

**METHYLATION OF TETRAZATHIAPENTALENES  
(10-S-3 SULFURANE) FUSED WITH PYRIDINE AND/OR  
PYRIMIDINE RINGS AND RESTRICTED ROTATION OF  
THE PYRIMIDINE RING: CHEMICAL EVIDENCES FOR  
N-S-N HYPERVALENT BOND**

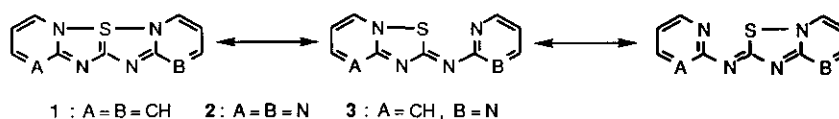
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**Abstract** - Methylation of the title compounds (10-S-3 sulfurane: **1-3**) took place exclusively on the nitrogen at 3(4)-position and selectively on the nitrogen bound to the more electron-withdrawing heterocycle. The activation energy of the hindered rotation in **5** was lower for the pyrimidine ring ( $\Delta G_c^\ddagger = 20.2 \text{ kcal mol}^{-1}$ ) bound to the methylated nitrogen than the other one ( $\Delta G_c^\ddagger = 22.9 \text{ kcal mol}^{-1}$ ).

Structure of the title compounds (**1**, **2**, and **3**) can be represented in terms of both resonance structure (no-bond resonance) and valence shell expanded structure (Scheme 1).<sup>1</sup> In preceding communications, we showed that the restricted rotation of the pyrimidine ring in symmetrical and unsymmetrical 10-S-3 sulfuranes (**2** and **3**) reflected hypervalent N-S-N bond energy.<sup>2</sup> Since these compounds have several reactive sites in the molecule, regioselectivity of methylation and estimation of the corresponding bond energy of methylated products are of interesting problems.

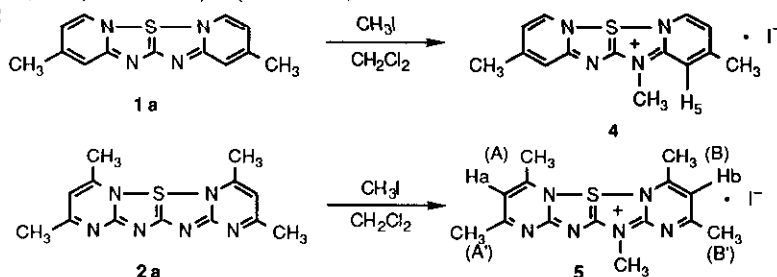
**Scheme 1**



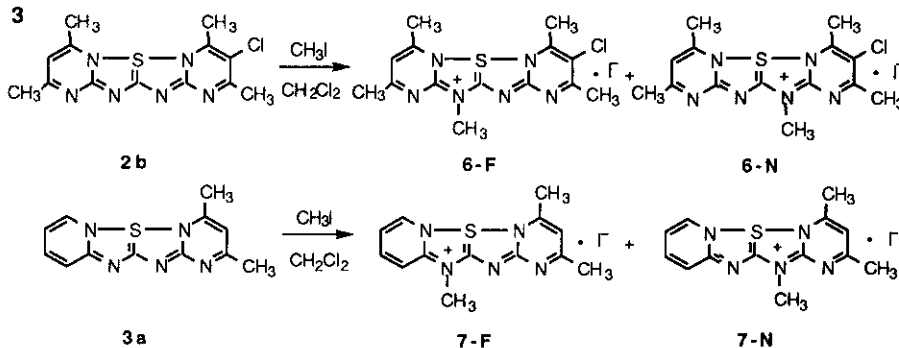
Treatment of **1a** with methyl iodide ( $\text{CH}_3\text{I}$ ) in  $\text{CH}_2\text{Cl}_2$  solution afforded *N*-methylated product (**4**) in 76% yield (Scheme 2).<sup>3,4</sup> Regiochemistry of methylation in **4** was confirmed by NOE experiments in  $^1\text{H}$  nmr spectrum.

The differential NOE spectrum of **4** showed an enhancement (6.1%) in the magnitude of the signal at  $\delta$  7.46 (**H**<sup>5</sup>) when the N-CH<sub>3</sub> signal at  $\delta$  4.07 was irradiated. This result indicates that methylation occurred exclusively at the nitrogen of 3-position instead of 1-position of tetrazathiapentalene framework. Reaction of **2a** with CH<sub>3</sub>I gave **5** in 78% yield (Scheme 2).<sup>4</sup> In <sup>1</sup>H nmr spectrum at 35 °C (CDCl<sub>3</sub>), **5** shows a pair of singlets at  $\delta$  2.65 (B'), 2.73 (A') and a pair of doublets at  $\delta$  3.03 (B) ( $J = 0.65$  Hz, 3H), 3.23 (A) ( $J = 0.66$  Hz, 3H) along with a singlet at  $\delta$  4.11 for the N-CH<sub>3</sub> group and a pair of quartet at  $\delta$  7.16 (**Hb**) ( $J = 0.65$  Hz, 1H), 7.30 (**Ha**) ( $J = 0.66$  Hz, 1H). Treatment of unsymmetrical sulfuranes **2b** and **3a** with CH<sub>3</sub>I furnished a mixture of isomers for each, i.e., 6-F,N and 7-F,N (Scheme 3).<sup>4</sup>

Scheme 2

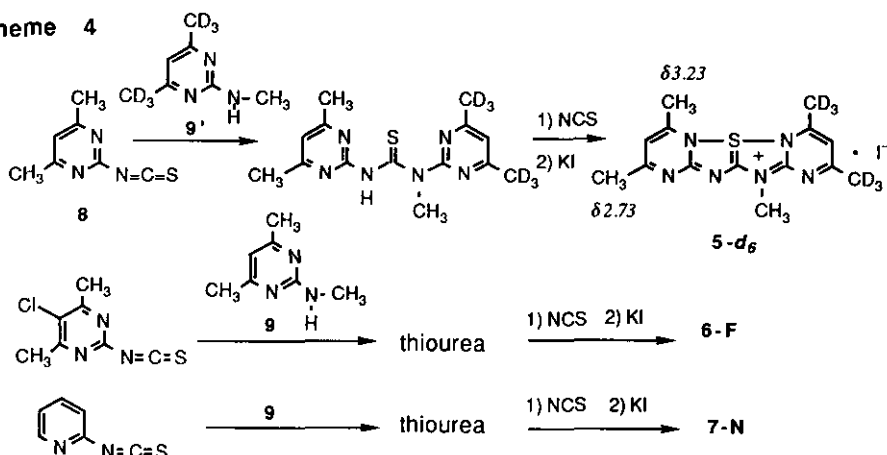


Scheme 3



The assignment of <sup>1</sup>H nmr spectra for these compounds was very difficult. Therefore, **5-d**<sub>6</sub>, **6F**, and **7-N** were prepared by alternative routes as shown in Scheme 4. Reaction of 4,6-dimethylpyrimidyl isothiocyanate (**8**) with 2-methylamino-4,6-dimethylpyrimidine-d<sub>6</sub> (**9'**) gave the corresponding thiourea which was converted to **5-d**<sub>6</sub> after oxidation with *N*-chlorosuccinimide. Similarly, **7-N** was prepared by the addition of 2-methylamino-4,6-dimethylpyrimidine (**9**) to the corresponding isothiocyanate followed by the oxidation as shown in Scheme 4.<sup>4</sup> By comparison of <sup>1</sup>H nmr spectra of these compounds with those of reaction products, the assignment of <sup>1</sup>H nmr spectra was firmly established.

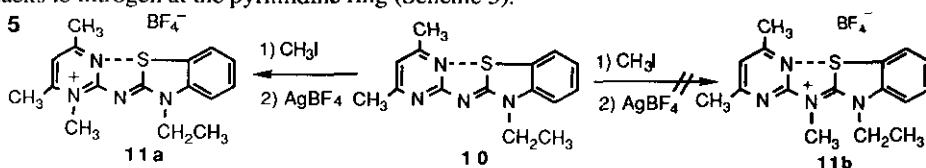
Scheme 4



Then, the ratios between the regioisomers were determined by comparison of the integral of the corresponding methyl signals. The ratios were the following; **6-F** : **6-N** = 1 : 2; **7-F** : **7-N** = 1 : 9, respectively. Now, it is concluded that methylation of tetrazathiapentalenes takes place more smoothly on the nitrogen at 3-(or 4-) position which is bound to the more electron-withdrawing pyrimidine ring. The result is contrary to the expectation based simply on the inductive effect of the heterocycle but it can be realized by the greater stability of the positive charge endowed by the resonance structures (Scheme 6; **5-i** > **5-ii**).

On the other hand, reaction of 3-ethyl-2-(4',6'-dimethyl-2'-pyrimidinylimino)benzothiazoline (**10**) with  $\text{CH}_3\text{I}$  did not afford **11b** but gave *N*-methylpyrimidinium derivative (**11a**), exclusively.<sup>5</sup> This regiochemistry is attributable to electronic features in the pyrimidine ring and it means that the N-S interaction in **10** is so weak that  $\text{CH}_3\text{I}$  attacks to nitrogen at the pyrimidine ring (Scheme 5).

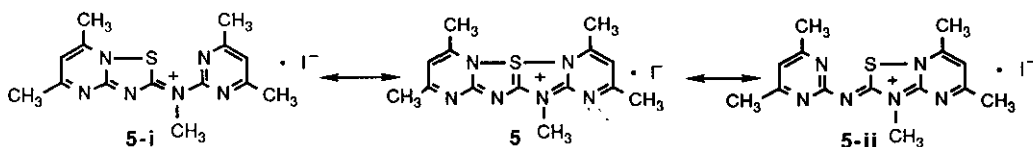
Scheme 5



Temperature dependence  $^1\text{H}$  nmr spectra were measured for **5**. Two pairs of methyl signals of **5**, i.e.,  $\text{CH}_3(\text{A})$ - $\text{CH}_3(\text{A}')$  and  $\text{CH}_3(\text{B})$ - $\text{CH}_3(\text{B}')$ , coalesced at 170 °C and 115 °C respectively and  $\Delta\text{Gc}^\ddagger$  values were calculated as 22.9 and 20.2 kcal·mol<sup>-1</sup> in  $\text{CD}_2\text{Cl}_2/\text{CD}_2\text{Cl}_2$ .<sup>6</sup> The coalescence process can only be explained by the rotation of the pyrimidine ring. Therefore, the energy of hypervalent N-S-N bond must be reflected in the kinetic data of the restricted rotation of the pyrimidine ring. Accordingly, the pyrimidine ring of the methylated side rotates more easily than the other pyrimidine ring in **5**. This difference is understandable in terms of the substituent effect on the rotational barrier in the 10-S-3 sulfurane. As the result of the stronger electron-withdrawing

property of the methylated side, the contribution of no-bond resonance structure (**5-i**) should be larger than **5-ii** and the hypervalent S-N bond should be elongated, therefore, the S-N bond of this side is weakened (Scheme 6). As expected from the regiochemistry of methylation in **10**, the rotation of the pyrimidine ring of **11b** as well as **10** about the C-N single bond did not suffer any hindrance until  $-60^{\circ}\text{C}$ .

Scheme 6



### ACKNOWLEDGMENTS

Partial support of this research by the Ministry of Education, Science, and Culture of the Japanese Government is heartily acknowledged (Nos. 03214101 and 03453029).

### REFERENCES AND NOTES

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- (a) K.-y. Akiba, M. Ohsugi, H. Iwasaki, and K. Ohkata, *J. Am. Chem. Soc.*, 1988, **110**, 5576. (b) K. Ohkata, M. Ohsugi, T. Kuwaki, K. Yamamoto, and K.-y. Akiba, *Tetrahedron Lett.*, 1990, **31**, 1605.
- Analytical and spectral data for new compounds were fully compatible with the given assignments.
- $^1\text{H}$  Nmr ( $\delta$ ,  $\text{CDCl}_3$ ) for **4** [mp  $285^{\circ}\text{C}$  (decomp.)]: 2.58 (s, 3H), 2.61 (s, 3H), 4.07 (s, 3H), 7.18 (d,  $J=6.3$  Hz), 7.20 (d,  $J=5.4$  Hz, 1H), 7.46 (s, 1H), 7.53 (s, 3H), 9.09 (d,  $J=5.4$  Hz, 1H), and 9.40 (d,  $J=6.3$  Hz, 1H); for **5** [mp  $242-245^{\circ}\text{C}$  (decomp.)]: 2.65 (s, 3H), 2.73 (s, 3H), 3.03 (d,  $J=0.65$  Hz, 3H), 3.23 (d,  $J=0.66$  Hz, 3H), 4.11 (s, 3H), 7.16 (q,  $J=0.65$  Hz, 1H), 7.30 (q,  $J=0.66$  Hz, 1H); for **6F**: 2.70 (s, 3H), 2.77 (s, 3H), 3.10 (s, 3H), 3.28 (s, 3H), 4.13 (s, 3H), 7.34 (s, 1H); for **6N**: 2.77 (s, 3H), 2.83 (s, 3H), 3.13 (s, 3H), 3.28 (s, 3H), 4.13 (s, 3H), 7.22 (s, 1H); for **7F**: 2.74 (s, 3H), 3.26 (s, 3H), 4.16 (s, 3H), 7.11 (s, 1H), 7.58 (t,  $J=6.0$  Hz, 1H), 7.70 (d,  $J=8.6$  Hz, 1H), 8.26 (t,  $J=8.6$  Hz, 1H), 9.82 (d,  $J=6.0$  Hz, 1H); for **7N**: 2.64 (s, 3H), 3.15 (s, 3H), 4.10 (s, 3H), 7.07 (s, 1H), 7.52 (t,  $J=6.2$  Hz, 1H), 7.84 (d,  $J=8.4$  Hz, 1H), 8.14 (t,  $J=8.4$  Hz, 1H), 10.29 (d,  $J=6.2$  Hz, 1H).
- H. Balli and F. Kersting, *Ann*, 1961, **647**, 1. **10** was prepared by condensation of 2-chloro-3-ethylbenzothiazolium tetrafluoroborate (**12**) with 2-amino-4,6-dimethylpyrimidine in 14% yield.  $^1\text{H}$  Nmr ( $\delta$ ,  $\text{CDCl}_3$ ) for **10** [mp  $168-169^{\circ}\text{C}$ ]: 1.42 (t,  $J=7.1$  Hz, 3H), 2.54 (s, 6H), 4.53 (q,  $J=7.1$  Hz, 2H), 6.65 (s, 1H), 7.18-7.61 (m, 4H).  $^1\text{H}$  Nmr ( $\delta$ ,  $\text{CDCl}_3$ ) for **11a** [mp  $190^{\circ}\text{C}$  (decomp.)]: 1.47 (t,  $J=7.2$  Hz, 3H), 2.64 (s, 3H), 2.68 (s, 3H), 3.98 (s, 3H), 4.64 (q,  $J=7.2$  Hz, 2H), 7.07 (s, 1H), 7.45-7.92 (m, 4H). **11b** was prepared by condensation of **9** with **12**.  $^1\text{H}$  Nmr ( $\delta$ ,  $\text{CDCl}_3$ ) for **11b** [mp  $175^{\circ}\text{C}$  (decomp.)]: 1.52 (t,  $J=7.2$  Hz, 3H), 2.16 (s, 6H), 3.88 (s, 3H), 4.51 (q,  $J=7.2$  Hz, 2H), 7.03 (s, 1H), 7.73-8.12 (m, 4H).
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Received, 14th March, 1994