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A Review Article on Preparation of Peptide–Metal Complex Conjugates using Solid-Phase synthesis

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Abstract:

Solid-phase synthesis is an easy and a well established method for the preparation of peptide-based compounds. Earlier attempts to use solid-phase synthesis to obtain, for example, (2,2-bispyridine) dichloro complexes of platinum(II) by Gallop failed at the cleavage step due to the more labile metal–ligand bonds of organometallic building blocks in relation to typical covalent bonds of organic molecules.

Recently, to prepare metal complexes based on peptide backbone ligands, solid-phase synthesis using insoluble resins as solid support has been used. These coordination compounds find applications in biochemistry as well as in medicinal chemistry. Resin-bound chelates were synthesised in such a manner that upon the addition of suitable metal salts, the target metal complexes were selectively released from the resin and used in, for example, fluorescence or radio imaging or oligonucleotide DNA/RNA binding studies.

It gives the flexibility to incorporate a metal ion chelator with exclusive site specificity in any amino acid sequence not just terminally or at one or more lysine or cysteine side chains. Additionally, peptides are often prepared most effectively by automated solid-phase synthesis.

We have made our survey by the metal ions used for complex formation, and the discussion between examples of solid-phase ligand synthesis with subsequent metallation and the use of metalcontaining amino acids for synthesis.

1.Chromium, Molybdenum and Tungsten (Group 6) Metal Complex–Peptide Conjugates:

1.1 N_{δ},N,O-L-Histidinate (His) Molybdenum Conjugate

The conjugates were prepared in very good yields and purities by two different solid-phase synthesis strategies. In one approach the neuropeptide enkephalin (enk) Tyr-Gly-GlyPhe-Leu, which is a natural ligand to the opiate receptor, was synthesized by standard Fmoc solid-phase methods on NovaSyn TGA resin with an HMBA linker. The metal complex Mo(Nε-C2H4CO2H-His)(allyl)(CO)2 was coupled to the resin-bound, fully deprotected enkephalin and afterwards cleaved from the resin by treatment with saturated ammonia solution in methanol.

1.2 Bis(2-picolyl)amine (bpa) Molybdenum Conjugate

In cases in which the attachment of a metal complex to the peptide on the solid support is not favourable with radioactive metal isotopes, for example –during solid-phase synthesis, an innocent anchoring group can be attached to the peptide. The ligand–peptide conjugate is then cleaved from the resin and purified.

1.3 Bidentate Schiff Base Metal Conjugates

A specific resin and linker system allows coordination and organometallic chemistry under solid-phase reaction conditions and the cleavage of the metal complex from the solid support. Bidentate Schiff base 5-R was used as the ligand. The phenolic hydroxy group allows the attachment to the solid support. A silyl etherbased linker was chosen, since it is stable under basic and acidic conditions and the potential to cleave it with fluoride ions, which are expected to be unreactive towards most metal complexes.High temperature conditions have to be avoided in solid-phase chemistry with polystyrene resins as the molybdenum precursors can react with the aromatic residues of the support.

Heinze and co-workersutilized,the molybdenum–carbonyl and molybdenum–isocyanide bonds molybdenum carbonyl complexes which are substitutionally inert metal–ligand bonds, to prepare di- and trimetallic homonuclear complexes. finally,on solid-phase mixed-metal dinuclear complexes prepared from chromium, molybdenum and tungsten and a directional bridging ligand were grouped stepwise and cleaved from the support.More reaction steps are required for the solid-phase synthesis (ligand immobilization and product release) and differently optimized reaction conditions are needed. However, it is much easier to accomplish, and solubility problems and purification of intermediates can be disregarded.

2.Manganese, Technetium and Rhenium (Group 7) Metal Complex–Peptide Conjugates

The manganese family comprisesof the most widely used metals for peptide complexation. Its applications range from rhenium- and technetium-labelled radiopharmaceuticals to organometallic PNA oligomers with rhenium and their interaction with complementary DNA and to peptide– manganese complexes with catalytic activity. The transition metals technetium and rhenium are among the most commonly used radioisotopes in medicine.

2.1Bpa Metal Conjugate

A solid-phase methodology was published by Valliant and coworkers in 2005 that aimed to incorporate lysine into the backbone of a peptide in such a manner that the ε-nitrogen could be selectively liberated and a metal-bpa-chelate added while the peptide was still linked to the resin. To protect lysine side chain ,Dde was used since it is stable to the conditions used in typical Fmoc solid-phase synthesis.

2.2 Quinoline-2-aldehyde (Q2A) Metal Conjugate

A method to prepare bioconjugates that can deliver the ligand to specific receptors was the objective. Such amino acid analogues that can be incorporated into peptide sequences by solid-phase peptide synthesis were represented by the SAACQ ligand and the SAACQ–Re complex .

The work is an example of the use of metal-containing amino acids in solid-phase peptide synthesis.

2.3 Hydrazinonicotinyl Acid (HYNIC) Technetium Conjugate

A novel solidphase synthesis approach was explained by Blower and co-workers recently in which a HYNIC derivative of Fmoc-lysine was used as a metal-binding amino acid analogue. By standard Fmoc solid-phase peptide chemistry the N-protected HYNIC derivative was successfully incorporated into a bioactive peptide.

The HYNIC was protected by a trifluoroacetate group during alkaline oxidation to the cyclic disulfide and was readily removed by mild acid treatment. After deprotection and cleavage of the amino acid sequence from the resin, the peptide was oxidized with air in $NaHCO_3$ (0.1 M) under high-dilution conditions to form the corresponding disulfide-cyclized peptide.

2.4 3,3-Bis(2-imidazolyl) Propionic Acid (bip-OH) Rhenium Conjugate

To couple $Re(bip)(CO)_3$ fragments to PNA decamers on Tentagel resin solid-phase synthesis was used with PAL linker and their interaction with complementary DNA was studied .Due to the excellent hybridization properties of PNA,such metal–PNA conjugates are of interest for the detection of complementary DNA or RNA.

3. Iron, Ruthenium and Osmium (Group 8) Metal Complex–Peptide Conjugates

3.1 4'-Aminomethyl-2,2'-bipyridyl-4-carboxylic Acid (Abc) Ruthenium Conjugate

Due to the possession of a number of favourable properties, including high stability, inertness to ligand exchange reactions, tuneable electronic structures, long lifetimes in fluid solution, and high quantum yields, Tris(diimine) metal complexes of 4'-aminomethyl-2,2'-bipyridyl-4-carboxylic acid (Abc) are of interest.

Solid-phase synthesis of these metallopeptides was performed on MBHA resin using BOP and ByBOP as coupling reagents since they give high-affinity binding sites for ruthenium(II). Metal complexation occurred in solution, and was followed by cleavage of the peptide from the solid support.

A dual oxidation strategy was employed To prepare the Abc . Firstly, 4,4'-dimethyl-2,2'-bipyridine was selectively oxidized to the 4'-monocarboxylic acid derivative . Secondly, the 4'-methyl group of was oxidized with excess selenium dioxide to form the aldehyde acid 4'-formyl-2',2-bipyridine-4-carboxylic acid . Oxime formation with hydroxylamine in ethanol/pyridine smoothly converted the reactantinto a compound. Lastly, oxime acid was transformed into the desired amino acid Abc by catalytic hydrogenation.

To demonstrate the utility of Abc in solid-phase peptide synthesis, a heptapeptide containing two Abc residues was synthesized to serve as a tetradentate caging peptide ligand for ruthenium(II) ions . Two aminohexanoic acid (Ahx) residues were arranged as a bridging tether just long enough to form cis-bridged meridonal metal complexes.

3.2 Metallocene (Ferrocene) Conjugate

Solid phase peptide synthesis was used to prepare Ferrocene-containing tripeptides containing one or two ferrocene building blocks. Heinze et al. incorporated the solid-phase peptide synthesis-compatible ferrocene building block Fmoc-protected 1'-aminoferrocene-1-carboxylic acid (Fca) into the backbones of tripeptidestide synthesis.

By solid-phase peptide synthesis Metallocene-peptide bioconjugates were prepared by Metzler-Nolte and co-workers in which the amino acid sequence ranged from three to five residues. By coupling of ferrocenecarboxylic acid hexafluorophosphate with the free amino group of the peptide, the ferrocene and the cobaltocenium groups were introduced at the N terminus while the peptide was attached to the solid support.

Later, Metzler-Nolte and co-workers hoped to arrive at small, easy available artificial AMPs with activities comparable to those of the best naturally occurring AMPs by addition of metallocenes to more active peptide sequences. The metallocene peptide conjugates were prepared on Rink amide resin, whereas the

ferrocenecarboxylicacid was attached by formation of an amide bond with the free N-terminal amino group of the solid support. The ferrocene moiety is stable towards deprotection reagents and to resin cleavage, although the ferrocenoyl peptides are only stable when phenol rather than water is used in the cleavage mixtures.

4. Cobalt and Rhodium (Group 9) Metal Complex–Peptide Conjugates

4.1 Metallocene (Cobaltocenium) Conjugate

Since thecobaltcenium cation has a much higher redox potential and better chemical stability than ferrocene, much work has been done on ferrocene bioconjugates, the closely related cobaltocenium group. The lipophilic nature of the ferrocenyl moiety acts as a mimic for the bulky Trp residue, whereas the positively charged cobaltocenium moiety is isostructural with the neutral ferrocene, thus allowing an assessment of additional positive charge, and acting as a bulky Arg mimetic. Capping of the N termini of Arg- and Trp-containing hexapeptide sequences results in net losses of one unit of positive charge in the case of the ferrocenoyl bioconjugates, but the cobaltocenium analogues retain the overall charges of the peptides, which is favourable for their antibacterial activities.

To prepare the cobaltocenium conjugate of a nuclear localization signal peptide, solid-phase peptide synthesis was used. The heptapeptide H-Pro-Lys-Lys-Lys-Arg-Lys-Val-OH was chosen as the antigen NLS, which serves as an "address label" for proteins and indicates their destination as the cell nucleus.

4.2 Phenanthrenequinone Diimine (Phi) Rhodium Conjugate

Barton et al. have worked on the development of peptide conjugates of rhodium(III) complexes as models for sequence-selective DNA binding proteins. To do so, a family of rhodium–peptide complexes was prepared by coupling short oligopeptides to the intercalating moiety to explore whether the side chain functionalities of small peptides may be used to augment metal complex recognition.

To conclude this work, DNA site-specificity depends on the peptide side chain functional groups. Moreover, the phi complexes of rhodium cleave DNA upon photoactivation. Barton and co-workers utilized two complementary solidphase peptide synthesis ideas for the covalent attachment of phi complexes of rhodium(III) complexes to specific sites on synthetic peptides.

The metal–peptide conjugates were synthesized by either the direct coupling method or by coordination method. In the direct coupling strategy, the coordinatively saturated metal complex is assembled first. The functionalized metal complex and the terminal amine of the peptide bound to the resin are then condensed in a way that is analogous to the addition of another residue to the growing peptide chain.

In the coordination strategy the chelating ligand is first coupled onto the amino terminus of the peptide on the resin. Then, the resin-bound peptide containing the chelating ligand is treated with [Rh(phi)2(DMF)2](OTf)3, in a manner similar to that used for the synthesis of the parent rhodium complex.

In conclusion, both strategies offer distinct advantages over solution-phase methods, in that functionalization of side chains is precluded.

4.3 (Diphenylphosphanyl)serine (Pps) Rhodium Conjugate

Rhodium was utilized to prepare the first peptide–phosphane–metal complexes. For the incorporation of a phosphane-containing amino acid building block it was required to prevent the undesirable formation of phosphane oxide. To overcome this problem, a temporary conversion of the phosphane into the phosphanesulfide gave rise to an amino acid that could be used in standard coupling procedures.

Reaction with sodium thiosulfate converted the phosphane into the phosphane sulfide . Acid is then converted into the amino acid by formation of the oxazolidinone . Cleavage of the chiral auxiliary and reduction of the azide with tin(II) chloride gives amino acid , which was finally converted into the Fmoc-protected amino acid ready for peptide synthesis.

4.4 Mixed Bidentate Pps,Cps-Based Rhodium Conjugate

The (diphenylphosphanyl)serine (Pps) group was later incorporated into the 12-residue peptide along with a (dicyclohexylphosphanyl)serine (Cps) unit . The synthesis of the peptide conjugate, as well as the rhodium complexation, was carried out as described before, but on polystyrene resin.

5. Nickel, Palladium and Platinum (Group 10) Metal Complex–Peptide Conjugates

5.1 Ethylenediamine Platinum Conjugate

In 2000 Reedijk et al. reported the first synthesis of a trimeric arginine-containing peptide-dichloroplatinum(II) complex with potential antitumor activity by solid-phase synthesis. The solid-phase peptide synthesis was performed on Rink amide resin with commercially available protected amino acids Fmoc-Arg(Pbf)-OH and Fmoc-Gly-OH by a standard Fmoc protocol.

Later, Reedijk and co-workers examined the scope and generality of the solid-phase platination approach by preparing a six by six array of individual dichloroplatinum peptide analogues. Unfortunately, these platinum peptide complexes showed no potential as cytotoxic agents, but only demonstrated the utility of solid-phase peptide synthesis for the preparation of platinum drugs.

5.2 Dinuclear $N_{\alpha,\varepsilon}$-L-Lysine Platinum Conjugate

Reedijk and co-workers described the first solid-phase peptide synthesis of dinuclearlysinebridgedplatinum(II) complexes.Platination of the lysine was achieved with a fivefold excess of activated transplatin to give the immobilized compound. Biological testing of the platinum complexes showed their potential as anticancer agents. However, in comparison with cisplatin ,the compound displayed a 60-fold decrease in activity. One of the main applications of metal complex cross-linking is to increase the affinity of an antisense oligonucleotide to its target.

5.3 Tetradentate Monoanionic “Pincer” NCN {[C6H2(CH2NMe2)2-2,6-R-4]–} Platinum Conjugate

Van Koten et al. reported a robust organoplatinum(II) biomarker that can be incorporated into peptides by standard solid-phase coupling techniques. For the almost instantaneous change of colour from colourless to deep purple, capping of only 6% of the available amine termini of the resin-bound peptide is sufficient. Furthermore, this colouration process is reversible by washing with DMF/Et3N or DMF/morpholine solutions.

6. Copper (Group 11) Metal Complex–Peptide Conjugates

6.1 IDA Copper Conjugate

To extend the scope of solid-phase synthesis of peptide–metal complex conjugates, König et al.reported their preparation from modified amino acids bearing metal complexes in their side chains.

The IDA motif, known for its ability to bind imidazole residues and N-terminal His, was chosen and converted into its copper complex as a SAAC. This modified amino acid was incorporated into a peptide sequence by standard solidphase peptide synthesis.

6.2 Bis(2-picolyl)amine (bpa) Metal Conjugate

The nls peptide used by Metzler-Nolte et al. in their work is a heptapeptide with the primary sequence H-Pro-LysLys-Lys-Arg-Lys-Phe-OH . The nls-bpabioconjugate was prepared by Fmoc solid-phase peptide synthesis.

The peptide synthesis cycle consisted of Fmoc removal with piperidine and TBTU coupling. Metal complexation was carried out in aqueous solution with $Cu(NO3)_2$. The formation of the complex was immediately apparent from the deep blue colour of the solution due to a blue shift of the Cu d–d transition in the Cu(bpa) complex.

7. Zinc (Group 12) Metal Complex–Peptide Conjugate

7.1 Bpa Zinc Conjugate

Kraemer and co-workers prepared conjugates of peptide nucleic acids (PNAs) and metal-binding ligands by solidphase synthesis. Synthesis of conjugates was accomplished through sequential coupling/deprotection steps with the required number of Fmoc-Gly-OH building blocks to the terminal amino group of the Rink resin-bound PNA.

The affinities of the metal–bpa conjugates towards were shown to be strongly dependent upon the nature of the metal, in the order Ni^{2+}, Zn^{2+},Cu^{2+} .

König et al. reported solid-phase peptide synthesis protocols in which the positions and numbers of SAACs and their metal complexes may be varied.Peptide–metal complex conjugates were obtained either by incorporation of the metal-coordinated SAAC followed by mild nucleophilic resin-cleavage, or by complexation in metal salt solution after cleavage from the resin.

7.2 Bis-bpa Zinc Conjugate

Bis(ZnII chloride)-SAAC 164 has also been successfully used in solid-phase peptide synthesis. Cleavage with a DIPEA/MeOH/DMF solution gave the metallated peptide bis-bpa zinc complex.

7.3 Bis(1,4,7,10-tetraazacyclododecane) Bis(cyclene) Zinc Conjugate

The solid-phase synthesis of metal-complex-containing peptides bearing cyclene moieties has been performed.[90] The amino acid complex was prepared from the previously reported triazene-bis(cyclene) by treatment with α-amino Z-protected L-Lys–OBn.

Preliminary attempts to couple amino acid to aliphatic amino acids using HBTU, TBTU and DIPEA as coupling reagents failed. The more efficient reagent HOAt was used instead of HOBt together with the onium salt HATU.

8. Samarium, Europium, Terbium and Gadolinium (Lanthanides) Metal Complex– Peptide Conjugates

8.1 N-(Isothiocyanatobenzyl)diethylenetriamineN,N',N",N"'-tetrakis(acetic acid) Metal Conjugate.

The chelates of certain lanthanides, such as Eu^{3+}, Tb^{3+}, Sm^{3+} and Dy^{3+}, have unique fluorescence properties. Hovinen et al. described the synthesis of oligopeptide building blocks that allow for the introduction of lanthanide(III) chelates into synthetic oligopeptides by standard automated solid-phase peptide synthesis. After the building block had been coupled to the amino terminus of the coding sequence with use of a prolonged reaction time, but otherwise standard HBTU/HOBt conditions, the oligopeptide was released from the resin. Treatment of the deblocked oligomer with europium(III) citrate converted the conjugate into the corresponding europium peptide chelate.

Karvinen et al. have paved the way to a multiparametric caspase assay by characterizing the fluorescence properties of a series of lanthanide (Ln^{3+}) chelates incorporated into peptides and testing their functionality in a caspase-3 assay. As the caspases and their substrates are a well characterized and interesting group of enzymes as potential drug targets.

Hovinen et al. modified the synthesis of the building block , allowing the introduction of photoluminescent europium(III) and samarium(III) chelates into synthetic oligopeptides on solid-phase by Fmoc chemistry.

8.2 1,4,7,10-Tetraazacyclododecane-N,N',N",N"'tetraacetic Acid (DOTA) Gadolinium Conjugate

Macrocyclic ligand forms complexes with exceptionally high binding affinities and kinetic stabilities with a variety of metal ions.Sherry et al. prepared Gd^{3+}-G80BP (Binding Peptide) by solid-phase peptide synthesis and demonstrated that magnetic resonance imaging (MRI) can detect the binding event of a Gd^{3+}-DOTA-labelled peptide (Gd3+G80BP) to its target protein Gal-80.

In a later work, Sherry et al. modified the Gal-80 binding peptide TFDDLFWKEGHR by introducing a DOTA-chelating group at three different residues . Conjugation of DOTA to the N terminus of the resinbound peptide was accomplished with DOTA-tris(tBu) ester by standard Fmoc solid-phase peptide synthesis.

Addition of Gd3+ to each peptide–DOTA conjugate, competitive binding experiments showed that the exo-peptide labelled with Gd3+–DOTA at the N terminus had a reasonable affinity for Gal-80, while those peptides labelled with Gd3+–DOTA at endo positions within the peptide sequence had no detectable binding affinity for Gal-80.

Abbreviations

Bhoc – N-Benzhydryloxycarbonyl
Boc – tert-Butoxycarbonyl
BOP – (Benzotriazol-1-yloxy)-tris(dimethylamino)phosphonium hexafluorophosphate
ByPOP – (Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate
DCC – N,N'-Dicyclohexylcarbodiimide
Dde – 1-(4,4-Dimethyl-2,6-dioxocyclohexyldiene)ethyl
Dhbt-OH – 3,4-Dihydro-3-hydroxy-4-oxo-1,2,3-benzotriazine
DIC – N,N'-Diisopropylcarbodiimide
DIPEA – N,N-Diisopropylethylamine

DMAP – 4-(Dimethylamino)pyridine
DMF – Dimethylformamide
DNA – Deoxyribonucleic acid
DSC – N,N-Disuccinimidyl carbonate
EDTA – Ethylenediaminetetraacetic acid
HATU – 2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate methanaminium
HBTU – 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HMBA – Hydroxymethylbenzoic acid
HOAt – 1-Hydroxy-7-azabenzotriazole
HOBt – 1-Hydroxybenzotriazole
MBHA – 4-Methylbenzhydrylamine
MeOH – Methanol
MSNT – 1-(Mesitylene-2-sulfonyl)-3-nitro-1,2,4-triazole Mtt – 4-Methyltrityl
NBD – 4-Halo-7-nitrobenzo-2-oxa-1,3-diazole
NEM – N-Ethylmorpholine
NHS – N-Hydroxysuccinimide
SAAC – Single amino acid chelate
SASRIN – Super acid-sensitive resin
SPPS – Solid-phase peptide synthesis
NMP – N-Methylpyrrolidone
TBTU – 2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate
TFA – Trifluoroacetic acid
TMS – Trimethylsilane
TSTU – N,N,N',N'-Tetramethyl-O-(succinimidyl)uronium tetrafluoroborate
XAL – Xanthenyloxyalkylamide

References :

[1] S. Reinhardt, K. Heinze, Z. Anorg. Allg. Chem. 2006, 632, 1465–1470.
[2] S. Tadesse, A. Bhandari, M. A. Gallop, J. Comb. Chem. 1999, 1, 184–187.
[3] K. Heinze, Chem. Eur. J. 2001, 7, 2922–2932.
[4] Comparison of solution and solid-phase synthesis of a metal complex precursor: M. Albrecht, P. Stortz, J. Runsink, P. Weis, Chem. Eur. J. 2004, 10, 3657; M. Albrecht, P. Stortz, J. Runsink, P. Weis, Chem. Eur. J. 2004, 10, 3666.
[5] W. E. P. Greenland, K. Howland, J. Hardy, I. Fogelman, P. J. Blower, J. Med. Chem. 2003, 46, 1751–1757.
[6] For recent reviews on post solid-phase metallation, see: a) M. Albrecht, P. Stortz, R. Nolting, Synthesis 2003, 1307–1320; b) M. Albrecht, P. Stortz, Chem. Soc. Rev. 2005, 496–506.
[7] D. R. van Staveren, N. Metzler-Nolte, Chem. Commun. 2002, 1406–1407.
[8] K. Heinze, Chem. Eur. J. 2001, 7, 2922–2932.
[9] a) K. Heinze, U. Winterhalter, T. Jannack, Chem. Eur. J. 2000, 6, 4203–4210; b) J. T. Randolph, K. F. McClure, S. J. Danishefsky, J. Am. Chem. Soc. 1995, 117, 5712–5719; c) S. J. Danishefsky, K. F. McClure, J. T. Randolph, R. B. Ruggeri, Science 1993, 260, 1307–1309; d) L. A. Thompson, F. L. Moore, Y.-C. Moon, J. A. Ellman, J. Org. Chem. 1998, 63, 2066–2067.
[10] K. Heinze, J. D. B. Toro, Angew. Chem. Int. Ed. 2003, 42, 4533– 4536.
[11] K. Heinze, J. D. B. Toro, Eur. J. Inorg. Chem. 2004, 3498–3507.
[12] a) S. M. Okarvi, Med. Res. Rev. 2004, 24, 685; b) S. Liu, D. S. Edwards, Chem. Rev. 1999, 99, 2235–2268; c) S. M. Okarvi, Nucl. Med. Commun. 1999, 20, 1093–1112.
[13] E. Deutsch, K. Libson, J. L. Vanderheyden, A. R. Ketring, H. R. Maxon, Nucl. Med. Biol. 1986, 13, 465–477.

[14] a) K. A. Stephenson, J. Zubieta, S. R. Banerjee, M. K. Levadala, L. Taggart, L. Ryan, N. McFarlane, D. R. Boreham, K. P. Maresca, J. W. Babich, J. F. Valliant, Bioconjugate Chem. 2004, 15, 128–136; b) A. J. Fischman, J. W. Babich, H. W. Strauss, J. Nucl. Med. 1993, 34, 2253–2263.
[15] J. F. Valliant, R. W. Riddoch, D. W. Hughes, D. G. Roe, T. K. Fauconnier, J. R. Thornback, Inorg. Chim. Acta 2001, 325, 155–163.
[16] a) K. A. Stephenson, J. Zubieta, S. R. Banerjee, M. K. Levadala, L. Taggart, L. Ryan, N. McFarlane, D. R. Boreham, K. P. Maresca, J. W. Babich, J. F. Valliant, Bioconjugate Chem. 2004, 15, 128–136; b) K. A. Stephenson, S. R. Banerjee, O. O. Sogbein, M. K. Levadala, N. McFarlane, D. R. Boreham, K. P. Maresca, J. W. Babich, J. Zubieta, J. F. Valliant, Bioconjugate Chem. 2005, 16, 1189–1195.
[17] K. A. Stephenson, S. R. Banerjee, N. McFarlane, D. R. Boreham, K. P. Maresca, J. W. Babich, J. Zubieta, J. F. Valliant, Can. J. Chem. 2005, 83, 2060–2066.
[18] a) B. W. Bycroft, W. C. Chan, S. R. Chhabra, N. D. Hone, J. Chem. Soc. Chem. Commun. 1993, 778–779; b) S. Peluso, P. Dumy, C. Nkubana, Y. Yokokawa, M. Mutter, J. Org. Chem. 1999, 64, 7114–7120; c) B. Rohwedder, Y. Mutti, P. Dumy, M. Mutter, Tetrahedron Lett. 1998, 39, 1175–1178.
[19] K. A. Stephenson, S. R. Banerjee, T. Besanger, O. O. Sogbein, M. K. Levadala, N. McFarlane, J. A. Lemon, D. R. Boreham, K. P. Maresca, J. D. Brennan, J. W. Babich, J. Zubieta, J. F. Valliant, J. Am. Chem. Soc. 2004, 126, 8598–8599.
[20] a) A. Davison, A. G. Jones, C. Orvig, M. Sohn, Inorg. Chem. 1981, 20, 1629–1632; b) N. Bryson, J. C. Dewan, J. ListerJames, A. G. Jones, A. Davison, Inorg. Chem. 1988, 27, 2154– 2161; c) T. N. Rao, D. Adhikesavalu, A. Camerman, A. R.

