

Selective binding of substrates using sodium salts of linked C₃ symmetric aryl oxides

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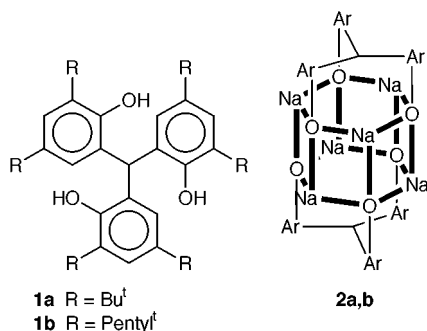
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Received (in Columbia, MO, USA) 14th September 1999, Accepted 3rd November 1999

Tris(3,5-dialkyl-2-hydroxyphenyl)methanes (*tert*-butyl, *tert*-pentyl) react with three equivalents of sodium hydride to give hexanuclear dimers; these bulky aggregates have six well-defined coordination 'pockets' which demonstrate selectivity toward a variety of ketones.

The design of molecules for the selective recognition of substrates has been an extremely active and growing area of research over the last number of years.¹ The utility of metal coordination chemistry, particularly aluminium, in a steric environment to give Lewis acidic selective reagents is clear, and a considerable body of work, largely pioneered Yamamoto,² regarding their use for a wide range of selective organic functional group transformations has been published.³ Less developed work, using lithium phenolates⁴ and zirconium naphtholates,⁵ amongst others, towards similar purposes have also been reported.

During our investigations⁶ of the alkali metal salts of tris(3,5-



dialkyl-2-hydroxyphenyl)methanes **1**,⁷ it was clear from X-ray structure determinations that the sodium salts **2** are hexanuclear aggregates, with six coordinated solvent molecules (THF) residing in identical binding sites; somewhat surprisingly, this Na₆O₆ core had been structurally characterized only once previously.⁸ From an examination of the structures, it was evident that the solvate molecules binding the metal atoms reside in a sterically crowded environment, offering the opportunity to prepare metal clusters capable of facilitating selective binding of a range of substrates. Herein we communicate our findings regarding these novel systems.

The reaction of tris(3,5-di-*tert*-butyl-2-hydroxyphenyl)methane **1a** with sodium hydride in Et₂O generates the dimeric, hexanuclear sodium salt **2a** in almost quantitative yield (¹H NMR).[†] When the bulkier tris(3,5-di-*tert*-pentyl-2-hydroxyphenyl)methane **1b** is used, refluxing THF is required for cluster formation. Examination of the crystal structures of the THF adducts of **2a** and **2b** reveals the solvent molecules reside in 'pockets' created by the aromatic rings and their aliphatic substituents. Complete removal of the coordinated solvent molecules can be readily achieved by evacuation with gentle warming.

The electrophilic nature of the coordinatively unsaturated sodiums is witnessed by their propensity to interact with very poor donor molecules. The solid state structure of the CH₂Cl₂

adduct of **2b** (Fig. 1)[‡] reveals that all six sodium atoms are associated by a solvent molecule with an Na...Cl distance of 2.891(1) Å. Furthermore, the aromatic rings are canted slightly to allow for weak *ipso*-interactions with the sodiums [Na...C(3) 2.771(3) Å]. The sodium atoms clearly adopt extremely distorted tetrahedral geometries, exemplified with a minimum angle for O(1')-Na-O(1) of only 93.21(7)°. When crystallized solely from Et₂O,⁶ the cluster is forced to distort even more dramatically to allow for the binding of Et₂O molecules to only two of the six sodium atoms, and in the absence of a donor molecule, the average distance of the remaining four metal centers to the *ipso*-carbon of the aryl ring decreases to 2.676(5) Å.

Accordingly, addition of 6 equiv. of a variety of oxygen donor substances of suitable size and shape (THF, acetone, benzaldehyde, acetophenone, *trans*-cinnamaldehyde or cyclohexyl methyl ketone) to **2a** in Et₂O readily yields the corresponding adducts.[§] In contrast, bulkier substrates, such as 2,5-dimethyltetrahydrofuran and 2,2,4,4-tetramethylpentan-3-one, fail to bind. Aromatic substrates immediately impart a color change upon coordination to **2a** or **2b**, with a distinctive absorption maxima evident in the visible region, providing a convenient avenue to rapidly screen binding affinities of new substrates. Et₂O and α,α,α-trimethylacetophenone bind only very poorly, and are readily displaced upon addition of more suitable molecules. Thus, addition of an equimolar mix of α,α,α-trimethylacetophenone and acetophenone to **2a** allows for complete separation of the two ketones by evaporation of the

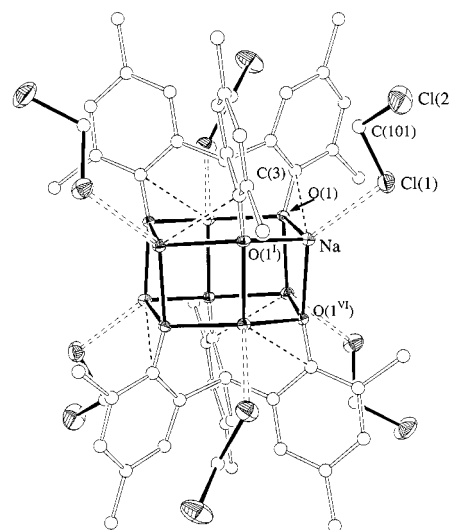


Fig. 1 Structure of **2b**·8.6CH₂Cl₂ (30% probability ellipsoids for Na, O and Cl). The molecule crystallizes on an S₆ symmetry position. Selected bond lengths (Å) and angles (°): Na...Cl(1) 2.891(1); Na...C(3) 2.771(3); Na-O(1) 2.326(2); Na-O(1') 2.280(2); Na-O(1'') 2.246(2); O(1)-Na-O(1') 112.88(9); O(1)-Na-O(1'') 93.21(7); O(1')-Na-O(1'') 94.47(7); O(1)-Na-Cl(1) 118.92(6); O(1')-Na-Cl(1) 103.91(6); O(1'')-Na-Cl(1) 131.19(6)°. *tert*-Pentyl groups, hydrogen atoms, and additional CH₂Cl₂ solvate molecules have been omitted for clarity.

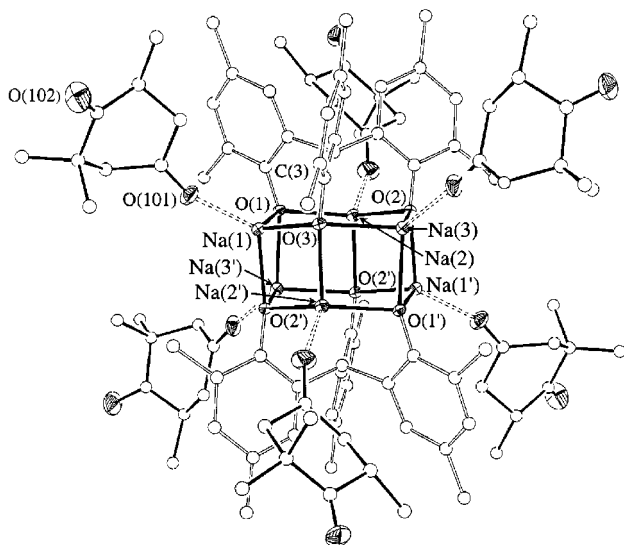


Fig. 2 Structure of **2b**·6C₉H₁₄O₂·0.4Et₂O (30% probability ellipsoids for Na and O). Selected bond lengths (Å) and angles (°): Na(1)···O(101) 2.257(3); Na(1)–O(1) 2.362(2); Na(1)–O(3) 2.297(2); Na(1)–O(2') 2.272(2); Na(1)···C(3) 2.748(3); O(1)–Na(1)–O(3) 116.82(8); O(1)–Na(1)–O(2) 93.49(7); O(3)–Na(1)–O(2') 96.27(8); O(1)–Na(1)–O(101) 116.67(9); O(3)–Na(1)–O(101) 109.54(9); O(2')–Na(1)–O(101) 122.15(9). The *tert*-pentyl groups, hydrogen atoms and Et₂O solvate have been omitted for clarity.

solvent, and subsequent washing of the residue with pentane, in which the acetophenone adduct of **2a** is insoluble. In solution, ¹H NMR investigations demonstrate that only acetophenone binds in this mixture and a spectrum identical to an authentic sample of **2a**·6C₈H₈O is observed.

Commercial 2,6-dimethylcyclohexanone is a thermodynamic mixture of isomers,⁹ which we determined by GC to be in the ratio of 81:19 for *cis*:*trans*. When this ketone is added to **2a** so that at least 6 equiv. of the *trans* isomer are present, following workup, GC and NMR analyses reveals that the ratio of isomers now clearly favors the *trans* by 1:5. This selectivity further highlights the relative rigidity and discrete size of the 'pockets', since the two isomers differ only subtly in size and shape. To demonstrate the utility of this separation, 6 equiv. of 2,4-dinitrophenylhydrazine were added to the dimethylcyclohexanone coordinated cluster, and after work-up and recrystallization, exclusively the *trans*-isomer of the corresponding hydrazone was obtained in 73% yield.

Finally, when 2,2,6-trimethylcyclohexane-1,4-dione, a diketone that features both sterically and non-sterically crowded carbonyl functionalities, is added to **2b**, only the non-bulky end was found to bind the sodium metal (Fig. 2).[¶] The ketone is obviously a much better donor than CH₂Cl₂ and maintains an average Na···O=C contact of 2.271(3) Å, a distance indistinguishable from the sodium–aryl oxide bonds. Despite the superior donor abilities of the carbonyl moiety in comparison to CH₂Cl₂, the Na–*ipso*-carbon interactions persist in this complex, with an average length of 2.749(3) Å. This system demonstrates the possibility for sterically protecting multifunctional group containing compounds, with the more reactive groups rendered inert, whilst chemistry at the less reactive sites is undertaken. The present compound, unfortunately, is only sparingly soluble, hindering reactivity studies.

In summary, we have synthesized coordinatively unsaturated sodium salts of bulky triaryloxymethanes, wherein the vacant coordination sites reside in discretely sized 'pockets'. The

compounds have been successfully used to selectively bind only molecules that possess a size and shape compatible with the 'pocket'. In addition to simple chemical separations, this selectivity may have utility for the protection of reactive functional groups in chemical reactions.

We thank the University of Florida, the National Science Foundation (CAREER Award 9874966) and the donors of the American Chemical Society Petroleum Research Fund for funding this research. Support from the Research Corporation is also gratefully acknowledged.

Notes and references

† General procedure for synthesis of **2a**: Tris(3,5-di-*tert*-butyl-2-hydroxyphenyl)methane was dissolved in anhydrous Et₂O (20 ml) and dry NaH (0.03 g, excess) added. The resulting mixture was stirred at room temperature for 17 h. The excess NaH was filtered off, to leave a solution of **2a**, which was sufficiently pure for further reactions. **2b**: Tris(3,5-di-*tert*-pentyl-2-hydroxyphenyl)methane was dissolved in THF (15 ml), and excess NaH added. The milky solution was refluxed under nitrogen for 1 h. The solvent was evaporated under vacuum, and the resulting dry residue was heated to 60 °C under vacuum for 3 h, to remove coordinated THF. The residue was dissolved in Et₂O, and the excess NaH filtered off, leaving a solution of **2b** which was sufficiently pure for further reactions.

‡ Crystal data for **2b**·8.6CH₂Cl₂: C_{106.6}H_{163.2}O₆Na₆Cl_{17.2}, *M* = 2288.45, *a* = 14.423(2), *c* = 50.468(8) Å, *V* = 9092(2) Å³, rhombohedral, space group *R*3̄ *Z* = 3, *T* = 173 K, final *R*1 = 0.0681 [for 3138 data *I* ≥ 2σ(*I*)], *wR*2 = 0.1928 (all 3568 reflections), GoF (on *F*²) = 1.098.

§ General procedure for synthesis of adducts: To an Et₂O solution of crude **2a** or **2b** was added 6 equiv. of aldehyde or ketone. The Et₂O was then slowly allowed to evaporate under a dry atmosphere, to give a crystalline residue. The crystals were then thoroughly washed with pentane producing the corresponding adduct.

¶ Crystal data for **2b**·6C₉H₁₄O₂·0.4Et₂O: C_{153.6}H₂₃₄O_{18.4}Na₆, *M* = 2519.13, *a* = 19.911(1), *b* = 15.528(1), *c* = 24.873(2) Å, β = 91.051(1)°, *V* = 7688.8(9) Å³, monoclinic, space group *P*2₁/*n*, *Z* = 2, *T* = 173 K, final *R*1 = 0.0746 [for 9656 data *I* ≥ 2σ(*I*)], *wR*2 = 0.2395 (all 15676 reflections), GoF (on *F*²) = 1.029. Both structures were solved using the direct methods option of SHELXS. Full-matrix least-squares refinements based on *F*² were subsequently performed using SHELXL-97. (ref. 10). All non-hydrogen atoms, with the exception of a disordered CH₂Cl₂ in **2b**·8.6CH₂Cl₂ and a disordered Et₂O molecule in **2b**·6C₉H₁₄O₂·0.4Et₂O, were assigned anisotropic temperature factors, with corresponding hydrogen atoms included in calculated positions. CCDC 182/1479. See <http://www.rsc.org/suppdata/cc/1999/2525/> for crystallographic data in .cif format.

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Communication 9/07476G