



Zirconium-mediated cyclomagnesiation of styrene using magnesacyclopentane and 1,4-di(brommagnesium)butane as a method for the preparation of macrocyclic organomagnesium compounds

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ARTICLE INFO

Article history:

Received 28 December 2009

Received in revised form 27 February 2010

Accepted 7 March 2010

Available online 11 March 2010

Keywords:

Zirconium complexes

Magnesacycloalkanes

Dimagnesium compounds

Homogeneous catalysis

ABSTRACT

Cyclometalation of styrene with 1,4-bis(brommagnesium)butane and magnesacyclopentane in the presence of Cp_2ZrCl_2 gives rise to the formation of magnesacycloalkanes, composed of one ethylene molecule and two, three or four styrene molecules.

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1. Introduction

To date, the literature contains numerous publications on the synthesis of the five-membered cyclic organomagnesium compounds (OMCs) via the cyclomagnesiation reaction of olefins, acetylenes and allenes using metal complex catalysts [1].

According to the report [2], magnesacyclopentanes and magnesacyclopentadienes actively enter into the reaction with electrophilic and nucleophilic reagents at the active Mg–C bond to afford both cyclic and acyclic heteroatomic compounds. The insertion reaction of olefins into Mg–C bond that would allow the directed design of various macrometallacarbo-cycles, practically, has not been studied.

Previously, we reported on selective cyclomagnesiation of styrene assisted by magnesacyclopentane in the presence of Cp_2ZrCl_2 [3]. The reaction of styrene with magnesacyclopentane (3 mol% Cp_2ZrCl_2 , 25 °C, 1.5 h) resulted in the formation of 2-phenylmagnesacyclopentane **1** (95%) and a small amount of 2,4-diphenylmagnesacycloheptane **2** (5%) in 75% total yield (Scheme 1).

In this paper we wish to report our attempts to accomplish homologation of magnesacyclopentane and 1,4-bis(brommagnesium)butane, generated during the magnesacyclopentane synthesis from styrene and ethylene in the presence of complex catalysts in order to develop the efficient methods for the synthesis of cyclic OMCs of large size.

2. Results and discussion

In view of the works published in the literature and taking into account our own findings [4] we studied the reaction of 1,4-di(brommagnesium)butane, together with magnesacyclopentane, and styrene in the presence of zirconium, titanium and hafnium complexes as catalysts in accordance with the Schlenk equilibrium to elaborate preparative procedures for obtaining previously inaccessible macromagnesacarbo-cycles.

Thus, the interaction between 1,4-bis(brommagnesium)butane and styrene (2:1 ratio) in the presence of 3 mol% Cp_2ZrCl_2 (THF, 25 °C, 12 h) was found to afford a mixture of three OMCs **2**, **3** and **4** in 98% total yield (Scheme 2 and Table 1).

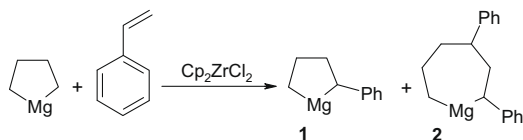
The product yields were determined by GLC analysis of the hydrolysis reaction mixture. The individual hydrolysis products (**5**, **6**, **7**) and deuterolysis products (**8**, **9**, **10**) were isolated by high-performance liquid chromatography.

The structure of OMCs obtained has been proven by analysis of IR, ^1H and ^{13}C NMR spectra as well as by GS–MS analysis of **5**–**10**.

The one-dimensional (^1H and ^{13}C NMR), two-dimensional homonuclear (COSY) and heteronuclear experiments (HSQC, HMBC) have been performed for compounds **5** and **8**. These experimental findings allowed making the complete ^1H and ^{13}C NMR assignments that unambiguously define the positions of the phenyl substituents. In COSY experiments the propyl fragment of the molecule **5** is characterized by the chain of cross-peaks between the methyl protons [δ (C^6H_3) 0.92], the methylene protons [δ (C^5H_2) 1.25, δ (C^4H_2) 1.64] and the methine proton [δ (C^3H) 2.63] interact-

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Scheme 1.

ing to each other. The triplet signal of the methylene protons [δ (C^1H_2) 2.54] correlates with the proton signals [δ (C^2H_2) 1.90–2.10] that fully confirms the 1,3-position of the phenyl groups. The ^{13}C NMR spectrum of the deuterolysis product **8** exhibit the characteristic triplet splitting of the signals at δ (C-1) 33.58 and δ (C-6) 13.95 ppm ($^1J_{\text{C-D}} = 19.5$ Hz).

Compound **3** is formed by the insertion of the styrene molecule into compound **2**. Theoretically, this reaction can occur as the “head-to-tail” and/or “head-to-head” type process. Hydrolysis of these compounds may result in the formation of two regioisomeric products: 1,3,5-triphenyloctane **6** or 1,3,6-triphenyloctane **6a**.

The one- and two-dimensional homonuclear COSY and also heteronuclear, HSQC and HMBC experiments, were crucial for the determination of the resultant regioisomer structure.

The observed doubling of signals in the ^{13}C NMR spectra attributable to the C_8 hydrocarbon chain indicates the formation of a 1:1 mixture of two diastereoisomeric compounds **6** [3S(R),5S(R) and 3S(R),5R(S)] or **6a**, which have two chiral centers at C-3 and C-5 and also at C-3 and C-6, respectively (Fig. 1).

The COSY experiments showed the correlation between the propyl protons [δ (C^6H_2) 1.63–1.73, δ (C^7H_2) 1.09–1.28, and δ (C^8H_3) 0.87–0.92] and the methine proton [δ (C^5H) 2.00–2.11] that confirm the formation of compound **6** with 1,3,5-arrangement of the phenyl substituents, in contrast with compound **6a**, which should demonstrate the correlation between the protons of the ethyl group at C-6 in a COSY experiment.

The ^{13}C NMR spectrum of the deuterated derivative **9** (as 1:1 diastereomeric mixture) exhibits two triplet signals: [δ (C^8) 13.99, 14.34] and [δ (C^1) 33.56, 33.68] with $^1J_{\text{C-D}} = 19.5$ Hz. The α -isotope shifts reach the magnitude of about 0.2–0.4 ppm (upfield).

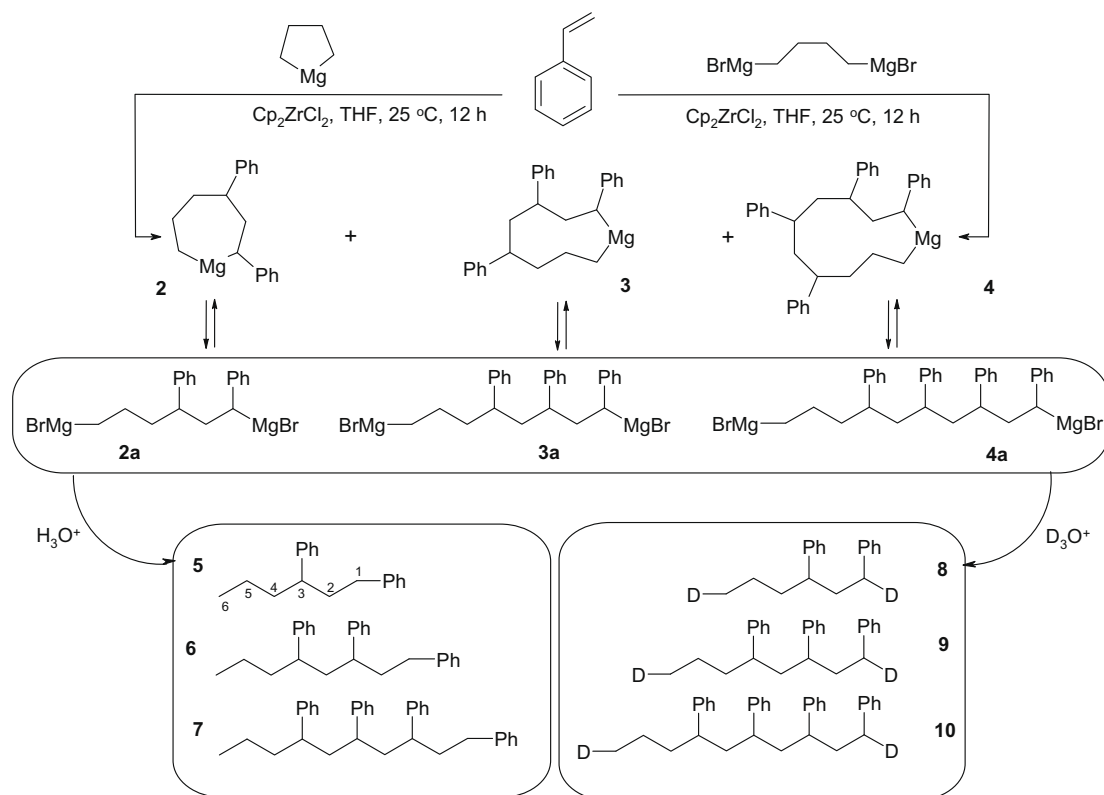
Such isotope effects are observed in the ^{13}C NMR spectra of 1,3,5,7-tetraphenyldecane **7** and its deuterated derivative **10**, which are also characterized by the increase in the number of non-equivalent signals. The formation of the four stereoisomers was found to occur due to the presence of three chiral centers (C-3, C-5, and C-7) in the molecules **7** and **10**.

Accordingly, magnesacycloalkanes **3** and **4** and/or dimagnesium compounds **3a** and **4a** are constructed from one ethylene and three styrene units and four styrene and one ethylene units, respectively. The predominant formation of **3** and **4** is observed under reaction conditions (25 °C, 3 mol% Cp_2ZrCl_2 , 12 h), while replacing 1,4-bis(brommagnesium)butane with magnesacyclopentane (Table 1).

Cyclomagnesiation of styrene at elevated temperatures (67–70 °C) afforded a complicated mixture of products. The decrease in temperature up to 0 °C causes an increase in selectivity providing predominant formation of **1** as a target product, albeit in low yield (up to 20%).

When testing catalysts and studying the influence of its central metal atom nature upon the yield and selectivity (Table 1) of magnesacycloalkanes synthesized (and/or the corresponding dimagnesium compounds), we concluded that Ti and Hf complexes, as compared with Cp_2ZrCl_2 , are less active and mediate formation of compounds **1**, **2** and **3** in low yields and selectivity. The $(\text{MeCp})_2\text{ZrCl}_2$ catalyst reduces the selectivity of the reaction leading to equilibrium mixture of **1**, **2**, **3** and **4**. Like the Hf-based catalyst, $(\text{Me}_5\text{Cp})_2\text{ZrCl}_2$ also revealed low effectiveness, but it showed high selectivity leading to the formation of **1** only.

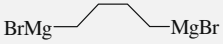
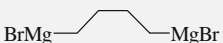

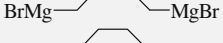
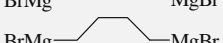
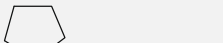




Our experiments and the results obtained allowed to propose the scheme of transformations of styrene and magnesacyclopent-



Scheme 2.

Table 1

The effect of the OMC structure, catalyst and ratio of the starting reagents on the yield and composition of the cyclomagnesiation products of styrene.

Nos.	OMC	Catalyst	Styrene:OMC molar ratio	Product yield (%)				Total yield (%)
				1	2	3	4	
1		Cp ₂ ZrCl ₂	1:1	–	10	20	20	50
			2:1	–	28	35	35	98
			3:1	2	35	41	22	100
			4:1	10	38	43	9	100
2		(MeCp) ₂ ZrCl ₂	2:1	20	23	23	27	93
			2:1	8	8	12	–	28
3		Cp ₂ HfCl ₂	2:1	–	–	–	–	–
4		(Me ₅ Cp) ₂ ZrCl ₂	2:1	30	–	–	–	30
5		Cp ₂ TiCl ₂	2:1	–	–	–	–	–
6		Ti(Pr ^t O) ₄	2:1	45	31	–	–	76
7		Cp ₂ ZrCl ₂	1,2:1	–	–	45	55	100
			1:1	–	–	36	59	95
			2:1	–	–	50	50	100
8		(MeCp) ₂ ZrCl ₂	1,2:1	25	30	25	20	95
			1,2:1	15	15	12	–	42
9		Cp ₂ HfCl ₂	1,2:1	–	–	–	–	–
10		(Me ₅ Cp) ₂ ZrCl ₂	1,2:1	38	2	–	–	40
			1,2:1	–	–	–	–	–

Reaction conditions: concentration of the OMC 0.6 mmol/ml, THF, 25 °C, 3 mol% catalyst, 12 h; catalyst = Cp₂ZrCl₂, (MeCp)₂ZrCl₂, Cp₂HfCl₂, Cp₂TiCl₂, Ti(*i*-PrO)₄.

tane (or 1,4-bis(brommagnesium)butane) in the presence of the Cp₂ZrCl₂ catalyst (Scheme 3 for magnesa-cyclopentane. All the arrows can be considered as equilibrium). According to this scheme, primarily, magnesa-cyclopentane enters into the transmetalation reaction with Cp₂ZrCl₂ to give 1,4-tetramethylene-bis(cyclopentadienyl)zirconium **11**, which under reaction conditions transforms into bis(ethylene) complex **12**. Being in the reaction mixture in excess, styrene displaces the ethylene molecule from **12**, which, through π -complex **13** and intramolecular cyclometalation, gives rise to zirconacyclopentane **14**. The insertion of the styrene molecule into the Zr–C bond of **14** affords complex **15**. The successive insertion of the styrene unit into **15** and **16** results in the corresponding the 9- and 11-membered tri- and tetraphenyl-substituted zirconacycloalkanes **16** and **17**, respectively, which undergo transmetalation with the excess of the starting OMC to produce the target magnesa-cycloalkanes and/or the corresponding dimagnesium compounds.

In conclusion, we suggest the efficient catalytic method to prepare macromagnesa-cycloalkanes and/or the corresponding dimagnesium derivatives via the interaction between magnesa-cyclopentane [and/or 1,4-bis(brommagnesium)butane] and styrene in the presence of the catalytic amount of the Cp₂ZrCl₂ complex. The OMCs obtained can be used for the synthesis of heterocyclic and bifunctional compounds [4].

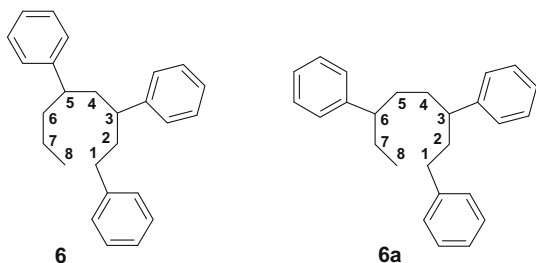


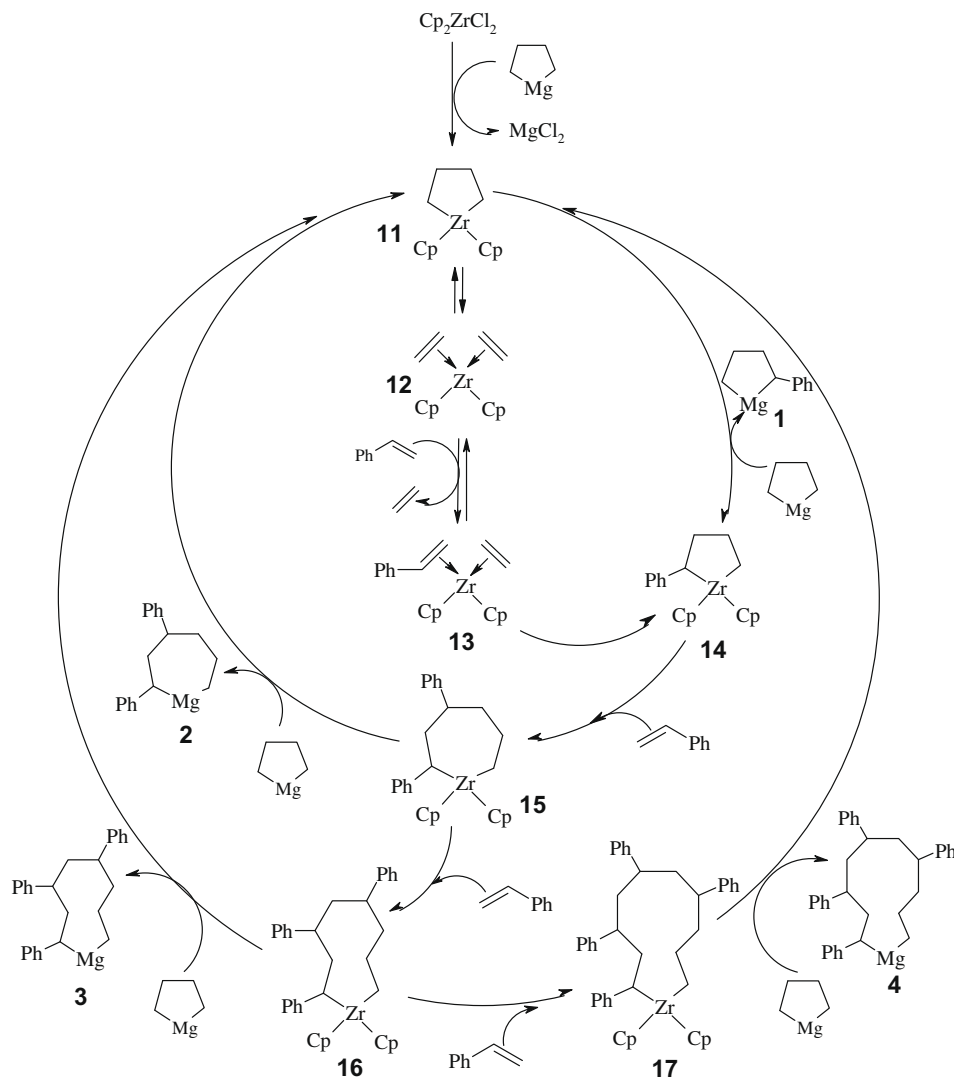
Fig. 1. The structures for compounds **6** and **6a**.

3. Experimental

All reactions were carried out under dry argon atmosphere. All solvents employed were purified and dried prior to use. Magnesa-cyclopentane and 1,4-bis(brommagnesium)butane was synthesized according to the method [5]. IR spectra of the compounds were recorded on a spectrometer Specord 75 IR. UV spectra were recorded on a spectrometer Lambda 750. Separation of the hydrolysis and deuterolysis products was performed by HPLC (preparative column: 21 × 250 mm, octadecyl/Si(100) polyol, 3 μ , detector – Lambda-Max 481 (λ 265 nm), eluent – acetonitrile (CH₃CN), flow rate 5 ml/min. The hydrolysis and deuterolysis products were analyzed on a chromatograph Chrom-5 in a stream of helium, column 1200 × 3 mm, 5% SE-30 on Chromaton N-AW. The ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a spectrometer Bruker Avance [400.13 MHz (¹H) and 100.62 MHz (¹³C)].

3.1. Synthesis of 1,3SR,5SR-triphenyloctane, **6**, 1,6-dideutero-1,3SR,5SR-triphenyloctane, **9**, 1,3SR,5SR,7SR-tetraphenyldecane, **7**, and 1,10-Dideutero-1,3SR,5SR,7SR-tetraphenyldecane, **10**

General procedure: A glass reactor, under a dry argon atmosphere at 0 °C, was charged under stirring with Cp₂ZrCl₂ (1.5 mmol, 0.438 g), styrene (50 mmol, 5.2 g), and magnesa-cyclopentane (60 mmol, 0.6 M solution in THF). The temperature was raised to 25 °C and the mixture was stirred for additional 12 h. Then, the reaction mixture was quenched by a 8% DCl in D₂O to identify magnesa-cycloalkanes (and/or dimagnesium compounds) obtained. The organic layer was separated. The aqueous layer was extracted with diethyl ether or hexane. The combined organics were washed with NaHCO₃ (until neutral) and dried over CaCl₂. The individual products were separated by preparative HPLC. Compounds **5** and **8**, additionally, were identified by comparison with the known samples [3]. Spectral data for **6**: Bp 168 °C (2 mm Hg). IR ν_{CO} (cm⁻¹ in thin film,): 3060, 3040, 2940, 2900, 2840, 1580, 1480, 1440, 1050, 1010, 745, 690. ¹H NMR (CDCl₃, in ppm,



Scheme 3.

400.13 MHz): $\delta = 7.19\text{--}7.52$ (m, 15H, Ph), 2.39–2.65 (m, 1H, CH-Ph), 2.38–2.62 (m, 2H, $\text{CH}_2\text{-Ph}$), 2.37–2.48 (m, CH_2 , C- $\text{CH}_2\text{-C}$), 2.0–2.11 (m, 1H, CH-Ph), 1.62–2.17 (m, 2H, C- $\text{CH}_2\text{-C}$), 1.63–1.73 (m, 2H, C- $\text{CH}_2\text{-C}$), 1.09–1.28 (m, 2H, C- $\text{CH}_2\text{-C}$), 0.87–0.92 (t, 3H, CH_3 , $^3J = 7.2$ Hz). ^{13}C NMR (CDCl_3 , in ppm, 100.62 MHz): $\delta = 146.09$, 145.86, 145.75, 145.38, 128.51, 128.46, 128.36, 128.28, 128.07, 127.77, 127.69, 126.16, 126.13, 125.93, 125.72, 125.63, 125.34, 43.69, 43.68, 43.36, 43.26, 43.02, 42.94, 40.31, 40.31, 39.95, 38.58, 33.95, 33.84, 20.70, 20.64, 14.64, 14.20. MS, m/z : 342 (M^+). Elemental Anal. Calc. for: C, 91.23; H, 8.77. Found: C, 91.29; H, 8.69%. Spectral data for **9**: Bp 169 °C (2 mm Hg). IR ν_{CO} (cm^{-1} in thin film): 3080, 3060, 3020, 2920, 2850, 2275 (C-D), 1620, 1515, 1480, 945, 780, 735. ^1H NMR (CDCl_3 , in ppm, 400.13 MHz): $\delta = 7.19\text{--}7.52$ (m, 15H, Ph), 2.38–2.64 (m, 1H, CH-Ph), 2.37–2.61 (m, 2H, CH_2), 2.37–2.84 (m, 2H, C- $\text{CH}_2\text{-C}$), 2.01–2.12 (m, 1H, CH-Ph), 1.64–1.88 (m, 2H, C- $\text{CH}_2\text{-C}$), 1.18–1.38 (m, 2H, $-\text{CH}_2-$), 0.92–1.03 (m, 2H, CH_2D). ^{13}C NMR (CDCl_3 , in ppm, 100.62 MHz): $\delta = 145.88$, 146.11, 145.39, 145.78, 128.52, 128.45, 128.35, 128.28, 128.07, 127.76, 127.68, 126.15, 126.12, 125.94, 125.73, 125.65, 125.33, 44.78, 44.69, 43.36, 43.42, 43.12, 43.02, 40.37, 37.82, 39.98, 38.65, 33.68 (t, $^1J_{\text{C-D}} = 19$ Hz), 33.56 (t, $^1J_{\text{C-D}} = 19$ Hz), 20.71, 20.65, 14.34 (t, $^1J_{\text{C-D}} = 19$ Hz), 13.99 (t, $^1J_{\text{C-D}} = 19$ Hz). MS, m/z : 344 (M^+). Elemental Anal. Calc. for: C, 90.70;

H, 8.14; D, 1.16. Found: 90.45; H+D, 9.27%. Spectral data for **7**: IR ν_{CO} (cm^{-1} in KBr): 3080, 3060, 3030, 2920, 2850, 1520, 1485, 955, 780, 750. ^1H NMR (CDCl_3 , in ppm, 400.13 MHz): $\delta = 7.33\text{--}6.90$ (m, 20H, Ph), 2.62–1.72 (m, 5H, CH-Ph), 1.08–1.59 (m, 10H, CH_2), 0.74–0.77 (m, 3H, CH_3). ^{13}C NMR (CDCl_3 , in ppm, 100.62 MHz): $\delta = 146.25$, 145.97, 145.89, 145.80, 145.63, 145.41, 145.21, 144.92, 142.58, 142.48, 128.35, 128.26, 128.11, 127.98, 127.81, 127.68, 127.63, 127.57, 127.55, 126.05, 125.97, 125.93, 125.87, 125.76, 125.61, 125.55, 45.37, 44.37, 44.01, 43.88, 43.82, 43.17, 42.89, 42.79, 41.63, 40.85, 40.85, 40.53, 40.29, 39.79, 39.09, 38.09, 37.38, 33.37, 33.42, 20.42, 20.35, 13.77. MS, m/z : 446 (M^+). Elemental Anal. Calc. for: C, 91.48; H, 8.52. Found: C, 91.39; H, 8.54%. Spectral data for **10**: IR ν_{CO} (cm^{-1} in KBr): 3080, 3060, 3030, 2920, 2850, 2275 (C-D), 1620, 1520, 1495, 950, 780, 760. ^1H NMR (CDCl_3 , in ppm, 400.13 MHz): $\delta = 7.34\text{--}6.91$ (m, 20H, Ph), 2.63–2.70 (m, 5H, CH-Ph), 1.06–1.58 (m, 10H, CH_2), 0.74 (m, 2H, CH_2D). ^{13}C NMR (CDCl_3 , in ppm, 100.62 MHz): $\delta = 146.24$, 145.39, 145.96, 145.87, 145.79, 145.62, 145.4, 145.19, 144.91, 142.57, 57, 142.47, 128.35, 128.52, 128.16, 128.10, 127.95, 127.80, 127.67, 127.62, 127.56, 127.54, 126.15, 126.04, 125.95, 125.91, 125.86, 125.75, 125.59, 125.53, 125.53, 45.35, 44.35, 44.00, 43.89, 43.16, 42.89, 42.79, 41.61, 40.83, 40.51, 40.28, 39.78, 39.08, 38.08, 37.77, 33.37 (t, $^1J_{\text{C-D}} = 19$ Hz), 33.42 (t, $^1J_{\text{C-D}} = 19$ Hz), 20.41,

20.33, 13.77 (t, $^1J_{C-D} = 19$ Hz). MS, m/z : 448 (M^+). Elemental Anal. Calc. for: C, 91.07; H, 8.03. Found: C, 91.10; H+D, 9.91%.

Acknowledgement

This work was financially supported by a Grant of the RF President (Sci.Sh.-2349.2008.3).

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