Highly Enantioselective Copper-Bisoxazoline Catalyzed Allylic Oxidation of Cyclic olefins with tert-Butyl p-*Nitroperbenzoate*

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Experimental Section

General Methods. Melting points were determined using a LD Meltemp II and are uncorrected. Optical rotations were recorded using a Perkin-Elmer 241 MC Polarimeter in $CHCl_3$. The $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. The NMR spectra were recorded in $CDCl_3$ at 300 MHz with chloroform-d_1 (δ 7.26, ^1H; δ 77.23, ^{13}C) as internal standard. The mass spectra were obtained using chemical ionization(CI) or electron impact (EI). Enantiomeric excess of the samples were determined by HPLC using a Chiralpak® AD™ and/or Chiralcel® OD-H columns. All reactions were performed under an atmosphere of oxygen-free nitrogen in flame-dried glassware twice evacuated and filled with nitrogen. *t*-butyl-*p*-nitroperbenzoate was made according to the procedure below. Olefins were distilled from calcium hydride and passed through activated alumina immediately before use. Solvents and solutions were transferred by syringe-septum and cannula techniques. All solvents for the reactions were of reagent grade and were dried and distilled immediately before use as follows: acetonitrile dichloromethane, pyridine, and triethylamine from calcium hydride; tetrahydrofuran (THF) from sodium/benzophenone ketyl. The organic extracts were dried over anhydrous sodium sulfate. Evaporation of the solvents was performed in reduced pressure. Yields are given for isolated products showing one spot on a TLC plate and no impurities were detectable in the NMR spectrum. Starting materials and reagents were purchased from Aldrich. Purification by radial chromatography was performed using 1 and/or 2 mm plates loaded with 230 - 400 mesh PF_{254} gypsum-bound silica.

Procedure for the Synthesis of *tert*-Butyl *p*-nitroperbenzoate:

CAUTION! Peroxy compounds present a serious detonation hazard. While peresters are not nearly as reactive as peracids, use of a blast shield and a teflon coated spatula for solid materials are recommended. A teflon needle was used for transferring all *tert*-butyl hydroperoxide solutions.

***tert*-Butyl *p*-nitroperbenzoate**: To a clear solution of *p*-nitrobenzoyl chloride (3.2 g, 17.2 mmol) in CH_2Cl_2 (35 mL) at –20 ^oC under N_2 was added pyridine (1.7 mL, 20.0 mmol). The reaction solution was stirred for 10 min. *tert*-Butyl hydroperoxide (5-6 M in nonane, 3.5 mL, 20.0 mmol) was added dropwise to the solution at -20 ^oC, and the reaction was stirred for 4 h. The reaction solution was diluted with CH_2Cl_2 (20 mL), and washed with water. The organic layer was separated, dried over $MgSO_4$, and evaporation of the solvent afforded crude yellow solid residue. Purification using flash chromatography (2-10% EtOAc/hexanes) afforded the desired product as a light yellow solid (mp 75-77 °C, 3.9g, 98% yield). ^1H NMR (200 MHz, $CDCl_3$) δ 8.35 (d, 2H), 8.15 (d, 2H), 1.45 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.3, 150.1, 133.2, 130.4, 123.9, 84.8, 26.3.

General Procedure for Enantioselective Allylic Oxidation of cycloolefins with *t*-butyl-*p*-nitroperbenzoate in the presence of bisoxazoline ligand - $Cu(CH_3CN)_4PF_6$ A solution of the bisoxazoline ligand (0.13 mmol) and $Cu(CH_3CN)_4PF_6$ (0.048 g, 0.13 mmol) in distilled acetonitrile (3.0 mL) was stirred at rt for 2 h (until TLC indicated that there was no free ligand present). The solution was cooled to - 25 ºC to - 30 ºC, followed by the addition of cycloolefin (4.3 mmol) and *t*-butyl-*p*-nitroperbenzoate (0.203 g, 0.85 mmol) sequentially. The solution was degassed by nitrogen and stirred at - 20 ºC for 8 to 10 days typically. The reaction was monitored by TLC during this reaction period. After the reaction was judged to be complete, the acetonitrile was removed by *vacuo*, and the crude material was dissolved in 10% NH_4OH, extracted with ether and the organic layer was dried over Na_2SO_4. Radial chromatography using ethyl acetate/hexanes (2-10%) was used to purify the products.

2-Cyclopentenyl-p-nitrobenzoate. mp 81- 83 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (bt, 2H), 8.20 (bt, 2H), 6.21 (m, 1H), 5.99-5.94 (m, 2H), 2.65-2.58 (m, 1H), 2.48-2.36 (2H), 2.05-1.96 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 164.8, 150.4, 138.8, 136.3, 130.9, 128.9, 123.7, 82.6, 31.4, 30.0. MS (EI), m/z (%) 233 (10, $M^{\bullet+}$), 150 (100, $C_7H_4NO_3$), 104 (22), 84 (58), 67 (83, C_5H_7). Obtained as a white solid in 99% ee (entry 6, table 2). The optical purity was determined by HPLC using a Chiralcel OD-H column. [hexane/MTBE 90:10; flow rate 0.5 ml/min; t_R = 18.80 min (*R*), 21.20 min (*S*)]: (82% ee sample) $[\alpha]^{25}_D$ - 169.7° (c 0.38, $CHCl_3$) [lit.[1] 2-cyclopentenyl-1-benzoate (93% ee); $[\alpha]^{25}_D$ - 179.0° (c 0.37, $CHCl_3$)].

2-Cyclohexenyl-p-nitrobenzoate. mp 75 - 76 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (bt, 2H), 8.22 (bt, 2H), 6.06 (m, 1H), 5.84 (m, 1H), 5.55 (m, 1H), 2.13 - 1.74 (m, 6H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 168,9, 155.6, 136.4, 133.9, 130.9, 125.2, 123.7, 70.0, 28.5, 25.1, 19.0. MS (EI), m/z (%) 247 (18, $M^{\bullet+}$), 161 (56), 150 (54), 81 (100, C_6H_9). Obtained as a white solid in 96% ee (entry 2, table 1). The optical purity was determined by HPLC using a Chiralpak AD column. [heptane/2-propanol 99.5 :0.5; flow rate 0.5 ml/min; t_R = 20.42 min (*R*), 24.27 min (*S*)]: (78% ee) $[\alpha]^{25}_D$ - 134.7° (c 0.38, $CHCl_3$) [lit.[1] 2-cyclohexenyl-1-benzoate (71% ee sample); $[\alpha]^{25}_D$ - 118.0° (c 0.45, $CHCl_3$)].

2-Cycloheptenyl-p-nitrobenzoate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (m, 2H), 8.22 (m, 2H), 5.97 - 5.88 (m, 1H), 5.80 - 5.76 (bd, 1H), 5.70 - 5.68 (bd, 1H), 2.21 (m, 2H), 2.00 (m, 2H), 1.88 - 1.73 (m, 4H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 164.2, 151.0, 136.3, 132.9, 132.8, 130.9, 123.7, 76.1, 32.9, 28.7, 26.8, 26.6. MS (EI), m/z (%) 261 (7, $M^{\bullet+}$), 150 (100, $C_7H_4NO_3$), 94 (34, C_7H_{10}), 84 (67), 79 (58). Obtained as a light yellow oil in 99% ee (entry 3, table 3). The optical purity was determined by HPLC using a Chiralcel OD-H column. [heptane/2-propanol 99.5 :0.5; flow rate 0.5 ml/min; t_R = 21.65 min (*R*), 25.48 min (*S*)]: (99% ee sample) $[\alpha]^{25}_D$ - 63.1° (c 0.65, $CHCl_3$) [lit.[2] 2-cycloheptenyl-1-benzoate (82% ee) $[\alpha]^{25}_D$ - 38.2° (c 1, $CHCl_3$)].

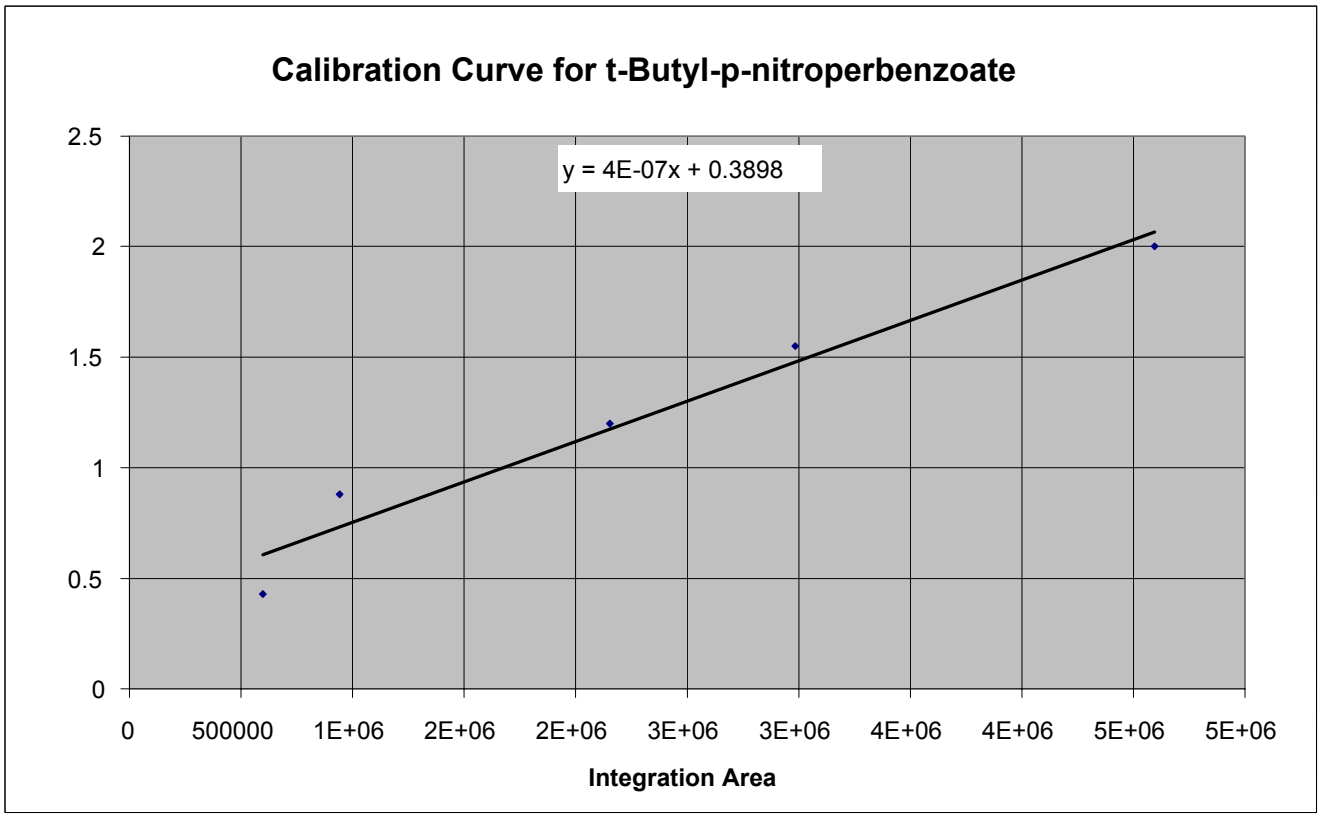
2,6 -Cyclooctadienyl-p-nitrobenzoate. mp 78 - 80 ° C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (bt, 2H), 8.22 (bt, 2H), 6.23 (m, 1H), 5.79 - 5.58 (m, 4H), 2.94 - 2.83 (m, 2H), 2.64 - 2.50 (m, 2H), 2.38 - 2.21 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.9, 130.9, 130.1, 128.6, 124.9, 123.7, ??, 74.4, 33.9, 28.8, 28.3, 28.0. MS (EI), m/z (%) 273 (7, $M^{\bullet+}$), 150 (100, $C_7H_4NO_3$), 104 (41, C_8H_8), 84 (51), 78 (33). It was obtained as a white solid in 94% ee (entry 1, table 4). The optical purity was determined by HPLC using a Chiralcel OD-H column. [heptane/2-propanol 99:1; flow rate 1.0 ml/min; t_R = 13.33 min (*S*), 16.09 min (*R*)]: (74% ee sample, entry 2) $[\alpha]^{25}_D$ + 18.5° (c 1, $CHCl_3$).

Procedure for Kinetic Resolution Experiment. Racemic sample of 2-cyclohexenyl-*p*-nitrobenzoate (0.05 g, 0.202 mmol) was added to a solution of the gem-dimethyl diphenyl bisoxazoline ligand (0.0303 mmol, 15 mol%)- $CuPF_6$ complex (0.0303 mmol) in acetonitrile (2.0 mL) followed by *t*-butyl-*p*-nitroperbenzoate (0.048 g, 0.202 mmol). The reaction mixture was stirred at - 20 °C for 11 d. The product was recovered after work-up in 91% yield following chromatography. No change in the chiral HPLC spectrum was observed. When 58% ee enriched 2-cyclohexenyl-*p*-nitrobenzoate was exposed to these conditions for 17 d, the material was recoved with 85% yield and was found to be further enriched to 84% ee.

Time Dependence for Reactivity and Selectivity. For the example in entry 3, table 1:

Days	Yield (%)	Selectivity (ee%)
1	29	70
3	41	70
5	44	70
7	43	73
9	44	74
11	45	77
13	54	88
15	55	95
17	55	95

Aliquots were withdrawn at the indicated times and the yields were estimated from an HPLC integration-concentration calibration curve. The selectivities were directly measured as before.



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