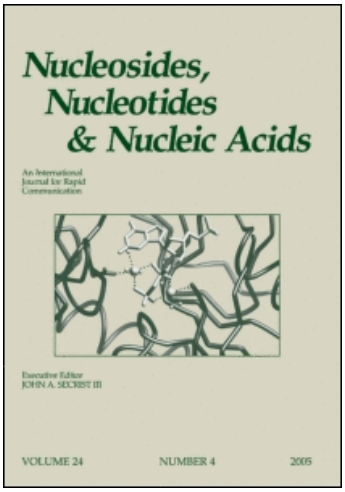

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Synthesis of (Dicarbonyl)(η⁵-cyclopentadienyl)Manganese Complex Stabilized Nucleoside Phosphite Esters

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Synthesis of (Dicarbonyl)(η^5-cyclopentadienyl)Manganese Complex Stabilized Nucleoside Phosphite Esters

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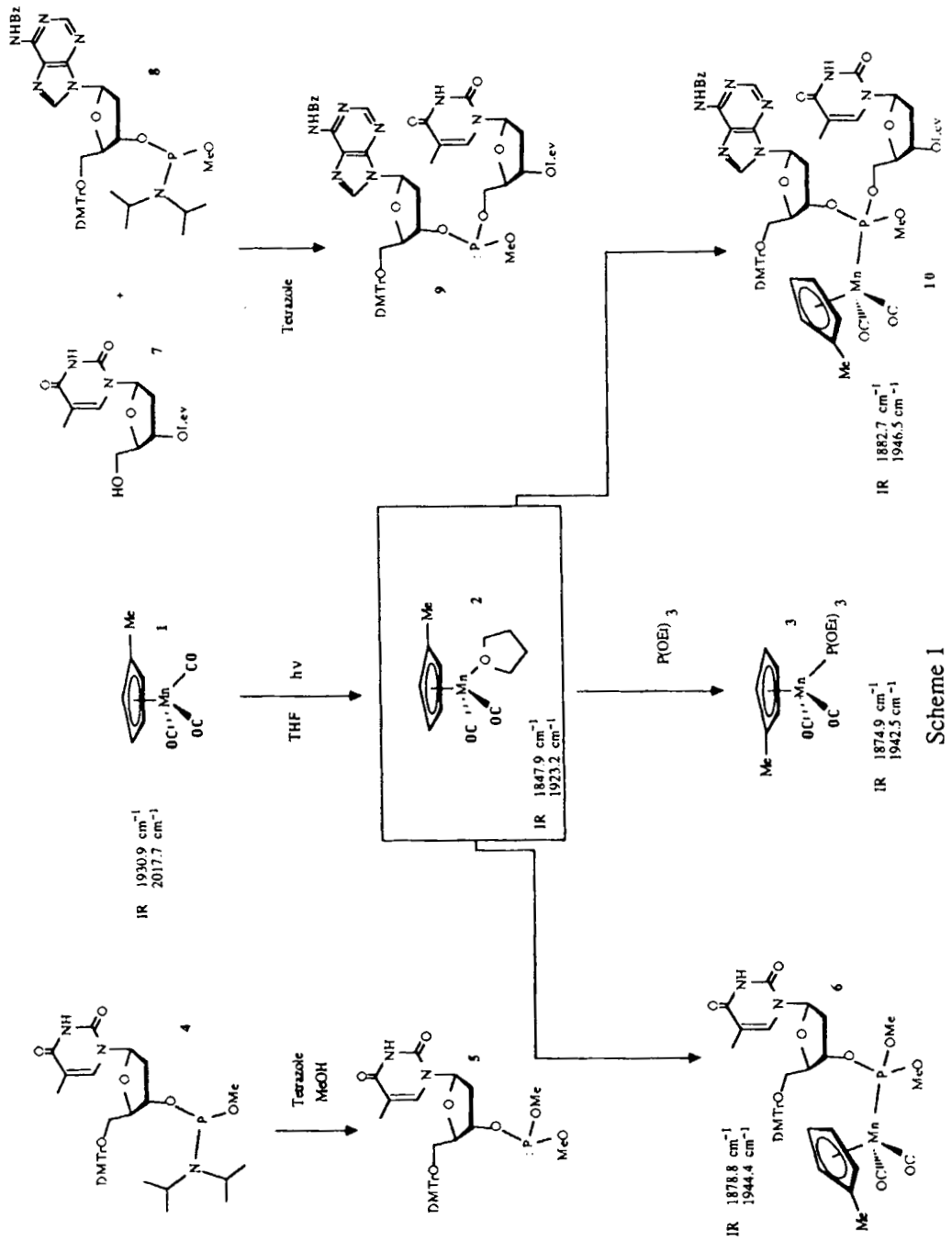
Abstract

We have found that stable nucleoside derived phosphite ester manganese complexes can be generated by the reaction of $Mn(CO)_2(THF)(\eta^5\text{-}C_5H_4R)$ with nucleoside phosphite esters. These complexes appear to be stable towards oxygen and reagents used for DNA synthesis and deprotection. The cyclopentadienyl ligand can be modified by a strong electron withdrawing group and still retain the photochemical and chemical properties necessary to complex readily to phosphite esters.

It occurred to us that we could confer a number of potentially interesting properties on oligonucleotide analogs if we could attach certain metal complexes directly to phosphorus. Cyclopentadienyl and carbonyl metal complexes can be designed which stabilize otherwise unstable phosphines, phosphite esters and related compounds to reagents such as oxygen.[1,2] Transition metal carbonyl complexes have recently been demonstrated to be effective FTIR sensitive probes with metal carbonyl labeled biomolecules capable of detection at levels as low as 100 fM.[3] Examples of the significance of transition metal linked oligonucleotides as synthetic nucleases and as potential therapeutics have appeared in the literature.[4,5,6,7,8,9]

Although there is a large body of literature on the reactions of metal ions and transition metal complexes with bases, nucleosides, nucleotides, and nucleic acids,[10,11] there are no previous accounts that we are aware of in which transition metals have been linked directly to phosphorus.

Most of our initial research has concentrated on the chemistry of the complex $Mn(CO)_2(THF)(\eta^5\text{-}C_5H_4CH_3)$ (**2**), which is readily prepared by photolysis of $Mn(CO)_3(\eta^5\text{-}C_5H_4CH_3)$ (**1**) in THF.[12,13] This compound reacts rapidly and specifically with phosphite esters in THF solution at room temperature. We have successfully accomplished the transformations shown in Scheme 1. The nucleoside derived phosphites **5** and **9** react selectively and in good yield with complex **2** to give complexes **6** and **10**, respectively.



Scheme 1

The (dicarbonyl)(η^5-cyclopentadienyl)manganese phosphite complexes appear to be stable to the conditions commonly used to construct oligonucleotides by phosphoramidite methodology. The model complex, (dicarbonyl)(η^5-methylcyclopentadienyl) (triethylphosphito)manganese (**3**) was synthesized and subjected to: a) 2% dichloroacetic acid in ethylene dichloride, b) acetic anhydride, DMAP, and pyridine, c) I_2, lutidine, H_20, and d) satd. methanolic ammonia. The compound remained unchanged in each case.

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