250 mg (1.5 mmol) of sodium iodide. After the mixture was refluxed overnight under nitrogen, the solvent was removed under reduced pressure. Anhydrous ether (25 mL) was added to the residue, and the mixture was filtered through Celite to give a yellow residue on removal of the solvent. TLC analysis (elution with hexanes–ethyl acetate, 9:1) showed product **3** (R_f 0.60) and a trace of **2** (R_f 0.25). Recrystallization from methanol–petroleum ether (9:1) gave 120 mg (63%) of (+)-**3**: mp 54–55 °C; lit.[13] mp 53–54 °C; $[\alpha]^{25}_D$ +1.47° (*c* 3.185, $CHCl_3$) [lit.[13] $[\alpha]^{20}_D$ +2.5° (*c* 10, $CHCl_3$)].

Diphenyl 1,2-Distearoyl-*sn*-glycero-3-phosphate ((+)-4). The iodide **3** (90 mg, 0.12 mmol) was dried over P_2O_5 in a desiccator and dissolved in 10 mL of dry refluxing benzene in a flask protected from light with aluminum foil. Silver diphenyl phosphate (175 mg, 0.35 mmol) was added, and the reaction mixture was refluxed for 4 h, after which time TLC analysis (hexanes–ethyl acetate, 4:1) showed complete conversion of **3** into the desired diphenyl phosphate ester **4** (R_f 0.50); traces of tosylate **2** present in **3** remained unreacted. The mixture was cooled to room temperature, filtered through a sintered-glass funnel packed with Celite, and washed with chloroform (3 × 50 mL). Removal of solvent left a white solid that was dissolved in hexanes–ethyl acetate (95:5) and purified by flash chromatography on silica gel in the same solvent system, yielding 60 mg (59%) of product **4**: $[\alpha]^{25}_D$ +1.55° (*c* 1.42, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.4–7.2 (m, 10 H, C_6H_5), 5.28–5.19 (m, 1 H, CH_2CHCH_2), 4.42–4.08 (m, 4 H, CH_2CHCH_2), 2.38–2.15 (m, 4 H, $COCH_2$), 1.7–1.1 (m, 60 H, $(CH_2)_{15}$), 0.92–0.80 (t, J = 7.3 Hz, 6 H, ω-CH_3). Anal. Calcd for $C_{51}H_{85}O_8P$: C, 71.46; H, 9.99; P, 3.61. Found: C, 71.86; H, 10.19; P, 3.40.

(+)-**4** was also prepared in 77% yield directly from tosylate (+)-**2** by refluxing for 6 h in dry xylenes with 2.5 equiv of silver diphenyl phosphate. Purification by flash chromatography (elution with hexanes–ethyl acetate, 95:5) gave a white solid: mp 55–56 °C (lit.[14a] mp 58–59 °C, lit.[14b] mp 54.5–55 °C; *rac*-**4** lit.[14c,d] mp 58–59 °C); $[\alpha]^{25}_D$ +0.52° (*c* 5.07, $CHCl_3$) (34% optical purity).

1,2-Distearoyl-*sn*-glycero-3-phosphatidic Acid (5). Adams catalyst (80 mg) was suspended in 10 mL of glacial acetic acid and reduced with hydrogen for about 1 h until black granules of platinum black appeared. A solution of 60 mg (0.070 mmol) of diphenyl phosphate **4** in 10 mL of cyclohexane–glacial acetic acid (1:1) was injected into the flask through a rubber septum. The mixture was stirred vigorously at room temperature for 3 h, filtered through a sintered-glass funnel packed with Celite, and washed with $CHCl_3$ (3 × 10 mL). The filtrate was concentrated, and the product was obtained by precipitation with 10 mL of cold (−20 °C) acetonitrile. After two precipitations, phosphatidic acid **5** (R_f ~0.5 in $CHCl_3$–CH_3OH–HCO_2H, 80:15:5) was obtained as a hygroscopic white solid (36 mg, 73%), which was used in the next step without further purification.

1,2-Distearoyl-*sn*-glycero-3-phosphocholine (6). Phosphatidic acid **5** (36 mg, 0.050 mmol) was dissolved by heating (oil bath) in dry pyridine (10 mL) at 50 ± 5 °C for 30 min. Choline tosylate (140 mg, 0.50 mmol), freshly dried over P_2O_5, and trichloroacetonitrile (2 mL) were added, and the reaction mixture was stirred for 48 h at 50 ± 5 °C. The solvent was removed under reduced pressure; to ensure complete removal of pyridine, the residue was dissolved three times successively in 25 mL of $CHCl_3$–CH_3OH (1:1), and the solvents were evaporated each time under vacuum. The residue was dissolved in THF–water (9:1) and purified by column chromatography on Amberlite MB-3 (20 g; THF–water, 9:1) to give (+)-**6** as a tan solid. Chromatography on silica gel, eluting with $CHCl_3$–CH_3OH (first 9:1, then 3:2), gave 32 mg (55%) of the desired phosphocholine **6** (R_f 0.37 in $CHCl_3$–CH_3OH–H_2O, 65:25:4). The suspended silica gel was removed by filtering a chloroform solution of **6** through a 0.45-μm Metricel filter. (+)-**6**: $[\alpha]^{25}_D$ +6.95° (*c* 0.097, $CHCl_3$–CH_3OH, 1:1) [an authentic sample purchased from Sigma Chemical Co. had $[\alpha]^{25}_D$ +6.80° ($CHCl_3$–CH_3OH, 1:1); lit.[6a] $[\alpha]^{29}_D$ +6.2° ($CHCl_3$–CH_3OH, 1:1); lit.[6i] $[\alpha]^{25}_D$ +6.4° ($CHCl_3$–CH_3OH, 1:1); lit.[7a] $[\alpha]^{25}_D$ +6.1° ($CHCl_3$–CH_3OH, 1:1); lit.[7b] $[\alpha]^{20}_D$ +6.95° ($CHCl_3$–CH_3OH, 1:1)]; ^1H NMR ($CDCl_3$) δ 5.30–5.18 (m, 1 H, CH_2CHCH_2), 4.62–4.42 (m, 2 H, CH_2OP), 4.40–4.25 (m, 2 H, CH_2N), 4.18–3.98 (m, 4 H, CH_2CHCH_2), 3.4 (s, 9 H, $N(CH_3)_3$), 2.74 (br s, H_2O), 2.38–2.20 (m, 4 H, $COCH_2$), 1.65–1.50 (m, 4 H, $COCH_2CH_2$), 1.38–1.0 (m, 56 H, $(CH_2)_{14}$), 0.92–0.80 (t, J = 7.8 Hz, 6 H, ω-CH_3). Anal. Calcd for $C_{44}H_{88}O_8NP{\cdot}3H_2O$: C, 62.60; H, 11.22; N, 1.65; P, 3.67. Found: C, 62.52; H, 11.31; N, 1.44; P, 3.53.

1-Stearoyl-2-lyso-*sn*-glycero-3-phosphocholine. The optical purity of phosphocholine (+)-**6** was examined by treatment with phospholipase A_2 (*Naja naja*, Sigma) in pH 7.4 buffer for 1 h at 38 °C as described previously.[15] TLC analysis ($CHCl_3$–CH_3OH–H_2O, 65:25:4) showed complete hydrolysis of **6** (R_f 0.37) to 1-stearoyl-2-lysophosphatidylcholine (R_f 0.12) and stearic acid (R_f 0.85), confirming retention of the natural *sn*-3 configuration in 1,2-distearoylphosphatidylcholine (**6**).

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Lactone Synthesis by α,ω-Diols with Hydrogen Peroxide Catalyzed by Heteropoly Acids Combined with Cetylpyridinium Chloride

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Recently, metal-catalyzed oxidations of a wide variety of substrates with aqueous hydrogen peroxide, which have received much attention from a synthetic and industrial perspective, were accomplished by the use of heteropoly acids such as 12-molybdophosphoric acid (MPA) or 12-tungstophosphoric acid (WPA) in combination with cetylpyridinium chloride (CPE).[1-4] Furthermore, similar oxidations[5-7] with dilute hydrogen peroxide by molybdenum and tungsten catalysts have been reported by Venturello[5,7] and Modena.[5,6] These methods permit the use of commercially available aqueous hydrogen peroxide (30–35% H_2O_2), which is inexpensive, environmentally clean, and easy to handle, as the oxidant.

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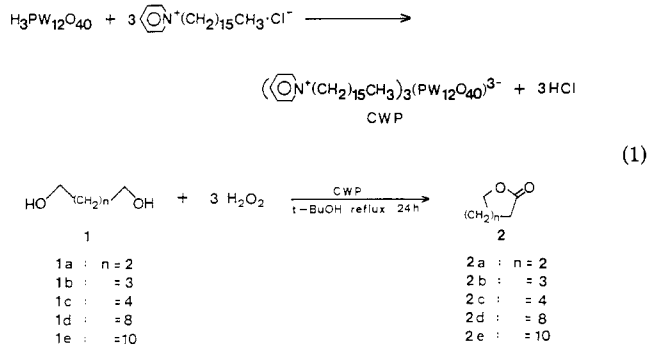
Table I. Lactonization of 1,4-Butanediol (1a) to γ-Butyrolactone (2a) with Hydrogen Peroxide Catalyzed by Heteropoly Acids under Several Reaction Conditions[a]

run	catalyst	solvent	conv (%)[b]	selectivity (%)[b]
1	CWP	t-BuOH	97	>98
2	CWP	$CHCl_3$	20	90
3	CWP	CH_3CN	18	89
4	CWP	dioxane	75	20
5[c]	CWP	benzene	26	30
6[d]	CWP	t-BuOH	75	71
7	WPA/3CPC	t-BuOH	72	77
8[e]	CWP + HCl	t-BuOH	50	80
9	WPA	t-BuOH	76	29
10	CMP	t-BuOH	25	82
11[c]	CMP	benzene	45	85

[a] **1a** (2 mmol) was allowed to react with 35% H_2O_2 (6 mmol) in the presence of catalyst (0.04 mmol) under refluxing temperature of solvent (15 mL) for 24 h. [b] Determined by GLC analysis. [c] t-BuOOH was used instead of H_2O_2. [d] CWP (0.02 mmol) was used. [e] 1 N HCl (0.12 mL) was added.

In the course of studies concerning the oxidation of alcohols and diols with hydrogen peroxide by tris(cetylpyridinium) 12-tungstophosphate (CWP), $[\pi\text{-}C_5H_5N^+\text{-}(CH_2)_{15}CH_3]_3(PW_{12}O_{40})^{3-}$, prepared from WPA and 3 equiv of CPC, α,ω-diols **1** were dehydrogenated to lactones **2** in good yields (eq 1). Several methods (e.g., silver carbonate,[8]

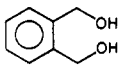
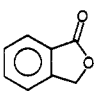
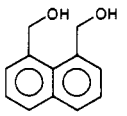
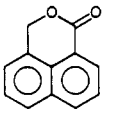


(1)

sodium bromate,[9] oxoaminium salts,[10] or Ni-mediated[11] oxidations, and Ru,[12] Pd,[13] Rh,[14] or Pt[15]-catalyzed reactions etc.) are available for selective lactonization, but the lactone synthesis by dehydrogenation of α,ω-diols with hydrogen peroxide is scarcely published. In this paper we describe a facile lactonization of α,ω-diols with 35% H_2O_2 catalyzed by heteropoly acids combined with CPC under homogeneous condition using *tert*-butyl alcohol as the solvent.

For examination of the potential of heteropoly acids as the catalyst for lactonization of α,ω-diols by hydrogen peroxide, the dehydrogenation of 1,4-butanediol (**1a**) to γ-butyrolactone (**2a**) was chosen as the model reaction. The representative results are summarized in Table I.

Table II. Lactonization of a Variety of α,ω-Diols with 35% H_2O_2 Catalyzed by CWP[a]

run	α,ω-diols	conv (%)[b]	product (selectivity, %)[b]
1	**1a**	97	**2a** (>98)
2	**1b**	78	**2b** (94)
3	**1c**	53	**2c** (70)
4	**1d**	47	**2d** (81)
5[c]	**1d**	52	**2d** (80)
6[d]	**1d**	60	**2d** (60)
7	**1e**	42	**2e** (64)
8	**3a**	80	**5a** (43), **4a** (41)
9	**3b**	82	**5b** (70), **4b** (20)
10	**6a**	96	**7a** (93)
11	**6b**	96	8 (75), **7b** (15)
12	 9	98	 10 (>98)
13	 11	98	 12 (>98)

[a] α,ω-Diols (2 mmol) were allowed to react with H_2O_2 (6 mmol) in the presence of CWP (0.04 mmol) in t-BuOH (15 mL) under reflux for 24 h. [b] Determined by GLC analysis. [c] for 72 h. [d] H_2O_2 (10 mmol) was used.

The lactonization of **1a** to **2a** could be achieved efficiently by the use of a 2-fold excess of 35% H_2O_2 and a catalytic amount of CWP (0.02 equiv) in *tert*-butyl alcohol at reflux temperature (run 1). Under two-phase conditions using chloroform as the solvent in which the epoxidation of allylic alcohols with H_2O_2 by CWP was successfully carried out,[1,2] the dehydrogenation of **1a** to **2a** was markedly retarded. Acetonitrile and 1,4-dioxane were not suited for the present lactonization reaction (runs 3 and 4). The use of a catalyst concentration of less than 0.02 equiv to **1a** resulted in the decrease of the yield of **2a** (run 6). The dehydrogenation catalyzed by WPA in the presence of 3 equiv of CPC (WPA/3CPC system), which produces CWP in situ with evolution of hydrogen chloride in the medium (eq 1), led to somewhat lower conversion and selectivity to **2a** (run 7). This observation suggests that the lactonization is depressed by the hydrogen chloride generated in the reaction system. Indeed, the reaction proceeded sluggishly by the addition of hydrochloric acid to the CWP-catalyzed reaction of **1a** (run 8). In contrast to these observations, the epoxidation of olefins with H_2O_2 by CWP catalysis was facilitated when hydrochloric acid was added to the reaction medium.[16] The oxidation of **1a** by WPA alone, although resulting in high conversion of **1a**, is characteristically unselective, giving **2a** in poor yield (run 9).

In comparing the catalytic features of tungsten- and molybdenum-based heteropoly acids for the lactonization, several observations are noteworthy. Molybdenum catalyst, tris(cetylpyridinium) 12-molybdophosphate (CMP), $[\pi\text{-}C_5H_5N^+(CH_2)_{15}CH_3]_3(PMo_{12}O_{40})^{3-}$, showed low activity for the lactonization of **1a** (run 10), while **1a** was converted to lactone **2a** in moderate yield when *tert*-butyl hydroperoxide was used in place of hydrogen peroxide as the oxidant. In contrast to the molybdenum-catalyzed lac-

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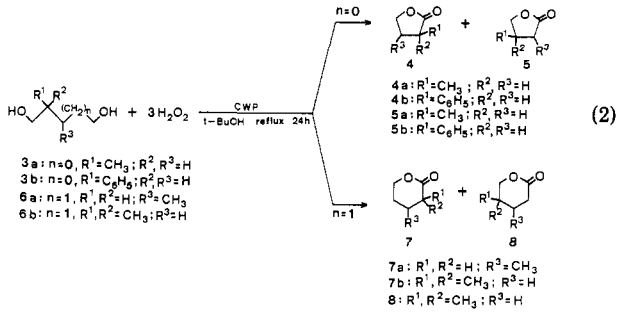
(16) The epoxidation of 1-octene with 35% H_2O_2 by the WPA/3CPC system took place more rapidly than that by CMP and was found to be facilitated in a weak acidic medium rather than under neutral condition.[4]

tonization, *tert*-butyl hydroperoxide was ineffective for the tungsten-catalyzed lactonization (run 5).

The lactonization of a variety of α,ω-diols with 35% H_2O_2 catalyzed by CWP under reflux of *tert*-butyl alcohol is shown in Table II.

Although **1a** was dehydrogenated to **2a** in nearly quantitative yield, dehydrogenation of α,ω-diols to lactones became successively difficult with an increase in the chain length of the diols. The yields of δ-valerolactone (**2b**) and ϵ-caprolactone (**2c**) from the corresponding diols, **1b** and **1c**, therefore, decreased somewhat compared with that of **2a**. The cyclization of 1,10-decanediol (**1d**) and 1,12-dodecanediol (**1e**) was difficult, giving lactones **2d** and **2e**, respectively, in low selectivities. The reaction was carried out under varying conditions (e.g., reaction time, temperature, and quantity of oxidant and catalyst etc.) to improve the yield of large-membered ring lactones. But this difficulty could not be overcome easily (runs 5 and 6). Only when the reaction was prolonged was the yield of **2e** slightly improved (run 5). In a similar manner as **1a**, the dehydrogenation of substituted 1,4-butanediols, **3a** and **3b**, having a methyl or phenyl substituent at the 2-position, respectively, could be achieved satisfactorily, but these lactonizations gave regioisomeric mixtures.

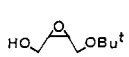
For examples, 2-methyl-1,4-butanediol (**3a**) produced a pair of isomers of 2- and 3-methyl-γ-butyrolactones, **4a** and **5a**, in about a 1:1 ratio, while 2-phenyl-1,4-butanediol (**3b**) was dehydrogenated with relatively high regioselectivity to form **5b** and **4b** (ca. 7:2) (eq 2). Thus, the phenyl



(2)

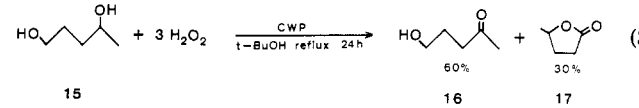
substituent at the 2-position of 1,4-butanediol offered somewhat greater regiocontrol than does the methyl substituent at the same position. For substituted 1,4-pentanediols, the reaction proceeded similarly to form lactones in good yields; 3-methyl-1,5-pentanediol (**6a**) was converted to 3-methyl-δ-valerolactone (**7a**) in high yield, and 2,2-dimethyl-1,5-pentanediol (**6b**) afforded the sterically encumbered lactones, **8**, as the principal product (**8**/**7b** = 5:1) (eq 2).

1,2-Benzenedimethanol (**9**) and 1,8-naphthalenedimethanol (**11**) were completely dehydrogenated to 1,2-phthalide (**10**) and 1,8-naphthalide (**12**), respectively, in almost theoretical yields. However, 2-butene-1,4-diol (**13**) was epoxidized by the present method to give 4-*tert*-butoxy-2,3-epoxybutanol (**14**) (60%) in which the alternative hydroxy group of **13** was substituted by the *tert*-butoxy group.



14

In order to obtain mechanistic information concerning the present lactonization, 1,4-pentanediol (**15**) possessing a secondary hydroxy group in the molecule was allowed to react under the same conditions as the lactonization of 1,5-pentanediol (**1b**). In a previous paper, we showed that the present catalyst–oxidant system prompted the preferential oxidation of a secondary hydroxy group rather than the primary one of alcohols and diols.[17] In the oxidation of **15**, the ketonization of the secondary hydroxy group took place in preference to the lactonization, giving 5-hydroxy-2-pentanone (**16**) and a small amount of γ-valerolactone (**17**) (eq 3).



15 **16** **17** (3)

The possibility of the conversion of hydroxy ketone **16** to lactone **17** was excluded by the independent oxidation of **16** which resulted in only a small consumption of **16** and no detectable formation of **17**. Consequently, the formation of **17** from **15** shows that the oxidation took place at the primary hydroxy group of **15** to form 4-hydroxypentanal (**18**),[18] which probably lies in equilibrium with hemiacetal **19**. Dehydrogenation of **19** appears to be easily effected, giving lactone **17**. In fact, the treatment of the hemiacetal **19** derived from **18** under the same conditions as the lactonization afforded **17** in good yield.

In conclusion, oxidative dehydrogenation of a wide variety of α,ω-diols with aqueous hydrogen peroxide by CWP provides a convenient method for the preparation of lactons.

Experimental Section

Melting points were determined with a Yanagimoto capillary melting point apparatus. All melting points are uncorrected. Infrared (IR) spectra were measured with a Jasco Model A-202 spectrometer. ^1H and ^{13}C NMR spectra were measured with JEOL PMX-60 and Hitachi R-90H spectrometers in $CDCl_3$ by using Me_4Si as the internal standard, respectively. GLC analyses were performed on a Yanagimoto G1800 chromatography, employing a thermal conductivity detector using a 3 mm × 3 m column (5% silicone OV-7 on Chromasorb W), or a Shimazu 12A gas chromatograph with a flame ionization detector using a 25-m HR-101 capillary column.

Materials. 2-Methyl-1,4-butanediol (**3a**), 2-phenyl-1,4-butanediol (**3b**), 2,2-dimethyl-1,5-pentanediol (**6b**), 1,2-benzenedimethanol (**9**), 1,8-naphthalenedimethanol (**11**), and 1,4-pentanediol (**15**) were prepared by $LiAlH_4$ reductions of methylsuccinic acid, phenylsuccinic acid, 2,2-dimethylglutaric acid, phthalic anhydride, 1,8-naphthalic anhydride, and γ-valerolactone, respectively.

CMP and CWP were prepared according to the methods reported previously.[1,2]

General Procedure for Oxidation of α,ω-Diols. To the stirred solution containing CWP (0.15 g, 0.04 mmol) were added 35% H_2O_2 (0.58 g, 6.0 mmol) in t-BuOH (15 mL) and the α,ω-diol (2.0 mmol) dropwise, and the mixture was allowed to react under refluxing conditions for 24 h. The reaction mixture was washed with a solution of saturated or 10% sodium thiosulfate to decompose the unreacted H_2O_2. After being washed with a solution of 10% sodium hydroxide, the products were extracted with ether or ethyl acetate. The products were isolated by distillation or by silica gel column chromatography (hexane/ethyl acetate = 10/1–2 eluent). Spectral data of each product were compared with authentic samples and literature values.[19,20]

τ-Decalactone (2d): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 177.3 (s), 61.9 (t), 33.6 (t), 31.9 (t), 29.1 (t), 28.9 (t), 28.7 (t), 28.6 (t), 25.3 (t), 24.3 (t); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.10–1.89 (m, 14 H), 2.16 (t,

(17) Although 2-octanol was oxidized to 2-octanone in 88% yield, the oxidation of 1-octanol took place with difficulty to give octanal in poor yield (16%). In the oxidation of 1,3-diols, such as 2-ethyl-1,3-hexanediol and 2,2,4-trimethyl-1,3-pentanediol possessing both the primary and secondary hydroxy groups, the secondary hydroxy groups were oxidized exclusively to give the corresponding hydroxy ketones, respectively, in good yields.[4]

(18) The present result may indicate that the primary hydroxy group of 1,4-diols is somewhat easily oxidized compared with that of 1,3-diols.

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2 H), 3.99 (t, 2 H); IR (NaCl) 1740 cm^{-1} (C=O).

β-Methyl-δ-valerolactone (7a): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 172.3 (s), 62.1 (t), 41.3 (d), 35.0 (t), 27.4 (t), 19.5 (q); ^1H NMR ($CDCl_3/Me_4Si$) δ 0.97 (d, 3 H), 1.33–2.40 (m, 5 H), 4.18 (t, 2 H); IR (NaCl) 1739 cm^{-1} (C=O).

1,2-Phthalide (10): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 170.9 (s), 146.4 (s), 133.8 (d), 128.7 (d), 125.3 (s), 125.2 (d), 122.1 (d), 69.6 (t); ^1H NMR ($CDCl_3/Me_4Si$) δ 5.38 (s, 2 H), 7.40–8.10 (m, 4 H); IR (NaCl) 1760 cm^{-1} (C=O).

1,8-Naphthalide (12): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 163.0 (s), 134.1 (s), 132.3 (s), 132.0 (s), 127.9 (s), 126.2 (d), 125.9 (d), 125.5 (d), 125.3 (d), 125.3 (d), 120.3 (d), 68.9 (t); ^1H NMR ($CDCl_3/Me_4Si$) δ 5.71 (s, 2 H), 7.17–8.50 (m, 6 H); IR (NaCl) 1725 cm^{-1} (C=O).

β-Methyl-γ-butyrolactone (5a): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 179.1 (s), 73.6 (t), 35.0 (t), 29.3 (d), 14.1 (g); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.10 (d, 3 H), 2.00–2.90 (m, 3 H), 3.82–4.03 (d, 2 H); IR (NaCl) 1775 cm^{-1} (C=O).

α-Methyl-γ-butyrolactone (4a): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 176.3 (s), 65.1 (t), 33.1 (d), 29.0 (t), 16.8 (q); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.29 (d, 3 H), 1.82–2.90 (m, 3 H), 4.03–4.43 (m, 2 H); IR (NaCl) 1740 cm^{-1} (C=O).

β-Phenyl-γ-butyrolactone (5b): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 175.3 (s), 135.5 (s), 127.3 (d), 126.6 (d), 125.4 (d), 65.4 (t), 44.3 (d), 30.3 (t); ^1H NMR ($CDCl_3/Me_4Si$) δ 2.60–2.98 (d, 2 H), 3.70–4.71 (m, 3 H), 7.15–7.42 (m, 5 H); IR (NaCl) 1770 cm^{-1} (C=O).

α-Phenyl-γ-butyrolactone (4b): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 176.3 (s), 138.3 (s), 127.8 (d), 127.6 (d), 12693 (d), 72.8 (t), 39.8 (d), 34.5 (t); ^1H NMR ($CDCl_3/Me_4Si$) δ 2.30–2.79 (m, 2 H), 3.52–4.53 (m, 3 H), 7.20–7.40 (m, 5 H); IR (NaCl) 1760 cm^{-1} (C=O).

α,α-Dimethyl-δ-valerolactone (7b): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 176.6 (s), 64.7 (t), 34.0 (s), 26.3 (t), 19.6 (t), 14.1 (q); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.23 (s, 6 H), 1.79–2.10 (m, 4 H), 4.45 (t, 2 H); IR (NaCl) 1730 cm^{-1} (C=O).

γ,γ-Dimethyl-δ-valerolactone (8): ^{13}C NMR ($CDCl_3/Me_4Si$) δ 170.0 (s), 59.3 (t), 26.7 (s), 23.8 (t), 19.9 (t), 13.1 (q); ^1H NMR ($CDCl_3/Me_4Si$) δ 0.91 (s, 6 H), 1.62 (t, 2 H), 3.72 (s, 2 H); IR (NaCl) 1730 cm^{-1} (C=O).

Registry No. **1a**, 110-63-4; **1b**, 111-29-5; **1c**, 629-11-8; **1d**, 112-47-0; **1e**, 5675-51-4; **2a**, 542-28-9; **2b**, 502-44-3; **2c**, 539-87-7; **2d**, 1725-03-7; **2e**, 1725-04-8; **3a**, 2938-98-9; **3b**, 6837-05-4; **4a**, 1679-47-6; **4b**, 6836-98-2; **5a**, 1679-49-8; **5b**, 1008-73-7; **6a**, 4457-71-0; **6b**, 3121-82-2; **7a**, 1121-84-2; **7b**, 4830-05-1; **8**, 1679-55-6; **9**, 612-14-6; **10**, 87-41-2; **11**, 2026-08-6; **12**, 518-86-5; **13**, 6117-80-2; **14**, 116503-38-9; **15**, 626-95-9; **16**, 1071-73-4; **17**, 108-29-2; **19**, 18545-25-0; CWP, 115031-77-1; WPA, 1343-93-7; CPC, 123-03-5; CMP, 88418-08-0.

A Convenient Synthesis of "Bis-homotris": 4-Amino-4-[1-(3-hydroxypropyl)]-1,7-heptanediol and 1-Azoniapropellane[1]

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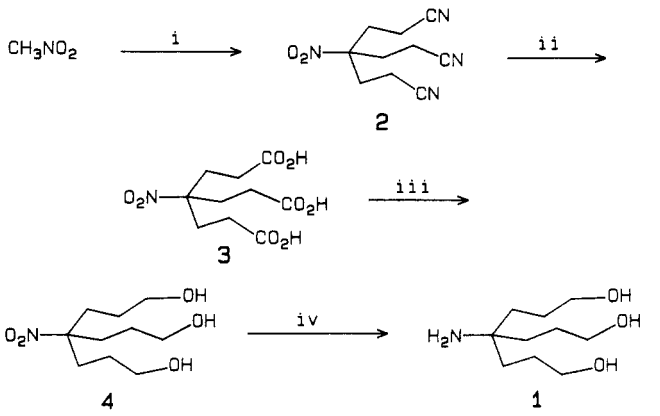
One of our research goals is the synthesis of unimolecular micelles based on the cascade methodology,[2] which involves successive multiplicative synthetic sequences,[3-5] in which an alkyl halide, or its equivalent, is alkylated with the carbanion of a trialkyl methanetricarboxylate, and then amidated with an appropriate multifunctional amine, such as tris(hydroxymethyl)aminomethane ("tris"). Subsequent transformation of the hydroxyl groups to better nucleofuges would allow repetition of the process; however, the nucleophilic displacement of such leaving groups (i.e. bromide) by a *C*-nucleophile does not readily occur under "reasonable" reaction conditions (<100 °C) due to the neopentyl moiety.[6] Tomalia, Hall, and co-workers[7] circumvented this limitation by the use of a "tied-back" oxy anion nucleophile under rigorous conditions.

It was initially surmised that a single carbon homologation[8] of "tris" should circumvent the substitution problem associated with a bulky carbon nucleophile. Unfortunately, work toward this end, confirmed by a search of the literature,[9] indicated that complete substitution by large nucleophiles, e.g. iodide, was still precluded due to steric hindrance. To bypass this problem, a convenient four-step, high-yield (93% overall) route to the convenient cascade building block, 4-amino-4-[1-(3-hydroxypropyl)]-1,7-heptanediol ("bis-homotris") (**1**) was devised and is reported herein.

Tris(β-cyanoethyl)nitromethane (**2**) was prepared (51%) by using a modified procedure adopted from Bruson and Riener,[10] in which the anion of nitromethane underwent a Michael reaction with 3 equiv of acrylonitrile, with tetrabutylammonium hydroxide.[11] Rigorous purification of **2** is imperative to obviate the arduous task of purifying subsequent products. Acid hydrolysis of **2** smoothly afforded (94%) the nitro triacid **3**, which was identified by the appearance in the ^{13}C NMR spectrum of a peak at 173.7 ppm attributable to the carbonyl carbon. Mild borane–THF[12] reduction of **3** gave triol **4** as evidenced by the ^{13}C NMR absorption at 60.6 ppm (Scheme I).

Various reduction procedures are available for the conversion of nitroalkanols to aminoalkanols,[13-22] employing

Scheme I[a]



[a] (i) $Bu_4N^+HSO_4^-$, KOH, H_2O, dioxane, 80–85 °C; (ii) HCl (concentrated), reflux; (iii) BH_3, THF, N_2, 0–25 °C; (iv) T-1 Raney Ni, EtOH, 25 °C, 72 h.

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