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## Vicinal Diamides as Lanthanide Complexers with Two Conformational States of Different Dipole Moments—Elements for new Molecular Switches

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Vicinal diamides rest in the ground state in an anti-parallel orientation with a small dipole moment; they are able to bind metal ions like lanthanide<sup>3+</sup> upon which they change to a parallel orientation with high dipole moments.

The development of molecular switches has become of much recent interest in view of their possible applications in synthetic allosteric systems, and potentially for information storage and transmission. Several supramolecular systems have been described already in which occupation of one binding site leads to conformational changes at another complexation site, with subsequent positive or negative cooperativity<sup>1,2</sup>. Many molecular switches reported until now are based on systems undergoing photoisomerism<sup>3</sup>. They have already shown impressive progress in spite of problems with slow or uncomplete interconversion/response, with lifetimes of the states, particularly at higher temperature, as well as with stabilities limited by photodecomposition processes etc. An ideal molecular device, in particular for elements of

“molecular computers”, should be distinguished by [i] well defined, if possible two-state equilibria, [ii] by sufficiently large barriers between the different states with, [iii], still fast response, [iv] sensitivity against external signals, and [v] high stabilities after many turnovers.

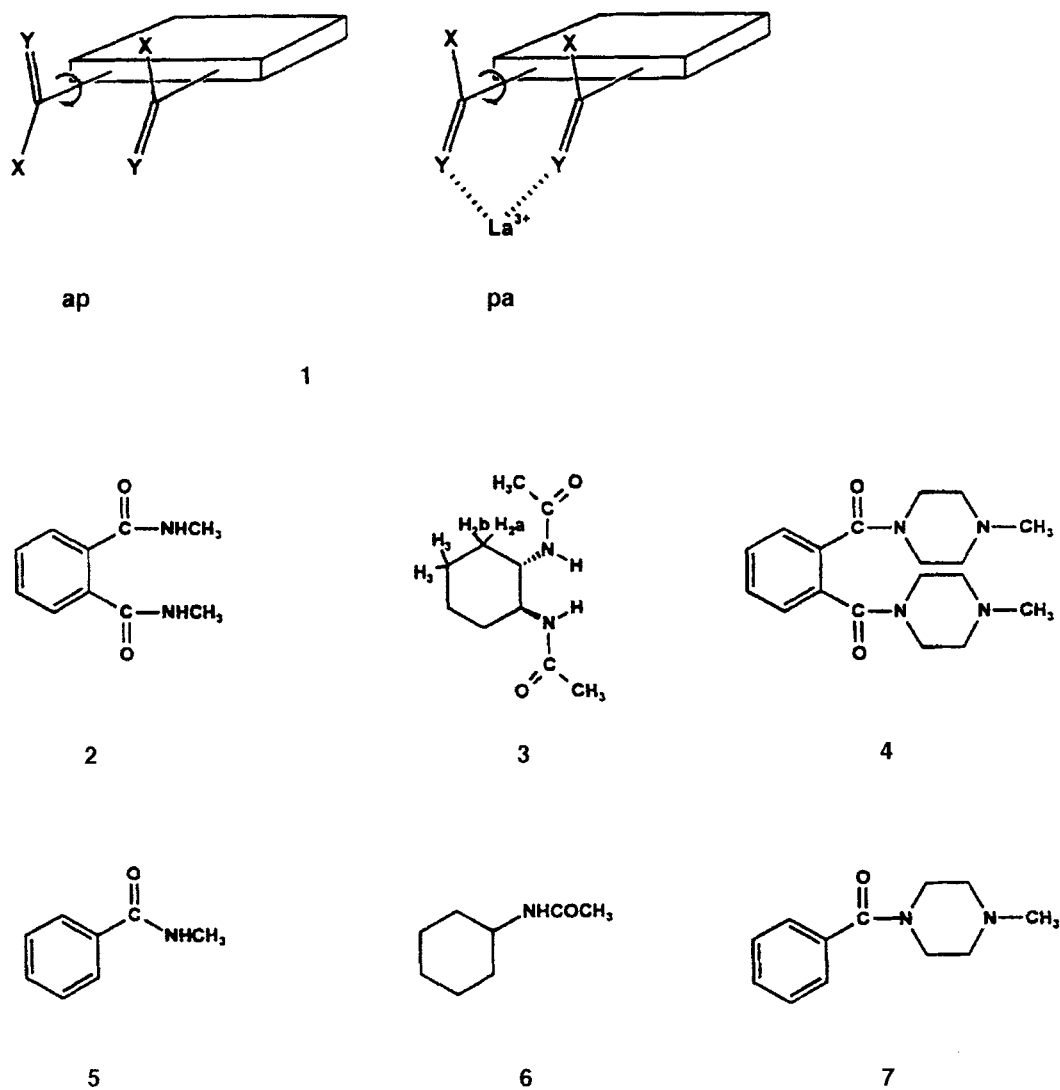
As a simple, non-photochemical strategy towards these goals we want to describe the use of vicinal dipolar functions which can be either in a parallel (**pa**) or antiparallel (**ap**) orientation (**1**, Scheme 1). The **ap** orientation should be preferred<sup>4</sup> in the ground state due to attraction between the dipoles, and to repulsion in the **pa** state. The latter can be populated by complexation with suitable guest compounds at one or both ends of the dipoles, by increasing the local dielectric of the microenvironment, and in principle also by strong external fields<sup>5</sup>.

In the present work we have investigated the use of vicinal diamides as a first step. Binding of cations to such diamides in protic solutions requires at least the presence of two of the electronegative amide oxygen functions in a proper

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orientation towards the cation, leading to the desired conversion from **ap** to **pa** states of the switch. The binding of lanthanide ions has also become of interest in view of the catalytic activities of such ions in the hydrolysis of phosphate esters and of DNA or RNA<sup>6</sup>. Morrows *et al.*<sup>7</sup> have recently shown that amide functions can indeed efficiently contribute to binding of lanthanide ions.

As starting point for such vicinal diamides we choose derivatives either of *o*-phthalic acid **2**, or of *trans*-1,2-diaminocyclohexane **3**. (Scheme 1). Preliminary molecular mechanics calculations with the CHARMM field show that indeed the **ap** conformations dominate in the ground state, with, however, small energy differences to **pa** (e.g. by 0.13 kcal/mol with an dielectric constant of  $\epsilon = 3$  D). In line with this, the CHARMM



SCHEME 1

calculated total energies for the 1.3- and the 1.4 phtalic diamides are almost the same as the for 1.2 diamide, indicating that the interaction between the vicinal diamides is small. Perrin et al have recently pointed out that large dipole moments of a molecule indeed do not necessarily lead to smaller stability<sup>4e</sup>. The CHARMM calculated barrier of interconversion between the two states is with  $\Delta G^* = 2.7$  kcal/mol also small. Similar results are obtained with the cyclohexyldiamides diamides 3.

Obviously, one should enhance both the ground state differences as well as, if possible, the barriers. As a first attempt to increase the electrostatic effects responsible for the **ap/pa** differences we prepared the diamide 4 by reaction of o-phthaloyl dichloride with N-methylpiperazine. The permanent charges at the protonated terminal nitrogen atoms can enhance the dipole moments of the interacting parts, and hence the **ap/pa** energy differences considerably. Other derivatives, such as those obtained from the reaction of trans-1,2 diaminocyclohexane and all 3 picolinic acids, were unfortunately not soluble enough for further studies.

Preliminary measurements with the diamides in methanol (*d*<sub>4</sub>-methanol) showed NMR shift changes below 0.003 ppm if eg. up to 0.2 M Zn<sup>2+</sup> salts were added, however substantial changes of up to 0.4 ppm if La<sup>3+</sup> salts were added. Several lanthanide ions are well known to produce NMR shifts as a consequence of shielding tensors from the f electrons. It was secured, that the shifts observed with the diamides 2 or 3 are not due to this by comparison with the mono-amide 5, which showed shift changes below 0.003 ppm even with 0.2 M Ln<sup>3+</sup> salts. This experiment also proves, that both amide oxygens are needed for effective complexation of the metal ion. Hence, the diamides indeed work as expected as switchable systems.

The shift changes observed with the diamides allowed to determine associations constants *K* and the corresponding free energies  $\Delta G$  with several independent NMR signals. The titrations

were carried out in CD<sub>3</sub>OD, and evaluated with usual protocols as described earlier. Figure 1

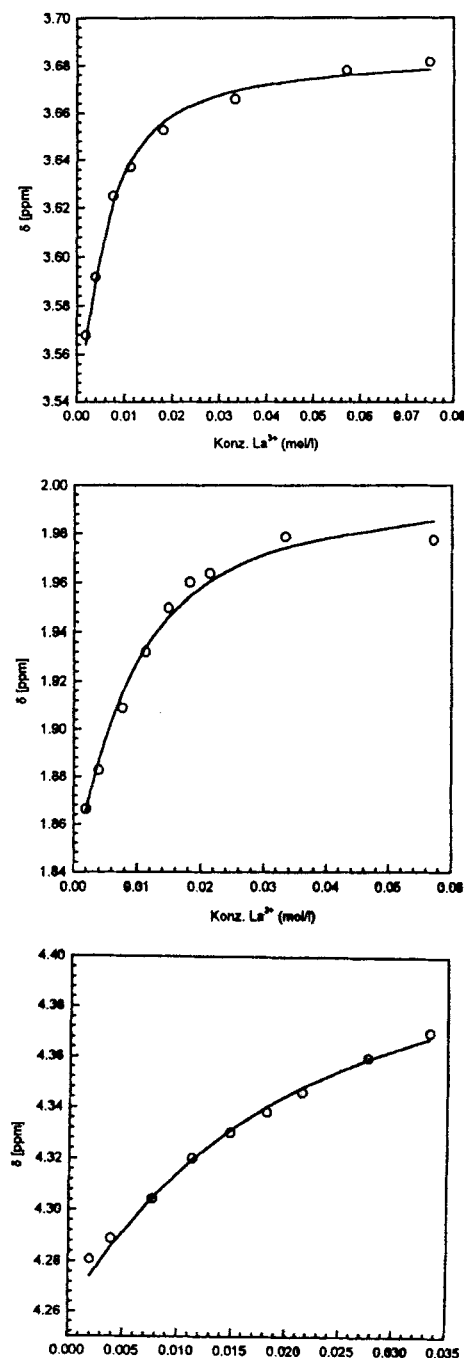


FIGURE 1 NMR Shift titrations with non-linear least squares fit. Representative examples: 1a) 2, CH<sub>3</sub>-signal; 1b) 3, H3 signal; 1c) 4, H2 signal.

TABLE I NMR-Titration of **3** with LaCl<sub>3</sub> (CD<sub>3</sub>OD, 300 K)

Proton	$\delta_0$	CIS [ppm]	K (10 <sup>2</sup> ) [l/mol]	$\Delta G$ [kJ/mol]
H <sub>1</sub>	4.096	0.450	0.80	11.0
H <sub>2a</sub>	2.458	0.450	1.10	11.8
H <sub>2b</sub>	2.276	-0.110	0.09	5.5
H <sub>3</sub>	1.840	0.162	1.60	12.8
CH <sub>3</sub>	2.431	0.196	0.90	11.3
			$\bar{K} = 0.9$	$\bar{\Delta G} = 10.5$

shows typical titration curves; the non-linear least square fit of these furnishes the corresponding complexation induced shifts (CIS values) and equilibrium constants **K** (Tables I–III).

The phthaldiamide **2** showed large shift changes at both the ArH and the NMe signals (aromatic signals were not separated even at 500 MHz). The **K** and  $\Delta G$  values obtained from the different signals were in sufficient agreement, and showed that these diamides can indeed function as switchable acceptors for lanthanides. The constants obtained by the same procedures as with the cyclohexyldiaminoderivative **3** can be based even on the evaluation of 4 signals, yielding rather consistent **K** or  $\Delta G$  values: only the H<sub>2b</sub> signal for unknown reasons shows unexpected deviations.

The piperazide **4** showed association constants with La which are decreased compared to the electroneutral **2**. This is in line with an additional repulsion between the piperazine charges in the metal-binding **pa** conformer. Addition of dicarboxylates to the La complexes, aiming at allosteric interactions, invariably was leading to insoluble material in methanol or similar sol-

vents. This was observed with terephthalic acid and even with less hydrophobic acids such as tartrates, and thus prevented until now the study of allosteric effects with these derivatives.

The results demonstrate that vicinal diamides show appreciable binding and switching from **ap** to **pa** conformations upon addition of e.g. lanthanoide cations, thus demonstrating the possibility to construct new and simple two state switches. We plan to increase the efficiency by modification of the isomerization centers, including e.g. the amide function itself as rotors, and by the use of longer “handles” in **1**. Enlarging the handles can provide both for higher barriers and for larger energy and dipole moment differences between the two states. The principle can be used with all systems featuring high and tunable steric hindrance of rotation, such as with 1,8-disubstituted naphthyl, 3,7-diazabicyclo[3.3.1]nonyl<sup>8</sup>, bicyclo[2.1.1]heptyl- or bicyclo[2.2.2]octyl<sup>9</sup> derivatives and those of cyclohexane-1,2 dicarboxylic acids<sup>10</sup>.

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TABLE II NMR-Titration of **4** with LaCl<sub>3</sub> (CD<sub>3</sub>OD, 300 K)

Proton	$\delta_0$	CIS [ppm]	K (10 <sup>2</sup> ) [l/mol]	$\Delta G$ [kJ/mol]
H <sub>a</sub>	8.055	0.005	1.75	13.0
H <sub>b</sub>	7.927	0.009	1.19	12.0
H <sub>1</sub>	3.887	0.125	0.97	11.5
H <sub>2</sub>	4.261	0.171	0.54	10.0
H <sub>3</sub>	2.966	0.206	1.47	12.6
H <sub>4</sub>	3.038	0.228	1.13	11.9
CH <sub>3</sub>	2.850	0.228	1.13	11.9
			$\bar{K}_m = 1.17$	$\bar{\Delta G} = 11.8$

TABLE III NMR-Titration of **2** with LaCl<sub>3</sub> (CD<sub>3</sub>OD, 300 K)

Proton	$\delta_0$	CIS [ppm]	K (10 <sup>2</sup> ) [l/mol]	$\Delta G$ [kJ/mol]
Ar.-H	81.60	0.140	5.9	16.1
CH <sub>3</sub>	35.31	0.155	3.0	14.4
			$\bar{\Delta}K = 4.45$	$\bar{\Delta}G = 15.3$

## References and Notes

- [1] Most of the early synthetic allosteric systems comprised cooperativity between two metal binding centers: (a) Vögtle, (1992). *Supramolekulare Chemie* 2. Aufl, Thieme Stuttgart; *Supramolecular Chemistry*, Wiley 1991; (b) Rebek, Jr. J. (1984). *Acc. Chem. Res.*, **17**, 258; (c) Shinkai, S. (1992). *Crown Ethers and Analogous Compounds*, **45**, 335.
- [2] Recent references for allosteric systems with binding centers also for organic substrates: Inouye, M., Konishi, T. and Isagawa, K. (1993). *J. Am. Chem. Soc.*, **115**, 8091; Bauer, H., Matz, V., Lang, M., Krieger, C. and Staab, H. A. (1994). *Chem. Ber.*, **127**, 1993; Baldes, R. R. and Schneider, H.-J. (1995). *Angew. Chem.*, **107**, 380; *Angew. Chem. Int. Ed. Engl.*, (1995), **34**, 321; Ikeda, T., Yoshida, K. and Schneider, H.-J. (1995). *J. Am. Chem. Soc.*, **117**, 1453.
- [3] Selected reviews on photosensitive switches see ref 1 and: (a) Feringa, B. L., Jager, W. F. and de Lange, B. (1993). *Tetrahedron*, **49**, 8267; (b) *Photochromism. Molecules and Systems in Organic Chemistry*, H. Dürr, H. Bouas-Laurent, Eds.; Elsevier Amsterdam 1990; (c) Shinkai, S. and Manabe, O. (1984). *Top. Curr. Chem.*, **121**, 67; (d) Balzani, V. and Scandola, F. (1991). *Supramolecular Photochemistry*, Ellis Horwood, Chichester.
- [4] Cf. electrostatic interpretations of the anomeric effect: a) Kirby, A. J. (1983). *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer: New York etc; (b) Perrin, C. L., Armstrong, K. B. and Fabian, M. A. (1994). *J. Am. Chem. Soc.*, **116**, 715; (c) Wiberg, K. B. and Marquez, M. (1994). *ibid.*, **116**, 2197; (d) Jorgensen, W. L., Morales de Tirado, P. I. and Severance, D. L. (1994). *ibid.*, **116**, 2199; (e) Perrin, C. L. and Young, D. B. (1995). *Tetrahedron Lett.*, **36**, 7185; and references cited therein.
- [5] The use of external electric fields for orientation of chromophores in thin films has been reported: Kurihara, S., Iwamoto, K. and Nonaka, T. (1995). *J. Chem. Soc., Chem. Commun.*, 2195.
- [6] (a) Bamann, E. and Trapmann, H. (1959). *Adv. Enzym.*, **21**, 169; (b) Breslow, R. and Huang, D. L. (1991). *Proc. Nat. Acad. Sci. USA*, **88**, 4080; (c) Komiyama, M., Matsumura, K., Matsumoto, Y., Ushida, H., Shiiba, T., Kodamam, T. and Yashiro, M. (1995). *J. Chem. Soc., Perkin Trans.*, **2**, 269; (d) Morrow, J. L., Buttrey, L. A., Shelton, V. M. and Berback, K. A. (1992). *J. Am. Chem. Soc.*, **114**, 1903; (e) Rammo, J., Hettich, R., Roigk, A. and Schneider, H.-J. (1996). *J. Chem. Soc., Chem. Commun.*, 105; and references cited therein.
- [7] Amin, S., Morrow, J. R., Lake, C.-H. and Churchill, M. R. (1995). *Angew. Chem.*, **824**; *Angew. Chem. Int. Ed. Engl.*, (1995), **33**, 773.
- [8] Cf. O. I. Levina, Pothekin, K. A., Kurkotova, E. N., Struchkov, Y. T., Baskin, I. I., Palyulin, V. A. and Zefirov, N. S. (1985). *Dokl. Akad. Nauk*, **281**, 1367; McCabe, P. H., Milne, N. J. and Sim, G. A. (1985). *J. Chem. Soc., Chem. Commun.*, 625.
- [9] Samoshin, V. V., Vereshchagina, Y. A., Lutsenko, A. I. and Zefirov, N. S. (1993). *Zh. Org. Khim.*, **29**, 1095, and references cited therein.
- [10] Cf. Samoshin, V. V., Chertkov, V. A., Vatlina, L. P., Dobretsova, E. K., Simonov, N. A., Kastorsky, L. P., Gremyachinsky, D. V. and Schneider, H.-J. (1996). *Tetrahedron Lett.*, **37**, 3981.