Tetrahedron Letters 51 (2010) 4617–4619

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

‘Click’ synthesis of ferrocenyl-, biferrocenyl-, and cobalticenyl-triazolyl-β-cyclodextrins

Abdou K. Diallo[a], Stéphane Menuel[b], Eric Monflier[b], Jaime Ruiz[a], Didier Astruc[a,*]

[a] *Institut des Sciences Moléculaires, UNMR CNRS No 5255, Université Bordeaux 1, 351 Cours de la Libération, 33405 Talence Cedex, France*
[b] *Unité de Catalyse et de Chimie du Solide, UMR CNRS No 8181, Université d'Artois, rue Jean Souvraz, SP18, 62307 Lens Cedex, France*

ARTICLE INFO

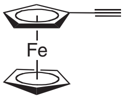
Article history:
Received 1 June 2010
Revised 22 June 2010
Accepted 23 June 2010
Available online 30 June 2010

Keywords:
Ferrocene
Cobalticinium
Alkyne
Cyclodextrin
Click reaction
Redox

ABSTRACT

Cu^I-catalyzed Huisgen-type dipolar ‘click’ reactions between azidomethyl-β-cyclodextrin and ethynylferrocene, ethylnylcobaltocenium hexafluorophosphate, and bis(ethynyl)-biferrocene yield the corresponding metallocenyl-1,2,3-triazolyl-β-cyclodextrins. The monometallocenyl 1,2,3-triazolyl-β-cyclodextrins are soluble in water, unlike the biferrocene derivative.

The combination between the supramolecular host properties of cyclodextrins[1] and the redox sensor properties of ferrocenes and other metallocenes[2] should enable monitoring the very useful encapsulation of guests in the cavities of these well-known natural receptors.[3] In addition, attachment of cyclodextrins to ligands can be applied to catalysis in aqueous solution, a key branch of ‘Green Chemistry’.[4] Therefore, we report here the use of the Huisgen-type[5] 1,3-dipolar ‘click’ cycloaddition reaction[6] between azidomethyl-β-cyclodextrin **1** and ethynylmetallocenes **2**–**4** to synthesize 1,2,3-triazolyl-metallocenes linked to β-cyclodextrin. In such ‘clicked’ derivatives, the 1,2,3-triazolyl ring is not only a link, but also a ligand,[7] with recently demonstrated useful coordination properties in the synthesis of catalytically active dendrimer-stabilized Pd nanoparticles (PdNPs).[8]



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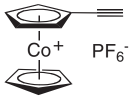

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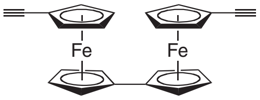

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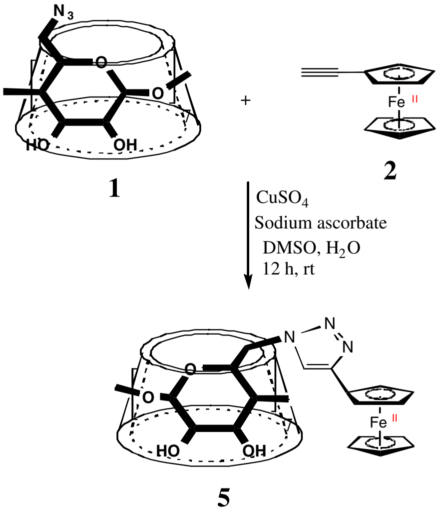
There are a number of reports of ‘click’ reactions between the azido derivative **1**[9] or its derivatives and various organic alkynes.[10] Likewise, multiple functionalities have been introduced.[11] Ferrocene is a guest of choice for β-cyclodextrin with a supramolecular interaction that has been abundantly studied.[12]

Reaction between azidomethyl-β-cyclodextrin, **1**, and commercial ethynylferrocene, **2**, was carried out in dimethylsulfoxide (DMSO)/H_2O (12:1) with stoichiometric amounts of hydrated Cu sulfate and sodium ascorbate under ambient conditions during 18 h (Eq. 1).



(1)

Lower amounts of catalyst do not lead to completion of the reaction, possibly due to catalyst inclusion into cyclodextrin (this feature was also noted recently in the case of ‘click’ reactions in

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* Corresponding author.
E-mail addresses: d.astruc@lcoo.u-bordeaux1.fr, d.astruc@ism.u-bordeaux1 (D. Astruc).

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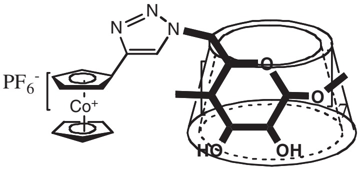
doi:10.1016/j.tetlet.2010.06.115

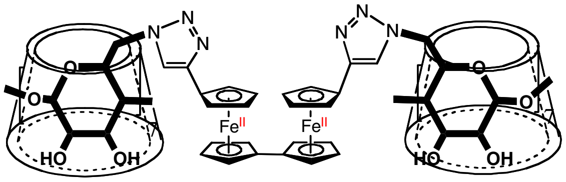
dendrimers).[7b,8] The solvents were removed under vacuum, the product was washed with dichloromethane, and the copper ions were removed as $[Cu(NH_3)_2(H_2O)_2]^{2+}$ by stirring overnight with aqueous ammonia. The water-soluble product was purified by chromatography over silica gel with water, giving **5**, as an orange powdery solid in 60% yield, that was characterized by the disappearance of the azide band at 2090 cm^{-1} in the infrared spectrum, ^1H NMR in D_2O (in particular the triazole proton at 8.31 ppm), ^{13}C NMR in DMSO-d_6 (see the Supplementary data), and its molecular peak in MALDI TOF spectroscopy (calcd for $C_{54}H_{79}FeN_3O_{34}$: 1370.068; found: 1391.75, major peak, calcd: 1392.38: MNa^+). Cyclic voltammetry (CV) of **5** was best carried out in DMSO solution with Pt electrodes, yielding a weak cyclic voltammogram of low intensity with little chemical reversibility ($E_{1/2} = 0.49$ mV vs decamethylferrocene).[13] Although a reduced intensity is expected because of the relatively large molecular weight, it is likely that it is mostly due to supramolecular polymer formation, ferrocene encapsulation in a β-cyclodextrin inhibiting a better observation (Fig. 1a).

The 'click' reaction of ethynylcobalticinium hexafluorophosphate **3**[14] with azidomethyl-β-cyclodextrin was carried out analogously, yielding 64% of the water-soluble product, cobaltoceniumtriazolyl-β-cyclodextrin hexafluoro-phosphate, **6**, as an orange powder. This complex was also characterized by the disappearance of the infrared azide band at 2090 cm^{-1}, the triazolyl proton at 8.39 ppm in ^1H NMR and its ^{13}C NMR spectrum (see Supplementary data). Its CV recorded with a dimethylformamide (DMF) solution showed a broad wave at $E_{1/2} = -0.88$ V vs decamethylferrocene (Fig. 1c).



6

Finally, bis(ethynyl)ferrocene, **4**,[15] also reacts with azidomethyl-β-cyclodextrin according to the same protocol, giving bis(ferrocenyltriazolyl-β-cyclodextrin, **7**,) as an orange powder in 61% yield.



7

This product **7** is not soluble in water, but only in DMSO and DMF, which allowed recording ^1H (triazole proton at 7.77 ppm) and ^{13}C NMR data in DMSO-d_6 (see Supplementary data). The MALDI TOF mass spectrum yielded the molecular peak: calcd for $C_{108}H_{156}Fe_2N_6O_{68}$: 2738.120; found: 2760.45, major peak, calcd: 2761.11: MNa^+). The CV of **7** recorded in DMSO provided only the first (more cathodic) biferrocenyl wave (weak) giving the mixed-valence 35-electron (Fe^{II}–Fe^{III}) species, the electroactivity of the second monoelectronic oxidation to the 34-electron Fe^{III}–Fe^{III} species being not accessible in DMSO (Fig. 1b).

In conclusion, ethynylmetallocenes yielded water-soluble triazolyl-bridged cyclodextrin-metallocene derivatives upon 'click' Huisgen-type 1,3-dipolar reactions under ambient conditions, but with stoichiometric amount of Cu^I 'catalyst', with the easily available azidomethyl-β-cyclodextrin. This reaction was also applied to the biferrocene compound, yielding a bis (1,2,3-triazolyl) derivative that was insoluble in water, but soluble in DMSO and DMF.

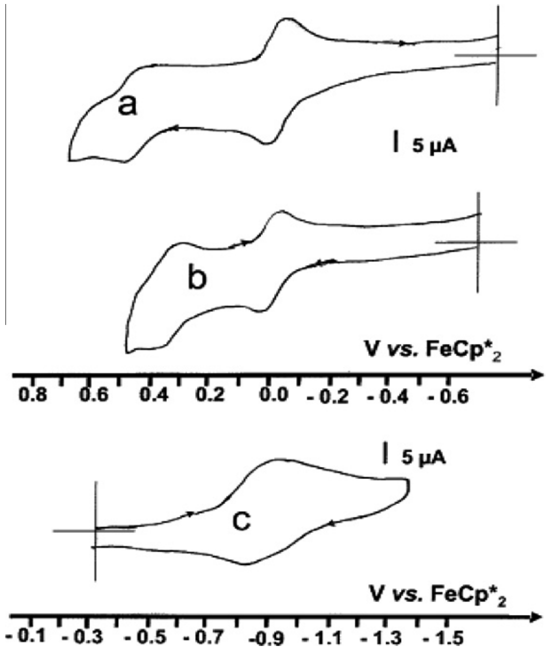


Figure 1. Cyclic voltammograms of the metallocenyltriazolyl-β-cyclodextrin complexes (concentration: 10^{-3} mol L^{-1}) using a PAR 273 potentiostat galvanostat; supporting electrolyte: 0.1 M [n-Bu_4N][PF_6]; 293 K). Pt working and counter electrodes; Ag reference electrode; scan rate: 0.2 V s^{-1}. $E_{1/2}$ vs decamethylferrocene as the internal reference. (a) **5** in DMSO; (b) **7** in DMSO; (c) **6** in DMF.

All the 'clicked' compounds showed weak electrochemical responses, suggesting head-to-tail supramolecular oligomeric structures involving the cyclodextrin cavities. Preliminary studies indicate that **5** coordinates Pd^{II} which can be reduced to water-soluble catalytically active Pd nanoparticles for Suzuki–Miyaura coupling under ambient conditions in an aqueous medium.[16]

Acknowledgment

Financial support from the Universities Bordeaux 1 and Artois, Centre National de la Recherche Scientifique and the Agence Nationale pour la Recherche (ANR-07-CP2D-05-01) is gratefully acknowledged.

Supplementary data

Supplementary data (^1H and ^{13}C NMR, MALDI TOF, and IR data and spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.115.

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