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1-Methyl-2-vinylpyrrole and 2-vinylthiophene showed remarkable differences in reactivity and regioselectivity upon reaction with methyl propiolate, respectively forming dimethyl 1-methylindole-4,7-dicarboxylate and dimethyl benzo[*b*]thiophene-4,6-dicarboxylate. 1-Methyl-2-(1-propenyl)pyrrole reacted with dimethyl acetylenedicarboxylate to give Diels-Alder and Michael-type adducts. On the other hand, 2-(1-propenyl)thiophene gave a 1:2 adduct which results *via* an initial cycloaddition and subsequent ene reaction.

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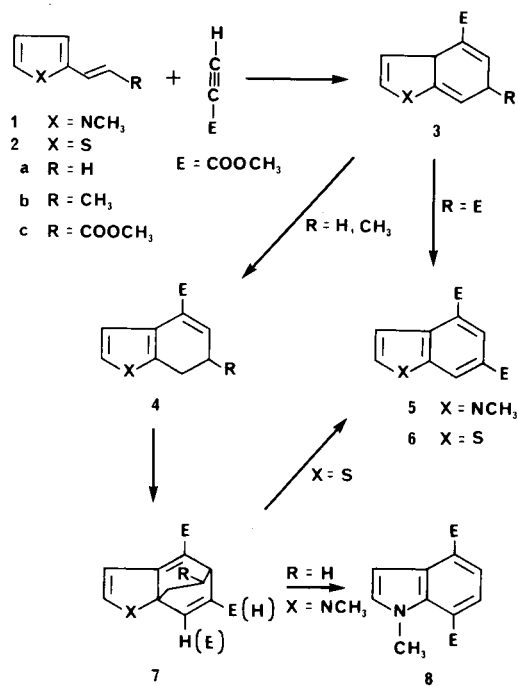
Cycloaddition reactions in which the diene is a heterocyclic aromatic five-membered ring compound have synthetic utilities and show interesting patterns of reaction [1]. For example, cycloaddition of furan with dimethyl acetylenedicarboxylate (DMAD) readily forms a 2:1 adduct [2], whereas *N*-methylpyrrole reacts with DMAD to form a 1:2 adduct [3]. Thiophene, however, does not react at all under conditions similar to those for furan or pyrrole [4]. This kind of striking difference in the reaction of five-membered monoheteroaromatic compounds was reported previously [5]. Vinylfurans or thiophenes having an electron-withdrawing group on the β -carbon do not undergo Diels-Alder reactions with DMAD or methyl propiolate (MP), but the corresponding pyrrole compounds form adducts. As we have extended our interest in the reaction of heteroaromatic compounds we have found that vinylpyrroles, in addition to having enhanced reactivity in cycloaddition reactions, show regioselectivity in the reaction that is quite different from that of vinylthiophenes.

One of the striking contrasts in the reaction of 1-methyl-2-vinylpyrrole (**1a**) and its thiophene analogue **2a** is the regioselectivity of the attacking dissymmetric dienophile, MP, toward the unisolated intermediates **4**. Jones and his coworkers isolated **8** from the reaction of **1a** and MP in refluxing benzene for 2 days in 73% yield [6]. However, 2-vinylthiophene (**2a**) and MP did not react under similar reaction conditions. Instead, polymerization of **2a** took place quite rapidly. When a neat 1:3 mixture of **2a** and MP was heated in a sealed tube at 110° for 4 days, compound **6** was isolated in 70% yield after recrystallization from methanol-ether (Scheme I). Vinylfuran did not give a compound similar to **5** or **8** in which two molecules of MP were involved [7].

Vinylpyrrole and vinylthiophene having electron-withdrawing substituents on the β -carbon are not suitable dienes for cycloaddition. General reaction conditions such as heating at reflux in benzene or carbon tetrachloride were not enough to force the reaction to take place. However, when a neat mixture of methyl (*E*)-3-(1-methyl-2-pyrrolyl)propenoate (**1c**) and MP was heated at reflux for 20

hours compound **5** was isolated in 29% [5]. Yet, these reaction conditions were not forceful enough for the thiophene analogue **2c**. A similar product **6** was isolated in 17% yield only after 4 days of heating at 100° in a sealed tube.

Scheme I



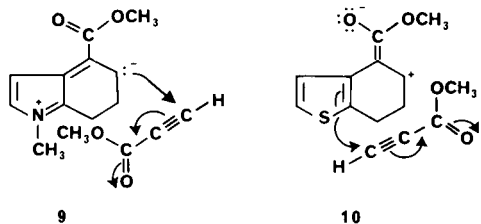
Formation of **5** and **6** from the acrylate ester of *N*-methylpyrrole **1c** and thiophene **2c**, respectively, may well define the positions of the two ester groups. However, the structural determinations of **8** and **5** are essential to confirmation of the observed regioselectivity in the reaction of MP with 1-methyl-2-vinylpyrrole (**1a**) and vinylthiophene (**2a**). Since the structures of **5** and its thiophene analogue **6** are closely related it seems logical to establish the different identities of 4,6-dicarboxylate **5** and 4,7-dicarboxylate **8** of 1-methylindole, and then to compare the similarity of 4,6-dicarboxylate of 1-methylindole (**5**) and that of the benzo[*b*]thiophene **6**. The different identities of

5 and **8** can be readily inferred by the melting point ranges, 84.5-85° [5] and 69-70° [6] for **5** and **8**, respectively. In addition, the ¹H-nmr (chloroform-*d*) spectrum of **8** showed four doublets at δ 6.98, 7.11, 7.48, and 7.70, each corresponding to 1H for 5-, 6-, 3-, and 2-H, respectively [6]. On the other hand, the chemical shifts of 5- and 7-H in **5** overlapped and appeared as a singlet at δ 7.18, while 3- and 2-H showed an AB pattern at δ 7.55 and 7.87 (*J* = 8 Hz) [5]. The ¹H-nmr spectrum of **6** was quite similar to **5** even though the chemical shifts appeared to be shifted further downfield. Thus, an AB pattern at δ 7.72 and 8.25 (*J* = 5.7 Hz) for 3- and 2-H, respectively and a singlet at 8.13 for 5- and 7-H of **6** represented well the positions of the two ester groups on the benzo[*b*]thiophene moiety of **6** should be identical to those on the indole **5**. The downfield shift in the thiophene **6** compared to the pyrrole **5** is not surprising [8].

The ir spectra of **5** and **6** showed strong, but narrow, bands at 1711 and 1726 cm⁻¹, respectively, indicating that the two ester groups in each compound are in very similar environments, *meta* to the hetero atoms.

The mass spectra of **5** and **6** also showed similarity. Compound **6** had fragments of *m/e* 250 (relative intensity 92%) and 219 (100%) corresponding to M⁺ and the loss of CH₃O from it, respectively. Compound **5** shows M⁺ at *m/e* 247 (100%) and a fragment 216 (69%) which is the loss of CH₃O. Other fragments are insignificant, having relative intensities of less than 20%.

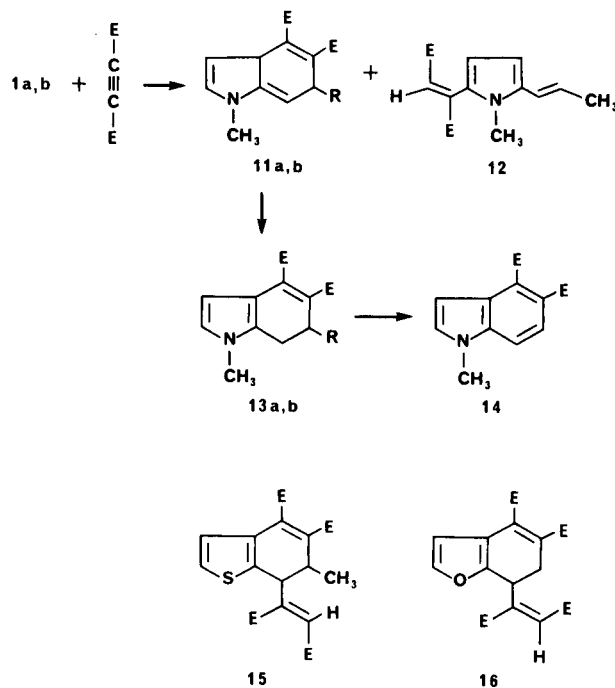
Similar to **2a** reaction of (*E*)-1-(2-thienyl)propane (**2b**) and MP gave **6** in 55% yield. Therefore, neither the regioselectivity (**4** to **7**) nor the retro-Diels-Alder cleavage from **7** to **6** seems to be affected by the replacement of H with a CH₃ group. The key factor that accounts for differences in regioselectivity between the pyrrole and the thiophene is proposed to be electron releasing ability through resonance. Much feasible mesomeric release of electrons from the nitrogen atom through the double bonds (*i.e.* **9**) may well favor the observed regioselectivity. On the other hand, resonance structure such as **10** in which the thiophene ring maintains the aromaticity seems to be more favorable than the one correspondent to **9**.



With DMAD, a stronger dienophile than MP, reaction of **1b** and **2b** showed remarkable differences. The pyrrole **1b** gave two isomeric 1:1 adducts **11b** and **12** upon reflux in ether for 38 hours. These products can be derived *via*

Diels-Alder and Michael-type addition reactions, respectively (Scheme II). The structure of the Diels-Alder adduct was readily confirmed as **11b**, not **13b**, by the complex pattern integrating for 3 protons in the region of δ 6.0-6.5 in the ¹H-nmr spectra. The uv spectrum also showed only rising end absorption, indicating lack of conjugation. On the other hand, the thiophene **2b** did not react under similar conditions. When a mixture of **2b** and DMAD was heated in a sealed tube for 4 days at 110°, a 1:2 adduct, **15**, was isolated. It is worthwhile to compare these reaction conditions to those for the preparation of **16** from vinylfuran; reflux in benzene for 24 hours [7]. Vinylthiophene (**2a**) polymerized as soon as it was mixed with DMAD, while vinylpyrrole (**1a**) gave a 6,7-dihydroindole **13a** [6]. In contrasting, vinylfuran gave an aromatized compound similar to **14** and a 7-oxabicyclo[2.2.1]heptadiene compound upon stirring with DMAD in ether at room temperature for 4 days [7].

Scheme II



Compounds **15** and **16** are ene reaction products from the intermediates corresponding to **11**. The ene reaction of thiophene compounds is not common in the literature [9]. The structure of **15** was readily confirmed by spectroscopic methods. Note that the two ester groups on the vinyl group are *cis*. This was supported by the chemical shift value (δ 5.37) of the vinyl proton [10]. It was δ 7.68 in **16** [7]. Furthermore, *w*-coupling of the vinyl proton with C₇-H was observed with *J* = 1.3 Hz. Although there can be four stereoisomers for **15**, the splitting of the peak corresponding to vinyl-H does not seem to be due to the presence of a diastereomeric mixture because the mp of **15** was

rather sharp. Furthermore, the C_6-CH_3 gave a clear doublet in the nmr spectrum at δ 1.16 with $J = 7.0$ Hz. This may be an evidence of the presence of a single diastereomer. The configuration of C_6 and C_7 were not determined in this research. The yield of **15** was 30% and the residue after isolation of **15** was a polymeric gum which does not move on tlc. Even though we were not able to confirm the presence of the *E* isomer of **15** by tlc, it is not certain if an O or S atom in the five-membered ring or the presence of an adjacent methyl group was responsible for different stereochemistry of the ene reaction products **16** and **15**, since the yield of **16** in the literature is only 3% [7].

EXPERIMENTAL

Melting points were determined on a Fisher MEL-TEMP apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 783 spectrophotometer, and ultraviolet-visible spectra were recorded on a Shimadzu double beam spectrophotometer. The 1H -nmr spectra were recorded on a JEOL FX-90Q spectrometer. Mass spectra were obtained on an AEI MS-30 spectrometer at 70 eV and 200°. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ, U.S.A. and Korea Research Institute of Chemical Technology, Chung Nam, Korea. Starting Materials.

Compounds **1a-c** and **2a-c** were prepared by literature methods [6,11-13]. Commercial DMAD and MP were distilled prior to use.

Dimethyl (*E*)-1-Methyl-5-(1-propen-1-yl)-2-pyrrolylbutenedioate (**12**) and Dimethyl 3a,b-Dihydro-1,6-dimethylindole-4,5-dicarboxylate (**11b**).

A solution of **1b** (0.20 g, 1.65 mmoles) and DMAD (0.40 g, 2.81 mmoles) in anhydrous ether (10 ml) was heated at reflux for 38 hours. The solvent was concentrated, the residue was chromatographed on preparative tlc plates (20 cm x 20 cm x 1 mm, silica gel, benzene) and three bands resulted. The first band, $R_f = 0.83$, was a mixture of **1b** and DMAD (0.13 g), which was confirmed by nmr analyses.

The second band, $R_f = 0.39$, was **12** (0.16 g, 37%), a yellow gum that did not solidify upon refrigeration at 4° for several days. The gum was purified by using a medium pressure liquid chromatography apparatus (100 psi) with a silica gel column (200-425 mesh, 0.7 x 25 cm, hexane:ethyl acetate = 4:1); ir (neat): 3030 w, 2975 w, 2820 w, 1748 s, 1685 s, 1612 ms, 1450 ms, 1275 ms, 1035 m, 970 s, 800 ms cm^{-1} ; 1H -nmr (chloroform-*d*): δ 1.87 (dd, 3H, C=CH-CH₃, $J = 6.5$ and 1.0 Hz), 3.30 (s, 3H, NCH₃), 3.62 and 3.77 (both s, 3H each, COOCH₃), 5.63 (d, 1H, C=CH-CH₃, $J = 12.0$ Hz), 6.22 (apparent s, 2H, C₃- and C₄-H), 6.91 (s, 1H, C=CH-COOCH₃); uv (methanol): 330 nm (ϵ 41000); ms: m/e (%) 263 (24, M⁺), 232 (96), 204 (100), 203 (94), 172 (21), 145 (15).

Anal. Calcd. for C₁₄H₁₇NO₄ (263.29): C, 63.86; H, 6.51; N, 5.32. Found: C, 64.18; H, 6.67; N, 5.05.

The third band, $R_f = 0.19$, gave **11b** (0.17 g, 40%) as a brown gum which was purified by chromatographic method similar to the purification of **12**; ir (neat): 3050 w, 2975 w, 2825 w, 1730 vs, 1620 m, 1445 ms, 1300 s, 1160 s, 1010 s, 820 nm cm^{-1} ; 1H -nmr (chloroform-*d*): δ 1.88 (d, 3H, C₆-CH₃, $J = 5.5$ Hz), 3.60 (s, 3H, NCH₃),

3.80 (m, 6-H) overlapping 3.75 (s, and 3.92 s, total 7H, COOCH₃), 5.88 (d, 1H, 3a-H, $J = 2.0$ Hz), 6.0-6.5 (m, 3H, 2-, 3-, and 7-H) uv (methanol): 230 nm rising end absorption; ms: m/e (%) 263 (5, M⁺), 261 (12), 232 (20), 204 (52), 203 (100), 202 (98), 188 (24).

Anal. Calcd. for C₁₄H₁₇NO₄ (263.29): C, 63.86; H, 6.51; N, 5.32. Found: C, 64.22; H, 6.48; N, 5.32.

Dimethyl Benzo[*b*]thiophene-4,6-dicarboxylate (**6**). From **2a**.

Vinylthiophene (**2a**, 0.61 g, 5.53 mmoles) and methyl propiolate (1.57 g, 18.67 mmoles) were placed in a stainless-steel tube (inner volume 45 ml). After sealing the tube, the mixture was heated in an oil-bath at 110° for 4 days. The reaction mixture was transferred to a small test tube, capped, and left at room temperature overnight to give white needles of **6** (0.95 g, 70%), mp 145-146°; ir (potassium bromide): 3100 w, 2970 w, 1726 vs, 1578 w, 1467 m, 1438 ms, 1286 vs, 1263 vs, 1205 s, 1142 m, 1129 m, 1118 ms, 1022 m, 985 m, 758 s cm^{-1} ; 1H -nmr (chloroform-*d*): δ 4.01 (s) and 4.04 (s, 3H, each, COOCH₃), 7.72 (d, 1H, 3-H, $J_{3,2} = 5.7$ Hz), 8.13 (s, 2H, 5- and 7-H), 8.25 (d, 1H, 2-H, $J_{2,3} = 5.7$ Hz); uv (methanol) 312 nm (ϵ 8630), 278 infl (2450), 243 infl (5440); ms: m/e (%) 250 (92, M⁺), 219 (100, M⁺ - CH₃O), 191 (16), 176 (13), 159 (26).

Anal. Calcd. for C₁₂H₁₀O₄S (250.27): C, 57.59; H, 4.03; S, 12.81. Found: C, 57.48; H, 4.01; S, 12.80.

From **2b**.

Compound **2b** (1.25 g, 100 mmoles) and methyl propiolate (2.15 g, 250 mmoles) were heated in a sealed stainless-steel tube at 110° for 4 days by similar procedure as for **2a**. Upon cooling and keeping the tube in a freezer (-5°) for 2 days **6** was isolated in 55% yield, mp 144-146°.

From **2c**.

A mixture of **2c** (2.03 g, 12.09 mmoles) and methyl propiolate (4.28 g, 50.91 mmoles) was heated in a stainless-steel tube at 110° for 4 days. The resulting gum was dissolved in abs. ethanol (30 ml) by heating and decolorized with charcoal once. Upon cooling the solution a white precipitate formed, which was filtered and then dried under vacuum to give **6** (0.52 g, 17%), mp 143°. The filtrate was mostly unreacted **2c**, as confirmed by tlc ($R_f = 0.26$, benzene). Compound **6** has $R_f = 0.18$ (silica gel, benzene).

Dimethyl (*Z*)-(6,7-Dihydro-4,5-dimethoxycarbonyl-6-methylbenzo[*b*]thiophen-7-yl)butenedioate (**15**).

A mixture of **2b** (1.25 g, 100 mmoles) and DMAD (2.82 g, 200 mmoles) was heated in a sealed stainless-steel tube at 110° for 4 days. The resin-like material was dissolved in methanol by heating, and ether was then added to cloudiness. Upon cooling of the solution white needles of **15** formed (1.30 g, 32%), mp 121.5-122.5°; ir (potassium bromide): 3100 w, 3005 w, 2965 m, 1730 s, 1720 s, 1710 s, 1642 m, 1616 m, 1524 w, 1440 ms, 1380 ms, 1375 s, 1340 s, 1303 s, 1278 s, 1265 s, 1210 ms, 1108 m, 1010 m, 972 m, 900 m, 791 m, 766 m, 759 m cm^{-1} ; 1H -nmr (chloroform-*d*): δ 1.16 (d, 3H, 6-CH₃, $J = 7.0$ Hz), 3.48 (m, 2H, 6- and 7-H), 3.66, 3.79, 3.81, and 3.89 (all s, 3H each, COOCH₃), 5.37 (d, 1H, vinyl-H, $J = 1.3$ Hz), 6.97 (d, 1H, 3-H, $J = 5.3$ Hz), 7.27 (d, 1H, 2-H, $J = 5.3$ Hz); uv (methanol): 316 nm (ϵ 4500), 282 (4200), 243 infl (9000), 237 (10300); ms: m/e (%) 408 (0.6, M⁺), 376 (19), 361 (28), 344 (23), 317 (30), 316 (81, M⁺ - CH₃OCHO, CH₃OH), 289 (12), 258 (11), 257 (32), 234 (15), 233 (100).

Anal. Calcd. for $C_{19}H_{20}O_8S$ (408.42): C, 55.88; H, 4.94; S, 7.85.
Found: C, 56.04; H, 5.03; S, 8.07.

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