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Functionalized Macroheterobicyclic Compounds

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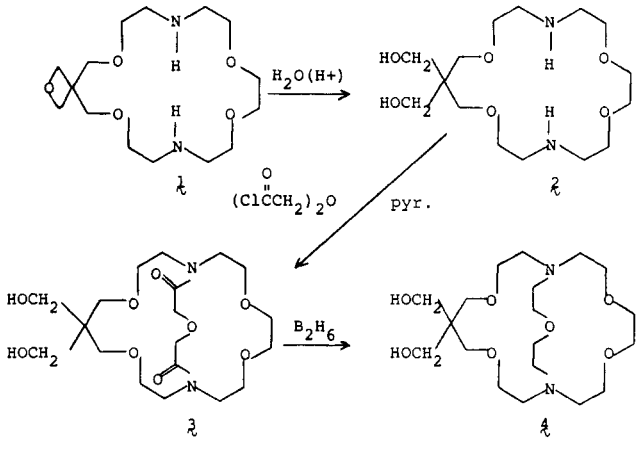
Heteromacrocycles containing two spirooxetane moieties have been converted to cage compounds with carbon at both bridgeheads and bearing hydroxymethyl functions to allow incorporation into polymers. A prototype cage compound with nitrogen at the bridgehead positions and *gem*-hydroxymethyl groups has been prepared from a heteromacrocycle containing one spirooxetane unit.

Synthetic schemes which allow easy access to macroheterocycles carrying one or two functions are desirable as routes to monomers and polymers containing macrorings. The previously described synthesis of macroheterocycles having an oxetane ring spiro to the macroring is a versatile source of such functionalized macrocycles containing varying numbers of oxygen, sulfur, and nitrogen atoms in the large ring.[1,2] The oxetane function in these compounds has been shown to be cleaved selectively to diol by acid-catalyzed hydrolysis.[3,4] Macrocycles containing the spirooxetane moiety are directly converted to polyoxetanes with cationic initiators,[5] while those containing the 1,3-diol function give polyesters by condensation–polymerization techniques.[3]

Both types of polymer are capable of solubilizing alkali metal salts with an efficiency related to that of the monomeric macrocyclic precursors, but such polymeric ligand/salt complexes have very limited stability in the presence of water. In view of the remarkable increases in stability constants attending the introduction of an additional strand to form macroheterobicyclic ligand/salt complexes in nonpolymeric systems,[6] routes to macroheterobicyclic compounds bearing functions suitable for incorporating the macrobicycle into polymers were of interest.[7] Two approaches are described in this paper.

Nitrogen Bridgehead Atoms. Diol **2**, obtained[4] by hydrolysis of the corresponding oxetane **1**, was condensed with diglycolyl dichloride. Despite the presence of impurities as well as reactive hydroxyl groups in the crude **2**, bridged bicyclic diol **3** was obtained in 14% yield (Scheme I). Attempts to reduce the amide groups in **3** with lithium aluminum hydride mainly gave recovered starting material; presumably insolubilization as the dilithium salt caused the reduction to be unusually slow. With diborane,[8] however, reduction of **3** proceeded readily to give **4**, a macroheterobicyclic compound with nitrogen at each bridgehead and a diol function available for further reactions. Bicyclic product **4** readily formed a crystalline 1:1 complex with sodium thiocyanate, in keeping with the assigned structure.

Scheme I



The synthesis[2] of **1** can be readily generalized to give the class of macroheterocycles **6**, since it allows variation in

(1) Krespan, C. G. *J. Org. Chem.* **1974**, *39*, 2351.
(2) Krespan, C. G. *J. Org. Chem.* **1975**, *40*, 1205.
(3) U.S. Patent 3 860 611, Jan 14, 1975; *Chem. Abstr.* **1975**, *82*, 157001.
(4) U.S. Patent 3 952 015, Apr 20, 1976; *Chem. Abstr.* **1976**, *85*, 46781.
(5) U.S. Patent 3 763 188, Oct 2, 1973; *Chem. Abstr.* **1974**, *80*, 71333.
(6) Lehn, J. M.; Sauvage, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6700.
(7) Tomoi, M.; Kihara, K.; Kakiuchi, H. *Tetrahedron Lett.* **1979**, 3485 and references therein describe some monofunctional cryptands and their incorporation into polymers. In particular, cage structures closely related to **4** were prepared.

(8) H. C. Brown and P. Heim (*J. Am. Chem. Soc.* **1964**, *86*, 3566) demonstrated the generality and efficiency of diborane in converting amides to amines.

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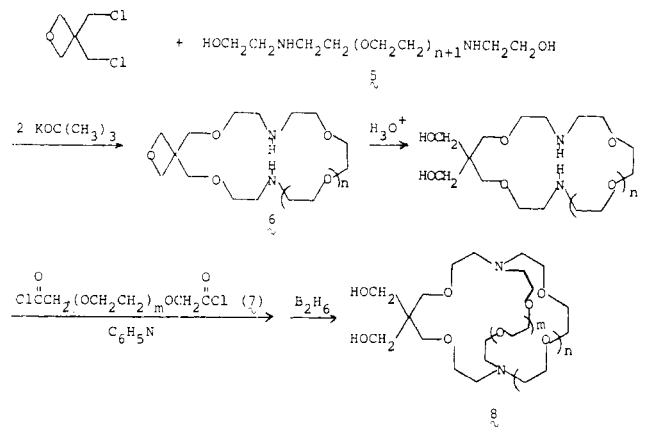
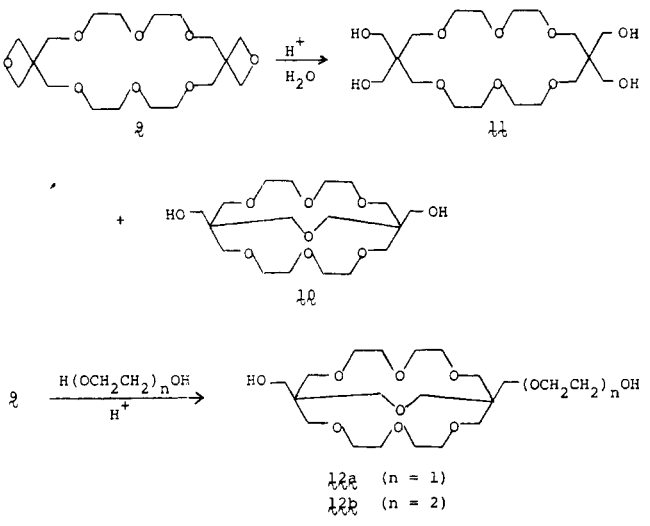
Scheme II



Scheme III



the chain length of intermediate **5**. The above scheme for converting **1** to **4** should be similarly adaptable to the synthesis of the class of macroheterobicyclic compounds **8** (Scheme II) by variations in the length of **7**. Therefore, considerable latitude appears to be available with respect to the length of the the two bridging strands in **8** and hence in the size of cavity within the bicyclic molecule.

Carbon at the Bridgeheads. The availability of macrocycles containing bis(spirooxetane) moieties[1] presented the possibility of preparing bicyclic derivatives by bridging reactions at the two oxetane rings. In the special case of bis(oxetane) **9**, simple hydrolysis conditions served to form bicyclic product **10** as well as tetraol **11** (Scheme III). The short bridge in **10** is presumably introduced by intramolecular attack of a protonated oxetane ring on a hydroxyl group from a previously hydrolyzed oxetane ring. The steric requirements for such attack are important since alcoholysis of **9** in ethylene glycol produced diol **12a** containing the same short bridge as in diol **10**. Bis(oxetane) containing a larger central macroring no longer adopts conformations favoring intramolecular reaction, so that the corresponding tetraol is obtained in over 70% yield.[3]

Similarly, alcoholysis of **9** in diethylene glycol gave diol **12b**. The isomeric diol with three equivalent bridges has been prepared by Coxon and Stoddart by a different procedure.[9]

Ammonia attacks an oxetane ring in an uncatalyzed thermal reaction to give 1,3-hydroxyamine from ring

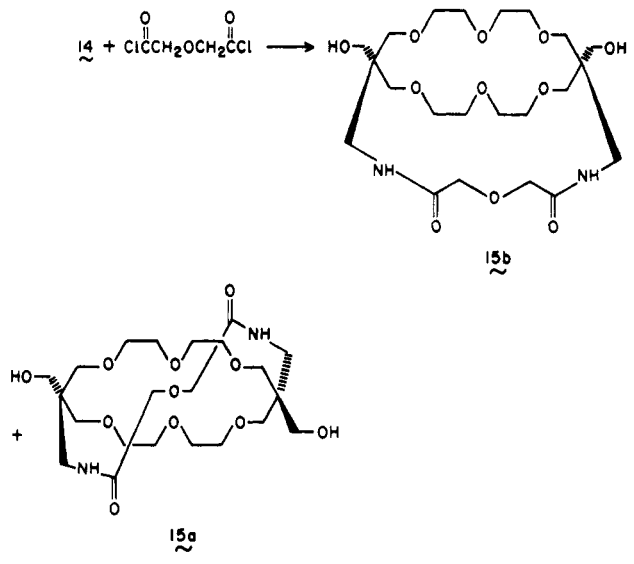
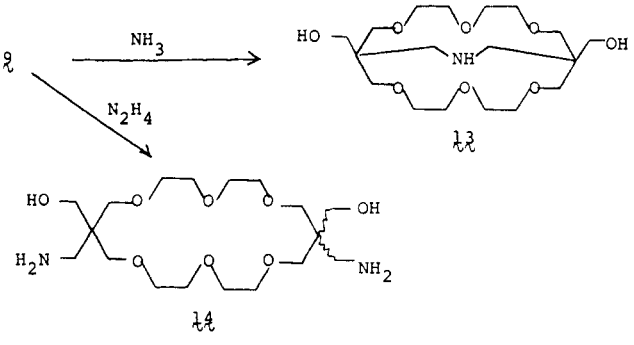


Figure 1.

Scheme IV



cleavage.[10] Addition of ammonia to **9** at 200 °C led to bicyclic amine **13** as the main product (Scheme IV). Cleavage of one oxetane ring introduced an aminomethyl group; intramolecular attack of this amine group on the second oxetane ring is sterically favored and competed effectively with excess ammonia to give **13**.

The reaction leading to **13** gave an oily byproduct which probably contained the stereoisomeric diamines **14**. A practical route to **14** was found in the high-temperature reaction of bis(oxetane) **9** with hydrazine. This reaction was carried out in an attempt to introduce two hydrazinomethyl groups, bridging being suppressed because of hindrance to intramolecular closure at the 1-nitrogen. Although the desired bis(hydrazine) appears to have been formed, the vigorous reaction conditions caused in situ reduction of the N–N bonds to give **14** directly.

Condensation of diamine **14** with diacid chlorides can give new macroheterobicyclic compounds containing two bridgehead carbon atoms, as was demonstrated by its reaction with diglycolyl dichloride to form **15** as a mixture of isomers (Figure 1). Fractional crystallization provided pure samples of the two diamides. The more soluble isomer was indicated to be trans (**15a**) by the fact that it formed only mono- and bis(trimethylsilyl) derivatives, while the less soluble isomer formed tris- and tetrakis-(trimethylsilyl) derivatives as well. The geometry assumed by **15a**, which resulted in marked hindrance to silylation, may have been of the type depicted in Figure 1 in which one bridge is threaded through the ring formed by the other two chains. This form corresponds to the out–out

(9) Coxon, A. C.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1974**, 537.

(10) Berlow, E.; Barth, R. H.; Snow, J. E. "The Pentaerythritols"; Reinhold: New York, 1958; pp 78, 90.

conformation of Park and Simmons.[11] An alternative conformation of the same structure, the out–in isomers having one hydroxymethyl group inside the molecular cavity, could be favored since a molecular model made from space-filling CPK atomic models indicates that the cavity is large enough to accommodate CH_2OH. It is also possible to convert this model from the out–out to the out–in conformation without breaking bonds. A related structure in which hydrogen occupies the bridgehead positions has indeed been interpreted as existing preferentially in the out–in conformation but as being capable of rapid out–in, in–out isomerization via out–out conformations.[12]

Experimental Section[13]

6,6-Bis(hydroxymethyl)-20,24-dioxo-4,8,14,17,22-pentaoxa-1,11-diazabicyclo[9.8.5]tetracosane (3). Solutions of 16.4 g (0.049 mol) of crude 12,12-bis(hydroxymethyl)-1,4,10,14-tetraoxa-7,17-diazacyclononadecane (**2**)[4] in 200 mL of purified CH_2Cl_2 and 8.4 g (0.049 mol) of diglycolyl dichloride in 210 mL of dry benzene were added dropwise and simultaneously to a vigorously stirred mixture of 25 mL of triethylamine and 1 L of benzene. After the addition was complete (3 h), the reaction mixture was stirred another 15 min and filtered, and the filtrate was evaporated to give 9.6 g of solid residue. Extraction with hot acetone and crystallization gave 3.0 g (14%) of **3** in two crops, the latter with a melting point of 177–179 °C. Two recrystallizations from methanol/acetone gave an analytical sample: mp 179.5–180.5 °C; IR (Nujol) 2.90 (OH), 6.01 (sh) and 6.07 (C=O), 8.6–9.6 μm (COC, COH). Mass spectrum (trimethylsilyl derivative), *m/e* 578 (disilylated M^+), 563 (disilylated $M^+ - CH_3$).

Anal. Calcd for $C_{19}H_{34}N_2O_9$: C, 52.52; H, 7.89; N, 6.45. Found: C, 52.52; H, 8.18; N, 6.22.

6,6-Bis(hydroxymethyl)-4,8,14,17,22-pentaoxa-1,11-diazabicyclo[9.8.5]tetracosane (4). Attempts to reduce the amide groups in **3** with $LiAlH_4$ in refluxing glyme for 8 h and in refluxing tetrahydrofuran for 3 days resulted in 62 and 55% recovery of **3**.

A suspension of 5.94 g (0.0137 mol) of diamide **3** in 50 mL of dry tetrahydrofuran was stirred at 0 °C under nitrogen while 100 mL of 1 M borane in tetrahydrofuran was added dropwise over a 40-min period. The ice bath was then removed and the mixture refluxed for 2 h, cooled, and allowed to stand over the weekend. Dropwise addition of 15 mL of concentrated HCl with simultaneous purging by nitrogen was followed by distillation of 100 mL of solvent at 1 atm. The reaction mixture was then cooled, 75 mL of concentrated HCl was added, and the mixture was heated to 65 °C to give a clear solution. Volatiles were removed under reduced pressure, 50 mL of water was added, evaporation under reduced pressure was repeated, and the residual moist solid was dissolved in 600 mL of distilled water. This solution was passed through 200 g of basic ion-exchange resin (Amberlite IRA-400), and the column was flushed with an additional 1 L of water. Evaporation of the aqueous solution at 50 °C (0.5 mm) gave 5.74 g of crude **4**. The product could not be induced to crystallize, but IR analysis showed only a trace of unreduced carbonyl to be present.

A solid 1:1 complex of diamine **4** with NaSCN was prepared by dissolving 0.81 g (ca. 0.002 mol) of crude **4** and 0.16 g (0.002 mol) of sodium thiocyanate in 20 mL of acetone, evaporating the solvent, and triturating the residue with 10 mL of tetrahydrofuran. The resulting crystals were recrystallized twice from small amounts of acetone to give 0.62 g (64% from crude **4** and 66% from diamide **3**) of product, mp 117.5–119 °C. Another recrystallization from acetone gave the following: mp 118.5–119.5 °C; IR (KBr) 2.97 and 3.06 (OH), 3.36, 3.46, and 3.52 (satd CH), 4.83 (SCN), 8.7–9.5 μm (COC, COH).

Anal. Calcd for $C_{20}H_{38}N_3NaO_7S$: C, 49.27; H, 7.85; N, 8.62; Na, 4.71. Found: C, 49.72; H, 8.16; N, 8.82; Na, 4.48.

9,9,19,19-Tetrakis(hydroxymethyl)-1,4,7,11,14,17-hexaoxacycloeicosane (11) and 1,11-Bis(hydroxymethyl)-3,6,9,13,16,19,22-heptaoxabicyclo[9.9.3]tricosane (10). A solution of 9.0 g (0.024 mol) of 2,6,9,12,16,19,22,25-octaoxadispiro[3.9:3.9]hexacosane (**9**) in 100 mL of water containing 0.5 mL of concentrated H_2SO_4 was refluxed for 8 h and then neutralized with barium hydroxide. Filtration and evaporation of water left a semisolid residue which was recrystallized three times from ether by continuous Soxhlet extractions. Another recrystallization from 1:1 ether/tetrahydrofuran afforded 1.6 g (16%) of tetraol **11**: mp 80–81 °C; IR (Nujol) 3.0 (br, OH), 8.7–9 μm (COC); ^1H NMR (acetone-d_6) 3.63–3.58 (m, 8 H, CH_2O), 2.92 ppm (s, 1 H, OH). Mass spectrum (trimethylsilyl derivative), *m/e* 700 (tetrasilylated M^+).

Anal. Calcd for $C_{18}H_{36}O_{10}$: C, 52.41; H, 8.80; O, 38.79. Found: C, 52.77; H, 8.64; O, 38.75.

Evaporation of the combined mother liquors and slow volatilization in a sublimer at 140 °C (0.025 mm) gave 1.55 g of solid, mp 114–118 °C, after 3 days. Further sublimation for 4 days gave an additional 0.72 g of solid, mp 85–110 °C, along with 1.01 g of less volatile crude **11**, mp 77–80 °C. Recrystallization of the combined higher melting solids from tetrahydrofuran gave 1.3 g (14%) of diol **10**, mp 121–123 °C. Two more recrystallizations from 1:1 ether/tetrahydrofuran provided an analytical sample: mp 123–124 °C; IR (Nujol) 2.88 (OH), 8.7–9 μm (COC); ^1H NMR (acetone-d_6) 3.67–3.18 (m, 16 H, CH_2O), 2.82 ppm (s, 1 H, OH), addition of D_2O shifted the 2.82-ppm band to 3.92 ppm; mass spectrum, *m/e* 394 (M^+); for trimethylsilyl derivative, *m/e* 538 (disilylated M^+).

Anal. Calcd for $C_{18}H_{34}O_9$: C, 54.81; H, 8.69; O, 36.50. Found: C, 55.79; H, 8.66; O, 36.75.

When the hydrolysis of **9** was carried out in refluxing dimethoxyethane for 1 day with only a tenfold excess of water present, the formation of tetraol **11** was repressed, and a higher yield (29%) of diol **10**, mp 118–122 °C, was obtained directly by fractional sublimation. Although the yield of **10** was improved, it remained limited because of a competing polymerization reaction.

1-(Hydroxymethyl)-11-(7′-hydroxy-2′,5′-dioxaheptyl)-3,6,9,13,16,19,22-heptabicyclo[9.9.3]tricosane (12b) and 1-(Hydroxymethyl)-11-(4′-hydroxy-2′-oxabutyl)-3,6,9,13,16,19,22-heptaoxabicyclo[9.9.3]tricosane (12a). A suspension of 18.8 g (0.05 mol) of bis(oxetane) **9** in 200 mL of diethylene glycol containing 0.2 mL of concentrated H_2SO_4 was stirred at 25 °C for 6 days. The resulting clear solution was neutralized with lithium hydroxide, and the volatiles were removed. Slow volatilization (2 weeks) at 170–180 °C (0.07 mm) gave 9.9 g of oil which solidified when scratched. Recrystallization from a small amount of acetone gave 5.4 g of colorless cubes, mp 79–81 °C. A second crop, recrystallized from acetone/ether, was 0.7 g for a total of 6.1 g (25%) of **12b**. An analytical sample was prepared by two recrystallizations from ether/acetone: mp 81.5–83 °C; IR (Nujol) 2.94 (OH), 9 μm (COC); ^1H NMR (acetone-d_6) 3.2–3.8 ppm (m, CH_2O and OH); addition of D_2O modified the pattern and moved OH signal to 3.82 ppm; mass spectrum (trimethylsilylated derivative), *m/e* 626 (disilylated M^+), 536 ($M^+ - (CH_3)_3SiOH$), 448 ($M^+ - 2(CH_3)_3SiO$); ^{13}C NMR (Me_2SO-d_6, external CS_2 reference) −147.2 (1, bridgehead C), −147.0 (1, bridgehead C), −133.0 (1, CH_2OH), −132.2 (1, CH_2OH), −125.0 to −120.3 ppm (m with at least seven peaks of varying intensity). The closely related **10** gave a simpler ^{13}C spectrum with the expected six lines at −147.4 (1, bridgehead C), −133.4 (1, CH_2OH), −124.4 (1, C in short bridge), and −125.3, −124.0, and −123.3 ppm (each 2, C in long bridges).

Anal. Calcd for $C_{22}H_{42}O_{11}$: C, 54.76; H, 8.77; O, 36.47; mol wt 482.6. Found: C, 54.90; H, 8.79; O, 36.53; mol wt 481 (ebullioscopic in benzene).

A mixture of 9.0 g (0.024 mol) of bis(oxetane) **9**, 100 mL of ethylene glycol, and 0.5 mL of concentrated H_2SO_4 was stirred at 25 °C for 6 days. The mixture was neutralized with barium

(11) Park, C. H.; Simmons, H. E. *J. Am. Chem. Soc.* **1972**, *94*, 7184.
(12) Gregory, B. J.; Haines, A. H.; Karntiang, P. *J. Chem. Soc., Chem. Commun.* **1977**, 918.
(13) Boiling points and melting points are uncorrected. NMR spectra were recorded on a Varian A-60 spectrometer with tetramethylsilane as internal reference and using approximately 20% solutions in the given solvent. Chemical shifts are given in parts per million with the downfield direction from Me_4Si taken as positive.

hydroxide, the solvent was removed, and the residue, 15.3 g, was extracted with ether (3 × 100 mL) and then with benzene (2 × 25 mL) to give 10.9 g of viscous oil. This residue was subjected to slow sublimation/distillation at 140 °C (0.5 mm) to give a moist solid. When pressed dry, triturated with ether, and recrystallized from a small amount of benzene/petroleum ether, the solid yielded crystalline diol **12a**, mp 96–98 °C. Evaporation of the ether and recrystallization of the residue from CCl_4 gave an additional crop of **12a** (mp 95–97 °C; total weight 1.6 g, 15%). An analytical sample was prepared by two recrystallizations from benzene: mp 97–98 °C; IR (Nujol) 2.95 (OH), 9 μm (COC); NMR (acetone-d_6) 3.2–3.8 ppm (m, CH_2O and OH); addition of D_2O modified the pattern and moved the OH signal to 4.20 ppm; mass spectrum (trimethylsilylated derivative), m/e 582 (disilylated M^+), 567 ($M^+ - CH_3$), 492 ($M^+ - (CH_3)_3SiO$), 448 ($M^+ - (OCH_2CH_2)_2O$).

Anal. Calcd for $C_{20}H_{38}O_{10}$: C, 54.78; H, 8.73; O, 36.49. Found: C, 54.91; H, 8.58; O, 35.93.

The symmetrical structure was ruled out for this product because of the similarity of both the method of synthesis and the ^{13}C NMR spectrum to those of the product from diethylene glycol (described above).

1,11-Bis(hydroxymethyl)-3,6,9,13,16,19-hexaoxa-22-azabicyclo[9.9.3]tricosane (13). A mixture of 18.8 g (0.05 mol) of **9** and 200 mL of concentrated aqueous NH_3 was heated in a metal tube at 200 °C for 20 h under autogenous pressure. Filtration of the reaction mixture gave 4.5 g of diol **13**, mp 149–150 °C. Evaporation of the filtrate to low volume and trituration of the residue with 5 mL of concentrated aqueous NH_3 gave crystals which were filtered and washed with a small amount of concentrated aqueous NH_3 to give an additional 4.3 g of **13**. Recrystallization of the off-colored product from methanol gave 8.5 g of colorless crystals, mp 149–150 °C. Concentration of the mother liquors and volatilization of the residue at 140 °C (0.25 mm) gave a mixture of solid and oil from which 1.2 g more of **13** was obtained by crystallization from acetone. The total yield of **13** was 9.7 g (49%). An analytical sample was prepared by recrystallization from methanol: IR (Nujol) 2.92 (OH), 3.03 (NH), 8.5–10 μm (COC); ^1H NMR (Me_2SO-d_6) 3.1–3.7 (m, 30 H, pattern similar to that of corresponding O-bridged compound), 2.33 ppm (s atop broad peak, 5 H, CH_2N and NH). Absence of an IR band near 6.2 μm for NH_2 eliminates the unsymmetrical isomer from consideration.

Anal. Calcd for $C_{18}H_{35}NO_8$: C, 54.94; H, 8.97; N, 3.56. Found: C, 54.86; H, 9.15; N, 3.67.

The volatile oily byproduct, 5.5 g, presumed to be mainly diamine isomers, could not be induced to crystallize. Neutralization with aqueous HCl gave a very viscous mixture of hydrochlorides which could not be crystallized.

9,19-Bis(aminoethyl)-9,19-bis(hydroxymethyl)-1,4,7,11,14,17-hexaoxacycloeicosane (14). A shaker tube loaded with 18.8 g (0.05 mol) of bis(oxetane) **9**, 100 mL of water, and 100 mL of hydrazine hydrate was heated at 200 °C for 20 h, cooled, and vented. The reaction mixture was filtered, evaporated to a thick oil, and allowed to crystallize. Filtration gave a moist solid which was recrystallized from tetrahydrofuran and then extracted thoroughly with ether, resulting in an ether-insoluble residue A: 4.1 g, mp 120–128 °C. Evaporation of the various filtrates and crystallization of the combined residues from toluene gave fraction B: 9.4 g, mp 107–122 °C. The total of mixed isomers of **14** was 13.5 g (66%). Recrystallization of A from toluene and then tetrahydrofuran gave an analytical sample: mp 118–127 °C; IR (Nujol) 2.98, 3.02, and 3.10 (OH and NH), 3.6–4 (H-bonded OH, NH), 6.12 (NH_2), 8.5–9.5 μm (COC, COH); mass spectrum (trimethylsilylated derivative), m/e 698 (tetrasilylated M^+), 596 ($M^+ - CH_2NHSi(CH_3)_3$).

Anal. Calcd for $C_{18}H_{38}N_2O_8$: C, 52.66; H, 9.33; N, 6.83. Found: C, 52.93; H, 9.33; N, 6.66.

For fraction B, the IR spectrum was similar to that of A, and the mass spectrum of silylated B was identical with that of A.

Anal. Found: C, 52.75; H, 9.41; N, 6.26.

The toluene filtrate from A deposited 0.1 g of bicyclic compound **13**, mp 147.5–149.5 °C (not depressed by authentic **13**), which was identified by IR. For **13**: mass spectrum (trimethylsilylated derivative), m/e 537 (M^+ with two silyl groups), 522 ($M^+ - CH_3$), 464 ($M^+ - Si(CH_3)_3$), 434 ($M^+ - CH_2OSi(CH_3)_3$). No peaks for mono- or trisilylated derivatives of **13** were found.

1,11-Bis(hydroxymethyl)-4,8-dioxo-3,9-diaza-6,13,16,19,22,25,28-heptaoxabicyclo[9.9.9]nonacosane Isomers 15b and 15a. Solutions of 4.2 g (0.0244 mol) of diglycolyl dichloride in 200 mL of dry benzene and 10.0 g (0.0244 mol) of **14** in 200 mL of hot glyme were added simultaneously and with vigorous stirring to a mixture of 14 mL of triethylamine and 800 mL of dry benzene in a creased flask. The addition was complete in 165 min, after which time the mixture was stirred an additional 30 min and then filtered. Evaporation of the filtrate gave 6.2 g of crude bisamides, mp 118–125 °C. Fractional crystallization from ether and then acetone separated the product into the less soluble isomer **15b** (1.2 g (10%), mp 170–173 °C) and the more soluble isomer **15a** (2.0 g (16%), mp 143–146 °C).

An analytical sample of **15b** was obtained from acetone/methanol: mp 174.5–176 °C; IR (Nujol) 2.92, 2.97, and 3.05 (OH, NH), 6.03 (C=O), 6.43 (amide II), 8.5–9.5 μm (COC, COH); mass spectrum (trimethylsilylated derivative), m/e 796 (tetrasilylated M^+), 724 (more intense, trisilylated M^+), 652 (very intense, disilylated M^+), 562 (disilylated $M^+ - HOSi(CH_3)_3$), 482 (unknown). The parent at m/e 652 was confirmed to be $C_{28}H_{56}N_2O_{11}Si_2$ by mass measurement (mol wt 652.3421 vs. calcd mol wt 652.3419). The spectrum suggests that the hydroxyls silylate rapidly and that the amide NH silylates more slowly; no change in the spectrum was seen after silylation had been allowed to proceed for several days.

Anal. Calcd for $C_{22}H_{40}N_2O_{11}$: C, 51.96; H, 7.93; N, 5.51. Found: C, 52.19; H, 8.01; N, 5.29.

An analytical sample of **15a** was obtained from acetone: mp 147–148.5 °C; IR (Nujol) 2.98 (sh), 3.01 (sh), and 3.03 (OH, NH), 5.95 and 6.02 (C=O), 6.4 (br, amide II), 8.6–9.5 μm (COC, COH); mass spectrum (trimethylsilylated derivative), m/e 652 (disilylated M^+), 562 (disilylated $M^+ - HOSi(CH_3)_3$), 482 (unknown). No higher mass peaks were observed, indicating the amide NH is too hindered to silylate or that only one OH and one amide NH are accessible to the reagent. The spectrum was unchanged after the silylation mixture had been allowed to stand for 10 days.

Anal. Calcd for $C_{22}H_{40}N_2O_{11}$: C, 51.96; H, 7.93; N, 5.51. Found: C, 52.12; H, 7.87; N, 5.38.

Registry No. 2, 59865-97-3; **3**, 72866-99-0; **3**, $(Me_3Si)_2$ derivative, 72867-00-6; **4**, 72867-01-7; **4**, NaSCN complex, 72869-06-8; **9**, 51652-72-3; **10**, 55064-12-5; **10**, $(Me_3Si)_2$ derivative, 72867-02-8; **11**, 55067-01-1; **11**, $(Me_3Si)_4$ derivative, 72867-03-9; **12a**, 72867-04-0; **12a**, $(Me_3Si)_2$ derivative, 72867-05-1; **12b**, 72867-06-2; **12b**, $(Me_3Si)_2$ derivative, 72867-07-3; **13**, 72867-08-4; **13**, $(Me_3Si)_2$ derivative, 72867-09-5; **14**, 72867-10-8; **14**, $(Me_3Si)_4$ derivative, 72881-49-3; **15a**, 72867-11-9; **15a**, $(Me_3Si)_2$ derivative, 72867-12-0; **15b**, 72904-11-1; **15b**, $(Me_3Si)_2$ derivative, 72904-12-2; **15b**, $(Me_3Si)_3$ derivative, 72881-50-6; **15b**, $(Me_3Si)_4$ derivative, 72881-51-7; diglycolyl dichloride, 21062-20-4; diethylene glycol, 111-46-6; ethylene glycol, 107-21-1; hydrazine hydrate, 7803-57-8.