Enzyme-Catalyzed Ring-Opening Polymerization of ε-caprolactone using Alkyne Functionalized Initiators

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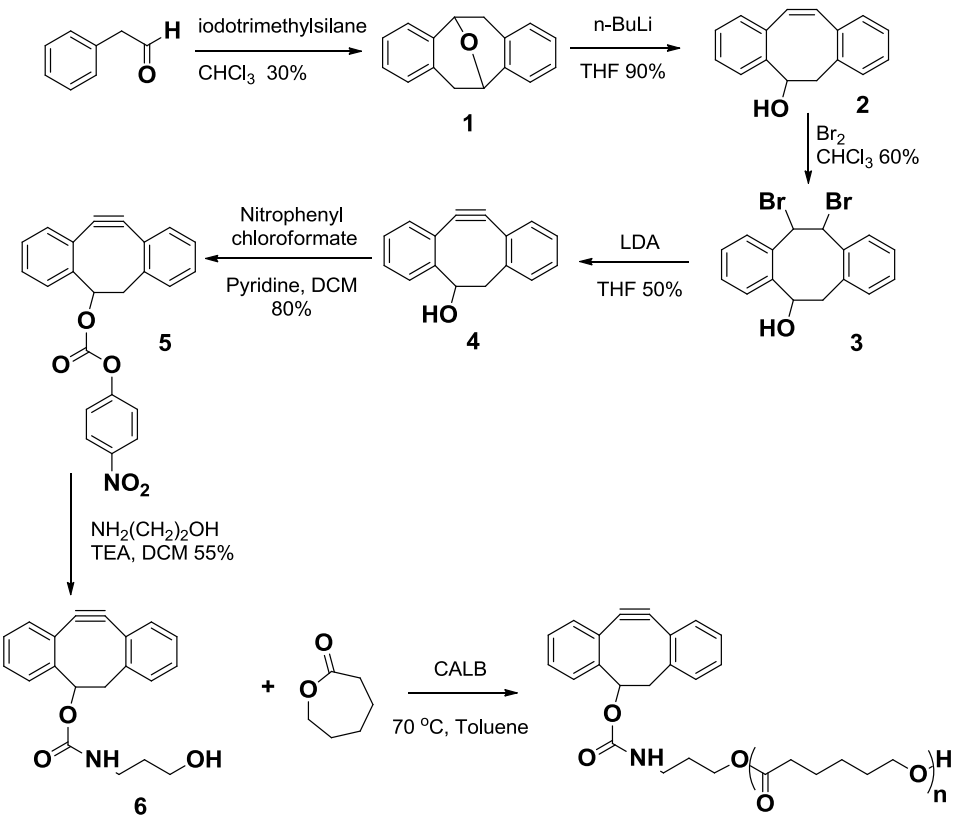
4-dibenzocyclooctynol (DIBO) was synthesized according to our work described previously but is included for simplicity and convenience[1].



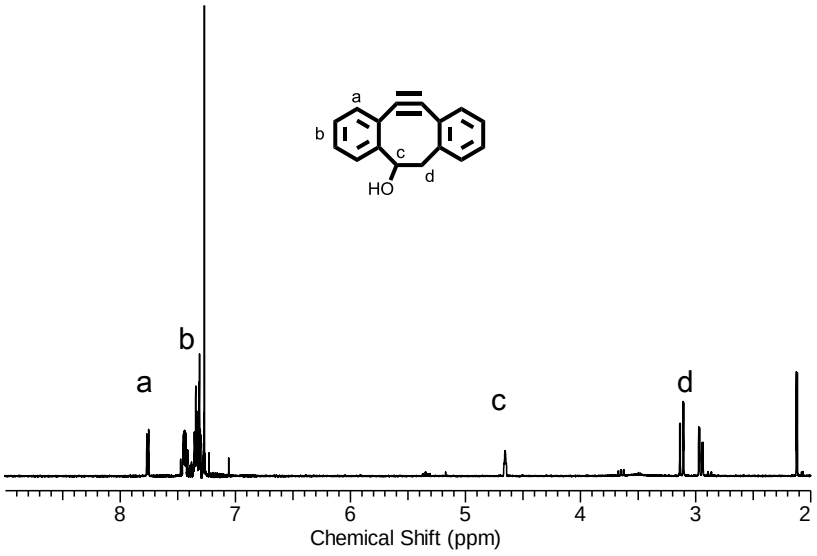
2,3:6,7-Dibenzo-9-oxabicyclo[3.3.l]nona-2,6-diene (1).
A 250 mL flask was flame dried and charged with argon. Phenylacetaldehyde (18.52 g, 0.154 mol) and 100 mL of chloroform (anhydrous) were then added via syringe. The reaction flask was cooled in an ice bath. Trimethylsilyl iodide (25 mL, 37.5 g, 0.188 mol) was added to the solution and the reaction was allowed to stand at 5 □C for 7 days. The reaction was monitored by TLC. After 7 days, sodium thiosulfate (1.0 M, 160 mL) and chloroform (200 mL) were added, and the mixture was stirred until the iodine color was discharged. The organic phase was sepa-

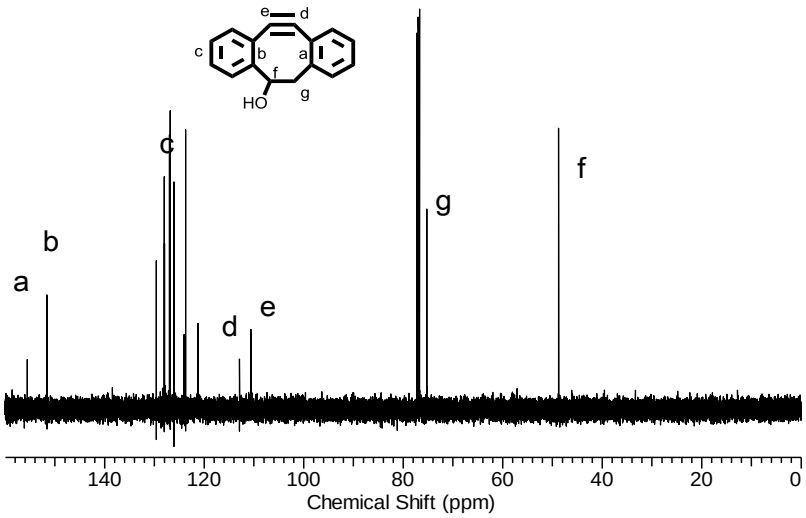
rated, dried (sodium sulfate), and concentrated in vacuum. Chromatography on silica gel eluting with chloroform yielded 6.1 g of the crystalline ether compound (35%).^{1}H NMR (300 MHz, CDC1$_3$) δ= 7.09 (m, 8H), 5.30(d, 2H, J=5.9 Hz, CH), 3.55(dd, 2H, J= 6.3, 16.2 Hz, CH_2), 2.75(d, 2H, J=16.4 Hz, CH_2); ^{13}C NMR (75MHz, CDC1$_3$) δ=137.98, 131.79, 129.28, 127.02, 126.16, 125.35, 69.75, 36.31. ESI MS m/z 245.1334 [M+Na$^+$]; calcd for $C_{16}H_{14}NaO^+$: 245.0942

3-Hydroxy-2',3',2",3"-tetramethox1y,-2 :5,6-dibenzocyclocta- 1,5,7-triene (2).
2,3:6,7-Dibenzo-9-oxabicyclo[3.3.l]nona-2,6-diene 1 (2.00 g, 5.84 mmol) in anhydrous THF (60 mL) was placed into a three-necked round bottom flask and cooled in an ice bath under argon. n-butyl lithium (4.92 mL, 2.5 M, 12.4 mmol) was added slowly via syringe. The reaction mixture was stirred at room temperature under argon for 4 h. The reaction was quenched by careful addition of water and extracted with 2X50mL $CHCl_3$. The combined organic phases were washed with 30 mL of brine, dried over Na2SO4, concentrated under vacuum and purified by column chromatography on silica gel CHC1$_3$ to yield 1.83 g of 3-Hydroxy-2',3',2",3"-tetramethox1y,-2 :5,6-dibenzocyclocta- 1,5,7-triene (90%).
^{1}H NMR (300 MHz, $CDCl_3$): δ=7.48 (m, 1 H), 7.10–7.30 (m, 7H), 6.86 (q, 2H, J=2.7, 12.0 Hz, CH), 5.31 (q, 1H, J=6.1, 10.0 Hz, CHOH), 3.45 (m, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): d=140.9, 136.9, 136.3, 134.6, 131.8, 131.7, 130.3, 129.9, 129.3, 128.8, 127.3, 127.2, 126.1, 125.9, 74.7, 42.7. ESI MS m/z 245.1277 [M+Na+]; calcd for $C_{16}H_{14}NaO$+: 245.0942.

11,12-Dibromo-5,6,11,12-tetrahydro-dibenzo[a,e]cycloocten-5-ol (3).
Bromine (0.51 mL, 10 mmol) was added dropwise to a stirred solution of 2 (2.22 g, 10 mmol) in $CHCl_3$ (50 mL). After stirring the mixture for 0.5 h, TLC analysis indicated completion of the reaction. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography over silica gel (2:1/1:2, v/v, hexanes/CH_2Cl_2) to yield 3 as a light-yellow oil (60%). ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.70–7.68 (2 H, aromatics), 7.39–6.88 (6 H, aromatics), 5.88 (d, 1H, J=5.4 Hz, CHBr), 5.47 (dd, 1H, J=3.6, 15.9 Hz, CHOH), 5.30 (d, 1H, J=5.4 Hz, CHBr), 3.60 (dd, 1H, J=3.7, 16.1 Hz, CH2), 2.87 (dd, 1H, J=3.7, 16.1 Hz, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ=142.2, 138.9, 138.2, 135.0, 134.3, 132.5, 132.3, 131.1, 128.8, 127.2, 124.7, 122.3, 80.3, 70.6, 60.1 36.0. ESI MS m/z 402.9749 [M+Na$^+$]; calcd for $C_{16}H_{14}Br_2NaO^+$:402.9309.

5,6-Dihydro-11,12-didehydro-dibenzo[a,e]cycloocten-5-ol (4).
Lithium diisopropylamide in tetrahydrofuran (2.0 M; 8.0 mL, 16 mmol) was added dropwise to a stirred solution of 3 (1.53 g, 4.0 mmol) in tetrahydrofuran (40mL) under an atmosphere of argon. The reaction mixture was stirred for 0.5 h, after which it was quenched by the dropwise addition of water (0.5 mL). The solvents were removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes/CH_2Cl_2 2:1/0:1, v/v) to yield 4 as a white amorphous solid (0.52 g, 60%).





Carbonic acid, 5,6-dihydro-11,12-didehydro-dibenzo[a,e]cyclo- octen-5-yl ester, 4-nitrophenyl ester (5). 4-Nitrophenyl chloroformate (0.4 g, 2 mmol) and pyridine (0.4 mL, 5 mmol) were added to a solution of 4 (0.22 g, 1 mmol) in CH_2Cl_2(30 mL). After being stirred for 4 h at room temperature, the mixture was washed with brine (210 mL) and the organic layer was dried (MgSO4). The solvents were evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate, 10:1, v/v) to afford 5 (0.34 g, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): d=8.23–8.18 (2H, aromatics), 7.56–7.54 (2H, aromatics), 7.46–7.18 (8H, aromatics), 5.52 (dd, J=3.9, 15.3 Hz, 1H, CHOH), 3.26 (dd, J=3.9, 15.3 Hz, 1H, CH2), 2.97 (dd, J=3.9, 15.3 Hz, 1H,CH2); ^{13}C NMR (75 MHz, $CDCl_3$): d=154.5, 150.7, 149.1, 148.7, 129.0,127.4, 127.3, 126.7, 126.5, 125.5, 125.2, 124.3, 124.0, 122.6, 122.4, 120.8, 120.6, 120.2, 112.2, 108.5, 80.6, 44.8; MALDI HRMS: m/z 408.0852 [M+Na+]; calcd for C_{23} H_{15} $NNaO_5$ +: 408.0842.

3-Hydroxypropyl-carbamic acid 5,6-dihydro-11,12-didehydro- dibenzo[a,e]cycloocten-5-yl ester (6): 3-Aminopropan-1-ol (15 mg, 0.2 mmol) and triethylamine (10 μL) were added to a stirred solution of 5 (38 mg, 0.1 mmol) in CH_2Cl_2 (15 mL). The reaction mixture was stirred at room temperature for 12 h, after which the solvents were evaporated under reduced pressure and the residue was purified by silica gel column chromatography (CH_2Cl_2 /CH_3 OH, 20:1, v/v) to afford 6 (55%).

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