

PUTTING SMALL METALLACARBORANES TO WORK: A REVIEW

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Dedicated to Professor Jaromír Plešek on the occasion of his 75th birthday in recognition of his outstanding contributions to boron chemistry.

1. Introduction	728
2. Small Metallacarborane Clusters as Construction Modules	729
2.1. Cage Functionalization and Linkage	733
2.2. Assembly of Polynuclear Complexes	733
2.3. Low-Energy Fusion: Large Clusters From Small Fragments	739
3. Small Metallacarboranes in Organic Synthesis	741
3.1. Olefin and Alkyne Hydrogenation Catalysis	742
3.2. Selective Hydrometallation of Alkenes and Alkynes: Analogues of Schwartz's Reagent	743
4. Small Metallacarboranes in Medicine	745
5. Conclusion	747
6. References	747

The prospects for developing useful applications based on the chemistry of transition metal complexes of *nido*-2,3-RR'C₂B₄H₄²⁻ and related small carborane ligands are reviewed, with primary emphasis on areas where their utility has been demonstrated in practice. Special attention is directed to the properties of small 6- and 7-vertex MC₂B₃ and MC₂B₄ clusters that distinguish them from their icosahedral metallacarborane congeners, and from structurally related metallocene sandwiches. A review with 43 references.

Keywords: Boron clusters; Carboranes; Metallacarboranes; Metal complexes; Metal sandwich compounds; Metallocenes.

1. INTRODUCTION

A conspicuous feature of polyhedral carborane chemistry from its inception nearly a half-century ago has been the heavy emphasis on large cage systems, especially those of 12 vertices (icosahedra). A vast literature has accu-

mulated on the $C_2B_{10}H_{12}$ isomers and their derivatives, with far less attention directed to their smaller homologues; a similar asymmetry is reflected in the metallocarboranes (carboranes having one or more metal atoms in the framework), where again the 12-vertex systems dominate¹. There is no mystery about this: icosahedral carboranes are commercially available and are easily prepared from decaborane(14) ($B_{10}H_{14}$), a readily accessible solid borane, while the routes to unsubstituted lower carboranes typically involve volatile, pyrophoric small boron hydrides such as B_2H_6 and B_5H_9 . However, in the case of *nido*-RR' $C_2B_4H_6$ dicarbahexaboranes and their metallocarborane derivatives, accessibility is less problematic because the essential precursor carboranes such as $Et_2C_2B_4H_6$ are now prepared in 50 to 100 gram lots from B_5H_9 and alkynes in organic solvents, a much safer procedure that avoids the use of raw boranes². Consequently, this area has seen extensive development in recent years³. The small metallocarboranes, far from simply mirroring the behavior of the icosahedral systems, show distinctive reactivities that open the way to some potentially useful roles^{3d,4}. This review is intended to highlight the main features of this chemistry, in a sense complementing the excellent discussion of large-carborane applications⁵ several years ago by Dr Jaromír Plešek, to whom the present issue is dedicated.

2. SMALL METALLACARBORANE CLUSTERS AS CONSTRUCTION MODULES

Studies of nanostructured materials that can be tailored to have specified electronic, magnetic, optical, or other properties are well under way in materials science, chemistry, and solid state physics laboratories⁶. A variety of synthetic approaches are under exploration, including the assembly of extended systems from small building-block molecules *via* covalently bound organic or inorganic linkers⁷. Such systems can be entirely organic (lacking metal content) or organometallic, incorporating metal centers that are capable of electronic or optical excitation. These covalently linked assemblies differ from other types (*e.g.* hydrogen-bonded supramolecular clusters⁸ or solid-state materials) in that they are *molecule-based* and are held together by strong electron-pair bonds. In general, they are soluble in nonaqueous solvents and, in typical organic fashion, retain their intramolecular atom connectivities in solution.

At least two important advantages of binding transition metals into covalently bound extended chains or other arrays are apparent. First, the techniques of synthetic molecular chemistry that have been developed over many years afford a high degree of control over structure – more so than is

usually possible in the assembly of supramolecular materials where the intermolecular binding is weak and less susceptible to manipulation. Second, in covalent systems the metal centers are effectively locked into relatively stable structures in which, under ambient conditions, no further bond-formation or bond-breaking occurs. To the extent that it is possible to vary the metals, linking groups, and molecular geometry, such systems allow considerable design flexibility. In many cases they can be studied both in solution, using NMR and other spectroscopies, and as crystalline solids, employing X-ray diffraction methods.

One problem that can arise with some types of molecular organometallic systems is a tendency toward instability upon oxidation or reduction; for example, attempts to oxidize Fe(II)–arene complexes in nearly all cases result in failure to react, or in decomposition⁹. In general, hydrocarbon–transition metal bonding is highly sensitive to changes in the metal and/or oxidation state; *e.g.* ferrocene [Cp₂Fe] is the only stable neutral Cp₂M complex of a first-row transition metal.

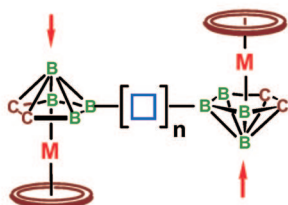
This limitation largely disappears when one replaces a Cp⁻ ($\eta^5\text{-C}_5\text{H}_5^-$) ligand with an isoelectronic 6-electron donor such as $\eta^5\text{-RRC}_2\text{B}_4\text{H}_4^{2-}$; thus, complexes of the type LM(RR'C₂B₄H₄) where L is Cp, Cp* ($\eta^5\text{-C}_5\text{Me}_5$), or an arene, are typically air-stable, robust compounds that undergo facile, reversible electrolytic oxidation and reduction. The underlying basis of this carborane-stabilization of organometallics has been reviewed elsewhere^{3a}. We anticipated that metallocarborane-based organometallic chains and networks would show similarly enhanced stability. Accordingly, we began several years ago in our laboratory to develop efficient synthetic routes to such systems *via* the introduction of suitable functional groups at specific locations on the carborane ligands; these substituents are then used to effect intermolecular covalent linkages. In parallel with the synthetic work, we have pursued collaborative investigations on the electrochemical and ESR properties of these compounds with other laboratories, principally those of W. E. Geiger at the University of Vermont and more recently P. Zanella at the University of Siena. Here I will outline our main synthetic approaches together with some observations on specific systems.

All of the systems to be described are based on metal complexes of the *nido*-2,3-RR'C₂B₄H₄²⁻ or *arachno*-2,3-RR'C₂B₃H₅⁴⁻ ligands, where R and R' are usually alkyl, aryl, or SiR₃ groups. These complexes incorporate 7-vertex *closo*-MC₂B₄, 7-vertex *closo*-MC₂B₃M', or 6-vertex *nido*-MC₂B₃ polyhedral clusters, as in the building-block modules that are shown in Charts 1 and 2. Chart 1 depicts several dimetallic types that consist of *closo*-MC₂B₄ cages linked through equatorial or apical boron vertices; the arrows indicate sites

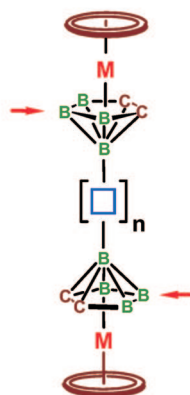
for metal stacking or BH locations that can easily be functionalized, allowing interconnection to form extended covalently bonded chains. Chart 2 shows modules having three or more metal centers. All of the types depicted in Charts 1 and 2 are represented in known compounds that are described below or in earlier reports.



equatorial B-linked



apical B-linked



$n = 0, 1, 2, \dots$

C_n ring-linked

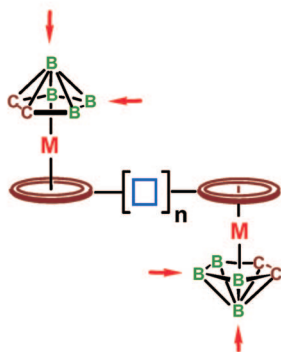


CHART 1
Dinuclear module types

B = BH, B

↑ = sites for intermolecular connection

C = C-Me, C-Et, C-SiR₃

⊖ = C₅H₅, C₅Me₅, C₆H₆, other arenes

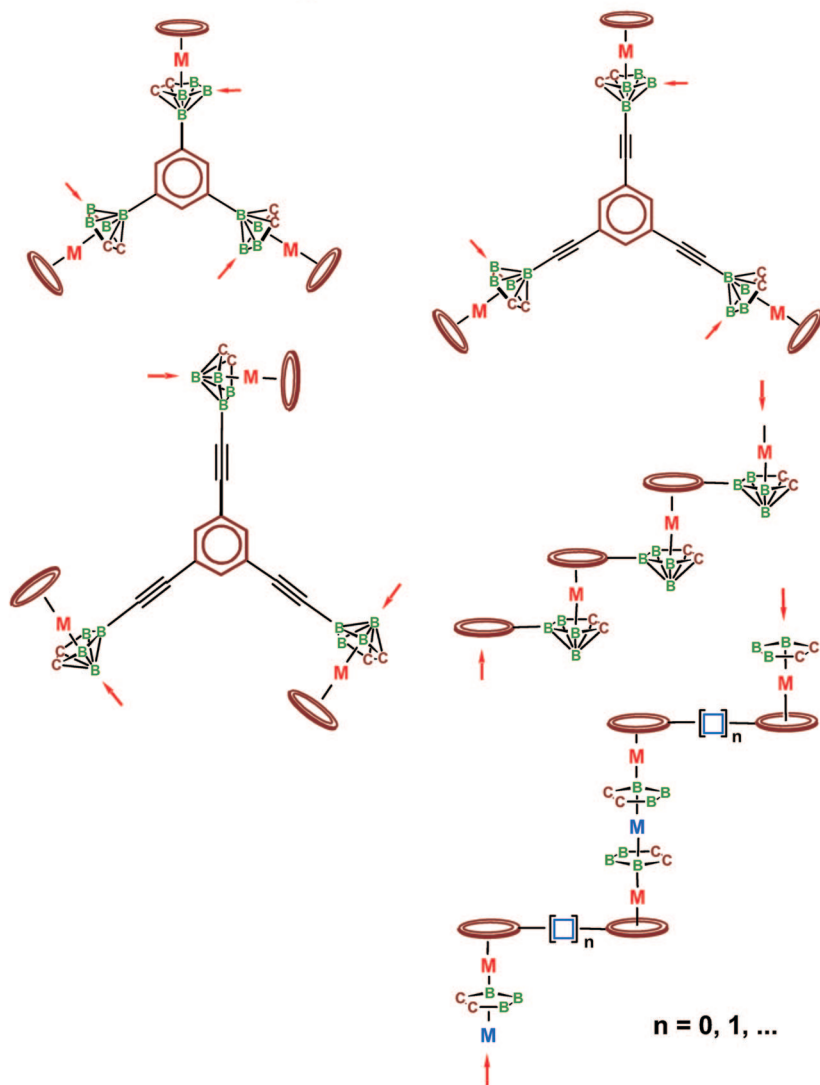


CHART 2

Trinuclear and polynuclear module types

2.1. Cage Functionalization and Linkage

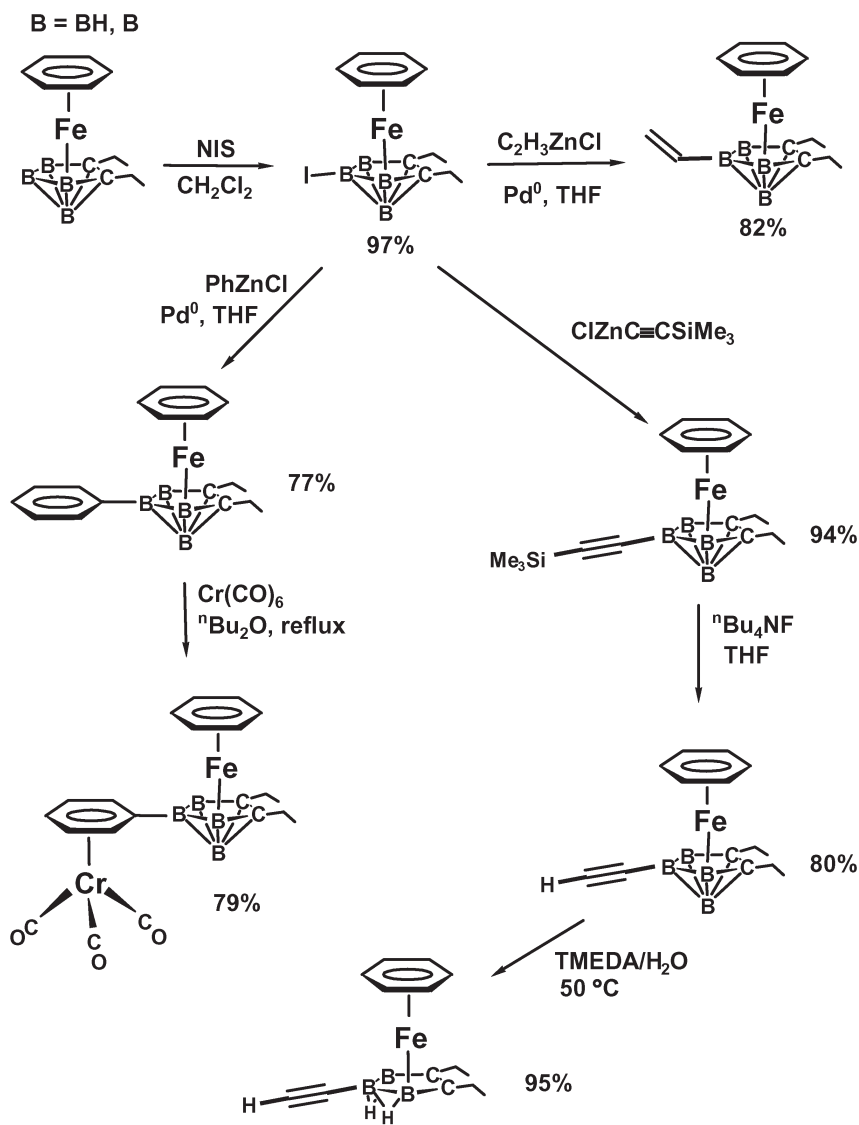
The modular approach to construction requires controlled methods for introducing active functional groups onto metallocarborane clusters. In principle these groups can be attached at the cage boron or carbon vertices, the metal center, or a hydrocarbon ligand (e.g., Cp or arene) bound to the metal. Substitution at cage carbon¹⁰, metal^{4,11}, or hydrocarbon ligand^{7c,12} locations on *closo*-LM(RR'C₂B₄H₄) complexes has been described, as has B-halogenation¹³. However, until recently B-organosubstituted derivatives of these *closo* clusters could be obtained only indirectly, *via* boron insertion into *nido*-LM(R₂C₂B₃H₃)²⁻ open-cage complexes to afford apically [B(7)] functionalized derivatives¹⁴.

Direct introduction of organic groups at boron vertices in LM(RR'C₂B₄H₄) systems, and their subsequent intermolecular linkage, has been accomplished with the aid of known metal-facilitated coupling chemistry that was originally developed for hydrocarbons¹⁵. This work has focused mainly on ferra- and cobaltacarborane clusters and is illustrated by the sequences depicted in Schemes 1–3. As shown in Scheme 1, the B(5)-iodo derivative (C₆H₆)Fe(Et₂C₂B₄H₃-5-I) is treated with zinc or palladium reagents to generate B(5)-organo derivatives¹⁶. Similar chemistry can be employed (Scheme 2) to attach two ferracarborane (or cobaltacarborane) units *via* an organic linker, or to link them directly *via* a B(5)–B(5) bond as shown¹⁶.

Scheme 3 shows sequences employed in the construction of a B(5,7)-dialkynyl complex whose acetylenic chains are aligned at 90° angles, making it a useful synthon for square planar assemblies (see below); corresponding cobalt systems having Cp*Co^{III} units in place of isoelectronic (arene)Fe^{II} groups have also been prepared^{16c}.

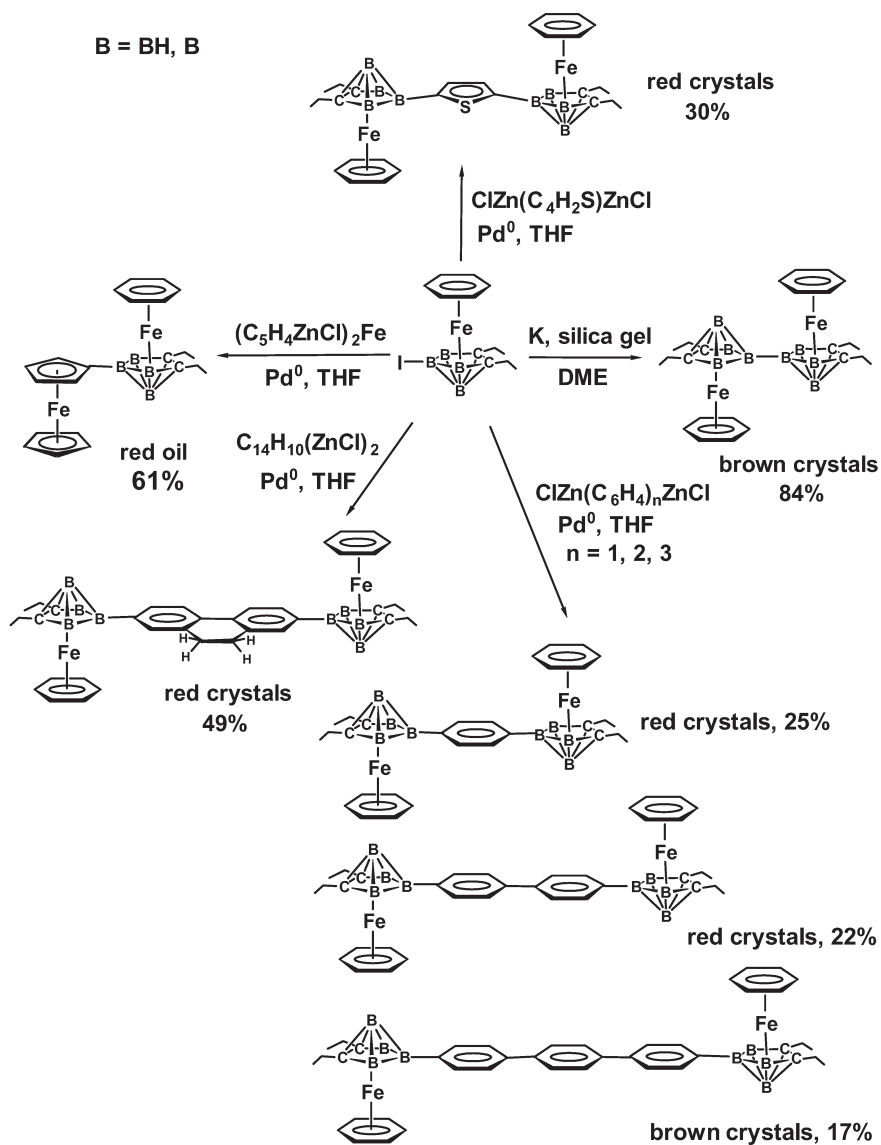
2.2. Assembly of Polynuclear Complexes

Our earliest efforts to link small metallocarborane clusters to create extended polymetallic oligomers and polymers utilized metal stacking reactions of *nido*-LM(R₂C₂B₃H₂-X)²⁻ complexes, where X is an electron-withdrawing group¹⁷. The products obtained are tetradeccker sandwiches of the type [LM(R₂C₂B₃H₂-R')]₂M'; this concept has also been employed to synthesize penta- and hexadeccker sandwiches employing C₂B₃¹⁸ or C₃B₂ (diborolyl) rings, the latter by Siebert and coworkers¹⁹. If metal stacking is conducted with bis(metallocarborane) species such as fulvalene-bridged [(C₅H₄)M(R₂C₂B₃H₂-R')]₂ complexes, one obtains hydrocarbon-soluble “staircase” oligomers^{12d} of the type shown at the bottom of Chart 2. When



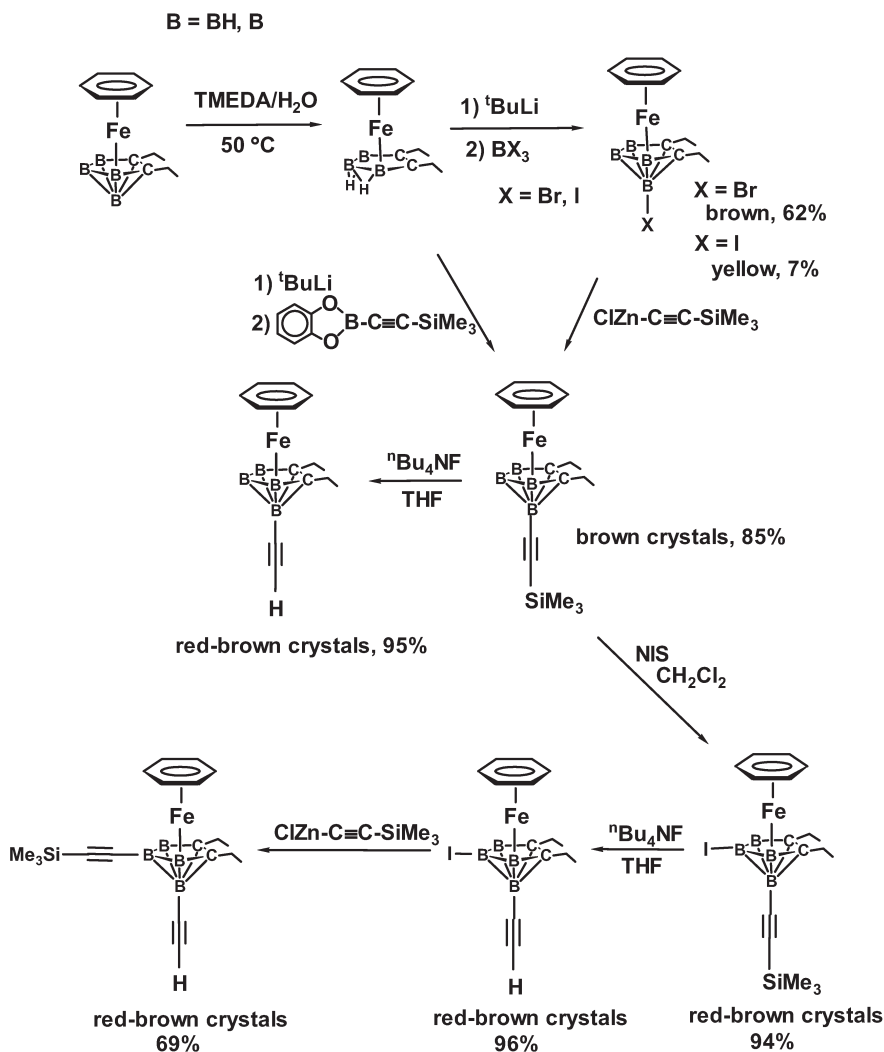
SCHEME 1

Introduction of alkenyl, alkynyl, and phenyl groups at B(5)



SCHEME 2
Synthesis of dimetallic building-block complexes

the outer metal M is Co^{III} and the central metal (shown in blue) is Co^{IV} , each tetradeccker unit is paramagnetic with one unpaired electron. If linking phenylene rings are present ($n = 1$), electrochemical data indicate that there

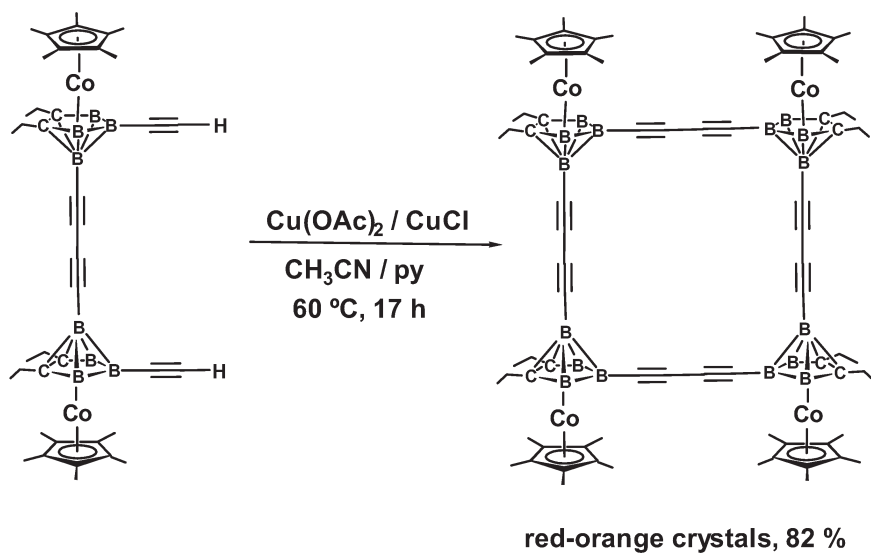


SCHEME 3
Synthesis of B(7)-alkynyl complexes

is communication within, but not between, the tetradeccker sandwiches²⁰; however, in corresponding fulvalene systems where the C₅ rings are directly linked ($n = 0$) there is extensive electron communication across the entire oligomeric chain²¹.

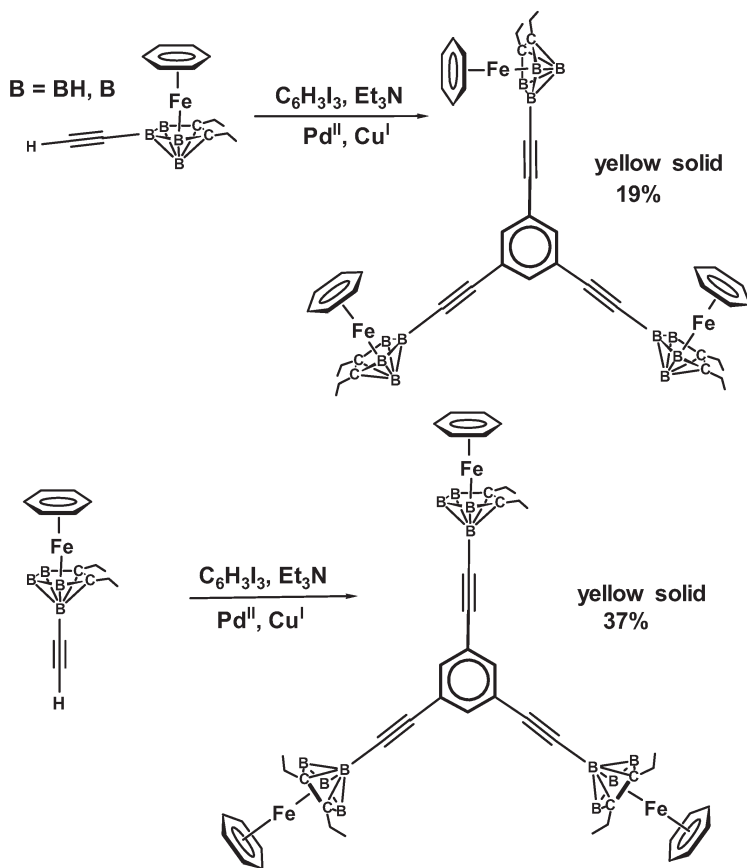
An alternative strategy for linking metallocarborane units, offering potentially more versatility than multidecker stacking, entails the use of boron-functionalized ferra- and cobaltacarborane modules. For example, Scheme 4 shows the efficient conversion of the bis(dialkynylcobaltacarborane) dimer into a square tetranuclear macrocycle whose structure has been assigned from NMR and mass spectra^{16b}. A different type of molecular architecture is expressed in the benzene-centered polycluster complexes shown in Schemes 5 and 6¹⁶, the first metallocarborane-based examples of which were described recently²².

The electronic properties of these and other small-metallocarborane based oligomeric structures are currently under study in collaboration with the laboratory of Prof. P. Zanella and will be reported in due course²³. Earlier work^{4a,24} revealed a wide variation in the nature of metal-metal interac-



SCHEME 4
Construction of a C₁₆B₈ macrocycle

tions in small mixed-valent metallacarboranes, extending from Robin-Day Class I (no communication) to Class III (full delocalization) behavior; there is considerable sensitivity to the choice of metals and metal oxidation states. For example, in mixed-valent bis(cobaltacarborane) systems, electron-delocalization in fulvalenediyl-bridged $\text{Co}^{\text{III}}\text{-Co}^{\text{II}}$ (d^6d^7) species is found to be significantly greater than is observed in corresponding $\text{Co}^{\text{IV}}\text{-Co}^{\text{III}}$ (d^5d^6) complexes²⁴. The question of how such trends carry over to large multi-nuclear systems is a subject of current investigation.

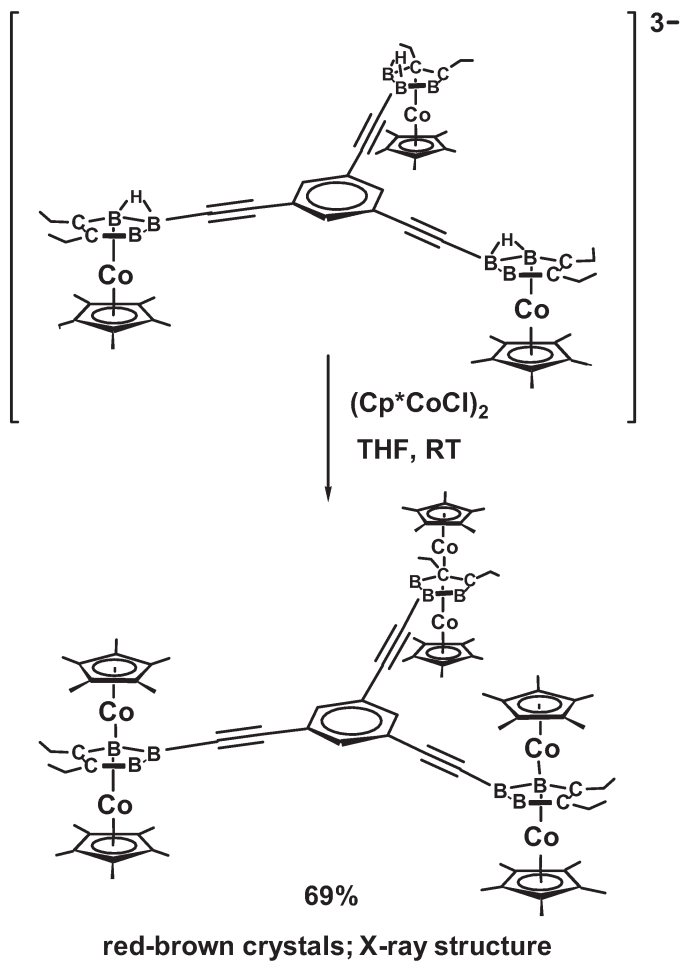


SCHEME 5

Construction of benzene-centered tris(ferracarborane) complexes

2.3. Low-Energy Fusion: Large Clusters from Small Fragments

A continuing challenge to synthetic boron chemists is the preparation of so-called supraicosahedral clusters. Boranes, metallaboranes, or carboranes having more than 12 vertices in a *single polyhedral cage unit* have not been prepared (“macropolyhedral” boranes composed of linked or conjoined B_9 , B_{10} or other fragments, such as $B_{18}H_{22}$ and $B_{20}H_{16}$, are long known)^{1b}. It is possible to break the “icosahedral barrier” if metal atoms are incorporated

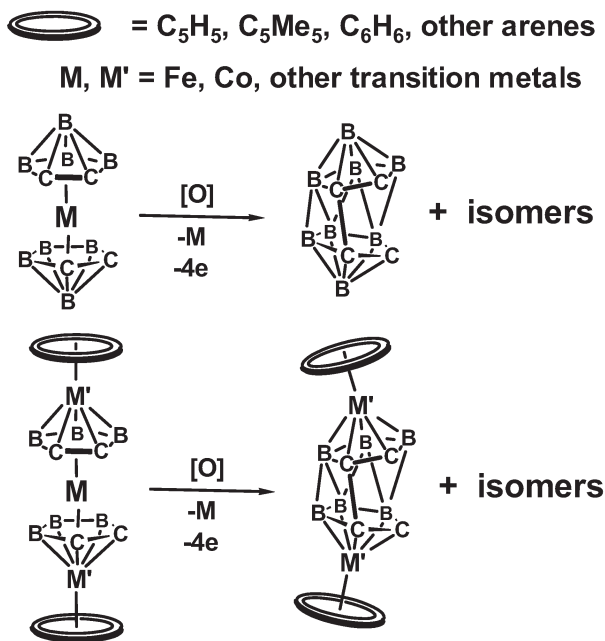


SCHEME 6

Construction of a triple-tripledecker sandwich system

into the cage; thus, 13- and 14-vertex²⁵ metallocarboranes have been prepared and characterized, with the most stable of the latter group adopting the geometry of a bicapped hexagonal antiprism^{25d}. These, however, fall far short of the very large clusters having dozens of boron atoms that have been predicted on the basis of molecular orbital calculations²⁶.

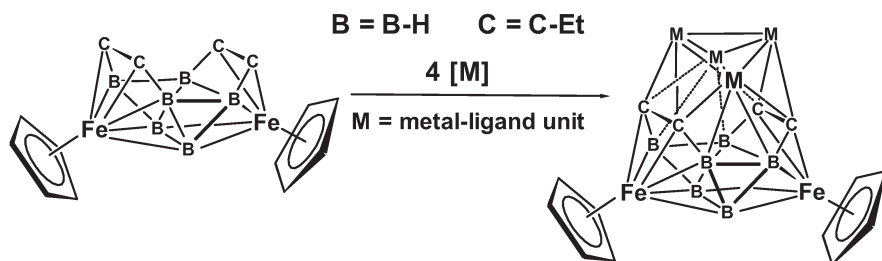
How might small metallocarboranes play a role in the construction of boron superclusters? The face-to-face metal-facilitated, low-temperature oxidative fusion of pentagonal pyramidal C_2B_4 or MC_2B_3 dianionic cluster anions, generating neutral 12-vertex C_4B_8 or $M_2C_4B_6$ cages (Scheme 7), was discovered serendipitously in 1974²⁷. In turn, these carbon-rich systems, some of which exhibit reversible room-temperature cage rearrangements, opened a new subarea of carborane and metallocarborane chemistry^{3d,27,28}. Metal-mediated cage fusion has been observed with small 5- or 6-vertex carborane or metallocarborane ligands and their borane counterparts²⁹ such as $B_5H_8^-$ and $B_6H_9^-$, but not with the $C_2B_9H_{11}^{2-}$ (dicarbollide) ions (which, however, can be oxidized to form edge-linked $(C_2B_9H_{11})_2^{2-}$ dimers³⁰).



SCHEME 7

Oxidative fusion of small carborane and metallocarborane ligands

The structures of some of the fused 12- to 14-vertex metallocarboranes suggest that they might be useful as templates for construction of still larger cages. As one example, the open 12-vertex $\text{Cp}_2\text{Fe}_2(\text{Et}_4\text{C}_4\text{B}_6\text{H}_6)$ cluster in Scheme 8, which is a fragment of a closo-16 vertex polyhedron, was prepared *via* metal-facilitated fusion of $\text{CpFe}(\text{Et}_2\text{C}_2\text{B}_4\text{H}_4)^{2-}$ dianions³¹. It has been suggested^{3d} that complexes of this type might be used to complete a 16-vertex polyhedral cage *via* addition of four metal vertices to the open C_4B_4 face, as shown.



SCHEME 8

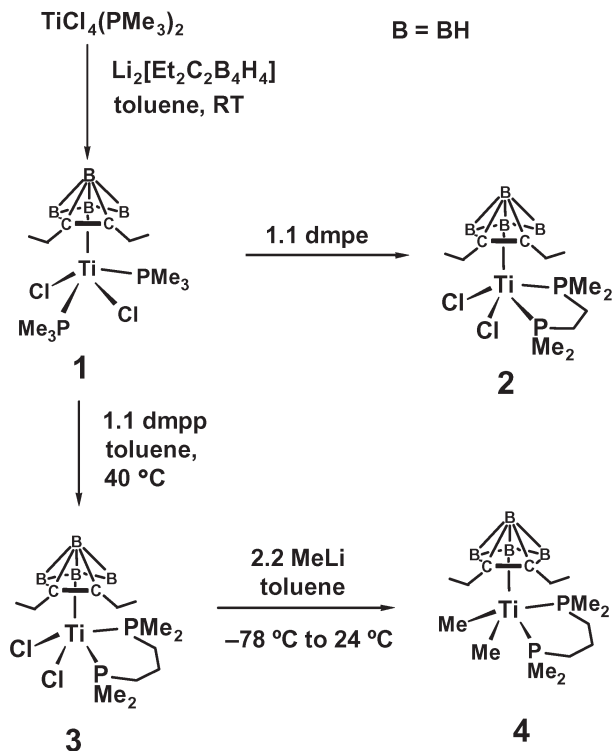
Proposed construction of a 16-vertex hexanuclear metallocarborane cluster

3. SMALL METALLACARBORANES IN ORGANIC SYNTHESIS

In addition to their potential use as synthons in the construction of extended systems including metallopolymers and nanostructured materials, small metallocarborane clusters also present opportunities for the development of novel organometallic reagents. In addition to their general chemical and thermal stability and solubility in organic solvents, the fact that (ligand) $\text{M}(\text{Et}_2\text{C}_2\text{B}_4\text{H}_4)$ complexes are readily tailorable *via* the introduction of functional groups affords a significant advantage. Furthermore, replacement of two Cp^- ligands in a metallocene sandwich with a single, less sterically demanding $\text{Et}_2\text{C}_2\text{B}_4\text{H}_4^{2-}$ unit opens additional metal coordination sites. It does not stretch the imagination unduly to see that this combination of properties might be exploited for purposes of organic synthesis, particularly as recoverable catalysts in industrially important processes. Indeed, the catalytic activity of metal complexes of related boron-containing ligands such as borataarenes³², borollides³³, and dicarbollides³⁴ in olefin hydrogenation has been demonstrated. The following discussion summarizes some recent work in our group in this area.

3.1. Olefin and Alkyne Hydrogenation Catalysis

In collaboration with Prof. M. G. Finn, our group has explored the catalytic properties of 14-electron phosphinotitanium and phosphinozirconium complexes such as $L_2Cl_2M(Et_2C_2B_4H_4)$ ($M = Ti$ or Zr ; $L_2 = 2 PMe_3$, $Me_2P(CH_2)_2PMe_2$, or $Me_2P(CH_2)_3PMe_2$) and $[Me_2P(CH_2)_3PMe_2]_2Me_2Ti(Et_2C_2B_4H_4)$, shown in Scheme 9. As we reported recently³⁵, these compounds are the first Ziegler–Natta catalyst precursors containing phosphine ligands, polymerizing ethylene at 1 atm pressure and room temperature in the presence of methylaluminoxane (MAO) cocatalyst. The dimethyl-dmpe complex **4**, whose molecular structure is depicted in Fig. 1, was found to be a far more active catalyst precursor than other phosphino-titanacarborane species such as **2**, **3**, and others prepared in our study³⁵ but not shown. Complex **4** is active even with low MAO concentrations. Thus, when the $[MAO]/[Ti]$



SCHEME 9

Synthesis of catalytically active phosphinotitanacarboranes

molar ratio is 2 500, ethylene at 25 °C and 1 atm is converted to polyethylene at a rate of *ca* 1 500 kg per mol of **4** per hour; remarkably, when [MAO]/[Ti] is reduced to only 100, the conversion rate is still over 1 000. Significantly, the polyethylene obtained from **4** is high molecular weight material (50,000 to 150,000) and the polydispersity (M_w/M_n) is low³⁵ (PDI = 2.3–2.6). Zirconium analogues of complexes **2**, **3**, and **4** are also catalytically active under similar conditions, but yield polyethylene of different physical characteristics from the products obtained using the titanium catalysts. The main point derived from these investigations is that the catalytic behavior is strongly affected by the nature of the phosphine ligand, creating opportunities for synthesizing families of olefin polymerization catalysts tailored to specific requirements.

3.2. Selective Hydrometallation of Alkenes and Alkynes: Analogues of Schwartz's Reagent

Another example that illustrates how small metallocarborane chemistry can be directed to specific synthetic purposes is the facile hydrometallation of unsaturated hydrocarbons by the hydridotantalum dimer

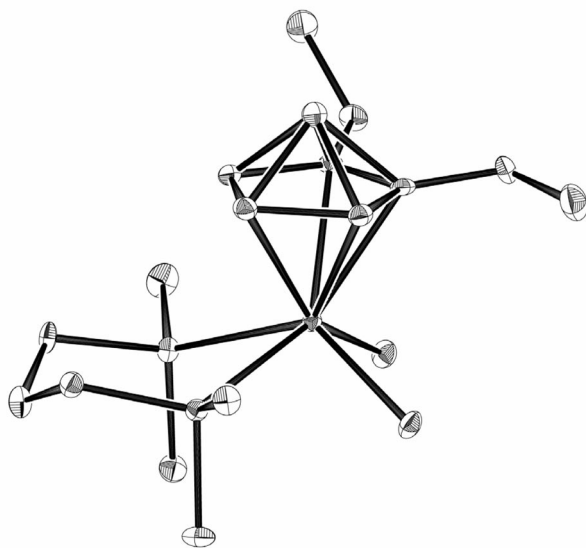
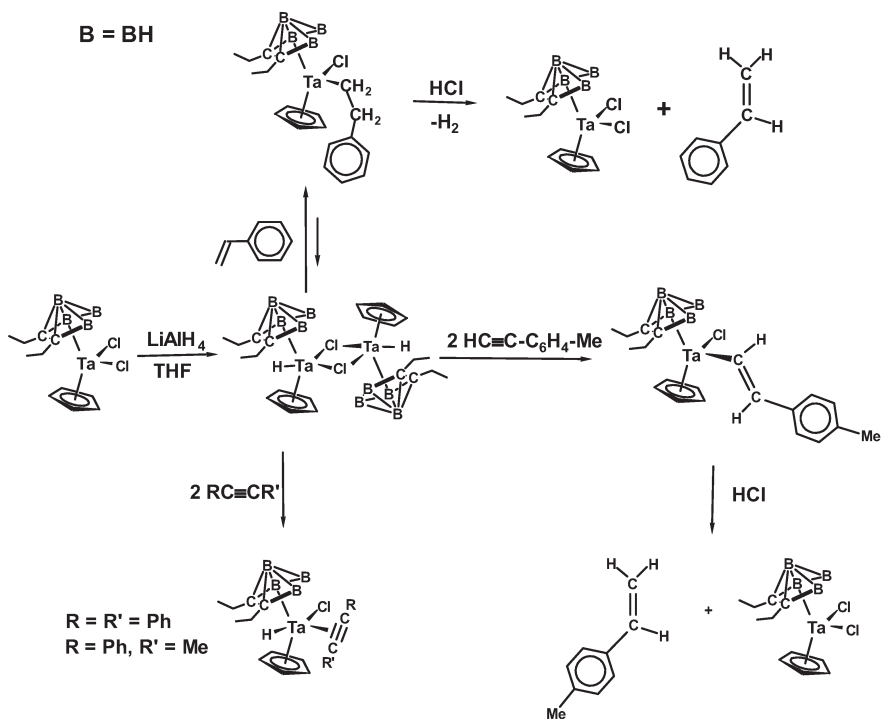


FIG. 1
ORTEP plot of $[\text{Ti}(\text{dmpp})\text{Me}_2(\text{Et}_2\text{C}_2\text{B}_4\text{H}_4)]$ (**4**) with thermal ellipsoids shown at the 30% probability level

$[\text{CpTa}(\text{H})(\text{Et}_2\text{C}_2\text{B}_4\text{H}_4)]_2(\mu\text{-Cl})_2$, shown in Scheme 10³⁶. As in the well-known insertion of alkenes and alkynes into the Zr–H bond of $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$ (Schwartz's reagent)³⁷, which generates alkenyl- or alkynylzirconium(IV) complexes from which the organic product is readily liberated by electrophiles, the dichloro-bridged tantalacarborane dimer undergoes alkene/alkyne insertion reactions. However, the carborane insertion products exhibit different chemistry from those obtained with the zirconocene system. Thus, *p*-tolylacetylene insertion undergoes *cis*-addition to Ta–H and forms exclusively the *trans* complex, which on treatment with HCl generates *p*-tolylethylene (Scheme 10, right)³⁶.

Treatment of the dimer with diphenylacetylene or methyl(phenyl)acetylene gives *stable, isolable* monomeric hydridotantalum–alkyne complexes (Scheme 10, bottom left) that are the first examples of alkyne π -coordination to a metal in a formal d^0 electronic state³⁶. Moreover, the reaction of the dimer with styrene to afford a β -phenylethyl-Ta complex (Scheme 10,



SCHEME 10

Hydridotantalum(V)-carborane alkene and alkyne insertion reactions

top) apparently proceeds *via* β -hydride elimination, rare for a neutral zirconocene derivative. This behavior, notably different from that of Schwartz's reagent, evidently reflects the higher electron density on Ta (notwithstanding its formal d^0 oxidation state) in the carborane complex. Although not catalytic, these reactions regenerate the original dichlorotitanacarborane monomer as shown, allowing its re-use. As in other applications described in this review, the formal replacement of Cp^- with the stronger electron-donor $Et_2C_2B_4H_4^{2-}$ has consequences that can be exploited to alter the properties of reagents in useful ways.

4. SMALL METALLACARBORANES IN MEDICINE

Polyhedral boron clusters in general – boron hydride anions, carboranes, metallocarboranes, and their functional derivatives – have attracted considerable interest for potential medical uses, for several reasons: they are exceptionally stable; they are “inorganic” and tend to resist metabolism in biological systems; they can be functionalized with organic and inorganic substituents; and they are boron-rich, supplying ^{10}B nuclei for use in boron neutron capture therapy³⁸ (BNCT). Most attention in this area has been directed to the development of BNCT (now in clinical trials in the U.S.A. and Europe), which centers primarily on organic derivatives of the icosahedral $C_2B_{12}H_{12}$ and $B_{12}H_{12}^{2-}$ systems. However, roles for metallocarboranes and metal-carborane sigma-complexes are emerging in such areas as medical imaging³⁹ and radioimmunotherapy⁴⁰. In recent years, Sneddon and Hall and co-workers in their groups have reported antitumor properties of tricarbon 11-vertex ferracarboranes of the type $CpFe^{III}(MeC_3B_7H_9)^+$ that are analogues of ferrocenium ion⁴¹.

Small 7-vertex bent-metallocene analogues having the general formula $Cp(Cl)_2M(R_2C_2B_4H_4)$ where $M = Ta$ or Nb and $R = Me, Et,$ or $SiMe_3$, prepared in our laboratory, were similarly shown to have anticancer activity^{42a}. These early findings prompted a much broader study^{42b} showing that numerous other 6- and 7-vertex metallocarboranes of $Fe, Co, Tl, Ta, Nb,$ and Mo originating in our group (Chart 3) also exhibit antitumor properties^{42b}. To varying degrees, these complexes show significant – in some cases, remarkably strong – activity (ED_{50} values of $\leq 4 \mu g/ml$) against the growth of a number of murine and human suspended cell tumors, including murine L1210 lymphoid leukemia, human HI-60 leukemia, acute monocytic leukemia THP-1, Hut-78 lymphoma, and HeLa-S³ uterine. Many of these compounds are more effective than standard clinical drugs, having ED_{50} values below 1.0 or even 0.5 $\mu g/ml$ in some cases^{42b}.

Certain of these complexes are also active against cultures derived from human solid tumors, *e.g.*, lung A549, lung MB9812, melanoma Sk-2, epidermoid skin A431, osteosarcoma bone, glioma UM-86, colon SW480 adenocarcinoma, and ovary 1-A9; the cytotoxicity levels against solid tumors vary considerably, with some compounds effective against particular cell lines and not at all against others. A mode of action study^{42b} involving P388 lymphocytic leukemia demonstrated that DNA synthesis is preferentially suppressed by the complexes, evidently *via* interference with ribonucleotide reductase and dihydrofolate reductase activities. Thus far it appears that the complexes do not directly attack DNA itself, as there is no evidence of intercalation between base pairs or cross-linking of DNA strands.

Viewed against the background of the well-known anticancer properties of neutral $(\eta^5\text{-C}_5\text{H}_5)_2\text{MX}_2$ complexes and salts of ferrocenium ion⁴³

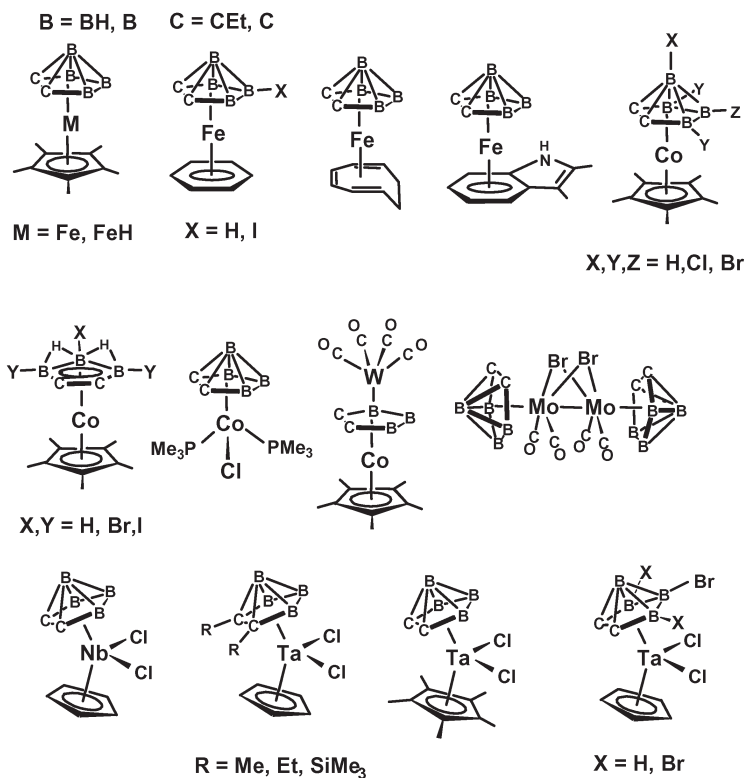


CHART 3

Complexes exhibiting antitumor activity in murine and human tissue cells

$\{[(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe}^+]\text{X}^-\}$, these data suggest that structurally and electronically related small metallocarboranes, which as a class are more stable and more easily derivatized^{3a} than the metallocenes, might be used to advantage as anticancer agents. The small size of the $\text{C}_2\text{B}_3\text{M}$ and $\text{C}_2\text{B}_4\text{M}$ clusters may facilitate interaction with enzymes and other biological agents, thereby affording a possible steric advantage (other things being equal) over icosahedral boron cage compounds in some pharmaceutical applications. This, however, remains to be demonstrated.

5. CONCLUSION

It is possible in a short review to explore only a few areas of possible application in a field as extensive as small metallocarborane chemistry. Several potentially important topics, including nonlinear optics, chiral reagents, metal extraction agents, and others, have not been touched on. Nevertheless, I hope that this article will serve to illustrate the remarkable scope of possibilities that exist for harnessing the lower metallocarboranes for useful purposes. One point is perhaps worth emphasizing: the range of available compound types, great though it is with a wide variety of metals and molecular architectures, is only part of the story. At least equally important has been the development of controllable routes for synthesizing the complexes and for introducing and modifying desired functional groups. This is clearly essential in a relatively exotic field such as polyhedral metallocarborane cluster chemistry, enabling it to advance beyond laboratory curiosities and to demonstrate wider relevance.

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