Entry to new *N*,*O*-ligands from oxygen-depleted calixarenes†

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We prepared and characterized titanium complexes of a new mixed *N*,*O*-ligand obtained from oxygen-depleted calixarenes, which show interesting catalytic activity compared with complexes of a "regular" calixarene ligand.

Metal complexes of multidentate ligands bearing both hard and soft two-electron donors have found numerous applications in catalysis.[1] Most commonly, the soft centers are comprised of neutral imine or phosphine atom, while the hard ones are usually the negatively charged alkoxide or amide groups. Omnipresent Salen and porphyrin molecules, which act as tetradentate dianionic donors in their metal complexes (Fig. 1(a) and (b)), can be viewed as typical representatives of such ligands.[2,3] A similar tetradentate dianionic motif is also found in a large number of reported metal complexes of calix[4]arene (calixarene) ligands, where the metal is coordinated to the lower rim oxygen atoms (Fig. 1(c)).[4–6] Yet, the catalytic properties of the calixarene metal complexes remain largely undeveloped. Several metal calixarene catalysts were reported, most notably by the groups of Neri,[7] Ladipo[8] and others,[9] however, the calixarene ligands failed to become on par with other multidentate ligands in catalytic applications. One possible reason for this is the presence of only hard oxygen donors in the calixarene ligand making metal complexation relatively weak. Because of these limitations, much of the focus in calixarene metal catalysis shifted toward calixarene molecules with pendant ligand groups.[10] From the structural point of view, the introduction of the pendant groups makes the metal complex more flexible. While not necessarily detrimental to the catalytic activity, this flexibility reduces the attractiveness of the calixarene platform as the three-dimensional analog of the rigid multidentate systems, such as Salen or porphyrin. To maintain this rigidity while improving the coordination properties, it would be desirable to introduce the soft donor atoms in place of one or more oxygen atoms of the calixarene lower rim. Herein we present the first example of a calixarene-based ligand having two of the oxygen atoms replaced by the soft nitrogen donors.

Although calixarenes lacking one or more oxygen atoms at the lower rim were previously reported the synthetic protocols toward such compounds are complicated, with the yields and selectivities being generally low.[11] Georghiou *et al.* recently reported the successful Sonogashira-type cross-coupling reaction on trifluoromethanesulfonate (triflate) substituted calixarene compounds.[12] Using our modified protocol,[13] we were able to introduce two trimethylsilyl (TMS) acetylene groups in 1,3-positions of the calixarene lower rim to give **1** (Scheme 1). The TMS protecting groups were removed by the reaction with K_2CO_3 in methanol–THF mixture giving compound **2**. Finally, the reaction with benzyl azide under the Sharpless-modified conditions for the Huesgen 1,3-cycloaddition gave the bis-triazole compound **3** (Scheme 1).

Compound **3** represents the first oxygen-depleted calixarene with the sp^2-hybridized nitrogens placed instead of the oxygen atoms. The X-ray crystal structure of **3**‡ is presented in Fig. 2. The conic conformation of the calixarene scaffold is clearly preserved. Importantly, the nitrogen atoms of the triazole units point toward the center of the calixarene lower rim, which is necessary for the successful metal complexation. Two of these atoms are involved in hydrogen bonding with the remaining two phenol groups of the calixarene. The conic conformation of **3** is also preserved in solution, as evident from its ^{1}H NMR spectrum. The calixarene methylene groups give rise to two apparent doublets at 3.37 and 3.96 ppm (J = 13.7 Hz), while the triazole benzyl groups show a singlet at 5.66 ppm. The OH groups hydrogen atoms give rise to a broad signal at 8.69 ppm.

To verify the ability of **3** to complex transition metals, we treated **3** with $TiCl_4$. Upon heating in toluene at 110 °C, the clean formation of the red Ti complex **4** was observed (Scheme 2). Complex **4** was characterized by the NMR spectroscopy, mass spectrometry and X-ray crystallography. The X-ray crystal structure of **4**‡ is shown in Fig. 3. The Ti center in **4** is in an octahedral environment, with the triazole ligands occupying axial positions. Atoms N34 and N46, previously involved in the hydrogen bonding, are now coordinated to the metal center. Due to the presence of the carbon atom between the calixarene aromatic ring and coordinated nitrogen atom, the N34–Ti–N46 angle of 161.02°. is significantly deviated from the ideal 180°. For comparison, the corresponding titanium complex of the regular dimethylcalixarene ligand, Calix$(OMe)_2O_2TiCl_2$, has an O–Ti–O angle of 170.8°.[14] Also, the rigid positioning of the

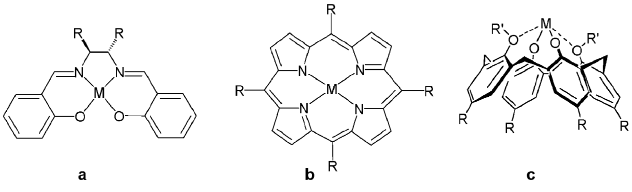

Fig. 1

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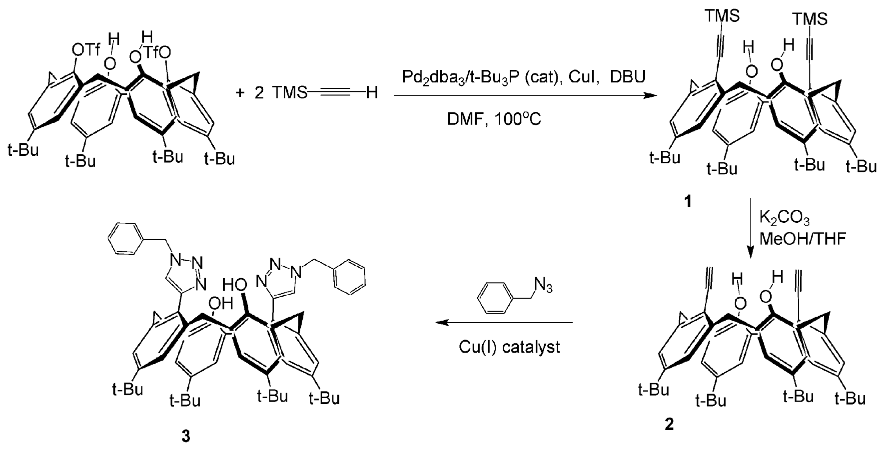


Scheme 1

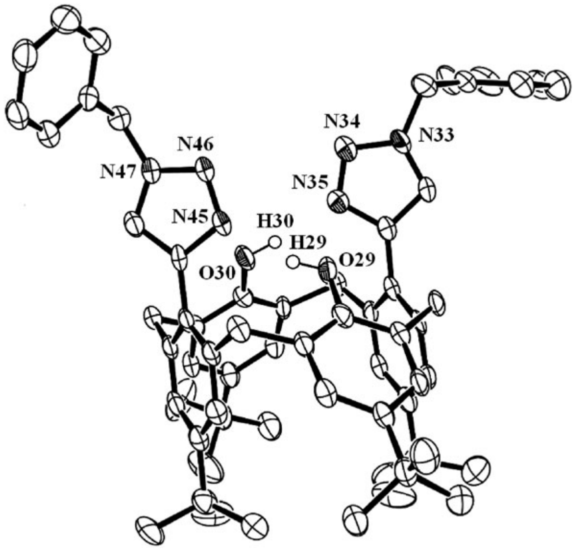
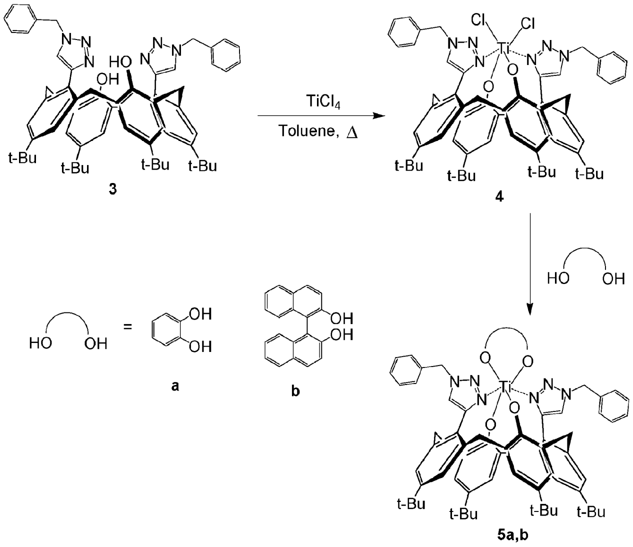


Fig. 2 ORTEP view of a molecule of **3** with thermal ellipsoids shown at 50% probability. Hydrogen atoms are omitted for clarity.



Scheme 2

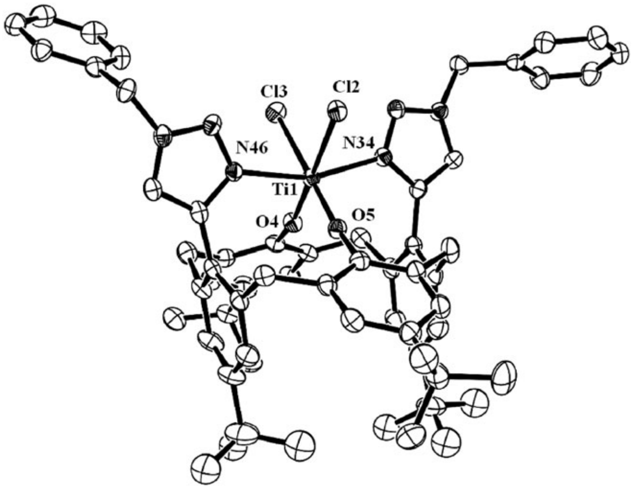
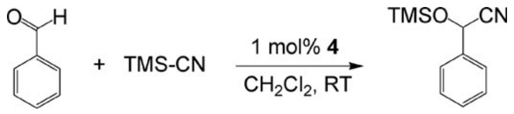


Fig. 3 ORTEP view of a molecule of **4** with thermal ellipsoids shown at 50% probability. Two of *tert*-butyl groups were refined isotropically. Solvent molecules and hydrogen atoms are omitted for clarity.

triazole group at the calixarene lower rim forces one of these groups away from the aromatic plane of the calixarene scaffold by more than 10°. Apart from this, the bond lengths and angles around the Ti center are quite similar to those in Calix$(OMe)_2O_2TiCl_2$.[14] Complexation to a metal center results in some changes in the ^1H NMR spectrum, such as 0.4 ppm up-field shift of the vinylic triazole hydrogen signal (7.24 ppm *vs.* 7.66 ppm in **3**). Other hydrogen atoms, more remote from the metal center, were only slightly affected by the complexation.

Complex **4** shows typical reactivity expected from a Ti(IV) dichloro complex. For example, it can be easily converted to complexes **5a,b** upon the reaction with catechol or BINOL, respectively (Scheme 2). We also tested the catalytic activity of **4** in addition of trimethylsilyl cyanide to aldehydes. Reaction



Scheme 3

of TMS cyanide with one equivalent of benzaldehyde in the presence of 1 mol% of **4** at room temperature resulted in the quantitative formation of the addition product **6** (Scheme 3). Interestingly, the titanium dichloro complex of a "regular" calixarene ligand, 1,3-dimethylcalixarene,[14] showed only minimal catalytic activity in the same reaction, demonstrating the advantages of the new ligand design for catalysis.

In summary, we prepared a new oxygen-depleted calixarene ligand with triazole groups attached to the lower rim. The ligand can be used to prepare a titanium(IV) complex which showed catalytic activity superior to that of the unmodified calixarene Ti(IV) complex. We are currently studying the catalytic activity of the new complexes in various organic reactions as well as working on the asymmetric version of the new ligand.

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Notes and references

‡ *Crystal structure data*: for **3**: $C_{62}H_{70}N_6O_2$, $M = 931.24$, $0.6 \times 0.3 \times 0.03$ mm^3, monoclinic, space group $P2_1/c$, $a = 11.6844(5)$, $b = 41.4198(15)$, $c = 10.9193(4)$ Å, $\beta = 98.280(2)°$, $V = 5229.5(4)$ Å^3, $Z = 4$, $D_c = 1.183$ g cm^{-3}, $2\theta_{max} = 25.06°$, Nonius KappaCCD, Mo-Kα radiation ($\lambda = 0.71073$ Å), graphite monochromator, $T = 110(2)$ K, 6705 collected reflections, 4505 unique reflections ($R_{int} = 0.0720$). $R1 = 0.0771$, $wR2 = 0.1661$ for data with $I > 2\sigma(I)$, and $R1 = 0.1232$, $wR2 = 0.1923$ for all unique data. The crystals are characterized by high mosaicity and very poor diffraction. Some of the *tert*-butyl groups exhibit partial orientational disorder, which could not be resolved. The low resolution of the dataset affects the reliability of the parameters calculated from the structure determination. The structure is used to show connectivity.

For **4**: $C_{62}H_{68}Cl_2N_6O_2Ti{\cdot}1.721(CHCl_3)$, $M = 1253.44$, $0.45 \times 0.35 \times 0.10$ mm^3, triclinic, space group $P\bar{1}$, $a = 12.3623(4)$, $b = 16.3201(4)$, $c = 19.1318(7)$ Å, $\alpha = 83.9380(19)$, $\beta = 75.0364(13)$, $\gamma = 71.1954(17)°$, $V = 3528.9(2)$ Å^3, $Z = 2$, $D_c = 1.181$ g cm^{-3}, $2\theta_{max} = 27.48°$, Nonius KappaCCD, Mo-Kα radiation ($\lambda = 0.71073$ Å), graphite monochromator, $T = 110(2)$ K, 15 836 collected reflections, 10 522 unique reflections ($R_{int} = 0.0440$). $R1 = 0.0753$, $wR2 = 0.2135$ for data with $I > 2\sigma(I)$, and $R1 = 0.1111$, $wR2 = 0.2349$ for all unique data. The crystal contains molecules of partly disordered chloroform solvent. It also contains additional crystallization solvent, which could not be modeled by discrete atoms. Two of the *tert*-butyl substituents also exhibit rotational disorder. Distance constraints were used in their crystallographic refinement.

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