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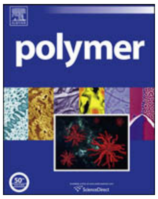

Polymer Communication

First [4 + 2] inverse electrodemand heterocycloaddition on oligoisoprenes

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ABSTRACT

The first [4 + 2] inverse electrodemand heterocycloaddition between hydroxytelechelic oligoisoprenes and the benzylidene pyruvic methyl ester promoted by tin tetrachloride is described. A partial hydrogenation of hydroxytelechelic oligoisoprenes was necessary to selectively promote the cycloaddition.

1. Introduction

The polymer design starting from a specific monomer can be sometimes a very difficult task due to both hard monomer synthesis and low polymerization process. Instead of monomer elaboration, an alternative route consists in the chemical modification of an existing polymer presenting electrophilic or unsaturated sites. In this respect, we are strongly involved in polyisoprene degradation leading to unsaturated oligomers [1] easy to handle and analyze. A simple and fast chain end chemical modification followed by polyaddition reactions can afford various polymers suchlike polyurethanes presenting elastomeric sequences. In this paper we focused on the double bonds' reactivity toward cycloaddition reactions and the possibility to build 6-membered rings along the oligoisoprene skeleton using reactive dienes. This kind of reaction is well described for small molecules elaboration either in homogeneous or in heterogeneous phase [2] but also in polymer chemistry [3]. Thus, 5 or 6-membered rings can be obtained with the opportunity of a large functional groups variety [4]. Dendrimers [5], various linear or crosslinked polymers [6] bearing either the diene or the dienophile part have been thus prepared. However, among the wide range of cycloaddition reactions performed, as far as we are concerned no mention of any [4 + 2] cycloadditions on polydienes is reported in the literature and only few examples implying [3 + 2] cycloadditions [7] are depicted. We present in this article the first [4 + 2] inverse electrodemand cycloaddition on oligoisoprenes implying the specific π-electron deficient benzylidene pyruvic methyl ester already used by Schreiber [8] and Dujardin [9] in their attempts to form substituted dihydropyrans on solid support.

2. Experimental section

2.1. Materials

Oligoisoprene precursor has been prepared according to a known procedure [1b]. Palladium on activated carbon (10%) and $SnCl_4$ 1 M in CH_2Cl_2 have been purchased from Acros and used without any further purification. Ethyl acetate, dichloromethane and tetrahydrofuran were used after standard distillation.

2.2. Instrumentation

2.2.1. Size exclusion chromatography (SEC)

Average molecular weights and molecular weight distributions of the different oligomers were measured using size exclusion chromatography (SEC) on a system equipped with a SpectraSYSTEM AS1000 autosampler, with a guard column (Polymer Laboratories, PL gel 5 µm Guard, 50 × 7.5 mm) followed by 2 columns (Polymer Laboratories, 2 PL gel 5 µm MIXED-D columns, 2 × 300 × 7.5 mm), with a SpectraSYSTEM RI-150 and a SpectraSYSTEM UV2000 detectors. The eluent used is THF at a flow rate of

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1 mL/min at 35 °C. Polystyrene standards (580–483 × 10^3 g/mol) were used to calibrate the SEC and molar masses are given in polystyrene equivalent (PS.Eq.).

2.2.2. NMR analysis

^{1}H NMR spectra were recorded on a Bruker 400 Fourier Transform spectrometer at 400.13 MHz, in $CDCl_3$ solutions using tetramethylsilane (TMS) as internal standard.

2.2.3. FTIR analysis

IR spectra were recorded on an FTIR Perkin–Elmer spectrophotometer, having a diamond ATR device (attenuated total reflection), between 4000 and 500 cm^{-1}.

2.2.4. Differential scanning calorimetry (DSC)

Differential scanning calorimetric determinations were performed on a Texas-Instrument DSC Q-100 with a heating rate of 10 °C/min under nitrogen atmosphere. The sample weight was about 20 mg. Calibration was achieved with indium as reference material.

2.3. Synthesis

2.3.1. Hydrogenation of oligoisoprene

2.3.1.1. Use of p-toluenesulfonyl hydrazide. To a solution of oligoisoprene **4** (2.01 g, $\overline{M}_n$: 1800 g/mol) in toluene (100 mL) is added *p*-toluenesulfonyl hydrazide (8.22 g, 44 mmol, 1.5 equiv) and the mixture is heated for 5 h. After filtration, the mixture is dried over $MgSO_4$, filtrated and evaporated under reduced pressure. The yellow viscous oil is dissolved in hexane and the oligomer is precipitated in methanol. The residue is again dissolved in hexane, dried over $MgSO_4$, filtrated and evaporated under reduced pressure to afford **5** in 46% yield.

2.3.1.2. Homogeneous phase catalytic reduction. A solution of oligoisoprene **4** (0.5 g, 7.35 mmol) and $RhCl(PPh_3)_3$ (0.07 g, 0.074 mmol, 1%) in AcOEt (15 mL) is mechanically stirred at 25 °C under hydrogen atmosphere (3 bars) for 48 h. The mixture is evaporated, dissolved in hexane and precipitated in methanol to afford **5** (see Table 1).

2.3.1.3. Heterogeneous phase catalytic reduction. A solution of oligoisoprene **4** (1.0 g, 14.7 mmol) and Pd/C (0.25 g, 1%) in toluene (15 mL) is mechanically stirred at 60 °C under hydrogen atmosphere (3 bars) for 5 h. The mixture is then filtrated and evaporated to afford **5** (see Table 1).

Table 1
Oligoisoprenes' partial hydrogenation.

Entry	Conditions	Hydrogenation rate (%) (isomerisation)[a]	Yield[b] (%)
1	*p*-Toluenesulfonyl hydrazide (1.5 equiv), toluene, reflux, 12 h	75 (67%)	67
2	*p*-Toluenesulfonyl hydrazide (1.5 equiv), toluene, reflux, 5 h	60 (46%)	46
3	H_2 (3 bars), $RhCl(PPh_3)_3$ (0.5%), AcOEt, 41 h, 25 °C	36 (7%)	100
4	H_2 (3 bars), $RhCl(PPh_3)_3$ (1%), AcOEt, 48 h, 25 °C	50 (17%)	100
5	H_2 (3 bars), Pd/C (10%), toluene, 24 h, 60 °C	95	82
6	H_2 (3 bars), Pd/C (10%), toluene, 5 h, 60 °C	54	79

[a] Remaining double bond isomerisation.

[b] Yield determined from the recovered materials' mass.

The partially hydrogenated oligoisoprene characterisation has been already fully described [1a]. $\overline{M}_n$ = 1900 g/mol; DPI = 1.7; T_g = −63 °C.

The hydrogenation rate is determined through NMR analysis by comparison of ethylenic proton integration at 5.1 ppm and that of the three protons of the methyl of the hydrogenated units at 0.85 ppm. Using the same methodology, the isomerisation rate is determined by comparison of different methyl integrations at 1.58 and 1.68 ppm.

Rate of hydrogenation: $(H_9/3)/((H_9/3)+H_3)$ where H_9 represents the integration value of the methylic protons of the hydrogenated units (9 in Fig. 1) and H_3 being the integration value of the ethylenic proton.

Rate of isomerisation: $H_{2trans}/(H_{2cis}+H_{2trans})$ where H_{2trans} is the integration value of the methyl of the *trans* 1,4-unit and H_{2cis} is the integration value of the methyl of the *cis* 1,4-unit.

2.3.2. Cycloaddition reactions

*2.3.2.1. Cycloaddition with 1-methylcyclohexene **1**.* $SnCl_4$ (100 µL, 0.1 equiv) is added to a mixture of benzylidene pyruvic methyl ester **2** (0.190 g, 1 mmol), and 1-methylcyclohexene (0.096 g, 1 mmol) in dichloromethane (4 mL) at an ice bath temperature. After 3 h stirring at 0 °C, a saturated $NaHCO_3$ solution is added. The aqueous phase is then extracted with dichloromethane (3 × 10 mL), and organic phases are dried over $MgSO_4$ and concentrated under reduced pressure to afford **1** as a yellow oil in 94% yield (270 mg) (Fig. 2).

^{1}H NMR of the major isomer ($CDCl_3$): 1.5 (m, 11H, H-6, H-7, H-8, H-9, H-10), 3.2 (m, 1H, H-4), 3.8 (s, 3H, H-11), 4.0 (m, 1H, H-5), 6.2 (s, 1H, H-3) and 7.3 (m, 5H, Ph).

*2.3.2.2. Cycloaddition on oligoisoprene **5**.* $SnCl_4$ 1 M in dichloromethane (210 µL, 0.1 equiv) is added to a mixture of benzylidene pyruvic methyl ester **2** (0.419 g, 2.1 mmol), and oligoisoprene **5** (0.342 g, 2.1 mmol) in dichloromethane (10 mL) at −23 °C. The mixture is then stirred for 24 h and additional $SnCl_4$ 1 M in dichloromethane (210 µL, 0.1 equiv) is again added. After 24 h, the solution is warmed to room temperature and hydrolysed with a saturated $NaHCO_3$ solution. The aqueous phase is then extracted with dichloromethane (3 × 20 mL), the organic phases are dried over $MgSO_4$ and concentrated under reduced pressure. The yellow oil is then washed with hexane to remove residual starting material leading to **5** in 83% yield (Fig. 3).

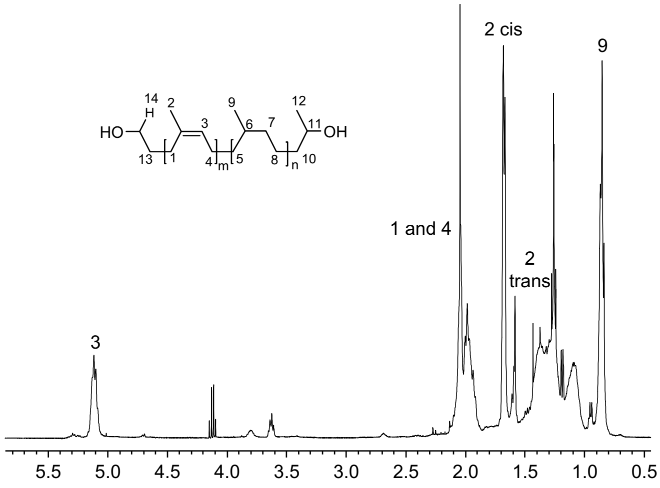


Fig. 1. 400 MHz proton NMR spectrum of partially hydrogenated oligoisoprene **5**.

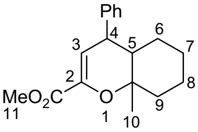
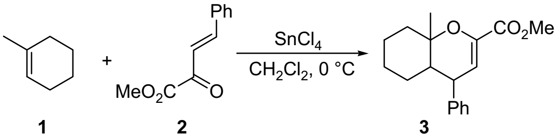
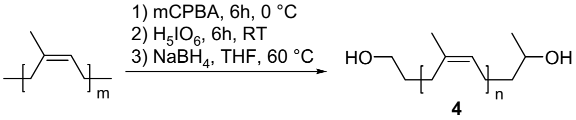


Fig. 2. Heteroadduct **3**.



Scheme 1. Heterocycloaddition between 1-methylcyclohexene and benzylidene pyruvic acid methyl ester.



Scheme 2. Preparation of oligoisoprene **4**.

^{1}H NMR (CDCl$_3$): 0.1–02 (m, aliphatic protons), 3.76–3.82 (m, H-17), 5.61–6.26 (m, H-16), 7.26 (m, H-18). IR: 3350, 1728, 1636, 1559, 1024 cm^{-1}. $T_g = 85$ °C. $\overline{M}_n = 2000$ g/mol.

3. Results and discussions

The first task was to demonstrate the ability of a dienophile to react with isoprene units in cycloaddition reaction (Scheme 1).

Assuming the fact that polyisoprene double bond presents a relatively low reactivity, we focused on benzylidene as a high reactive diene. A model reaction was performed using 1-methylcyclohexene in the presence of 0.1 equiv of tin tetrachloride by simply mixing the diene and dienophile in dichloromethane at 0 °C. The reaction was found to regioselectively proceed in 75% yield and the ^{1}H NMR analysis of the crude mixture revealed the presence of four diastereoisomers.

The first attempt performed on the oligoisoprene **4** (obtained in three steps from polyisoprene, Scheme 2) itself was conducted at room temperature using 1 equiv of diene. After 4 h reaction, no characteristic signals evolving from a cycloadduct moiety were observed by ^{1}H NMR analysis of the crude product despite a significant disappearance of the ethylenic protons. However, a very broad signal appearing between 0.5 and 2 ppm already mentioned by Christianson [10] tended to demonstrate that internal cyclisation evolved prior to cycloaddition (Scheme 3).

When the reaction was performed at lower temperature (0 °C, −78 °C) similar results were observed together with a decrease of the reaction rate as illustrated by high starting material recovery. This tends to demonstrate that intermediate tin derivatives evolved to more stable derivatives than cycloadducts.

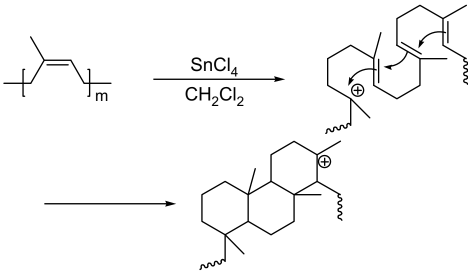
In order to overcome this non desired internal reaction, a partial hydrogenation of oligoisoprenes was undertaken using different hydrogenating systems. A 50% hydrogenation was focused so that no contiguous isoprenic entities remained. We first investigated a stoichiometric homogeneous hydrogenation using reactive diimide [11] obtained in situ by thermal decomposition of *para*toluene sulfonylhydrazide (TSH). However for this method, an excess of hydrazide was found to be necessary to partially hydrogenate the substrate, which renders the purification difficult and the yield moderate as already mentioned by Phinyocheep et al. [12]. In addition, a partial double bond isomerisation occurred during the reaction.

A catalytic homogeneous hydrogenation was then investigated using 1% Wilkinson catalyst in order to avoid any purification difficulties. In that case the desired hydrogenation rate was obtained, the reaction oligomers presenting nevertheless a predictable double bond isomerisation due to the rhodium intermediate β-elimination during the catalytic process [13].

Finally a standard heterogeneous hydrogenation was performed using palladium over charcoal by varying the reaction time (Table 1, entries 5 and 6). After 5 h stirring, the oligoisoprene **5** was obtained with the expected hydrogenation rate and without any further byproducts (Scheme 4).

This new half hydrogenated oligoisoprene **5** was finally engaged in a cycloaddition reaction with the benzylidene pyruvic methyl ester **2** as dienophile. Various reaction conditions were investigated (Table 2).

The first attempt realized after 3 h stirring at 0 °C (entry 1, Table 2) revealed by ^{1}H NMR analysis a complete disappearance of the isoprenic units double bond and the presence of the expected



Scheme 3. Example of internal cyclisation on polyisoprene structure.

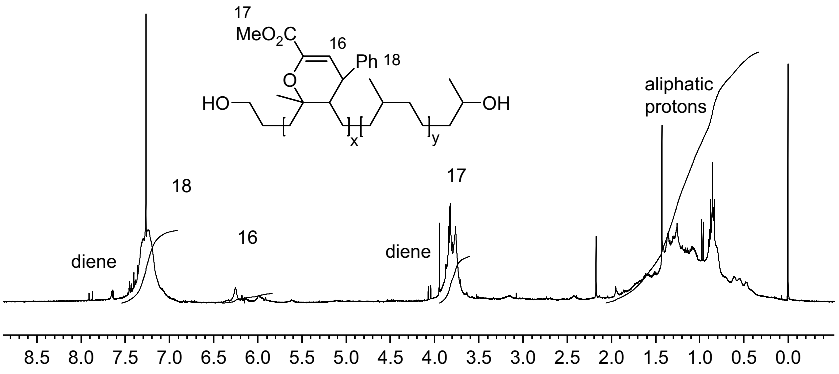
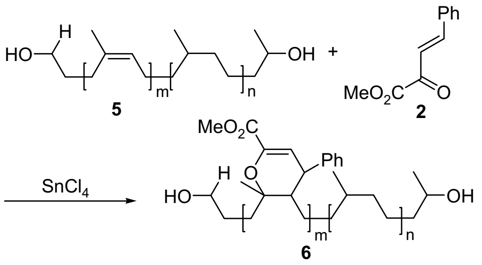


Fig. 3. 400 MHz proton NMR spectrum of oligoisoprene **6**.



Scheme 4. Cycloaddition on oligoisoprenes.

Table 2
Heterocycloaddition conditions.

Entry	Conditions	Promotor (equiv)	Conversion (%) (yield (%))
1	3 h, 0 °C	0.5	100 (76)
2	7 h, 0 °C	0.1	100 (80)
3	20 h, −23 °C	0.1	78 (85)
4	72 h, −23 °C	0.1	75 (92)
5	72 h, −23 °C	2 × 0.1	100 (83)

heterocyclic adducts. However an unidentified byproduct was obtained in significant amount. To minimize its formation, the amount of $SnCl_4$ was reduced in the second attempt (Table 2, entry 2). Furthermore the reaction temperature was lowered and the reaction time increased in the third attempt (Table 2, entry 3). This last experiment showed an almost total disappearance of ^{1}H NMR signals corresponding to this byproduct with concomitant presence of the cycloadducts. Finally, to reach a complete cycloaddition conversion, $SnCl_4$ in solution was added twice for 24 h at low temperature (Table 2, entry 5).

In this paper, we have described the first inverse electron demand [4 + 2] heterocycloaddition of a *cis*-1,4-oligoisoprene by the way of a selective partial hydrogenation leading to new polyheterocycles. Further investigations on these polyheterocycle modifications are in progress.

Acknowledgments

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