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Synthesis of (pentacarbonyl)tungstate(−1) and (pentacarbonyl)molybdate(−1) dinucleotides

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ABSTRACT

New methods for preparation of metallo dinucleotides with transition metals directly bonded to phosphorus are presented. (Pentacarbonyl)tungstate(−1) and (pentacarbonyl)molybdate(−1) dimers are prepared by the reaction of dinucleotide-H-phosphonate with $M(CO)_5(THF)$ (M = W, Mo). These syntheses can be completed in solution or on solid-phase.

1. Introduction

DNA, apart from being a natural biological information carrier, has also been shown to be highly useful as building material in the field of nanotechnology. Molecular recognition, self-assembly, and predictable structure make DNA a particularly promising candidate for constructing complex nanostructures.[1–4] Another application is to use DNA as a nanowire for connecting quantum devices to macroscopic electrodes or other devices.[5,6] The deposition of silver,[7] gold,[8] platinum,[5,9] and palladium[10,11] metal on DNA has been investigated as a potential approach for creating conductive nanowires. Incorporation of transition metal-containing moieties to oligonucleotides has also been used for the study of DNA-mediated energy and electron transfer processes[12] as well as the development of DNA hybridization probes or sensors.[13–16] Moreover, metalloimmunoassays involving carbonyl transition metal complexes conjugated to biomolecules have successfully demonstrated the detection of such complexes in biological samples using FTIR in the picomole range.[17,18] Thus, metallocarbonyl oligonucleotides would be of potential interest in nanotechnology as nanowires or other nanochemical devices and also in biology as probes or biosensors.

The preparation of dBdT (B = A, T) dinucleotides having (pentacarbonyl)tungsten and (dicarbonyl)(η^5-cyclopentadienyl)manganese complexes joined covalently to phosphorus was reported previously.[19,20] Dinucleotide-phosphite triesters were prepared by the phosphoroamidite condensation method and oxidized with $W(CO)_5$(η^2-cis-cyclooctene) and $Mn(CO)_2$(η^5-cyclopentadienyl)(THF), respectively. However, the reaction of dinucleotide-phosphite triesters with metal complexes in solution and on solid-phase afforded products in low yield (~25%). Therefore, we decided to change synthesis strategies and employ H-phosphonate chemistry.

Simple dialkylphosphites react with $M(CO)_6$ (M = W, Mo) under heating to afford appropriate (pentacarbonyl)tungstate and (pentacarbonyl)molybdate derivatives.[21,22] Under the same conditions, we did not observe formation of dinucleotide-(pentacarbonyl)tungstate and (pentacarbonyl)molybdate derivatives. Therefore we used a protocol established earlier for the synthesis of boranophosphate oligonucleotides.[23] Dinucleotide-H-phosphonates[24] **1a–d** were activated with *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and then treated with $M(CO)_5(THF)$ (Scheme 1). By this simple method we prepared all eight (pentacarbonyl)tungstate (**2a–d**) and (pentacarbonyl)molybdate (**2e–h**) dimers in good yields (Scheme 1). The ^{31}P NMR spectra of (pentacarbonyl)tungstate (**2a–d**) and (pentacarbonyl)molybdate (**2e–h**) dimers indicated formation of metal-phosphorus bond with signals at ~105 ppm and ~130 ppm, respectively. Moreover, (pentacarbonyl)tungstate dimers **2a–d** exhibited characteristic $J(^{31}P–^{183}W)$ coupling constants equal to ~178 Hz (natural abundance of ^{183}W is 14.3%).

The next step in extending this procedure to oligonucleotides was to determine if the method would be applicable on automated synthesis of oligonucleotides on solid-phase. Thus dinucleotide-H-phosphonates[24] **3a–d** were synthesized on dT-Q-linker support[25] in the DMT OFF form, and treated with BSA and $M(CO)_5(THF)$ (M = W, Mo) in THF. Release from the support with aqueous ammonia afforded fully deprotected (pentacarbonyl)tungstate (**4a–d**) and (pentacarbonyl)molybdate (**4e–h**) dimers in good yields (Scheme 2).

Under basic conditions, we observed hydrolysis of dimers **4a–h** to appropriate dinucleoside-phosphates and cleavage of internucleotide linkages in various amounts. In general, (pentacarbonyl)molybdate dimers **4e–h** were less stable in aqueous ammonia than (pentacarbonyl)tungstate dimers **4a–d** (Scheme 2). Moreover, metallo dinucleotides were rapidly cleaved with strong bases and fluoride anions. Based on these results, synthesis of longer, mixed-sequence oligonucleotides will require the introduction of new protecting system that do not use either basic con-

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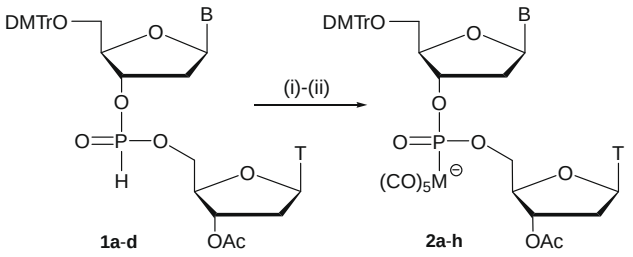
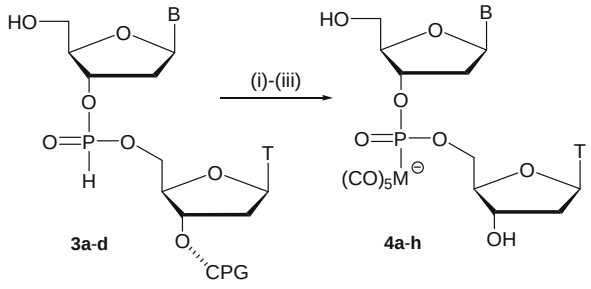


Entry	Substrate		Product			Yield[a]
	B	No.	B	M	No.	(%)
1	A^{Bz}	**1a**	A^{Bz}	W	**2a**	66
2	T	**1b**	T	W	**2b**	79
3	C^{Bz}	**1c**	C^{Bz}	W	**2c**	56
4	G^{iBu}	**1d**	G^{iBu}	W	**2d**	67
5	A^{Bz}	**1a**	A^{Bz}	Mo	**2e**	54
6	T	**1b**	T	Mo	**2f**	62
7	C^{Bz}	**1c**	C^{Bz}	Mo	**2g**	49
8	G^{iBu}	**1d**	G^{iBu}	Mo	**2h**	58

[a] Isolated yield.

Scheme 1. Reagents and conditions: (i) BSA, THF, 10 min, rt; (ii) $M(CO)_5(THF)$, THF, M = W 8 h, rt; M = Mo 16 h, 55 °C.



Entry	Substrate		Product			Yield[a]
	B	No.	B	M	No.	(%)
1	A^{Bz}	**3a**	A^{Bz}	W	**4a**	85
2	T	**3b**	T	W	**4b**	92
3	C^{Bz}	**3c**	C^{Bz}	W	**4c**	79
4	G^{iBu}	**3d**	G^{iBu}	W	**4d**	78
5	A^{Bz}	**3a**	A^{Bz}	Mo	**4e**	52
6	T	**3b**	T	Mo	**4f**	59
7	C^{Bz}	**3c**	C^{Bz}	Mo	**4g**	51
8	G^{iBu}	**3d**	G^{iBu}	Mo	**4h**	68

[a] Yield was determined by HPLC.

Scheme 2. Reagents and conditions: (i) BSA, THF, 10 min, rt; (ii) $M(CO)_5(THF)$, THF, M = W 8 h, rt; M = Mo 16 h, 55 °C; (iii) aq NH_3, B = T 20 min rt; B = (A^{Bz}, C^{Bz}, Gi^{Bu}) 2 h, 55 °C.

ditions or fluoride anion cleavage for deprotection of nucleobases and release from the support.

In conclusion, we have successfully employed H-phosphonate chemistry for the preparation of (pentacarbonyl)tungstate and (pentacarbonyl)molybdate dinucleotides both in solution and on solid-phase. A search for new nucleobase protecting groups and a support linker which would allow synthesis of longer metallo oligonucleotides is under way.

2. Experimental

2.1. Preparation of $M(CO)_5(THF)$[26]

0.1 M solution of $M(CO)_6$ in THF was irradiated for 1 h with a high-pressure mercury lamp (450 W) and used without further purification.

2.2. Preparation of metallo dinucleotides 2a–h in solution

BSA (2.5 mmol) was added under stirring to a solution of dinucleotide-H-phosphonate (**1a–d**, 0.5 mmol) in THF (5 ml). After 10 min, 0.1 M $M(CO)_5(THF)$ (2.5 mmol) in THF was added. The mixture was stirred for 8 h at rt (M = W), or heated for 16 h at 55 °C (M = Mo). The reaction was quenched by addition of 2 M TEAB (1 ml). Product was purified by chromatography on silica gel (elution with a gradient of 0–20% methanol in chloroform).

2.3. Preparation of metallo dinucleotides 4a–h on solid-phase

Dinucleotide-H-phosphonates (**3a–d**) were synthesized on dT-Q-linker CPG (1 μmol) in DMT OFF form. BSA (50 μl) was added to a suspension of the support in THF (1 ml) and after 10 min 0.1 M $M(CO)_5(THF)$ (2.5 ml) in THF was added. The mixture was shaken for 8 h at rt (M = W) or heated for 16 h at 55 °C (M = Mo). The support was washed with THF (3 × 1 ml) and treated with aqueous ammonia [B = T 20 min, rt; B = (A^{Bz}, C^{Bz}, G^{iBu}) 2 h, 55 °C]. Ammonia was evaporated and the products were purified by preparative HPLC (A = 0.05 M TEAA, B = acetonitrile; A to 50% B in 50 min).

Acknowledgments

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Supplementary data

Supplementary data (complete spectral data, copies of NMR spectra, and HPLC chromatograms of dimers prepared on solid-phase) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.089.

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