Journal of Inclusion Phenomena and Molecular Recognition in Chemistry **14**: 141–147, 1992.

A Schiff Base *p-tert*-Butylcalix[4]arene. Synthesis and Metal Ion Complexation

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(Received: 8 April 1992; in final form: 30 September 1992)

Abstract. This communication describes the synthesis of Schiff base calix[4]arene (**1**) in which the Schiff base unit bridges two opposite hydroxy groups of *p-tert*-butylcalix[4]arene. The synthesis of (**1**) has been achieved by refluxing in acetonitrile–methanol the appropriate 1,3-dicarbaldehyde-*p-tert*-butylcalix[4]arene (**4**) with 1,3-diaminopropane. The yield of the reaction is 19%. Ligand (**1**) possesses a compartment containing two nitrogen atoms, four ether-type oxygen atoms, and two ionizable hydroxy groups likely to complex metal cations.

Key words. 1,3-bridged calix[4]arene, Schiff-base, alkaline and alkaline-earth cations, transition metals, stability constants, biphasic transfer.

1. Introduction

Since the preliminary communication of Alfieri *et al.* [1] reporting the synthesis of the first member of a new class of macrocyclic crown compounds by bridging two opposite OH groups of *p-tert*-butylcalix[4]arene with a pentaethylene glycolic chain, extensive work has been reported on the synthesis of 1,3-bridged calix[4]arenes. Thus, 1,3-capping of calix[4]arenes at the lower rim has been achieved with poly(oxyethylene) chains (calix crown ethers [2], calix doubly crowned [3], double calix crown [4]), with a terphenyl unit (calix spherands [5]), with a metallocene unit (metallocene calixarene [6]), and with disulphonyl chloride and diacetyl dichloride [7]. Calix(aza-)crowns have been reported to be ionophores for divalent and trivalent cations [8]. Similarly, 'double cavity' calixarenes have been prepared by Gutsche *et al.* [9]. The treatment of *p-tert*-butylcalix[4]arene with 3,5-dinitrobenzoyl chloride affords the 1,3-diaroylate in excellent yield, which is further transformed, after reduction and reaction with diacetyl dichloride, into 'double cavity' calixarenes [9].

In this communication we report the synthesis of a Schiff base calix[4]arene (**1**) in which the Schiff base unit bridges two opposite hydroxy groups of *p-tert*-butylcalix[4]arene. Nijenhuis *et al.* [10] have presented a compound related to (**1**) in which the calix[4]arene is bridged by a salophene moiety. However, its synthesis was not given. In addition to the synthesis of (**1**), we report its binding properties towards selected cations.

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2. Experimental

2.1. MATERIAL FOR THE SYNTHESIS

p-tert-Butylcalix[4]arene was prepared as described in the literature [11]. 1,3-Diaminopropane, salicylaldehyde, potassium carbonate, and the solvents were commercial reagents and used without further purification.

2.2. ANALYTICAL PROCEDURES

The metling points (mps) were taken on a Büchi 500 apparatus in capillaries sealed under nitrogen. Silica columns were prepared with Kieselgel Merck (Art. 9385). The eluent is specified in the experimental procedures. Elemental analyses were performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg. The ^{1}H-NMR spectra were recorded at 200 MHz on a Bruker SY200 spectrometer. The FAB mass spectra were obtained on a VG-Analytical ZAB HF apparatus.

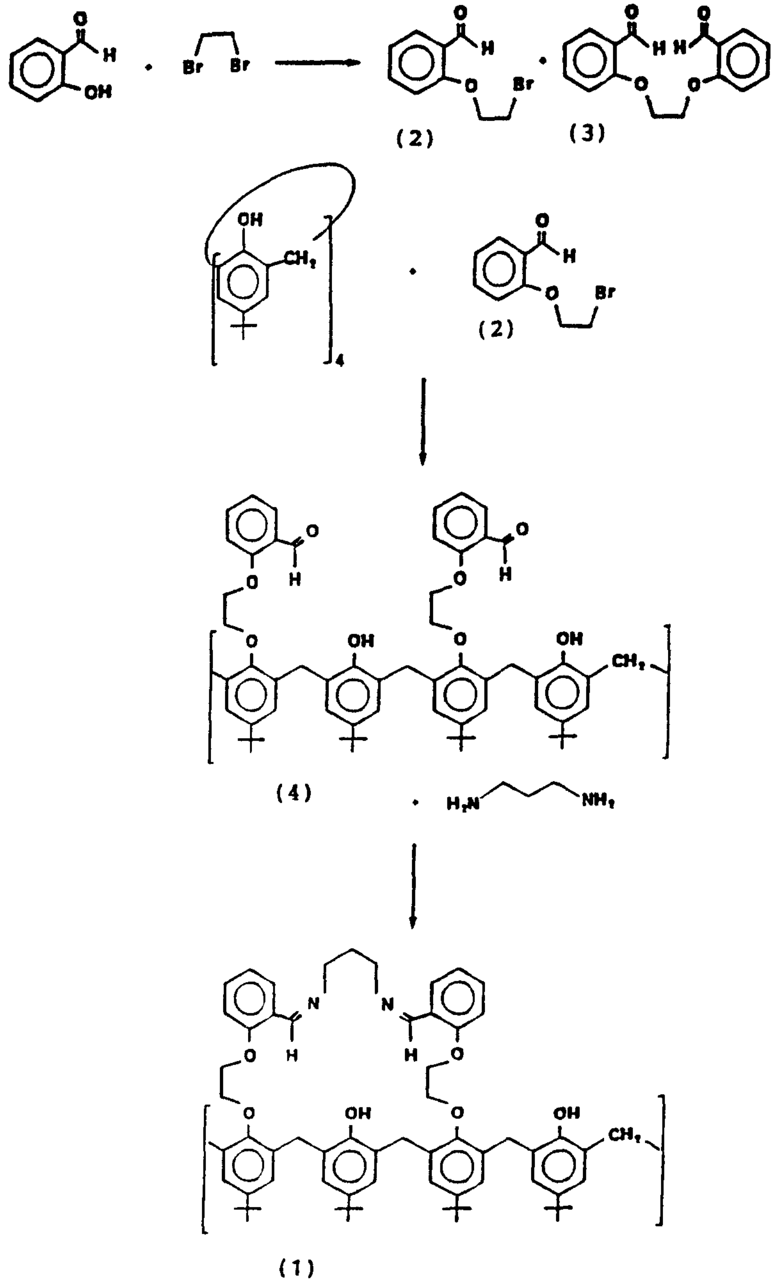
2.3. EXTRACTION EXPERIMENTS AND STABILITY CONSTANT DETERMINATIONS

The complexing power of receptor (**1**) towards various metal ions was first estimated by experiments measuring the extraction of the corresponding picrates from water into dichloromethane. Two of the most efficient systems have been characterized by the stability constants of the complexes in methanol, measured by UV–visible absorption spectrophotometry. The experimental details have already been published [4, 12].

2.4. PREPARATION OF 2-((2′-BROMO)ETHOXY)BENZALDEHYDE (**2**)

A 1-L, two-necked round-bottom flask was equipped with a condenser and a dropping funnel, and charged with acetonitrile (250 mL), salicylaldehyde (14.80 g, 121.2 mmol), and potassium carbonate (23.10 g, 167.0 mmol). 1,2-Dibromoethane (206.35 g, 1098 mmol) was then added dropwise over 30 min. The contents were stirred for 7 h with reflux under nitrogen. The reaction mixture was cooled to room temperature and filtered. The filtered solution was concentrated on a rotatory evaporator (45°C bath) to yield an oily black residue (26.73 g). An aliquot (6.12 g) of this residue was chromatographed on a silica column (310 g) with chloroform as eluent. Pure 2-((2′-bromo)ethoxy)benzaldehyde (**2**) (1.59 g) was eluted first and obtained as a transparent oil. *Yield* 25%. ^{1}H-NMR ($CDCl_3$) 10.54 (*s*, 1H, C*H*O), 8.28–6.93 (*m*, 4H, aromatics), 4.42 (*t*, 2H, $J_{H-H} = 6.2$ Hz, OCH_2CH_2Br), 3.70 (*t*, 2H, $J_{H-H} = 6.2$ Hz, OCH_2CH_2Br). MS (70 eV): 228 (10%), 149 (100%). *Elemental analysis*: *calcd.* for $C_9H_9BrO_2$ C 47.18, H 3.96. *Found* C 47.06, H 4.07.

The second product eluted is pure 2,2′-(1,2-dioxyethane)bisbenzaldehyde (**3**) (0.502 g) as a transparent oil which solidified over time. Mp 42–44°C. *Yield* 13%. ^{1}H-NMR ($CDCl_3$) 10.44 (*s*, 2H, C*H*O), 7.86–7.04 (*m*, 8H, aromatics), 4.53 (*s*, 4H, OCH_2CH_2O). MS (70 eV): 270 (30%), 121 (100%). *Elemental analysis*: *calcd.* for $C_{16}H_{15}O_4$ C 70.83, H 5.57. *Found* C 70.16, H 5.22.



Scheme I. Synthesis of Schiff base *p-tert*-butylcalix[4]arene (**1**).

2.5. PREPARATION OF 26,27-DI((2-ETHOXY)BENZALDEHYDE)-*p-tert*-BUTYLCALIX[4]ARENE (4)

A 250-mL, two-necked round-bottom flask was equipped with a condenser and a dropping funnel, and charged with acetonitrile (50 mL), *p-tert*-butylcalix[4]arene

(1.95 g, 3.00 mmol) and potassium carbonate (3.32 g, 24.00 mmol). The mixture was stirred for 20 min. The brominated derivative (**2**) (1.59 g, 6.94 mmol), dissolved in acetonitrile (25 mL), was then added dropwise over 30 min. The contents were refluxed under nitrogen for 18 h. After cooling to room temperature, the reaction mixture was filtered off and washed with acetone and dichloromethane. The filtrate was concentrated and the residue was dissolved in dichloromethane and precipitated by addition of methanol yielding the pure dialdehyde calixarene derivative (**4**) (1.55 g). Mp 201–202°C. *Yield* 55%. ^{1}H-NMR ($CDCl_3$) 10.51 (*d*, 2H, $J_{H-H} = 0.6$ Hz, C*H*O), 7.86 (*dd*, 2H, $J_{H-H} = 8.2$ Hz, $J_{H-H} = 0.6$ Hz, H on C6), 7.56–7.47 (*m*, 2H, H on C3), 7.54 (*s*, 2H, ArO*H*), 7.06–6.96 (*m*, 4H, H on C4 and C5), 7.02 (*s*, 4H, HOAr*H*), 6.88 (*s*, 4H, ROAr*H*), 4.42–4.40 (*m*, 8H, OCH_2CH_2O), 4.21 and 3.31 (AB system, $J_{H-H} = 13.6$ Hz, 8H, $ArCH_AH_BAr$), 1.26 (*s*, 18H, HOAr-*t*-C_4H_9), 1.03 (*s*, 18H, ROAr-*t*-C_4H_9). FAB positive: 944.5. *Elemental analysis calcd.* for $C_{62}H_{72}O_8{\cdot}CH_3OH$: C 77.42%, H 7.83%. *Found* C 77.54%, H 7.79%.

2.6. PREPARATION OF THE SCHIFF BASE *p-tert*-CALIX[4]ARENE (1)

A 500-mL, two-necked round-bottom flask was equipped with a condenser and a dropping funnel, and charged with acetonitrile (90 mL), methanol (70 mL), and the dialdehyde calixarene derivative (**4**) (953 mg, 1.01 mmol). After dissolution of the reacting mixture, 1,3-diaminopropane (81.6 mg, 1.1 mmol, 0.092 mL) dissolved in methanol (40 mL) was added dropwise over 30 min. The contents were refluxed for 18 h. The solvents were then evaporated to dryness under reduced pressure and the residue was recrystallized three times from acetonitrile. The recrystallizations took place in about 12 h. Pure Schiff base *p-tert*-butylcalix[4]arene (**1**) (190 mg) was filtered off by suction. Mp 301–302°C with decomposition. *Yield* 19%. ^{1}H-NMR ($CDCl_3$) 8.72 (*s*, 2H, C*H*N), 7.83 (*d*, 2H, $J_{H-H} = 8$ Hz, H on C6), 7.26 (*s*, 4H, ROAr*H*), 6.86–6.61 (*m*, 10H, H on C3, C4 and C5, HOAr*H*, and ArO*H*), 4.46 and 3.27 (AB system, $J_{J-H} = 13.7$ HZ, 8H, $ArCH_AH_BAr$), 4.29 (*s*, 8H, OCH_2CH_2O), 4.29 (broad *s*, 4H, NCH_2), 3.26 (*m*, 2H, $CH_2CH_2CH_2$), 1.31 (*s*, 18H, HOAr-*t*-C_4H_9), 0.88 (*s*, 18H, RoAr-*t*-C_4H_9). FAB positive: 983.5. *Elemental analysis calcd.* for $C_{65}H_{78}O_6$: C 79.39%, H 7.99% *Found* C 79.12%, H 8.05%.

3. Results and Discussion

The synthesis of (**1**) was conducted according to Scheme I. Salicylaldehyde was refluxed for 7 h under nitrogen with an excess of 1,2-dibromoethane in acetonitrile in the presence of potassium carbonate as base. After the usual work up, the reaction residue was chromatographed on a silica column to afford pure 2-((2′-bromo)ethoxy)benzaldehyde (**2**) and 2,2′-(1,2-diethoxyethane)-bis-benzaldehyde (**3**) in 25% and 13% yields, respectively. In a second step, *p-tert*-butylcalix[4]arene was alkylated with the bromoaldehyde derivative (**2**) by refluxing the two components during 18 h in acetonitrile in the presence of potassium carbonate as base. Precipitation from methanol of the crude mixture afforded pure 25,27-di((2-ethoxy)benzaldehyde)-*p-tert*-butylcalix[4]arene (**4**) in 55% yield as a white solid melting at 201–202°C. Dialdehyde calixarene (**4**) was treated with 1 eq. of 1,3-diaminopropane in a mixture of acetonitrile–methanol under reflux for 18 h. Bridged

Schiff base *p-tert*-butylcalix[4]arene (**1**) was obtained pure in 19% yield after recrystallization from acetonitrile.

All the products were characterized by ^{1}H-NMR spectroscopy, fast atomic bombardment mass spectrometry, and elemental analysis. From its ^{1}H-NMR spectrum, dialdehyde calixarene (**4**) was deduced to be *O*-dialkylated in two opposite positions due to the presence of only two singlets at 1.03 ppm and 1.26 ppm for the *tert*-butyl groups and of one AB system at 3.31 ppm and 4.21 ppm with $J_{H-H} = 13.6$ Hz for the methylene protons of the macrocyclic structure, indicative of a *cone conformation* for the calixarene unit.

Similarly, from its ^{1}H-NMR spectrum, Schiff base *p-tert*-butylcalix[4]arene (**1**) was shown to be bridged on two opposite positions due to the presence of only two singlets at 0.88 ppm and 1.31 ppm for the *tert*-butyl groups and of one AB system at 3.27 ppm and 4.46 ppm with $J_{H-H} = 13.7$ Hz for the methylene protons of the macrocyclic structure, also indicative of a *cone conformation* for the calixarene unit.

In this structure, Schiff base *p-tert*-butylcalix[4]arene (**1**) presents a compartment containing two nitrogen atoms, four ether-type oxygen atoms, and two ionizable hydroxy groups. We therefore decided to investigate the binding properties of ligand (**1**) towards metal ions.

Preliminary extraction results, expressed as percentages, %*E*, of cation, transferred from water to the dichloromethane phase, are listed in Table I. They show the low level of extraction of alkali and alkaline-earth cations. However, a slight selectivity for Rb^+ is observed within the alkali series. Among the transition and heavy metal cations, which are expected to be better complexed by a Schiff base containing ligand [13, 14], Cu^{2+} and Pb^{2+} are the best extracted, with %*E* values around 21 and 15, respectively. Eu^{3+} is extracted better than Pr^{3+}.

The complexing properties of (**1**) towards Cu^{2+}, Pb^{2+}, and Eu^{3+} have been investigated. With Cu^{2+} the spectra varied with time and no proper equilibrium state could be reached, preventing reliable interpretation of the data. The spectral changes of ligand (**1**) upon addition of metallic salts generally lead to new absorption maxima and several isosbestic points between 250 and 400 nm, as illustrated in Figure 1 for the case of Eu^{3+}. The data are satisfactorily interpreted assuming the formation of 1 : 1 complexes in both cases, with stability constants $\log K = 5.0$ for the lead complex and $\log K = 4.8$ for the europium complex.

Table I. Percentage extraction, %*E*, of metal picrates (2.5×10^{-4} M) by ligand (**1**) (2.5×10^{-4} M) from water into dichloromethane

Na^+	6	Cd^{2+}	8	Mn^{2+}	3
K^+	7	Pb^{2+}	15	Fe^{2+}	9
Rb^+	9	Pr^{3+}	6	Co^{2+}	6
Cs^+	7	Eu^{3+}	13	Ni^{2+}	9
Ca^{2+}	4			Cu^{2+}	21
Sr^{2+}	4			Zn^{2+}	9
Ba^{2+}	4				

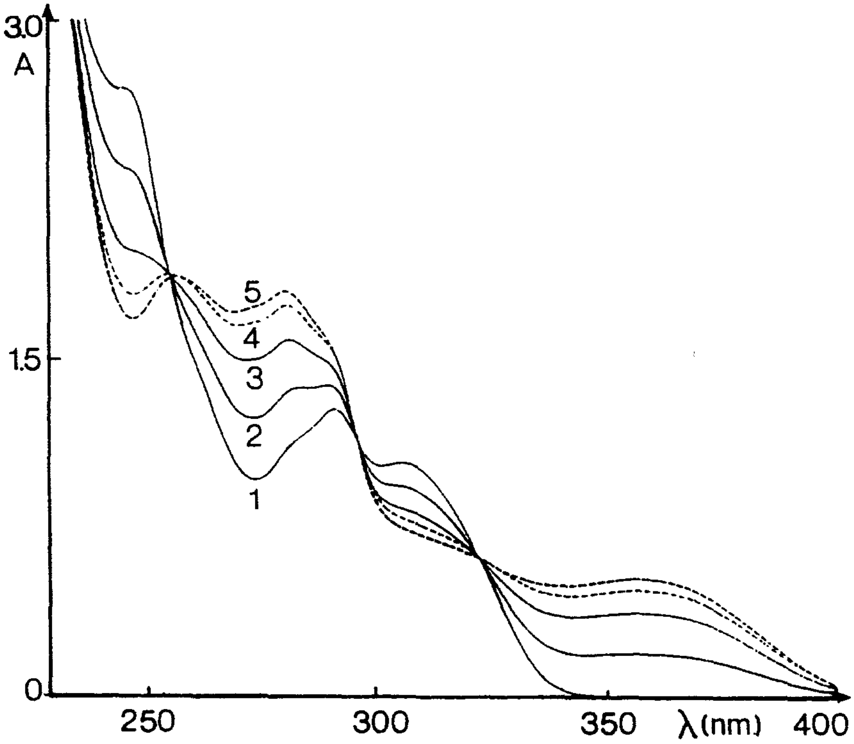


Fig. 1. Change in the UV absorption spectrum of (1) upon addition of $Eu(CF_3SO_3)_3$ in methanol: $C_{(1)} = 1.25 \times 10^{-4}$ M. Spectra 1–5 correspond to $0 \leqslant C_{Eu}/C_{(1)} \leqslant 2$.

As a result of the complexation studies, experimental work is currently being devoted to the preparation of a series of Schiff base calix[4]arenes by varying the nature of the bridge linking the imino functions.

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