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A NEW AND REACTIVE DIELS-ALDER DIENE, N,N-DIMETHYLAMINO-3-METHYLTHIOBUTADIENE

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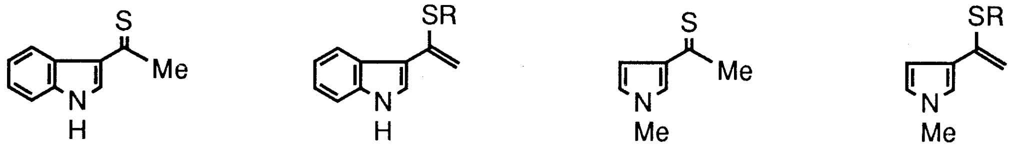
Reactivities of a new diene N,N-dimethylamino-3-methylthiobutadiene (**7**), prepared *in situ* by treatment of the methiodide of thioenaminone **5** with triethylamine, with several dienophiles as a Diels-Alder diene, were investigated. In general, the cycloaddition reactions were completed at low temperature for short periods, which showed that the diene has a high reactivity as a Diels-Alder diene.

KEYWORDS thiobutadiene; thioenaminone; Diels-Alder diene; dienophile; cycloaddition; anthraquinone; naphthazarine; acetylene dicarboxylate; maleic anhydride; N-methylmaleinimide

Recent works showed that 3-thioacetylindole (**1**) and N-methyl-3-thioacetylpyrrole (**3**) yield dienes by alkylation reactions, and the resulting dienes **2** and **4** undergo Diels-Alder reactions with appropriate dienophiles to give the functionalized carbazoles and indoles.1,2) (Chart 1) These behaviors to form the dienes from **1** and **3** by the alkylation reactions may be attributable to the character of the thioenaminone nucleus. Thus, we planned to synthesize a simple diene from a suitable thioenaminone such as 4-(N,N-dimethylamino)-3-butene-2-thione (**5**). This paper describes preparation of a new diene, N.N-dimethylamino-3-methylthiobutadiene (**7**; ATBD), from thioenaminone **5**, and investigations on the reactivity of **7** as a Diels-Alder diene with several dienophiles.



(1) (2) (3) (4)

Chart 1

ATBD **7** was best prepared3) *in situ* from the methiodide **6**4)of thioenaminone **5**,5) prepared by the reaction of 4-(N,N-dimethylamino)-3-buten-2-one with Lawesson's reagent,6) by the treatment with triethylamine. Preparation of ATBD and a general cycloaddition reaction with a dienophile was carried out as follows. Triethylamine (360 mg, 3.6 mmol) was slowly added to a solution of the methiodide **6** (813 mg, 3 mmol) and a dienophile (3.6 mmol) in 18 ml dry methylene chloride with stirring under ice-cooling for an appropriate time. Dil-HCl was added to the reaction mixture and the whole was extracted with chloroform. The organic layer was washed with brine, then dried and concentrated. The residue was subjected to silica gel column chromatography using an appropriate solvent.

The results of the cycloaddition reactions of ATBD with several dienophiles are shown in Chart 2. Reactions of ATBD with naphthoquinone at 0 °C for 2 h gave 2-methylthio-9,10-anthraquinone (**8**)[7,8] in 87% yield, and with naphthazarine at -20 °C for 3 min afforded 1,4-dihydroxy-6-methylthio-9,10-anthraquinone (**9**)[8,9] in 56% yield. Reaction of ATBD with dimethyl acetylenedicarboxylate at 0 °C for 30 min afforded dimethyl 4-methylthiophthalate (**10**)[10] in 22% yield. Reaction of ATBD with maleic anhydride at 0 °C for 5 min, followed by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) for 30 min, gave 4-methylthiophthalic anhydride (**11**)[11] in 18% yield. Reaction of ATBD with N-methylmaleinimide at 0 °C for 5 min, then reflux for 30 min followed by the treatment with DDQ for 30 min afforded N-methyl-4-methylthiophthalimide (**12**)[12] in 97% yield. Reaction of ATBD with β-nitrostyrene at 0 °C for 5 min gave 1-methylthio-4-nitro-5-phenyl-1,3-cyclohexadiene (**13**)[13] in 18% yield. In general, reactions were completed at low temperature for short periods, which showed that ATBD possesses a high reactivity as a Diels-Alder diene.

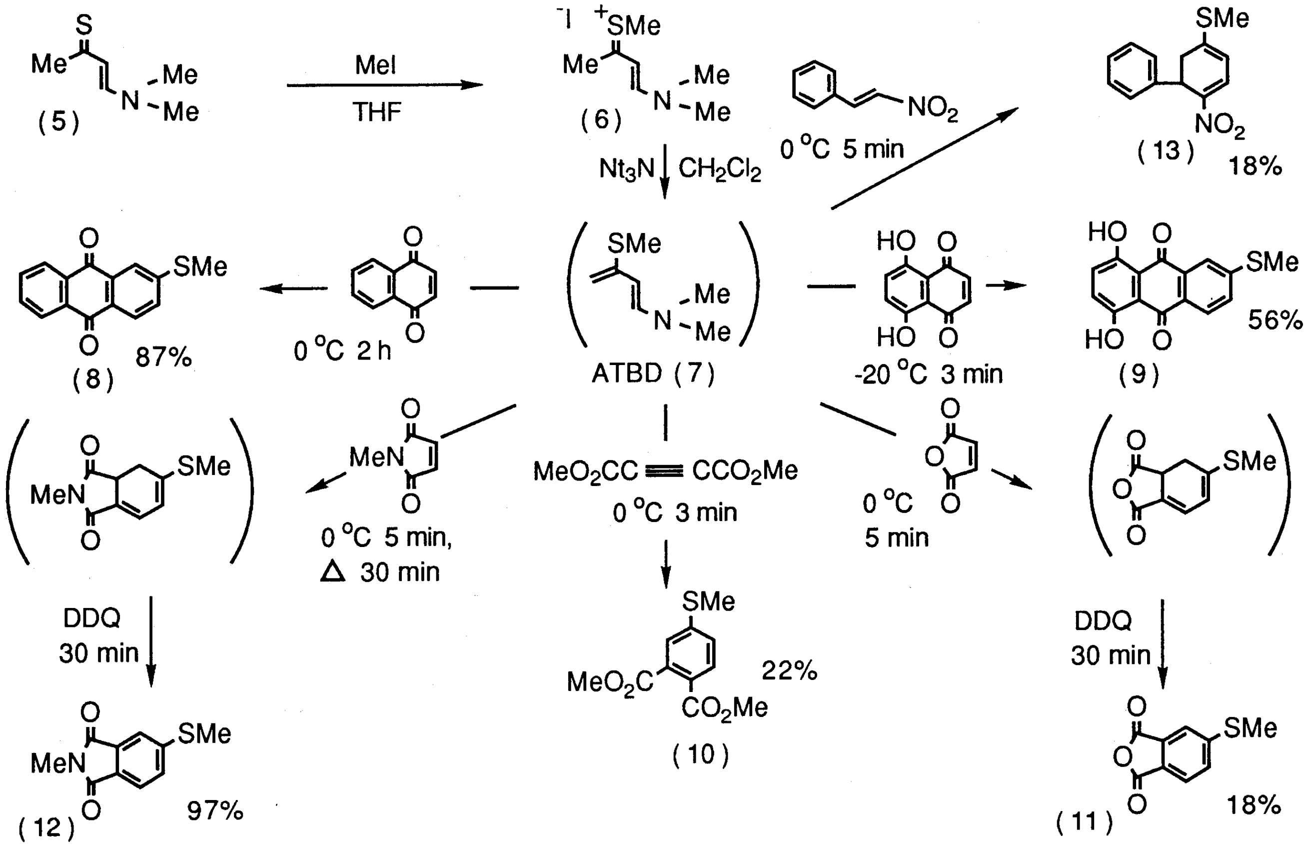
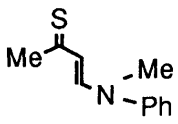


Chart 2

Although yield of the cycloaddition reaction of ATBD with dimethyl acetylenedicarboxylate by the general method was very low, the reaction result was improved by an alternative procedure as follows. That is, potassium carbonate (414 mg, 3 mmol) was added to a solution of **6** (542 mg, 2 mmol) and dimehyl acetylenedicarboxylate (341 mg, 2.4 mmol), and the whole was kept at room temperature overnight. The solution was worked up, and the residue was subjected to silica gel column chromatography to give the ester **10** in 61.8 % yield.

Related thioenaminones **14**, **15**, and **16**[14] were prepared to examine reactivities of their dienes which may result from corresponding methiodides of the thioenaminones. Reaction of the diene derived from the methiodide of 4-(N-methyl-N-phenylamino)-3-butene-2-thione (**14**) with naphthoquinone by a procedure similar to ATBD preparation at

O °C for 10 min afforded the anthraquinone **8** in 40% yield. On the other hand, reactions of the dienes derived from the methiodides of **15** and**16** with naphthoquinone failed to give the cycloaddition products. Their unreactivities may be attributable to difficulty in maintaining the cisoid diene structures on account of the steric hindrance of the methyl group.



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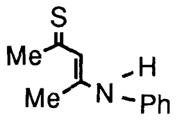

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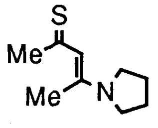

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1) M. Murase, T. Hosaka, T. Koike, and S. Tobinaga, *Chem . Pharm. Bull.,* **37**, 1999 (1989).
2) M. Murase, S. Yoshida, T.Hosaka, and S. Tobinaga, *Chem. Pharm. Bull.,* **39**, 489 (1991).
3) ATBD can be obtained by treatment of the thioenaminone 5 with NaH and MeI, alternatively.
4) Green powder, mp 147-148 °C. (dec.). ^{1}H-NMR (d_6-DMSO) δ : 2.36 (3H, s, C-Me or S-Me), 2.5 (3H, s, C-Me or S-Me), 3.30 (3H, s, N-Me), 3.43 (3H, s, N-Me), 5.96 (1H, d, J=12 Hz, olefinic H), 8.26 (1H, d, J=12 Hz, olefinic H).
5) Obtained from the enaminone as red needles (ether), mp 89 °C, in 80% yield.
6) M. C. Cava and M. I. Levinson, *Tetrahedron,* **22**, 5061 (1985).
7) Yellow needles (benzene-hexane), mp 166 °C. ^{1}H-NMR ($CDCl_3$) δ : 2.62 (3H, s, SMe), 7.57 (1H, dd, J= 8.3 and 1.96 Hz, C-3H), 7.75-7.82 (2H, m, C-6H and C-7H), 8.04 (1H, d, J=1.96 Hz, C-1H), 8.18 (1H, d, J=8.3 Hz, C-4H), 8.27-8.31 (2H, m, C-5H and C-8H). MS *m/z*: 254 (M^+). *Anal.* Calcd for $C_{15}H_{10}O_2S_1$: C, 70.84; H, 3.96. Found: C, 71.00; H, 4.00.
8) In these reactions, spontaneous oxidation reactions were taking place.
9) Violet plate (benzene), mp 201-203 °C. ^{1}H-NMR ($CDCl_3$) δ : 2.64 (3H, s, SMe), 7.30 (2H, s, C-2H and C-3H), 7.61 (1H, dd, J=8.3 Hz and 2.2 Hz, C-7H), 8.09 (1H, d, J=2.2 Hz, C-5H), 8.21 (1H, d, J=8.3 Hz, C-8H), 12.83 (1H, s, -OH), 12.98 (1H, s,-OH). MS *m/z*: 286 (M^+). *Anal.* Calcd for $C_{15}H_{10}O_4S_1$: C, 62.93; H, 3.52. Found: C, 63.01; H, 3.56.
10) Light yellowish oil. ^{1}H-NMR ($CDCl_3$) δ : 2.50 (3H, s, SMe), 3.88 (3H, s, CO_2Me), 3.90 (3H, s, CO_2Me), 7.1-7.4 (2H, m, C-3H and C-5H), 7.63 (1H, d, J=8.0 Hz, C-6H). MS *m/z*: 240 (M^+). Calcd for $C_{11}H_{12}O_4S_1$: 240.0412, Found 240.0443.
11) Yellowish needle (chloroform-hexane), mp 166-167 °C. ^{1}H-NMR (CD_3COCD_3) δ : 2.68 (3H, s, SMe), 7.66-7.76 (3H, m, aromatic H). MS *m/z*: 194 (M^+). *Anal.* Calcd for $C_9H_6O_3S_1$: C, 55.66; H, 3.11. Found: C, 55.54; H, 3.13.
12) White needle (ether-hexane) mp 144-145 °C. ^{1}H-NMR ($CDCl_3$) δ : 2.57 (3H, s, SMe), 3.16 (3H, s, NMe) 7.45 (1H, dd, J=7.91 and 1.5 Hz, C-5H), 7.62 (1H, d, J=1.5 Hz, C-3H), 7.7 (1H, d, J=7.9 Hz, C-6H), MS *m/z*: 207 (M^+). *Anal.* Calcd for $C_{10}H_9N_1O_2S_1$: C, 57.95; H, 4.38; N, 6.76. Found: C, 57.99; H, 4.25; N, 6.70.
13) Yellow needles (CH_2Cl_2-hexane), mp 123-125 °C. ^{1}H-NMR (CD_3COCD_3) δ : 2.42 (3H, s, SMe), 2.63 (1H, dd, J=17.34 and 1.71 Hz, C-6Ha), 3.36 (1H, ddd, J=17.34, 9.76 and 2.44 Hz, C-6Hb), 4.88 (1H, dd, J=9.76 and 1.71 Hz, C-5H), 5.97 (1H, dd, J=6.84 and 2.44 Hz, C-2H), 7.27 (5H, s, aromatic H), 7.85 (1H, d, J=6.84 Hz, C-3H). MS *m/z*: 247 (M^+). Calcd for $C_{13}H_{13}N_1O_2S_1$: 247.0666. Found: 247.0696.
14) **14** as a red oil. ^{1}H-NMR ($CDCl_3$) δ : 2.7 (3H, s, CMe), 3.4 (3H, s, NMe), 6.5 (1H, d, J=12 Hz, C-3H), 7.0-7.58 (5H, m, aromatic H), 8.16 (1H, d, J=12 Hz, C-4H). MS *m/z*: 191 (M^+). Calcd for $C_{11}H_{13}N_1S_1$: 191.0778, Found: 191.0768. **15** as orange plate (hexane) mp 58-59 °C. ^{1}H-NMR ($CDCl_3$) δ : 2.1 (3H, s, C-5Me), 2.6 (3H, s, C-1Me), 6.2 (1H, s, C-3H), 7.2 (5H, m, aromatic H), 8.9 (1H, br, NH). MS *m/z*: 191 (M^+). Calcd for $C_{11}H_{13}N_1S_1$: 191.0766. Found: 191.0746. **16** as orange plate (ether-hexane) mp 93 °C. ^{1}H-NMR ($CDCl_3$) δ : 1.9-2.2 (4H, m, -CH_2-), 2.64 (3H, s, C-1Me), 2.84 (3H, s, C-5Me), 3.28-3.64 (4H, m, -CH_2-), 6.22 (1H, s, C-3H). MS *m/z*: 169 (M^+). Calcd for $C_9H_{15}N_1S_1$: 169.0926, Found: 169.0944.

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