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# Studies on the Reactions of Heterocyclic Compounds. XIV.[1] 1,3-Dipolar Cycloaddition of Some Isoquinolinium Ylides with Methyl Propiolate[2]

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In the cycloaddition reaction of isoquinolinium bis(methoxycarbonyl)methylide (VI) and isoquinolinium cyano(methoxycarbonyl)methylide (VIII) with methyl propiolate (II), the primary adducts, trimethyl-3,10b-dihydropyrrolo[2,1-*a*]isoquinoline-1,3,3-tricarboxylate (VII) and dimethyl 3-cyano 3,10b-dihydropyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylate (IX), were isolated. The stability of the primary adduct was found to be affected by the kind of substituent at 3-position.

In previous papers we reported the isolation of the primary adducts, the isomerized products, the rearranged products, and the aromatized products in the 1,3-dipolar cycloaddition of some isoquinolinium ylides with acetylenic compounds (dimethyl acetylenedicarboxylate and dicyanoacetylene) and the stabilities of the primary adducts for acid, base, and heat.[4-8] In the present work, the reaction between various isoquinolinium ylides and methyl propiolate (II) was investigated to examine the effect of the substituents on the stabilities of primary adducts, and we found that, when isoquinolinium bis(methoxycarbonyl)methylide (VI)[9] or isoquinolinium cyano(methoxycarbonyl)methylide (VIII) was used, the primary adducts were obtained, while isoquinolinium mono-substituted methylides gave aromatized products (Chart 1).

When 2-(methoxycarbonylmethyl)isoquinolinium bromide (I) was made to react with II in the presence of triethylamine in the dichloromethane–acetonitrile mixture at room temperature for two hours, only an aromatized compound (III) by air oxidation of the primary adduct was obtained but no primary adduct. The position of the methoxycarbonyl group was determined from the appearance of the signal of the proton at 10-position of III at a lower magnetic field (δ 9.08) by the magnetically anisotropic effect in the nuclear magnetic resonance (NMR) spectrum.[5]

When 2-(cyanomethyl)isoquinolinium bromide (IV) was treated with II in the presence of triethylamine in the dichloromethane–acetonitrile mixture under ice-cooling for four and a half hours, only an aromatized compound (V) was obtained as in the case of I. The structure of V was determined from the appearance of the signal of the proton at 10-position at a lower magnetic field (δ 9.61) by the magnetically anisotropic effect of the carbonyl group in the NMR

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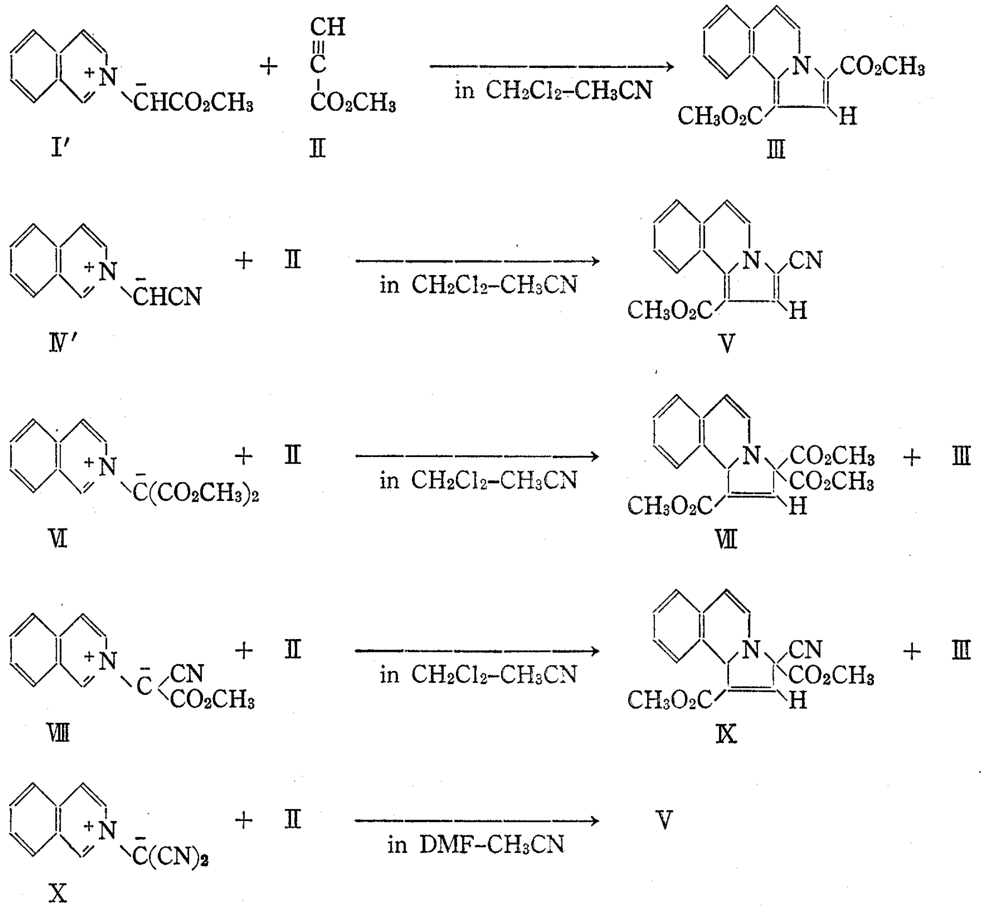

Chart 1

spectrum5) and the presence of carbonyl and cyano groups in the infrared (IR) spectrum and by elemental analyses.

It is assumed that the easy occurrence of isomerization and dehydrogenation prevented the primary adduct from being obtained when mono-substituted ylides like I' and IV' were used. Therefore, we attempted the reaction of isoquinolinium bis(methoxycarbonyl)methylide (VI) with II in the dichloromethane–acetonitrile mixture at room temperature for five hours to obtain the primary adduct (VII) in 73.8% yield, together with a small amount of III. When VII was dissolved in dichloromethane and allowed to stand for two hours in the presence of alumina at 0°, it was converted to III. VII was also converted to III in the presence of silica gel. VII showed the absorption maxima at 316 nm (log $\varepsilon$: 3.90) in the ultraviolet (UV) spectrum.5) Since the stability of the primary adduct depended on the substituent of the ylide,5,6) an ylide possessing cyano and methoxycarbonyl groups and II were treated in the dichloromethane–acetonitrile mixture at room temperature for eleven hours, and the primary adduct (IX) was obtained. In this case, a small amount of III was obtained as a by-product.

When isoquinolinium dicyanomethylide (X), which has two cyano groups, was treated with II in the dimethylformamide–acetonitrile mixture for forty-eight hours, only V was obtained by elimination of hydrogen cyanide from the primary adduct.

As the result, it can be said that the primary adduct tends to be oxidized, causing isolation impossible, when a C-monosubstituted ylide is used. In the case of an ylide with two methoxycarbonyl groups or one methoxycarbonyl group and one cyano group as electron-withdrawing group, the primary adduct was obtained. Dicyano ylide gave no primary adduct. Therefore, by replacing both methoxycarbonyl groups with cyano groups, the primary adduct is made unstable.

## Experimental

**Dimethyl Pyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylate (III)**——To a suspension of 2-(methoxycarbonylmethyl)isoquinolinium bromide (I) (282 mg) in $CH_2Cl_2$ (5 ml), a solution of triethylamine (101 mg) in $CH_2Cl_2$ (5 ml) was added dropwise at room temperature under stirreing. When a solution of methyl propiolate (II) (84 mg) in $CH_3CN$ (10 ml) was slowly added dropwise to the above solution, crystals were precipitated out 10 min later. After the stirring was continued for 2 hr, $CH_2Cl_2$ and $CH_3CN$ were evaporated *in vacuo* (below 40°). The precipitated crystals by adding $CH_3OH$ were filtered and recrystallization from $CH_2Cl$-$CH_2Cl$ afforded pale yellow prisms (III, mp 214.5°). Yield 75.5 mg (26.7%). III was identified with the authentic specimen[4] by admixture.

**Methyl 3-Cyanopyrrolo[2,1-*a*]isoquinoline-1-carboxylate (V)**——a) To a suspension of 2-(cyanomethyl)-isoquinolinium bromide (IV) (249 mg) in $CH_2Cl_2$ (10 ml), a solution of triethylamine (101 mg) in $CH_3CN$ (5 ml) was added dropwise at room temperature under stirring. Then, a solution of II (84 mg) in $CH_3CN$ (5 ml) was slowly added dropwise under ice-cooling. The stirring was continued for 4.5 hr. When the reaction was completed, $CH_2Cl_2$ and $CH_3CN$ were evaporated *in vacuo* (below 30°) and the residue was chromatographed over silica gel. When the $CH_2Cl_2$ layer was concentrated to dryness *in vacuo*, the residue was recrystallized from $CH_3OH$ to afford colorless plates (V) of mp 159.5°. Yield, 29.5 mg (12%). IR $cm^{-1}$: $\nu_{C\equiv N}$ 2227, $\nu_{C=O}$ 1715 (KBr). NMR ($d_6$-DMSO) $\delta$: 3.86 (3H, s), 7.58 (1H, d, $J$=7.5 Hz, 6-H), 7.84 (4H, m, 2-, 7-, 8-, and 9-H), 8.29 (1H, d, $J$=7.5 Hz, 5-H), 9.61 (1H, m, 10-H). *Anal.* Calcd. for $C_{15}H_{10}O_2N_2$: C, 71.99; H, 4.03; N, 11.20. Found: C, 71.77; H, 3.98; N, 11.16.

b) To a solution of isoquinolinium dicyanomethylide (X) (290 mg) in dimethyl formamide (DMF) (10 ml) and $CH_3CN$ (5 ml), II in $CH_3CN$ (5 ml) was added dropwise and the mixture was stirred at room temperature for 48 hr. After the reaction was completed, DMF and $CH_3CN$ were evaporated *in vacuo*. When $CH_3OH$ was added to the residue, crystals (X) was obtained (69.3 mg, 23.9%). The filtrate was concentrated to dryness *in vacuo* and the residue was recrystallized from $CH_3COCH_3$ to afford V of mp 162—165°. Yield, 228 mg (60.8%).

**Trimethyl 3,10b-Dihydropyrrolo[2,1-*a*]isoquinoline-1,3,3-tricarboxylate (VII)**——To a solution of isoquinolinium bis(methoxycarbonyl)methylide (VI) (518 mg) in $CH_2Cl_2$ (15 ml), a solution of II (168 mg) in $CH_3CN$ (15 ml) was added dropwise and the mixture was stirred at room temperature for 5 hr. The reaction mixture was concentrated to dryness *in vacuo*, and the residue was recrystallized by adding $CH_3OH$ (5 ml) to afford pale-yellow needles of VII (472 mg). The filtrate was concentrated to dryness *in vacuo* and chromatographed over silica gel to afford III (5 mg) and VII (34 mg). Yield of VII, 506 mg (73.8%). IR $cm^{-1}$: $\nu_{C=O}$ 1731, 1748 (KBr). UV $\lambda_{max}^{CH_3CN}$ nm (log $\varepsilon$): 316 (3.90). NMR ($CDCl_3$) $\delta$: 3.60 (3H, s), 3.84 (3H, s), 3.91 (3H, s), 5.65 (1H, s, 10b-H), 5.86 (1H, d, $J$=7.5 Hz, 6-H), 6.64 (1H, d, $J$=7.5 Hz, 5-H), 7.06 (5H, m, 2-, 7-, 8-, 9-, and 10-H). *Anal.* Calcd. for $C_{18}H_{17}O_6N$: C, 62.97; H, 4.99; N, 4.08. Found: C, 63.09; H, 5.09; N, 3.97.

**Dimethyl 3-Cyano-3,10b-dihydropyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylate (IX)**——To a solution of isoquinolinium cyano(methoxycarbonyl)methylide (VII) (339 mg) in $CH_2Cl_2$ (10 ml) and $CH_3CN$ (5 ml), II (126 mg) in $CH_3CN$ (5 ml) was added dropwise and the mixture was allowed to stand for 11 hr at room temperature under stirring. After the reaction was completed, $CH_2Cl_2$ and $CH_3CN$ were removed *in vacuo*. When $CH_3OH$ was added to the residue, pale-yellow prisms (III) precipitated out. Yield, 25 mg (5.7%). Recrystallization of the filtrate after concentration afforded yellow needles (IX) of mp 157°. Yield, 294 mg (63.3%). IR $cm^{-1}$: $\nu_{C\equiv N}$ 1990, $\nu_{C=O}$ 1760, 1737 (KBr). NMR ($CDCl_3$) $\delta$: 3.95 (6H, s), 5.75 (1H, s, 10b-H), 6.10 (1H, d, $J$=6.6 Hz, 6-H), 6.39 (1H, d, $J$=6.6 Hz, 5-H), 6.95 (4H, m, 7-, 8-, 9-, 10-H). *Anal.* Calcd. for $C_{17}H_{14}O_2N$: C, 65.85; H, 4.62; N, 9.12. Found: C, 65.81; H, 4.58; N, 9.03.