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Article

Oxacalix[3]arene Complexes with the $Re^I(CO)_3$ Fragment†

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Oxacalix[3]arenes *p*-methyloxacalix[3]arene (L^1), *p*-isopropyloxacalix[3]arene (L^2), and *p*-ethoxycarbonyloxacalix[3]arene (L^3) are able to bind the $Re^I(CO)_3$ moiety with two of their three phenol-O atoms and one of their ether-O atoms. The monoanionic complexes were isolated in the salts $(DBUH)[Re(CO)_3(L^1H_{-2})]\cdot L^1$ (**1**) and $(NEt_4)[Re(CO)_3(L^2H_{-2})]\cdot L^2\cdot 0.5$ MeCN (**2**) (DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene). Over the course of its reaction with $(NEt_4)_2[Re(CO)_3Br_3]$ and DBU, *p*-ethoxycarbonyloxacalix[3]arene decomposes to form $[\{Re(CO)_3(L^4H_{-2})\}_2]$ (**3**) {L^4 = 1-(5-ethoxycarbonyl-2-hydroxy-3-hydroxymethyl-benzyl)-2,3,4,6,7,8,9,10-octahydro-pyrimido[1,2-a]azepin-1-ium. The expected monoanion $[Re(CO)_3(L^3H_{-2})]^-$ (**4**) was identified by ^{13}C NMR and mass spectra.

Introduction

Interest in calixarenes has grown immensely in the last 20 years.[1] Of the two main conformers, the partial-cone and cone structures, the latter bears a cavity which is able to bind various ions and neutral molecules, such as toluene,[2] and various cations.[3,4] Furthermore, the crystal structures of several calix[4]arenes give evidence for the existence of aromatic π hydrogen bonding from a water donor inside the cone toward two aromatic rings as the acceptors.[5] Oxacalix[3]arenes are able to bind alkali metal ions[6,7] and quaternary ammonium ions.[8] Many different possible functionalizations exist for both the upper and the lower rim of an oxacalix[3]arene molecule, resulting in a variety of metal derivatives[1,9−11] including compounds that mimic enzymatic activity.[12,13]

Rhenium is an important metal in the field of nuclear medicine. The two β^- emitting isotopes Re-186 and Re-188 have physical decay properties that open the door for their use as potential radiopharmaceuticals.[14] Especially, the relatively easy synthesis of $[Re(CO)_3(H_2O)_3]^+$, and therefore, the availability of the $Re^I(CO)_3$ moiety[14] has led to intense efforts to synthesize new complexes of this fragment.[15] For application purposes, it is necessary to develop ligands which, on one hand, are suitable in terms of the stability of the resulting complexes and, on the other hand, offer functional groups that can act as anchoring points for the coupling to larger biomolecules such as peptides. In an approach using calixarenes, the Reinhoudt group attached metal-chelating functions to the calix[4]arene core and coordinated an oxorhenium(V) fragment to the functionalized oxacalixarene derivative.[9] Assuming an analogy between the hydroxy-group patterns of underivatized oxacalixarenes and carbohydrate-based OH assemblies that were found to be suitable for rhenium binding,[16] we tried to use the intrinsic hydroxy

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† Dedicated to Professor Hansgeorg Schnöckel on the occasion of his 65th birthday.

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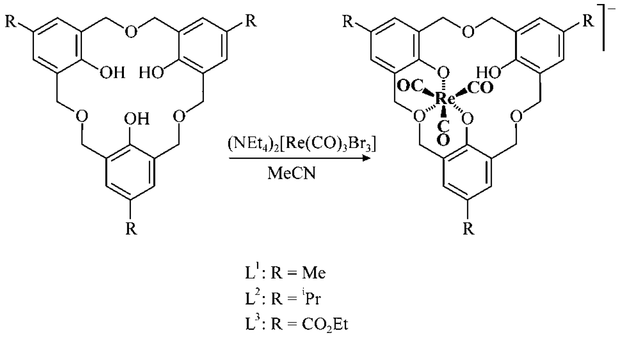
Scheme 1. Synthesis of $Re^I(CO)_3$ Complexes of Oxacalix[3]arenes with Various Substituents



groups of an oxacalixarene as the rhenium-binding site. Scheme 1 gives a sketch of the resulting coordination behavior of the $Re^I(CO)_3$ core observed in this work toward oxacalix[3]arenes that bear additional noncoordinating groups at the opposite rim.

Experimental Section

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) and *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O) and triethylamine (NEt_3) were used as supplied by Fluka; diethyleneglycoldimethyl ether (diglyme, Aldrich), decacarbonyldirhenium (Strem), and tetraethylammoniumbromide (Merck) were used as supplied as well. Solvents were dried (molecular sieve) and deoxygenated. Acetonitrile was supplied by Fisher Scientific; tetrahydrofurane (THF), ethyl acetate (EtOAc), toluene, and dichloromethane were purchased from Fluka. Bromopentacarbonyl-rhenium(I) was prepared according to standard procedures.[17] Standard Schlenk techniques (nitrogen as the inert gas) were used. Ethyl-3,5-bis(hydroxymethyl)-4-hydroxybenzoate[7] and the oxacalix[3]arenes, *p*-methyloxacalix[3]arene and *p*-isopropyloxacalix[3]arene, were synthesized according to previously described methods.[6]

$(NEt_4)_2[Re(CO)_3Br_3]$. The general method of ref 18 was used. $[Re(CO)_5Br]$ (4.90 g, 12.1 mmol) was suspended in diglyme (80 mL) and heated to 50 °C. NEt_4Br (5.47 g, 26.0 mmol) was suspended in diglyme (250 mL) and heated to 70 °C. The suspensions were combined and heated to 115 °C under stirring. A colorless precipitate formed over the course of 5 h. The precipitate was filtered off, washed three times with diglyme and ether, and dried in vacuo. Excess NEt_4Br was removed by suspending the solid in ethanol (40 mL), followed by in vacuo drying of the resulting powder. The product obtained was a colorless powder (7.36 g, 9.55 mmol, 79.3% yield). Anal. Calcd for $C_{19}H_{40}Br_3N_2O_3Re$: C, 29.6; H, 5.2; N, 3.6; Br 31.1. Found: C, 29.7; H, 5.2; N, 3.6; Br 30.9. IR (KBr, carbonyl valence absorptions): $\tilde{\nu}$ 2000 (s), 1866 (s) cm^{-1}.

$(DBUH)[Re(CO)_3(L^1H_{-2})]\cdot L^1$ (1). DBU (46 mg, 0.30 mmol) and *p*-methyloxacalix[3]arene (45 mg, 0.10 mmol) were suspended in 4 mL of acetonitrile. $(NEt_4)_2[Re(CO)_3Br_3]$ (154 mg, 0.200 mmol) was added, and the suspension was stirred at room temperature for 5 h. After 1 h, the suspension became a pale yellow solution. After filtration, the solvent was evaporated in vacuo, and the pale yellow residue was dissolved in 2 mL of CH_2Cl_2. The crystallization of the product follows an elaborate crystallization protocol. To crystallize NEt_4Br, the solution was kept at 4 °C, and diethyl ether vapors were allowed to diffuse into it. After 1 day, the solution was filtered off from the white solid, and diethyl ether vapors were again allowed to diffuse into it at 4 °C. After 24 h, colorless crystals of (DBUH)Br were filtered off, and 1 mL of diethyl ether was added to the resulting solution. This mixture was filtered, and the solution was layered with hexane (1 mL) and stored at 4 °C again; the solvents were allowed to slowly evaporate. Over the course of one month, a few colorless platelets formed. FAB^-: *m*/*z* calcd for $C_{30}H_{28}O_9Re = [Re(CO)_3(L^1H_{-2})]^-$ 718.7. Found: 718.7 with a typical Re_1 pattern. ^{13}C NMR (67.93 MHz, MeCN): δ 164.1 (C22/23), 156.5 (C24), 131.61, 131.56, 130.6, 129.3, 128.8, 128.7, 125.0, 123.3 (Ar−C), 74.9 (C2/3), 70.0, 69.9 (C9/10/16/17), 20.5, 20.4 (C25/26/27). IR (KBr, carbonyl valence absorptions): $\tilde{\nu}$ 2007 (s), 1882 (s), 1869 (s) cm^{-1}.

$(NEt_4)[Re(CO)_3(L^2H_{-2})]\cdot L^2\cdot 0.5MeCN$ (2). *p*-Isopropyloxacalix[3]arene (107 mg, 0.20 mmol) and $(NEt_4)_2[Re(CO)_3Br_3]$ (77 mg, 0.10 mmol) were suspended in 2 mL of acetonitrile. After the addition of DBU (30 mg, 0.20 mmol), the mixture was heated at 85 °C for 2 h. At a temperature of about 70 °C, the suspension became a pale yellow solution. During the reaction time, a white solid appeared which was filtered off after the mixture was cooled to room temperature. The resulting pale yellow solution was kept at room temperature. Colorless crystals grew over the course of 1 day (18 mg, 0.006 mmol, 12.1% yield). Crystals of **2** also grew from a batch with a molar Re/L^2 ratio of 1:1 after the addition of ca. 0.2 mL of water. Anal. Calcd for $C_{78}H_{103.5}N_{1.5}O_{15}Re$: C, 62.9; H, 7.0; N, 1.4. Found: C, 62.6; H, 6.9; N, 1.4. FAB^-: *m*/*z* calcd for $C_{36}H_{40}O_9Re = [Re(CO)_3(L^2H_{-2})]^-$ 802.9. Found: 802.8 with a typical Re_1 pattern. ^{13}C NMR (100.63 MHz, MeCN): δ 164.4 (C22/23), 156.7 (C24), 140.1, 134.8, 129.0, 128.8, 128.0, 124.7 (Ar−C), 75.0 (C2/3), 70.4, 70.3 (C9/10/16/17), 33.9, 33.8 (C25/28/31), 24.8, 24.7, 24.6 (C26/27/29/30/32/33). IR (KBr, carbonyl valence absorptions): $\tilde{\nu}$ 2002 (s), 1878 (s), 1853 (s) cm^{-1}.

***p*-Ethoxycarbonyloxacalix[3]arene (L^3).** Ethyl-3,5-bis(hydroxymethyl)-4-hydroxybenzoate (2.00 g, 8.8 mmol) and *p*-TsOH·H_2O (35 mg, 0.19 mmol) were suspended in 90 mL of dry toluene. This mixture was heated to 125 °C for 1 h, during which it became a solution. After the mixture was cooled to room temperature, the solvent was removed and the resulting solid was dried in vacuo. The solid was suspended in 10 mL of $CHCl_3$. This mixture was subjected to a flash chromatography on silica gel (EtOAc/$CHCl_3$ 1:9, $R_f = 0.53$). The fractions were combined, and the solvent was removed in vacuo. The product obtained was a colorless solid (172 mg, 0.275 mmol, 9.4%). Anal. Calcd for $C_{33}H_{36}O_{12}$: C, 63.5; H, 5.8. Found: C, 63.8; H, 5.6. FAB^+: *m*/*z* calcd for L^3 624.6. Found: 625.5 $[M + H^+]$. ^{13}C NMR (67.93 MHz, $CDCl_3$): δ 166.0 (*C*OO), 159.9 (*C*−OH), 131.7 (C_{Ar}), 123.8 (C_{Ar}−CH_2), 122.1 (*C*−COO), 71.0 (CH_2−O−CH_2), 61.0 (CH_2−CH_3), 14.4 (CH_3). ^1H NMR (270.17 MHz, $CDCl_3$): δ 9.18 (*s*, 3H, Ar−OH), 7.85 (*s*, 6H, Ar−H)), 4.75 (*s*, 12H, −OCH_2−), 4.33 (*q*, $J = 7.1$, 6H, CH_2), 1.36 (*t*, $J = 7.1$, 9H, CH_3).

$[\{Re(CO)_3(L^4H_{-2})\}_2]$ (3). *p*-Ethoxycarbonyloxacalix[3]arene (62 mg, 0.10 mmol) and $(NEt_4)_2[Re(CO)_3Br_3]$ (77 mg, 0.10 mmol) were suspended in 2 mL of acetonitrile. After the addition of DBU (46 mg, 0.30 mmol), the suspension turned into a pale yellow solution. This solution was heated at 85 °C for 6 h. After it was cooled to room temperature, the solution was filtered and kept at ambient temperature. A few small, colorless crystals grew overnight. The poor yield of crystals was sufficient for crystal-structure and mass-spectral analysis only. Hence, for this decomposition product, no other analytical data are available. FAB^+: *m*/*z* calcd for $[Re(CO)_3(L^4H_{-2})]_2$ 1259.4. Found: 1258.7 = $[M^+]$.

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Solution of $[Re(CO)_3(L^3H_{-2})]^-$ (4). a. *p*-Ethoxycarbonyloxacalix[3]arene (62 mg, 0.10 mmol) and $(NEt_4)_2[Re(CO)_3Br_3]$ (77 mg, 0.10 mmol) were suspended in 2 mL of acetonitrile. After the addition of NEt_3 (30 mg, 0.30 mmol), the suspension was stirred at room temperature for 24 h. After filtration, a pale yellow solution was obtained.

b. *p*-Ethoxycarbonyloxacalix[3]arene (31 mg, 0.05 mmol) and $(NEt_4)_2[Re(CO)_3Br_3]$ (39 mg, 0.05 mmol) were suspended in 2 mL of acetonitrile. After the addition of NEt_3 (15 mg, 0.15 mmol), the suspension was stirred at 85 °C. It became a solution within 1 h. After 2 h, a white solid appeared, probably unreacted L^3. The reaction was stopped by cooling to room temperature. During this procedure, fine, small, colorless needles grew which were filtered off. After filtration, a pale yellow solution was obtained. Evaporation of the solution produced a pale yellow solid. FAB^-: *m/z* calcd for **4** 892.9. Found: 892.6 with a typical Re_1 pattern. ^{13}C NMR (100.53 MHz, MeCN): δ 171.6 (C22/23), 167.4, 167.0 (*C*OO), 163.1 (C24), 132.7, 132.4, 132.3, 129.5, 127.7, 125.0, 121.9, 116.7 (Ar−C), 75.0 (C2/3), 69.6, 69.4 (C9/10/16/17), 61.3, 60.9 (CH_2-CH_3), 14.8, 14.7 (CH_3). IR (KBr, carbonyl valence absorptions): $\tilde{\nu}$ 2012 (s), 1869 (s) cm^{-1}.

Spectroscopy. $^{13}C\{^1H\}$ spectra were recorded using 1 mL of filtered reaction mixture in a 5 mm tube. The following equipment was used: ^{13}C NMR JEOL EX-400, GSX 270, 400e; mass spectra JEOL JMS-700 (ionization method FAB^-/ FAB^+); IR Jasco FT/IR-460plus. NMR shift differences are given according to $\Delta\delta = \delta(\text{complex}) - \delta(\text{free oxacalix[3]arene})$. ^{13}C NMR chemical shifts are listed for oxacalix[3]arene carbon atoms only. The signal of the methyl carbon atom of acetonitrile was used as the chemical shift standard (1.79 ppm).

Crystal Structure Determination and Refinement. Crystals suitable for X-ray crystallography were selected by means of a polarizing microscope, mounted on the tip of a glass fiber, and investigated on a Nonius KappaCCD diffractometer using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The measurement temperature was 200 K. The structures were solved by direct methods (SHELXS) and refined by full-matrix least-squares calculations on F^2 (SHELXL-97). Anisotropic displacement parameters were refined for all non-hydrogen atoms. No restraints were applied in structure refinements. Crystallographic data are collected in Table 3. The values of R_{int}, mean $\sigma(I)/I$, and $R_w(F^2)$ refer to weakly diffracting crystals. The maximum electron densities are located near the Re atoms in **2** and **3** or as an isolated "cluster" in **1** (obviously acetonitrile), withstanding any refinement procedure. A numerical absorption correction in the crystal structure analysis of **3** failed and therefore SCALEPACK was applied.

Results and Discussion

Re^I(CO)$_3$ Derivative of *p*-Methyloxacalix[3]arene 1.

p-Methyloxacalix[3]arene (L^1) was chosen as a starting point to examine the complexation of the $Re^I(CO)_3$ moiety. It is a prototypical representative of the class of oxacalix[3]arenes, and except for its three phenol groups, no other functional groups are present that could disturb or hinder complexation. In our experience, a base must always be added to the reaction mixture or the ^{13}C NMR spectra will not indicate coordination. Acetonitrile was used as the solvent because of the competing formation of the oxorhenium clusters $[Re_3(CO)_9(\mu_3\text{-}OH)(\mu\text{-}OH)_3]^-$ and $[Re_2(CO)_6(\mu\text{-}OH)_3]^-$ in aqueous solution at higher pH values.[19] The same species also exist with methoxo instead of hydroxo ligands, so the use of an aprotic polar solvent is obviously required when base addition is necessary. To synthesize oxacalix[3]arene−rhenium complexes, molar Re/L^1/base ratios of 2:1:3 and 1:1:3 were used. DBU was used as the base.

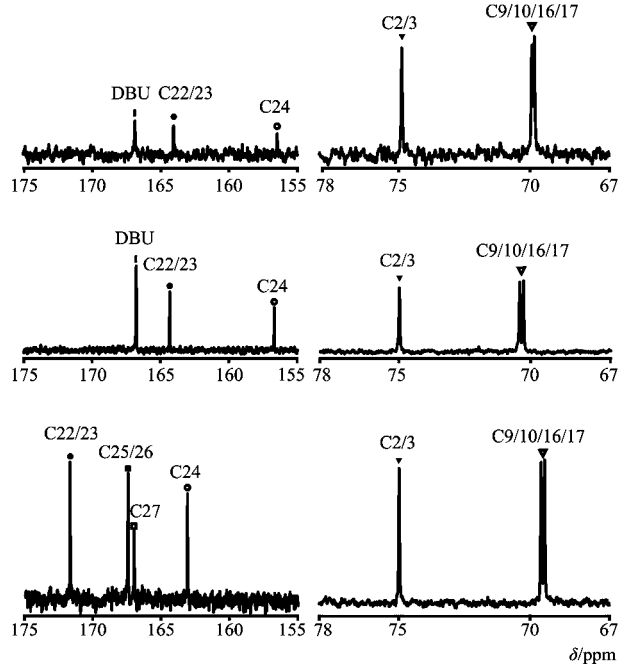

Figure 1. ^{13}C NMR spectra of the three coordinated oxacalix[3]arenes. The typical regions of the carbon atoms bonded to the phenol-O atoms (left part) and the inner cyclic methylene groups (right part) are shown: (top) $(DBUH)[Re(CO)_3(L^1H_{-2})]$, (middle) $(NEt_4)[Re(CO)_3(L^2H_{-2})]$, and (bottom) solution of $[Re(CO)_3(L^3H_{-2})]^-$. DBU signals that occur in the oxacalix[3]arene range are depicted with filled rectangles: (●) C atoms bonded to the coordinated phenol-O atoms, (○) C atoms bonded to the noncoordinated phenol-O atoms, (▼) C atoms bonded to the coordinating ether-O atoms, (▽) C atoms bonded to noncoordinating ether-O atoms, (■) the two identical carboxy-C atoms in **4**, and (□) residual carboxy-C atom in **4**.

Surprisingly, in both experiments, the ^{13}C NMR spectra showed a species that is asymmetrically coordinated. No C_3 axis was present regardless of the molar ratio used. With this result, it was obvious that upon coordination of L^1 not all of its phenol-O atoms were bonded to rhenium(I). While small amounts of free oxacalix[3]arene were still visible with the 1:1:3 ratio, the ^{13}C NMR spectrum of the 2:1:3 batches shows only signals of coordinated L^1. According to the ^{13}C NMR spectrum there was no total loss of symmetry. There were 10 signals in the aromatic region, three in the aliphatic region of the methylene groups, and two signals for the methyl groups from the coordinated L^1, indicating a 2-fold axis or a mirror plane. Figure 1 shows the most meaningful regions in the ^{13}C NMR spectra of the reaction batches. The signals of the carbon atoms bonded to the phenol-O atoms (left part), as well as the signals of the inner cyclic methylene groups (right part), indicate a coordination of two phenol-O atoms and one ether-O atom. This leads to a higher shift (coordination-induced shift, CIS) of those carbon atoms that bind to the rhenium-bonded oxygen atoms (C2/3/22/23) and a lower one for those carbon atoms whose oxygen atom does

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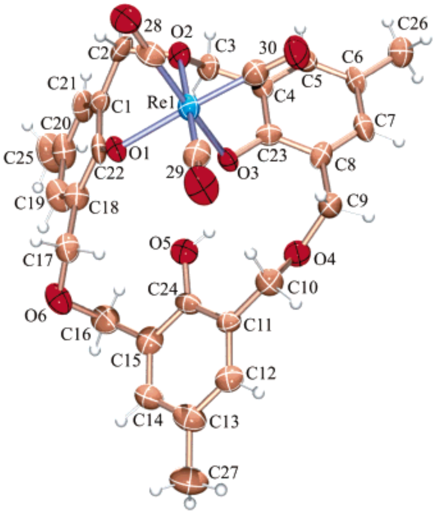

Figure 2. Structure of one of two $[Re(CO)_3(L^1H_{-2})]^-$ anions in the asymmetric unit of **1** (40% probability ellipsoids; the number *n* at the carbonyl ligands should be read as C*n* and O*n*). Distances (Å) and angles (deg) of complex 1 [complex 2]: Re1−O1 = 2.162(6) [2.105(6)], Re1−O2 = 2.248(7) [2.225(7)], Re1−O3 = 2.118(7) [2.136(7)]; O1−Re1−O2 = 84.2(3) [80.8(3)], O1−Re1−O3 = 85.1(2) [83.5(3)], O2−Re1−O3 = 79.6(3) [84.0(3)]; mean $Re-C_{CO}$ = 1.892 [1.889], mean $C-O_{CO}$ = 1.166 [1.161].

Table 1. ^{13}C NMR Chemical Shifts (ppm) in a MeCN Solution of **1**[a]

	C22/23	C24	C2/3	C9/10/16/17		C25/26/27	
δ	164.1	156.5	74.9	70.0	69.9	20.5	20.4
$\Delta\delta$	**9.9**	2.3	**3.1**	−1.8	−1.9	0.1	0.0

[a] Free L^1: C22/23/24, 154.2; C2/3/9/10/16/17, 71.8; C25/26/27, 20.4. The boldface values are the $\Delta\delta$ values of carbon atoms that bear a rhenium-binding oxygen atom.

not bind to rhenium(I) (C9/10/16/17/24). The crystal structure analysis of **1** confirmed these considerations (Figure 2). The *p*-methyloxacalix[3]arene ligand binds with two of its phenol-O atoms (O1, O3) and one of its ether-O atoms (O2). The hydroxy function with O5 does not participate in the coordination but acts as a donor in a bifurcated hydrogen bond toward one of the two free ether-O atoms (O4) and one coordinated phenol-O atom (O3) as the acceptors. As expected, the bond from Re to the ether-O atom O2, is about 0.1 Å longer than that for the phenolato-O atoms O1 and O3. The crystal structure corresponds to the ^{13}C NMR spectrum (Figure 1, top). The predicted symmetry element is a noncrystallographic mirror plane that includes the atoms O2, Re1, C29, O29, O5, C24, C13, and C27. Fifteen signals are in agreement with a C_s symmetrical product (Scheme 1).

The chemical shifts and the coordination-induced shift (CIS) values are given in Table 1 for those carbon atoms that bind to oxygen atoms; the shifts of methyl carbon atoms are given as well. It can be seen that the two signals of the four carbon atoms that bear a rhenium-binding oxygen atom are more downfield shifted than the signals of the other carbon atoms. The phenol-O-related signal is about 7 ppm more downfield shifted than the signal stemming from the rhenium-binding ether oxygen atom. The residual signals of the methylene groups experience a high-field shift of nearly 2 ppm relative to the free L^1. The unexpected downfield shift of the C24 signal is noteworthy: although C24 is distant from the Re center in terms of bonds, the signal shift exceeds the shifts of any other noncoordinated function (Table 1).

Table 2. ^{13}C NMR Chemical Shifts (ppm) in a MeCN Solution of **2**[a]

	C22/23	C24	C2/3	C9/10/16/17		C25/C28/C31		C26/27/29/30/32/33		
δ	164.4	156.7	75.0	70.4	70.3	33.9	33.8	24.8	24.7	24.6
$\Delta\delta$	**10.0**	2.3	**3.0**	−1.6	−1.7	−0.1	−0.2	0.3	0.2	0.1

[a] Free L^2: C22/23/24, 154.4; C2/3/9/10/16/17, 72.0; C25/28/31, 34.0; C26/27/29/30/32/33, 24.5. The boldface values are the $\Delta\delta$ values of carbon atoms that bear a rhenium-binding oxygen atom.

Crystals grew from a batch with a molar 2:1:3 ratio of Re/L^1/DBU. Unexpectedly, because of the absence of free L^1 in terms of ^{13}C NMR spectra, the asymmetric unit in the crystal structure contains two uncoordinated L^1 in addition to two complex molecules. So, during the elaborate crystallization process, a significant part of the product decomposed to free L^1 and Re-containing species. The two complex molecules of the asymmetric unit are almost identical. Figure 1 thus shows one of these complex anions only.

$Re^I(CO)_3$ Derivative of *p*-Isopropyloxacalix[3]arene (L^2) 2. For the following introduction of a substituent which allows coupling of the oxalix[3]arene to larger biomolecules, the influence of sterically demanding residues other than methyl on the ligand's coordination properties was investigated first. Experiments were made with the 1:1:3 and 2:1:3 molar ratios of Re/L^2/DBU, L^2 being the isopropyl analogue. The ^{13}C NMR spectra of these experiments indicated the same coordination pattern as for the L^1 ligand. In the 1:1 Re/L^2 experiments, the ^{13}C NMR spectra showed an excess of free L^2 over the coordinated one. However, in the case of the 2:1 Re/L^2 experiments, no signals of free L^2 were observed. Both series of experiments showed the same signals of coordinated L^2 in the ^{13}C NMR spectra. Moreover, the signal pattern resembled the one in the L^1 experiments (Figure 1, middle). The only noticeable difference was the existence of only 8 signals in the aromatic region in the case of the 2:1 Re/L^2 experiment instead of 10, which was caused by accidental signal overlap. Significant chemical shifts and CIS values are listed in Table 2. The apparent constancy of the CIS values in Tables 1 and 2 should be noted as well as the $\Delta\delta$ value of the C24 signal. As expected, the isopropyl signals were not significantly shifted upon coordination of the ligand.

Figure 3 shows the molecular structure of the complex anion in crystals of **2**. The crystals grew from a 1:1:3 batch of Re/L^2/DBU which contained non-rhenium-bonded L^2. Like **1**, the asymmetric unit contains two free L^2 molecules and two complex molecules. Both complex anions have the same shape, so only one of them is depicted in Figure 3. The coordination is the same as that for the L^1 ligand showing the constant coordination pattern of this ligand class with the $Re^I(CO)_3$ moiety. The resulting products and the ^{13}C NMR spectra gave no hint of any other product; therefore, obviously, the substituents do not influence the coordination behavior of the oxacalix[3]arenes.

Reactions of the *p*-Ethoxycarbonyloxacalix[3]arene (L^3) with the $Re^I(CO)_3$ Moiety. We saw that the oxacalix[3]-

Table 3. Crystallographic Data

	1	**2**	**3**
net formula	$C_{66}H_{75}N_2O_{14}Re$	$C_{78}H_{103.5}N_{1.5}O_{15}Re$	$C_{46}H_{54}N_4O_{14}Re_2$
M_r (g mol^{-1})	1322.513	1495.368	1259.354
cryst size (mm)	0.15 × 0.05 × 0.05	0.14 × 0.12 × 0.10	0.15 × 0.12 × 0.06
cryst syst	triclinic	triclinic	triclinic
space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a (Å)	16.6126(2)	14.1272(2)	9.1852(3)
b (Å)	18.5955(3)	23.5791(4)	9.9042(3)
c (Å)	23.9217(4)	24.6058(5)	15.9634(5)
α (deg)	76.8060(5)	109.9521(6)	82.3567(16)
β (deg)	83.1942(5)	100.2614(6)	75.3812(16)
γ (deg)	74.9826(7)	96.7309(6)	74.8731(14)
V (Å^3)	6935.23(18)	7439.5(2)	1353.01(7)
Z	4	4	1
calcd density (g cm^{-3})	1.26664(3)	1.32887(4)	1.54562(8)
μ (mm^{-1})	1.813	1.698	4.530
abs correction	numerical	numerical	none
transm factor range	0.8002−0.9536	0.7403−0.8844	
reflns measured	93 595	103 208	10 740
R_{int}	0.1575	0.1819	0.0851
mean $\sigma(I)/I$	0.2776	0.2949	0.1126
θ range	3.1−27.5	3.2−27.5	3.3−27.6
obsd reflns	12343	11835	4473
x, y (weighting scheme)	0.1114, 0	0.0887, 0	0.0958, 2.4713
reflns in refinement	31 339	33 287	6053
params	1514	1722	301
$R(F_{obs})$	0.085	0.095	0.062
$R_w(F^2)$	0.2522	0.2352	0.1717
S	0.972	0.989	1.034
shift/error$_{max}$	0.001	0.001	0.001
max electron density (e Å^{-3})	1.734	1.055	2.567
min electron density (e Å^{-3})	−0.698	−1.030	−1.999

arenes exhibit a new and unexpected coordination behavior unique to the $Re^I(CO)_3$ fragment not involving all of the phenol-O atoms in the coordination of the central metal. We proceeded to synthesize a product according to **1** and **2** with a functionalized oxacalix[3]arene. For this purpose, the oxacalix[3]arene with three *p*-ethoxycarbonyl groups, L^3, was synthesized. In the course of the ligand synthesis, we found it suitable to follow a procedure starting from a byproduct of an oxacalix[8]arene synthesis[20] instead of the procedure reported for L^3, varying only the starting material and the solvent.[7]

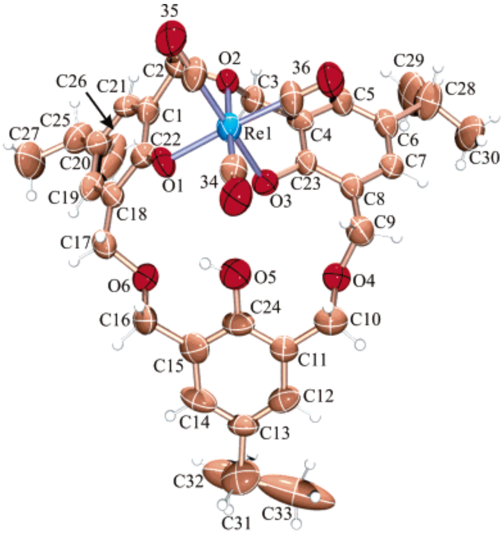

Figure 3. Structure of one of two $[Re(CO)_3(L^2H_{-2})]^-$ ions in the asymmetric unit of **2** (40% probability ellipsoids; the number *n* at the carbonyl ligands should be read as C*n* and O*n*). Distances (Å) and angles (deg) of complex 1 [complex 2]: Re1−O1 = 2.108(6) [2.114(7)], Re1−O2 = 2.214(7) [2.199(8)], Re1−O3 =2.140(6) [2.134(6)] ; O1−Re1−O2 = 83.9(2) [83.9(3)], O1−Re1−O3 = 82.3(2) [83.2(3)], O2−Re1−O3 = 81.4(2) [81.4(3)]; mean Re−C_{CO} = 1.900 [1.857], mean C−O_{CO} = 1.169 [1.187].

Decomposition of the Oxacalix[3]arene Ring by Use of DBU. The 1:1:3 ratio of Re/L^3/DBU was tested, and reactions were carried out in acetonitrile either at 85 °C or at room temperature. As a result, the ^{13}C NMR spectra indicated no unreacted oxacalix[3]arene in either case. On the other hand, the expected signal pattern of the attempted product was not present. When $(NEt_4)_2[Re(CO)_3Br_3]$ was used as the Re starting material, few colorless crystals grew over the course of 1 day at room temperature. The molecular structure of the complex in crystals of $[\{Re(CO)_3(L^4H_{-2})\}_2]$ (**3**) are shown in Figure 4 and Scheme 2 (L^4 = 1-(5-ethoxycarbonyl-2-hydroxy-3-hydroxymethyl-benzyl)-2,3,4,6,7,8,9,10-octahydro-pyrimido[1,2-a]azepin-1-ium. There it can be seen that the DBU base induced an ether cleavage so that the oxacalix[3]arene ring decomposed into L^4 fragments bonded to rhenium. The DBU base is bonded with its sp^2 nitrogen atom (N1) to a former ether methylene group (C11) leading to a positive formal charge at N1. The resulting molecule acts as a bidentate ligand forming a dimeric complex with two $Re^I(CO)_3$ moieties. This structure motif is related to the $[Re_2(CO)_6(\mu\text{-}OH)_2(H_2O)_2]$ species reported by Alberto and Hegetschweiler[19] and to the carbohydrate complex $[Re_2(CO)_6(\kappa^4O\text{-}L\text{-}ThreH_{-3})]^-$ (Thre = threitol).[16] The coordination is carried out with two deprotonated alcohol groups one of which is a former ether-O atom (O1) bridging the two Re

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(20) Tsue, H.; Enyo, K.; Hirao, K.-i. *Helv. Chim. Acta* **2001**, *84*, 849−859.

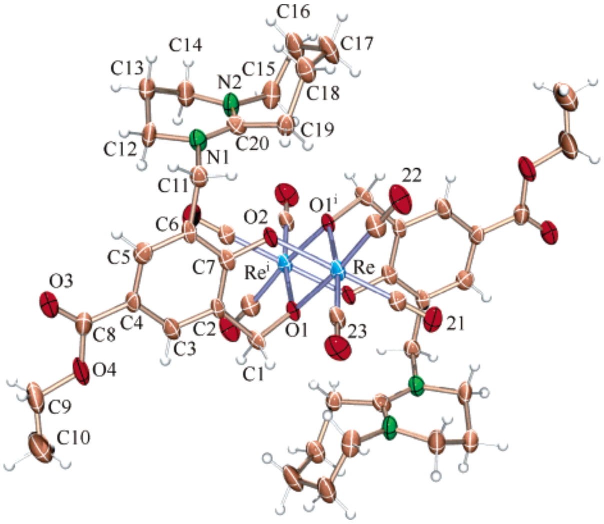
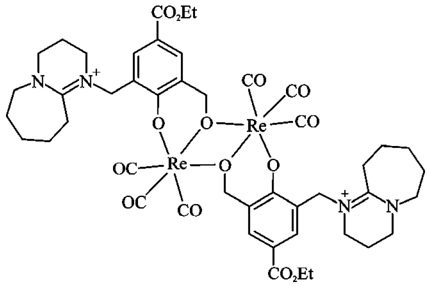


Figure 4. Structure of [{Re(CO)$_3$(L^{4}H$_{-2}$)}$_2$] (**3**) (40% probability ellipsoids; the number *n* at the carbonyl ligands should be read as C*n* and O*n*). Distances (Å) and angles (deg): Re−O1 = 2.128(6), Re−O1^i = 2.150(6), Re−O2 = 2.118(6); Re−O1−Re^i = 105.7(2)°; mean Re−C$_{CO}$ = 1.913, mean C−O$_{CO}$ = 1.150, nonbonded Re−Re^i distance = 3.410(2). Symmetry code: i −*x*, −*y*, 1 − *z*.

Scheme 2. Complex **4**[a]



[a] The conjugate acid of the ligand 1-(5-ethoxycarbonyl-2-hydroxy-3-hydroxymethyl-benzyl)-2,3,4,6,7,8,9,10-octahydro-pyrimido[1,2-a]azepin-1-ium (L^4) is formed by decomposition of L^3 (Scheme 1).

centers. The phenol-O atom O2 which is more acidic than O1 is bonded to only one Re atom.

A rhenium-free mixture of 1:3 L^3/DBU was heated in acetonitrile at 85 °C for 5.5 h to investigate the effect of the Re^I(CO)$_3$ moiety on the observed ether cleavage. The ^{13}C NMR spectra showed signals of deprotonated L^3 only, and no decomposition product was observed. As discussed later, the replacement of DBU by NEt$_3$ in the presence of the Re^I(CO)$_3$ fragment did not result in the decomposition of L^3. These experiments support the assumption that the ether cleavage is caused by the combined effects of the DBU base and the Re^I(CO)$_3$ starting material.

Synthesis of [Re(CO)$_3$(L^{3}H$_{-2}$)]$^-$ (4). In terms of the ^{13}C NMR signal pattern, the exchange of DBU by NEt$_3$ yielded the intact *p*-ethoxycarbonyloxacalix[3]arene bonded to the rhenium fragment in the desired way. The reaction could be carried out either at room temperature or at 85 °C. Decomposition of the oxacalix[3]arene ring was not observed under either of the conditions.

In the case of the room-temperature reaction, the reaction time was increased to 24 h because the L^3 ligand did not dissolve completely in acetonitrile. Even after that time, the reaction mixture was not a clear solution. However, the ^{13}C NMR spectrum of the filtrate showed the exact signal pattern that indicates the attempted coordination with two phenol-O and one ether-O atoms (Figure 1, bottom). The same signal pattern was observed after the reaction mixture was heated for 2 h at 85 °C. That means that under the same reaction conditions, DBU is able to deprotonate unfunctionalized oxacalix[3]arenes without decomposition. It seems unsuitable, however, to act merely as a simple base in case of L^3.

Conclusions

It was demonstrated that the oxacalix[3]arenes *p*-methyloxacalix[3]arene, *p*-isopropyloxacalix[3]arene, and *p*-ethoxycarbonyloxacalix[3]arene coordinate to the Re^I(CO)$_3$ moiety. Unexpectedly, the oxacalix[3]arenes do not act as tridentate tris(phenoxo) ligands but offer a new coordination behavior preferring one ether-O atom to the third phenol-O atom. These results appear to be unique to the Re^I(CO)$_3$ moiety, since other central metals such as the highly charged vanadium(V)[10] or titanium(IV)[11] are found in the expected bonding mode.

Furthermore, we reported an unusual ether cleavage of the functionalized oxacalix[3]arene L^3 by the use of DBU producing 1-(5-ethoxycarbonyl-2-hydroxy-3-hydroxymethyl-benzyl)-2,3,4,6,7,8,9,10-octahydro-pyrimido[1,2-a]azepin-1-ium (L^4) which acts as a bidentate ligand for the rhenium(I) center as identified by crystal-structure analysis. Coordination of the intact ligand L^3 can be achieved by the use of NEt$_3$ leading to the observed coordination behavior of this ligand class.

A problem that remains to be solved prior to attempts to bind biomolecules to functionalized forms of the title compounds is the hydrolytic behavior of the latter. In the course of the development of suitable crystallization protocols, we examined the action of added water to the crystallization batches since such an addition had proven to be beneficial in the case of carbohydrate complexes of the Re^I(CO)$_3$ moiety.[16] The oxacalixarene compounds were, possibly dependent on the para substituents, completely or partly hydrolyzed in the presence of water. As a result of partial hydrolysis, cocrystallization products of the respective rhenium complexes and the free ligand were isolated.

Supporting Information Available: Additional crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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