

Jerald S. Bradshaw*, Krzysztof E. Krakowiak [1] and Reed M. Izatt

Department of Chemistry, Brigham Young University,
Provo, UT 84602 USA
Received March 27, 1989

A simple and convenient method to prepare polyaza-crowns and cyclams containing one or two unsubstituted macroring nitrogen atoms or a hydroxy group is described. The process involves the reaction of a *bis*-chloroamide with a *bis*-secondary amine followed by reduction of the cyclic diamide. The *bis*-chloroamide resembles a crab with two reactive organochloride groups poised and ready to react, hence the term "crab-like" cyclization. Nine new polyaza-crowns and cyclams were prepared.

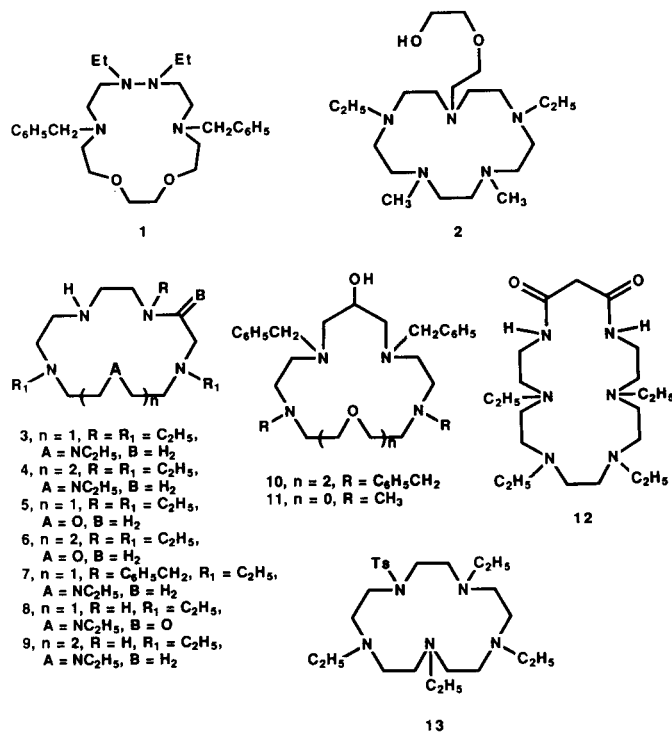
J. Heterocyclic Chem., **26**, 1431 (1989).

There is considerable interest in simple and inexpensive methods to prepare the polyaza-crowns and cyclams [2-6]. The polyaza-crowns are important because they have cation complexation properties that are intermediate between the cyclams, which complex strongly with the heavy metal cations, and the all oxygen crowns, which complex strongly with the alkali and alkaline earth metal ions [7]. Aza-crowns containing one or two reactive functional groups are used to prepare the cryptands [8,9], lariat crown ethers or cyclams [10-12] and for attachment to solid supports [5,13,14] or to biological tissues [15,16].

The usual methods to prepare the functionalized aza-crowns and cyclams include the Richman-Atkins tosylamide procedure [17,18], the Stetter diacid chloride-diamine ring closure reaction followed by reduction [19] and certain template ring closure reactions [20,21]. A method especially designed to prepare cyclams is the condensation of diesters (such as malonate) and polyamines [22-24]. Some of the above mentioned reactions have disadvantages such as the use of nitrogen protecting groups, which require two additional steps in the overall reaction sequence, the need for high dilution techniques or a low yield in the ring closure step. The various methods used to prepare the aza-crowns have been reviewed [6].

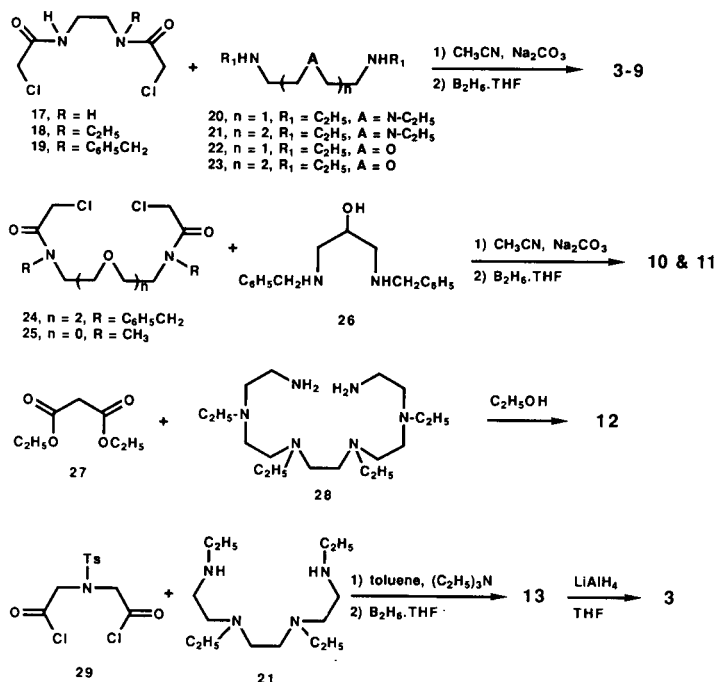
We have published several new procedures for the preparation of aza-crowns and, in one instance, cyclams using only a few steps. In most cases, high dilution techniques were not required [5,25-31]. Some of the compounds we have prepared include diaza-crowns in three or four steps [5,25,29], triaza- and tetraaza-crowns in a few steps [26,30], hydrazino crowns (like 1, Figure 1) [27] and polyaza-crowns and cyclams containing a hydroxyalkyl substituent on one of the macroring nitrogen atoms, 2, [28]. In all of these syntheses, per *N*-alkyl-substituted polyaza-crowns and cyclams were prepared. Thus, nitrogen protecting groups were not necessary. It is important to note that complexation of metal cations by aza-crowns containing *N*-alkyl substituents is about the same as complexation of the same cations by aza-crowns without these substituents [7].

Figure 1. Polyaza-Crowns and Cyclams



We now report the synthesis of a series of polyaza-crowns and cyclams each containing one or two unsubstituted macroring nitrogen atoms, 3-9, or a reactive hydroxy group, 10 and 11. *Bis*-chloroamides 17-19, 24 and 25 (Scheme 1) proved to be important synthons for the preparation of these new functionalized aza-crowns and cyclams. It is important to note that the amide portion of these *bis*-chloroamides function as protecting groups for the nitrogen atoms. These amide groups also increase the reactivity of the chloro atoms without the blistering problem of the β -chloro- or β -bromoamines. These *bis*-chloroamides were easy to prepare and, as mentioned, they are quite reactive towards the *bis*-secondary amines to form the intermediate macrocyclic diamides which were reduced to prepare 3-11 (Scheme 1). The starting *bis*-chloro-

Scheme 1. Preparation of Macrocycles



amides resemble a crab with the reactive chlorine atoms poised and ready to "grab" the amine groups, hence the term "crab-like" cyclization.

Results and Discussion.

The new mono- and difunctionalized macrocycles were prepared by reacting the appropriate crab-like *bis*-chloroamides and *bis*-secondary amines as shown in Scheme 1. These reactions were carried out in two steps. First, the *bis*-chloroamide and *bis*-secondary amine were reacted in acetonitrile using a carbonate base to form the macrocyclic *bis*-amide in good yields. The cyclic *bis*-amide was reduced in the second step using borane-THF to form the final polyaza macrocycle, **3-11**. The ¹H nmr spectra, molecular weights and combustion analyses were consistent for the proposed structures of the new polyaza-crowns and cyclams.

The crab-like cyclization reactions were carried out without using high dilution techniques and at room temperature. The reactants and the base were stirred together in acetonitrile. The yields of the intermediate macrocyclic diamides were in the 40-60% range. Changing the base from sodium carbonate to potassium carbonate did not change the yields more than about 5%. The reaction also was carried out in the presence of a tertiary amine. The crude intermediate macrocyclic diamides were separated quickly using flash silica gel chromatography and the products were reduced to the polyaza-crown or cyclam with borane-THF. In one case, for the preparation of **8**, only

the product with one of the two amide groups reduced was isolated on column chromatography. The fully reduced product was not isolated but a second product was observed on tlc.

The cyclization reactions gave good yields. It is possible that the *bis*-chloroamide and the *bis*-secondary amine reactants could associate by hydrogen bonding between the two amine hydrogen and the two amide oxygen atoms [32]. This association would place the chlorine atoms and the amine groups in position to react forming the cyclized *bis*-amide. In the case of *bis*-chloroamides **17-19**, an internal hydrogen bond between one amide hydrogen and the other amide oxygen would keep the two chloride units in the crab-like form needed for the cyclization reaction.

The starting crab-like *bis*-chloroamides are important synthons not only for the new macrocycles reported in this paper but for many other types of macrocyclic ligands. We have used these types of synthons previously to prepare hydrazinoaza-crown **1** [27], *N*-[2-(2-hydroxyethoxy)ethyl]-substituted cyclam **2** [28] and *N*-(2-ethylamino)ethyl-substituted triaza-crowns and cyclams [34]. Other important macrocycles containing propylene bridges, aromatic units, proton-ionizable groups or chiral moieties could also be prepared using these new crab-like synthons.

The crab-like *bis*-chloroamides were easily prepared by reacting an excess of chloroacetyl chloride with *bis*-*N*-alkyl secondary amines in stirred water-chloroform solvent using potassium carbonate as the base. This method is a modification of that reported by Cottrell and Gill [35] and

Table I
Starting Diamine, Eluant Solvent and ^1H nmr Data For
Bis-Chloroamide Products **18**, **19**, and **24**

Product	Diamine (source)	Eluant solvent [a]	^1H nmr
18	$\text{C}_2\text{H}_5\text{NHCH}_2\text{CH}_2\text{NH}_2$ (Fluka)	T/E: 25:1	1.2 (dt, 3 H), 3.45 (m, 6 H), 4.0 (t, 4 H), 7.2 (b, 1 H)
19	$\text{C}_6\text{H}_5\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$ (Kodak)	T/E: 10:1	3.5 (m, 4 H), 4.0 (m, 4 H), 4.6 (s, 2 H), 7.0 (b, 1 H), 7.3 (m, 5 H)
24	$[\text{C}_6\text{H}_5\text{CH}_2\text{NHCH}_2\text{CH}_2\text{OCH}_2]_2$ (Ref [25])	T/E: 20:1	3.5 (m, 12 H), 4.05 (d, 2 H), 4.3 (d, 2 H), 4.65 (d, 4 H), 7.2 (m, 10 H)

[a] T = toluene, E = ethanol.

Lin and co-workers [36] for similar compounds. The macrocycle prepared from each of these *bis*-chloroamides gave satisfactory combustion analyses. The *bis*-secondary amines used to prepare all macrocycles were either purchased or prepared by known procedures.

For comparison purposes, macrocyclic *bis*-amide **12** and cyclam **3** were prepared by procedures reported previously for those types of compounds (Scheme 1). Many cyclams have been prepared starting with diethyl malonate followed by reduction [22-24]. We prepared cyclic diamide **12** to compare the yields of the cyclization step. Starting from **27** and **28**, we obtained **12** in a 17% yield while the macrocyclic diamides leading to **3-9** were obtained in 40-60% yields. For example, the initial diamide product which contains four *N*-ethyl and two *N*-H groups from the reaction of **17** and **21** was produced in a 47% yield.

Macrocycle **3** was prepared by the Stetter method [19] by first reacting *N*-tosyl diacid chloride **29** with **21** followed by reduction to give tosyl-substituted macrocycle **13** in a 14% overall yield (see Scheme 1). The tosyl group was reductively removed using lithium aluminum hydride to give **3** in a 37% yield. The overall yield for the preparation of **3** from this process (about 5%) is way below the 30% of **3** obtained in our crab-like cyclization.

EXPERIMENTAL

Infrared (ir) spectra were obtained on Beckman Aculab 2 or Perkin Elmer FT 1600 spectrometers. The proton nuclear magnetic resonance (^1H nmr) spectra were obtained on a Varian Gemini 200 spectrometer using deuteriochloroform. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Molecular weights were determined by the electron impact method on a Finnegan 8430 High Resolution Mass Spectrometer. Starting diamines were purchased when available or synthesized as indicated. Starting *bis*-chloroamides **17** and **25** were prepared as reported [35,36]. The other starting materials were prepared as follows.

General Procedure to Prepare *Bis*-Chloroamides **18**, **19** and **24**.

Chloroacetyl chloride (Fluka) (0.3 mole) in 120 ml of chloroform and 33 g of potassium carbonate in 120 ml of water were each simultaneously added through dropping funnels to a stirred solution of 0.1 mole of the appropriate diamine in 100 ml of chloroform at 0°-5° over a four-hour period. The mixture was stirred an additional two hours at 25°. The chloroform layer was separated and washed twice with 50 ml portions of water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated under vacuum at 60° to give crude product in about 90% yield. The residue was chromatographed on silica gel where necessary. The crude *bis*-chloroamide products were used to prepare the appropriate macrocycles without further purification. The specific starting materials, eluant solvents (where used) and ^1H nmr data for the *bis*-chloroamides are given in Table I.

Preparation of 7,10,13,16-Tetraethyl-1,4,7,10,13,16-hexaazahexadecane (**28**) (Scheme I).

A mixture of 3.84 g (14.9 mmoles) of **21** (Phaltz and Bauer), 3.0 g (32 mmoles) of chloroacetamide (Aldrich) and 15 g of anhydrous sodium carbonate were refluxed in 100 ml of acetonitrile for two days. The mixture was evaporated under reduced pressure and 50 ml of methylene chloride was added to the residue. The mixture was filtered and the methylene chloride solvent was evaporated. The resulting residue was chromatographed on neutral alumina (toluene/ethanol: 50/1 then 10/1) to give 3.5 g (63%) of 4,7,10,13-tetraethyl-2,15-dioxo-1,4,7,10,13,16-hexaazahexadecane as an oil; ^1H nmr (δ): 1.0 (m, 12 H), 2.5 (m, 20 H), 3.0 (s, 4 H), 5.75 (b, 2 H), 8.0 (b, 2 H). The crude diamide was reduced with 1.6 g of lithium aluminum hydride in 50 ml of THF at 0° for 4 hours and then 16 hours at reflux temperature. The mixture was cooled to 5° and 6 ml of 5% aqueous sodium hydroxide was added. The mixture was filtered and the residue was washed with hot THF. The solution was evaporated and the residue was distilled to give 1.8 g (56%) of **28**, bp 136-141°/0.065 mm; ^1H nmr (δ): 1.0 (m, 12 H), 1.5 (b, 4 H), 2.5 (m, 24 H), 2.65 (m, 4 H). Compound **28** was used to prepare **12** without further purification.

General Procedure to Prepare Macrocycles **3-11** (Scheme I).

A mixture of 0.01 mole of the appropriate *bis*-chloroamide, **17-19**, **24** or **25**, 0.01 mole of the appropriate polyamine, **20-23** or **26**, and 20 g of sodium carbonate or 25 g of potassium carbonate was stirred at room temperature in 150 ml of acetonitrile for

48-72 hours. The mixture was filtered, the solvent evaporated and 50 ml of chloroform was added. The mixture was again filtered and evaporated. The crude cyclic bis-amide product was chromatographed on silica gel (isopropyl alcohol/ethanol). The resulting bis-amide was reduced by the borane-THF complex (60-80 ml of a 1 M solution). Water (5-10 ml) was added to the THF solution to decompose the excess borane. The solvent was evaporated and 30-60 ml of 18% aqueous hydrochloric acid was carefully added. The mixture was refluxed for 2-5 hours and evaporated. Water (15-20 ml) was added and the mixture was stirred and filtered. Ammonium hydroxide solution (28%) was added to the filtrate until a pH of 9 or 10 was reached. The solution was then extracted several times by 80 ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate, filtered and evaporated to give the product. In some cases, the residue was chromatographed on a short 250 mesh silica gel column (methanol/ammonia). The specific reactants, yields and spectral data are listed below for each product.

1,4,7,10-Tetraethyl-1,4,7,10,13-pentaazacyclopentadecane (3) (Scheme 1).

Macrocycle 3 was prepared from 18 and 20 (Alfa) to give 1.1 g (34%) of the product; ^1H nmr: (δ) 1.00 (t, 12 H), 2.55 (m, 29 H).

Anal. Calcd. for $\text{C}_{18}\text{H}_{31}\text{N}_5 \cdot 0.5 \text{H}_2\text{O}$: C, 64.24; H, 12.28; mol wt, 327.56. Found: C, 64.15; H, 12.16; mol wt, 328.

1,4,7,10,13-Pentaethyl-1,4,7,10,13,16-hexaazacyclooctadecane (4).

Macrocycle 4 was prepared from 18 and 21 (Pfaltz and Bauer) to give 1.3 g (33%) of the product; ^1H nmr: (δ) 0.95 (t, 15 H), 2.50 (m, 35 H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{30}\text{N}_6$: C, 66.28; H, 12.64; mol wt, 398.68. Found: C, 66.30; H, 12.43; mol wt, 398.

4,10,13-Triethyl-1-oxa-4,7,10,13-tetraazacyclopentadecane (5).

Macrocycle 5 was prepared from 18 and 22 [37] to give 0.93 g (31%) of the product; ^1H nmr: (δ) 1.00 (t, 9 H), 2.60 (m, 23 H), 3.45 (m, 2 H), 3.55 (m, 2 H).

Anal. Calcd. for $\text{C}_{16}\text{H}_{30}\text{N}_4\text{O}$: C, 63.95; H, 12.01; mol wt, 300.49. Found: C, 63.77; H, 11.96; mol wt, 300.

7,10,16-Triethyl-1,4-dioxa-7,10,13,16-tetraazacyclooctadecane (6).

Macrocycle 6 was prepared from 18 and 23 [38] to give 1.2 g (35%) of the product; ^1H nmr: (δ) 1.00 (t, 9 H), 2.60 (m, 23 H), 3.55 (m, 8 H).

Anal. Calcd. for $\text{C}_{18}\text{H}_{40}\text{N}_4\text{O}_2$: C, 62.75; H, 11.70; mol wt, 344.93. Found: C, 62.70; H, 11.76; mol wt, 344.

1-Benzyl-4,7,10-triethyl-1,4,7,10,13-Pentaazacyclopentadecane (7).

Macrocycle 7 was prepared from 19 and 20 to give 1.48 g (38%) of the product; ^1H nmr: (δ) 1.00 (m, 9 H), 2.50 (m, 27 H), 3.60 (s, 2 H), 7.4 (m, 5 H).

Anal. Calcd. for $\text{C}_{23}\text{H}_{43}\text{N}_5$: C, 70.90; H, 11.12; mol wt, 389.63. Found: C, 70.78; H, 10.95; mol wt, 390.

4,7,10-Triethyl-1,4,7,10,13-pentaazacyclopentadecan-2-one (8).

Macrocycle 8 was prepared from 17 and 20 to give 0.57 g (18%) of the product; ^1H nmr: (δ) 1.00 (m, 9 H), 2.30 (b, 1 H), 2.50 (m, 18 H), 2.70 (t, 2 H), 3.00 (s, 2 H), 3.40 (m, 2H), 8.10 (b, 1 H).

Anal. Calcd. for $\text{C}_{16}\text{H}_{35}\text{N}_5\text{O}$: C, 61.31; H, 11.24; mol wt, 313.45. Found: C, 61.09; H, 11.34; mol wt, 313.

1,4,7,10-Tetraethyl-1,4,7,10,13,16-hexaazacyclooctadecane (9).

Macrocycle 9 was prepared from 17 and 21 to give 0.67 g (18%) of the product; ^1H nmr: (δ) 1.00 (t, 12 H), 2.40 (b, 2 H), 2.60 (m, 28 H), 2.70 (s, 4 H).

Anal. Calcd. for $\text{C}_{20}\text{H}_{46}\text{N}_6$: C, 64.81; H, 12.51; N, 22.68; mol wt, 370.62. Found: C, 64.70; H, 12.35; N, 22.57; mol wt, 371.

7,10,14,17-Tetrabenzyl-15-hydroxy-1,4-dioxa-7,10,14,17-tetraazacyclononadecane (10).

Macrocycle 10 was prepared from 24 and 26 to give 2.60 g (40%) of the product; ^1H nmr: (δ) 2.7 (m, 16 H), 3.6 (m, 17 H), 4.5 (b, 1 H), 7.3 (m, 20 H).

Anal. Calcd. for $\text{C}_{35}\text{H}_{55}\text{N}_4\text{O}_2$: C, 75.65; H, 8.36; mol wt, 650.96. Found: C, 75.62; H, 8.10; mol wt, 650.

1,10-Dibenzyl-4,7-dimethyl-12-hydroxy-1,4,7,10-tetraazacyclotridecane (11).

Macrocycle 11 was prepared from 25 and 26 to give 1.0 g (26%) of the product; ^1H nmr: (δ) 2.05 (s, 6 H), 2.2-3.1 (m, 16 H), 3.3 (d, 2 H), 3.65 (m, 3H), 5.5 (b, 1 H), 7.3 (m, 10 H).

Anal. Calcd. for $\text{C}_{25}\text{H}_{39}\text{N}_4\text{O}$: C, 73.13; H, 9.33; mol wt, 410.60. Found: C, 73.21; H, 9.52; mol wt, 410.

1,4,7,10-Tetraethyl-1,4,7,10,13,16-hexaazacyclononadecane-17,19-dione (12).

A mixture of 1 g (2.9 mmoles) of 28 and 0.47 g (2.9 mmoles) of 27 (Aldrich) was refluxed for 4 days in 100 ml of ethanol. The solvent was removed under reduced pressure and the residue was chromatographed on neutral alumina (toluene/ethanol: 20/1 then 10/1) to yield 0.2 g (17%) of 15 as an oil; ^1H nmr: (δ) 1.0 (m, 12 H), 2.35 (m, 24 H), 3.1 (s, 2 H), 3.25 (m, 4 H), 7.6 (s, 2 H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{44}\text{N}_6\text{O}_2$: C, 61.12; H, 10.73; mol wt, 412.61. Found: C, 61.29; H, 10.73; mol wt, 412.

1-Tosyl-4,7,10,13-tetraethyl-1,4,7,10,13-pentaazacyclopentadecane (13) and its Reduction to 3.

Compound 29 [39] (3.24 g, 0.01 mole) in 100 ml of toluene and a mixture of 2.58 g (0.01 mole) of 21 and 3.03 g (0.03 mole) of triethylamine in 100 ml of toluene were each simultaneously dropped into 400 ml of toluene over a 5 hour period. The mixture was filtered, the residue was washed with hot toluene and the filtrate was evaporated under reduced pressure. The residue was chromatographed on neutral alumina (toluene/ethanol: 40/1) to give 1 g (19%) of the intermediate cyclic diamide; ^1H nmr: (δ) 1.0 (m, 12 H), 2.4 (m, 15 H), 3.3 (m, 8 H), 4.3 (m, 4 H), 7.5 (dd, 4 H); ms: 509, 354. This diamide (0.6 g, 1.1 mmoles) in 10 ml of THF was dropped into 18 ml of 1 M borane-THF solution and the mixture was refluxed for 18 hours. Water was added and the mixture was evaporated under reduced pressure. The residue was mixed with 20 ml of 18% aqueous hydrochloric acid and refluxed for 2 hours. The mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a minimum of THF and passed through an Amberlit column. Product 13 was chromatographed on neutral alumina (THF/toluene: 2/3 then THF) to give 0.4 g (71%) of 13; ^1H nmr: (δ) 0.95 (t, 12 H), 2.5 (m, 27 H), 3.2 (t, 4 H), 7.5 (dd, 4 H); ms: 481, 326. Compound 13 (0.4 g, 0.9 mmole) in 20 ml of THF was dropped into 0.5 g of lithium aluminum hydride in 20 ml of THF and the resulting mixture was refluxed for 18 hours. Water was then added to destroy the excess lithium aluminum hydride. The mixture was filtered and the residue was washed with hot THF. The filtrate was evaporated and the residue was chromatographed on a short neutral alumina column (ethanol) to give 0.1 g (37%) of 3 which had the same spectral

properties as **3** prepared above.

Acknowledgement.

The authors thank the Centers of Excellence Program of the State of Utah for supporting this work.

REFERENCES AND NOTES

- [1] Permanent address for K. E. K.: Department of Chemical Technology, School of Medicine, 90134 Lodz, Poland.
- [2] S. Kulstad and L. A. Malmstein, *Tetrahedron Letters*, **21**, 643 (1980).
- [3] J. Jazwinski, J. M. Lehn, R. Meric, J. P. Vigneron, M. Cesario, J. Guilhem and C. Pascard, *Tetrahedron Letter*, **28**, 3489 (1987).
- [4] J. Jazwinski, J. M. Lehn, D. Lilienbaum, R. Ziessel, J. Guilhem and C. Pascard, *J. Chem. Soc., Chem. Commun.*, 1691 (1987).
- [5] J. S. Bradshaw, K. E. Krakowiak, R. L. Bruening, B. J. Tarbet, P. B. Savage and R. M. Izatt, *J. Org. Chem.*, **53**, 3190 (1988).
- [6] K. E. Krakowiak, J. S. Bradshaw and D. J. Zamecka-Krakowiak, *Chem. Rev.*, **89**, 929 (1989).
- [7] R. M. Izatt, J. S. Bradshaw, S. A. Neilsen, J. D. Lamb, J. J. Christensen and D. Sen, *Chem. Rev.*, **85**, 271 (1985).
- [8] B. Dietrich, J. M. Lehn, J. P. Sauvage and J. Blanzat, *Tetrahedron*, **29**, 1629 (1973).
- [9] D. A. Babb, B. P. Czech and R. A. Bartsch, *J. Heterocyclic Chem.*, **23**, 609 (1986).
- [10] R. A. Schultz, B. D. White, D. M. Dishong, K. A. Arnold and G. W. Gokel, *J. Am. Chem. Soc.*, **107**, 6659 (1985).
- [11] A. K. Basak and T. A. Kaden, *Helv. Chim. Acta*, **66**, 2086 (1983).
- [12] D. Tschudin, A. Basak and T. A. Kaden, *Helv. Chim. Acta*, **71**, 100 (1988).
- [13] J. S. Bradshaw, R. L. Bruening, K. E. Krakowiak, B. J. Tarbet, M. L. Bruening, R. M. Izatt and J. J. Christensen, *J. Chem. Soc., Chem. Commun.*, 812 (1988).
- [14] R. M. Izatt, R. L. Bruening, M. L. Bruening, B. J. Tarbet, K. E. Krakowiak, J. S. Bradshaw and J. J. Christensen, *Anal. Chem.*, **60**, 1825 (1988).
- [15] J. R. Morphy, D. Parker, R. Alexander, A. Bains, A. F. Carne, M. A. Eaton, A. Harrison, A. Millican, A. Phipps, S. K. Rhind, R. Titmas and D. Weatherby, *J. Chem. Soc., Chem. Commun.*, 156 (1988).
- [16] M. K. Moi and C. F. Meares, *J. Am. Chem. Soc.*, **110**, 6266 (1988).
- [17] J. E. Richman and T. J. Atkins, *Org. Synth.*, **58**, 86 (1978).
- [18] M. Hediger and T. A. Kaden, *Helv. Chim. Acta*, **66**, 861 (1983).
- [19] H. Stetter and J. Marx, *Ann. Chem.*, **607**, 59 (1957).
- [20] E. K. Barefield, F. Wagner and K. D. Hodges, *Inorg. Chem.*, **15**, 1370 (1976).
- [21] R. J. Gue, T. W. Hambley, J. M. Harrowfield, A. M. Sargeson and M. R. Snow, *J. Am. Chem. Soc.*, **106**, 5478 (1984).
- [22] I. Tabushi, H. Okino and Y. Kuroda, *Tetrahedron Letters*, 4339 (1976).
- [23] I. Tabushi, Y. Taniguchi and H. Kato, *Tetrahedron Letters*, 1049 (1977).
- [24] E. Kimura, M. Shinoya, M. Okamoto and H. Nada, *J. Am. Chem. Soc.*, **110**, 3679 (1988).
- [25] J. S. Bradshaw and K. E. Krakowiak, *J. Org. Chem.*, **53**, 1808 (1988).
- [26] K. E. Krakowiak, J. S. Bradshaw and R. M. Izatt, *Tetrahedron Letters*, **29**, 3521 (1988).
- [27] J. S. Bradshaw, K. E. Krakowiak, G. Wu and R. M. Izatt, *Tetrahedron Letters*, **29**, 5589 (1988).
- [28] J. S. Bradshaw, K. E. Krakowiak and R. M. Izatt, *Tetrahedron Letters*, **30**, 803 (1989).
- [29] J. S. Bradshaw, K. E. Krakowiak and R. M. Izatt, *J. Heterocyclic Chem.*, **26**, 565 (1989).
- [30] K. E. Krakowiak, J. S. Bradshaw, E. V. Forsnes and R. M. Izatt, *J. Heterocyclic Chem.*, **26**, 661 (1989).
- [31] C. W. McDaniel, J. S. Bradshaw, K. E. Krakowiak, R. M. Izatt, P. B. Savage, B. J. Tarbet and R. L. Bruening, *J. Heterocyclic Chem.*, **26**, 413 (1989).
- [32] J. Zabicky, "The Chemistry of Amides", Wiley Interscience, 1970, p 230.
- [33] J. S. Bradshaw, P. Huszthy and R. M. Izatt, *J. Heterocyclic Chem.*, **23**, 1673 (1986).
- [34] K. E. Krakowiak, J. S. Bradshaw, N. K. Dalley, W. Jiang and R. M. Izatt, *Tetrahedron Letters*, in press.
- [35] T. L. Cottrell and J. E. Gill, *J. Chem. Soc.*, 129 (1947).
- [36] W. O. Lin, J. A. A. Figueira and H. G. Alt, *Monats. Chem.*, **116**, 217 (1985).
- [37] K. Krakowiak and B. Kotelko, *Acta Polon. Pharm.*, **40**, 685 (1983).
- [38] T. Kikui, H. Maeda, Y. Nakatsuji and M. Okahara, *Synthesis*, 74 (1984).
- [39] J. M. Lehn, J. Simone and J. Wazner, *Nouveau J. Chem.*, **1**, 14 (1977).