glucose oxidase[4] and by the characteristic absorption spectra of the reaction product of L-rhamnose in the cysteine–sulfuric acid test.[5] These results indicate that the product from the 1-hour incubation mixture is essentially pure thymidine diphosphate glucose and the product from the 5-hour incubation is apparently a mixture of thymidine diphosphate glucose and thymidine diphosphate rhamnose.

TABLE II

MOLAR RATIOS OF HYDROLYTIC PRODUCTS FROM THYMIDINE DIPHOSPHATE HEXOSE COMPOUNDS FROM THE 1- AND 5-HR. REACTION MIXTURES

Hr.	Thymidine monophosphate	Inorganic phosphate	Total hexose	Rhamnose
1	1.00	0.94	1.05	0.06
5	1.00	0.93	0.96	0.28

That the D-glucosyl unit of thymidine diphosphate glucose is converted to the rhamnosyl unit has been established by the results shown in Table III. In these experiments, samples of 0.8 micromole of thymidine diphosphate glucose in 0.05 ml. of enzyme extract were incubated for 5 hours with 0.15 or 0.3 micromole of the compounds listed in the table. The thymidine diphosphate hexose fraction from each reaction mixture was separated chromatographically and L-rhamnose and D-glucose in the fractions were determined quantitatively.[3] The values in Table III show that the disappearance of glucose was accompanied by a stoichiometric increase in L-rhamnose in the reaction mixture.

TABLE III

MICROMOLES OF L-RHAMNOSE AND D-GLUCOSE IN THE HYDROLYSATES OF THYMIDINE DIPHOSPHATE HEXOSE FRACTIONS PREPARED AS DESCRIBED IN THE TEXT

Compound added	μmoles of L-rhamnose	μmoles of D-glucose	Conversion to L-rhamnose,[a] %
None	0.03	0.79	0
TPNH (0.15 μM.)	.17	.64	17
TPNH (0.3 μM.)	.24	.58	26
DPNH (0.3 μM.)	.18	.64	19
Dialyzed[b] + TPNH (0.3 μM.)	.11	.71	11
Dialyzed + DPNH (0.3 μM.)	.04	.79	1
Glutathione (0.3 μM.)	.05	.73	3
G-1-P (0.3 μM.)	.03	.78	0

[a] The figures have been corrected for the small amount of L-rhamnose initially detected in the TDPG preparation by the colorimetric procedure employed. [b] The enzyme extract was dialyzed for 24 hours in water and for 3 hours in 0.1 *M* phosphate buffer containing 0.05 *M* magnesium chloride.

On the basis of these findings, a reaction sequence suggested for the conversion of D-glucose to L-rhamnose by the enzyme system of *S. faecalis* is outlined in the accompanying equations

$$G + ATP \longrightarrow G\text{-}6\text{-}P \longrightarrow G\text{-}1\text{-}P \quad (1)$$

$$TTP + G\text{-}1\text{-}P \longrightarrow TDPG + P\text{-}P \quad (2)$$

$$TDPG + TPNH \longrightarrow TDPRh + TPN^{+} \quad (3)$$

This reaction sequence is consistent with the observation that specifically labeled glucose is converted to L-rhamnose without randomization of the label[6] and probably accounts for the occurrence of thymidine diphosphate rhamnose in several strains of bacteria.[7,8,9] In this scheme, reaction 1 illustrates the formation of glucose-1-phosphate (G-1-P) from glucose (G) and adenosine triphosphate (ATP) via hexokinase to yield glucose-6-phosphate (G-6-P) and via mutase to yield G-1-P. Reaction 2 indicates the synthesis of thymidine diphosphate glucose (TDPG) by a mechanism similar to that for the synthesis of uridine diphosphate glucose. The enzyme which catalyzes this reaction may be appropriately termed a thymidine diphosphate glucose pyrophosphorylase. Reaction 3 is a diagrammatic representation for a series of reactions resulting in the conversion of the glucosyl moiety of TDPG to the rhamnosyl moiety of thymidine diphosphate rhamnose (TDPRh). These reactions result in epimerizations at positions 3, 4, and 5 and reduction at position 6 of the glucosyl moiety of TDPG. Reduced triphosphopyridine nucleotide (TPNH) is required for this series of reactions and in the crude reaction mixture is probably supplied by other metabolic reactions occurring in the system. The thymidine diphosphate rhamnose probably participates in transglycosylation reactions as a donor of rhamnosyl units in the biosynthesis of heteropolysaccharides.

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(10) Dow Chemical Co. Fellow, University of Nebraska, 1959–1960.

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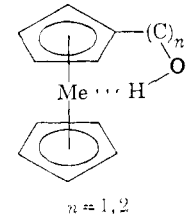
METAL-HYDROGEN BONDING IN METALLOCENE COMPOUNDS[1]

Sir:

Evidence provided by our infrared spectral studies on a wide range of ferrocene and some related metallocene derivatives has established a revealing example of the active electronic role which can be exercised by the metal atom in appropriate reactions of these metallocene systems. Study of the hydrogen bonding characteristics of ferrocene and related derivatives has shown the metal atom to be the site of a substantially strong intramolecular hydrogen bond involving the electrons of the metal atom acting as proton acceptor.



$n = 1, 2$

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The occurrence of this interesting type of hydrogen bond which appears to be a first example of a metal atom bonding in this manner is also of wider significance since it demonstrates the probable similar availability of the metal electrons for other coördination and bonding. For example, these results have led us to studies, recently reported,[2] on the role of the iron atom on rate and stereochemistry where metal electron participation is shown to be a very general and dominant phenomenon for metallocene reactions proceeding via α-cationic intermediates, both with respect to anchimeric rate enhancement and metal-bonded cation structure.

Representative ferrocenyl alcohols were examined in the fundamental hydroxyl stretching region in dilute CCl_4 solution (*ca.* 0.005 *M*) using a Perkin-Elmer Model 21 spectrometer equipped with LiF prism. Under these conditions of high resolution and dilution, precluding any intermolecular hydrogen bonding, certain metallocenyl alcohols, depending on structure, can be observed to exhibit unusual hydroxyl absorption frequencies and multiplicity resulting from the availability of two intramolecular hydrogen bonding sites of the hydroxyl group—one to the metal electrons and the other to the π-electrons of the carbocyclic ring to which the substituent-bearing chain is attached. π-Electron hydrogen bonding occurs analogously here in metallocene aromatic compounds[3] as in benzene aromatic[3,4] and carbon–carbon π-electron systems.[5]

The spectrum which best presents together the three representative hydroxyl bands typical of metallocenyl alcohols is that of 2-ferrocenylethanol whose separately resolved peaks at 3632, 3605 and 3533 cm.$^{-1}$ correspond, respectively, to the free, π-bonded and Fe-bonded hydroxyl absorptions.

Unequivocal assignment of the respective π-bonded and metal-bonded absorption bands of the metallocenyl alcohols comes from the spectra of the isomeric *exo*- and *endo*-1,2-(α-hydroxytetramethylene)-ferrocenes,[2] in which only one each of the respective bonding modes is possible because of the fixed *exo*- and *endo*- positions of the hydroxyl groups on the non-rotating side chain. The *endo*-hydroxyl, suitably positioned for metal-bonding, gives rise to the lower frequency bonded absorption peak, while the *exo*-hydroxyl produces the weaker, higher frequency π-hydrogen bond. In addition, intermolecular ferrocene π-bonding data with pri., sec., and tert. alcohols provide limiting values for the strength of this type of π-hydrogen bond ($\Delta\nu$ = 52–38 cm.$^{-1}$) and confirms the metal-assignment of the stronger, higher $\Delta\nu$ absorption bands. Finally, comparative spectra in diethyl ether solvent, where all available hydroxyl hydrogens completely bond intermolecularly to the ether, directly demonstrate that the metal-modified hydroxyl band originates from a hydrogen-metal interaction, *i.e.*, an authentic hydrogen bond, rather than from a conceivable oxygen-metal interaction.

One-carbon side chain ferrocenyl alcohols give intramolecular Fe · · H-bonds with $\Delta\nu$ values of 57, 48 and 43 cm.$^{-1}$, respectively, for ferrocenylcarbinol, ferrocenylmethylcarbinol and ferrocenyldimethylcarbinol, the decreasing sequence following normal hydrogen bond acidity dependence. Increasing the side chain length by an additional carbon atom in 2-ferrocenylethanol increases the $\Delta\nu$ to 99 cm.$^{-1}$ as a result of better bonding geometry. However, increased $-\Delta S$ leads to lower concentration of bonded species, with Fe-bonding no longer detectable in 3-ferrocenylpropanol. Ferrocene does not hydrogen bond intermolecularly with alcohols or phenol at the Fe site but exhibits only π-bonding. The greater accessibility of the π-ring electrons compared with the more sterically hindered Fe atom must account for this observation.

Hydrogen bond strengths to other metal atoms of various metallocenyl types could provide interesting and informative comparisons. Thus far we have examined ruthenocene and several of its derivatives and have found markedly stronger metal–hydrogen bonding for ruthenium compared to iron. In analogous alcohols the Ru *vs.* Fe $\Delta\nu$ values are 102 *vs.* 48 cm.$^{-1}$ and 171 *vs.* 99 cm.$^{-1}$ for the metallocenylmethyl carbinols and 2-metallocenylethanols, respectively.[6] Conversely, the π-bonding of the ruthenocene aromatic ring is substantially weaker than that of ferrocene, consistent with lower Friedel–Crafts activity.[7]

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