Tetrahedron 65 (2009) 8402–8406

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Photoswitchable ionophores based on 1,3-alternate calix[4]arenes bearing acridane units at the wide rim and bridged at the narrow rim by glycol chains

L. Grubert [a], H. Hennig [a], U.-W. Grummt [b], W. Abraham [a,*]

[a] Humboldt-Universität zu Berlin, Institute of Chemistry, Brook-Taylor-Str. 2, 12489 Berlin, Germany
[b] Institute of Physical Chemistry, Friedrich-Schiller-University, Jena, Germany

ARTICLE INFO

Article history:
Received 13 July 2009
Received in revised form 30 July 2009
Accepted 31 July 2009
Available online 6 August 2009

Keywords:
Calixarene
Acridinium salt
Acridanes
Photoswitch
Cation receptor

ABSTRACT

The complexation with alkali metal ions by calix[4]arenes with 1,3-alternate conformation bearing acridinium and acridane substituents at one rim and a glycol chain at the other rim has been studied by isothermal calorimetry. The thermodynamic parameters and the stoichiometry of the complexes are strongly influenced by the nature of the substituent (acridane or acridinium), by the solvent and by the length of the glycol chain. Both 9-methoxyacridane substituents are involved in the photoheterolysis leading to the corresponding acridinium calixcrowns. The nucleophilic attack of the methoxide leaving group reverses the reaction thermally. Therefore, the different complexation properties of acridane and acridinium calixcrowns can be switched on and off.

1. Introduction

The selective recognition of alkali metals is a central research interest not only in biological systems but also in artificial chemical systems, as, for example, in the development of artificial ion channels or of selective extractants for caesium for nuclear waste remediation.[1,2] Because crown ethers are well-known macrocycles, which are able to complex cations, the more or less pre-organized scaffold of calixarenes has been hybridized to crown ethers resulting in calixcrowns.[1] Calixcrowns have been applied in ion sensing and recognition and for use as ionophores in ion selective electrodes for various cations.[1] Dependent on the calixarene conformation, a Na^+ or a K^+ selectivity can be observed.[3] Efforts were made to control complexation strength and selectivity. Molecular switching of crowns and calixarenes involves changes in charge state, conformation, or structure that enable or prevent cation complexation.

Proton switchable calix[4]arenes bearing pyridinium units have been developed for anion binding.[4]

Photochemical control of complexation is of particular interest. The advantage of light driven systems is that no chemicals are necessary and no waste products are formed. To the best of our knowledge, only two photoswitchable systems have been synthesized thus far. In 1992, Shinkai et al. synthesized a photoswitchable calixcrown based on the photodimerization of anthracene substituents.[5] Light-switched Ag^+-tunnelling across the π-basic tube of 1,3-alternate calix[4]arenes has also been demonstrated.[6]

Azobenzene and stilbene units are widely used for switching because cis–trans photoisomerization leads to changed geometries of macrocycles such as crowns.[7] Photo-regulated metal binding has been shown with an azobenzene-capped calix[4]arene.[8] However, cis–trans isomerization is limited by the formation of a photo-equilibrium, which does not allow a complete switch. Photochromism and metal ion binding ability have been connected in calixarenes bearing chromene units at the wider rim.[9]

Recently, we synthesized photoresponsive calix[4]crowns **1** (Scheme 1) bearing the 9-alkoxy-9-aryl-10-methyl-9,10-dihydroacridine(-acridane) as the switch.[10] Upon photoexcitation with light of 313 nm, the acridane unit is converted into the acridinium alkoxides **2**, which are characterized by the typical absorption band of the electronic transition localized in the acridinium moiety. Charge transfer from the 9-aryl-substituent towards the acridinium unit does not play a significant role.[11] The longest wavelength absorption band of the acridinium ion is at 430 nm. Accordingly, the colourless solution of the acridanes changes to yellow upon irradiation.

Due to the formation of acridinium units at the wide rim of the 1,3-alternate calix[4]crowns, the access towards the cavity of the calixarene may be blocked.[10] Herein, we present complexation and photochemistry studies of calix[4]arenes having the acridane/acridinium-photoswitch at the wide rim.

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[*] Corresponding author. Tel.: +49 30 2093 7348; fax: +49 30 2093 7266.
E-mail address: abraham@chemie.hu-berlin.de (W. Abraham).

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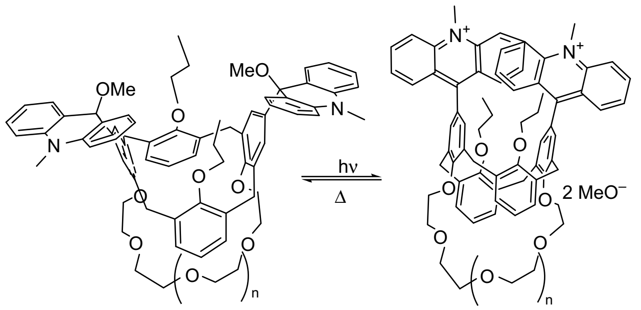
doi:10.1016/j.tet.2009.07.096



1a(O5) n = 1
1b(O6) n = 2
1c(O7) n = 3

2a(O5) n = 1
2b(O6) n = 2
2c(O7) n = 3

Scheme 1. Photolytic conversion of acridane substituted calix[4]arenes into the corresponding acridinium methoxides and their thermal reset.

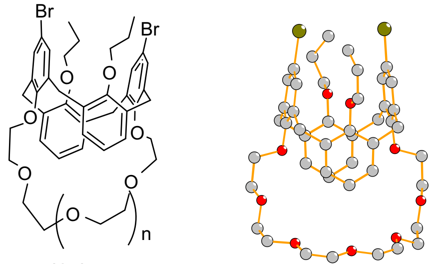
2. Results and discussion

2.1. Conformation

The 1,3-alternate conformation of calixarenes **1** and **2** is determined by the synthetic route chosen.[10] Within compound **3**, which is the precursor of the calixarene **2c**, the phenyl groups are nearly parallel to each other, as revealed by the crystal structure (Fig. 1). Unfortunately, we were not able to produce suitable single crystals of calixarenes **1** and **2**. However, we assume that, due to the given 1,3-alternate conformation, the structure of the calixcrowns is very similar.

Density functional theory (DFT) structure optimizations (B3LYP/6-31g(d)) result in the stable conformers shown in Figure 2. Both the acridane and the acridinium calixcrown-5 exhibit a slightly opened square cavity.

Although compounds **1** and **2** differ only in the length of their glycol chains, the substituents at the wide rim are affected by the chain length because of steric stress of the large groups at the wide rim. For example, the ionogenic equilibrium of **1** in methanol solution is strongly influenced by the chain length.[10] Furthermore, while *p*-alkoxyphenylacridinium salts are nonfluorescent, compound **2b(O6)** exhibits a weak fluorescence. However, the fluorescence quantum yield of **2a(O5)** is five times higher than that of **2b(O6)** (see Supplementary data).



3c(O7), n = 3

Figure 1. Structure of compound **3c(O7)**.

2.2. Complexation

Calixcrowns are bitopic hosts. The π-basic cavity can be used to bind guests, such as organic cations.[12] However, in the case of calixcrowns bearing acridinium and acridane substituents at the wide rim, the cavity seems to be blocked by the large substituents.[10] Accordingly, we found that organic cations such as acetylcholine, *N*-methylquinoline and *N*-methylacridinium ions were not complexed by **1** and **2**. In contrast, metal ions are known to interact with the glycol chain at the narrow rim mainly by electrostatic attraction between oxygen atoms and the cation favoured by the calixarene skeleton. Electronic effects caused by substituents at the wide rim may influence the electron density at the phenol oxygens and also affect the complexation capability of the glycol chain. It is known that small changes in substituents at the wide or narrow rim can result in dramatic changes in binding properties.[13] Therefore, we expected that acridinium and acridane substituted calixcrowns **1** and **2** would interact differently with alkali metal ions.

We determined exemplarily thermodynamic parameters (i.e., complex stability constant (K), standard free energy (ΔG^0), enthalpy (ΔH^0) and entropy changes (ΔS^0)) of the complexation of some alkali-metal cations in acetonitrile solution by use of isothermal titration calorimetry (ITC). We have mainly focussed our studies on the complexation differences between the acridane and acridinium substituted calixacrowns. Therefore only selected metal cations were included. In fact the data in Tables 1 and 2 indicate that the complexation is strongly influenced both by the chain length of the calixcrown and the nature of the substituent at the wide rim. A comparison of the complexation data given in Tables 1 and 2 reveals that the introduction of the acridane unit at the wide rim results in a higher selectivity of alkali-metal cation binding (Table 1, entries 1,3,4 vs Table 2, entries 1–3).

Generally, the complexation is driven by the enthalpic gains, mostly with accompanying losses in entropy. Notably, two bromo-substituted calixcrown molecules are needed to bind one alkali metal ion with rather high association constants (see Table 2). Because the length of the glycol chain controls the binding, the interaction of the cation with the two glycol chains of both host molecules is assumed. The two chains must adopt to the size of the cation.

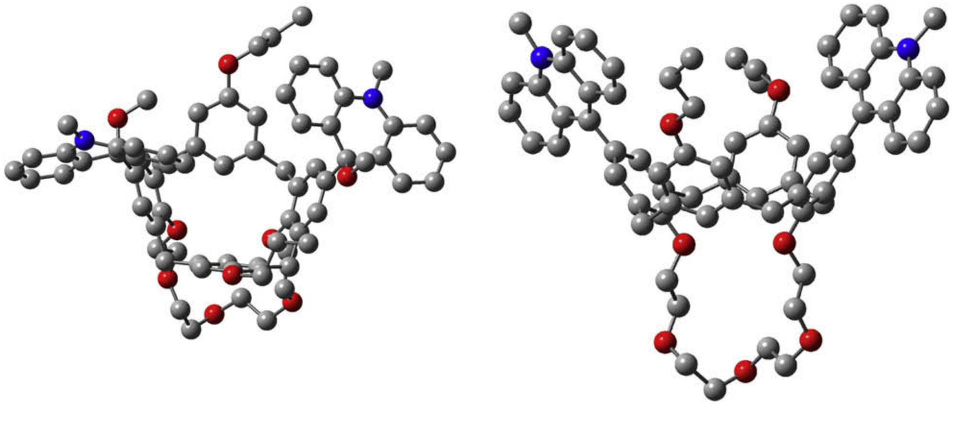


Figure 2. Optimized structures of **1a(O5)** (left) and **2a(O5)** (right).

Table 1
Thermodynamic parameters of complexes between hosts **1** and **2** and different alkali metal ions (*n* denotes the ratio of guest to host in the complex). All measurements were performed at 298 K using acetonitrile as the solvent, unless noted otherwise

Entry	Host	Ion	log K	$-\Delta H$ [kcal mol^{-1}]	$T\Delta S$ [kcal mol^{-1}]	*n*
1	**1a(O5)**	K^+	6.10	9.1	−0.78	0.5
2	**1a(O5)**[b]	K^+	<2	[a]	[a]	[a]
3	**1a(O5)**	Rb^+	<2	[a]	[a]	[a]
4	**1a(O5)**	Cs^+	<2	[a]	[a]	[a]
5	**1b(O6)**	K^+	<2	[a]	[a]	[a]
6	**1b(O6)**	Rb^+	4.37	7.2	−1.28	0.5
7	**1b(O6)**[b]	Rb^+	4.45	5.65	0.42	0.65
8	**1b(O6)**	Cs^+	5.37	6.3	1.07	0.5
9	**1b(O6)**[b]	Cs^+	5.03	7.1	−0.24	0.65
10	**1c(O7)**	Cs^+	3.94	8.4	−3.07	0.5
11	**2a(O5)**	K^+	<2	[a]	[a]	[a]
12	**2a(O5)**[b]	K^+	4.70	5.29	1.13	0.49
13	**2a(O5)**	Rb^+	<2	[a]	[a]	[a]
14	**2b(O6)**	K^+	<2	[a]	[a]	[a]
15	**2b(O6)**[b]	K^+	<2	[a]	[a]	[a]
16	**2b(O6)**	Rb^+	3.29	8.3	−3.87	1
17	**2b(O6)**[b]	Rb^+	3.77	3.21	1.94	1
18	**2b(O6)**	Cs^+	4.36	6.0	−0.06	1
19	**2b(O6)**[b]	Cs^+	4.11	6.93	−1.31	1
20	**2c(O7)**	Rb^+	<2	[a]	[a]	[a]
21	**2c(O7)**	Cs^+	<2	[a]	[a]	[a]

[a] Not measurable.
[b] Solvent MeCN/EtOH 4:1.

Table 2
Thermodynamic parameters of complexes between hosts **3** and different alkali metal ions (solvent acetonitrile) measured at 298 K

Entry	Host	Ion	log K	$-\Delta H$ [kcal]	$T\Delta S$ [kcal mol^{-1}]	*n*
1	**3a(O5)**	K^+	7.20	10.81	−1.00	0.65
2	**3a(O5)**	Rb^+	6.73	10.7	−1.51	0.69
3	**3a(O5)**	Cs^+	4.66	11.6	−5.33	0.63
4	**3b(O6)**	K^+	3.19	2.46	3.30	0.65
5	**3b(O6)**	Rb^+	4.10	5.16	2.13	0.5
6	**3b(O6)**	Cs^+	5.03	7.62	0.37	0.57
7	**3c(O7)**	Rb^+	<2	—	—	—
8	**3c(O7)**	Cs^+	3.90	7.04	−1.72	0.79

Most interesting is the difference of complexation parameters between the acridane and the acridinium substituted calixcrowns **1** and **2** (Table 1). The acridane substituted calixcrown-5 (**1a(O5)**) has the highest binding capability for K^+ in acetonitrile solution (Table 1, entry 1), and forms 2:1-complexes like the bromo-substituted calixcrowns. All complexes of the acridane substituted calixcrowns are substantially more stable than corresponding acridinium counterparts in acetonitrile solution. The complexation constants of K^+ are comparable with values reported for other calixcrowns with 1,3-*alternate* conformation.[14] However, compared with simple calixcrowns the selectivity for alkali-metal cations is more pronounced for the acridane substituted calixcrowns.[14]

In contrast to **1a(O5)**, the corresponding acridinium compound **2a(O5)** does not bind the potassium ion (Table 1, entry 11).

The interaction of the cation with the host molecules results in shifts of proton signals both of the calixarene skeleton and the acridane moiety at the wide rim. Accordingly, Job plots using complex induced shifts of ^1H NMR signals of the host molecule (CH_2-group of the glycol chain) are suitable to confirm the formation of 2:1-complexes (see Fig. 3).

Both the photoheterolysis of the acridane calixcrowns as well as the thermal back reaction afford the presence of alcoholic solvents. With this in mind, the complexation properties in acetonitrile/ethanol solution (4:1) are of particular interest. Surprisingly, the addition of ethanol (20%) reversed the ratio of the complexation of acridinium and acridane substituted calixcrown-5 (Table 1, entry 2 vs entry 12). Now, two acridinium substituted calixcrown-5 (**2a(O5)**) host molecules are required to bind one K^+-ion while in all other cases the acridinium substituted calixcrowns **2** form 1:1-complexes. Because the acridane substituted calixcrown-5 (**1a(O5)**) does not bind K^+ the photolysis of **1a(O5)** leading to **2a(O5)** would result in the acquisition of potassium ions from the solution and a switchable ion receptor would be created.

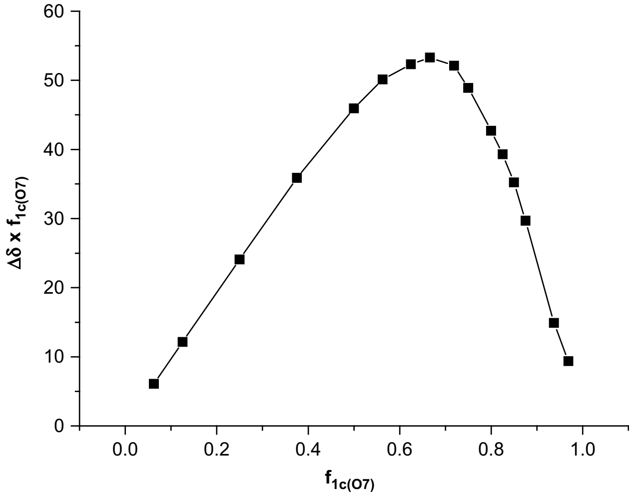


Figure 3. ^1H NMR–Job plot of the complexation of Cs^+ by two calixcrown-7 molecules (**1c(O7)**) in acetonitrile solution ($f_{\mathbf{1c(O7)}}$—mole fraction; $\Delta\delta=\delta_{obsd}-\delta_{\mathbf{1c(O7)}}$).

The subtle influences of solvents and substituents at the wide rim are not fully understood, but the acridane substituted calixcrowns seem to possess a generally higher binding capability for alkali ions in acetonitrile solution and the positively charged acridinium units at the wide rim suppress the complexation of cations at the narrow rim.

2.3. Photoreaction

Upon photoexcitation with light between 254 and 330 nm, 9-alkoxy acridane compounds undergo heterolytic bond fission, yielding the corresponding acridinium alkoxide with high quantum yields.[15] The alkoxide attacks the acridinium moiety, reverting to the starting acridane compound. The rate of the back reaction depends strongly on the solvent.[15] Complete recovery of the starting compound requires the presence of a small amount of an alcohol. The outcome of the reaction can easily be followed by UV–vis-spectroscopy (see Fig. 4).

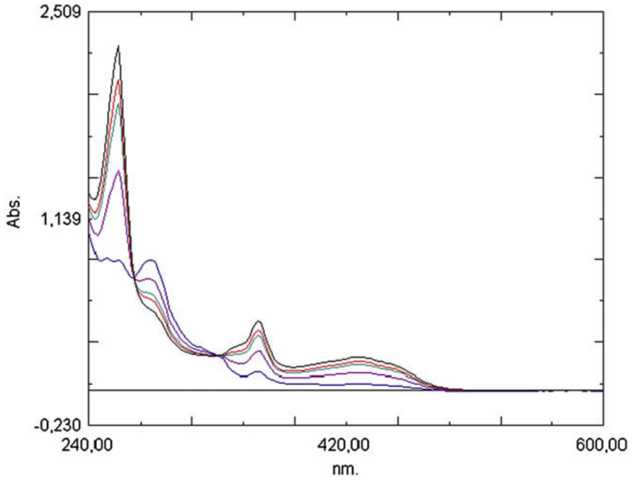


Figure 4. UV–vis absorption spectra recorded after consecutive irradiation (HBO 500 mercury arc source) of compound **1a(O5)** in MeCN/EtOH (4:1) solution; formation of the acridinium compound: blue 0 s; pink, 1 s; green, 2 s; red, 3 s; black, 10 s.

The reaction can also be performed in pure alcohols such as methanol and ethanol. However, in these cases the lifetime of the acridinium alkoxide is considerably shorter compared with mixtures of acetonitrile with methanol or ethanol. For instance, the lifetime in methanol is 50 s, in ethanol, 600 s, and in acetonitrile containing 20% ethanol, 70 min. If the solution contains ethanol and the methoxide leaving group is used, the latter is replaced by the ethoxy group. However, the nature of the leaving alkoxide does not influence the photoheterolysis.

Because the presented calixcrowns possess two acridane units the question arises as to whether both photoactive groups undergo heterolytic bond fission. Because of the thermal back reaction, the light intensity controls the conversion of the acridane to the acridinium units. With high light intensities (high pressure mercury lamp, HBO 500), turnovers of about 70% are obtained with solutions in the range between 2 and 8×10^{-5} M. These results clearly show that both acridane units are involved. However, the photolysis efficiency of the second acridane unit appears to be smaller than that of the first photoactive unit. The second photoionization may be regarded as an upper state reaction because the lowest excited state is now essentially generated by the acridinium moiety. Obviously, the reactive state is localized at the acridane substituent and decoupled from the other chromophore. Additionally, energy transfer to the acridinium moiety can only inefficiently compete with the fast bond cleavage.

We were not able to prepare pure calixcrowns with one acridane and one acridinium group. But, by interrupting the slow reaction of the bis-acridinium compound **2a(O5)** with ethanol (20%) in acetonitrile solution in the presence of $NaHCO_3$ a mixture has been obtained, which according to the ^{1}H NMR spectrum (Fig. 2, Supplementary data) consists of 71% acridinium/acridane-calix[4]arene crown-5, 18% bis-acridinium calixarene and 10% bis-acridane compound **1a(O5)**. The irradiation of this mixture in acetonitrile/ethanol (4:1) solution with light of comparable intensity as used for the photoreaction of pure **1a(O5)** (5 s HBO 500 mercury arc source) resulted in a considerably smaller conversion into **2a(O5)** (18% vs 50%). The formation of the bis-acridinium compound can easily be followed by UV–vis spectroscopy at the wavelength of 435 nm. The conversion is 18%, considerably higher than would be expected if only 10% of the bis-acridane compound had reacted.

Neither the photoreaction nor the thermal back reaction was influenced by the presence of salts such as $KClO_4$ (Fig. 3, Supplementary data). Accordingly, the conversion of **1a(O5)** to **2a(O5)** leads to an uptake of potassium ions, which will be released by the recovery of the starting acridane calix[4]crown-5. Also the differences of the binding capabilities between **1b(O5)** and **2b(O5)** for Cs^+ and Rb^+ (Table 1) can be switched on and off by the combined photo- and thermal reaction in acetonitrile/ethanol (4:1) solution.

3. Conclusions

Calix[4]arene crowns exhibiting the 1,3-*alternate* conformation and bearing acridinium and acridane substituents at the wide rim were studied regarding their response to photoexcitation. All compounds with acridane groups at the wide rim underwent photoheterolysis to give the corresponding acridinium methoxides, which reverted to the acridane moieties in a thermal reaction. Acridane and acridinium calixcrowns are different in their complexation of alkali cations. Both the binding capability and the stoichiometry of the complexes depend on the nature of the substituent at the wide rim and on the solvent composition. Drastic changes occur in the case of the crown-5 derivative. While the acridane substituted host does not bind potassium ions in acetonitrile solution containing 20% ethanol, the binding constant of the corresponding acridinium substituted host is high. Two host molecules bind a single K^+. Therefore, due to photolysis of the acridane substituted calixcrown-5, K^+ ions are abstracted from the solution and released after the thermal reset.

4. Experimental

4.1. General

Commercially available chemicals and solvents (UVASOL, Merck) were used as received unless otherwise noted; solvents were dried according to standard procedures. Calixarene compounds were available in our laboratory from earlier studies.[10] NMR spectra were recorded on a Bruker Advance 400(400 MHz) instrument. UV–vis measurements were performed with a Shimadzu UV 2101 PC spectrometer. Irradiations of the calixarene solutions were carried out with a conventional mercury arc (HBO 500 or HBO 200) combined with a cut-off filter of 300 nm. The thermal reactions were followed by UV–vis spectroscopy using the kinetics-program of the spectrometer. The absorption decay curves at the wavelength of 360 nm were analyzed by nonlinear regression fits (Origin 6.0, Microcal Software, Inc.). Transient absorption spectra between 340 and 500 nm were recorded with the UV 2101 PC spectrometer using the fastest scan mode.

4.2. Microcalorimetric measurements

An isothermal calorimetry instrument VP-ITC (MicroCal) was used. The Differential Power axis (DP in $\mu cal\, s^{-1}$) of the ITC instrument was calibrated electrically using an internal electric heater. Enthalpy and equilibrium constants were determined from the titration curves using the Origin plotting software. At least three independent measurements were carried out at 298 K. A constant volume (1 μL/injection) of the metal salt acetonitrile solution was injected into the cell (1.4255 mL) charged with the calixarene solution (acetonitrile, 2×10^{-4} M). The heat of dilution caused by the addition of the metal salt solution to the blank solution without the calixarene was determined in each run. The dilution enthalpies were subtracted from the enthalpies measured during the titration experiment. Maximum errors for the K and ΔH values were estimated as ±7%.

4.3. X-ray crystallographic studies

Single crystals of compound **3c(O7)** were obtained by slow cooling of the warm acetonitrile solutions. Data were collected with a STOE-diffractometer using graphite-monochromated Mo Kα radiation (details are given in Supplementary data). The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least squares techniques against F^2 (SHELXL-97).[16] The hydrogen atoms were included at calculated positions. All other nonhydrogen atoms were refined anisotropically. The X-STEP-Program was used for structure representation.

Acknowledgements

Financial support provided by Deutsche Forschungsgemeinschaft is gratefully acknowledged.

Supplementary data

Fluorescence, UV–vis, NMR spectra as well as crystallographic data are available in supplementary data. Supplementary data in the form of a CIF have been deposited with the Cambridge Crystallographic Data Centre for **3** (CCDC 739500). Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.07.096.

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