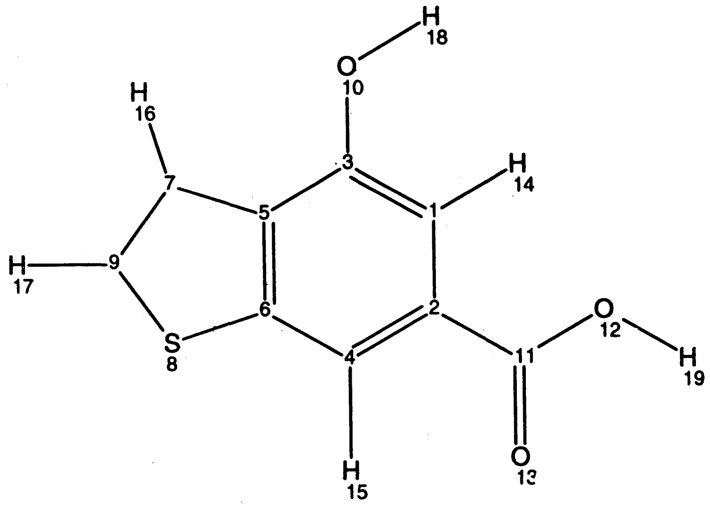

Fig. 2. The molecular structure of 4-hydroxybenzothiophene-6-carboxylic acid

The computed atomic charge density data along with ^{1}H NMR chemical shifts for these two molecules were tabulated in Tables 1 and 2. From these tables, it is observed that there is no appreciable difference in charge density data computed by both AM1 and PM3 method. In methyl-4-acetoxybenzothiophene-6-carboxylate, the charge density of aromatic hydrogen atoms H_{18}, H_{19}, H_{20} and H_{21} are 0.8418, 0.8434, 0.8263 and 0.8205, respectively. The NMR chemical shifts due to these hydrogen atoms are observed in the expected range[9], *i.e.*, 7.25–8.45 δ. It is also evident that methyl protons in $OCOCH_3$ group have higher values (0.9719, 0.9783 and 0.9424) compared to $COOCH_3$ groups (0.9265, 0.9195 and 0.9318), hence chemical shifts for hydrogen in $OCOCH_3$ is less than the $COOCH_3$ group hydrogen atoms.

TABLE-1
ELECTRON DENSITY OF METHYL-4-ACETOXYBENZOTHIOPHENE-6-CARBOXYLATE BY AM1 AND PM3 METHOD

Atom No.	Type	AM1	PM3	^{1}H NMR chemical shifts
1	C	4.1279	4.1039	
2	C	4.1236	4.1219	
3	C	3.9193	3.9163	
4	C	4.0459	4.0127	
5	C	4.0619	4.0637	
6	C	4.3169	4.2168	
7	C	4.1337	4.0938	
8	S	5.4622	5.7041	
9	C	4.3880	4.2562	
10	O	6.2084	6.1846	
11	C	3.6982	3.6464	
12	O	6.2795	6.3169	
13	C	4.2546	4.1398	
14	C	3.6617	3.6016	
15	O	6.2764	6.3139	
16	O	6.2487	6.2342	
17	C	4.0710	3.9493	
18	H	0.8418	0.8713	7.6
19	H	0.8434	0.8716	7.25
20	H	0.8263	0.8604	7.75
21	H	0.8205	0.8502	8.45
22	H	0.8804	0.9265	2.4
23	H	0.8749	0.9195	2.4
24	H	0.8907	0.9318	2.4
25	H	0.9246	0.9719	3.91
26	H	0.9335	0.9783	3.91
27	H	0.8859	0.9424	3.91

In 4-hydroxybenzothiophene-6-carboxylic acid, the charge densities of aromatic hydrogen atoms H_{14}, H_{15}, H_{16} and H_{17} are 0.8620, 0.8657, 0.8792 and 0.8529, respectively and their chemical shifts are 7.81, 7.52, 7.3 and 8.05 δ respectively. But the hydrogen atoms attached to the oxygen atom possess lesser charge density because of electronegative properties of oxygen bearing the proton causes a downward shift. So they are deshielded and hence its chemical shifts are higher than the aromatic hydrogen. The computed charge density data are in good agreement with the literature.

TABLE-2
ELECTRON DENSITY OF 4-HYDROXYBENZOTHIOPHENE-6-CARBOXYLIC ACID BY AM1 AND PM3 METHOD

Atom No.	Type	AM1	PM3	1H NMR chemical shifts
1	C	4.1164	4.1053	
2	C	4.0753	4.0744	
3	C	3.8983	3.8712	
4	C	4.0651	4.0434	
5	C	4.1117	4.1278	
6	C	4.2981	4.1905	
7	C	4.1525	4.1060	
8	S	5.4675	5.7107	
9	C	4.3859	4.2560	
10	O	6.2418	6.2176	
11	C	3.6488	3.5729	
12	O	6.3109	6.3003	
13	O	6.3643	6.3946	
14	H	0.8257	0.8620	7.81
15	H	0.8352	0.8657	7.52
16	H	0.8477	0.8792	7.30
17	H	0.8240	0.8529	8.05
18	H	0.7771	0.7972	10.38
19	H	0.7537	0.7722	12.80

Thermodynamic functions: Thermodynamic functions are of great importance to study the chemical kinetics and chemical equilibrium[10]. The direct and experimental measurements of thermodynamic functions are usually tedious and may not be reliable. The total energy in a system is given by the sum of energies due to translational, rotational, vibrational and electronic energies of a system. The partition function in terms of energy may be evaluated separately and hence the corresponding thermodynamic functions are calculated. Then, each contribution to the thermodynamic functions has been added to get the total value. The calculated values of the thermodynamic functions for the title molecules have been shown in Table-3.

As the temperature increases, entropy increases indicating the vapourisation process. The entropy value of methyl-4-acetoxybenzothiophene-6-carboxylate is higher than 4-hydroxybenzothiophene-6-carboxylic acid; hence 4-hydroxybenzothiophene-6-carboxylic acid is stable compared to methyl-4-acetoxybenzothiophene-6-carboxylate. It is clearly confirmed by heats of formation of these compounds. The enthalpy function represents the total energy stored in a system. When a system is brought from solid into vapour state, the enthalpy function of the system increases. Similar trend is reflected in Table-3 for the title molecules as the temperature increase from 100–1000 K.

TABLE-3
THERMODYNAMIC PROPERTIES OF METHYL-4-ACETOXY BENZOTHIOPHENE-6-CARBOXYLATE AND 4-HYDROXYBENZOTHIOPHENE-6-CARBOXYLIC ACID

Temp. (K)	Methyl 4-acetoxybenzo thiophene-6-carboxylate			4-Hydroxybenzothiophene -6-carboxylic acid		
	ΔHf	H	S	ΔHf	H	S
100	–117.63	1.578	80.34	–91.25	1.196	70.94
200	–114.31	4.905	102.73	–88.89	3.560	86.82
300	–109.28	9.933	122.88	–85.26	7.190	101.37
400	–102.64	16.575	141.88	–80.45	11.996	115.12
500	–94.58	24.628	159.80	–74.65	17.793	128.02
600	–85.36	33.846	176.58	–68.05	24.390	140.02
700	–75.20	44.013	192.23	–60.82	31.624	151.16
800	–64.26	54.952	206.83	–53.07	39.371	161.50
900	–52.68	66.528	220.45	–44.91	47.536	171.11
1000	–40.58	78.634	233.21	–36.40	56.046	180.08

Units of (ΔHf): Heats of formation in kcal/mol; (H): Enthalpy in kcal/mol and (S): entropy in cal/K/mol.

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