Crystal Structure of 2-(Chloromethyl)-5-(phthalimidomethyl)thiophene. No Evidence for Intramolecular 1,4-S···N Attraction

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The crystal structure of 2-(chloromethyl)-5-(phthalimidomethyl)thiophene (**1**), as an example of a 2,5-disubstituted thiophene, together with data from semi-empirical and *ab initio* calculations provide strong evidence against an intramolecular S···N attraction in 2-formylthiophene semicarbazone (**2**), as well as in other five-membered heterocycles.

2-(Chloromethyl)-5-(phthalimidomethyl)thiophene (**1**) was prepared by chlormethylation of 2-phthalimidomethylthiophene.[1] The crystal structure of (**1**) (Figure 1) shows that both substituents are on one side of the aromatic ring.† This structure is also the global minimum on the potential energy surface according to MNDO and AM1 calculations.[2,3] Any structure having the substituents in the plane of the aromatic ring is not a minimum on the energy surface. A planar structure is expected and observed if the nitrogen is conjugated to the aromatic π-system as in 2-formylthiophene semicarbazone (**2**). However Koziol *et al.*[4] pointed out that the near planarity in (**2**) is the result of an S···N attraction and not of π-conjugation (Figure 2). Comparing the structures of (**1**) and (**2**) we cannot support their arguments.

In the crystal structure of (**1**) the C(1)–C(2)–S and the C(6)–C(5)–S angles are identical within experimental error [121.6(3)°]. The value is equivalent to the corresponding S–C(1)–C(5) angle [121.9(3)°] of (**2**). Therefore the angle in (**2**) is not unusually small and should not be used as an argument for an S···N attraction. Moreover, if an S···N interaction did exist in (**2**), a shortening of the S–C(1) distance and a lengthening of the S–C(4) bond would be expected which is not observed.

The C(5)–C(6) distance in (**1**) (Figure 1) is 1.504 Å. The bond is considerably longer than the corresponding one in (**2**) (1.447 Å, Figure 2), but the difference is easily explained by conjugation of the heteroaromatic ring and the side chain in (**2**) and does not require additional S···N attraction.

If the small S···N distance of 3.037 Å (Figure 2) indeed arises from a interaction between these two atoms, it could be expected that there should also be an analogous bond shortening in suitably substituted furans. The sum of the van der Waals radii of sulphur and nitrogen is 3.4 Å; for oxygen and nitrogen the value is 2.9 Å. In some 2-substituted furans an N–O distance of 2.8 Å and smaller has been observed where no N···O interaction has been postulated.[5]

By applying semi-empirical and *ab initio* methods we investigated a suitable model compound. Different geometries of 2-formylthiophenemine (**3**) were fully optimized with MNDO and AM1, the planar ones being the most stable forms. The *s-cis* form is favoured by 0.11 kcal/mol (cal = 4.184 J) according to AM1; the *s-trans* form is favoured by MNDO by 0.02 kcal/mol (Table 1). A planar geometry however is not

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† *Crystal data* for (**1**): $C_{14}H_{10}ClNO_2S$, $M = 291.75$, monoclinic, space group $P2_1/c$, $a = 1130.4(5)$, $b = 803.1(3)$, $c = 1546.1(7)$ pm, $\beta = 110.46(3)^\circ$, $U = 1314 \times 10^6$ pm^3, $D_c = 1.47$ g cm^{-3}, $Z = 4$, $R = 0.054$, $R_w = 0.040$, Mo-K_α - radiation, graphite monochromator, Nicolet R 3m/V diffractometer, 3172 reflections ($4^\circ < 2\theta < 56^\circ$), 1969 observed with $F > 4\sigma(F)$. 199 Parameters refined. The structure was solved by direct methods (SHELXS-86), anisotropic refinement of the non-H atoms. H-Atoms were included using a riding model. Further details have been deposited at the Fachinformationszentrum Energie, Physik, Mathematik GmbH, D-7514 Eggenstein-Leopoldshafen 2, Federal Republic of Germany. Any request for this material should quote the full literature citation and the reference numbers CSD 53256. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

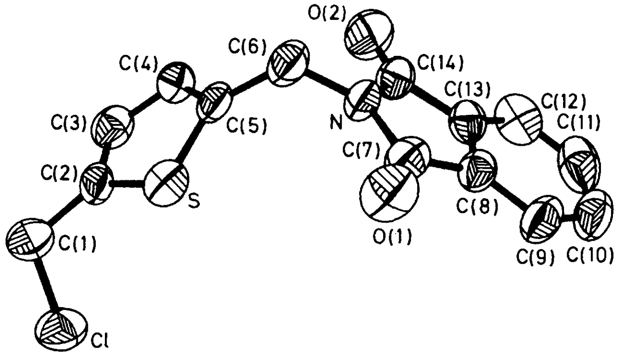

Figure 1. The crystal structure of 2-(chloromethyl)-5-(phthalimidomethyl)thiophene (**1**). Selected bond lengths: Cl–C(1), 180.3(4); S–C(2), 172.6(3); S–C(5), 171.5(3); O(1)–C(7), 119.7(3); O(2)–C(14), 120.0(3); N–C(6), 146.7(4); N–C(7), 139.2(4); N–C(14), 138.3(4); C(1)–C(2), 147.4(4); C(2)–C(3), 134.1(4); C(3)–C(4), 139.0(4); C(4)–C(5), 135.0(4); C(5)–C(6), 150.4(4); C(7)–C(8), 148.9(4); C(8)–C(9), 137.4(4); C(8)–C(13), 137.9(4); C(9)–C(10), 138.4(4); C(10)–C(11), 136.5(5); C(11)–C(12), 136.9(5); C(12)–C(13), 137.8(4); C(13)–C(14), 148.6(4) pm. Selected bond angles: C(5)–S–C(2), 91.2(2); C(7)–N–C(6), 123.0(3); C(14)–N–C(6), 123.7(3); C(14)–N–C(7), 113.1(2); C(2)–C(1)–Cl, 112.9(2); C(1)–C(2)–S, 121.6(3); C(3)–C(2)–S, 111.0(2); C(3)–C(2)–C(1), 127.4(3); C(4)–C(3)–C(2), 113.4(3); C(5)–C(4)–C(3), 113.4(3); C(4)–C(5)–S, 110.9(3); C(6)–C(5)–S, 121.6(3); C(6)–C(5)–C(4), 127.4(3); C(5)–C(6)–N, 114.2(3); N–C(7)–O(1), 124.9(3); C(8)–C(7)–O(1), 130.2(3); C(8)–C(7)–N, 104.8(3); C(9)–C(8)–C(7), 130.5(3); C(13)–C(8)–C(7), 108.5(3); C(13)–C(8)–C(9), 121.0(3); C(10)–C(9)–C(8), 117.4(4); C(11)–C(10)–C(9), 121.0(4); C(12)–C(11)–C(10), 122.0(4); N–C(14)–O(2), 125.2(3); C(13)–C(12)–C(11); 117.1(4); C(8)–C(13)–C(14), 108.3(3); C(12)–C(13)–C(8), 121.4(3); O(2)–C(14)–C(13), 129.5(3); C(14)–C(13)–C(12), 130.3(3); N–C(14)–C(13), 105.3(3)°.

a minimum for the corresponding aminomethyl compound; in this case the amino group is rotated away from the aromatic plane, regardless of the starting geometry.[6] 2-Formylthiophene semicarbazone (**2**) was also calculated both with MNDO and AM1 and the relative energies of s-*cis* and s-*trans* forms obtained were very similar to those of (**3**). Therefore, we think that conclusions drawn from an *ab initio* analysis of (**3**) should also be applicable to (**2**).

Compound (**3**) was optimised by *ab initio* methods at the 3-21G and 6-31G levels (C_s symmetry). In these calculations the stability of the s-*cis* and the s-*trans* forms differed only by 1.07 kcal/mol at the 3-21G level and 0.99 kcal/mol at the 6-31G level, the s-*cis* form being the most favoured in both cases (Table 1).

Second-order pertubation theory analysis of the Fock matrix in NBO basis[7] of *cis*-(**3**) at 3-21G and at 6-31G shows that the bond orders between nitrogen and sulphur are practically zero. The most important fact is that 2-formylthiopheneimine can be considered as a simple heteropolyenic system. No stabilization is found by the interaction of the sulphur lone pairs with either the π-system or the nitrogen lone pair within the limits of the NBO analysis.

We conclude from both experimental and theoretical results that a small S···N distance in iminic derivatives of 2-formylthiophene is not a result of an S···N interaction. The planar structure of these compounds is a consequence of conjugation.

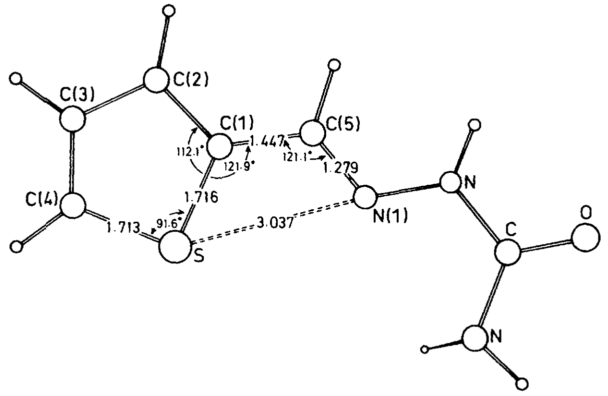

Figure 2. Crystal geometry of (**2**) (taken from ref. 4).

Table 1.[a] Calculated heats of formation and total energies.

	MNDO	AM1	3-21G	6-31G
(**2**) s-*cis*	19.59	40.50	—	—
(**2**) s-*trans*	19.82	40.65	—	—
(**3**) s-*cis*[b]	44.34	58.24	−640.83215	−644.03233
(**3**) s-*trans*[b]	44.32	58.37	−640.83050	−644.03075

[a] MNDO and AM1 energies are given in kcal/mol, *ab initio* energies in atomic units (1 a.u. = 627.49 kcal/mol).

[b] *E*-configuration at the imine double bond.

The energy difference between s-*cis* and s-*trans* conformers is very small, but S···N attraction is not required to stablize the *cis*-form.

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