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Nitrogen-Capped π-Prismands: Syntheses and Conformational Analyses

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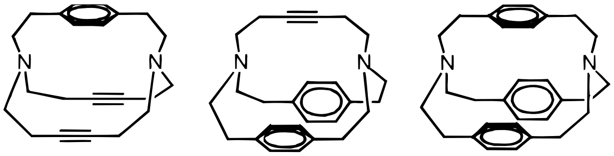
ABSTRACT

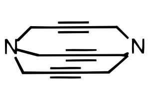


5 **6** **7**

The one-pot syntheses of the new diazabicyclophanes 5–7 are described. The benzene rings incorporated in the bridging chains exhibit rotational motion which is examined by means of variable-temperature NMR experiments and semiempirical calculations. X-ray analysis and NMR studies indicate that the metal ion in the endohedral silver(I) complex of 7 fluctuates between the two nitrogen atoms.

The detailed investigation of 1,(k+2)-diazabicyclo[k,l,m]-alkanes[1] proved that for k, l, m = 3−5 the *in*,*in*-conformation[2] of the nitrogen bridgeheads is more stable than the *out*,*out*-conformation. These studies also reveal that mono- and diprotonation depend on the intrabridgehead distance and on the conformation at the nitrogen atoms. Although quite a number of medium sized bicyclic diazaalkanes have been prepared,[1,2] no host−guest complexes with suitable metal ions were encountered so far. We ascribe this observation to the fact that the space-filling alkane chains prevent the penetration of metal ions and, furthermore, in most cases more than two coordination sites in a cage molecule are required to give stable metal complexes.

To probe this assumption we recently synthesized a number of bicyclic compounds with nitrogen at both bridgehead positions, in which triple bonds are incorporated in the middle of the alkane chains, such as 1,6-diazabicyclo-[4.4.4]tetradeca-3,8,12-triyne (**1**),[3] 1,8-diazabicyclo[6.6.4]-octadeca-4,11,16-triyne (**2**),[4] and 1,8-diazabicyclo[6.6.6]-eicosa-4,11,17-triyne (**3**).[5]



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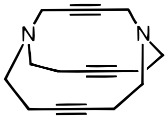

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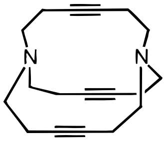

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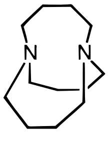

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The triple bonds have two functions: they expand the cage of the corresponding diazabicycloalkane along the N···N axis and they act as additional soft donors forming a "π-belt" around the cavity. In the case of **3**, which resembles a stretched 1,4-diazabicyclo[4.4.4]tetradecane (**4**), the intrabridgehead distance allows not only double *in*,*in*-protonation but also strong complexation of copper(I) and silver(I) in the center of the molecule.[6]

Besides alkyne units we also took into consideration 1,4-substituted benzene rings as linear and rigid spacer groups. In this Letter we report congeners of **3** in which the triple bonds are replaced successively by benzene systems. This leads to 17-(1,4)benzena-1,8-diazabicyclo[6.6.5]nonadecaphane-4,11-diyne (**5**), 11,16-(1,4)dibenzena-1,8-diazabicyclo-[6.5.5]octadecaphane-4-yne (**6**), and 4,10,15-(1,4)tribenzena-1,7-diazabicyclo[5.5.5]heptadecaphane (**7**).[7] Compared to the triyne **3**, the introduction of benzene rings should cause a

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[1] (a) Alder, R. W.; East, S. P. *Chem. Rev.* **1996**, *96*, 2097 and references therein. (b) Alder, R. W. *Acc. Chem. Res.* **1983**, *16*, 321.

[2] Simmons, H. E.; Park, C. H.; Uyeda, R. T.; Habibi, M. F. *Trans. N.Y. Acad. Sci. Ser. II* **1970**, *32*, 521.

[3] Gleiter, R.; Hövermann, K.; Ritter, J.; Nuber, B. *Angew. Chem.* **1995**, *107*, 867; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 789.

[4] Wolfart, V.; Gleiter, R.; Krieger, C.; Pritzkow, H. *Tetrahedron Lett.* **1998**, *39*, 513.

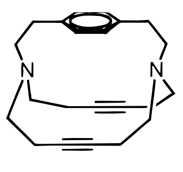
[5] Wolfart, V.; Gleiter, R.; Irngartinger, H.; Oeser, T.; Krieger, C. *Eur. J. Org. Chem.* **1998**, 2803.

[6] Kunze, A.; Gleiter, R.; Rominger, F. *Chem. Commun.* **1999**, 171.

[7] For the bicyclic systems we follow the 1998 IUPAC recommendations: *Pure Appl. Chem.* **1998**, *70*, 1513.

10.1021/ol991360y CCC: $19.00

further elongation of the cage while the soft coordination sites are maintained.



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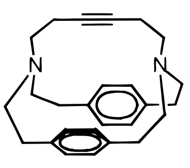

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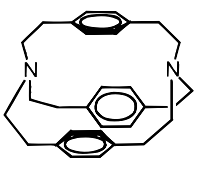
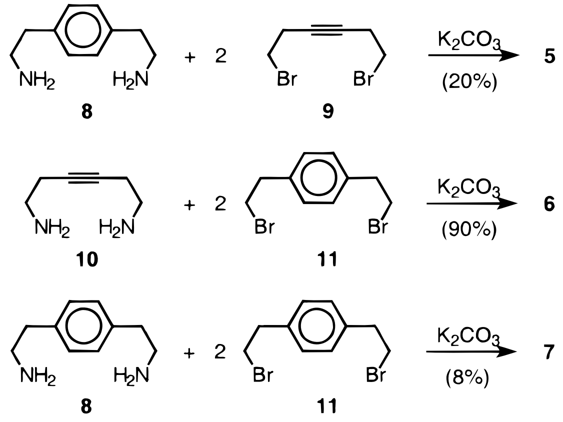


7

Our synthesis of the bicyclophanes **5**−**7** was rather straightforward. Three-component condensation of the appropriate terminal diamines and dibromides in refluxing acetonitrile employing potassium carbonate as base gave the bicyclic products in one step (Scheme 1).

Scheme 1



As starting materials we used 1,4-bis(2-aminoethyl)benzene (**8**),[8] 1,6-dibromohex-3-yne (**9**),[9] 1,6-diaminohex-3-yne (**10**),[10] and 1,4-bis(2-bromoethyl)benzene (**11**),[11] which were reacted in 0.01−0.05 M solutions for 3−6 days.

The yields obtained by these one-step cyclizations were low to satisfactory, ranging from 8% for the tribenzena derivative to a remarkable 90% for the bicycle **6**. The low yield in the case of **7** is possibly a consequence of steric repulsion between the three aromatic systems.

Table 1 lists relevant spectroscopic data for bicyclophanes **5**−**7**.[12] The UV spectroscopy provided early evidence of ring bending in aromatic systems.[13] Our spectral data point out that the benzene rings in all three compounds are rather unstrained since the absorption maxima are similar to that of *p*-xylene (λ_{max} 268 nm).

Table 1. Comparison of Selected Spectroscopic Data for Bicyclophanes **5**−**7**

compd	UV λ_{max} (nm)[a]	^1H NMR H_{ar} (δ)
5	266	7.04[b]
6	268	7.04/6.87[c]
7	268	6.54[b]

[a] Recorded in methylene chloride. [b] Recorded in methylene chloride-d_2 at room temperature. [c] Recorded in chloroform-d_1 at room temperature.

The ^1H NMR spectra measured at room temperature reveal that the chemical shifts of the aromatic protons (H_{ar}) in **5** (AA′A″A‴ system) and **6** (AA′BB′) are located in the normal aromatic region, while those of **7** (AA′A″A‴) exhibit a very high field resonance in comparison. The upfield shift indicates the occurrence of a mutual transannular shielding effect of the benzene rings, which is understandable if they are considered as internal rotors and the observed singlet for H_{ar} represents an average value at various rotational conformations.

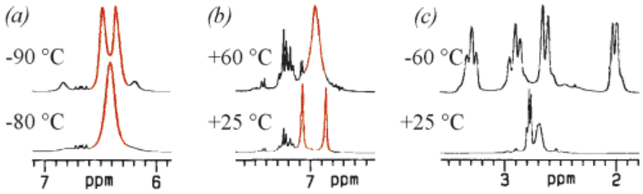


Figure 1. Aromatic region of the ^1H NMR spectra of bicyclophanes **7** (a) and **6** (b) and methylene group resonances of **7** (c) at different temperatures. The resonances of H_{ar} are shown in red.

To explore the conformational dynamic processes in the bicyclophanes **5**−**7** we conducted variable-temperature ^1H NMR experiments (Figure 1).[14] In the case of **7**, two different conformational changes were detected. On one hand, we found that the singlet of the aromatic protons resolves into two signals of equal intensity below −82 °C, separated by 0.12 ppm, a phenomenon which can be rationalized with a major or frozen “lateral” conformation of the formerly

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(8) Ruggli, P.; Prijs, B. *Helv. Chim. Acta* **1945**, *28*, 674.

(9) Brudermüller, M.; Musso, H.; Wagner, A. *Chem. Ber.* **1988**, *121*, 2239.

(10) To our knowledge, this is the first time that compound **10** is reported in the literature. A detailed description of the synthesis and spectral and analytical data can be found in the Supporting Information.

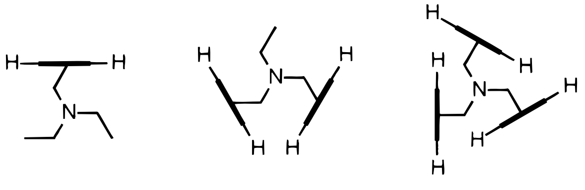
(11) Longone, D. T.; Küsefoglu, S. H.; Gladysz, J. A. *J. Org. Chem.* **1977**, *42*, 2787.

(12) Selected spectroscopic data for **5**: ^1H NMR (300 MHz, in CD_2Cl_2) δ 7.04 (4H, s, H_{ar}), 2.80−2.58 (8H, m, $PhCH_2CH_2N$), 2.31−2.13 (16H, m, $CCCH_2CH_2N$); ^{13}C NMR (75 MHz, in CD_2Cl_2) δ 137.0 ($C_{ar,q}$), 128.3 ($C_{ar,t}$), 78.4 (C_{CC}), 54.5 (CH_2N_{Ph}), 51.4 (CH_2N_{CC}), 32.8 ($PhCH_2$), 18.1 ($CCCH_2$); FAB-HRMS $[C_{22}H_{29}N_2]^+$ calcd 321.2330, found 321.2348. Selected spectroscopic data for **6**: ^1H NMR (500 MHz, in $CDCl_3$) δ 7.04 (4H, s, H_{ar}), 6.87 (4H, s, H_{ar}), 2.82−2.50 (16H, m, $PhCH_2CH_2N$), 2.13 (4H, m, CH_2N_{CC}), 2.06 (4H, t, ^3J = 5.6 Hz, $CCCH_2$); ^{13}C NMR (125 MHz, in $CDCl_3$) δ 137.1 ($C_{ar,q}$), 129.7 ($C_{ar,t}$), 128.1 ($C_{ar,t}$), 78.1 (C_{CC}), 53.9 (CH_2N_{Ph}), 49.8 (CH_2N_{CC}), 33.1 ($PhCH_2$), 18.0 ($CCCH_2$); FAB-HRMS $[C_{26}H_{33}N_2]^+$ calcd 373.2644, found 373.2650. Selected spectroscopic data for **7**: ^1H NMR (500 MHz, in CD_2Cl_2) δ 6.54 (12H, s, H_{ar}), 2.84 (12H, t, ^3J = 5.6 Hz, $PhCH_2$), 2.67 (12H, br s, CH_2N); ^{13}C NMR (125 MHz, in CD_2Cl_2) δ 136.2 ($C_{ar,q}$), 128.3 ($C_{ar,t}$), 52.3 (CH_2N), 31.8 ($PhCH_2$); FAB-HRMS $[C_{30}H_{37}N_2]^+$ calcd 425.2957, found 425.2966.

(13) As was observed in small meta- and paracyclophanes, shortening of the bridge leads to a distinctive bathochromic shift in the UV spectra which is associated with the increasing out-of-plane deformation of the benzene ring: (a) Bickelhaupt, F.; de Wolf, W. H. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 459 and references therein. (b) Allinger, N. L.; Sprague, J. T.; Liljefors, T. *J. Am. Chem. Soc.* **1974**, *96*, 5100.

(14) 300 MHz ^1H NMR spectra were recorded at a variety of temperatures from 173 K (in methylene chloride-d_2) to 413 K (in dimethylformamide-d_7).

rotating π-systems with respect to one another as illustrated in Figure 2. In this model, one set of *ortho*-protons is forced to reside in the diamagnetic region of the adjacent benzene ring and thus should absorb at a higher field than the other.



5 **6** **7**

Figure 2. Schematic drawing of proposed conformations of the benzene rings in bicyclophanes **5**−**7** referring to the NMR spectroscopic data. Viewed along the N···N-axis.

Furthermore, we observed an interesting splitting of the resonances of each of the two sets of methylene groups below −20 °C. The resulting signal pattern (Figure 1c) proves that the geminal methylene protons become diastereotopic on the NMR time scale. This matches with a torsional motion of the entire bridging chains that is frozen on the NMR time scale to give rise to a conformation that displays either C_{3h} or D_3 symmetry.

At room temperature the ^{1}H NMR spectrum of compound **6** contains two signals of the same intensity for H_{ar} suggesting that both benzene rings prefer to adopt a "face" conformation with regard to the center of the cage (Figure 2). These two resonances coalesce to a singlet (δ 6.96) at 48 °C in what is attributed to a relatively fast internal rotation of the aromatic rings within the NMR time scale.

The singlet for H_{ar} in compound **5** detected at room temperature appears to be invariant toward heating or cooling within the examined temperature range. Thus, it is not possible to determine whether the benzene system is rotating on the 1,4-axis or if it is frozen in a "face" conformation at a certain temperature (Figure 2).

The results of the dynamic NMR studies are summarized in Table 2. The free energies of activation to torsional motion of the aromatic rings estimated by the coalescence method[15] are compared with theoretically calculated values[16] for various thinkable rotational processes.

Table 2. Comparison of the Free Energies of Activation to Rotation of the Benzene Rings in Bicyclophanes **5**−**7** Derived from Experimental and Computational Analysis (kcal/mol)

compd	T_c [a]	$\Delta\nu$ [b]	$\Delta G^{\ddagger}_{exp}$ [c]	Ar_{rot} [d]	$\Delta G^{\ddagger}_{PM3}$ [e] (NIMAG) [f]	$\Delta G^{\ddagger}_{AM1}$ [e] (NIMAG) [f]
5				1	23.0 (1)	25.0 (1)
6	321	68	15.6	1	20.5 (1)	16.4 (1)
				2	62.1 (2)	52.3 (1)
7	191	36	9.3	1	6.7 (1)	8.9 (1)
				2	51.5 (1)	57.5 (1)
				3	84.0 (5)	103.9 (3)

[a] In K. [b] In Hz. [c] Reference 15. [d] Number of rotating benzene rings. [e] Reference 16. Zero-point energy corrections and thermal corrections included. [f] NIMAG = number of imaginary frequencies.

Semiempirical PM3 and AM1 calculations assign the torsional barriers to rotation of one benzene ring, while the other bridges are not involved in the rotational motion. Frequency calculations were performed to verify that the optimized structures are true transition states (one imaginary frequency was found). There is good agreement with the experimental values especially for the AM1-calculated values.

The calculated barrier for **5** is 25.0 kcal/mol. This increase of the activation barrier from **7** to **5** is associated with the shorter N···N distance and the greater out-of-plane bending of the benzene rings for the smaller bicycles. Furthermore, the transition states for the correlated rotation of two or three benzene rings were calculated to be higher in energy, which means that these correlated torsional motions are not likely to take place at moderate temperature.[17]

The structural assignment of the tribenzena bicycle is confirmed by X-ray analysis of single crystals of **7** (Figure 3). In fact, a "trilateral" conformation of the aromatic systems is utilized in the solid state. Analogous to the triyne **3**, the two nitrogen atoms adopt the *in*,*in*-conformation, but the intrabridgehead distance (6.14 Å)[18] has been enlarged by about 1.1 Å due to the substitution of the triple bonds by benzene units.

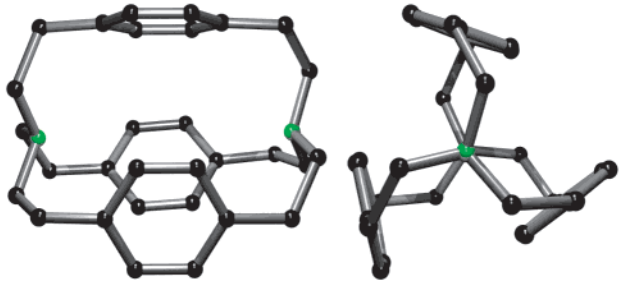


Figure 3. Solid-state structure of **7** as determined by X-ray analysis (solvent molecules and hydrogen atoms omitted for clarity).

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[15] $\Delta G^{\ddagger}_{exp}$ were determined by using the simplified Eyring equation: Kessler, H. *Angew. Chem.* **1970**, *82*, 237.

[16] Gaussian 98, Revision A.7, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1998.

[17] For a further discussion of rotational motion in related diazabicyclophanes, see: Buhleier, E.; Wehner, W.; Vögtle, F. *Chem. Ber.* **1979**, *112*, 546.

[18] Mean value due to four independent molecules in the unit cell.

To test the capability of enclosing a soft metal ion we synthesized a 1:1 complex of **7** with silver triflate.[19] The structural properties of **7**·AgOTf were ascertained by means of X-ray crystallography and NMR spectroscopy.[20] In the solid state, the most striking result is that the silver ion resides not exactly in the center of the cage as was observed in the related endohedral silver complex of **3** but is disordered over two equivalent positions, each displaced toward the bridgeheads, and thus reduces the symmetry from C_{3h} to C_3 (Figure 4).

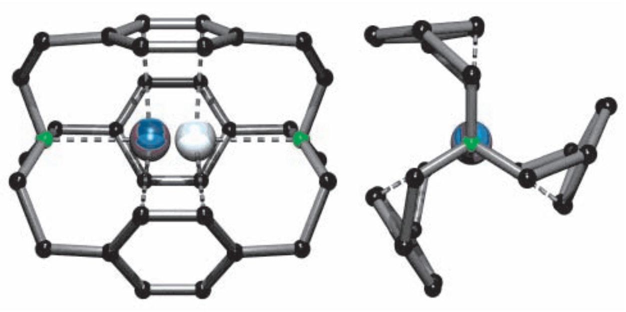

Figure 4. Solid-state structure of **7**·AgOTf as determined by X-ray analysis (counterion, disordered parts, and hydrogen atoms omitted for clarity). The two equivalent positions of the disordered silver ion are marked with different colored spheres.

In contrast, the NMR spectra of **7**·AgOTf in solution show no perturbation of the mirror symmetry. The signal pattern and the chemical shifts are similar to that obtained for the free bicyclophane except for the singlet of the aromatic protons which is shifted downfield to $\delta = 6.95$.

At this point we suppose that a relatively fast intramolecular tunneling of the silver ion through the bicyclophane "π-belt" occurs in solution as well as possibly in the solid state at room temperature.[21] The ^{1}H NMR of **7**·AgOTf exclusively contains broadened resonances which reflect a dynamic process in solution. According to low-temperature NMR studies, only torsional motion of the framework seems to be involved. The proposed fluctuation of the silver ion could not be resolved down to −100 °C.[14] Since the separation of the two silver positions in the crystal structure is small (1.05 Å) and the tunneling path is flanked by mobile π-systems on three sides, the activation energy to the intramolecular exchange process should be relatively low.

The spatial arrangement of the benzene rings in bicyclophane **7** is closely related to that in [2_3](1,4)cyclophane[22] (π-prismand) and [2_6](1,2,4,5)cyclophane.[23] Interestingly, both compounds form silver complexes in which the metal ion lies exterior to the cyclophane moiety and undergoes rapid exchange in solution. In the case of **7**·AgOTf, the two nitrogen bridgeheads "cap" the cavity and force the silver ion to stay near the center of the cage, thus preventing an intermolecular exchange.

We are now expanding the scope of this preliminary work to other suitable metals for encapsulation and attempting to extend the concept of nitrogen-capped π-prismands to the smaller bicyclophanes **5** and **6**.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft (SFB 247), the Fonds der Chemischen Industrie, and the BASF Aktiengesellschaft, Ludwigshafen, for financial support.

Supporting Information Available: Synthesis and analytical properties of compound **10**, details of the semiempirical calculations, and data, in CIF format, for the X-ray crystal structures of **7** and **7**·AgOTf. This material is available free of charge via the Internet at http://pubs.acs.org.

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[19] Stirring an equimolar mixture of **7** and AgOTf under argon in dry CH_2Cl_2 at room temperature for 30 min and evaporation of the solvent leads to the light- and air-stable endohedral 1:1 complex in quantitative yield.

[20] Selected spectroscopic data for **7**·AgOTf: ^{1}H NMR (500 MHz, in CD_3OD) δ 6.95 (12H, br s, H_{ar}), 2.90 (12H, br s, $PhCH_2$), 2.77 (12H, br s, CH_2N); ^{13}C NMR (125 MHz, in CD_3OD) δ 138.0 ($C_{ar,q}$), 127.7 ($C_{ar,t}$), 53.8 (CH_2N), 31.8 ($PhCH_2$); FAB-HRMS $[C_{30}H_{36}N_2{}^{107}Ag]^+$ calcd 531.1929, found 531.1915.

[21] X-ray analysis of **7**·AgOTf was undertaken at 25 °C.

[22] (a) Cohen-Addad, C.; Baret, P.; Chautemps, P.; Pierre, J.-L. *Acta Crystallogr., Sect. C* **1983**, *39*, 1346. (b) Pierre, J.-L.; Baret, P.; Chautemps, P.; Armand, M. *J. Am. Chem. Soc.* **1981**, *103*, 2986.

[23] Kang, H. C.; Hanson, A. W.; Eaton, B.; Boekelheide, V. *J. Am. Chem. Soc.* **1985**, *107*, 1979.