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A selective convenient ruthenium-mediated synthesis of mixed acetals

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ABSTRACT

Addition of alcohols and phenols to allyl ethers catalyzed mainly by ruthenium complexes was studied. Complexes of ruthenium generated *in situ* from precursors such as $\{[RuCl_2(1,5\text{-}COD)]_x\}$ or $[Ru_3(CO)_{12}]$ and from external ligands such as phosphines (e.g. PPh_3, PBu_3, BINAP) or phosphites (e.g. $P(OPh)_3$, $P(OMe)_3$) were found to be particularly efficient catalysts of the studied reactions. Transacetalization reaction could be practically completely eliminated by the addition of a base (particularly Na_2CO_3) to the catalytic systems. It was observed that the selectivity of mixed acetals formation increases with increasing value of Θ parameter of phosphines. Especially interesting results (0–5% of transacetalization) have been obtained for catalytic systems generated from $\{[RuCl_2(1,5\text{-}COD)]_x\}$ or $[Ru_3(CO)_{12}]$, phosphines (PPh_3, BINAP, dppe, tris(2,4,6-tri-metylphenyl)phosphine, or dppf) and Na_2CO_3. The mechanism of mixed acetals formation has been investigated using deuterated reagents. It is postulated that the examined reaction is a nucleophilic addition of ROH to a hydrido-π-allyl complex formed during oxidative addition of allyl substrate to metal complex. As a result, a new, selective, and convenient method of the synthesis of symmetrical and, in particular, unsymmetrical (mixed) acetals has been developed. Mixed acetals $CH_3CH_2CH(OR^1)(OR^2)$ may be obtained in the reaction of R^1-*O*-allyl with R^2OH or R^1OH with R^2-*O*-allyl, depending on the structure of R^1 and R^2.

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1. Introduction

Mixed (unsymmetrical) acetals are widely used in synthetic organic chemistry [1–3]. Also, in the fragrance [4,5] and pharmaceutical [6] industries, acetals are used both as intermediates and as end products. Acetals are recognized as good carbonyl protecting groups [7,8]. There are many methods of the synthesis of acetals [9–11] described in the literature. However, selective synthesis of mixed acetals of $RCHOR^1(OR^2)$ type is still difficult. Application of classical methods of the synthesis of these compounds is not satisfactory, as a concomitant transacetalization reaction leads to a mixture of symmetrical and unsymmetrical acetals, which can be difficult to separate. So far, only two reports describing a selective method for the preparation of several mixed acetals [12,13] have been published. Fujioka et al. obtained mixed acetals by reaction of dimethyl (or diethyl) acetals of $R^1CH(OMe)_2$ type with TESOTf and 2,4,6-collidine and then by treating the obtained salt with R^2OH [12]. Ledneczki and Molnár obtained mixed acetals by reaction of various primary and secondary alcohols with four different dialkoxymethanes; the desired mixed acetals were rapidly formed at reflux temperature [13].

A few attempts using transition metal complexes for the synthesis of mixed acetals have not been successful. Chang obtained various symmetrical and unsymmetrical acetals, in the reactions of $R^1OCH_2CH{=}CHR^2$ with methanol, catalyzed by cobalt complexes generated from $[Co_2(CO)_8]$ in the presence of hydrogen and carbon monoxide [14]. However, the syntheses of unsymmetrical acetals of type EtCH(OMe)(OR) in reactions of allyl ethers with MeOH were very unselective (transacetalization was observed) [14]. A symmetrical diethyl acetal was also obtained by reaction of allyl ether (n-$C_6H_{13}COCH{=}CHCH_2OMe$) with 95% EtOH in the presence of $[RhCl(PPh_3)_3]$ [15].

In this paper we have shown that in the addition reaction of alcohols or phenols to allyl ethers it is possible to synthesize mixed acetals of $R^1CH_2CH(OR^2)(OR^3)$ type with high selectivity and, what is most important, the application of a proper catalytic system (ruthenium complex and base) allows for practically complete elimination of undesirable transacetalization reaction which results in the formation of acetal mixture.

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2. General information and experimental

For Tables S1–S7, materials and full experimental details including the physical data, see supporting information.

Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. All reactions were carried out under dry argon. Solvents were dried with appropriate drying agents (molecular sieves or CaH_2) and distilled prior to use.

3. Results and discussion

In our two previous communications we have described the isomerization of allyloxy alcohols to cyclic acetals (formally an intramolecular addition of OH group to the double bond) and addition of alcohols and phenols to allyl ethers (formally intermolecular addition of OH group to the double bond) leading to mixed or symmetrical acetals [16,17]. These reactions were effectively catalyzed by the nonhydride ruthenium complex—$[RuCl_2(PPh_3)_3]$ [16,17], while the hydride complex – $[RuClH(CO)(PPh_3)_3]$ – catalyzed mainly double bond migration in allyl substrates [16].

In the present paper we have described the results of our studies on more catalytic systems for the synthesis of mixed acetals which could be more effective than $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$. We paid particular attention to the catalytic systems generated *in situ* from stable precursors and different ligands since these systems are particularly promising for controlling the rate and, in particular, the selectivity of the reaction, as found in our previous studies on the double bond migration in *N*-allyl amides [18] and allyl ethers [18,21]. We have thoroughly analyzed the influence of donor–acceptor and steric parameters of the ligands (particularly phosphines) on the selectivity of mixed acetals formation. We have also studied the influence of the structure of the allyl reagent and the nucleophile (i.e. alcohol or phenol) on the rate and selectivity of the reaction. The influence of the reaction conditions was also analyzed.

3.1. Catalytic system

We have studied the catalytic activity of nonhydride transition metal (Re, Ru, Os, Rh) complexes in a model reaction of allyl butyl ether with *m*-cresol (Scheme 1). The products of the reactions were—A: mixed acetal, a desired product; B: (*E*)- and (*Z*)-butyl-1-propenyl ether, the product of double bond migration in allyl ether molecule (undesired product, which can be, however, easily separated from mixed acetals); and C: a symmetrical acetal (the product of transacetalization, highly undesirable, usually difficult to separate from mixed acetals). On the other hand, we did not observe the formation of a symmetrical acetal $CH_3CH_2CH(OAr)_2$ (Ar = *m*-MePh)—therefore it was not included in Scheme 1.

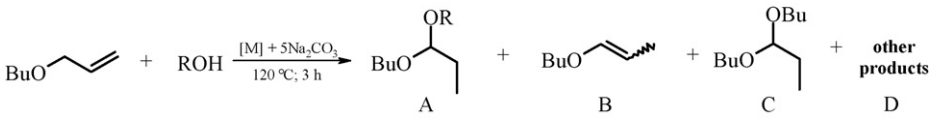
Moreover, in the reactions in which the degree of transacetalization was particularly large we have observed various products of consecutive side reactions—the issue of competitive and consecutive reactions is discussed in Section 3.6. We have tested different stable precursors and complexes generated *in situ* from these precursors and triphenylphosphine. In the studied catalytic systems always present was also Na_2CO_3—as we have shown it enhances selectivity of mixed acetals formation (decreases the contribution of transacetalization reaction) [17]. The results of the screening of catalytic systems are given in Table S1 (see supporting information).

The results show that the most promising catalysts of this reaction is $[RuCl_2(PPh_3)_3]$ and the catalytic systems generated from stable, easily accessible precursors, i.e. $\{[RuCl_2(COD)]_x\}$, $[Ru_3(CO)_{12}]$, $\{[OsCl_2(COD)]_x\}$ and triphenylphosphine. Therefore, in further studies we have tested catalytic systems generated from two ruthenium precursors, i.e. ($\{[RuCl_2(COD)]_x\}$ and $[Ru_3(CO)_{12}]$) and from different ligands: P, As, Sb and N-donors (phosphines, phosphites, triphenylstibine, triphenylarsine, and amines). We have not done detailed examination of catalytic systems generated from $\{[OsCl_2(COD)]_x\}$ and phosphines due to the toxicity of osmium compounds and the ease of the synthesis of analogical ruthenium complex. However, the activity and high reaction selectivity (only 2% of transacetalization) of this catalytic system is noteworthy. Results of the studies on the catalytic systems generated from $\{[RuCl_2(COD)]_x\}$ and different phosphine ligands and $SbPh_3$ are contained in Table S2 which can be found in the supporting information.

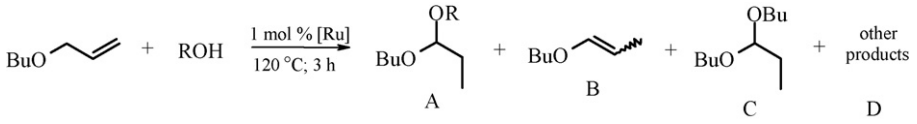
Our data show that both the precursor and practically all the catalytic systems generated from phosphines and from triphenylstibine allow the synthesis of unsymmetrical acetal without transacetalization (the yield of undesirable symmetrical acetal formation is 0–2%). Only in the case of the application of tributylphosphine as a ligand the contribution of transacetalization is comparatively high (5%). This means that strong donor ligands are not advantageous in this reaction. A similar result, i.e. an adverse effect of the strongly donor phosphine (significant contribution of transacetalization—8%), we have obtained for $[Ru_3(CO)_{12}]$–tricyclohexylphosphine system (see Table S4 in supporting information). What is of importance is the presence of the external ligand in the $[Ru_3(CO)_{12}]$–phosphine systems suppressed the competitive unwanted double bond migration. The yield of allyl ether isomerization product decreases with increasing Θ angle of the phosphine (Table S3 in supporting information). A particularly spectacular result (only 1% of both isomerization and transacetalization) we have obtained if the ligand was tris(2,4,6-trimethylphenyl)phosphine—the phosphine with highest Θ angle.

This suggests that the relative contribution of two competitive reactions, i.e. addition of ROH and double bond migration is governed by steric factors and not by electron factors. What is important, application of phosphines with large Θ angles allows limiting both transacetalization and double bond migration.

We have also studied the influence of the type of external ligand on the catalytic activity of the systems generated from $[Ru_3(CO)_{12}]$ (Table S4 in supporting information). It was found that phosphine complexes formed *in situ* from this precursor and PPh_3 allow synthesis of unsymmetrical acetal with significantly greater selectivity than in the reaction catalyzed only by $[Ru_3(CO)_{12}]$. Also, the catalytic system generated from the precursor and $SbPh_3$ is very attractive—no transacetalization is observed. What is interesting and important, in the case of catalytic systems obtained from $\{[RuCl_2(COD)]_x\}$ or $[Ru_3(CO)_{12}]$ and external ligands, both double bond migration and, most of all, transacetalization could be significantly limited. In contrast to $\{[RuCl_2(COD)]_x\}$, $[Ru_3(CO)_{12}]$ alone catalyzes also transacetalization reaction (the problem of transac-



Scheme 1. Reaction of allyl butyl ether with *m*-cresol catalyzed by 1 mol% transition metal complexes: screening of catalytic systems. BuOallyl:ROH = 1:1.5.



Scheme 2. Reaction of allyl butyl ether with several alcohols and phenols (R = alkyl or aryl; [Ru] = ruthenium complexes). BuOallyl:ROH:Ru:Na_2CO_3 = 100:150:1:5.

etalization reaction is discussed in Section 3.6). As in the case of the systems formed from {$[RuCl_2(COD)_x]$}, the application of phosphines with large Θ angles is particularly advantageous. On the other hand, strong donor PCy_3 is not a good ligand—the transacetalization contribution was as large as 7%.

The influence of [Ru]:[P] ratio was more important for the catalytic system generated from $P(OPh)_3$ than from corresponding phosphines (PPh_3, dppe). Namely, for the ratio Ru:$P(OPh)_3$ = 1:3 we have observed a drastic decrease of activity of the catalytic system. For the catalytic systems containing phosphines, the increase of [P]:[Ru] ratio was also unfavorable—the contribution of isomerization reaction increased while the conversion of allyl system was quantitative.

3.2. Influence of base

A very important component of the catalytic systems studied is the base—its presence allows limiting or even complete elimination of the transacetalization reaction. We have examined the influence of the presence of different bases on the model reaction of allyl butyl ether with *m*-cresol (see Table S5 in supporting information).

Introduction of alkali metal carbonates, particularly NaOH, into the catalytic systems examined had a very advantageous influence on the results of the studied reactions. It allowed practically complete elimination of very unfavorable transacetalization. However, in the case of the application of Li_2CO_3, and in particular Cs_2CO_3, the contribution of competitive (and adverse) isomerization noticeably increased. On the other hand, NaOH did not appear to be universal, e.g. in the reaction of 2-phenylethanol addition to allyl butyl ether isomerization was solely observed. So far our studies on the influence of the addition of NaOH and M_2CO_3 on the reaction of ROallyl with ROH indicate that the more the base is soluble in the reaction mixture, the greater is the contribution of double bond migration. Cs_2CO_3 was completely soluble in the reaction mixture, therefore the contribution of isomerization was highest. On the other hand NaOH underwent homogenization, e.g. in the reaction of $PhOCH_2CH_2O$allyl and BuOH. For both of this bases as a result, we have obtained only, or mainly, the products of double bond migration, mixed acetals (up to 30%), and other unidentified compounds. Therefore, in further studies we have always added Na_2CO_3, which in all reactions had advantageous influence on the selectivity by eliminating transacetalization.

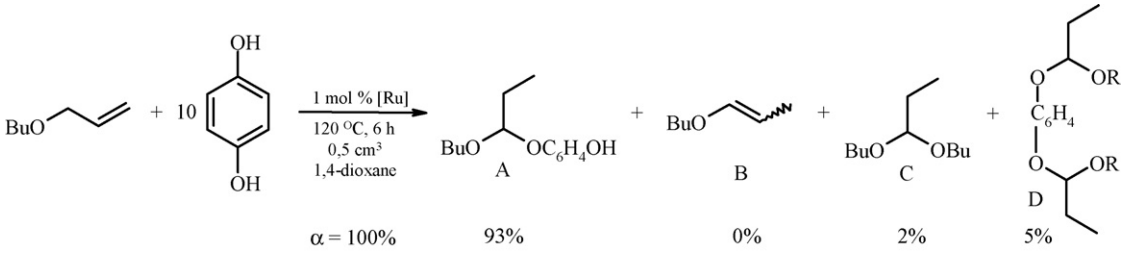
Very important was also thorough removal of oxygen from the reaction mixture. The reaction in the presence of air was unselective, i.e. transacetalization contribution increased strongly (see Table S6 in supporting information)

Interestingly, in the presence of oxygen the double bond migration product was not formed. Previous studies on double bond migration in alkenes mediated by $[RuCl_2(PPh_3)_3]$ have shown that some amount of oxygen (or peroxides) enhances isomerization reaction [19].

3.3. Structure of the reagent undergoing addition and the result of the reaction with O-allyl system

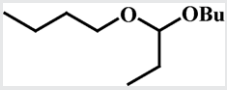
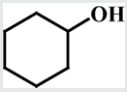
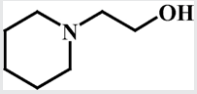
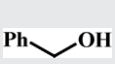
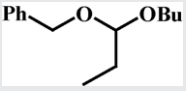
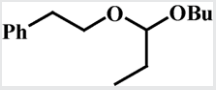
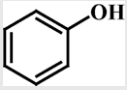
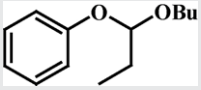
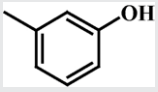
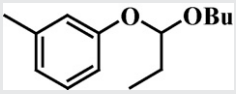
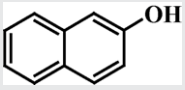
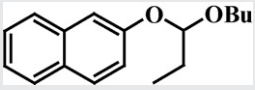
We have also studied which alcohols and phenols undergo addition to allyl ethers and which mixed acetals can be selectively obtained this way. The model reaction was the addition of several alcohols and phenols to allyl-butyl ether catalyzed by $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$ (Ru^1) (Schemes 2 and 3 and Table 1). We have used other catalytic systems (Ru^2, Ru^3 or Ru^4—see Table 1) in this model reaction if the result of the reaction with Ru^1 was not satisfactory.

The data contained in Table 1 indicate that products of the reaction of allyl butyl ether with varied ROH are very different. In the reaction with methanol and secondary alcohol (cyclohexanol) and tertiary alcohol (*t*-butanol) (*E*)- and (*Z*)-butyl-1-propenyl ethers, the products of double bond migration in the allyl substrate, were exclusively formed. In the case of methanol it was certainly the result of transformation of $[RuCl_2(PPh_3)_3]$ into hydride complex, which catalyzed double bond migration but not addition to the double bond [19]. On the other hand, in the case of secondary and tertiary alcohols the reaction products were controlled probably by steric factors. Steric hindrance noticeably decreased the ratio of acetal formation, therefore only the product of much faster double bond migration was present in the post-reaction mixture. Although the addition of ROH to 1-propenyl ether also occurs (see Section 3.6) but it is much slower than to allyl ether. On the other hand it is difficult to explain the absence of the product of addition in the case of 2-phenoxyethanol and 2-*N*-piperidinylethanol. Probably these systems strongly complex ruthenium, as we have observed in the isomerization reactions of allyl ethers of diols [20]. Mixed acetals were easily formed with high selectivity (with the absence or with only a slight contribution to transacetalization) in the reactions of allyl butyl ether with phenols and with some primary alcohols. In the next part of this paper we have shown that the problems with the synthesis of acetals from some ROH may be, however, easily overcome, which significantly extends the scope of the developed



Scheme 3. Synthesis of mixed acetal from bifunctional nucleophile. [Ru] = $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$.

Table 1
Influence of the structure of alcohols and phenols on their addition to allyl butyl ether catalyzed with ruthenium complexes[a,b]

ROH	Mixed acetal	[Ru]	A (%)	B (%)	C (%)	D[c] (%)
CH_3OH	–	$[Ru]^1$	0	100	0	0
		$[Ru]^1$	100	0	–	–
	–	$[Ru]^{1,2,3}$	0	100	0	0
	–	$[Ru]^{1,2,3}$	0	100	0	0
	–	$[Ru]^1$	0	100	0	0
		$[Ru]^1$	78	10	6	6
		$[Ru]^1$	81	13	3	3
	–	$[Ru]^{1,2,3}$	0	100	0	0
		$[Ru]^3$	89	5	3	3
		$[Ru]^3$ $[Ru]^4$	97 77	1 21	1 1	1 1
		$[Ru]^1$	80	20	0	0

Reaction conditions—Scheme 2. $[Ru]^1 = [RuCl_2(PPh_3)_3] + 5Na_2CO_3$; $[Ru]^2 = [RuCl_2(PPh_3)_3] + 5NaOH$; $[Ru]^3 = \{[RuCl_2(1,5\text{-}COD)]_x\} + P(2,4,6\text{-}MeC_6H_2)_3 + 5Na_2CO_3$; $[Ru]^4 = [Ru_3(CO)_{12}] + 3PPh_3 + 5Na_2CO_3$.

[a] Conversion of allyl ether was quantitative.

[b] Reaction conditions: 120 °C, 3 h, without solvent.

[c] Propene, butanol, and other unidentified products.

method of mixed acetal synthesis. For example, the addition of *t*-butanol to allyl butyl ether does not occur but the corresponding acetal may be easily obtained in the reaction of allyl-*t*-butyl ether with *t*-butanol (see Section 3.4). Similarly, the addition of cyclohexanol to allyl butyl ether does not occur, but the required acetal may be easily formed in the reaction of allyl cyclohexyl ether with 1-butanol. Generally, mixed acetals of $CH_3CH_2CH(OR^1)(OR^2)$ type cannot be synthesized with our method from secondary and tertiary alcohols and other strongly coordinating ROH. In such a case it is required and possible to change reagents, i.e. use R^2Oallyl and R^1OH instead of R^1Oallyl and R^2OH.

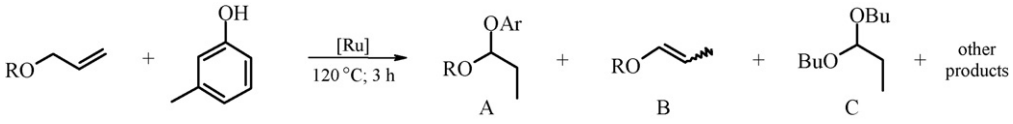
Moreover, if the nucleophile is bifunctional, e.g. hydroquinone, it is possible to obtain with high yield a mixed acetal which is a product of addition of only one OH group (see Scheme 3).

However, synthesis of an acetal following Scheme 3 requires at least 10-fold excess of a nucleophile relative to allyl substrate. Necessary was also a solvent which allowed intensive mixing of the reaction mixture, thereby enabling a high selectivity of the reaction.

3.4. Structure of allyl reagent and the product of the reaction with ROH

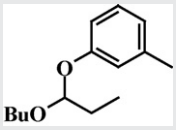
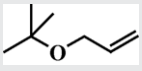
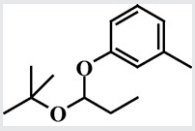
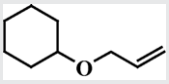
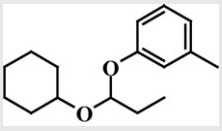
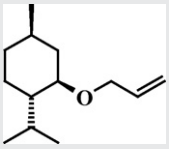
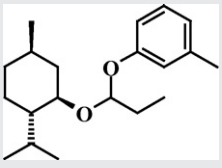
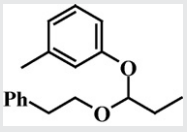
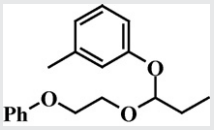
We have also analyzed which allyl reagents (allyl ethers) may be used in the synthesis of mixed acetals *via* addition of alcohols and phenols to allyl ethers. We have studied the influence of the structure of allyl reagent on the reaction products with ROH using the model reaction of various allyl ethers with *m*-cresol, catalyzed by $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$ $[Ru^1]$ (Scheme 4 and Table 2). We applied other catalytic systems if the product obtained using 1 mol% of Ru^1 was unsatisfactory.

As indicated by the data contained in Table 2, mixed acetals of $CH_3CH_2CH(OR^1)(OR^2)$ type may be obtained from ethers of primary, secondary, and tertiary alcohols. It is also possible to synthesize an acetal from the ether of $R^1OCH_2CH{=}CHR^2$ type, i.e. with one substituent at γ carbon of the allyl system (see Scheme 5). On the other hand, allyl ether of $ROCH_2CH{=}CRR$ type, e.g. butyl 3,3-dimethylallyl ether is com-



Scheme 4. Reaction of *m*-cresol with several nucleophiles of ROH type mediated by ruthenium complexes. ROallyl:*m*-cresol = 1:1.5.

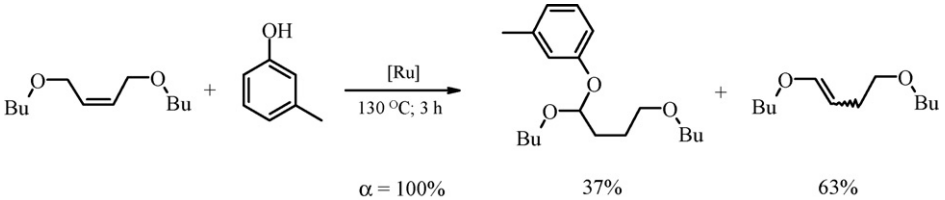
Table 2
Reaction of *m*-cresol with several allyl ethers mediated by ruthenium complexes[a]

RO	Mixed acetal	[Ru]	A (%)	B (%)	C (%)	D[b] (%)
BuO		[Ru]^3	97	1	1	1
		[Ru]^4	77	21	1	1
		[Ru]^1	90	10	0	0
		[Ru]^1	95	5	0	0
		[Ru]^1	90	4	3	3
Ph		[Ru]^1 [Ru]^4	78 26	14 74	4 0	4 0
Ph		[Ru]^1	74	12	7	7

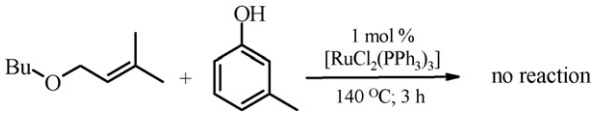
[Ru]^1 = $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$; [Ru]^2 = $[RuCl_2(PPh_3)_3] + 5NaOH$; [Ru]^3 = $\{[RuCl_2(1,5\text{-}COD)]_x\} + P(2,4,6\text{-}MeC_6H_2)_3 + 5Na_2CO_3$; [Ru]^4 = 0.33% $[Ru_3(CO)_{12}] + 3PPh_3 + 5Na_2CO_3$.

[a] Conversion of allyl ether was quantitative.

[b] Propene, ROH, and other unidentified compounds.



Scheme 5. Reaction of *m*-cresol with (*Z*)-2-butene-1,4-diol catalyzed by [Ru] = 1 mol% $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$ (synthesis of acetal from allyl ether of $R^1OCH_2CH{=}CHR^2$ type). Allyl ether:*m*-cresol = 1:1.5.



Scheme 6. Reaction of allyl aryl ethers with ROH (R = Bu or *m*-MePh) in the presence of $[RuCl_2(PPh_3)_3]$.

pletely nonreactive—neither addition nor isomerization occurs Scheme 6.

Our previous studies have shown that isomerization of ethers of this type on ruthenium complexes occurs only at 160–180 °C [19]. In these conditions, however, acetals heated with ruthenium complexes undergo significant changes—aldehydes, alkenes, phenols or alcohols, and other unidentified compounds are formed.

We have also found that the addition of ROH (R = Bu or *m*-MePh) to allyl aryl ethers does not occur at all (see Scheme 7). The only products of these reactions we have identified were 1-propenyl ethers, phenol, and propene (at 130 °C). Increasing the temperature up to 140 °C or even to 160 °C and extension of the reaction time did not yield expected effect—aryl-1-propenyl ethers were found to be completely nonreactive in the reaction of ROH addition which was to yield acetals.

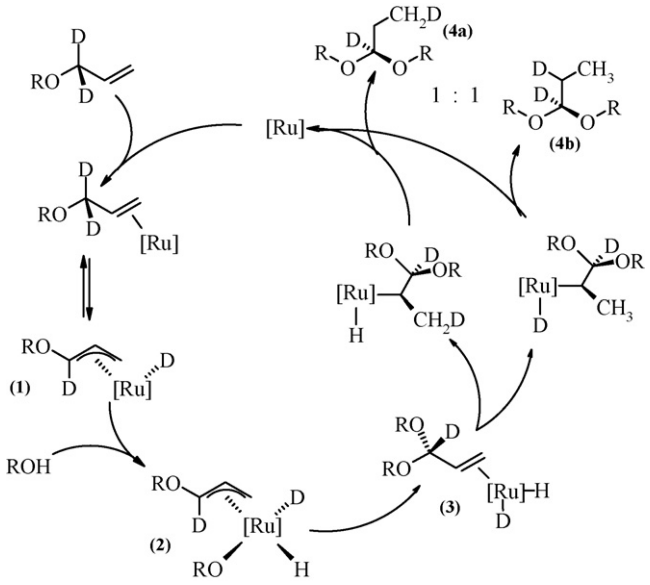
On the other hand, we have observed formation of the products of C—O bond cleavage in allyl aryl ethers, i.e. phenols and propene and other unidentified products. In our previous studies on the isomerization of allyl aryl ethers in the presence of ruthenium complexes we have also noticed such changes, especially in the case of allyl pentachlorophenyl or hexafluoropropyl ethers [18].

3.5. Reaction conditions: temperature and reaction time

We have also analyzed the influence of temperature and reaction time on allyl ether conversion and, most of all, the selectivity of mixed acetal formation in a model reaction (see Scheme 1 and Table S7 in supporting information). We have shown that the advantageous reaction conditions are 120 °C for 1 h ($[Ru^3]$) or 3 h ($[Ru^1]$ and $[Ru^2]$). The loss of the yield of the double bond migration product with increasing temperature and reaction time suggests that 1-propenyl ether also undergoes addition (but much slower than allyl ether [16]). It is possible, however, that 1-propenyl ether is nonreactive and the decrease of its concentration is a result of the reversibility of the reaction of double bond migration (therefore addition to allyl ether takes place).

3.6. Mechanism of mixed acetals formation

Our previous studies have unambiguously shown that the studied reaction is not a simple, two-stage addition of alcohol or phenol to 1-propenyl ether formed in the first stage since we have shown that *O*-vinyl systems are completely nonreactive—they

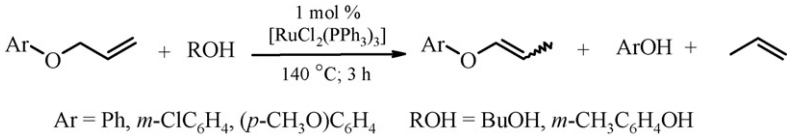


Scheme 9. Formation of mixed acetals in the reaction of allyl ethers with nucleophiles of ROH or ArOH type—suggested mechanism of a model reaction (addition of benzyl alcohol to α,α-dideuteroallyl benzyl ether).

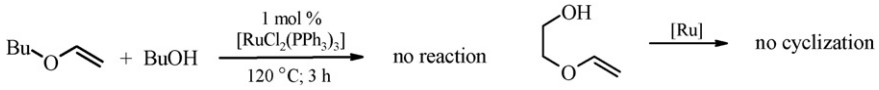
undergo neither intermolecular nor intramolecular addition of ROH (Scheme 8) [16,17].

It is also interesting that the addition of ROH or ArOH to allyl alkyl ethers is catalyzed by nonhydride complexes of transition metals (particularly those of ruthenium), while hydride complexes catalyze double bond migration. It clearly shows that addition of ROH to ROallyl may proceed through π-allyl complexes. By studying of the addition of benzyl alcohol to α,α-dideuteroallyl benzyl ether we have shown that the product of this reaction is an equimolar mixture of (**4a**) and (**4b**) acetals (see Scheme 9).

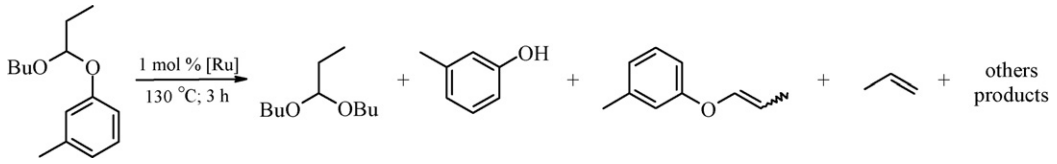
Thus, the addition of alcohols and phenols to allyl alkyl ethers leading to mixed acetals may follow that shown in Scheme 9. In the first stage of the reaction the oxidative addition of allyl ether to metal complex takes place—a hydride–π-allyl complex is formed (**1**). In the next stage ROH (or ArOH) undergoes coordination—alkoxy (or aryloxy)dihydride–π-allyl complex is formed (**2**). In the next stage alkene complex is obtained (**3**) as a result of the migration of coordinated nucleophile (RO or ArO) to coordinated allyl system. Finally, as a result of transfer of two hydride ligands the equimolar mixture of mixed acetal (**4a**) and (**4b**). Double bond migration in allyl ethers which accompanies acetal formation is a competitive reaction and according to us it follows hydride-π-allyl mechanism, as found for complexes of $[RuCl_2(PPh_3)_3]$ type [19,21]. We have also shown that heating of a mixed acetal $CH_3CH_2CH(OBu)(OAr)$ with $[RuCl_2(CO)_3]_2$, which is a



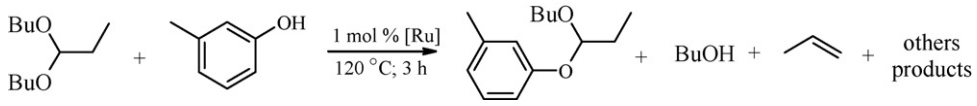
Scheme 7. Reaction of allyl aryl ethers with ROH (R = Bu or *m*-MePh) in the presence of $[RuCl_2(PPh_3)_3]$.



Scheme 8. Reaction of vinyl ethers with ruthenium complex: no OH addition (only destruction and polymerization products) [16,17].

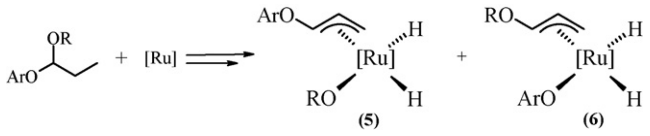


Scheme 10. Reaction of 1-butoxy-1-(3-methylphenoxy)propane with ruthenium complex: symmetrical acetal, enol ether, propene, and other (unidentified) product formation. [Ru] = $[RuCl_2(PPh_3)_3]$ or $[RuCl_2(CO)_3]_2 + 5Na_2CO_3$.



Scheme 11. Reaction of 1,1-dibutoxypropane with *m*-cresol—transacetalization. [Ru] = $[RuCl_2(CO)_3]_2$ or $[RuCl_2(CO)_3]_2 + 5Na_2CO_3$.

Scheme 12. Reaction of allyl aryl ethers with ruthenium complex: double bond migration and C—O bond cleavage. Ar = Ph, 2-bromophenyl, 2,4,6-tribromophenyl; [Ru] = $[RuCl_2(CO)_3]_2$ or $[RuCl_2(PPh_3)_3] + 5Na_2CO_3$.



Scheme 13. Formation of side products—a suggested mechanism.

particularly active transacetalization catalyst (see Table S1 in supporting information), or with $[RuCl_2(PPh_3)_3]$ leads to the formation of a symmetrical acetal $CH_3CH_2CH(OBu)_2$, ArOH, propene, and other unidentified products (Scheme 10).

Moreover, we have noticed that heating of a symmetrical acetal $CH_3CH_2CH(OBu)_2$ with *m*-cresol and $[RuCl_2(CO)_3]_2$ leads to the formation of a mixed acetal $CH_3CH_2CH(OBu)(OAr)$, propene, 1-butanol, and other unidentified products (see Scheme 11).

We have also shown that allyl aryl ethers heated with $[RuCl_2(CO)_3]_2$ (and Na_2CO_3) undergo slow destruction—the C—O bond is cleaved and phenols, propene and other unidentified products are formed (see Scheme 12).

Similar results of the reaction of some allyl aryl ethers and alkyl and aryl sulfides with ruthenium complexes have already been described by us [21,22]. Cleavage of C—O and C—S bond (in allyl esters, ethers and sulfides) by low valent ruthenium complexes was also reported by other authors [23].

In our opinion, symmetrical acetals and other products of consecutive reactions (phenols, propene, and other unidentified) may be formed as a result of typical complex transformations (**5**) or (**6**) (Scheme 13).

Complexes (**5**) and (**6**) may be easily formed in the reaction beginning from a reversible oxidative addition of [Ru] to C—O or C—H bonds in molecules of mixed acetals. We will continue the studies on the mechanism of the reaction of allyl ethers with alcohols and phenols.

4. Conclusions

The paper shows that the addition of alcohols and phenols to allyl ethers catalyzed by ruthenium complexes is a convenient and effective method of the synthesis of mixed acetals of $CH_3CH_2CH(OR^1)(OR^2)$ and $RCH_2CH_2CH(OR^1)(OR^2)$ type. Especially effective addition catalysts are phosphine complexes of ruthenium generated *in situ* from easily accessible and stable precursors, $[Ru_3(CO)_{12}]$ and $\{[RuCl_2(COD)_x]\}$, and phosphines with large Θ angles, e.g. tris(2,4,6-trimethylphenyl)phosphine. Application of these catalytic systems (with the addition of Na_2CO_3) allowed complete or almost complete elimination of transacetalization, a main problem occurring in almost all known methods of the synthesis of mixed acetals. Formation of mixed acetals in the addition reaction of ROH to allyl ethers is accompanied by undesirable double bond migration in allyl substrate. However, 1-propenyl ethers formed in this competitive side reaction can be easily separated from mixed acetals by distillation. What is of importance, acetals of $CH_3CH_2CH(OR^1)(OR^2)$ type may be obtained in the reaction of R^1Oallyl with R^2OH or in the reaction of R^1OH with R^2Oallyl (depending on the reactivity of ROallyl and ROH) which significantly broadens the scope of the method described in this paper. The results obtained so far suggest that mixed acetals are formed as a result of an attack of a ROH nucleophile (possible previously coordinated) on the π-allylic complex formed in the oxidative addition of allyl substrate to catalytic metal complex. It was shown that mixed acetals do not form in the result of the addition of ROH to 1-propenyl ethers formed in the isomerization of allyl ethers.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2008.04.020.

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