Pergamon

Tetrahedron Letters 42 (2001) 5497–5500

TETRAHEDRON
LETTERS

Intra- and intermolecular interactions between a thiocarbonyl group and a pyridinium nucleus

Shinji Yamada* and Tomoko Misono

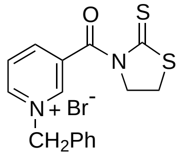
Department of Chemistry, Faculty of Science, Ochanomizu University, Bunkyo-ku, Tokyo 112-8610, Japan

Received 2 May 2001; revised 13 June 2001; accepted 15 June 2001

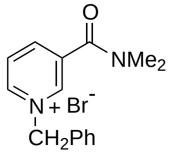
Abstract—An intramolecular interaction between a thiocarbonyl group and a pyridinium nucleus was found in nicotinium salt **1** having a 1,3-thiazolidine-2-thione moiety, which was elucidated by comparing the ^{1}H NMR chemical shifts and the X-ray structure with those of standards **2** and **3**. Moreover, an intermolecular interaction of the C=S···Py$^+$ was also found in crystalline state. © 2001 Elsevier Science Ltd. All rights reserved.

Nonbonding S···N,[1] S···O,[2] S···S[3] and S···π[4] interactions have recently been explored in various organosulfur compounds. These interactions play significant roles in controlling the molecular conformation, packing structure in crystals, and molecular recognition. Moreover, these interactions are interesting in relation to the bioactivity of a variety of compounds containing sulfur atoms.

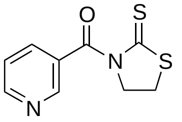
During our studies on the stereoselective reaction of pyridinium salts having a 1,3-thiazolidine-2-thione moiety with nucleophiles, we presumed an intramolecular interaction between the pyridinium and the thiocarbonyl groups.[5] Recently, an intramolecular C=S···S interaction has been elucidated in the crystal structure of 1,3-thiazolidine-2-thione derivatives by Nagao and his co-workers.[3a] Therefore, confirmation of our prediction will provide insights into further properties of a thiocarbonyl group. As to pyridinium cations, since they are observed in a wide variety of organic molecules such as NAD$^+$, pyridoxal phosphate, bioactive compounds, host–guest compounds and ionic liquids, disclosure of a new type of interaction with respect to a pyridinium cation would be of significant interest. In this communication, we describe the existence of attractive intra- and intermolecular C=S···Py$^+$ interactions, which were elucidated by ^{1}H NMR spectroscopy and X-ray crystallographic analysis.



1



2



3

As a model compound we selected *N*-benzyl salt **1**[6] prepared from **3** because of its sufficient stability and crystallizability for ^{1}H NMR spectroscopic measurements and X-ray analysis. Salt **2**[7] and amide **3**[8] are standards for ^{1}H NMR and X-ray analysis, respectively. Table 1 shows the ^{1}H NMR chemical shifts for **1** and **2** and the $\Delta\delta$ values that represent the difference in the chemical shifts between **1** and **2**. Plots of the $\Delta\delta$ values to the pyridinium protons are given in Fig. 1. It is obvious that the $\Delta\delta$ values are very different in terms of the position in the pyridinium nucleus. Remarkable is that $\Delta\delta_{H2}$ is very large (1.06), whereas $\Delta\delta_{H6}$ is a negatively very large value (−0.86) in $CDCl_3$. On the other hand, $\Delta\delta_{H4}$ and $\Delta\delta_{H5}$ are close to zero. The $\Delta\delta$ values are significantly dependent on the solvent employed; as the solvent polarity increased, the absolute values of $\Delta\delta_{H2}$ and $\Delta\delta_{H6}$ decreased. This indicates that the polar solvent disturbs the intramolecular interaction by solvation with the pyridinium ring. Since the *N*-benzyl group of **1** and **2** can rotate about the C–N bond freely, the unusual values of the $\Delta\delta_{H2}$ and $\Delta\delta_{H6}$ in $CDCl_3$ will not be ascribed to the magnetic anisotropic effect of the benzyl group. Indeed, the ^{1}H NMR spectrum for the corresponding *N*-methyl pyridinium salt also showed similar tendency. Therefore, the unusual downfield shift of H2 and upfield shift of H6 in $CDCl_3$ will be attributable to the intramolecular interaction

---

Keywords: thiocarbonyl compounds; pyridinium salts; X-ray crystal structures; intramolecular interaction; intermolecular interaction; neighboring group effects.

* Corresponding author. Tel.: +81-3-5978-5349; fax: +81-3-5978-5715; e-mail: yamada@cc.ocha.ac.jp

0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(01)01066-8

Table 1. ^{1}H NMR chemical shifts of **1** and **2** and the $\Delta\delta$ values (ppm)[a]

Solv.	Proton	δ_1	δ_2	$\Delta\delta$[b]
$CDCl_3$	H2	10.81	9.75	1.06
$CDCl_3$	H4	8.51	8.57	−0.06
$CDCl_3$	H5	7.91	8.19	−0.28
$CDCl_3$	H6	8.93	9.79	−0.86
CD_3CN	H2	9.48	9.53	−0.05
CD_3CN	H4	8.61	8.57	0.04
CD_3CN	H5	8.08	8.14	−0.06
CD_3CN	H6	8.93	9.40	−0.47
DMSO-d_6	H2	9.63	9.64	−0.01
DMSO-d_6	H4	8.80	8.75	0.05
DMSO-d_6	H5	8.25	8.30	−0.05
DMSO-d_6	H6	9.26	9.46	−0.20

[a] ^{1}H NMR chemical shifts are measured at 400 MHz.
[b] Subtracted δ_2 from δ_1.

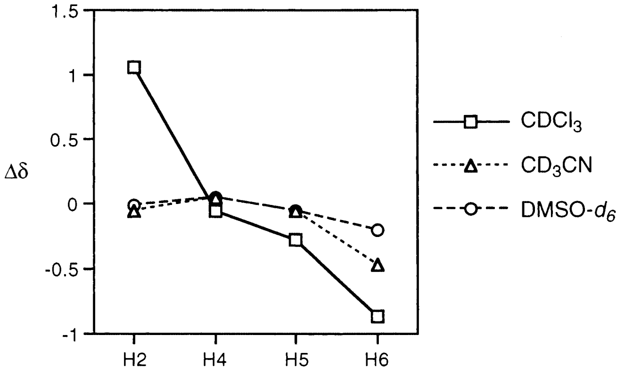


Figure 1. Plots of $\Delta\delta$ values for pyridinium hydrogens.

between the thiocarbonyl group and the pyridinium nucleus.

Comparison of X-ray structures between **1** and **3** led to unambiguous evidence for the noncovalent C=S···Py$^+$ interaction.[9] Fig. 2 shows the ORTEP representations.[10] Their geometries are very different in the relative position of the sulfur atom toward the pyridinium nucleus; while the S atom of **3** is on the side of the pyridinium ring, that of **1** is almost on the middle of the pyridinium ring. The S···C3 distance of 3.051(5) Å for **1** is surprisingly shorter than the sum of van der Waals radii of the sulfur and carbon atoms (3.65 Å).[11] On the other hand, the S···C3 distance of 3.211(3) Å for amide **3**, is much longer than that of **1**.[12] Significant structural difference is also observed in the bond angles around the amide carbonyl groups. As shown in Fig. 3, the N1-C1-C3 angle of 116.4(4)° for **1** is smaller and the N1-C1-O1 angle of 121.6(4)° is larger than those of **3** [118.8(3)° and 119.1(4)°, respectively]. The corresponding general bond angles for *N*-acyl-1,3-thiazolidine-2-thiones are in the range of 119–120° and 117–118°, respectively.[13] The shorter S···C3 distance and the bond angle deformation can be attributable to the attractive force of the thiocarbonyl with the pyridinium ring. Additional evidence for the C=S···Py$^+$ interaction is that the torsion angle of the carbonyl group relative to the pyridinium ring for **1** [C2-C3-C1-O1 58.0(7)°] is much larger than the corresponding angle for **3** [33.7(4)°]. This torsion angle deformation in **1** arises from the rotation of the C1–C3 bond so that the thiocarbonyl group efficiently approaches the pyridinium nucleus at the sacrifice of resonance stabilization of the pyridinium with the carbonyl groups. All of these characteristic

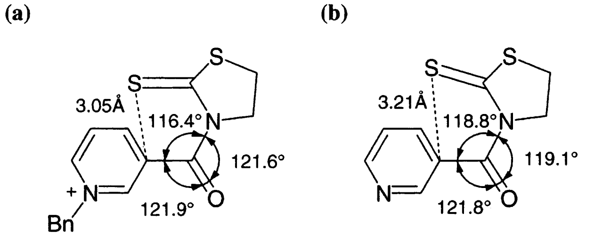


Figure 3. Bond angles around amide carbonyls (a) for **1** and (b) for **3**.

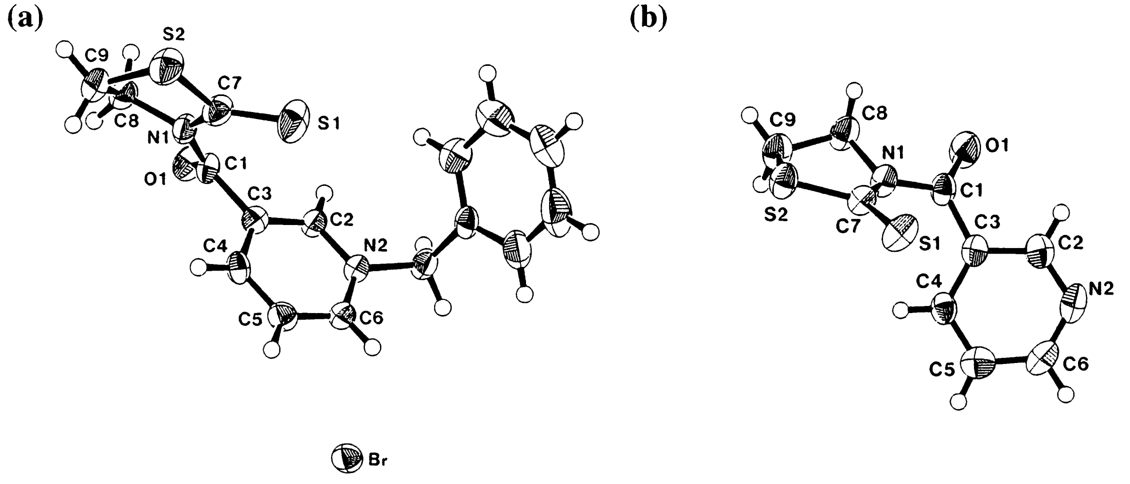


Figure 2. (a) ORTEP representation of **1** at the 50% probability level. Selected interatomic distances (Å): S1···C3 3.051(5), S1···C2 3.494(5), S1···C4 3.426(6), S1···C5 4.109(6), S1···C6 4.382(5), S1···N2 4.085(5); (b) ORTEP representation of **3** at the 50% probability level. Selected interatomic distances (Å): S1···C2 4.073(3), S1···C3 3.211(3), S1···C4 3.287(3), S1···C5 4.182(3), S1···C6 4.829(3), S1···N2 4.800(3).

structural features in **1**, the short S1···C3 distance, the smaller N1-C1-C3 angle, and the larger twist angle in the carbonyl group, strongly suggest the existence of the intramolecular C=S···Py^+ interaction.

The X-ray packing structure for **1** apparently shows not only the existence of an intramolecular interaction but also an intermolecular interaction in the crystal. As can be seen from Fig. 4, the sulfur atom of the thiocarbonyl group is sandwiched by the two pyridinium nuclei. The S1···C6′ distance of 3.65 Å is an almost similar value to the sum of van der Waals radii. The sulfur atom is placed on the line connecting C3 and C6′, which is the shortest line between the two pyridinium nuclei, indicating the sulfur atom is attracted by both pyridinium rings. It is remarkable that another sulfur atom S2 in the thiazolidine ring is very close to C4′ with the interatomic distance of 3.46 Å, suggesting the contribution of two sulfur atoms to the intermolecular interaction. No such intermolecular interaction was observed in **3**. Stoddart and his co-workers have reported that tetracationic cyclophane, cyclobis(paraquat-*p*-phenylene), makes an inclusion complex with tetrathiafulvalene with a higher free energy of complexation than the other π-components, and the distance between the sulfur atom and the pyridinium ring in the complex is 3.54 Å.[14] These observations seem to be related to our results and might support the intermolecular C=S···Py^+ interaction in the crystalline state described above.

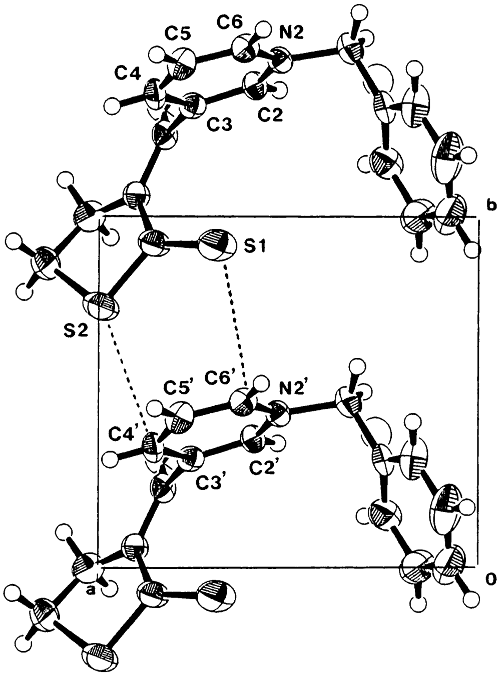


Figure 4. Crystal structure of **1** viewed along the c axis with selected interatomic distances between two molecules (Å): S1···N2′ 3.794(5), S1···C2′ 4.221(5), S1···C3′ 4.593(6), S1···C4′ 4.472(6), S1···C5′ 3.982(5), S1···C6′ 3.645(5), S2···N2′, 4.584(5), S2···C2′ 4.259(5), S2···C3′ 3.735(4), S2···C4′ 3.464(4), S2···C5′ 3.814(5), S2′···C6′ 4.389(5).

The observed unusual chemical shifts for H2 and H6 described earlier can be explained as resulting from following: (1) the C=S···Py^+ interaction would change the charge densities of the pyridinium protons; (2) X-ray structure of **1** indicates that H2 lies in a deshielding area, which would result in downfield shift of H2. Although the origin of the C=S···Py^+ interaction is still unclear, one of possible attractive force may be a cation-π interaction[15] because of the large polarizability of the thiocarbonyl group.

Further studies on the origin of the force of this C=S···Py^+ interaction are now in progress.

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research (No. 11304046) from Ministry of Education, Science, and Culture, Japan.

References

1. Ohkata, K.; Ohsugi, M.; Yamamoto, K.; Ohsawa, M.; Akiba, K.-y. *J. Am. Chem. Soc.* **1996**, *118*, 6355 and references cited therein.
2. (a) Minyaev, R. M.; Minkin, V. I. *Can. J. Chem.* **1998**, *76*, 776; (b) Nagao, Y.; Hirata, T.; Goto, S.; Sano, S.; Kakehi, A.; Iizuka, K.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *120*, 3104 and references cited therein.
3. (a) Nagao, Y.; Nishijima, H.; Iimori, H.; Ushirogochi, H.; Sano, S.; Shiro, J. *J. Organometallic Chem.* **2000**, *611*, 172; (b) Rovira, C.; Novoa, J. J. *Chem. Eur. J.* **1999**, *5*, 3689; (c) Wudl, F.; Srdanov, G.; Rosenau, B.; Wellman, D.; Williams, K.; Cox, S. D. *J. Am. Chem. Soc.* **1988**, *110*, 1316 and references cited therein.
4. Breinlinger, E. C.; Keenan, C. J.; Rotello, V. M. *J. Am. Chem. Soc.* **1998**, *120*, 8606.
5. Yamada, S.; Ichikawa, M. *Tetrahedron Lett.* **1999**, *40*, 4231.
6. Compound **1**: mp 197.3–198.2°C; IR (KBr) 3374, 3031, 1681, 1364, 1329, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50°C): δ 3.89 (t, $J=7.3$ Hz, 2H), 4.71 (t, $J=7.3$ Hz, 2H), 6.12 (s, 2H), 7.59 (m, 3H), 7.64 (m, 2H), 7.91 (dd, $J=7.6$, 5.9 Hz, 1H), 8.51 (d, $J=7.6$ Hz, 1H), 8.93 (d, $J=5.9$ Hz, 1H), 10.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2, 56.9, 64.5, 127.7, 129.7, 129.8, 130.4, 132.1, 134.9, 143.9, 144.2, 147.4, 164.3, 204.9; MS *m*/*z* 224 ([M−Br−Bn]$^+$, 48), 213 (15), 123 (28), 106 (92), 91 (100), 78 (51); HRMS calcd for $C_9H_8N_2OS_2$ ([M−Br−Bn]$^+$) 224.0078, found 224.0084.
7. Compound **2**: mp 158.0–159.0°C; IR (KBr) 2911, 1645, 1495, 1455, 1401 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.03 (s, 3H), 3.09 (s, 3H), 6.42 (s, 2H), 7.38–7.26 (m, 3H), 7.79 (d, $J=4.9$ Hz, 2H), 8.19 (dd, $J=7.9$, 6.1 Hz, 1H), 8.57 (d, $J=7.9$ Hz, 1H), 9.75 (d, $J=6.1$ Hz, 1H), 9.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.8, 40.1, 63.9, 128.7, 129.5 129.7, 129.9, 133.0, 136.4, 143.2, 144.1, 145.7, 163.8; MS *m*/*z* 150 ([M−Br−Bn]$^+$, 15), 106 (29), 91 (100), 78 (18); HRMS calcd for $C_8H_{10}N_2O$ ([M−Br−Bn]$^+$) 150.0793, found 150.0754.

8. Compound **3**: mp 103.0–104.0°C; IR (KBr) 2362, 1677, 1588 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.50 (t, J=7.3 Hz, 2H), 4.58 (t, J=7.3 Hz, 2H), 7.35 (ddd, J=8.0, 4.9, 0.8 Hz, 1H), 7.95 (ddd, J=8.0, 2.2, 1.6 Hz, 1H), 8.71 (ddd, J=4.9, 1.6 Hz, 1H), 8.87 (dd, J=2.2, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.7, 56.2, 130.0, 136.6, 149.9, 152.6, 169.4, 202.3; MS m/z 224 (M^+, 93), 106 (100), 78 (70); HRMS calcd for $C_9H_8N_2OS_2$ 224.0078, found 224.0084.
9. Crystal data for **1**: $C_{16}H_{15}BrN_2OS_2$, M=395.33, monoclinic, Pn; a=8.132(3), b=7.399(2), c=14.431(3) Å, β=101.49(2)°, V=850.9(4) Å^3, Z=2, μ(Cu-Kα)=5.603 mm^{-1}, Dc=1.543 Mg m^{-3}. Crystal data for **3**: $C_9H_8N_2OS_2$, M=224.24, orthorhombic, $P2_12_12_1$, a=9.778(2), b=14.647(4), c=7.0557(6) Å, V=1010.5(3) Å^3, Z=4, μ(Cu-Kα)=3.098 mm^{-1}, Dc=1.474 Mg m^{-3}. The 1343 and 1314 independent reflections [$2\theta<135°$]; [$\mathrm{I}Fo^2\mathrm{I}>3\sigma\mathrm{I}Fo^2\mathrm{I}$] were measured on a Rigaku AFC7R diffractometer using Cu-Kα radiation and an ω–2θ scan at 293 K. The structures were solved by direct methods with the SHELXS-86 and refined on F^2 using the SHELXL-93. Non-hydrogen atoms were refined anisotropically by full-matrix least-squares method. Final R indices [$I>2\sigma(I)$]: $R_1(wR_2)$=0.024(0.090) for **1** and $R_1(wR_2)$=0.045(0.131) for **3**. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-145061(**1**) and CCDC-160669(**3**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
10. The reversed absolute structure was indicated for **3** to facilitate the structural comparison between **1** and **3**.
11. Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.
12. Although the S···C3 distance is still shorter than the sum of van der Waals radii, this would be ascribed to its intrinsic steric demand.
13. (a) Yamada, S. *J. Org. Chem.* **1996**, *61*, 941; (b) Yamada, S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1083.
14. (a) Balzani, V.; Credi, A.; Mattersteig, G.; Matthews, O. A.; Raymo, F. M.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **2000**, *65*, 1924; (b) Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1584.
15. For a review, see: Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303.