Salicylaldiminato Derivatives of Cyclotriveratrylene: Flexible Strategy for New Rim-Metalated CTV Complexes

D. Scott Bohle* and Daniel J. Stasko

Department of Chemistry, University of Wyoming, Laramie, Wyoming 82071-3838

Received May 17, 2000

The amino-derivatized cyclotriveratrylene analogue, triaminotrimethoxytribenzocyclononene [$CTV(NH_2)_3(OMe)_3$], **1**, is readily converted into triply substituted imine compounds [$CTV(sal)_3(OMe)_3$], **2**, in high yield by treatment of the acid salt of **1** with a variety of substituted salicylaldehydes. Cleavage of the protecting methoxy group generates the tristridentate chelate $CTV(sal)_3(OH)_3$, **3**, which is readily converted into new rim-metalated species $CTV(sal)_3(ONiL)_3$, **4a** (**a**, L = pyrrolidine; **b**, L = 1-*n*-butyl-imidazole). Taken together, these results illustrate the remarkable synthetic flexibility that is possible for the CTV-based metal complexes by alteration of the metal, the salicylaldehyde component of the CTV ligand, or the ancillary ligands coordinated to the metal.

The considerable current interest in supramolecular chemistry stems from many sources, chief among which is the desire to mimic the multilevel order and regulation found in biological systems. Coupled with this motivation are the recent advances in macromolecular crystallography and related key spectroscopic techniques; it is now possible to study systems with hithertofore unknown complexity and scale. As our understanding of the individually weak, but cumulatively significant, forces that control intermolecular communication and recognition improve, the design of newer and more selective hosts is becoming easier. One molecule that has been used to better understand host−guest interactions is the cavitand cyclotriveratrylene (CTV, **1a**), shown in Figure 1.[1] This versatile framework has been known for some time to form a wide range of solid-state inclusion complexes,[2] and its derivatives engage in varying degrees of solid- and solution-state host−guest interactions. The growing list of compounds known to form host−guest interactions with the CTV framework includes buckministerfullerene,[3] carboranes,[4] halocarbons,[5] anions,[6] and cationic organometallic sandwich complexes.[7] While the organic derivatization of CTV is extensive, the use of inorganic constituents to improve or alter the properties of this host system is not nearly as well developed. This is surprising in light of the fact that metal structural components offer many advantages over classical organic derivatives.[8] Metal-derivatized cyclotriveratrylene compounds have, until recently, fallen into two basic categories: (1) molecules with pendant chelates or metal-containing groups attached to the rim of the CTV bowl;[9,10] (2) molecules that take advantage of the aromatic portion of the CTV framework to form π-arene metal complexes.[7] We have recently developed a third strategy[11] for the synthesis of metalated CTV derivatives that take advantage of the rim functionality inherent to the CTV scaffold to form rim-metalated CTV derivatives that have substantially extended cavities, with ca. 10-fold greater volumes, and new electrochemical properties as well as showing novel solution- and solid-state interactions.[12] Unfortunately, it is difficult to introduce systematic electronic and steric alterations at the metal binding and cavity sites without radically altering the synthetic strategy because of the limitation of the CTV framework itself. Herein, we describe a series of new triimido-derivatized CTV compounds and their rim-metalated derivatives (Figure 2). These complexes illustrate the synthetic potential for variation in the metal binding site in this cavitand.

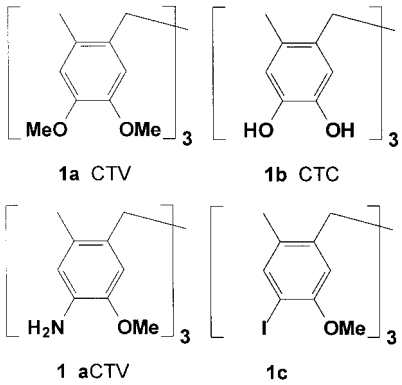


Figure 1. Key cyclotriveratrylene derivatives.

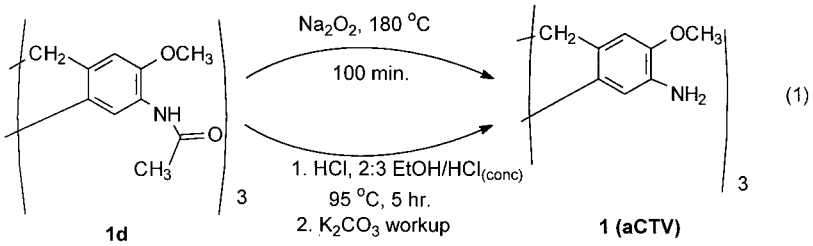
Results and Discussion

Cyclotriveratrylene (CTV, **1a**) can be derivatized to initially produce a tricatecholate analogue (CTC, **1b**) that can be subsequently elaborated to give a diverse array of cavitands.[13,14]

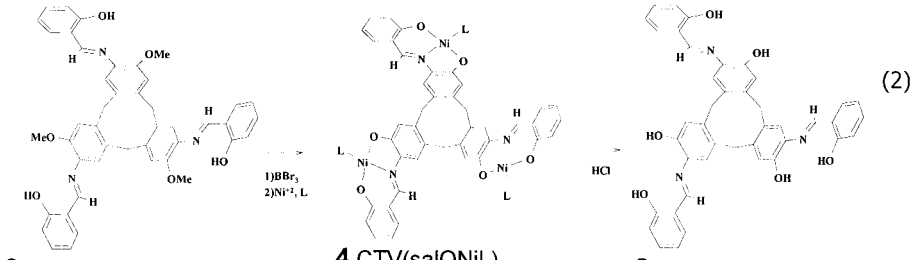
(1) Lindsey, A. S. *J. Chem. Soc.* **1965**, 1685−1688.
(2) Steed, J. W.; Zhang, H.; Atwood, J. L. *Supramol. Chem.* **1996**, *7*, 37.
(3) Atwood, J. L.; Barnes, M. J.; Gardiner, M. G.; Raston, C. L. *Chem. Commun.* **1996**, 1449.
(4) Blanch, R. J.; Williams, M.; Fallon, G. D.; Gardiner, M. G.; Kaddour, R.; Raston, C. L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 504.
(5) Cram, D. J.; Weiss, J.; Helgeson, R. C.; Knobler, C. B.; Dorigo, A. E.; Houk, K. N. *J. Chem. Soc., Chem. Commun.* **1988**, 407.
(6) Atwood, J. L.; Holman, K. T.; Steed, J. W. *Chem. Commun.* **1996**, 1401.
(7) Holman, K. T.; Steed, J. W.; Atwood, J. L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1736.
(8) Jones, C. J. *Chem. Soc. Rev.* **1998**, *27*, 289−299.
(9) Holman, K. T.; Orr, G. W.; Steed, J. W.; Atwood, J. L. *Chem. Commun.* **1998**, 2109−2110.
(10) Wytko, J. A.; Boudon, C.; Weiss, J.; Gross, M. *Inorg. Chem.* **1996**, *35*, 4469.
(11) Bohle, D. S.; Stasko, D. J. *Chem. Commun.* **1998**, 567−568.
(12) Bohle, D. S.; Stasko, D. J. Manuscript in preparation.
(13) Collet, A. *Tetrahedron* **1987**, *43*, 5725.

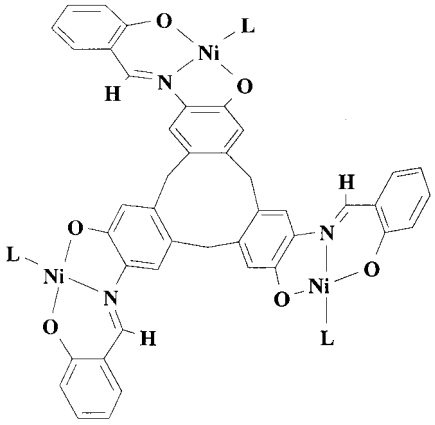
10.1021/ic0005240 CCC: $19.00
Published on Web 11/17/2000

Scheme 1



Scheme 2





1 CTV(OMe)$_3$(NH$_2$)$_3$ **2** CTV(sal)$_3$(OMe)$_3$
1a CTV(OMe)$_6$ **2a** CTV(tbsal)$_3$(OMe)$_3$
1b CTC(OH)$_6$ **2b** CTV(napsal)$_3$(OMe)$_3$
1c CTV(OMe)$_3$I$_3$ **3** CTV(sal)$_3$(OH)$_3$
1d CTV(OMe)$_3$(NHAc)$_3$ **4** CTV(salONiL)$_3$
1e CTV(OMe)$_3$(NH$_3$Cl)$_3$

Figure 2. Projected structure of cup shaped rim-metalated cavitands.

The rim-metalation strategy that we previously employed[11] used the inherent catecholate moiety of **1b**. To prepare further derivatives, we found it desirable to introduce a more flexible synthon into the rim to increase the range of metal binding and cavity characteristics. One of the most synthetically versatile functional groups is the amino group, a CTV derivative that is known, the C_3 symmetric tri(amino)tri(methoxy) CTV, (aCTV, **1**).[15] In principle aCTV can be used to prepare new classes of symmetrical trisubstituted CTVs such as the triiodo compound **1c**;[16] however, we are aware of no reports describing this strategy.

The amino derivative aCTV has been prepared by a four-step synthesis from commonly available starting materials.[15] However, in our hands, the final conversion of the triamide into the amine with sodium peroxide requires harsh conditions and leads to highly variable yields with numerous intractable side products. In particular, the final amide cleavage step with sodium peroxide results in the formation of an unknown and inseparable yellow material. As a prelude to our further studies, we sought to improve the access to **1**, that is, to optimize the final conversion of the triamide CTV derivative **1d** into aCTV, **1** (Scheme 1). It was found that **1d** can be easily converted into the hydrochloride salt of **1** by acid hydrolysis in ethanol, which eliminates the need for the harsh cleavage conditions.

Treatment of **1e** with triethylamine and salicyaldehyde in warm DMSO leads to the formation of the triimine derivative CTV(sal)$_3$(OMe)$_3$, **2**. The bright-yellow Schiff's base compound, **2**, can be precipitated with methanol or water and isolated in 85% yield after recrystallization. In an analogous manner it is possible to isolate the di-*tert*-butylsalicylaldimine (CTV(tbsal)$_3$-(OMe)$_3$, **2a**, 60%) and the 2-hydroxynaphthylaldimine derivatives (CTV(napsal)$_3$(OMe)$_3$, **2b**, 83%) by reaction with the respective aldehydes.

Although **2** easy to synthesize and purify, it is ineffective as a chelate for group 10 square planar divalent centers, and this is possibly due to the presence of the methoxy group attached to the CTV framework. As with other CTV derivatives, removal of this protecting group proceeds readily with boron tribromide to afford CTV(sal)$_3$(OH)$_3$, **3**. Unlike the trimethoxy derivative **2**, the isolation of **3** is complicated by the formation of stable borate esters[17] as well as the low solubility of the desired product, both of which lead to a low overall yield ($\leq$10%). A suitable solution to this problem, one that allows for the isolation of **3** in 72% yield (two steps), is to generate **3** in situ followed by formation of the nickel pyrrolidine complex, **4a** (79%). This can then be separated from the borate residues and purified readily and then converted back to **3** by treatment with hydrochloric acid and isolated in 91% yield (Scheme 2).

The tridentate nature of the new imine derivatives is analogous to other monomeric imine compounds.[18] For example, the CTV imine derivative **3** can be stirred with nickel(II)

(14) Collet, A., Ed.; *Comprehensive Supramolecular Chemistry*; Pergamon: Oxford, 1996; Vol. 6, pp 281−303.
(15) Garcia, C.; Malthête, J.; Collet, A. *Bull. Soc. Chim. Fr.* **1993**, *130*, 93−95.
(16) Garcia, C.; Collet, A. *Bull. Soc. Chim. Fr.* **1995**, *132*, 52−58.
(17) Wei, P.; Atwood, D. A. *Inorg. Chem.* **1997**, *36*, 4060−4065.
(18) Erlerman, Y.; Paulus, E.; Fuess, H. *Acta Crystallogr. C* **1991**, *47*, 70−72.

chloride and suitable ligands to generate the pyrrolidine (**4**), 1-butyl imidazolate (**4a**), and 1-benzyl imidazolate (**4b**) forms of the nickel complexes of **3**.

Summary

The new CTV-based imine derivatives **2**−**4** allow for rapid synthesis of highly variable rim-metalated derivatives. These new compounds show that it is possible to introduce synthetic variation at three distinct positions within the complex: through the salicylaldehyde portion, through the metal, and through the metal ligand set. The availability of a wide range of aldehydes also opens up the possibility of introducing chelation environments other than that of the salicylaldehyde substituent.

Experimental Section

The general experimental techniques and instrumentation used in this research are similar to those that have been described before.[19] Fast atom bombardment mass spectroscopy determinations were measured by the Washington University Mass Spectrometry Resource and NIH Research Resource (Grant P41RR0954).

Preparative Chemistry. (±)-3,8,13-Triammonium-2,7,12-trimethoxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene chloride, 1e. The triamide CTV, **1d** (520 mg), prepared according to literature methods,[15] was placed in ethanol (20 mL) and treated with concentrated hydrochloric acid (30 mL). The clear solution was heated at reflux for 5 h, and the resulting white suspension was cooled, filtered, and washed successively with 2 mL each of ethanol, ether, and methylene chloride to give 470 mg (93%). This product is spectroscopically identical to that previously reported;[15] however, the product from this preparation is colorless rather than the previously reported yellow. Analytically pure samples were obtained by recrystallization from acidic water. Anal. Obsd (calcd) for $C_{24}H_{29}N_3O_3Cl_3\cdot(HCl\cdot H_2O)$: C, 51.02 (50.63); H, 5.69 (5.84); N, 7.30 (7.38).

(±)-3,8,13-Triamino-2,7,12-trimethoxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, aCTV, 1. Compound **1** can be made by suspending the triammonium salt **1e** in 1 mM aqueous potassium carbonate solution. The colorless insoluble white solid is filtered, washed with water and ether, and dried. This colorless material is spectroscopically identical to that reported for the light-yellow product isolated from the sodium peroxide method.[15]

(±)-3,8,13-Tris(salicylaldimino)-2,7,12-trimethoxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, 2. The triammonium salt **1e**, 253 mg, is dissolved in 10 mL of DMSO containing 0.6 mL of salicylaldehyde. To this yellow solution 1 mL of triethylamine was added dropwise, and the resulting mixture was heated at 80 °C for 3 h. The ensuing orange solution was cooled and then poured into methanol (400 mL) to give a yellow precipitate that was then collected by filtration and washed with methanol, water, methanol, and then ether. Feathery yellow needles of **2** (303 mg, 85%) are prepared by recrystallization from methylene chloride/methanol. Anal. Obsd (calcd) for $C_{45}H_{39}N_3O_6\cdot(^1/_3CH_2Cl_2)$: C, 72.82 (72.92); H, 5.29 (5.36); N, 5.69 (5.63). FAB MS (M^+): obsd, 723.3; calcd, 723.3. ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 13.67 (s, 3H, O*H*), 8.63 (s, 3H, N═C*H*), 7.34 (m, 6H, SalC*H*), 7.17 (s, 3H, CTVC*H*), 7.00 (d, 3H, $^3J_{HH}$ = 8.3, SalC*H*), 6.94 (s, 1H, CTVC*H*), 6.92 (t, 3H, $^3J_{HH}$ = 7.4, SalC*H*), 4.81 and 3.7 (ab quartet, 6H, $^2J_{HH}$ = 14, CH_2), and 3.85 (s, 9H, OCH_3). Key IR bands (KBr, cm^{-1}): 1620s, 1490s, 752 s.

(±)-3,8,13-Tris(salicylaldiminato(nickel(II)pyrrolidine))-2,7,12-trimethoxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, 4a. Under an atmosphere of nitrogen a solution of **2**, 0.05 g, in 15 mL of dry benzene was treated with 0.25 mL of neat boron tribromide (3.3 equiv). The yellow solution darkened and was heated to reflux for 3 h, after which the mixture was cooled and methanol (30 mL) was added slowly. To this mixture nickel acetate (200 mg), pyrrolidine (2 mL), and potassium carbonate (200 mg) were added, and the mixture was again brought to reflux for 18 h. The green solution is then cooled, filtered, and washed with methanol to give a red solid. Following filtration of its dichloromethane solution, the complex was recrystallized from methylene chloride/carbon tetrachloride mixtures to give 59 mg (79%) of desired product. Anal. Obsd (calcd) for $C_{54}H_{51}N_6O_6Ni\cdot(CH_2Cl_2)$: C, 58.10 (57.74); H, 5.11 (4.93); N, 7.27 (7.35). FAB MS (M^+): obsd, 1059.1; calcd, 1059.6. ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 8.1 (s, 3H, N═C*H*), 7.43 (s, 3H, CTVC*H*), 7.41 (d, 3H, $^3J_{HH}$ = 8.0, SalC*H*), 7.15 (t, 3H, $^3J_{HH}$ = 8.1, SalC*H*), 6.78 (d, 3H, $^3J_{HH}$ = 8.0, SalC*H*), 6.35 (m, 6H, CTVC*H* and SalC*H*), 4.56 and 3.48 (ab quartet, 6H, $^2J_{HH}$ = 14, CH_2), 3.32 (b, 6H, NiNHC$_4$H$_8$), 2.94 (b, 6H, NiNH,C$_4$H$_8$), 2.07 (b, 3H, NiNH), 1.86 (b, 6H, NiNHC$_4$H$_8$), and 1.68 (b, 6H, NiNHC$_4$H$_8$). Key IR bands (KBr, cm^{-1}): 1606s, 1528s, 1489s, 1323s, 1148m, 755s.

(±)-3,8,13-Tris(salicylaldimino)-2,7,12-trihydroxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, 3. The red nickel complex **4a**, 100 mg, was dissolved in methylene chloride (10 mL) and treated with 0.2 mL of concentrated HCl. The clear red solution quickly became yellow, and a fine orange-yellow material precipitated. This solid was collected by filtration, washed with methylene chloride, water, and methanol to yield 58 mg of the desired compound (91%). This material was for all practical purposes insoluble in common organic solvents and only sparingly soluble in DMSO, making further purification difficult. ^{1}H NMR (DMSO, 400 MHz): δ 13.63 (s, 3H, ArO*H*), 9.55 (s, 3H, ArO*H*), 8.93 (s, 3H, N═C*H*), 7.60 (s, 3H, $^3J_{HH}$ = 8.0, SalC*H*), 7.38 (t, 3H, $^3J_{HH}$ = 8, SalC*H*), 7.33 (m, 6H, CTVC*H* and SalC*H*), 7.06 (s, 3H, CTVC*H*), 6.96 (t, 3H, $^2J_{HH}$ = 8,SalC*H*), 6.92 (t, 3H, $^2J_{HH}$ = 8, SalC*H*), 4.75 (d, 3H, $^2J_{HH}$ = 14, ArCH_2).

(±)-3,8,13-Tris(salicylaldiminato(nickel(II){1-*n*-butylimidazole})-2,7,12-trimethoxy-10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, 4b. The yellow salicylaldiminato complex **3**, 10 mg, was suspended in methanol (10 mL) and treated with nickel(II) acetate (50 mg) and 1 mL of 1-butylimidazole. The mixture was then refluxed for 5 h, and the resulting green solution was filtered to remove the red precipitate, which was then washed with methanol. The red solid was dried and recrystallized from methylene chloride/methanol to give 14 mg of a red-orange powder. Yield: 77%. FAB MS (M^+): obsd, 1218.1; calcd, 1218.3. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06 (s, 3H, imine ArNC*H*Ar), 7.63 (s, 3H, imine Ar*H*), 7.43 (s, 3H, CTV Ar*H*), 7.41 (d, $^3J_{HH}$ = 8.06, 3H, sal*H*), 7.1 (t, $^3J_{HH}$ = 8.56, 3H, sal*H*), 7.05 (s, 3H, imine Ar*H*), 6.84 (d, $^3J_{HH}$ = 8.56, 3H, sal*H*), 6.79 (s, 3H, imine Ar*H*), 6.74 (s, 3H, CTV Ar*H*), 6.61 (t, $^3J_{HH}$ = 8.06, 3H, sal*H*), 4.58 and 3.51 (ab doublet, $^2J_{HH}$ = 14.0, 3H, ArCH_aH$_x$Ar), 3.89 (t, $^3J_{HH}$ = 7.55 Hz, 6H, imine CH_2CH$_2$CH$_2$CH$_3$), 1.74 (p, $^3J_{HH}$ = 7.55, 6H, imine CH$_2$CH_2CH$_2$CH$_3$), 1.33 (sx, $^3J_{HH}$ = 7.55, 6H, imine CH$_2$CH$_2$CH_2CH$_3$), 0.92 (t, $^3J_{HH}$ = 7.55, 9H, imine CH$_2$CH$_2$CH$_2$CH_3).

Acknowledgment. We gratefully acknowledge support from the DOE (Grant DE-FCO2-91ER).

IC0005240

(19) Bohle, D. S.; Carron, K. T.; Christensen, A. N.; Goodson, P. A.; Powell, A. K. *Organometallics* **1994**, *13*, 1355−1373.