Synthesis of a Water-Soluble Derivative of Cyclohexatriacontane-1,2,13,14,25,26-hexone[1]

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Received February 12, 1986

Cyclotrimerization of cyclododecyne and cyclopentadecyne to the corresponding benzene derivatives is catalyzed by $Co_2(CO)_8$ and by $TiCl_3$. Ozonolysis of these aromatic compounds, followed by reductive workup and treatment with derivatives of *o*-phenylenediamine gives in ~3% yield macrocyclic ring compounds: cyclohexatriaconta[1,2,13,14,25,26-*b*,*b*',*b*'']trisquinoxaline (**9**), cyclohexatriaconta[1,2,13,14,25,26-*b*,*b*',*b*'']tris(1*H*,3*H*-2-oxoimidazo[4,5-*g*]quinoxaline-1,3-di-α-acetate) (**17**), and cyclopentatetraconta[1,2,16,17,31,32-*b*,*b*',*b*'']trisquinoxaline (**10**). These compounds do not show shape selectivity in facilitated transport of representative hydrocarbons in water.

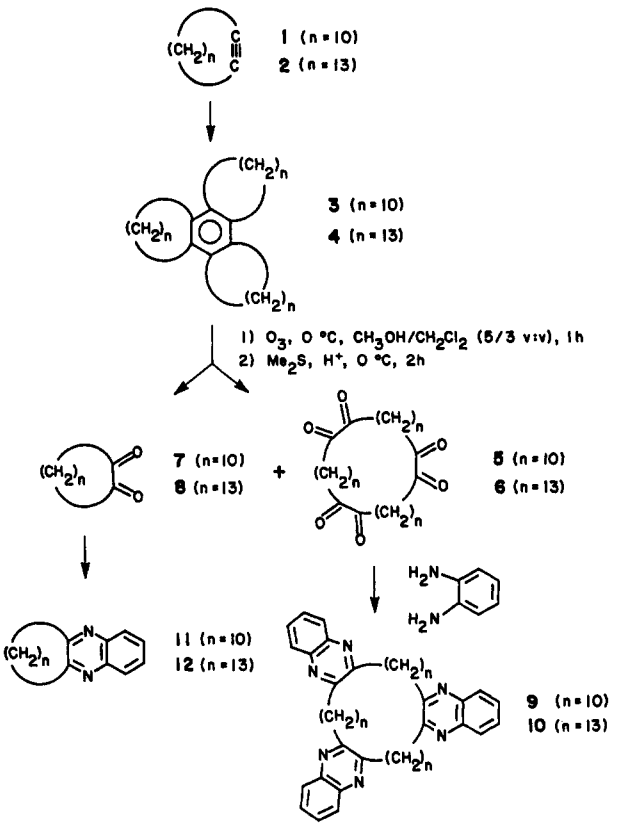
This paper describes straightforward but low-yield syntheses of tris(symmetrically functionalized)cyclohexatriacontanes and cyclopentatetracontanes from readily available starting materials. We prepared these compounds to test their activity as size-selective carriers for small organic molecules: that is, as hydrophobic "hosts" or structured micelles.[3-6] They do not, in the event, seem to show size selectivity in passive facilitated transport of hydrocarbons in U-tube experiments, presumably because their flexibility allows the C_{36} or C_{45} carbocyclic rings to collapse in aqueous solution: good performance in a host molecule seems to require a rigid, open cavity.[7-10] Nonetheless, the compounds are unusual representatives of the class of large-ring macrocycles, and the synthetic routes developed to them are practical, if low in overall yield.

The syntheses proceed from the cyclic acetylenes cyclododecyne (**1**) and cyclopentadecyne (**2**) via a sequence involving a cyclotrimerization reaction to yield the benzene derivatives **3** or **4** (Scheme I). These compounds are treated with ozone, and the resulting tris(α-diketones) **5** and **6** are generated as components in a complex mixture of products. Rather than attempting to isolate these unstable compounds, we converted them to water-soluble quinoxalines by acid-catalyzed reaction with *o*-phenylenediamines.

Results

Cyclic Acetylenes. A number of syntheses of cyclic acetylenes have been developed,[11-15] but those proceeding in best yields require the relatively inaccessible α-diketones as starting materials.[16-21] We prepared **1** and **2** from the corresponding monoketones by initial conversion to the corresponding 1,1-dichloride by treatment with phosphorus pentachloride[22] followed by dehydrohalogenation with potassium *tert*-butoxide in Me_2SO.[23] Compound **1** was prepared in 60% overall yield (mixed with 20% of the corresponding allene); **2** was obtained in 79% yield, with no contamination by allene. Cyclotridecyne was prepared

Scheme I. Syntheses of Macrocyclic Trisquinoxalines



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0022-3263/86/1951-3257$01.50/0

Table I. Relative Rates of Passage of Hydrocarbons through an Aqueous Barrier[a]

compound	additive		
	none	17	19
cyclopentane	1.0	1.4	1.2
n-pentane	0.3	0.6	0.5
toluene	1.4	3.5	2.8
p-xylene	0.35	1.5	1.0
naphthalene	0.2	1.5	0.7

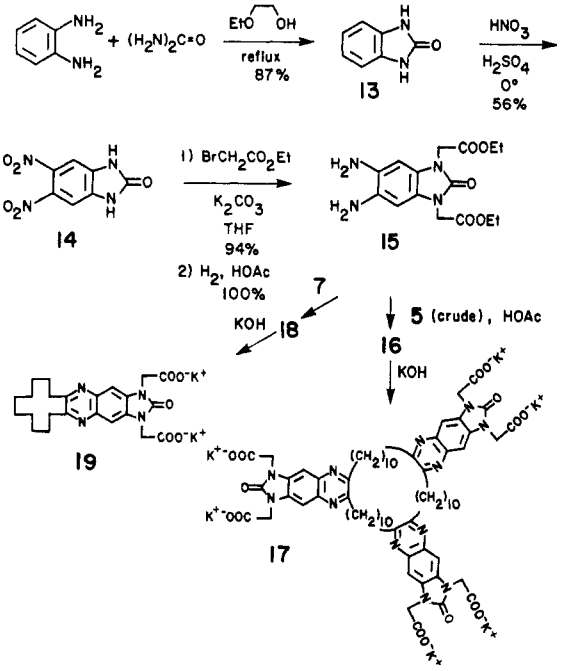
[a] All rates of transport are relative to cyclopentane in the absence of possible carriers.

by the procedure of Noyori.[24]

Cyclotrimerizations. Of the approximately ten catalysts reported to be active in cyclotrimerization of acetylenes that were examined in this work,[25-39] the two giving the best yields of **3** from **1** were $Co_2(CO)_8$ (85%) and $TiCl_3$ (92%). A mixture of **1** and the corresponding cyclic allene gave 74% of **3** based on **1**.

Ozonolyses. Optimization of the ozonolysis reaction was difficult: the tris-α-diketones desired products (**5** and **6**) were unstable compounds produced in low yield and were not readily distinguished from the monocyclic α-diketones (**7** and **8**). Our strategy in developing these reactions was to convert all of the α-diketone moieties present in the reaction mixture to a stable derivative. After examination of a number of derivatizing reactions, we settled on conversion to quinoxaline by acid-catalyzed reaction with *o*-phenylenediamine.[40] This reaction proceeds in quantitative yield under mild conditions and yields volatile, easily analyzed products (**11**, **12**). We optimized ozonolysis conditions by maximizing the yield of **11** from **3** (optimized yield = 12%). We assumed that the yield of **9** and **10** followed a parallel course (optimized yield of **9** from **3** = 3.6%). The optimum reaction solvent comprised a protic solvent (methanol) containing large quantities of methylene chloride to dissolve the cycloalkyne cyclotrimer. The ozonolysis was best performed at 0 °C in the presence of a trace of methanesulfonic acid to catalyze formation of the hydroperoxymethoxy ketal.[41] The amount of ozone required for complete ozonolysis of starting **3** was slightly less than 2 equiv. Varying reaction times, reaction temperatures, solvent polarity, solvent acidity, hydrogen donor capacity of the solvent, and solvent composition (when mixed solvent systems were used) did not increase the yield. The reaction was worked up by reduction with Me_2S;[41] use of phosphites, phosphines, and related species does not increase the yield.

Scheme II. Synthesis of a Water-Soluble Macrocyclic Trisquinoxaline



Compound **9** was isolated as a solid with correct elemental analysis. Its molecular weight was estimated as 800 and 840 (theory 805) in two experiments using freezing point depression in camphor.[42] It had a ^1H NMR spectrum indistinguishable from that of **11** and a ^{13}C NMR spectrum consistent with the assigned structure.

Preparation of a Water-Soluble Derivative of 5. We prepared a water-soluble derivative of **5** by substituting the functionalized *o*-phenylenediamine **15** for unsubstituted *o*-phenylenediamine (Scheme II). The yield of the corresponding trisquinazoline hexaester from **5** was high; the overall yield from **3** to **16** was 3.4%. Saponification of **16** yielded the hexaacid **17** with adequate water solubility (>10 g/L at 25 °C for both **17** and **19**) for facilitated transport experiments.

Facilitated Transport. We measured the relative rates of transport of several hydrocarbons through an aqueous barrier containing added **17** and **19** by using standard U-tube techniques (Table I). It is evident that **17** shows no significant selectivity for *n*-pentane. This series suggests, if anything, a small, similar, nonspecific facilitation of transport of aromatic molecules by both **17** and **19**.

Experimental Section

General Methods. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian T-60 spectrophotometer; carbon-13 NMR spectra were recorded on a Bruker HFX-90 spectrophotomer. Hydrogenations were performed on a Parr catalytic hydrogenation apparatus. Satisfactory elemental analyses were obtained for all compounds indicated by "Anal".

Cyclododecanone, *o*-phenylenediamine, ethyl bromoacetate, and phosphorus pentachloride were from Aldrich. Cyclopentadecanone was purchased from the Columbia Organic

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Chemical Co. Cyclododecane was purchased from Chemical Samples Co. Potassium *tert*-butoxide was purchased from MSA Research Corp. Platinum oxide and 10% palladium on carbon were purchased from Englehard Industries. All solvents were reagent grade and were used without further purification unless otherwise noted.

1,1-Dichlorocyclododecane. Cyclododecanone (91 g, 0.50 mol) was dissolved in 450 mL of benzene or methylene chloride. The solution was cooled in an ice bath to 5 °C and phosphorus pentachloride (156 g, 0.70 mol) was added in one portion with stirring.[43] Stirring was continued at 0 °C for 4 h and then the reaction was allowed to warm to room temperature and stirred for an additional 24 h.[44] The reaction was cooled to about 5 °C in an ice bath again and water (500 mL) was added dropwise with vigorous stirring. CAUTION: *The hydrolysis of the phosphorus oxychloride and excess phosphorus pentachloride is very exothermic.* After addition of the water was complete, the mixture was stirred at 0 °C for 1 h and then allowed to warm to ambient temperature. The mixture was stirred for an additional 24 h and the organic layer was separated and washed 3 times with 250-mL portions of water. The organic layer was dried ($MgSO_4$) and the solvent was removed at reduced pressure on a rotary evaporator at 25 °C or less. 1,1-Dichlorocyclododecane was obtained as a pale yellow oil, yield 116 g (98%), and was used without further purification. The IR spectrum showed only a very small peak (greater than 99% transmittance) in the carbonyl region.

Cyclododecyne (1). Dimethyl sulfoxide (1 L) was degassed by bubbling a slow stream of prepurified nitrogen through the stirred liquid at ambient temperature for 30 min. Potassium *tert*-butoxide (185 g, 1.65 mol) was added. The mixture was stirred until most of the potassium *tert*-butoxide had dissolved. The solution was cooled in a water bath (20 °C) and 1,1-dichlorocyclododecane was added in one portion with vigorous stirring. The internal reaction temperature did not exceed 50 °C. The dark red solution which resulted was stirred at ambient temperature for 24 h. A mixture of ice and water (500 mL) was added and stirring was continued for 1 h at which time hexane (500 mL) was added. The organic layer was separated, washed twice with 250-mL portions of water, and dried ($MgSO_4$). The hexane was removed at reduced pressure on a rotary evaporator to yield a mixture of cyclododecyne and 1,2-cyclododecadiene. GLPC analysis showed these two compounds to be the only major components (>95%) of the mixture. The NMR spectrum was used to determine the relative amounts of allene and acetylene. The ratio of allene to alkyne was found to be 1:3. Distillation of the oil, bp 119 °C/14 torr (lit.[21] bp 106–109 °C/11 torr) afforded a mixture of cyclododecyne and cyclododeca-1,2-diene in the same ratio as previously and in 81% yield (66 g). GLPC analysis showed the product consisted of greater than 99.5% of the allene–alkyne mixture.

Cyclopentadecyne (2). 1,1-Dichlorocyclopentadecane was prepared from cyclopentadecanone (26.4 g, 0.118 mol) in 99% yield in the same manner used for the preparation of 1,1-dichlorocyclododecane. Cyclopentadecyne was prepared in the same way as cyclododecyne from 1,1-dichlorocyclopentadecane in 79% yield after distillation (bp 168 °C/19 torr; lit.[18] bp 106–108 °C/1 torr) via a potassium *tert*-butoxide elimination isomerization. NMR analysis showed no 1,2-cyclopentedecadiene present in the product.

Tris(decamethylene)benzene (3) (Cyclododecyne Cyclotrimer). Dry, oxygen-free heptane (400 mL, distilled from sodium benzophenone dianion) was cooled to 0 °C in an ice bath with stirring. Triisobutylaluminum (13 mL of a 25% solution in heptane) and titanium tetrachloride (1.3 mL, 2.2 g, 11 mmol) were added via syringe to the cooled, stirred liquid. A mixture of cyclododecyne and cyclododeca-1,2-diene, prepared as described previously (82 g, 0.50 mol), was added over a period of time so that the temperature was kept below +20 °C. The mixture was allowed to warm to ambient temperature and stirred for 24 h under a positive pressure of prepurified nitrogen. The reaction was quenched with 50 mL of methanol and poured into 500 mL of water. Methylene chloride was added to dissolve any **3** which precipitated. The organic layer was separated, washed twice with 250-mL portions of water, and dried over anhydrous $MgSO_4$. The heptane and methylene chloride were removed at reduced pressure on a rotary evaporator and the residual solid was recrystallized from methyl ethyl ketone to yield 45 g (74%) of **3**; mp 166.5–167.0 °C (lit.[49] mp 164–165 °C). The yield was based on a starting composition of **1** that was 74% alkyne and 26% allene. The mother liquors from the recrystallizations were concentrated and distilled to yield cyclododeca-1,2-diene (19 g, 90%) which was present in the starting **1**. Compound **3**, had the following: NMR ($CDCl_3$) δ 1.57 (broad, 48 h) and 2.60 (broad, 12 H); IR (KBr) 2930 (vs), 2860 (s), 1610 (w), 1460 (m), 1440 (m), 1340 (m), 725 (m) cm^{-1}.

Tris(tridecamethylene)benzene (4) (Cyclopentadecyne Cyclotrimer). Cyclopentadecyne was cyclotrimerized in a manner analogous to that for the cyclotrimerization of cyclododecyne to yield **4** in 72% yield which had the following: mp 157.0–8.5 °C; NMR (CCl_4) δ 1.42 (broad, 66 H), 2.44 (broad, 12 H); IR ($CDCl_3$) 2930 (vs), 2860 (s), 1455 (s), 1350 (m) cm^{-1}. Anal.

2,3-Decamethylenequinoxaline (11). Cyclododecane-1,2-dione[45] (1.00 g, 5.1 mmol) and *o*-phenylenediamine (0.55 g, 5.1 mmol) were dissolved in 10 mL of absolute ethanol. Concentrated hydrochloric acid (0.1 mL) was added and the mixture was refluxed for 12 h. Water (4 mL) was added to the hot solution and the mixture was cooled to 5 °C. The solid which crystallized was collected by filtration and dried to yield 1.33 g (100%) of 2,3-decamethylenequinoxaline. Recrystallization from ethanol afforded an analytical sample that had the following: mp 84–85 °C; NMR ($CDCl_3$) δ 1.45 and 1.95 (br, 16 H total), 2.99 (t, 4 H, J = 7 Hz), 7.70 (symmetrical m, 4 H); IR ($CDCl_3$) 3060 (w), 2930 (s), 2860 (s), 1480 (m), 1465 (m), 1445 (m), 1395 (m), 1350 (m), 1205 (m), 1120 (m) cm^{-1}; UV λ_{max} 241 nm (ϵ 30 000), 321 nm (ϵ 9600). Anal.

Benzimidazolone (13) was prepared by the method of Smith.[46]

5,6-Dinitrobenzimidazolone (14) was prepared in a variation of the method of Efros and El'tsov.[47] Benzimidazolone (67 g, 0.50 mol) was dissolved in 250 mL of concentrated sulfuric acid. The dark solution was cooled to 5 °C in an ice bath and 90% nitric acid (white fuming, 67 mL) in 220 mL of sulfuric acid was added dropwise to the cooled, stirred solution over an 8-h period. The reaction temperature was not allowed to go above 10 °C during the addition. Immediately after the addition of the nitric acid was complete the cold solution was poured onto 3 kg of ice. The yellow solid that precipitated was collected via filtration and washed thoroughly 4 times with 1-L portions of cold water. Drying yielded 63 g (56%) of 5,6-dinitrobenzimidazolone that was recrystallized from 60% aqueous acetone to give crystals that melted at 344 °C dec (lit.[47] mp >315 °C).

Diethyl 5,6-Dinitrobenzimidazolone-1,3-di-α-acetate. 5,6-Dinitrobenzimidazolone (11.2 g, 0.050 mol) was dissolved in 500 mL of THF. Potassium carbonate (13.8 g, 0.20 mol) was added with vigorous stirring. Ethyl bromoacetate (20.0 g, 0.12 mol) was added and the mixture was refluxed for 48 h. The resulting mixture was filtered while hot and the solution was concentrated on a rotary evaporator at reduced pressure. Ethanol (95%, 100 mL) was added and the resulting crystals were filtered and air-dried to yield 18.6 g (94%) of diethyl 5,6-dinitrobenzimidazolone-1,3-di-α-acetate which the following: mp 201–202 °C; NMR ($CDCl_3$) δ 1.32 (t, 6 H, J = 8 Hz), 4.25 (q, 4 H, J = 8 Hz),, 4.97 (s, 4 H), 7.66 (s, 2 H); IR ($CDCl_3$) 1740 (s), 1620 (w), 1540 (s), 1510 (m), 1410 (m), 1340 (s), 1205 (s) cm^{-1}. Anal.

Diethyl 5,6-Diaminobenzimidazolone-1,3-di-α-acetate (15). The corresponding nitro compound (1.98 g, 5.00 mmol) was dissolved in 60 mL of warm (60 °C) acetic acid. Catalyst (10% Pd on C, 0.020 g) was added and the warm mixture was hydrogenated at 45 psi of H_2 (uptake = 30 mmol of H_2). The acetic

(43) Best results are obtained with overhead stirring but a Teflon-coated magnetic stirring bar may be used if a powerful magnetic stirrer (e.g., Cole-Parmer 6 × 6) is used.

(44) At this point the solution should show virtually no carbonyl peak in the IR. Additional phosphorus pentachloride may be added if necessary to effect total conversion.

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acid solution of 15 thus prepared was used without isolation or further purification after removal of the catalyst via filtration.

Diethyl 1*H*,3*H*-2-Oxoimidazo[4,5-*g*]cyclododeca[*b*]quinoxaline-1,3-di-α-acetate (18). A solution of 15 (5.00 mmol) in 60 mL of acetic acid prepared as described previously was filtered into a flask containing 0.98 g (5.00 mmol) of cyclododecane-1,2-dione. The resulting solution was stirred at ambient temperature for 1 h and then refluxed for 1 h. The acetic acid was removed at reduced pressure on a rotary evaporator and the resulting solid was recrystallized from MEK/ethanol to yield 2.4 g (96%) of 18 with the following: mp 198–199 °C; NMR ($CDCl_3$) δ 1.30 (t, J = 7 Hz), 1.50 and 2.13 (broad, 22 H), 3.05 (t, 4 H, J = 7 Hz), 4.24 (t, 4 H, J = 7 Hz), 4.74 (s, 4 H), 7.40 (s, 2 H); IR ($CDCl_3$) 2930 (s), 2850 (m), 1725 (vs), 1600 (w), 1485 (m), 1430 (m), 1350 (m), 1205 (s), 1195 (s), 1015 (m) cm^{-1}. Anal.

1*H*,3*H*-2-Oxoimidazo[4,5-*g*]cyclododeca[*b*]quinoxaline-1,3-di-α-acetic Acid (19). Potassium hydroxide (1.9 g, 30 mmol) and 18 (1.50 g, 3.00 mmol) were refluxed in 100 mL of water for 24 h with stirring. The solution of 19 thus formed was filtered while hot and excess HCl (5 mL) was added. The mixture was allowed to cool to ambient temperature and the solid material was collected via filtration and air-dried to yield 1.07 g (2.44 mmol, 82%) of 19 with the following: mp >340 °C; NMR (Me_2SO-d_6/$CDCl_3$) δ 1.47 and 1.93 (broad, 16 H), 3.02 (broad, 4 H), 4.75 (broad s, 4 H), 7.57 (s, 2 H); IR (KBr) 2910 (s), 2850 (s), 2700–2500 (m), 1710 (vs), 1600 (m), 1480 (s), 1430 (s), 1195 (s), 840 (w) cm^{-1}.

Preparative-Scale Ozonolysis of 3. Compound 3 (9.84 g, 20.0 mmol) was dissolved in 600 mL of methylene chloride. Methanol (200 mL) and methanesulfonic acid (2 drops) were added. The resulting solution was cooled to 0 °C in an ice bath with stirring. Ozone[48] (1.4 mmol/min) was bubbled through the cooled, stirred solution for 120 min (168 mmol of O_3, theory = 60 mmol). The ozone flow was stopped and prepurified nitrogen was bubbled through the solution for 15 min. Dimethyl sulfide (44.6 mL, 37.2 g, 600 mmol) was added and the solution was stirred at 0 °C for an additional 2 h. The solvent was removed at ambient temperature and reduced pressure on a rotary evaporator. The residual oil was derivatized.

2,3-Decamethylenequinoxaline (11) and Cyclohexatriaconta[1,2,13,14,25,26-*b*,*b*′,*b*″]trisquinoxaline (9) by Condensation of the Ozonoysis Product of 3 with *o*-Phenylenediamine. *o*-Phenylenediamine (12.96 g, 120.0 mmol) was added to the crude ozonolysis product prepared as previously described. Absolute ethanol (200 mL) and concentrated HCl (1 mL) were added, and the resulting solution was refluxed for 1 h with stirring. The solution was allowed to cool and the solvent was removed at reduced pressure on a rotary evaporator. Hydrochloric acid (4 N, 300 mL) and methylene chloride (300 mL) were added and the organic phase was separated. The methylene chloride solution was washed twice with 300-mL portions of water and dried over anhydrous $MgSO_4$. The solvent was removed at reduced pressure on a rotary evaporator. The crude oil thus obtained was dissolved in a minimum of chloroform and loaded on a silica gel column (Woelm, activity I, 0.063–0.2 mm, 225 g, column dimensions: approximately 4 × 50 cm) and chromatographed. Compound 11 (1.5 g, 9.5%) eluted in 5% THF/hexane (1 L) after application of 1 L of hexane and 2 L of 2.5% THF/hexane. Compound 9 (0.63 g, 3.7%) eluted in 20% THF/hexane after application of an additional 1 L of 2.5% THF/hexane and 2 L of 10% THF/hexane.

Compound 9 was isolated from the crude column eluent by brief trituration with ether and had the following: NMR ($CDCl_3$) δ 1.55 (broad, 48 H), 3.02 (distorted t, 12 H), 7.81 (symmetrical m, 12 H); IR (KBr) 3060 (s), 2930 (s), 2860 (s), 1485 (m), 1465 (m), 1390 (m), 1340 (m), 1205 (m); UV λ_{max} 241 nm (ε 84 000) and 319 (ε 26 000); mp 132.5–133.5 °C. An analytically pure sample was recrystallized from ethanol/water. Anal.

Diethyl 1*H*,3*H*-2-Oxoimidazo[4,5-*g*]cyclodeca[*b*]quinoxaline-1,3-diacetate (18) and Cyclohexatriaconta-[1,2,13,14,25,26-*b*,*b*′,*b*″]tris(diethyl 1*H*,3*H*-2-oxoimidazo-[4,5-*g*]quinoxaline-1,3-di-α-acetate) (16). Condensation of the Ozonolysis Product of 3 with 15. Compound 15 (60 mmol) in 750 mL of acetic acid was prepared as previously described. Compound 3 (20 mmol) was ozonolyzed as previously described and the acetic acid solution of 15 was filtered directly into the crude ozonolysis product. The solution was refluxed with stirring for 1 h. Most of the acetic acid was removed at reduced pressure on a rotary evaporator. Hydrochloric acid (4 N, 300 mL) and methylene chloride (300 mL) were added. The organic phase was separated, washed twice with 300-mL portions of water, dried ($MgSO_4$), and concentrated at reduced pressure on a rotary evaporator. The residual oil was dissolved in a minimum of chloroform and loaded on a silica gel (Woelm, activity I, 225 g, column dimensions: approximately 4 × 50 cm) column and chromatographed using a stepped THF/benzene gradient. Compound 16 (0.99 g, 3.4%) eluted in 20% THF/benzene.

Compound 18 had spectral and analytical data in accord with the data described earlier. Compound 16 was isolated by titration with ether and had the following: NMR ($CDCl_3$) δ 1.32 (t, J = 7 Hz), 1.55 and 2.17 (broad, 22 H), 3.07 (t, 4 H, J = 7 Hz) 4.27 (q, 4 H, J = 7 Hz), 4.87 (s, 4 H), 7.56 (s, 2 H); IR (KBr) 3060 (w), 2930 (s), 2860 (s), 1720 (vs), 1585 (m), 1470 (m), 1435 (m), 1380 (m), 1335 (m), 1205 (s), 1180 (s), 1020 (m), 925 (m), 840 (m) cm^{-1}; mp 307–309 °C.

2,3-Tridecamethylenequinoxaline (12) and Cyclopentatetraconta[1,2,16,17,31,32-*b*,*b*′,*b*″]trisquinoxaline (10). Ozonolysis of 4 and Condensation with *o*-Phenylenediamine. A solution of 4 (6.19 g, 10.0 mmol) in 300 mL of methylene chloride and 100 mL of methanol was prepared. Methanesulfonic acid (2 drops) was added and the stirred solution was cooled to 0 °C. Ozone was bubbled into the solution in the same manner used for the ozonolysis of 3, and the crude ozonolysis product was reduced and isolated as described for 3. *o*-Phenylenediamine (6.48 g, 60.0 mmol), ethanol (200 mL), and concentrated HCl (1 mL) were added to the crude ozonolysis product and the mixture was treated in the same manner as described for the preparation of 11 and 9. Column chromatography on 225 g of silica gel afforded 2,3-tridecamethylenequinoxaline (12) [mp 47.5–8.5 °C; NMR ($CDCl_3$) δ 1.57 (broad, 22 H), 3.04 (distorted t, 4 H), 7.78 (symmetrical m, 4 H); IR (KBr) 3060 (w), 2920 (vs), 2850 (s), 1735 (w), 1620 (m), 1560 (w), 1480 (m), 1460 (s), 1395 (m), 1350 (m), 1205 (m), 1125 (m), 760 (s) cm^{-1}] and 0.090 g (0.9%, 10 mmol = 100%) of 10 [mp 139–141 °C; NMR ($CDCl_3$) δ 1.32 (broad, 66 H), 3.05 (distorted t, 4 H), 7.83 (symmetrical m, 4 H); IR 2920 (s), 2850 (s), 1630 (m), 1525 (m), 1460 (m), 760 (m) cm^{-1}]. Anal.

Cyclohexatriaconta[1,2,13,14,25,26-*b*,*b*′,*b*″]tris(1*H*,3*H*-2-oxoimidazo[4,5-*g*]quinoxaline-1,3-di-α-acetic acid)hexakis-potassium Salt (17). The crude oil 16 eluted with 20% THF in benzene was rechromatographed on 50 g of silica gel (Woelm, activity I). The oil thus obtained (50–80% pure) was stirred with 20 equiv of KOH in 25 mL of water at 85 °C for 24 h. The resulting solution was allowed to cool to ambient temperature and filtered. Acidification of the yellow solution with excess, concentrated hydrochloric acid caused precipitation of the macrocyclic hexaacid. The free acid was separated by filtration, washed once in the funnel with 5 mL of water, and redissolved in about 20 mL of water containing the minimum amount of KOH necessary to effect solution. The acidification process was repeated and the free acid collected as before. The solution–precipitation process was repeated 2 times more to yield 150 mg (from 9.8 g of 3) of the macrocyclic hexaacid which had the following: NMR (Me_2SO-d_6/$CDCl_3$) δ 1.45 and 1.93 (broad, 48 H), 3.11 (broad, 12 H), 4.75 (broad s, 12 H), 7.55 (s, 6 H) and IR (KBr) 2920 (s), 2855 (s), 3200 (2550?) (broad, m), 1705 (broad, vs), 1490 (m), 1435 (m), 1200 (m), 780 (m) cm^{-1}.

Transfer Experiments. Three aqueous solutions were prepared. Solution I consisted of KOH (85%, 0.13 g, 20 mmol) in 25.0 mL of water. Solution II consisted of 19 (0.150 g, 0.34 mmol) in 25.0 mL of water containing KOH (0.13 g, 20 mmol). Solution III consisted of 17 (0.150 g, 0.11 mmol) in 25.0 mL of water containing KOH (0.13 g, 20 mmol). Four organic solutions were prepared. Solution A consisted of cyclopentane (3.5 g, 0.050 mol), cyclohexane (4.2 g, 0.050 mol), and *n*-undecane (1.56 g, 0.010 mol). Solution B consisted of toluene (4.6 g, 0.050 mol), *p*-xylene (5.3 g, 0.050 mol), mesitylene (6.0 g, 0.050 mol), durene (6.7 g, 0.050 mol), and *n*-undecane (1.56 g, 0.10 mol). Solution A had a density

(48) The ozone was prepared by using a Welsbach ozone generator operating at 4 psi of oxygen with a flow rate of 0.02 and at a potential of 80 V.

(49) Regen, S. L. Ph.D. Thesis, Massachusetts Institute of Technology, 1972, p 55.

of 0.72 g/mL and therefore was 3.9 M in both cyclopentane and cylohexane. Solution B had a density of 0.85 g/mL and was therefore 1.75 M in each of the aromatic hydrocarbons present. Solution C consisted of *n*-pentane (3.6 g, 0.050 mol), *c*-pentane (3.5 g, 0.050 mol), *cis*-decalin (6.9 g, 0.50 mol), and *trans*-decalin (6.9 g, 0.050 mol). Solution D consisted of toluene (9.2 g, 0.10 mol), *p*-xylene (10.6 g, 0.10 mol), and naphthalene (6.4 g, 0.050 mol). Solution C had a density of 0.81 g/mL and was therefore 1.9 M in each of the hydrocarbons present. Solution D had a density of 0.89 g/mL and was therefore 3.4 M in toluene and *p*-xylene and 1.7 M in naphthalene.

Three U-tubes, each equipped with a Teflon-coated magnetic stirring bar, were set up so that a single magnetic stirrer would stir all three at the same rate. Equal amounts (~12 mL) of solutions I, II, and III were placed in each U-tube. Two separate experiments were then performed in succession to determine the relative rates of transfer of the various hydrocarbons through the aqueous phases. The first experiment was to place 2.0 mL of solution A and 2.0 mL of solution B on opposite sides of each of the three U-tubes already containing solutions I, II, and III. Stirring was then commenced and continued for several days. The stirring rate was controlled so that no vortexing occurred.

The same experiment was also performed with solution C and D being used in place of A and B, respectively. After being stirred for several days, the organic solutions were analyzed by GLPC to determine the quantities of each organic compound which was transported through the aqueous phase. The relative rates of transport of each of the organic compounds are listed in Table I. The unfacilitated rate of transport of cyclopentane through aqueous KOH was given the arbitrary value of 1.0.

Registry No. 1, 1129-90-4; 2, 6573-73-5; 3, 65975-29-3; 4, 102652-58-4; 9, 102652-59-5; 10, 102682-72-4; 11, 7215-74-9; 12, 102652-60-8; 13, 43135-91-7; 14, 3705-86-0; 15, 102652-61-9; 16, 102652-62-0; 17, 102682-73-5; 18, 102652-63-1; 19, 102682-74-6; 1,1-dichlorocyclododecane, 60223-10-1; cyclododeca-1,2-diene, 1129-91-5; 1,1-dichlorocyclopentadecane, 102652-64-2; cyclopentadecanone, 502-72-7; cyclododecane-1,2-dione, 3008-41-1; *o*-phenylenediamine, 95-54-5; diethyl 5,6-dinitrobenzimidazolone-1,3-di-α-acetate, 1848-95-9.

Synthesis of Polynitro Compounds. Hexasubstituted Benzenes

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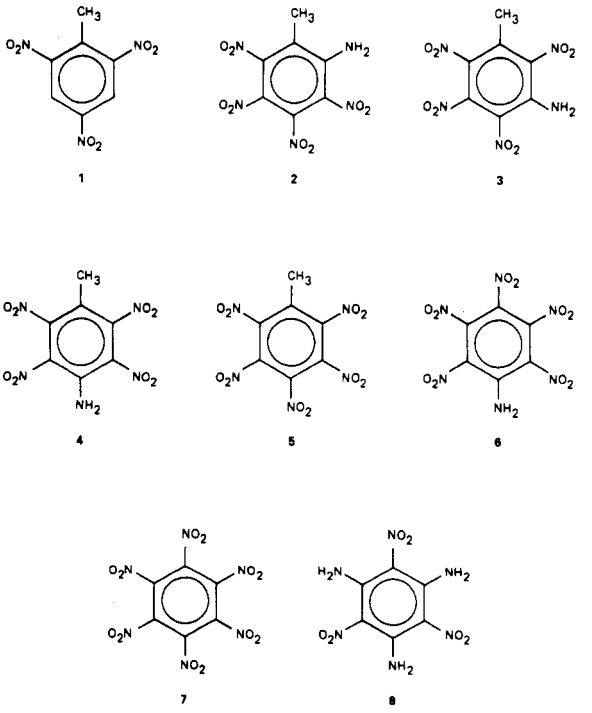
Received March 11, 1986

The synthesis of the three isomeric aminotetranitrotoluenes by nitration of an appropriate aminodinitrotoluene is presented, and the apparent ipso nitration of 4-amino-2,6-dinitrotoluene to give pentanitroaniline is also discussed. The oxidation of the isomeric aminotetranitrotoluenes to pentanitrotoluene is described, as is the ammonolysis of pentanitroaniline and of pentanitrotoluene.

Our continuing interest in highly nitrated species, energetic materials which have explosive and propellant applications, has prompted us to investigate methods of preparation of pernitrated aromatic systems.[2-5] Polynitroaromatic analogues of 2,4,6-trinitrotoluene (TNT, 1) and polyaminopolynitroaromatic compounds are expected to show improved properties of density, power, sensitivity and stability, but few of these species have been synthesized. This study deals, then, with the synthesis and reactions of the isomeric 2-amino-3,4,5,6-, 3-amino-2,4,5,6-, and 4-amino-2,3,5,6-tetranitrotoluenes (**2**, **3**, and **4**) and their oxidation to 2,3,4,5,6-pentanitrotoluene (**5**). We also discuss the apparent ipso nitration of **4** to 2,3,4,5,6-pentanitroaniline (**6**) from which hexanitrobenzene (**7**) and 1,3,5-triamino-2,4,6-trinitrobenzene (TATB, **8**) may be prepared.

Successive direct nitration by electrophilic substitution of an aromatic ring system, of course, becomes progressively more difficult due to the deactivating influence of the nitro groups already in place. Such difficulties can, however, be overcome by the stategic inclusion of a suitable activating group, as exemplified by the Flürscheim synthesis of **6** from 3,5-dinitroaniline, **9**.[6]

Chart I



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