

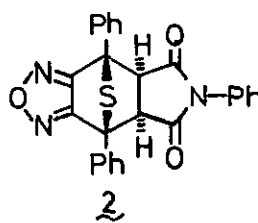
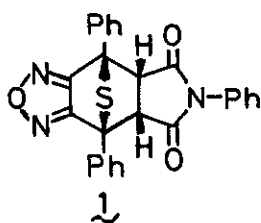
REACTIONS OF STRAINED 1,2,5-OXADIAZOLES OF THIANORBORNANE SERIES WITH OLEFINS
AND UNSYMMETRICAL ACETYLENES¹

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Abstract — The strained 1,2,5-oxadiazoles of thianorbornane series, which were obtained from diphenylthieno[3,4-c]-1,2,5-oxadiazole containing tetra-valent sulfur and N-phenylmaleimide, reacted with olefins and unsymmetrical acetylenes in refluxing xylene to give the corresponding isoxazoline and isoxazole derivatives arising from cycloadditions of olefins and acetylenes to the nitrile oxide moieties generated from the strained oxadiazoles.

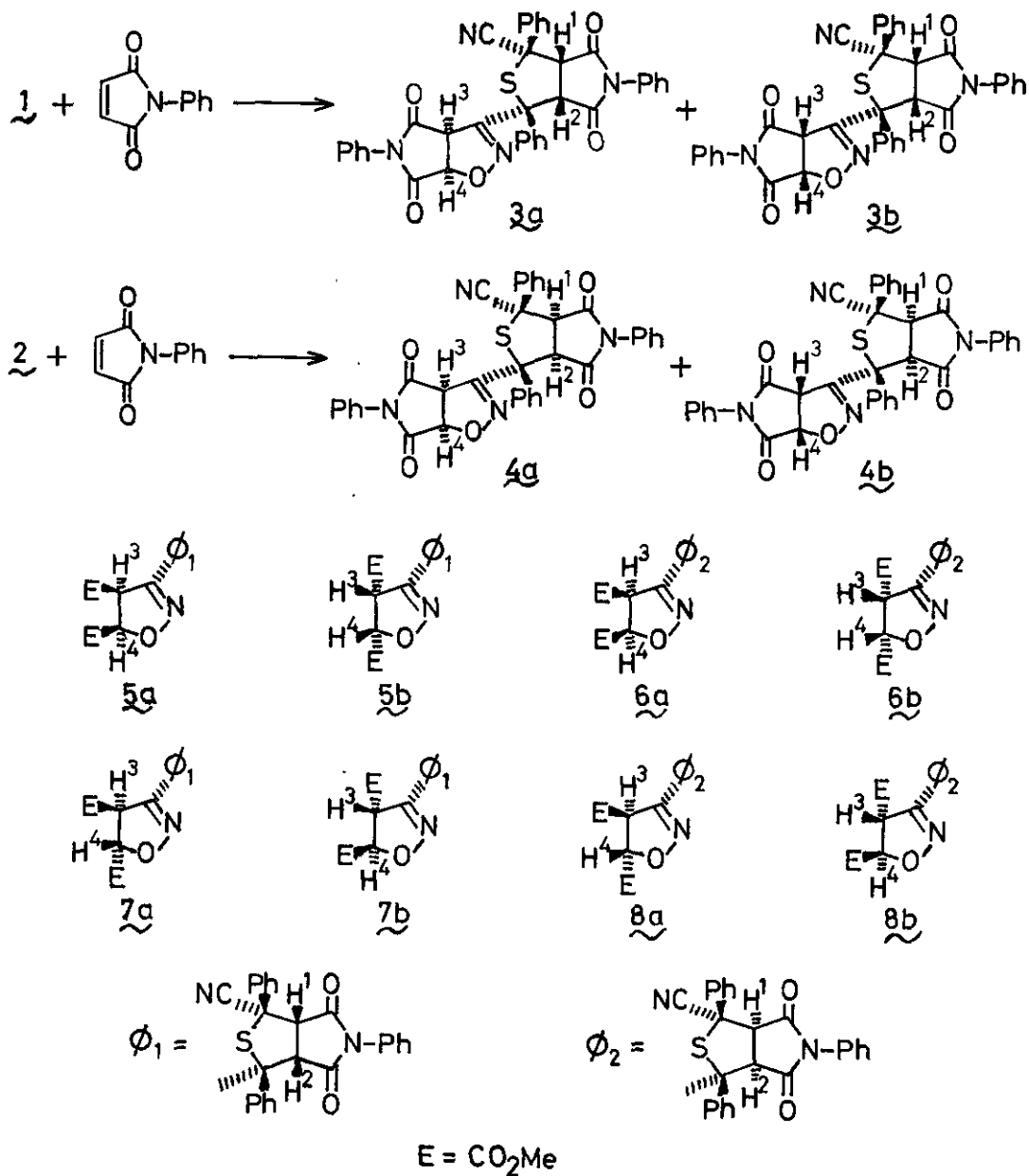
Recently, it has been found^{2,3} that thermolysis of the strained 1,2,5-oxadiazoles **1** and **2**, which were easily obtained from diphenylthieno[3,4-c]-1,2,5-oxadiazole containing tetravalent sulfur and N-phenylmaleimide⁴, under mild conditions resulted in ring cleavage of the oxadiazole ring to nitrile and nitrile oxide moieties which could be captured as 1,3-cycloadducts to dimethyl acetylenedicarboxylate, respectively.



In the present paper we wish to report on capturing nitrile oxide moiety, generated from **1** or **2**, with olefins or unsymmetrical acetylenes.

When a solution of equimolar amounts of *endo*-adduct **1** or *exo*-adduct **2** and N-phenylmaleimide (NPMI) in xylene was refluxed under nitrogen, two isomeric 1:1 adducts, **3a** and **3b** or **4a** and **4b**, were obtained respectively. The IR spectra of all 1:1 adducts exhibited a very weak band ascribable to $\nu_{C\equiv N}$ absorption as observed in the 1:1 adducts of **1** and **2** to dimethyl acetylenedicarboxylate². It is thus reasonable to conclude that the 1:1 adducts, **3a**, **3b**, and **4a**, **4b**, are isoxazoline deriva-

tives arising from 1,3-dipolar cycloadditions of NPMI to the nitrile oxide moieties generated from **1** and **2** respectively. The ^1H NMR spectra strongly supported the assigned structures⁵. Similarly, **1** and **2** reacted with dimethyl maleate (DMA) or fumarate (DFA) to give the corresponding two isomeric 1:1 adducts, **5a** and **5b**, **6a** and **6b**, or **7a** and **7b**, **8a** and **8b**, respectively (Scheme 1). Structural elucidation of **5**, **6**, **7**, and **8** was accomplished on the basis of their spectral data.



Scheme 1

The yields, physical and spectral data of 1:1 adducts 3-8 are listed in Tables 1 and 2⁶.

Table 1. Reactions of Strained Oxadiazoles 1 and 2 with Olefins^a

Oxadiazole	Olefin	Reaction time, h	Product		
			Yield, %	Mp., °C	
<u>1</u>	NPMI	8	<u>3a</u>	70	187-189(dec)
			<u>3b</u>	27	> 300
<u>2</u>	NPMI	12	<u>4a</u>	68	277-279(dec)
			<u>4b</u>	19	293-295(dec)
<u>1</u>	DMA	16	<u>5a</u>	73	141-144(dec)
			<u>5b</u>	6	178-180(dec)
<u>2</u>	DMA	24	<u>6a</u>	64	262-264(dec)
			<u>6b</u>	7	251-252(dec)
<u>1</u>	DFA	1.5	<u>7a</u>	30	228.5-230.5(dec)
			<u>7b</u>	54	232.5-234.5(dec)
<u>2</u>	DFA	3	<u>8a</u>	24	257-259(dec)
			<u>8b</u>	47	249-251(dec)

^aA solution of equimolar amounts of 1 or 2 and an olefin in xylene was refluxed.

Stereochemistry of all 1:1 adducts was deduced on the basis of ¹H NMR spectra. The inspection of the Dreiding models indicates that A and B are more favorable conformations for the adducts derived from endo-adduct 1 and exo-adduct 2 respectively, and that the dihedral angle (θ) between H¹ and H² is about 15° in A, whereas it is about 40° in B. The calculated J₁₂ values are 11.5 and 7.3 Hz when θ s are 15° and 40°, respectively⁷. The observed J₁₂ values (11.0-12.0 Hz) in the adducts derived from 1, and those (7.0-7.5 Hz) in the adducts derived from 2 are compatible with the respective calculated values. Thus, it may be concluded that the perhydrothienopyrroledione moieties in adducts have similar configurations in a- and b-types. As seen in Table 2, the H³ proton (δ 3.86-4.35) in the b-type adduct appeared at a higher field than that (δ 4.68-5.01) in the correspond-

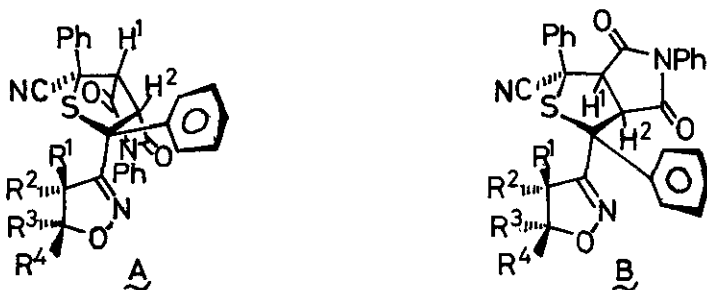


Table 2. Spectral Data of 1:1 Adducts 3-8

Adduct	$\nu_{\text{C}\equiv\text{N}}^{\text{a}}$ cm^{-1}	^1H NMR (DMSO-d_6), δ	M^+ m/e
3a ^b	2220	4.68(1H, d, J=10.2 Hz, H ³), 4.84(2H, s, H ¹ , H ²), 5.82(1H, d, J=10.2 Hz, H ⁴), 6.9-8.1(20H, m)	624
3b	2220	4.35(1H, d, J=9.0 Hz, H ³), 4.80, 5.05(each 1H, d, J=12.0 Hz, H ¹ , H ²), 5.82(1H, d, J=9.0 Hz, H ⁴), 7.0-8.1(20H, m)	624
4a	2230	4.41, 5.10(each 1H, d, J=7.5 Hz, H ¹ , H ²), 5.01(1H, d, J=9.5 Hz, H ³), 5.90(1H, d, J=9.5 Hz, H ⁴), 6.7-8.1(20H, m)	624
4b	2230	4.11(1H, d, J=9.6 Hz, H ³), 4.47, 5.11(each 1H, d, J=7.2 Hz, H ¹ , H ²), 5.80(1H, d, J=9.6 Hz, H ⁴), 6.75-7.95(20H, m)	624
5a	2230	2.94, 3.64(each 3H, s), 4.65, 5.06(each 1H, d, J=11.5 Hz, H ¹ , H ²), 4.87(1H, d, J=11.5 Hz, H ³), 5.61(1H, d, J=11.5 Hz, H ⁴), 7.2-8.1(15H, m)	595
5b ^c	2230	3.49, 3.65(each 3H, s), 4.14(1H, d, J=11.0 Hz, H ³), 4.93(2H, s, H ¹ , H ²), 5.70(1H, d, J=11.0 Hz, H ⁴), 7.1-8.1(15H, m)	595
6a ^d	2230	2.89, 3.60(each 3H, s), 4.36, 5.14(each 1H, d, J=7.4 Hz, H ¹ , H ²), 4.80(1H, d, J=11.4 Hz, H ³), 5.64(1H, d, J=11.4 Hz, H ⁴), 6.75-7.9(15H, m)	595
6b	2230	3.56, 3.67(each 3H, s), 3.86(1H, d, J=11.5 Hz, H ³), 4.58, 5.10(each 1H, d, J=7.5 Hz, H ¹ , H ²), 5.76(1H, d, J=11.5 Hz, H ⁴), 6.8-8.0(15H, m)	595
7a	2230	2.99, 3.67(each 3H, s), 4.67, 5.03(each 1H, d, J=11.0 Hz, H ¹ , H ²), 4.80(1H, d, J=6.5 Hz, H ³), 5.65(1H, d, J=6.5 Hz, H ⁴), 7.3-8.0(15H, m)	595
7b	2230	3.68, 3.70(each 3H, s), 4.28(1H, d, J=7.0 Hz, H ³), 4.67, 4.96(each 1H, d, J=11.0 Hz, H ¹ , H ²), 5.54(1H, d, J=7.0 Hz, H ⁴), 7.25-8.0(15H, m)	595
8a	2230	2.95, 3.67(each 3H, s), 4.37, 5.13(each 1H, d, J=7.0 Hz, H ¹ , H ²), 4.86(1H, d, J=8.0 Hz, H ³), 5.71(1H, d, J=8.0 Hz, H ⁴), 6.9-7.9(15H, m)	595
8b	2240	3.59, 3.73(each 3H, s), 4.05(1H, d, J=8.0 Hz, H ³), 4.45, 5.03(each 1H, d, J=7.5 Hz, H ¹ , H ²), 5.58(1H, d, J=8.0 Hz, H ⁴), 6.85-7.95(15H, m)	595

^aA very weak absorption band in all adducts.

^b ^1H NMR (CDCl_3): δ 4.35, 4.47(each 1H, d, J=12.0 Hz, H¹, H²), 4.81(1H, d, J=10.0 Hz, H³), 5.59(1H, d, J=10.0 Hz, H⁴), 6.9-7.85(20H, m).

^c ^1H NMR (CDCl_3): δ 3.50, 3.75(each 3H, s), 4.01(1H, d, J=11.0 Hz, H³), 4.43, 4.58(each 1H, d, J=10.5 Hz, H¹, H²), 5.25(1H, d, J=11.0 Hz, H⁴), 7.0-7.9(15H, m).

^d ^{13}C NMR (DMSO-d_6): δ 52.0, 52.2(OCH_3), 55.5, 65.4(quant. $\underline{\text{C}}$), 54.8, 58.2, 58.5, 82.8(tert. $\underline{\text{C}}$), 121($\text{C}\equiv\text{N}$), 157.2(isoxazoline 3- $\underline{\text{C}}$), 165.9, 166.8, 169.2, 171.0($\underline{\text{C}}=\text{O}$), 126.4, 127.2, 128.2, 128.8, 129.1, 130.2, 130.7, 131.5, 131.6.

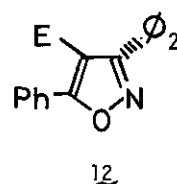
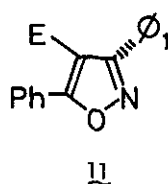
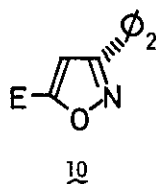
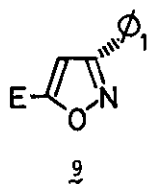
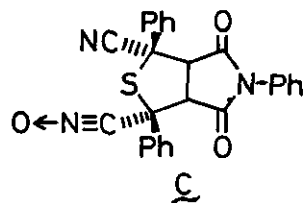
ing g-type adduct, because of anisotropy effect of the respective phenyl group at the 3-position of perhydrothiophene ring.

In addition, it may be concluded that the cycloaddition of olefins to the nitrile oxide moiety in C generated from 1 or 2 proceeds stereospecifically from the results of reactions of DMA and DFA.

Next, it has been investigated the reactions of 1 and 2 with methyl propiolate in refluxing benzene (36 h) or xylene (6 h);

the corresponding 1:1 adduct 9 or 10 was obtained as the sole isolated product respectively.

Similarly, the reaction of 1 or 2 with methyl phenylpropiolate in refluxing xylene for 24 or 48 h gave the sole 1:1 adduct 11 or 12 respectively.



E, ϕ_1 , ϕ_2 (see Scheme 1)

9: yield 83%; mp 138-140^o; IR (KBr) 2220 cm⁻¹ (very weak); ¹H NMR (DMSO-d₆) δ 3.90 (3H, s)⁸, 4.93, 5.16 (each 1H, d, J=12.0 Hz), 7.3-8.1 (16H, m, ArH + isoxazole ring 4-H)⁸.

10: yield 65%; mp 258-260^o (dec); IR (KBr) 2230 cm⁻¹ (very weak); ¹H NMR (DMSO-d₆) δ 3.89 (3H, s)⁸, 4.54, 5.37 (each 1H, d, J=7.0 Hz), 6.9-8.1 (16H, m, ArH + isoxazole ring 4-H)⁸; ¹³C NMR (DMSO-d₆) δ 52.9, 59.4 (tert. C), 55.4, 63.6 (quart. C), 57.1 (OCH₃), 109.7 (isoxazole ring 4-C), 119.8 (C=N), 156.3, 160.7, 168.2, 169.4, 171.2 (C=O, isoxazole ring 3- and 5-C).

11: yield 30%; mp 142-144^o; IR (KBr) 2230 cm⁻¹ (very weak); ¹H NMR (DMSO-d₆) δ 3.30 (3H, s)⁸, 4.80, 5.10 (each 1H, d, J=11.0 Hz), 7.3-8.2 (20H, m).

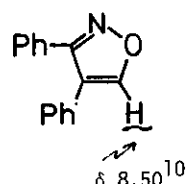
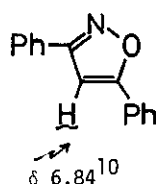
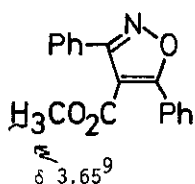
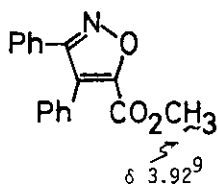
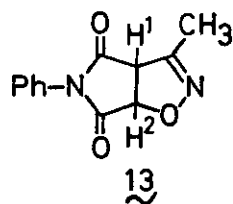
12: yield 29%; mp 247-249^o (dec); IR (KBr) 2220 cm⁻¹ (very weak); ¹H NMR (DMSO-d₆) δ 3.37 (3H, s)⁸, 4.51, 5.31 (each 1H, d, J=8.0 Hz), 6.95-8.1 (20H, m).

On the basis of the above spectral data, especially of ¹H NMR spectra⁸, 9 and 10 or 11 and 12 were assigned to be the corresponding 1-cyano-3-{3-(5-methoxycarbonylisoxazolyl)}- or 1-cyano-3-{3-(4-methoxycarbonyl-5-phenylisoxazolyl)}-perhydrothienopyrroledione compounds respectively.

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References and Notes

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5. The ^1H NMR spectrum ($\text{DMSO}-d_6$) of 13 (mp $177-178^\circ$), prepared by the cycloaddition of acetonitrile oxide to N-phenylmaleimide, showed signals at δ 2.09 (3H, s), 4.72 (1H, d, $J=10.0$ Hz, H^1), 5.55 (1H, d, $J=10.0$ Hz, H^2), and 7.2-7.7 (5H, m).
6. All the compounds in this paper gave satisfactory elemental analyses.
7. The calculated values of J_{12} were obtained by the following equation:
 $J=12.4\cos^2\theta$ ($0^\circ \leq \theta \leq 90^\circ$) (K. Kuriyama, E. Kondo and K. Tori, Tetrahedron Lett., 1963, 1485).
8. The reported ^1H NMR spectral data of isoxazole derivatives are as follows.



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