Technological aspects of synthesis of poly(ethylene glycol) mono-1-propenyl ether monomers

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For the first time, the technological aspects of the highly productive and selective synthesis of UV-reactive poly(ethylene glycol) mono-1-propenyl ether monomers was developed. The solvent-free isomerization of model commercial available 2-allyloxyethanol and allyloxypoly(ethylene glycol) derivatives, type Allyl–$[OCH_2CH_2]_n$–OH, n = 1–5, into a 1-propenyl derivative under the homogeneous catalysis conditions using the ruthenium complexes were evaluated. The effect of a various reaction conditions (i.e. the concentration of [Ru] complex, the reaction temperature, reaction gas atmosphere) together with trace amounts of allyl hydroperoxides formed via autoxidation reaction of allyl substrates on the productivity of catalyst was examined in detail. Moreover, the significant role of the allyl substrate structures on the catalytic activity of ruthenium catalysts were also recognized. The optimal parameters of the scaled-up synthesis together with productivity of catalyst were first established.

Keywords: polyethylene glycol allyl ether, 1-propenyl ether, isomerization, ruthenium complex, photopolymerization.

INTRODUCTION

Due to an increase of the environmental restrictions, the technology of UV-initiated radical or cationic polymerizations have attracted an increasing attention from years. These solvent-free and low-energy processes have employed in many thin film industrial applications such as coatings, adhesives, printing ink and many others because they could essentially eliminate air and water pollution[1–3]. The cationic photopolymerization process presents some industrial important advantages over the radical one, however, the growth of popularity of this method is hindered by the lack of easily available and highly reactive monomers, especially multifunctional ones. The most popular cationic UV-polymerizable resins are cycloaliphatic epoxides, vinyl ethers, oxetanes, oxazolines and others[1–3]. However, recently the structurally similar compounds, namely 1-propenyl ether monomers have been developed as a promising alternative to the vinyl monomer especially due to their high reactivity in photocurable applications[1–4] and very attractive from technological point of view methodology of the synthesis *via* isomerization of corresponding allyl ethers catalysed by ruthenium complexes under homogeneous conditions (Scheme 1)[5–7]. This strategy with using readily available of allyl ethers of alcohols, diols and polyols from both natural and synthetic sources and [RuCl$_2$(PPh$_3$)$_3$] was originally initiated and investigated by Crivello group[4] and postulated as easy and versatile method of synthesis of the UV-reactive mono-, di- and multifunctional 1-propenyl ether monomers. Our work in this area focused on wide and comprehensive studies of the reactions of multi-functional *O*-allyl systems with [Ru] complexes together with technological aspects of this processes[8–14] and also application of 1-propenyl ether monomers in UV curing polymeric systems[15–19].
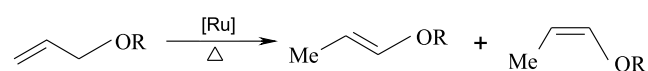
The 1-propenyl ethers bearing free hydroxyl groups of $CH_3CH=CH$-O-A-OH type (hydroxyalkyl 1-propenyl ethers, 1-propenyloxyalcohols) are the most desire as the reactive diluents for photopolymerizable systems with enhanced reactivity[15] or intermediates for the synthesis of hybrid monomers for special applications[1, 3]. It is well-known that the structure of A linker has decisive influence on its physicochemical properties, the course and rate photopolymerization, and also the structure and resulting properties of the cross-linked polymers[1, 3]. In this work, the low-molecular weight poly(ethylene glycol) (PEG) with precisely-defined numbers of PEG units were used as A linker. Generally, PEG is an industrially produced, relatively inexpensive, low or high molecular weight hydrophilic linear oligomer or polymer with a widely technical and medical applications[20–23]. Due to its excellent solubility in aqueous and organic media, flexibility of the main chain, non-toxicity and biocompatibility, the incorporation of PGE into 1-propenyl ether molecule give way for the commercial utility of these product as valuable fine chemicals for special applications.

As was mentioned above, the catalytic isomerization of allyloxyalcohol substrates is recognized as the best method of 1-propenyloxyalcohol synthesis. The low-molecular-weight poly(ethylene glycol) monoallyl ethers (APEG) with defined-length PGE are commercially produced via ethoxylation of allyl alcohol by ethylene oxide at the presence of alkaline catalysts such as NaOH KOH or Na$_2$CO$_3$[20]. Despite 2-allyloxyethanol is the simplest example of an ethoxylated alcohol containing an allyl ether group, only a few reports of its isomerization have been found in the literature. For example the using Pd/C (5%) as the heterogeneous palladium catalyst gave only 41% yield of the 2-(1-propenyloxy)ethanol during 2 h under harsher conditions at 150°C[24]. Interestingly, under homogeneous conditions only a few soluble Ru(II) complexes[10, 12, 25] or non-technological *t*-BuOK in DMSO system[22] were applied. Besides our preliminary reports regarding the quantitative yielded and solvent-less synthesis of 1-propenyloxyethanol with [RuClH(CO)(PPh$_3$)$_3$][8]

Scheme 1. The general scheme of the isomerization of allyl ethers catalyzed by the ruthenium complexes

or $[RuH_2(CO)(PPh_3)_3]^{12}$, only $[Ru(H_2O)_6(tos)_2]$ at a very high amount of 7 mol.% in water at the temperature of 40^oC during 6 h was used[25]. Thus, the synthesis of 1-propenyloxyethanol is still a challenging task. Moreover, the information regarding the isomerization of other allyloxyalcohols functionalized by linear poly(ethylene glycol) (PEG) chain are very scarce in the literature. Therefore, the aim of this study was to investigate in detail the isomerization reaction of 2-allyloxyethanol, 2-[2-(allyloxy)etoxy]ethanol and also other allyloxypoly(ethylene glycol) derivatives with precisely-defined numbers of PEG units, type Allyl–$[OCH_2CH_2]_n$–OH, $n = 1–5$, catalyzed by soluble ruthenium(II) complexes with some important technological aspects of this process (vide infra).

EXPERIMENTAL

Materials

The allyloxyalcohol substrates (purity>98%) (commonly called as allyloxy(polyethylene oxide) or allyl alcohol polyoxyethylene ethers, APEG, CAS#27274-31-3) i.e. 2-allyloxyethanol (Allyl-PEG_1-OH), 2-[2-(allyloxy)etoxy]ethanol (Allyl-PEG_2-OH), 2-{2-[2-(allyloxy)etoxy]ethoxy}ethanol (triethylene glycol monoallyl ether, Allyl-PEG_3-OH), tetraethylene glycol monoallyl ether (Allyl-PEG_4-OH), pentaethylene glycol monoallyl ether (Allyl-PEG_5-OH), the ruthenium catalyst precursors and also K_2CO_3 were commercial products (Aldrich, Merck, POCh Gliwice) or were obtained via well-known method synthesis describes in the literature. The concentration of allyl hydroperoxides (AHP) in allyl substrate was determined via Quantofix® peroxides test sticks colorimetric method. The traces of AHP were removed by reduction with PPh_3 (0.5 wt%) at room temperature with using magnetic stirrer and next vacuum distillation (2-allyloxyethanol bp: 46^oC/5 mmHg; Allyl-PEG_2-OH bp: 72^oC/0.5 mmHg; Allyl-PEG_3-OH bp: 107^oC/1 mmHg; Allyl-PEG_4-OH bp: 142^oC /0.8 mmHg; Allyl-PEG_5-OH bp: $141–143^oC$/0.16 mmHg). For generating of AHP at the required concentration of 25 ppm, the pure allyl substrates were sonicated at frequencies of 40 kHz during appropriate time at the temperature in the range $25–55^oC$, if necessary.

The general methodology of isomerization reaction

The isomerization reactions were conducted under solvent-free conditions and under the air or argon atmosphere using the Schlenk method according to the procedure described by us previously[12–14]. The allyl substrate (5 mmole) was placed into screw-capped glass ampoules together with ruthenium complex and stirred for given period time (the reaction conditions are given in footnotes of Table 1 and 2). In turn, all experiments in preparative scale were conducted using 0.3 mole (31 g) of 2-allyloxyethanol in a round-bottom flask with a red rubber septa (Sigma-Aldrich) and a magnetic stirrer under the argon atmosphere. The samples were taken at various times during the experiment using a glass syringe and analyzed.

The isomerization reactions were monitored by gas chromatography (Trace Ultra GC (Thermo Scientific), column Rtx-1 with length: 30 m, diameter: 0.53 mm, thickness of the film: 1,5 μm (Restek) and FID detector) or/and ^1H NMR (Bruker DPX-400 spectrometer in $CDCl_3$ containing TMS as the chemical shift standard, and K_2CO_3 as the HCl scavenger) or/and GC-MS analyses (optional) (gas chromatograph Hewlett Packard 6890 coupled to a mass spectrometer HP 5973 with electron impact ionization). The main 1-propenyloxyalcohol products obtained as an mixture of *Z* and *E* isomers were purified via vacuum distillation above ruthenium catalyst (for spectroscopic data see reference[14]).

The isomerization progress was evaluated in terms of the allyl group conversion (α_{AE}), the selectivity of the reaction to 1-propenyloxyalcohol (S_{PA}) together with the stereoselectivity given as the percentage of *E*-1-propenyl group (*%E*) and the selectivity of the reaction to products of intra- and/or intermolecular addition of an OH group to the double bond (S_{AP}). Moreover, the activity of [Ru] pre-catalyst, determined as the turnover number (TON) and the turnover frequency (TOF, h^{-1}) was calculated according to the following formulas:

$$TON = n_p / n_{[Ru]} \cdot y_p \qquad TOF = TON / \tau$$

where:

n_p – the number of moles of the 1-propenyloxyalcohol product formed; $n_{[Ru]}$ – the number of mole of the [Ru]

Table 1. The activity of selected ruthenium complexes as homogeneous pre-catalysts in the reaction of 2-allyloxyethanol under various reaction conditions

Pre-catalyst (0.1 mol%)	time (h)	Temperature of 80˚C			Temperature of 120˚C		
		argon atmosphere	argon atmosphere	air atmosphere	argon atmosphere	argon atmosphere	air atmosphere
		0 ppm AHP	25 ppm AHP	0 ppm AHP	0 ppm AHP	25 ppm AHP	0 ppm AHP
		α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)
[RuClH(CO)(PPh_3)_3]	0.5	100, 100 (44),	100, 100 (39), –	100, 100 (44), –	100, 100 (44), –	100, 99 (44), 1	100, 100 (44), –
	2	100, 100 (44), –	100, 100 (42), –	100, 100 (44), –	100, 99 (44), 1	100, 96 (45), 4	100, 98 (44), 2
[RuClH(CO)(AsPh_3)_3]	0.5	63, 100 (80), –	55, 100 (89), –	50, 100 (78), –	100, 90 (62), 10	93, 84 (65), 16	100, 93 (56), 7
	2	73, 100 (79), –	64, 100 (86), –	74, 100 (75), –	100, 81 (57), 19	100, 36 (83), 65	100, 89 (51), 11
[RuH_2(CO)(PPh_3)_3]	0.5	22, 100 (43), –	5, 100 (38), –	14, 100 (43), –	54, 100 (42), –	20, 100 (46), –	46, 100 (44), –
	2	44, 100 (44), –	10, 100 (43), –	29, 100 (42), –	82, 100 (42), –	46, 100 (44), –	64, 100 (44), –
[RuH_2(PPh_3)_4]	0.5	10, 100 (54), –	0, –, –	10, 100 (53), –	38, 100 (48), –	18, 100 (47), –	38, 100 (47), –
	2	14, 100 (48), –	8, 100 (65), –	14, 100 (51), –	68, 100 (44), –	41, 100 (47), –	58, 100 (49), –
[RuCl_2(PPh_3)_3]	0.5	100, 100 (44), –	64, 100 (59), –	78, 100 (46), –	100, 84 (44), 16	100, 74 (57), 26	100, 88 (44), 12
	2	100, 94 (47), 6	83, 100 (58), –	86, 94 (52), 6	100, 82 (44), 18	100, 35 (65), 65	100, 83 (44), 17
{[RuCl_2(*p*-Cym)]_2}	0.5	12, 56 (100), 44	38, 68 (100), 32	13, 58 (100), 42	100, 47 (72), 53	96, 37 (67), 63	98, 58 (64), 42
	2	66, 36 (100), 68	75, 57 (100), 43	64, 46 (100), 54	100, 37 (51), 63	100, 32 (52), 68	100, 57 (50), 43

The reaction conditions: 5 mmole scale of allyl ether; 0.1 mol% of [Ru]; AHP – the allyl hydroperoxides from allyl substrate ; α_{AE} – the conversion of allyl substrate, S_{PA} – the reaction selectivity to 1-propenyloxyalcohol, (%E) – the percentage of *(E)*-1-propenyl group, S_{AP} –the reaction selectivity to cyclic 2-ethylacetal;

Table 2. The activity of selected ruthenium complexes as homogeneous pre-catalysts in the isomerization of 2-[2-(allyloxy)etoxy] ethanol under various reaction conditions

Pre-catalyst (0.1 mol%)	time (h)	Temperature of 80°C			Temperature of 120°C		
		argon atmosphere	argon atmosphere	air atmosphere	argon atmosphere	argon atmosphere	air atmosphere
		0 ppm AHP	25 ppm AHP	0 ppm AHP	0 ppm AHP	25 ppm AHP	0 ppm AHP
		α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)	α_{AE}, S_{PA} (%E), S_{AP} (%)
[RuClH(CO)(PPh$_3$)$_3$]	0.5	100, 100 (38), –	100, 100 (39), –	100, 100 (38), –	100, 98 (43), 2	100, 98 (43), 2	100, 100 (43), –
	2	100, 100 (43), –	100, 100 (43), –	100, 100 (43), –	100, 93 (42), 7	100, 92 (42), 13	100, 94 (42), 6
[RuClH(CO)(AsPh$_3$)$_3$]	0.5	99, 99 (80), 1	95, 100 (73), –	94, 100 (78), –	100, 87 (56), 13	100, 86 (69), 14	100, 91 (55), 9
	2	100, 98 (74), 2	100, 98 (70), 2	99, 98 (69), 2	100, 64 (48), 36	100, 49 (69), 51	100, 70 (51), 30
[RuH$_2$(CO)(PPh$_3$)$_3$]	0.5	51, 100 (36), –	6, 100 (33), –	24, 100 (40), –	100, 100 (40), –	46, 100 (50), –	100, 100 (40), –
	2	87, 100 (32), –	10, 100 (31), –	68, 100 (45), –	100, 100 (42), –	92, 100 (48), –	100, 100 (41), –
[RuH$_2$(PPh$_3$)$_4$]	0.5	18, 100 (51), –	9, 100 (52), –	15, 100 (53), –	84, 100 (42), –	31, 100 (52), –	77, 100 (46), –
	2	31, 100 (42), –	14, 100 (47), –	37, 100 (51), –	98, 100 (42), –	77, 100 (47), –	93, 100 (46), –
[RuCl$_2$(PPh$_3$)$_3$]	0.5	100, 98 (61), 2	86, 98 (57), 2	100, 98 (61), –	100, 59 (42), 41	100, 62 (42), 38	100, 68 (42), 32
	2	100, 94 (46), 6	100, 90 (54), 10	100, 94 (57), 6	100, 23 (43), 77	100, 21 (43), 79	100, 39 (49), 61
{[RuCl$_2$(p-Cym)]$_2$}	0.5	33, 77 (74), 23	45, 68 (100), 32	27, 80 (100), 20	71, 15 (100), 85	65, 24 (100), 76	94, 25 (64), 75
	2	62, 52 (100), 47	69, 48 (100), 52	51, 61 (88), 39	100, 11 (82), 89	96, 8 (100), 92	100, 15 (53), 85

The reaction conditions: 5 mmole scale of allyl ether; 0.1mol% of [Ru]; AHP – the allyl hydroperoxides from allyl substrate; α_{AE} – the conversion of allyl substrate, S_{PA} – the reaction selectivity to 1-propenyloxyalcohol, (%E) – the percentage of (*E*)-1-propenyl group, S_{AP} –the reaction selectivity to cyclic 2-ethylacetal.

catalyst; y_p – the yield of 1-propenyloxyalcohol product; τ – the reaction time.

RESULTS AND DISCUSION

Generally, the difficulty of the conducting high selective and yielded the isomerization of the allyloxyalcohols at the presence of [Ru] complexes is connected with the fact that this reaction could leads to 1-propenyl derivatives and also products of the intra- and/or intermolecular addition of an OH group to the double bond, depending on kind of [Ru] catalyst and the temperature of reaction[10–12] (Scheme 2). Moreover, in the case of the 2-allyloxyethanol and its allyloxypoly(ethylene glycol) derivatives the activity of ruthenium catalysts and the relative rates of isomerization reactions could be strongly affected both by temporary chelation of ruthenium by the oxygen atoms from ethoxy groups (or/and C=C of η^3-allylic bond) (postulated for the diallyl ethers in the literature previously[26], including our work[9]) and also by the availability of the OH-group to formation (or reproduction) of the hydride or dihydride active species of the ruthenium catalyst. On the other hand, the allyloxypoly(ethylene glycol) derivatives type Allyl–[OCH$_2$CH$_2$]$_n$–OH, n = 1–5 are very good allyl substrates for the [Ru]-catalyzed isomerization due to fact, that they undergo the autoxidation reaction very slowly or they do not practically react with oxygen during storage of a pure substrate. Therefore, the concentration of allyl hydroperoxides (AHP), which often cause decrease or even deactivate of the [Ru] catalyst is ultra-traces. For example, in the case of Allyl-PEG$_3$-OH only 5–10 ppm
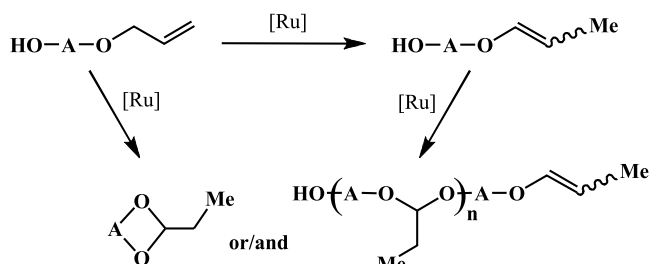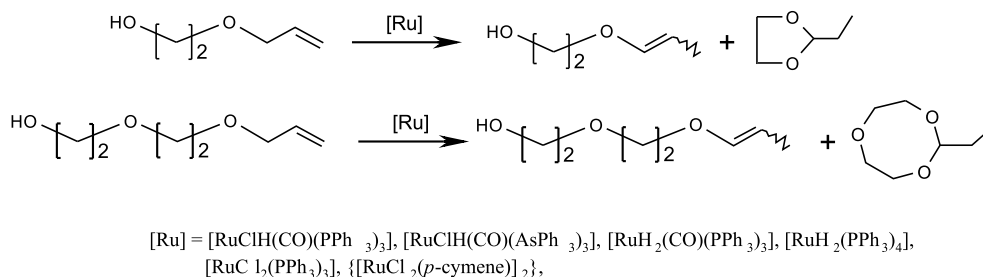
of AHP were detected within 10 months of storage under refrigeration and air atmosphere, while Allyl-PEG$_5$-OH did not undergoes autoxidation.

So, in order to explore the efficacy of [Ru] pre-catalyst the detailed screening of the reaction parameters on the 1-propenyl ethers product yields was conducted. Initially, the allyl substrate i.e. the 2-allyloxyethanol (Allyl-PEG$_1$-OH) and 2-[2-(allyloxy) ethoxy]ethanol (Allyl-PEG$_2$-OH) were used together with the ruthenium complexes (hydride [RuClH(CO) (PPh$_3$)$_3$], [RuClH(CO)(AsPh$_3$)$_3$], dihydride [RuH$_2$(CO) (PPh$_3$)$_3$], [RuH$_2$(PPh$_3$)$_4$], and non-hydride (dichloride) [RuCl$_2$(PPh$_3$)$_3$], {[RuCl$_2$(p-cymene)]$_2$}) as homogeneous pre-catalysts, under solvent-free oxidative or non--oxidative conditions. The isomerization reactions were conducted at the concentration of [Ru] complex of 0.1 mol% and at moderate temperature of 80°C or 120°C under argon or air atmosphere. Moreover, the possibility of using allyl substrate containing allyl hydroperoxides (AHP) and without additional purification was also tested as one of the key technological aspects of this process. The results for Allyl-PEG$_1$-OH and Allyl-PEG$_2$-OH were collected in Table 1 and Table 2, respectively.

Firstly in should be pointed that the reaction of 2-allyloxyethanol and 2-[2-(allyloxy)etoxy]ethanol with [Ru] complexes run exclusively towards the isomerization products i.e. 1-propenyloxyalcohols given as mixture of *Z* and *E* isomers of 2-(1-propenyloxy)ethanol and 2-[2-(1-propenyloxy)ethoxy]ethanol) and/or towards the intramolecular addition of an OH group to the double bond (cyclization) products given as 2-ethylacetals i.e. 2-ethyl-1,3-dioxolane and 2-ethyl[1,3,6]trioxane, respectively (Scheme 3). Secondly, the results revealed in Table 1 and Table 2 have clearly shown that the catalytic activity of [Ru] complexes varied dramatically depending on the allyl substrate structure, the pre-catalyst used and also the reaction conditions, especially the reaction temperature. Moreover, the presence of the oxidative factors i.e. the allyl hydroperoxide (the allyl substrate impurities) or the oxygen from the air have also a significant effect on the activity of the catalyst but they no change essentially the reaction chemoselectivity towards 1-propenyl ethers or acetals. And finally, the comparison the results obtained

Scheme 2. The general scheme of the reaction of hydroxyalkyl allyl ethers (allyloxyalcohols) with the ruthenium(II) complexes

[Ru] = [RuClH(CO)(PPh₃)₃], [RuClH(CO)(AsPh₃)₃], [RuH₂(CO)(PPh₃)₃], [RuH₂(PPh₃)₄],
[RuCl₂(PPh₃)₃], {[RuCl₂(p-cymene)]₂},

Scheme 3. The transformations of 2-allyloxyethanol and 2-[2-(allyloxy)etoxy]ethanol in the presence of the [Ru] complexes

showed also that in general 2-[2-(allyloxy)etoxy]ethanol is a much more reactive as 2-allyloxyethanol.

So, in the case of Allyl-PEG₁-OH and Allyl-PEG₂-OH at the reaction temperature of 80°C only [RuClH(CO)(PPh₃)₃] appeared to be the most active and selective pre-catalyst – the reaction proceeded with a quantitative yield of 1-propenyl ether derivatives within a very short reaction time of 0.5 h (Table 1 and Table 2). What is important, regardless of the oxidative reaction conditions the activity and the chemoselectivity of reaction was maintained for prolonged time of 2 h. However, at the higher temperature of 120°C, reaction of Allyl-PEG₁-OH with [RuClH(CO)(PPh₃)₃] was stopped on the isomerization step in contrast to Allyl-PEG₂-OH, where the 2-ethyl[1,3,6]trioxane with the relatively high yields from 2 to 13% was observed. Remarkably, the very fast and selective isomerization towards the 1-propenyl derivative was also detected for [RuCl₂(PPh₃)₃] – at the temperature of 80°C the reaction time of 0.5 h was sufficient to obtain the yield of 100% of 2-(1-propenyloxy)ethanol under non-oxidative reaction conditions (Table 1). However, at the higher temperature of 120°C and in the case of 2-[2-(allyloxy)etoxy]ethanol and the reaction selectivity was unacceptable – the mixture of 1-propenylalcohol and cyclic acetal was observed (Table 2). The use of the oxidative conditions practically did not affect the selectivity values. Moreover, the most significant differences in the reactivity of allyl substrates tested were revealed for less active ruthenium complexes such as hydride [RuClH(CO)(AsPh₃)₃] or dihydride [RuH₂(CO)(PPh₃)₃] and [RuH₂(PPh₃)₄]. Surprisingly, these pre-catalysts exhibited an unexpectedly low activity in the 2-(1-propenyloxy)ethanol synthesis, especially at lower temperature of 80°C (Table 1). Interestingly, the introduction into hydride ruthenium molecule of [RuClH(CO)L₃] of triphenylarsine ligand instead triphenylphosphine caused not only lower yield of 1-propenyl product up to ca. 73% but also a substantial changes in the stereoselectivity of isomerization (the thermodynamically favored *E*-isomer was the major product, %*E* amounted ca. 80–90% at temperature of 80°C) and also in the selectivity of cyclization (the yield of 2-ethyl-1,3-dioxolane equaled even 65% at temperature of 120°C and at the presence of AHP at the concentration as low as 25 ppm) (Table 1). The similar trend was observed for Allyl-PEG₂-OH/[RuClH(CO)(AsPh₃)₃] reaction system, however the practically quantitative conversion values were noted (Table 2). In turn, the using dihydride [Ru] complexes, especially [RuH₂(CO)(PPh₃)₃] as extremely selective isomerization pre-catalysts are the more technologically attractive catalytic systems of the 1-propenyloxyalcohols synthesis but they require the application of the higher temperatures of reaction

(minimum at 120°C). It should be also noted that the quantitative yield of 2-(1-propenyloxy)ethanol was detected for a prolonged reaction time of 3 h (after 2 h: the yield of only 82% was achieved under non-oxidative conditions, see Table 1) while a more reactive 2-[2-(1-propenyloxy)ethoxy]ethanol underwent a rapid and 100% yielding isomerization under AHP-free conditions within only 0.5 h and also under air atmosphere (Table 2). In a group of the non-hydride dichloride [Ru] complexes, contrary to [RuCl₂(PPh₃)₃], the non-phosphine complex such as {[RuCl₂(p-cymene)]₂} exhibited a high activity in the studied reactions only at the higher temperature of 120°C, but the main products were cyclic acetals, so it is not appropriate for 1-propenylalcohols synthesis.

From the process development perspective, the most active and selective [Ru] pre-catalysts such as [RuClH(CO)(PPh₃)₃], [RuH₂(CO)(PPh₃)₃] and [RuCl₂(PPh₃)₃] were selected for the isomerization of other tri-, tetra and penta(ethylene glycol) monoallyl ethers (Allyl-PEGₙ-OH, n = 3,4,5) under the same reaction conditions. However, it should be noted that the autoxidation reaction of those allyloxyalcohols with forming allyl hydroperoxides at the desired concentration of 25 ppm proceeded very slow during storage of a pure substrate. As was mentioned above, in the case of Allyl-PEG₃-OH only 5–10 ppm of AHP were detected within 10 months of storage under refrigeration and air atmosphere. For accelerating the autoxidation reaction and obtaining the Allyl-PEG₃-OH containing 25 ppm of allyl hydroperoxides, the sonification method at frequencies of 40 kHz within 3 days was successfully used. However, Allyl-PEG₄-OH and Allyl-PEG₅-OH practically did not undergo this reaction even under ultrasound conditions within 10 days. So, the reaction of both Allyl-PEG₄-OH and Allyl-PEG₅-OH with [Ru] complexes were conducted only under argon (non-oxidative conditions) or air (oxidative conditions) atmosphere.

Generally, the obtained results for allyloxyalcohols with tri-, tetra and penta(ethylene glycol) chains confirm the catalytic behavior of [RuClH(CO)(PPh₃)₃], [RuH₂(CO)(PPh₃)₃] and [RuCl₂(PPh₃)₃] complexes observed previously for 2-allyloxyethanol and 2-[2-(allyloxy)etoxy]ethanol. Consequently, the hydride complex [RuClH(CO)(PPh₃)₃] appeared to be the most active and selective pre-catalyst for the isomerization of all tested allyloxy tri-, tetra and penta(ethylene glycol) derivatives, the dihydride complex [RuH₂(CO)(PPh₃)₃] was the most selective but less active than both [RuClH(CO)(PPh₃)₃] and [RuCl₂(PPh₃)₃], and [RuCl₂(PPh₃)₃] exhibited very high activity (the allyl group conversions was 100%) but low selectivity toward 1-propenyl products. However, it is also important to noted that in the presence of

[RuCl$_2$(PPh$_3$)$_3$] the oligomeric linear acetal products of intermolecular addition of an OH group to the double bond together with oligomerization reaction were formed even at the lower temperature of 80°C. Thus, the popular ruthenium complex i.e. neat [RuCl$_2$(PPh$_3$)$_3$] can be not recommended for the reaction of these high molecular weight allyloxyalcohol substrates.

Figure 1 and Figure 2 present the values of 1-propenyoxyalcohols yield formed during isomerization reaction of AHP-free allyl substrates type Allyl-PEG$_n$-OH, where n = 3,4,5 catalyzed by 0.1 mol% [RuClH(CO)(PPh$_3$)$_3$] under argon or air atmosphere at temperature of 80°C or 120°C, respectively (the results for the Allyl-PEG$_1$-OH and Allyl-PEG$_2$-OH given in Table 1 and Table 2 were also added for comparison). As can be seen in Figure 1, the hydride complex [RuClH(CO)(PPh$_3$)$_3$] exhibits very high activity and selectivity in the isomerization of all tested allyloxy tri-, tetra and penta(ethylene glycol) derivatives, but in the first step of the reaction at the temperature of 80°C after a short reaction time of 0.5 h the values of allyl substrate conversion gradually decre-
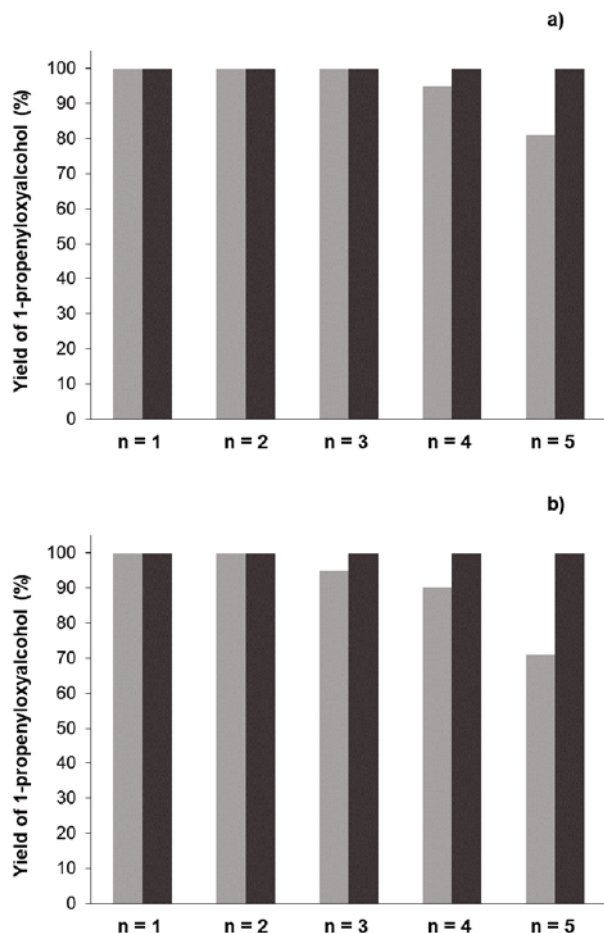
ased with the length of PEG chain under both argon and air atmosphere. However, the prolongated reaction time of 2 h was enough to obtain a 100% yield values of 1-propenyloxyalcohols. On the other hand, at 120°C the activity of [RuClH(CO)(PPh$_3$)$_3$] was practically the same, independently of the allyl substrate and the reaction gas atmosphere. The quantitative values of allyl group conversion and the yield of 1-propenyl products were determined but after 2 h of processes the values of selectivity of isomerization dropped from 100% to ca. 93–98% (Fig. 2).

The selected results of catalytic activity of [RuH$_2$(CO)(PPh$_3$)$_3$] in the isomerization of allyloxy tri-, tetra and penta(ethylene glycol) derivatives under non-oxidative conditions at the reaction temperature of 80°C and 120°C were presented on Figure 3 (for clarification, the values of yield of 1-propenyloxyalcohols under air atmosphere were slightly lower than under argon atmosphere, especially during the initial reaction period, so, for this reason these results were disregarded on the graph). The comparison of 1-propenyloxyalcohols yield values shows
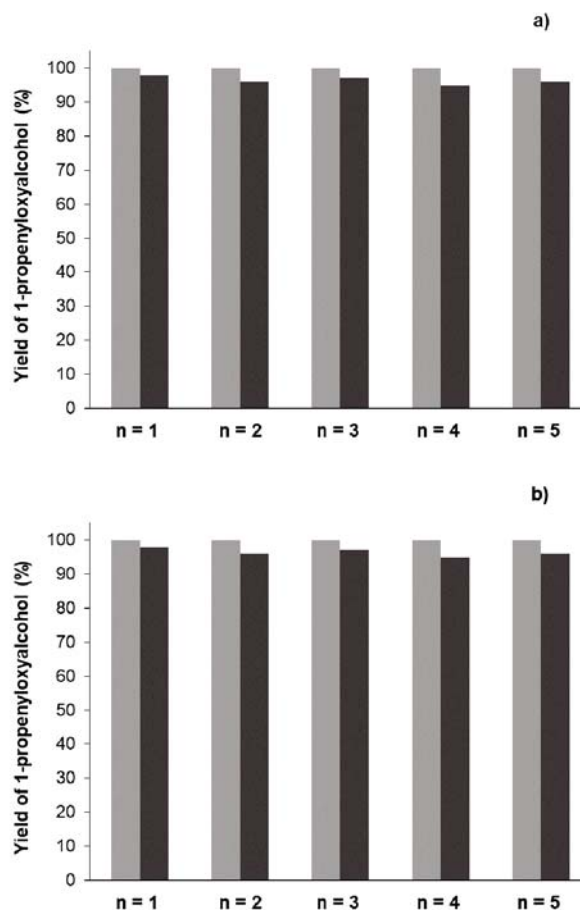

Figure 1. Variation of the yield of 1-propenyloxyalcohols achieved during the solvent-free isomerization of hydroperoxide-free allyloxypoly(ethylene glycol) derivatives type Allyl-PEG$_n$-OH where n = 1, 2, 3, 4, 5 catalyzed by 0.1 mol% of [RuHCl(CO)(PPh$_3$)$_3$] at reaction temperatures of 80°C under argon (a) or air (b) atmosphere after reaction time of 0.5 h (▨) and 2 h (■) (the reaction conditions: scale 5 mmole, the ratio of *Z* and *E* isomers in the all post-reaction mixture was practically constant ca. 60–62% of *Z* isomer)

Figure 2. Variation of the yield of 1-propenyloxyalcohols achieved during the solvent-free isomerization of hydroperoxide-free allyloxypoly(ethylene glycol) derivatives type Allyl-PEG$_n$-OH where n = 1, 2, 3, 4, 5 catalyzed by 0.1 mol% of [RuHCl(CO)(PPh$_3$)$_3$] at reaction temperatures of 120°C under argon (a) or air (b) atmosphere after reaction time of 0.5 h (▨) and 2 h (■) (the reaction conditions: scale 5 mmole, the ratio of *Z* and *E* isomers in the all post-reaction mixture was practically constant ca. 60–62% of *Z* isomer)

that at the temperature of 80°C the isomerization rate visibly increased in the order 2-allyloxyethanol < tri-, tetra and penta(ethylene glycol) monoallyl ethers << 2-[2-(allyloxy)ethoxy]ethanol (after 2 h the yield values equaled 44%, ca. 60% and 87%, respectively) while at the temperature of 120°C and reaction time of 2 h the differences in reactivity of tri-, tetra and penta-PEG and di-PEG allylalcohol derivatives are much smaller ca. 1−4% (vs. 80% for 2-allyloxyethanol). Interestingly, in the presence of $[RuH_2(CO)(PPh_3)_3]$ only 2-[2-(allyloxy)ethoxy]ethanol undergoes very fast isomerization reaction with a quantitative yield of corresponding 1-propenyloxy-alcohol. Therefore, it is clear that the structure of allyl substrate (here − the number of PEG groups in the molecule only) has a crucial influence on the reaction rate, especially in the first step of the reaction up to 30 min. and at lower temperature of 80°C. Moreover, it is reasonable to suggest that the temporary decreasing of isomerization rate is connected with the chelation of ruthenium by the oxygen atoms from ether and the
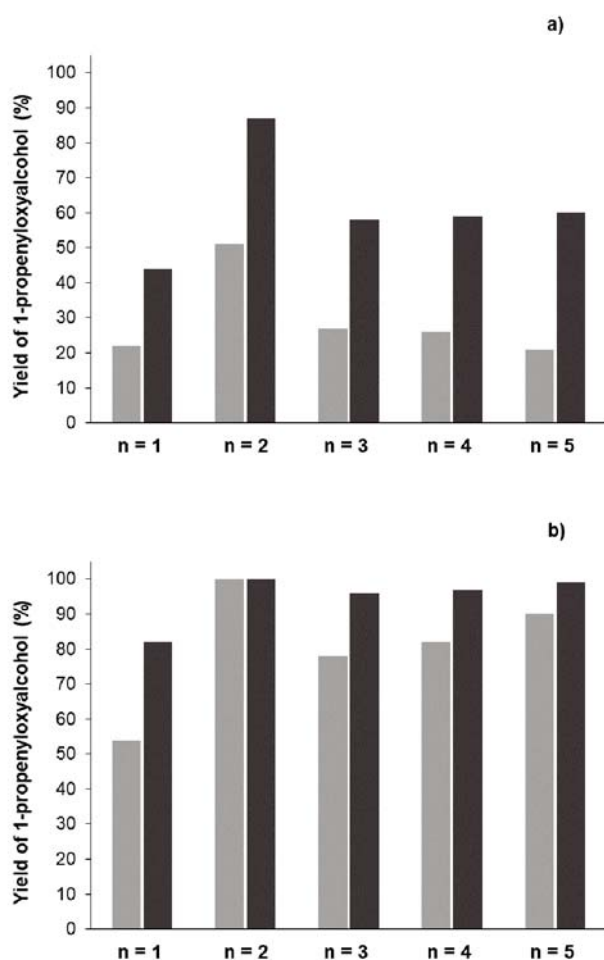
OH-group and also by the double bond carbon atoms. To confirm our hypothesis the minimum energy structure of tested poly(ethylene glycol) mono allyl ethers can be determined from MM calculation using the MM2 program[27] (Fig. 4) together with models of plausible ruthenium complex with them temporary formed during reaction[28] (Fig. 5).

As can be seen, the low reactivity of 2-allyloxyethanol could be first explain by relatively strong coordination of Ru by oxygen atoms with forming temporarily stable five-member ring, additionally stabilized by Ru–(C=C) bond from allyl or 1-propenyl group (3-dentate structure) (Fig. 5). In turn, in the case of 2-[2-(allyloxy)ethoxy] ethanol simultaneous oxygen atoms chelation together with C=C bond to form 3- or 4-dentate structure of eight-member ring has relatively low probability and in consequence the isomerization rate substantially increase
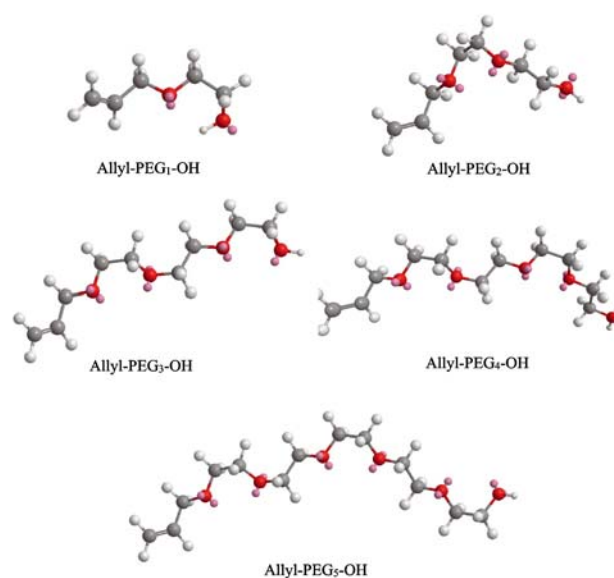

Figure 4. Proposed energy minimized (MM2) structures of allyloxypoly(ethylene glycol) derivative substrates

(Fig. 5). For the remaining allyl substrates containing 3, 4 or 5 of ethoxy spacers in molecule the chelation of Ru by oxygen atoms is also negligible. Moreover, it was demonstrated in the literature[5–7, 26] and also in our papers[9, 12–14] that the double bond migration reaction catalysed by hydride transition metals complexes do-minantly runs via the hydride addition – β elimination mechanism (1,2-hydrogen shift) with the preferential *Z* isomer formation. Additionally, the hydroxyl group of the allyloxyalcohol substrate (functional primary alkyl alcohol) might play the key role in the formation (or reproduction) of the hydride or dihydride active spe-cies of the catalyst in situ. Thus, in contrast to other tested allyloxyalcohols, the very easily availability of the -OH group to Ru atom in 2-[2-(allyloxy)ethoxy]ethanol molecule maintains or increases the activity of ruthenium hydride or dihydride catalyst and, in this way, contribute to acceleration of isomerization (Fig. 5).

Considering the technological aspects of the efficient high-yielded synthesis of 1-propenyloxyalcohols func-tionalized by linear poly(ethylene glycol) (PEG) chain some experiments were undertaken including the deter-
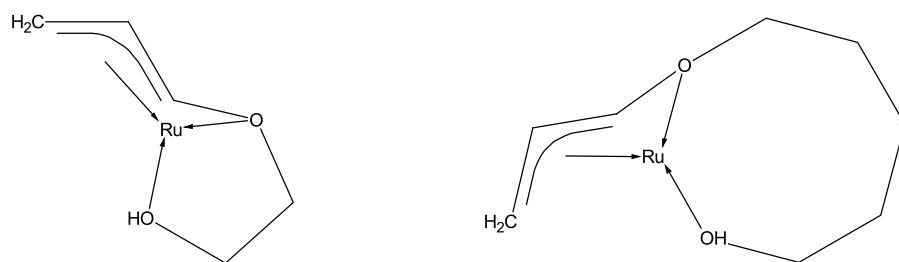

Figure 3. Variation of the yield of 1-propenyloxyalcohols achieved during the solvent-free isomerization of hydroperoxide-free allyloxypoly(ethylene glycol) derivatives type Allyl-PEG_n-OH where n = 1, 2, 3, 4, 5 catalyzed by 0.1 mol% of $[RuH_2(CO)(PPh_3)_3]$ at reaction temperatures of 80°C (a) or 120°C (b) under argon atmosphere after reaction time of 0.5 h (▨) and 2 h (■) (the reaction conditions: scale 5 mmole, the ratio of *Z* and *E* isomers in the all post-reaction mixture was practically constant ca. 50–60% of *Z* isomer)

Figure 5. Plausible structure of complexes formed via temporary coordination of ruthenium by 2-allyloxyethanol or 2-[2-(allyloxy) etoxy]ethanol

mination of the optimized reaction conditions with the high effectiveness of Ru catalyst, the possibility of using allyl substrate without additional purification (containing AHP) and also the scaling up of process. For this purpose, the solvent-free isomerization of the 2-allyloxyethanol catalyzed by a particularly active [RuClH(CO)(PPh₃)₃] was selected as a model reaction system. All experiments were conducted using 0.3 mole of 2-allyloxyethanol. The reaction was investigated in the range of minimal pre--catalyst concentration of 0.01–0.05 mol% under non--oxidative reaction conditions or when the allyl substrate contained the traces of allyl hydroperoxides at the level of ca. 10 ppm (we had established that only a trace amount ca. 5–10 ppm of the AHP was detected during storage of a pure substrate during ca. 3 months). The reaction was conducted in a reasonable time to achieve the highest possible yield of 1-propenyl product. The selected results are collected in Table 3.

As can be seen, [RuClH(CO)(PPh₃)₃] showed an excellent selectivity and a relatively high catalytic activity in the studied reaction under non-oxidative reaction conditions and at minimal loading of 0.01 mol%. A high TON values of approximately 10 000 were obtained both at the moderate temperature of 80°C and also at the higher temperature of 120°C (entries 1 and 2 in Table 3, respectively). However, the time required to complete the reaction was three times longer at the lower temperature, than at the higher one, giving the highest TOF values of 6 667 h⁻¹ at 80°C vs. 20 000 h⁻¹ at 120°C. Moreover, the presence of AHP traces dramatically reduced the progress of the isomerization regardless of the reaction temperature (entries 3 and 4). Depending on the temperature of 80°C or 120°C, the isomerization practically stopped after 4 h or 5 h when only ca. 55% or 80% of the allyl substrate was

converted. Nevertheless, it was found that a relatively low pre-catalyst loading of 0.025 mol% at lower temperature of 80°C was sufficient to eliminate completely the effect of allyl hydroperoxides on the isomerization rate and the same values of TON and TOF (4 000 and 4 000 h⁻¹, respectively) were obtained (entry 6). In the case of AHP-free allyl substrate the reaction occurs very fast with high TOF values of 8 000 h⁻¹ (entry 5). Although the higher activity of [RuClH(CO)(PPh₃)₃] noted it is important to emphasized that further raising of the pre-catalyst amount to 0.05 mol% is unreasonable from the technological point of view (entries 7 and 8).

On the other hand, it was interestingly to verify the catalytic activity of cheaper and well-known complex [RuCl₂(PPh₃)₃] in the isomerization of 2-allyloxyethanol. As was demonstrated in the screening research given in Table 1, at the reaction temperature of 80°C under non--oxidative conditions the 100% yield of 1-propenylethanol was noted after only 30 min. (TON = 1 000, TOF = 2 000 h⁻¹). Surprisingly, contrary to [RuClH(CO)(PPh₃)₃], [RuCl₂(PPh₃)₃] pre-catalyst using a 2-fold lower amount below 0.1 mol% exhibited an unexpectedly low activity in the 1-propenylethanol synthesis (entries 9–12 in Table 3). The best results with the quantitative conversion of allyl substrate were obtained at the [Ru] concentration of 0.05 mol% at 80°C within 2.5 h but the product yield was slightly lower (ca. 99%) due to the traces of cyclic acetal (2-ethyl-1,3-dioxolane) formed during prolonged reaction times. The TON value equaled 1 980, but TOF value was only 792 h⁻¹ (entry 10). In turn, in the presence of a lower [Ru] loading of 0.025 mol% the prolongation of the reaction time was required to obtain the high values of allyl group conversion but simultaneously contributed to considerable decrease of the isomerization selectivity (entry 9). Thus, according to our

Table 3. The catalytic acivity of [RuClH(CO)(PPh₃)₃] or [RuCl₂(PPh₃)₃] in the solvent-free isomerization of the 2-allyloxyethanol to 2-(1-propenyloxy)ethanol: the optimization of the reaction conditions

Entry	Pre-catalyst (mol%)	AHP amount (ppm)	t (°C)	Time	α (%)	S (%) (%E)	TON	TOF (h⁻¹)
1	[RuClH(CO)(PPh₃)₃] (0.01)	0	80	1.5 h	100	100 (38)	10 000	6 667
2			120	30 min	100	100 (37)	10 000	20 000
3		10	80	4 h	55	100 (49)	5 550	1 375
4			120	5 h	80	100 (45)	8 000	1 650
5	[RuClH(CO)(PPh₃)₃] (0.025)	0	80	30 min	100	100 (41)	4 000	8 000
6		10	80	1 h	100	100 (42)	4 000	4 000
7	[RuClH(CO)(PPh₃)₃] (0.05)	0	80	15 min	99.5	100 (40)	1 990	7 960
8		10	80	45 min	100	100 (42)	2 000	2 667
9	[RuCl₂(PPh₃)₃] (0.025)	0	80	5 h	79	91 (57)	2 876	575
10	[RuCl₂(PPh₃)₃] (0.05)	0	80	2.5 h	100	99 (43)	1 980	792
11	[RuCl₂(PPh₃)₃] + 10 K₂CO₃ (0.01)	0	120	3 h	11	100 (100)	1 100	367
12	[RuCl₂(PPh₃)₃] + 10 K₂CO₃ (0.025)	0	120	4 h	91	100 (44)	3 640	910

The reaction conditions: 0.3 mole scale of allyloxyalcohol containing 0 ppm or 10 ppm of AHP, argon atmosphere, magnetic stirrer.

previous findings that the base can effectively eliminate the undesirable cyclization reaction via scavenging of its real catalyst such as HCl[11], the effect of addition of inorganic base such as K_2CO_3 on the catalytic activity of $[RuCl_2(PPh_3)_3]$ was tested. Moreover, the using of the catalytic system $[RuCl_2(PPh_3)_3] + K_2CO_3$ allowed to conduct the reaction at the higher reaction temperature of 120°C, and to achieve a reasonable reaction rate at the lower [Ru] concentration. However, the negligible productivity of the 0.01 mol% of $[RuCl_2(PPh_3)_3] + 10$ K_2CO_3 catalytic system was revealed and the yield of 1-propenyloxyethanol of 11% only after 3 h was detected (entry 11). An increase of the [Ru] loading to 0.025 mol% caused a significant increase of the isomerization rate, resulting in the 1-propenyl product yield of 91% (entry 12). The TON and TOF values of 3 640 and 910 h^{-1}, respectively were determined (a considerably lower than in the case of 0.25 mol% $[RuClH(CO)(PPh_3)_3]$, see entries 5 and 6). Thus, the less expensive $[RuCl_2(PPh_3)_3]$ pre-catalyst used in the range of loading of 0.01–0.05 mol%. was not effective enough for practical applications in the reaction studied.

Summing up, the neat simple $[RuClH(CO)(PPh_3)_3]$ exhibited a high catalytic productivity with TON of 10 000 and TOF of 20 000 h^{-1} in the solvent-free isomerization of low reactive 2-allyloxyethanol. Due to fact that for large-scale production of medium-value fine chemicals the TON values between 10 000 and 50 000 and TOF > 10 000 h^{-1} are required[29–30], $[RuClH(CO)(PPh_3)_3]$ can be recommended for an efficient and selective scaled up synthesis of 2-(1-propenyloxy)ethanol.

CONCLUSIONS

The catalytic double bond isomerization is an important atom-efficient, one-pot and solvent-less reaction fulfilling both sustainability criteria and a widespread application in the industry. Particularly effective catalysts for this reaction are soluble ruthenium complexes. However, the information regarding the optimal and technologically attractive reaction conditions are still very scarce in the literature. In this work, we have chosen commercially available poly(ethylene glycol) monoallyl ethers with well-defined PGE units from 1 to 5 as allyloxyalcohol substrates for obtaining 1-propenyloxyalcohols type $CH_3–CH=CH–[OCH_2CH_2]_n–OH$, $n = 1–5$, as valuable fine chemicals with unique properties for special applications. We have first demonstrated extensive screening experiments allowing to determine the importance of individual parameters of a highly productive synthesis of title 1-propenyloxyalcohols via the solvent-less [Ru]-catalyzed isomerization of appropriate allyl substrates. It was confirmed that previously postulated by us the hydride ruthenium complexes such as $[RuClH(CO)(PPh_3)_3]$[7–13] is an extremely versatile, high active and selective catalyst also for the this reaction. However, theoretical considerations and the experimental evidence suggest that the structure of allyl substrate i.e. number of PGE spacer is a key factor affecting the reaction rate. The most reactive substrate was 2-[2-(allyloxy)etoxy]ethanol in the contrary to 2-allyloxyethanol, for which the isomerization was the slowest process. Moreover, the loading of [Ru] pre-catalyst, the presence and the concentration of allyl

hydroperoxides and also the temperature of reaction are significant limiting factors in the selectivity, productivity and reproducibility of the reaction. Finally, it was also demonstrated that under optimized conditions, neat $[RuClH(CO)(PPh_3)_3]$ selectively and effectively catalyzes the isomerization of low reactive 2-allyloxyethanol with relatively high TON of 10 000 and high TOF value of 20 000 h^{-1}, what is sufficient for large-scale production of valuable fine chemicals. This results opens the door for further studies of its technological efficiency using other much more reactive poly(ethylene glycol) monoallyl ether substrates dedicated to large-scale process development.

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27. The energy minimized structures of allylalcohol substrates were generated via molecular mechanics of MM2 program in Chem3D Pro software (in ChemBioDraw Ultra 13.0 Cambridge software) using the set functions.

28. Plausible structure of complexes formed via temporary coordination of ruthenium by 2-allyloxyethanol or 2-[2-(allyloxy)etoxy]ethanol were determined in ChemSketch (ACD/Labs 2018.1.1 software) with using 3D optimization function.

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