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Synthesis and ^{1}H-NMR Complexation Studies of Alkalimetal Bithioxanthylidene Crown Ether Complexes

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Abstract: Two synthetic routes to a novel class of sterically overcrowded alkenes, bithioxanthylidene crown ethers **1**, are described. The ^{1}H spin-lattice relaxation times (T_1) of the crown ethers as well as those of the corresponding complexes with Li^+, Na^+, K^+, Rb^+ and Cs^+ in $CDCl_3$ were measured and the results were interpreted in terms of complexation affinities.

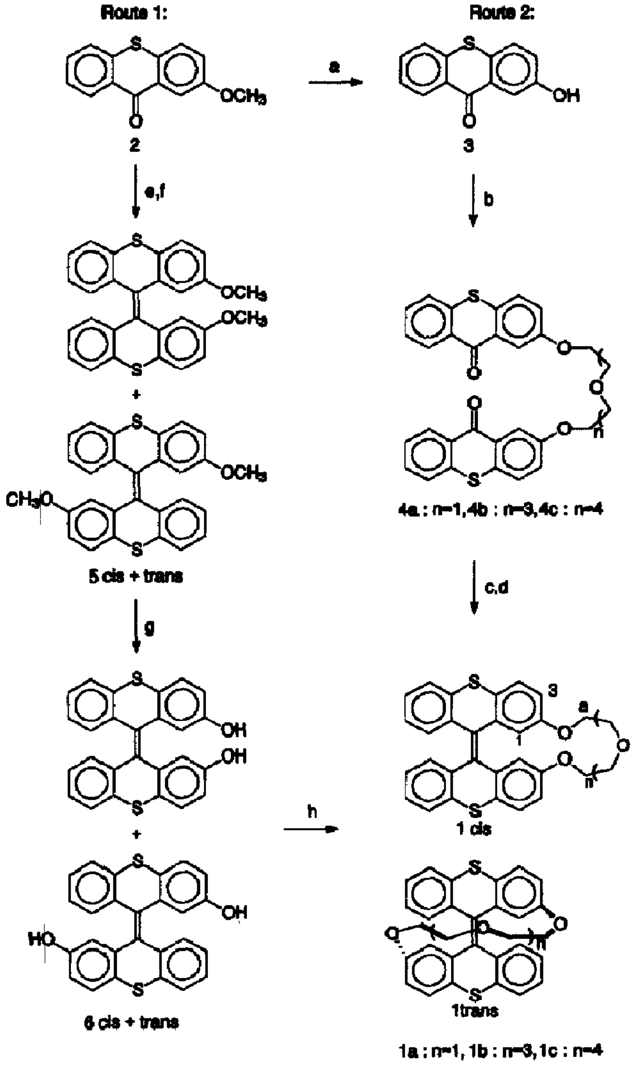
The development of molecular switching devices has attracted considerable attention, due to the challenge to achieve optical data storage on a molecular level.[1] Extensive research efforts on inherently dissymmetric overcrowded alkenes in our group resulted in the development of the first chiroptical molecular switches.[2] A highly desirable property of photochromic compounds is gated response[1,3], which means that photoresponsive effects are blocked upon irradiation unless another external stimulation, either chemical or physical, is applied. Recently Lehn and co-workers published the first dual-mode electro-optic switch that is completely stable at room temperature.[4]

In order to achieve a chemical gated response in the chiroptical switches, we decided to explore the possibilities of crown ether coupled overcrowded ethylenes. It can be imagined that the information written by light can reversibly be locked by ion complexation at the crown ether unit of the molecular switch.[5] In order to investigate the synthetic accessibility of crown ether bound overcrowded ethylenes and to study ion complexation synthetic routes to bithioxanthylidene crown ethers **1** were developed.

Two routes to bithioxanthylidene crown ethers **1** with three different crown ether sizes were accomplished (Scheme 1). The crucial step in these syntheses is the formation of the central olefinic bond of the bithioxanthylidene part of the molecule. The carbonyl groups of the upper and lower half are converted to the corresponding geminal dichlorides and subsequently coupled in *p*-xylene with copper bronze to yield an olefin.[6] In route 1 coupling and deprotection to **6** was followed by reaction with ditosylates using Cs_2CO_3 in DMF (60-70°C) to afford pure *cis* **1**. The stereoselectivity may be explained by a cesium template effect.[7] The intramolecular coupling (route 2) using bis-thioxanthones **4** generally resulted in lower yields of *cis/trans* mixtures of **1** and polymeric side products.[8]

Cis and *trans* **1** were distinguished by ^{1}H NMR and by comparison with the spectra of bismethoxybithioxanthylidene **5**. It was possible to make the assignment for the *cis* and *trans* isomers of **5** unequivocally, since the structure of *trans* **5** could be solved by X-ray analysis.[9] We focussed on the characteristic protons H_1 in **1** and **5** (Scheme 1), which are the most upfield shifted aromatic absorptions with a small long range coupling with H_3. The H_1 doublet of the *trans* isomer is shifted more upfield than the H_1 doublet of *cis* both for **1** and **5**.

Bithioxanthylidene crown ethers **1b** and **1c** (pure *cis* isomers) were subjected to complexation studies with alkalimetal triflates. ^{1}H NMR longitudinal relaxation times were determined for **1b** and **1c** in the absence and presence of Li^+, Na^+, K^+, Rb^+ and Cs^+ cations in order to study selectivity of complexation of different cations.[10]



Scheme 1

a) HBr, CH_3CO_2H, $(CH_3CO)_2O$, Δ, 5h, 76%.[11] b) $TsOCH_2(CH_2OCH_2)_nCH_2OTs$, DMF, K_2CO_3, reflux, 72h, **4a**: 74%, **4b**: 86%, **4c**: 89%. c) $C_2O_2Cl_2$, reflux, 2h, evaporation of excess $C_2O_2Cl_2$. d) copper bronze powder, p-xylene, reflux, 16h, **1a**: 22%, **1b**: 4%, **1c**: 38%. e) $C_2O_2Cl_2$, reflux, 2h, evaporation of excess $C_2O_2Cl_2$. f) copper bronze powder, p-xylene, reflux, 5h, 70%, *cis/trans* : 38/62.[12] g) BBr_3 (10 eq), CH_2Cl_2, RT, 2 days, 70%, *cis/trans* : 50/50. h) $TsOCH_2(CH_2OCH_2)_nCH_2OTs$, DMF, Cs_2CO_3, **1a**: 70°, 7 days, 71%, **1b**: 60°C, 24h, 58%, **1c**: 70°C, 7 days, 62%.

The relaxation times for all signals in the ^{1}H NMR spectra were measured,[13] but specific signals were selected for the complexation experiments. In the aliphatic region H_a (Scheme 1), the protons directly adjacent to the aromatic part of the molecules, were used. In the aromatic part the doublet caused by H_1, was chosen and the most upfield signal was used. The results are summarized in tables 1 and 2.

The effects on the relaxation times caused by the interactions with the alkalimetal cations are expressed as the percentages by which the relaxation times of the free crown ethers dropped upon complexation with the cations (T_1 drops (%)).

Table 1 *Relaxation times and relaxation time drops for* **1c** *(H_a 3.71 ppm; H_1 6.39 ppm)*

	H_a T_1 (s)	T_1drop (%)	H_1 T_1 (s)	T_1drop (%)
Free ligand	0.878±0.048		1.484±0.047	
Li	0.606±0.007	31.0±5.8	1.490±0.053	-0.4±4.7
Na	0.582±0.028	33.7±6.4	1.270±0.040	14.4±4.2
K	0.493±0.040	43.8±7.4	1.119±0.035	24.6±4.1
Rb	0.528±0.032	39.9±7.0	0.934±0.062	37.1±5.4
Cs	0.591±0.025	32.7±6.4	1.438±0.044	3.1±4.3

It is clearly shown in table 1 that crown ether **1c** exhibits preferential complexation with potassium and rubidium ions. This is in accordance with the well known perfect fit of potassium ions in 18-crown-6.[14]

Table 2 *Relaxation times and relaxation time drops for* **1b** *(H_a 3.70 ppm; H_1 6.41 ppm)*

	1:1 complex				2:1 complex	
	H_a		H_1		H_1	
	T_1 (s)	T_1drop (%)	T_1 (s)	T_1drop (%)	T_1 (s)	T_1drop (%)
Free ligand	0.733±0.010		1.633±0.055			
Li	0.528±0.011	27.9±2.0	1.401±0.051	14.2±4.6		
Na	0.636±0.005	13.2±1.5	1.405±0.057	14.0±4.9		
K	0.636±0.011	13.2±2.0	1.502±0.054	8.0±4.7	1.053±0.020	35.5±3.8
Rb	0.699±0.011	4.6±2.0	1.583±0.059	3.1±5.0	1.090±0.021	33.3±3.8
Cs	0.665±0.015	9.3±2.5	1.566±0.049	4.1±4.5	1.038±0.015	36.4±3.7

Bithioxanthylidene crown ether **1b**, with the smaller polyether ring, can form both 1:1 and 2:1 complexes, depending on the size of the cation. This is concluded from the ^{1}H NMR spectra of the samples containing potassium, rubidium and cesium ions, respectively. A second H_1 doublet was observed in these spectra, due to 2:1 complex formation. This interpretation seems to be plausible since sandwich complexation was observed for benzo-15-crown-5 with potassium and rubidium cations as well.[14]

With regard to the 1:1 complexation it can be concluded that lithium ions seem to fit well in the crown ether cavity. Sodium and potassium ions cause a less strong decrease in relaxation times, while rubidium and cesium show no 1:1 complexation with **1b**.

It can be concluded that the bithioxanthylidene crown ether **1b** exhibits preferential complexation abilities with lithium ions, while **1c** prefers complexation with potassium and rubidium ions. Applications in dual-mode chiroptical switches are currently investigated.

References and notes

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6. All new compounds showed spectroscopic and analytical data in accordance with the structures: **1b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.48-3.82 (m, 16H), 6.40 (d, J = 2.7 Hz, 2H), 6.77 (dd, J = 7.5, 1.2 Hz, 2H), 6.81 (dd, J = 8.7, 2.8 Hz, 2H), 7.10 (ddd, J = 7.5, 7.6, 1.2 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H); HRMS Calcd for $C_{34}H_{30}O_5S_2$: 582.153, found 582.153. **1c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.46-3.78 (m, 20H), 6.38 (d, J = 2.7 Hz, 2H), 6.79 (dd, J = 8.6, 2.7 Hz, 2H), 6.87 (ddd, J = 7.6, 7.6, 1.2 Hz, 2H), 7.09 (ddd, J = 7.5, 7.5, 1.2 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 7.50 (dd, J = 7.7, 0.6 Hz, 2H); HRMS Calcd for $C_{36}H_{34}O_6S_2$: 626.180, found 626.180.
7. Piepers, O; Kellogg, R.M. *J. Chem. Soc Chem. Commun.* **1978**. 383. The fact that the product is pure *cis* (starting from a 1:1 *cis/trans* mixture of **6**) can be explained when it is supposed that this cesium template effect applies only for the reaction of *cis* **6**. Since the reaction temperature is high enough to allow *cis/trans* isomerization of **6**, it seems plausible that the *cis/trans* equilibrium is shifted to the *cis* isomer, as only *cis* **6** reacts with the ditosylates.
8. All spectroscopic data suggest the unexpected formation of *trans* **1a** in route 2. The *cis/trans* product ratio for this reaction of 5/1 confirms the fact that this *trans* isomer is positively disfavoured as expected for sterical reasons.
9. Crystallization of mixtures of *cis* and *trans* **5** from hexane/dichloromethane 1:1 afforded small slightly green crystals of *trans* **5**, point group $P2_1/a$. The structure was solved to a final R index of 0.042 and will be published elsewhere.
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13. Longitudinal relaxation time (T_1) measurements were performed at 300 MHz on a Varian VXR-300 spectrometer using the inversion recovery technique, (T = 30 ± 0.1°C). Pulse delay times of 10000 s and ten different pulse intervals between 0.025 and 12.8 s were used for each individual measurement. For each pulse interval 100 scans were used in order to obtain an acceptable signal-to-noise ratio. T_1-values were determined by a linear least-squares; a two-parameter fit of the experimental data was used. The samples (0.016 M crown ether and one equivalent of triflate salt in 1 mL $CDCl_3$) were prepared in a glove box under a nitrogen atmosphere.
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