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Asymmetric Diels-Alder Reaction of 5,5,5-Trichloro-3-penten-2-one and Its Related Compound

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Diels-Alder reactions of 5,5,5-trichloro-3-penten-2-one and ethyl 4,4,4-trichloro-2-butenoate with cyclopentadiene in the presence of a chiral Lewis acid gave *exo*-2-acetyl-*endo*-3-trichloromethyl-bicyclo[2.2.1]hept-5-ene and *exo*-2-ethoxycarbonyl-*endo*-3-trichloromethylbicyclo[2.2.1]hept-5-ene with 40% and 7% e.e., respectively.

key words: *asymmetric reaction, Diels-Alder reaction, asymmetric Diels-Alder reaction, chiral Lewis acid, trichloromethyl group*

1. INTRODUCTION

Diels-Alder reaction[1,2] is a most popular [2+4] cycloaddition reaction. Asymmetric Diels-Alder reactions[1,2] by the use of chiral Lewis acid catalysts[3-6] containing elements such as boron,[7] aluminum,[8] titanium,[9] and magnesium et al.[10] are well known.

We reported a convenient synthesis of 5,5,5-trichloro-3-penten-2-one (**1**) and ethyl 4,4,4-trichloro-2-butenoate (**2**) by the reaction of 1,3-dicarbonyl compounds with chloral in the presence of potassium carbonate.[11] Compounds **1** and **2** are good dienophiles because of the presence of trichloromethyl and carbonyl groups. In 1974, we reported the Diels-Alder reaction of **1** with some dienes.[12]

Here we report asymmetric Diels-Alder reaction of **1** and **2** with cyclopentadiene in the presence of a chiral Lewis acid.

2. RESULTS AND DISCUSSION

The Diels-Alder reaction of **1** with cyclopentadiene afforded *exo*-2-acetyl-*endo*-3-trichloromethyl-bicyclo[2.2.1]hept-5-ene (**3**) with high stereoselectivity.[12] And the Diels-Alder reaction of ethyl 4,4,4-trichloro-2-butenoate (**2**) with cyclopentadiene also afforded *exo*-2-ethoxycarbonyl-*endo*-3-trichloro-methylbicyclo[2.2.1]hept-5-ene (**4**) predominantly.

The reaction of **1** with cyclopentadiene in the presence of a chiral Lewis acid: (*R*)-MS-free BINOL-Ti[13] gave the cycloaddition product **3** in a good yield with 40% e.e. The reaction of **2** with cyclopentadiene in the presence of (*R*)-MS-free BINOL-Ti was also tried to give the cycloaddition product **4** with 7.0% e.e.

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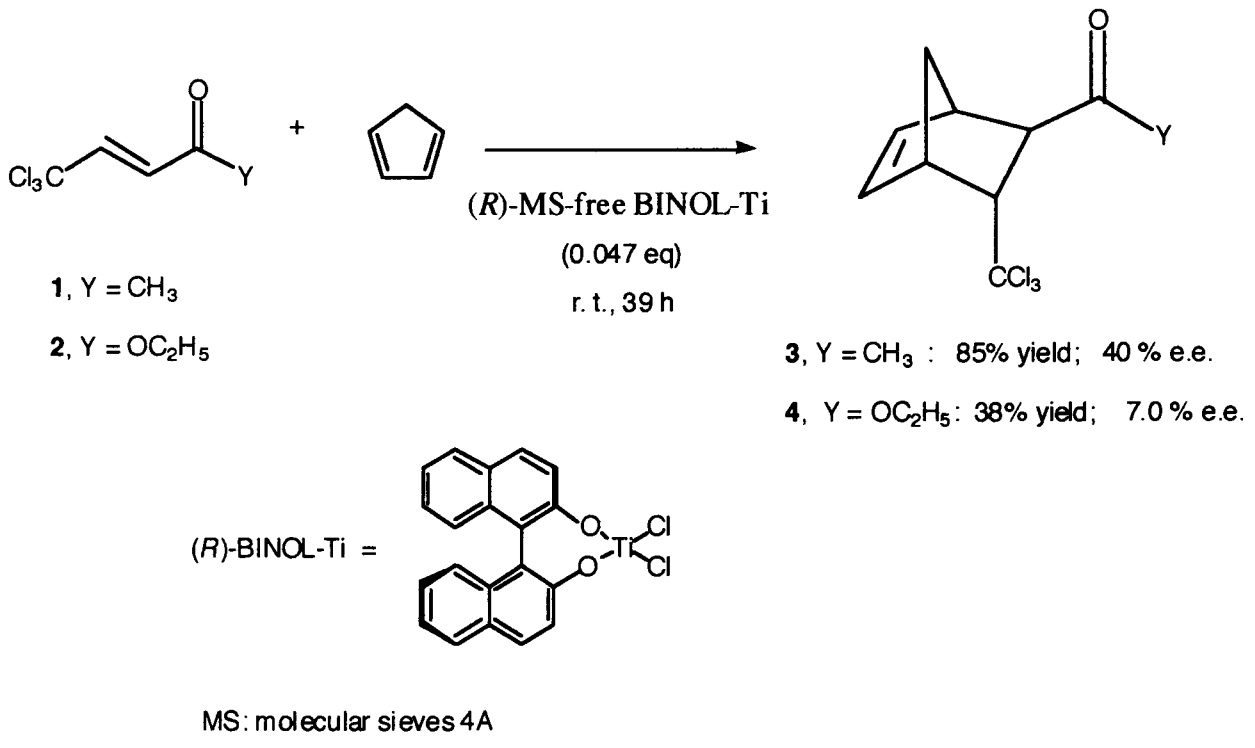

3. EXPERIMENTAL

All IR spectra were recorded on a JASCO FT/IR-5000 infrared spectrophotometer as films. ^{1}H NMR (200 MHz & 500 MHz) spectra and ^{13}C NMR spectra were recorded on a Varian Gemini-200 spectrometer or Varian Gemini-500 spectrometer using $CDCl_3$ ($CHCl_3$, δ = 7.26) as a solvent unless otherwise noted and chemical shifts are given in ppm relative to $CDCl_3$ (7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 Mz) spectra were recorded on a JEOL AL300 spectrometer. Splitting patterns are designated as br, s, d, t, and m; these symbols indicate broad, singlet, doublet, triplet, and multiplet, respectively. Elemental analysis were performed on Perkin Elmer 2400 series II CHNS/O analyser . For thin layer chromatography aluminum sheets Merck silica gel coated 60 F254 plates were used and the plates were visualized with UV light and phosphomolybdic acid (5% in EtOH). Merck silica gel 60 N (spherical, neutral) (40-50 μm) was used for the flash chromatography. The progress of the reaction was monitored by GC-MS Shimazu QP 5000 at 70 ev. Some stereoisomers of synthesized olefin were separated by preparative GC (Yanagimoto G-2800): column (6/5 mmϕ x 2 m) packed with 10% liq. phase Apieson Grease L supported on chromosorb W. Enantiomeric excess was determined by GC analysis: Shimazu GC-18A; column (0.25 mmϕ x 60 m) packed with CYCLODEXB at 170 °C, carrier gas; He (17 ml/sec).

All reactions were carried out in oven-dried, septum-capped flasks under N_2. All liquid reagents were transferred via oven dried syringes. Solvents and reagents were dried and distilled before use. THF was distilled from Na-benzophenone ketyl before use.

5,5,5-Trichloro-3-penten-2-one (1).[11]

In a typical experimental procedure, 1.30 g (9.38 mmol) of anhydrous potassium carbonate and 0.64 mL (6.25 mmol) of 2,4-pentanedione in 5 mL of anhydrous THF were placed in a 10 mL round bottomed flask. To this mixture, 0.73 mL (7.5 mmol) of chloral was added at room temperature via syringe under N_2 atmosphere. After 2 days, the reaction mixture was diluted with 10-15 mL of water and extracted with ether (20 mL x3). After removal of the solvent, the residue was subjected for column chromatography over silica gel using hexane and then hexane-ethyl acetate (10-12%) as an eluent to furnish the title compound as an yellow oil: the ketone **1** (0.867 g) (74%)

(*E*/*Z*=100/0); *Rf* 0.45 (hexane/EtOAc, 4/1); IR (neat) ν 3044, 3012, 1709, 1682, 1630, 1427, 1363, 1305, 1267, 1255, 1174, 1096, 1046, 1023, 1002, 965, 911, 853, 768, 729 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.37 (s, 3H), 6.59 (d, J = 15.0 Hz, 1H), 7.03 (d, J = 15.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.79, 92.58, 128.0, 144.3, 196.5.

Ethyl 4,4,4-Trichloro-2-butenoate (2).[11]

Potassium carbonate (43.7 g, 0.316 mol) was placed in a 300 ml round bottom flask, and dry THF (167 ml) was added. To a stirred mixture was added ethyl benzoylacetate (36.0 ml, 40.0 g, 0.208 mol) and chloral (25.0 ml, 38.0 g, 0.258 mol). The mixture was stirred at room temperature for 6 days, and then poured into water. The organic layer was extracted with ethyl acetate, and dried over $MgSO_4$. After removal of the solvent, the residue was distilled to give a colorless oil (36.7 g, 81.2%) at 85-86°C/10 mmHg; *Rf* 0.60 (hexane/EtOAc, 4/1); IR (neat) ν 2986 (C-C), 1729 (ester C=O), 1657 (C=C), 1468 (C=C), 1448 (C=C), 1396 (C=C), 1371 (C=C), 1309 , 1276 , 1183, 1096, 1033, 965, 866, 816, 774cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.33 (3H, t, J = 7.0 Hz, $OCH_2\underline{CH_3}$), 4.27 (2H, q, J = 7.0 Hz, $O\underline{CH_2}CH_3$), 6.39 (1H, d, J = 15.0 Hz, $Cl_3CCH{=}C\underline{H}$), 7.22 (1H, d, J = 15.0 Hz, $Cl_3CC\underline{H}{=}CH$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.13, 61.54, 92.16, 121.70, 146.01, 164.70.

Diisopropoxytitanium (IV) Dichloride.[14]

To a solution of titanium(IV) isopropoxide (4.5 ml, 15.2 mmol) in hexane (14 ml) was added titanium(IV) chloride (1.7 ml, 15.4 mmol) slowly at room temperature. On addition of titanium(IV) chloride, heat was evolved. After stirring for 10 min, the solution was allowed to stand for 6 h at room temperature, and the precipitate was then collected. The precipitate was washed with hexane (5 ml x 2) and recrystallized from hexane (5 ml). The wet powder (1.96 g) was dried under reduced pressure to give 1.93 g of white powder, which was dissolved in toluene (27.2 ml) to give a 0.3 M toluene solution.

(*R*)-MS-free BINOL-Ti.[13]

A 100 ml round-bottomed flask equipped with a magnetic stirring bar and nitrogen inlet was charged with powdered molecular sieves 4A (15.95 g), (*R*)-(+)-binaphthol (0.838 g, 2.93 mmol), and 52 ml of dichloromethane. After the mixture was stirred for 20 min at ambient temperature, the above solution (0.3 M, 10 ml) of diisopropoxytitanium dichloride in toluene was added into the resulting suspension in one portion. At this point, the reaction mixture became a red-brown suspension. After being stirred for 1.5 h at that temperature, the resultant suspension was transferred with syringe to a centrifugating tube capped with a rubber septum. By centrifugation at 4000 rpm for 20 min, molecular sieves were sedimented. The resultant supernatant was transferred with syringe to a 100 ml round-bottomed flask. The mixture was evaporated at 0°C to room temperature under reduced pressure to give a deep reddish residue. The resulting residue was suspended by adding 30 ml of hexane. The suspension was stirred for 20 min, and hexane was then decanted with a syringe. The resulting precipitate was vacuum-dried to give the binaphthol-titanium complex (0.67 g, 56.7% yield) and used as a catalyst.

***exo*-2-Acetyl-*endo*-3-trichloromethylbicyclo[2.2.1]hept-5-ene (3).**[12]

To a toluene solution (4 ml) of 5,5,5-trichloro-3-penten-2-one (**1**) (0.396 g, 2.11 mmol), the (*R*)-MS-free BINOL-Ti[13] (42 mg, 0.10 mmol, 0.047 eq) was added at room temperature. After 5 min, cyclopentadiene (0.33 ml, 3.98 mmol) was added in the reaction mixture. After being stirred for 38.5 h at room temperature, the resultant mixture was diluted with ether and brine. The organic layer was extracted three times with ether. The extract was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Separation of the residue by silica gel column chromatography (hexane/EtOAc,10/1) gave 0.456 g (85.3%) of **3** as an yellow oil : IR (neat) 2984, 2361, 1711, 1682, 1630, 1453, 1365, 1265, 1247, 1173 cm^{-1}; ^1H NMR (200 Mz, $CDCl_3$) δ 1.45 (dq, 1H, J = 8.9 Hz, J = 1.8 Hz, H_8), 1.73 (dbs, 1H, J = 8.8 Hz, H_7), 2.32 (s, 3H, *exo*$COCH_3$), 2.65 (dd, J = 5.6 Hz, J = 1.6 Hz, H_2), 2.95 (bs,

1H, H_1), 3.29 (bs, 1H, H_4), 4.02 (dd, 1H, J = 5.6 Hz, J = 3.0 Hz, H_3), 6.29 (t, 2H, H_5 and H_6, J = 13.4 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ 30.10, 47.28, 47.69, 48.44, 56.03, 63.35, 101.8, 135.4, 135.7, 207.1; $[\alpha]^{21.7}_D$ = -38.0 (c = 1.0, $CHCl_3$); e.e. = 40%.

***exo*-2-Ethoxycarbonyl-*endo*-3-trichloromethylbicyclo[2.2.1]hept-5-ene (4).**

To a toluene solution (4 ml) of ethyl 4,4,4-Trichloro-2-butenoate (0.447 g, 2.06 mmol), the (*R*)-MS-free BINOL-Ti[13] (39 mg, 0.097 mmol, 0.047 eq) was added at room temperature. After 5 min, cyclopentadiene (0.33 ml, 3.98 mmol) was added to the reaction mixture. After being stirred for 58 h at room temperature, the resultant mixture was diluted with ether and brine. The organic layer was extracted three times with ether. The extract was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Separation of the residue by silica gel column chromatography (hexane/EtOAc, 10/1) gave 0.223 g (38.1%) of **4** as a pale yellow oil: IR (neat) 2983, 2360, 1731, 1456, 1394, 1376, 1249, 1178 cm^{-1}; ^{1}H NMR (300 Mz, $CDCl_3$) δ 1.29 (t, 3H, J = 7.2 Hz, CH_3), 1.51 (dq, 1H, J = 8.7 Hz, J = 1.8 Hz, H_8), 1.89 (d, 1H, J = 8.7 Hz, H_7), 2.44 (dd, 1H, J = 6.0 Hz, J = 1.8 Hz, H_2), 3.04 (bs, 1H, H_1), 3.34 (bs, 1H, H_4), 3.93 (dd, 1H, J = 5.7 Hz, J = 3.0 Hz, H_3), 4.21 (dq, 2H, J = 7.0 Hz, J = 2.4 Hz, CH_2), 6.27 and 6.27 (dd, 2H, J = 15.9 Hz, J = 5.7 Hz, J = 3.0 Hz, H_5 and H_6); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.21, 47.38, 48.29, 48.66, 49.46, 61.10, 64.98, 101.6, 135.1, 135.9, 173.9. $[\alpha]^{22.6}_D$ = -20.6 (c 1.1, $CHCl_3$); e.e. = 7.0%.

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