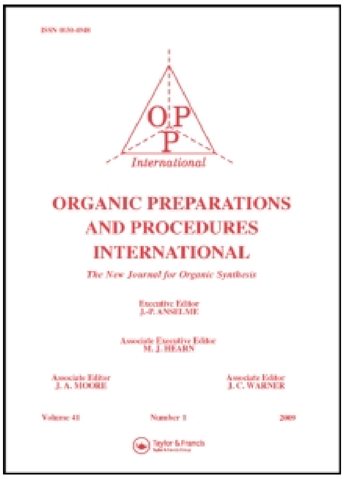

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SYNTHESIS OF DIBENZOHEPTALENE BISLACTONES *via* A DOUBLE INTRAMOLECULAR CANNIZZARO REACTION

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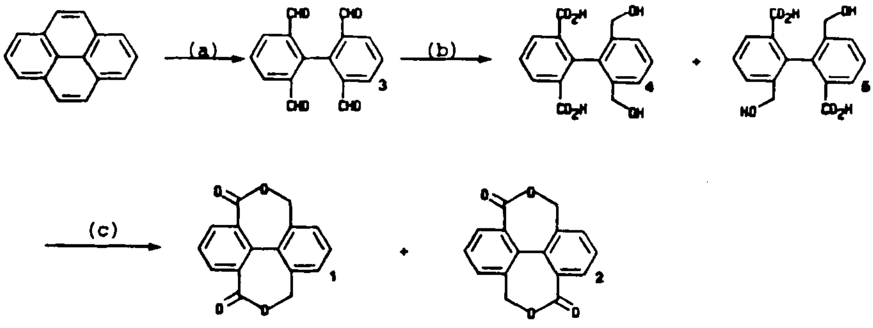
As parts of programs to produce novel difunctional compounds for condensation polymerization and remote catalysis studies, two isomeric bislactones: 4,6,10,12-tetrahydro-4,12-dioxo-5,11-dioxadibenzo[*ef*,*kl*] heptalene (1) and 4,6,10,12-tetrahydro-4,10-dioxo-5,11-dioxadibenzo [*ef*,*kl*] heptalene (2) were synthesized. These molecules are examples of well studied doubly bridged biphenyls.[1] However, 1 and 2 are unusual because the bridging groups are unsymmetrical. Although not obvious from planar representations, bislactones 1 and 2 are chiral, atropisomeric molecules. The racemization barriers of these molecules have been studied by variable



a) 1. O_3 2. KI, AcOH b) 1. NaOH 2. HCl c) H^+, $-H_2O$

temperature ^1H NMR, and their crystal structures have been determined by X-ray analysis.[2]

The scheme depicts the synthesis of the bislactones. 1,1'-Biphenyl-2-2',6,6'-tetracarboxaldehyde (3) was prepared by adaptation of literature procedures,[3] but on a larger scale. Typically, 20 g of pyrene in dry methylene chloride was treated with ozone at -78°, until a blue color persisted in the solution (approximately 5 hrs). Reductive workup with Kl/CH_3CO_2H produced 3 in 40-60% yields. The highest yields were obtained by careful temperature control during ozonolysis.

The key step in the synthesis of 1 and 2 was the double intramolecular Cannizzaro reaction of tetraaldehyde 3. There have been several previous reports of intramolecular Cannizzaro reactions with dialdehydes, notably those on phthaladehyle,[4] and on 2,2-biphenyl-dicarboxaldehyde[5] and its derivatives.[6] However, to our knowledge, no examples of such reactions on tetraaldehydes have been reported. When 3 was stirred at room temperature with excess of 6N aqueous NaOH, an immediate, mildly exothermic reaction occurred, and all of the tetraaldehyde dissolved. A mixture of hydroxy acids 4 and 5 was obtained in 65% yield after acidification of the reaction solution and recrystallization of the resulting precipitate. Separation and complete characterization of 4 and 5 was not attempted because of the tendency of the acids to cyclize partially to the lactones. The mixture was cyclized to 1 and 2 by the azeotropic removal of water in the presence of an acid catalyst in toluene. The resulting bislactones were separated by preparative HPLC,[7] eventually producing 41% of 1 and 24% of 2.

EXPERIMENTAL SECTION

Melting points were measured in open capillary tubes, and are uncorrected. IR and UV spectra were taken on Perkin-Elmer model 298 and 552 spectrophotometers, respectively. NMR spectra were obtained on a Varian XL-200 spectrometer, operating at 200 MHz for ^1H and 25.37 MHz for ^{13}C spectra.

Mass spectra were obtained on a Hewlett-Packard model 5987 integrated GC/MS; ionization was by 70 eV electron impact. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. TLC was done on pre-coated silica gel plates obtained from Eastman Kodak Co. Plates were developed in closed chambers which were presaturated with the appropriate solvent. The plates were visualized under ultraviolet light. Preparative HPLC was done on a Waters Prep LC 500A system, using a PrePak column (57 mm X 30 cm silica gel). Amberlyst-15 strongly acidic ion exchange resin was obtained from the Rohm and Haas Company.

2,2'-Bishydroxymethyl-1,1'-biphenyl-6,6'-dicarboxylic Acid (4) and 2,6-Bishydroxymethyl-1,1'-biphenyl-2',6'-dicarboxylic Acid (5).- The tetra-aldehyde 3 (25.8 g, 96.9 mmol) was dissolved in 400 mL of 6 N aqueoue NaOH at 25°. The solution warmed with the heat of reaction. After 30 min., concentrated HCl was added dropwise to the stirred solution until the pH of the mixture reached 2 (pH paper). The cream colored precipitate was collected and recrystallized from boiling water. After drying in vacuo over P_2O_5 overnight, 18.7 g (64%) of a tan solid was obtained, mp. 204-206°. TLC (ethanol) produced two spots, R_f = 0.56 and 0.36. Equivalent weight by titration 161 (calcd. 151). IR (KBr): 3280 s, br (OH), 1675 s (acid C=O) cm^{-1}. ^1H NMR, $(CD_3)_2SO$: δ4.13 (s, 4H, CH_2), 7.36 (m, 2H), 7.55 (m, 2H), 7.90 (m, 2H) (aromatic H).

4,6,10,12-Tetrahydro-4,12-dioxo-5,11-dioxadibenzo[*ef*,*kl*]heptalene (1) and 4,6,10,12-Tetrahydro-4,10-dioxo-5,11-dioxadibenzo[*ef*,*kl*]heptalene (2).- The mixture of bishydroxyacids 4 and 5 (3.90 g, 12.9 mmol) was placed in a 500 mL round-bottomed flask with 200 mL of toluene and 1.2 g (0.23 eq) of Amberlyst-15 resin. The flask was fitted with a Dean-Stark trap and condenser, and water was removed as an azeotrope with toluene. After 48 hrs, the solution was filtered hot, and the solvent was removed to give 3.40 g (98%) of a crude solid. TLC [40% Hexanes/60% ethyl acetate (v/v)] produced two spots, R_f = 0.62 and 0.42. The crude solid was dissolved in a minimum amount of dichloromethane and separated by preparative HPLC using 50% hexanes/50% ethyl acetate (v/v) as eluent.[7] Two fractions were collected, and after solvent was removed at reduced pressure, the residues were recrystallized from acetonitrile/toluene to give two white solids.

<u>1</u> (major isomer, eluted first): yield 1.41 g (41%), mp. 284-287° IR (KBr): 1705 s (lactone C=O), cm^{-1}. MS: 266 (100%, M^+, 237 (15%), 207 (17%), 193 (27%), 165 (32%), 151 m/e (15%). ^1H NMR ($(CD_3)_2SO$): δ 5.12 (AB quartet, 4H, $_{AB}20.3$ Hz, J_{AB} = 12.4 Hz, CH_2), 7.60 (t, 1H, J = 7.0 Hz, C^8H), 7.76 (m, 3H, C^1H-C^3H), 8.09 (d, 2H, J = 7.0 Hz, C^7H, C^9H). ^{13}C NMR ($CDCl_3$): δ 69.6 (CH_2), [129.6, 130.6, 132.0, 132.2, 135.6, 135.8, 136.0] (arom. C), 169.5 (C=O). UV (CH_3CN): 303 sh (ε = 12600), 208 nm (ε = 42000).

<u>Anal</u>. Calcd. for $C_{16}H_{10}O_4$: C, 72.18, H, 3.79

Found: C, 71.84, H, 3.73

<u>2</u> (minor isomer, eluted last): yield 0.80 g (24%), mp. 256-258°. IR (KBr): 1720 s (C=O) cm^{-1}. MS: 266 (100%, M^+), 237 (20%), 193 (14%), 180 (27%), 165 (43%), 152 m/e (13%). ^1H NMR ($(CD_3)_2SO$): δ 5.12 (AB quartet, 4H, δ_{AB} = 53.5 Hz, J_{AB} = 12.5 Hz, CH_2), 7.74 (dd, 2H, $J \simeq 7.0$ Hz, C^2H, C^8H), 7.96 (m, 4H, C^1H, , C^3H, C^7H, C^9H). ^{13}C NMR ($CDCl_3$), [130.0, 132.4, 133.0, 133.2, 134.3, 135.3] (arom. C), 169.5 (C=O). UV (CH_3CN): 295 sh (ε = 3530), 248 sh (ε = 12100), 212 nm (ε = 44500).

<u>Anal</u>. Calcd. for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79

Found: C, 71.89; H, 3.78

<u>Acknowledgements</u>.- We thank Dr. Herbert Schwartz for assistance with the NMR spectra, Mr. Saveley Goldin for obtaining the mass spectra, and Dr. Sidney Archer for the use of his chromatograph. The NMR spectrometer used in this work was purchased with funds provided by the National Science Foundation, and by the Camille and Henry Dreyfus Foundation.

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7. Attempts to separate 1 and 2 by flash chromatography and by dry column chromatography failed, probably because of the tendency of these compounds to tail on silica gel, as observed during preparative HPLC.

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