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Journal of Organometallic Chemistry 689 (2004) 4872–4876
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Note

Introduction of a planar chirality onto steroid substrates: synthesis of (*S*) and (*R*)-2′-formylcymantrenyl-17α-ethynylestradiols using (*S*) and (*R*)-1-formyl-2-iodo-cymantrenes

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Received 23 August 2004; accepted 24 September 2004

Abstract

We report the synthesis and characterisation of (*S*) and (*R*)-2′-formylcymantrenyl-17α-ethynylestradiol synthesized using the Sonogashira cross-coupling reaction between optically pure (*S*) and (*R*) 1-formyl-2-iodo cymantrenes and ethynylestradiol. (*S*) and (*R*) 1-formyl-2-iodo cymantrenes were obtained from the same precursor: (2R,4R)-4-(methoxymethyl)-2-cymantrenyl-1,3-dioxane.

Keywords: Cymantrene; Planar chirality; Ethynylestradiol; Bioorganometallics

1. Introduction

Owing to their particular electrochemical, spectroscopic, and radiopharmaceutical properties, ferrocene, cymantrene, and cyrhetrene derivatives are useful series in the emerging domain of bioorganometallic chemistry which deals with the biological properties of organometallic compounds [1]. These structures can also present planar chirality, mainly developed for asymmetric catalysis. In this context, ferrocenes have been particularly studied and their syntheses well exemplified, namely by Kagan et al. and Ugi et al. [2–6]. Some examples of cymantrenes presenting planar chirality, by using a chiral amide group and a ligand transfer reaction between a ferrocene compound and $[Mn(CO)_3Ar]^+$, have been reported [7]. However, to our knowledge, only two examples of planar chiral cyrhetrene are known in the literature [8].

In our ongoing work in the bioorganometallic field, we became interested in the recognition by the estrogen receptor of this unnatural type of chirality and its ability to differentiate between stereomers. Therefore we have envisaged the tethering of a planar chiral organometallic moiety to 17α-ethynylestradiol in view of further application in breast cancer treatment. The 17α position is tolerant to organometallic modification and the $CpMn(CO)_3$ series allows a newly described metal exchange reaction [1e]. We now present the ready attachment of functionalized enantiomeric cymantrene units to steroids.

The presence of a formyl substituent in position 2′ or 5′ not only generates a planar chirality, but also induces the formation of two diastereomers (Chart 1). One may anticipate the separation of these two diastereomers to be difficult. This situation can be avoided if the optically pure organometallic precursor can be separately prepared. We present now the synthesis of hormone complexes bearing a disubstituted cymantrene group in optically pure form.

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doi:10.1016/j.jorganchem.2004.09.057

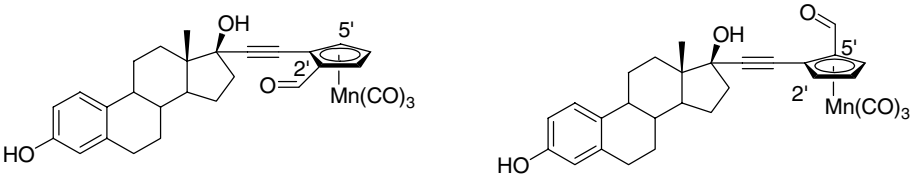


Chart 1.

2. Results and discussion

2.1. (R)-1-formyl-2-iodo-cymantrene

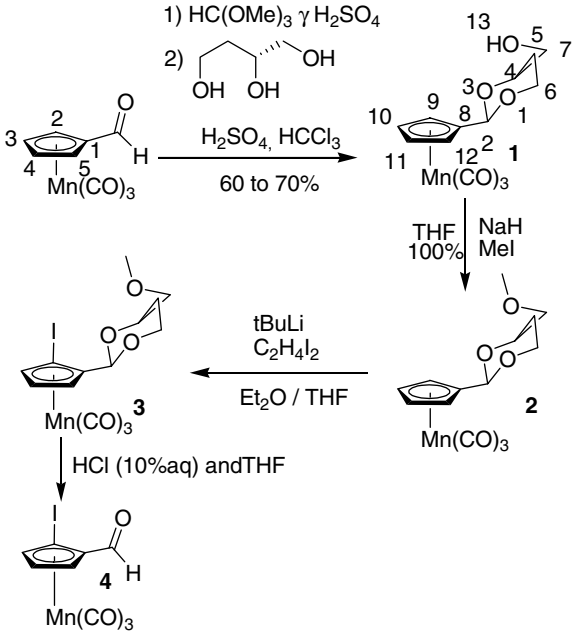
The synthesis of the precursor (*R*) 1-formyl-2-iodo cymantrene has been inspired by Riant and Kagan's procedure in ferrocene series [3]. Scheme 1 shows our synthetic pathway. Cymantrene carboxaldehyde was first reacted with (*R*) 1,2,4-butantriol to give ketal **1**. The addition of NaH to the ketal **1** solution followed by MeI addition produced the ether compound **2**. The attachment of a second substituent in the ortho position was achieved by adding a base, for example *t*-BuLi, followed by the reaction of a nucleophile with the lithium intermediate. Addition of *t*-BuLi to the etheral solution of **2** at −78 °C, followed by addition of diiodoethane, gave almost only iodo ketal **3**. Finally, removal of the ketal group by diluted HCl gave 1-formyl-2-iodo-cymantrene **4**.

The synthetic pathway for the ferrocene series is suitable for cymantrene series. Dioxane **1** was obtained in 70% yield from cymantrene carboxaldehyde. Only one epimer was observed by ^{1}H NMR. Theorically, *t*-BuLi can react with **2** either at position 2 or at position 5. But the methoxy group of the chiral substituent preferably stabilizes the lithium compound at position 2 (with *R* butanetriol). Therefore, only 2-iodo ketal **3** was formed. From this synthetic pathway, the formyliodocymantrene **4** obtained was in its *R* form.

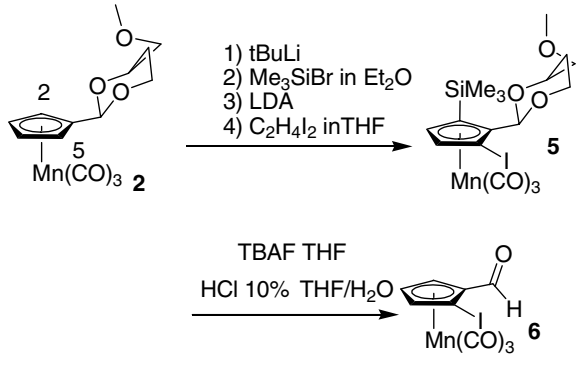
2.2. (S)-1-formyl-2-iodo-cymantrene 6

To obtain the second enantiomer, 1-formyl-5-iodo-cymantrene **6**, one can imagine using (*S*) 1,2,4-butantriol instead of (*R*) 1,2,4-butantriol. But this method requires the repetition of the whole synthetic pathway starting from formylcymantrene. In order to avoid this tedious method, we have designed a different and straightforward method to prepare **6** from **2** (Scheme 2).

We first introduced the trimethylsilyl group at position 2 in order to block, temporarily, this position. In this way, LDA may be directed toward the 5 position (Fig. 1). When diiodoethane was added, one compound was formed, the trisubstituted **5**, in 60% yield. The removal of trimethylsilyl group was achieved with TBAF



Scheme 1.



Scheme 2. Ortho iodation of cymantrene.

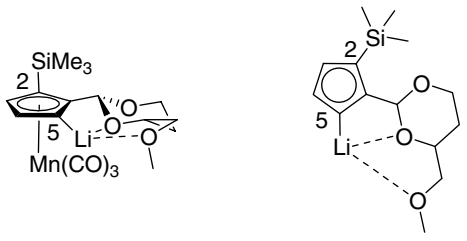


Fig. 1.

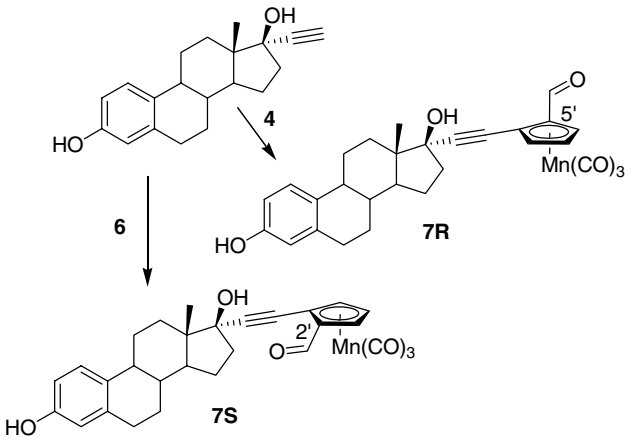
(2 eq, 1 M in THF). Finally, the chiral group was removed with diluted HCl to produce **6**.

We show here that the use of a trimethylsilyl group as a temporary position-blocking group is very convenient. Starting from the same precursor **2**, it is possible to prepare either (*R*) 1-formyl-2-iodo-cymantrene **4** or (*S*) 1-formyl-2-iodo-cymantrene **6**.

2.3. Cross-coupling reaction

Having now the two enantiomers **4** and **6**, the hormone complexes can be prepared by a cross-coupling reaction between ethynylestradiol and the iodo compounds (Scheme 3). Following the Sonogashira coupling reaction, ethynylestradiol and the respective iodo compound were heated in diisopropylamine in the presence of $PdCl_2(PPh_3)_2$ and $Cu(OAc)_2$. The yields of the hormone complexes are given in Table 1.

We found that the Sonogashira coupling is suitable in this case. Indeed, the hydroxyl group of ethynylestradiol does not need to be protected prior the coupling reaction. Compound **7R** was obtained in fairly good yield, 68%, but compound **7S** was isolated in only 43% yield. To improve the yields one might consider the use of a Stille reaction, but, in that case, ethynylestradiol must be transformed first into the tin derivative [9]. Both **7R** and **7S** exhibit very similar NMR spectra.



Scheme 3. Cross-coupling reaction with ethynylestradiol.

Table 1
Sonogashira coupling

Molecules	Yield (rd Cy_R/Cy_S)
7R	68% (>95/5)*
7S	43% (>5/95)*

Coupling condition in Sonogashira coupling: 5% $PdCl_2(PPh_3)_2$ 10% $Cu(OAc)_2 \cdot H_2O$ refluxing in degassed diisopropylamine 2 h.

* Diastereoisomer undetectable by NMR Spectroscopy.

3. Conclusion

We have, for the first time introduced planar chirality to a selected position of a steroid hormone. The high selectivity of the chiral auxiliary and the use of a silyl group as a blocking group allowed us to synthesize, separately, (*S*)-2′-formylcymantrenyl-17α-ethynylestradiol and (*R*)-2′-formylcymantrenyl-17α-ethynylestradiol. This work will be extended to other metal complexes, in particular to cyclopentadienylrhenium and ferrocene compounds and receptor binding affinities analyzed.

4. Experimental

4.1. General considerations

All manipulations, except acid deprotection, were performed under argon using standard Schlenk techniques. NMR spectra were obtained on a Bruker 300 MHz instrument. The starting materials were prepared according to the literature. Work up consisted in washing the a diethylether phase three times with water. Cymantrene carboxaldehyde was prepared according to the literature procedure [10].

4.2. (2R,4R)-4-(hydroxymethyl)-2-cymantrenyl-1,3-dioxane (*1*)

Cymantrene carboxaldehyde (2820 mg, 12.2 mmol) was dissolved, in trimethylorthoformate (20 mL) and 1 drop of H_2SO_4. The mixture was stirred for 3 h at room temperature and solid dry K_2CO_3 was slowly added. The mixture was filtered through celite and the solvent was removed under reduced pressure. The crude oil obtained was dissolved in dry chloroform (15 mL) and *R*-(+)-butane-1,2,4-triol was added followed by sulphuric acid (1 drop). The mixture was stirred overnight before neutralisation with K_2CO_3 and filtration through celite. The filtrate was diluted with diethylether (50 mL) and washed with water (3×20 mL). The organic phase was dried on $MgSO_4$ and evaporated under reduced pressure. The crude product was purified on silica gel column by eluting with pentane and ethylacetate (1/1). Compound **1** was obtained as a yellow oil (2735 mg, yield 70%). NMR ^1H (δ in ppm) : 1.39 (m, 1H, H5eq); 1.87 (dq, 1H, $J = 5.2$ Hz, $J = 12.3$ Hz, H5ax); 2.13 (t, 1H, $J = 7.4$ Hz, OH); 3.64 (m, 2H, H10); 3.87 (m, 2H, H6eq and H4ax); 4.19 (dd, 1H, $J = 4.8$ Hz, $J = 11.3$Hz, H6ax); 4.64 (br s, 2H, H10 and H11); 4.95 and 4.98 (two s, 2H, H9 and 12); 5.24 (s, 1H, H2). NMR ^{13}C (δ in ppm): 26.4 (C5); 77.4 (C4); 65.6 (C7); 66.4 (C6); 81.2 (C10); 81.6 (C11); 82.6 (C9); 82.9 (C12); 96.2 (C2); 102.1 (C8); 224.9 (CO).

4.3. (2R,4R)-4-(methoxymethyl)-2-cymantrenyl-1,3-dioxane (**2**)

Product **1** (2400 mg, 7.6 mmol) was dissolved in THF (20 mL) was added dropwise at room temperature, under argon, on a suspension of sodium hydride (60% in mineral oil, 454 mg, 11.3 mmol) in THF (4 mL). The mixture was stirred for 1 h before addition of methyl iodide (706 μL, 11.3 mmol) at room temperature. The reaction was stirred at room temperature overnight and quenched with water followed by a work-up. The crude product was purified by filtration on silica gel with dichloromethane quantitatively yielding a lemon yellow solid. (m.p. < 50 °C). NMR ^{1}H (δ in ppm): 1.47 (m, 1H, H5ax); 1.79 (dq, 1H, J = 5.0 Hz, J = 12.0 Hz, H5eq); 3.40 (dd, 1H, J = 5.9 Hz, J = 10.3 Hz, H7); 3.40 (s, 3H, H11); 3.51 (dd, 1H, J = 5.9 Hz, J = 10.3 Hz, H7′); 3.87 (dt, 1H, J = 2.1 Hz, J = 14.3 Hz, H6eq); 3.97 (m, 1H, H4); 4.19 (dd, 1H, J = 4.5 Hz, J = 11.1 Hz, H6ax); 4.62 (t, 2H, J = 2.1 Hz, H10); 4.96 (q, 2H, J = 2.0 Hz, H9); 5.23 (s, 1H, H2). NMR ^{13}C (δ in ppm): 27.7 (C5); 59.5 (C7); 66.6 (C6); 75.4 (C4); 76.1 (C10); 81.2 (C11); 82.6 (C9); 96.2 (C2); 102.6 (C8); 218.7 (CO). IR ($HCCl_3$ in cm^{-1}): ν_{CO} = 2024.3; 1943.1. $[\alpha]_D^{25} = -2°$ (c = 7.0 g/L, $CHCl_3$). Anal. Calc. for $C_{14}H_{15}MnO_6$: C, 50.31; H, 4.52. Found: C, 50.34; H, 4.59%.

4.4. (2R,4R,R_{Cy})-4-(methoxymethyl)-2-(α-iodocymantrenyl)-1,3-dioxane (**3**)

Product **2** (200 mg, 0.9 mmol) was dissolved in diethylether (4 mL), under argon, and cooled to −78 °C. Then ^{t}BuLi (0.48 mL, 0.72 mmol) was added dropwise. The mixture was stirred for 10 min at this temperature and 45 min at room temperature giving a pale yellow precipitate. In a dry Schlenk tube, 1,2 diodoethane (219 mg, 0.78 mmol) was dissolved in dry THF (2 mL) under argon. This solution was added dropwise to the mixture. After 10 min the cooling bath was removed and the mixture was stirred at room temperature for 2 h. An aqueous saturated solution of $Na_2S_2O_3$ was finally added before aqueous classical work up. The crude product was purified by chromatography on silica gel by eluting with pentane:diethylether (8:2) yielding a yellow oil (180 mg) which crystallized in pentane giving 62% yield (m.p. < 50 °C). NMR ^{1}H (δ in ppm): 1.52 (br d, 1H, J = 13.2 Hz, H5eq); 1.83 (dq, 1H, J = 5.1 Hz, J = 12.0 Hz, H5ax); 3.43 (m, 1H, H7); 3.46 (s, 3H, H11); 3.57 (m, 1H, H7′); 3.91 (td, 1H, J = 2.1 Hz, J = 12.0 Hz, H6eq); 4.01 (m, 1H, H4ax); 4.25 (dd, 1H, J = 4.8 Hz, J = 11.4 Hz, H6ax); 4.67 (s, 2H, H10); 5.00 (s, 2H, H9); 5.28 (s, 1H, H2). NMR ^{13}C (δ in ppm): 27.6 (C5); 59.4 (C13); 66.8 (C6) ; 75.2 (C7); 76.5 (C4); 81.2 (C12); 81.3 (C10); 82.4 (C11); 89.1 (C9); 97.7 (C2); 103.8 (C8); 212.9 (CO). Anal. Calcd: (C, 50.31; H, 4.52%) found: (C, 50.32; H, 4.59%). IR ($HCCl_3$ in cm^{-1}): ν_{CO} = 2028.2; 1950.6. $[\alpha]_D^{25} = +11.5°$ (c = 7.0 g/L, $CHCl_3$). Anal. Calc. for $C_{14}H_{14}IMnO_6$: C, 36.55; H, 3.07. Found: C, 36.67; H, 3.11%.

4.5. R-iodocymantrenecarboxaldehyde (**4**)

Product **3** (100 mg, 0.22 mmol) was dissolved in THF (10 mL) and HCl (10% in water, 10 mL) was added. The mixture was stirred 48 h at room temperature in dark. K_2CO_3 was added to neutralize the acid. The product was extracted with diethylether and filtered trough silica gel. In order to avoid decomposition, the yellow oil obtained was directly used in the cross-coupling reaction. ^{1}H NMR (δ in ppm, 300 Hz): 5.02 (dd, 1H, J = 1.72 Hz, J = 4.88 Hz, H5), 5.16 (dd, 1H, J = 1.80 Hz, J = 2.51 Hz, H3), 5.45 (dd, 1H, J = 2.00 Hz, J = 3.19 Hz, H4), 9.62 (s, 1H, CHO). $[\alpha]_D^{25} = +47.1°$ (c = 24.0 g/L, $CHCl_3$).

4.6. (2R,4R,S_{Cy})-4-(methoxymethyl)-2-[α-5′-(trimethylsilane)-2′-(iodo)-cymantrenyl]-1,3-dioxane (**5**)

Product **2** (200 mg, 0.60 mmol) was dissolved in diethylether (5 mL) and cooled to −78 °C. Then ^{t}BuLi (0.48 mL, 0.72 mmol) was added dropwise. The mixture was stirred for 10 min at this temperature and 45 min at room temperature giving a yellow precipitate. The mixture was cooled to −78 °C and trimethylsilylbromide was added dropwise (106 μL), under argon. After 10 min the cooling bath was removed and the mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure. The crude oil was dissolved, under argon, in THF (5 mL) and the solution was cooled to −78 °C. LDA (0.4 mL, 0.72 mmol) was added dropwise and the mixture was stirred at this temperature for 10 min and at room temperature for one hour giving a brown yellow solution. At room temperature, the diiodoethane (252 mg, 0.9 mmol) was added under argon. The cooling bath was removed and the mixture was stirred for 3 h. A classical aqueous work up was performed. The crude oil was purified on silica gel column with pentane/diethylether as eluent (1/9) giving a pale yellow oil (175 mg) in 55% yield. NMR ^{1}H (δ in ppm): 0.29 (s, 9H, SiMe); 1.60 (br d, 1H, J = 16.5 Hz, H5eq); 1.93 (m, 1H, H5ax); 3.37 (s, 3H, H13); 3.42 (dd, 1H, J = 7.3 Hz, J = 12.7 Hz, H7); 3.58 (dd, 1H, J = 5.3 Hz, J = 9.9 Hz, H7′); 3.93 (td, 1H, J = 2.5 Hz, J = 11.2 Hz, H6eq); 4.04 (m, 1H, H4); 4.25 (dd, 1H, J = 5.0 Hz, J = 11.2 Hz, H6ax); 4.79 (d, 1H, J = 2,7 Hz, H10); 4.92 (d, 1H, J = 2.7 Hz, H11); 5.21 (s, 1H, H2). NMR ^{13}C (δ in ppm): 0.9 (C14); 27.8 (C5); 59.1 (C13); 65.9 (C6); 74.8 (C7); 85.1 (C12); 89.9 (C10) ; 93.2 (C11); 97.3 (C9); 99.4 (C2) ; 111.2 (C8); 224 (CO). $[\alpha]_D^{25} = +5.7°$ (c = 7.0 g/L, $CHCl_3$). IR ($HCCl_3$ in cm^{-1}): ν_{CO} = 2026.3; 1949. Anal. Calc. for $C_{17}H_{22}I$- MnO_6Si: C, 38.36; H, 4.17. Found: C, 38.12; H, 4.01%.

4.7. S-iodocymantrenecarboxaldehyde (**6**)

Product **5** (134 mg, 0.25 mmol) was dissolved in THF (10 mL) then TBAF (1 M in THF, 0.50 mL) was added dropwise. The mixture was stirred for 2 h at room temperature giving a brown yellow solution. A classical aqueous workup was performed. The crude product was filtrated on silica gel eluting with dichloromethane giving a pal yellow oil. This product was dissolved in THF (10 mL) and HCl (10% in water, 10 mL) was added. The mixture was stirred 48 h at room temperature in dark. K_2CO_3 was added to neutralize the acid. The product was extracted with diethylether and filtered trough silica gel. In order to avoid decomposition, the yellow oil obtained was directly used in the cross-coupling reaction. ^{1}H NMR (δ in ppm, 300 Hz): 5.02 (dd, 1H, J = 1.72 Hz, J = 4.88 Hz, H5), 5.16 (dd, 1H, J = 1.80 Hz, J = 2.51 Hz, H3), 5.45 (dd, 1H, J = 2.00 Hz, J = 3.19 Hz, H4), 9.62 (s, 1H, CHO). $[\alpha]_D^{25} = -44.8^\circ$ (c = 5.0 g/L, $CHCl_3$).

4.8. S-(α-(17-α-ethynylestradiol))cymantrenecarboxaldehyde (7**S**)

Ethynylestradiol (65 mg, 0.21 mmol) and (*S*)-iodocymantrenecarboxaldehyde (90 mg, 0.25 mmol) were dissolved in degased diisopropylamine (5 mL). Thus diacetatecuprous monohydrate and di-chloro-bis-triphenylphosphine-palladium were added to the mixture. The reaction was refluxed, under argon, for 2 h. The reaction was ended by addition of water. Aqueous classical work up. The crude product was purified by preparative TLC with pentane/diethylether (2/8) yielding 47 mg (43%) of a pale yellow solid. NMR ^{1}H (δ in ppm): 0.92 (s, 3H, H18); 1.26–2.36 (m, 13H); 2.80 (m, 2H, H6); 4.91 (t, 1H, J = 3.2 Hz, H3′); 5.06 (dd, 1H, J = 1.7 Hz, J = 2.6 Hz, H4′); 5.43 (dd, 1H, J = 1.7 Hz, J = 3.2 Hz, H2′); 6.57 (s, 1H, H4); 6.63 (dd, 1H, J = 2.6 Hz, J = 8.5 Hz, H2); 7.16 (d, 1H, J = 8.5 Hz, H1); 9.83 (s, 1H, CHO). NMR ^{13}C (δ in ppm): 12.9 (C18); 15.3; 23.0; 26.4; 27.2; 29.6 (C6); 33.2; 39.3; 39.5; 43.5; 47.8; 50.0; 66.0; 67.2; 75.5; 80.6; 83.6 (C3′); 84.4 (C4′); 86.3 (C2′); 89.8 (C1′); 91.3 (C5′); 98.3; 112.8; 115.3; 126.6; 132.5; 138.3; 153.5; 186.5 (CHO); 222.1 (Mn–CO). IR ($HCCl_3$ in cm^{-1}): ν_{CO} = 2035.9; 1962.8. $[\alpha]_D^{25} = +116^\circ$ (c = 5.0 g/L, $CHCl_3$). Anal. Calc. for $C_{29}H_{27}MnO_6$ + 1Et_2O: C, 65.99; H, 6.21. Found: C, 65.63; H, 6.33%.

4.9. R-(α-(17-α-ethynylestradiol))cymantrenecarboxaldehyde (7**R**)

Ethynylestradiol (65 mg, 0.21 mmol) and (*R*)-iodocymantrenecarboxaldehyde (90 mg, 0.25 mmol) were dissolved in degased diisopropylamine (5 mL). Thus diacetatecuprous monohydrate and dichloro-bis(triphenylphosphine)palladium were added to the mixture. The reaction was refluxed under argon for 2 h. The reaction was ended by addition of water. Aqueous classical work up. The crude product was purified by preparative TLC with pentane/diethylether (2/8) yielding 75 mg (68%) of a pale yellow solid. NMR ^{1}H (δ in ppm): 0.92 (s, 3H, H18); 1.26–2.36 (m, 13H) 2.80 (m, 2H, H6); 4.92 (t, 1H, J = 3.2 Hz, H3′); 5.07 (dd, 1H, J = 1.7 Hz, J = 2.6 Hz, H4′); 5.44 (dd, 1H, J = 1.7 Hz, J = 3.2 Hz, H2′); 6.56 (s, 1H, H4); 6.63 (dd, 1H, J = 2.6 Hz, J = 8.5 Hz, H2); 7.16 (d, 1H, J = 8.5 Hz, H1); 9.84 (s, 1H, CHO). NMR ^{13}C (δ in ppm): 12.8 (C18); 15.3; 23.0; 26.4; 27.2; 29.6 (C6); 33.2; 39.3; 39.4; 43.5; 47.8; 50.0; 65.9; 67.2; 75.5; 80.6; 83.6 (C3′); 84.5 (C4′); 86.5 (C2′); 89.8 (C1′); 91.3 (C5′); 98.2; 112.8; 115.3; 126.6; 132.5; 138.3; 153.5; 186.4 (CHO); 222.6 (Mn–CO). IR ($HCCl_3$ in cm^{-1}): ν_{CO} = 2035.9; 1962.9. $[\alpha]_D^{25} = -247^\circ$ (c = 6.1 g/L, $CHCl_3$). Anal. Calc. for $C_{29}H_{27}MnO_6$) + 1 Et_2O: C, 65.99; H, 6.21. Found: C, 65.61; H, 6.21%.

Acknowledgement

Financial support from the Ministere de la Recherche and the Centre National de la Recherche Scientifique are gratefully acknowledged.

References

[1] (a) S. Top, A. Vessières, G. Leclercq, J. Quivy, J. Tang, J. Vaissermann, M. Huché, G. Jaouen, Chem. Eur. J. 9 (2003) 5223;
(b) N. Metzler-Nolte, Angew. Chem., Int. Ed. 40 (2001) 1040;
(c) G. Jaouen, R.H. Fish, J. Organomet. Chem. 668 (2003) 1;
(d) K. Severin, R. Bergs, W. Beck, Angew. Chem. Int. Ed. Engl. 37 (1998) 1634;
(e) S. Top, El B. Kaloun, S. Toppi, A. Herrbach, M.J. McGlinchey, G. Jaouen, Organometallics 20 (2001) 4554;
(f) G. Jaouen, S. Top, A. Vessières, R. Alberto, J. Organomet. Chem. 600 (2000) 23.

[2] (a) D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann, I. Ugi, J. Am. Chem. Soc. 2 (1970) 5389;
(b) D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann, I. Ugi, Angew. Chem., Int. Ed. Engl. 9 (1970) 371.

[3] (a) O. Riant, O. Samuel, H.B. Kagan, J. Am. Chem. Soc. 115 (1993) 5835;
(b) O. Riant, O. Samuel, T. Flessner, S. Taudien, H.B. Kagan, J. Org. Chem. 62 (1997) 6733.

[4] K. Schlögl, Topics Stereochem. 1 (1967) 39.

[5] T. Ferrocenes, A. Hayashi, A. Togni (Eds.), VCH, Weinheim, 1995.

[6] For review O. Delacroix, J. Gladysz, Chem. Commun. (2003) 66.

[7] Seung Uk Son, Kang Hyun Park, Seung Jung Lee, Young Keun Chung, Dwight A. Sweigart, Chem. Commun. (2001) 1290.

[8] (a) C. Bolm, L. Xiao, L. Hintermann, T. Focken, G. Raabe, Organometallics 23 (2004) 2362;
(b) C. Bolm, M. Kesselgruber, M. Hermanns, J.P. Hildrebrand, G. Rabe, Angew. Chem., Int. Ed. 40 (2001) 1488.

[9] S. Top, H. El Hafa, A. Vessières, J. Quivy, J. Vaissermann, D.W. Hughes, M.J. McGlinchey, J.-P. Mornon, E. Thoreau, G. Jaouen, J. Am. Chem. Soc. 117 (1995) 8372.

[10] N.C. Kolobova, Z.P. Valueva, M.Ya. Solodova, Bull. Acad. Sci. USSR, Div. Chem. 29 (1981) 1701.