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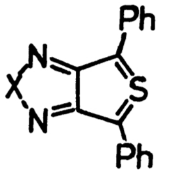
CYCLOADDITION REACTIONS OF 4,6-DIPHENYLTHIENO[3,4-c]-1,2,5-OXADIAZOLE AND -1,2,5-THIADIAZOLE WITH 6,6-DIPHENYLFULVENE AND TROPONE[1]

Otohiko TSUGE*, Toshiaki TAKATA, and Michihiko NOGUCHI
Research Institute of Industrial Science, Kyushu University 86, Hakozaki, Higashi-ku, Fukuoka 812

4,6-Diphenylthieno[3,4-c]-1,2,5-oxadiazole (**1**) reacts as a thiocarbonyl ylide with 6,6-diphenylfulvene to give the *exo*-[4 + 2] adduct *via* a stereoselective and regiospecific cycloaddition. The *exo*-adduct undergoes thermal cleavage of the oxadiazole ring to nitrile and nitrile oxide moieties which can be trapped as 1,3-cycloadducts to the fulvene and dimethyl acetylenedicarboxylate. The reaction of 4,6-diphenylthieno[3,4-c]-1,2,5-thiadiazole (**2**) with the fulvene affords a mixture of analogous *exo*- and *endo*-adducts which are subject to a retro-cycloaddition reaction. On the other hand, **1** reacts with tropone to give the corresponding [4 + 6] adduct which is susceptible to a retro-cycloaddition reaction. However, **2** did not react with tropone.

Recently, 10π-electron condensed thiophenes containing tetravalent sulfur have become considerable practical and theoretical interest.[2] Previously, we have reported that 4,6-diphenylthieno-[3,4-c]-1,2,5-oxadiazole (**1**)[3] containing tetravalent sulfur is a reactive substrate for cycloadditions, behaving as a thiocarbonyl ylide.[3,4] It has also been found that both the *endo*- and *exo*-adducts obtained from **1** and N-phenylmaleimide undergo thermal cleavage of the oxadiazole ring to nitrile and nitrile oxide moieties which can be captured as 1,3-cycloadducts by olefins and acetylenes,[5,6] whereas analogous cycloadducts formed from 4,6-diphenylthieno[3,4-c]-1,2,5-thiadiazole (**2**)[7] and the maleimide are subject to a retro-cycloaddition reaction.[5]

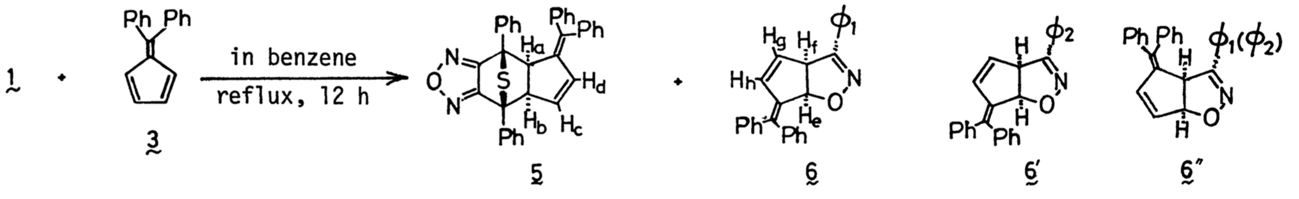


1: X=O
2: X=S

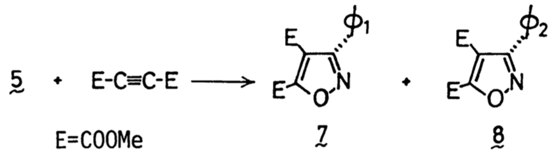
It has recently been recognized by several workers that the fulvene[8-10] and tropone systems[11-13] can function as either a 2π- or 6π-addend with several 1,3-dipoles. Thus, the fulvene and tropone systems seemed to be interesting substrates in the cycloadditions of **1** and **2** behaving as a thiocarbonyl ylide. In the present paper we wish to report the cycloaddition reactions of **1** and **2** with 6,6-diphenylfulvene (**3**) and tropone (**4**).[14]

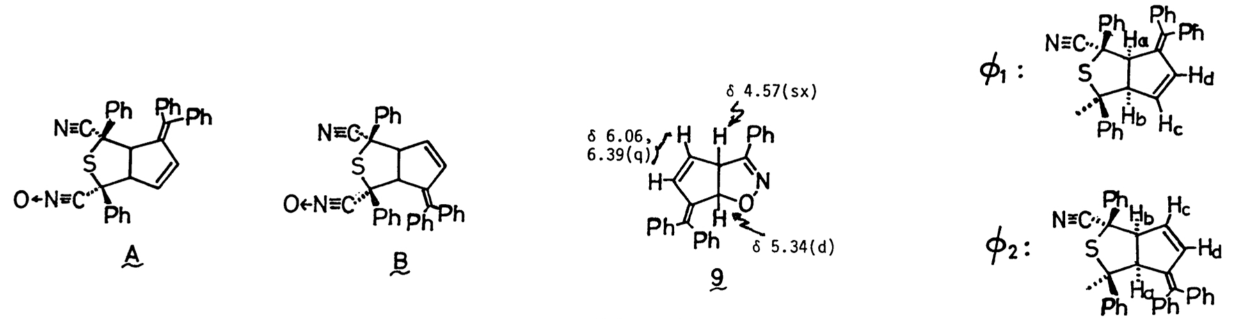
Reaction with Fulvene **3**. When a solution of **1** and **3** in benzene was refluxed, under nitrogen, for 12 h, a 1:1 adduct **5** was obtained as the major product, accompanied by a 1:2 adduct **6**. In the reaction employing excess of **1**, **5** was obtained as the sole product (Scheme 1). The ^{1}H and ^{13}C NMR spectra of **5** exclude both the [4 + 2] adduct to the exocyclic C=C bond of **3** and [6 + 4] adduct from possible structures for **5**, and are compatible with either *exo*- or *endo*-[4 + 2] adducts. On the basis of comparison of ^{1}H NMR spectral data with those of analogous cycloadducts of **2** to **3** described below, however, it was concluded that *exo* structure is more reasonable than *endo* structure.

On the other hand, 1:2 adduct **6** was assigned as an isoxazoline derivative arising from a 1,3-cycloaddition of **3** to a nitrile oxide moiety generated from **5** on the basis of the following evidences. The reaction of **5** with **3** afforded a 23% yield of **6** as an isolable product.[15] In addition, **5** reacted with dimethyl acetylenedicarboxylate (DMAD) to give two 1:1 adducts **7** and **8** in 48 and 15% yields respectively. The IR spectra of 6 as well as of 7 and 8 exhibited a weak band ascribable to $\nu_{C\equiv N}$ absorption as observed in the 1:2 adducts of 1 to acetylenes.[4] It is thus reasonable to conclude that 6 or 7 and 8 are cycloadducts of 3 or DMAD to a nitrile oxide moiety generated from 5, respectively.



1/3 mol/mol	Yield, % 5	 6	Recovery, % 1	 3
1/1	23	11	24	23
2/1	51	trace	40	—
3/1	52	—	54	—





Scheme 1

Now, the generation of two isomeric nitrile oxides, A and B, is possible from 5. On the basis of NMR spectral data, 7 and 8 were assigned as the isoxazole derivatives arising from A and B respectively. Differences in chemical shifts of Ha and Hb in 7 and 8 can be accounted for by considering the effects of isoxazole ring and phenyl group on the exo-methylene moiety. Based on the similarities of the ^{1}H NMR pattern with those of 7 (for Ha and Hb) and the reported adduct 9[9] (for He — Hh), the 1:2 adduct was assigned as 6 but not 6' nor 6". Stereochemistry of the isoxazoline moiety in 6 was based on the comparison of ^{1}H NMR spectral data of the isoxazoline derivatives obtained from the reaction of the exo-adduct of 1 to N-phenylmaleimide with olefins.[6]

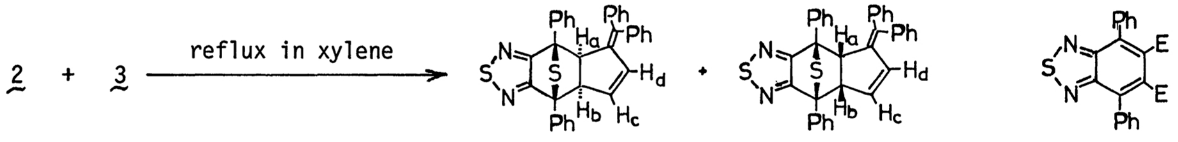
5: mp 191-194°C(dec); ^{1}H NMR($CDCl_3$) δ 4.04(1H, ddd, H_b, J=6, 2.5, 1.5 Hz), 4.54(1H, d, H_a, J=6 Hz), 5.56(1H, dd, H_c, J=6, 2.5 Hz), 6.75(1H, dd, H_d, J=6, 1.5 Hz), 6.3-6.5(2H, m), 6.8-7.7(18H, m); ^{13}C NMR ($CDCl_3$) δ 55.41, 63.79(tert. C), 66.61, 68.85(quat. C), 165.97, 166.32(C=N).

6: mp > 300°C; IR(KBr) 2220 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 4.63(1H, dd, H_g, J=5.5, 2 Hz), 4.73(1H, ddd, H_f, J=7.5, 2, 2 Hz), 5.02(2H, broad s, H_a, H_b), 5.40(1H, d, H_d, J=6 Hz), 5.54(1H, d, H_e, J=7.5 Hz), 6.00 (1H, dd, H_h, J=5.5, 2 Hz), 6.33(1H, d, H_c, J=6 Hz), 6.9-7.6(30H, m); ^{13}C NMR($CDCl_3$) δ 57.38, 59.93, 64.26, 86.74(tert. C), 57.56, 67.25(quat. C), 121.58(C≡N), 160.99(C=N).

7: mp 135-137°C(dec); IR(KBr) 2220 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 3.50, 3.94(each 3H, s), 5.00(1H, ddd, H_b, J=6, 2.5, 2 Hz), 5.12(1H, d, H_a, J=6 Hz), 5.35(1H, dd, H_d, J=6, 2 Hz), 6.35(1H, dd, H_c, J=6, 2.5 Hz), 6.6-7.5(20H, m).

8: mp 283-285°C(dec); IR(KBr) 2220 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 3.38, 3.91(each 3H, s), 4.33(1H, ddd, H_b, J=6, 2.5, 2 Hz), 5.33(1H, dd, H_d, J=6, 2 Hz), 6.20(1H, d, H_a, J=6 Hz), 6.26(1H, dd, H_c, J=6, 2.5 Hz), 6.45-7.8(20H, m).

Next, our attention was directed toward the reaction of 2 with 3. When a solution of 2 and 3 in xylene was refluxed under nitrogen, two isomeric [4 + 2] adducts 10 and 11 like 5 were obtained. On the basis of ^{1}H NMR spectral data, 10 and 11 were assigned as the exo- and endo-adducts respectively. Thus, the protons H_a and H_b in 11 appear at low field than those in 10, because of the deshielding effect of the sulfur bridge. Analogous effects have been noted for other related exo-endo adducts pairs containing a sulfur bridge.[3, 16] As mentioned above, the protons H_a and H_b in 5 appear at δ 4.54 and 4.04 respectively, positions very close to those in exo-adduct 10.



10 11 12

Reaction conditions		Yield, %		Recovery, %	
2/3(mol/mol)	time, h	10	11	2	3
1/1	6	16	7	56	52
1/1	18	13	21	40	42
1/4	18	26	59	—	42

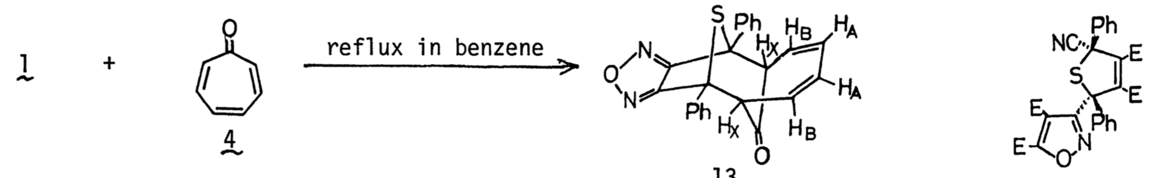
Scheme 2

10: mp 204-205°C(dec); ^{1}H NMR($CDCl_3$) δ 4.08(1H, ddd, H_b, J=5.5, 2.5, 1.5 Hz), 4.52(1H, d, H_a, J=5.5 Hz), 5.51(1H, dd, H_c, J=6, 2.5 Hz), 6.69(1H, dd, J=6, 1.5 Hz), 6.3-6.5(2H, m), 6.75-7.65(18H, m).

11: mp 194-195°C(dec); ^{1}H NMR($CDCl_3$) δ 4.86(1H, dd, H_b, J=7.5, 2.5, 1.5 Hz), 5.47(1H, d, H_a, J=7.5 Hz), 5.66(1H, dd, H_c, J=6, 2.5 Hz), 5.89(1H, dd, H_d, J=6, 1.5 Hz), 6.65-8.0(20H, m).

As shown in Scheme 2, the 10/11 ratio depended on reaction time, indicating that both the adducts 10 and 11 are subject to a retro-cycloaddition reaction to yield 2 and 3, which undergo re-cycloaddition. In fact, when a solution of endo-adduct 11 in xylene was refluxed with DMAD, under nitrogen, for 18 h, benzothiadiazole derivative 12[4], which was formed from the reaction of 2 with DMAD, was obtained in 48% yield.

Reaction with Tropone 4. When a solution of 1 and 4 in benzene was refluxed under nitrogen, a 1:1 adduct 13, mp 138-140°C (dec), was obtained together with recovery of starting materials (Scheme 3). The structure of 13 was deduced to be the [4 + 6] adduct on the basis of spectral data. The IR spectrum of 13 showed the bridging carbonyl absorption at 1730 cm^{-1}, while the ^{1}H NMR spectrum ($CDCl_3$)



13 14 (E=COOMe)

Reaction conditions		Yield, %	Recovery, %	
1/4(mol/mol)	time, h	13	1	4
1/1	16	2	78	98
1/1	48	15	68	73
1/3	48	30	44	85

Scheme 3

indicating $A_2B_2X_2$ spin system at δ 3.93 (2H, d, J=6.5 Hz), 5.38 (2H, H_B), and 6.24 (2H, H_A) demonstrated the symmetrical nature of the adduct, and corresponded closely to the NMR spectra of the [6 + 6] photodimer of 4[17] and [6 + 4] adduct of 4 to a cyclopentadienone.[18]

It has also been found that 13 undergoes a retro-cycloaddition reaction. Upon heating 13 in refluxing benzene for 48 h, 1 and 4 were formed in 48 and 44% yields respectively, besides recovery of 13 (48%). Furthermore, when a solution of 13 in benzene was refluxed with an excess of DMAD for 24 h, isoxazole derivative 14[6] corresponded to a 1:2 adduct of 1 to DMAD was formed in 34% yield.

References and Notes

1. Studies on 10π-Electron Heterocycles Containing Tetravalent Sulfur. Part 5. Part 4: Ref. 4.
2. M. P. Cava and M. V. Lakshmikantham, Acc. Chem. Res., 8, 139 (1975).
3. O. Tsuge, T. Takata, and M. Noguchi, Heterocycles, 6, 1173 (1977).
4. O. Tsuge and T. Takata, J. Org. Chem., in press.
5. O. Tsuge, T. Takata, and I. Ueda, Chem. Lett., 1979, 1029.
6. O. Tsuge and T. Takata, Heterocycles, 14, 423 (1980).
7. J. D. Bower and R. H. Schlessinger, J. Am. Chem. Soc., 91, 6891 (1969).
8. K. N. Houk and L. J. Luskus, Tetrahedron Lett., 1970, 4029.
9. P. Caramella, P. Frattini, and P. Grünanger, ibid., 1971, 3817.
10. N. Dennis, B. Ibrahim, and A. R. Katritzky, J. Chem. Soc. Perkin I, 2307 (1976).
11. M. Franck-Neumann, Tetrahedron Lett., 1970, 2143.
12. D. Mukherjee, C. R. Watts, and K. N. Houk, J. Org. Chem., 43, 817 (1978).
13. C. De Micheli, R. Gandolfi, and P. Grünanger, Tetrahedron, 30, 3765 (1974).
14. All new compounds in this paper gave satisfactory elemental analyses.
15. In the reaction of 1 with an equimolar amount of 3 as well as in this case, a mixture of 1:2 adducts ($\nu_{C\equiv N}$ 2220 cm^{-1}, ^1H NMR ($CDCl_3$) complex signals at δ about 3.8 and 4.5-6.5) other than 6 was obtained. However, attempts to isolate pure adduct(s) were unsuccessful.
16. M. P. Cava, N. M. Pollack, O. A. Mamer, and M. J. Mitchell, J. Org. Chem., 36, 3932 (1971); M. P. Cava, N. M. Pollack, and G. A. Dieterle, J. Am. Chem. Soc., 95, 2558 (1973); M. P. Cava, M. Behforonz, G. E. M. Husbands, and M. Srinivasan, ibid., 95, 2561 (1973).
17. T. Mukai, T. Tezuka, and Y. Akasaki, J. Am. Chem. Soc., 88, 5025 (1966).
18. K. N. Houk and R. B. Woodward, J. Am. Chem. Soc., 92, 4145 (1970).

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