1,3-Dipolar cycloadditions are a useful class of synthetic reactions for the construction of functionalized five-membered heterocycles. Although cycloadditions using nitrile oxides, azomethine ylides, carbonyl ylides, nitrones, and nitroalkenes as dipoles have been well studied, the use of diazoalkanes as dipoles has not been extensively examined. Because of the instability of the initial \([3+2]\) adduct, synthetic applications of these dipoles have typically been limited to the preparation of the derived cyclopropanes or pyrazoles obtained by nitrogen extrusion or aromatization, respectively. During the course of our studies on the reactivity of 2-methylene-1,3-dicarbonyl compounds \(^1\) we investigated the reaction with ethyl diazoacetate and obtained relatively stable pyrazoline derivatives (Chart 1).

2-Methylene-1,3-dicarbonyl compounds \(^1\) were reacted with ethyl diazoacetate in CH\(_2\)Cl\(_2\) at room temperature to give 1,3-dipolar cycloadducts in good yields regardless of \(R\) (methyl, phenyl, alkoxy groups) (Table 1). In the \(^1\)H-NMR spectrum of the adduct from \(1\) \((R=\text{OMe})\), signals at 3.50 and 4.07 ppm show geminal coupling constant (18.3 Hz), and the latter shows long-range coupling (1.5 Hz) with NH which appeared at 7.42 ppm. In addition the frontier molecular orbital (FMO) theory\(^10\) predicts the adduct should be 3. From these facts the final product is thermodynamically more stable \(2\) \((2\text{a} \text{ from } 1\text{a})\) which is isomerized from 3. The other possible regioisomers 4 and 5 must show different \(^1\)H-NMR spectra.

We earlier succeeded in the enantioselective catalytic Diels–Alder reaction,\(^11\) and next we examined the chiral Lewis acid catalyzed dipolar addition reactions. As \(1\text{b}\) gave almost the same result under the identical conditions shown in Table 1, except for the reaction temperature (entry 4), the chiral Lewis acid catalyzed reaction of \(1\text{b}\) was carried out by slowly adding ethyl diazoacetate using MgI\(_2\) and bis(oxazoline) \(6\) as a chiral ligand (Table 2). However, the products (entries 1—3) show no specific optical rotation. This means the reactivity of \(1\text{b}\) is too reactive to introduce the chirality into the adduct.

**Experimental**

NMR spectra were measured on a JEOL GX-270 spectrometer for samples in CDCl\(_3\) solution at 270 MHz for \(^1\)H and 67.89 MHz for \(^1\)C, and chemical shifts are expressed in \(\delta\)-units using tetramethylsilane or chloro-
form as an internal standard. IR spectra were recorded on a JASCO FT/IR-410 spectrometer. High-resolution mass spectra (HR-MS) were obtained with a JEOL JMS-700 spectrometer. MgSO₄ was used to dry organic layers after extraction. Preparative thin layer chromatography (p-TLC) was performed with Merck Silica Gel 60 F₂₅₄ (0.5 mm).

**Reaction of 2-Methylene-1,3-dicarbonyl Compounds with Diazotized Chloramine T**

**General Procedure A** solution of ethyl diazocateate (0.6 mmol) in CH₂Cl₂ (3 ml) was added to a solution of 2-methylene-1,3-dicarbonyl compounds (0.5 mmol) in CH₂Cl₂ (4 ml) during a period of 15 min at room temperature. As soon as the addition was completed the solvent was evaporated off and the resulting residue was applied to p-TLC. The adducts were obtained in the yields shown in Table 1.

- **5-Benzoyl-4,5-diethyl-1H-pyrazole-3,5-dicarboxylic Acid Ethyl Ester**
  - **(2a)**: A yellow oil. IR (neat): 1736, 1691 cm⁻¹. ¹H-NMR δ: 1.13 (3H, t, J=7.1 Hz, CH₃), 1.33 (3H, t, J=7.1 Hz, CH₃), 1.52 (1H, d, J=18.3 Hz, 4-H), 4.06 (1H, dd, J=18.3, 1.5 Hz, ArH), 4.29 (2H, q, J=7.1 Hz, OCH₂), 7.69 (2H, t, J=7.5 Hz, ArH), 7.89 (2H, dd, J=7.5, 1.5 Hz, ArH). ¹³C-NMR δ: 13.4, 39.2, 53.4, 61.1, 78.2, 128.7, 131.8, 134.0, 142.7, 161.1, 169.0, 191.6. HR-MS m/z: CaIed for C₁₇H₂₀N₂O₅: 304.1059. Found: 304.1066.

- **5-Benzoyl-4,5-diethyl-1H-pyrazole-3,5-dicarboxylic Acid Diethyl Ester**
  - **(2b)**: A yellow oil. IR (neat): 1736, 1692 cm⁻¹. ¹H-NMR δ: 1.13 (3H, t, J=7.1 Hz, CH₃), 1.33 (3H, t, J=7.1 Hz, CH₃), 1.52 (1H, d, J=18.3 Hz, 4-H), 4.06 (1H, dd, J=18.3, 1.5 Hz, 4-H), 4.11 (2H, q, J=7.1 Hz, OCH₂), 4.29 (2H, q, J=7.1 Hz, OCH₂), 7.40 (1H, br s, NH), 7.49 (2H, t, J=7.5 Hz, ArH), 7.60 (1H, tt, J=7.5, 1.5 Hz, ArH), 7.88 (2H, dd, J=7.5, 1.5 Hz, ArH). ¹³C-NMR δ: 13.4, 13.8, 39.1, 61.1, 62.7, 78.3, 128.8, 131.5, 133.9, 142.7, 161.1, 168.4, 192.1. Anal. CaIed for C₁₇H₂₀N₂O₅: C, 60.7; H, 5.7; N, 8.80. Found: C, 60.4; H, 5.8; N, 8.46. HR-MS m/z: CaIed for C₁₇H₂₀N₂O₅: 318.1216. Found: 318.1198.

- **5-Benzoyl-4,5-diethyl-1H-pyrazole-3,5-dicarboxylic Acid 3-Ethyl Ester**
  - **(2c)**: A yellow oil. IR (neat): 1736, 1691 cm⁻¹. ¹H-NMR δ: 1.01 (3H, d, J=6.3 Hz, CH₃), 1.19 (3H, d, J=6.3 Hz, CH₃), 1.34 (3H, t, J=7.2 Hz, CH₃), 3.51 (1H, d, J=18.3 Hz, 4-H), 4.04 (1H, dd, J=18.3, 1.5 Hz, 4-H), 4.29 (2H, q, J=7.2 Hz, OCH₂), 5.06 (1H, heptet, J=6.3 Hz, OCH₃), 7.37 (1H, br s, NH), 7.48 (2H, t, J=7.5 Hz, ArH), 7.62 (1H, t, J=7.5, 1.3 Hz, ArH), 7.89 (2H, dd, J=7.5, 1.3 Hz, ArH). ¹³C-NMR δ: 14.2, 21.1, 21.3, 39.3, 61.6, 71.2, 78.7, 129.0, 129.1, 131.9, 134.2, 143.3, 161.5, 168.1, 192.5. HR-MS m/z: CaIed for C₁₇H₂₀N₂O₅: 332.1372. Found: 332.1377.

- **5-Benzoyl-4,5-diethyl-1H-pyrazole-3,5-dicarboxylic Acid 5-Cyclopentyl Ester**
  - **(2d)**: A yellow oil. IR (neat): 1736, 1692 cm⁻¹. ¹H-NMR δ: 1.33 (3H, t, J=7.1 Hz, CH₃), 1.18—1.81 (8H, m, CH₃), 3.51 (1H, d, J=18.1 Hz, 4-H), 4.05 (1H, dd, J=18.1, 1.5 Hz, 4-H), 4.29 (2H, q, J=7.1 Hz, OCH₂), 5.21 (1H, m, OCH₂), 7.35 (1H, br s, NH), 7.48 (2H, t, J=7.3 Hz, ArH), 7.62 (1H, tt, J=7.3, 1.5 Hz, ArH), 7.88 (2H, dd, J=7.3, 1.5 Hz, ArH). ¹³C-NMR δ: 13.9, 22.7, 22.8, 24.7, 30.7, 39.1, 61.2, 78.5, 128.7, 128.8, 131.7, 133.9, 142.8, 161.2, 167.9, 192.2. HR-MS m/z: CaIed for C₂₀H₂₄N₂O₅: 372.1685. Found: 372.1694.

References


