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Introduction

Alcohols are important building blocks for synthetic organic and pharmaceutical chemistry to build advanced organic structures.^{1,2} The transformation of commercially available alcohol derivatives to functional compounds using transition metal-based catalysts have been intensively studied over the last decade.3-5 Acceptorless dehydrogenative alcohol coupling reaction is one of the most important processes for the synthesis of carboxylic acids, ketones, esters, lactones and substituted mono-alcohol derivatives in an efficient manner. Several transition metal catalysts based on cobalt, manganese, iridium, ruthenium are mostly used in dehydrogenative alcohol coupling reactions.⁶⁻¹² Among these transition based metal catalysts, ruthenium is the most frequently used catalyst in dehydrogenative alcohol coupling reactions. Verpoort, Madsen and Möller have utilized different N-heterocyclic carbene/ruthenium-arene complexes to build carboxylic acids through dehydrogenative alcohol coupling reactions of primary alcohols in the presence of strong bases such as KOH and NaOH.¹³⁻¹⁵ In 2011, Madsen et al. used RuCl₂(IPr)(p-cymene) for acceptorless dehydrogenative alcohol coupling reactions of primary alcohols to obtain functional ester derivatives.¹⁶ Later on, Madsen et al. reported the



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In this study, *in situ* formed ruthenium hydride species that were generated from Grubbs type catalysts are used as efficient catalysts for dehydrogenative alcohol coupling and sequential cross-metathesis/ dehydrogenative coupling reactions. The selectivity of Grubbs first generation catalysts (G1) in dehydrogenative alcohol coupling reactions can be tuned for the ester formation in the presence of weak bases, while the selectivity can be switched to the β -alkylated alcohol formation using strong bases. The performance of Hoveyda–Grubbs 2nd generation catalyst (HG2) was improved in the presence of tricyclohexylphosphine for the selective synthesis of ester derivatives with weak and strong bases in quantitative yields. Allyl alcohol was used as self and cross-metathesis substrate for the HG2 catalyzed sequential cross-metathesis/dehydrogenative alcohol coupling reactions to obtain γ -butyrolactone and long-chain ester derivatives in quantitative yields.

self-coupling of secondary alcohols to yield racemic ketones through dehydrogenative Guerbet reactions.¹⁷ In 2017, protic NHC ruthenium complexes were used in dehydrogenative alcohol coupling reactions of secondary alcohols and coupling of primary and secondary alcohols to yield functional ketone derivatives.¹⁸ Ruthenium hydride complexes bearing unsymmetrical tridentate (NNN) ligands were used as alternative catalysts for the coupling of primary and secondary alcohols through β-alkylation reactions.¹⁹ In addition to specially designed ruthenium catalysts, commercially available RuCl₂(PPh₃)₃ performed the dehydrogenative coupling reactions of primary alcohols to give Guerbet alcohol derivatives in the presence of potassium-tert-butoxide.²⁰ As can be seen from literature examples, dehydrogenative coupling reactions can be manipulated through the selection of suitable catalysts and reaction conditions for the selective formation of ester and Guerbet alcohols.

As an important alcohol-transformation reaction, crossmetathesis of unsaturated alcohols that are catalyzed by welldefined metathesis catalysts can be used for the formation of unsaturated functional molecules in a highly efficient way.^{21–24} Unsaturated alcohols are considered as challenging substrates for cross-metathesis reactions owing to their ability to form ruthenium hydride species in the presence of Grubbs catalyst, which triggers the undesired olefin isomerization reactions.²⁵ In 2020, tandem cross-metathesis/hydrogenation reactions of allyl alcohol with 1-octene in the presence of binary catalytic system HG2/PtO₂ to form long-chain primary alcohols were reported as an efficient catalytic protocol for the synthesis of fatty alcohols.²⁶



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Considering the importance of unsaturated alcohol derivatives in various transformation reactions, the combination of dehydrogenative coupling and cross-metathesis reactions in a one-pot procedure will lead to the formation of various functional materials. The proposed sequential reactions can be possible by the in situ transformation of Grubbs catalysts to ruthenium hydride species to catalyze the dehydrogenative coupling reactions after cross-metathesis reactions. In this study, we have evaluated the performance of Grubbs catalysts on dehydrogenative alcohol coupling reactions for the first time in literature. Dehydrogenative alcohol coupling and crossmetathesis reactions were combined in a one-pot procedure for the synthesis of functional ester molecules from unsaturated alcohol derivatives using ruthenium based olefin metathesis catalysts. Various saturated and unsaturated alcohol derivatives and a set of different bases (NaOH, KOH, Cs₂CO₃, K₂CO₃, KOtBu, NaOMe) were used for the optimization of the dehydrogenative alcohol coupling reactions. The mechanistic aspects of Grubbs catalyzed dehydrogenative alcohol coupling reactions were investigated in detail. To the best of our knowledge, this study represents the first example of one-pot cross-metathesis/dehydrogenative alcohol coupling reactions using Grubbs type catalysts.

Results and discussion

Ruthenium based metathesis catalysts have emerged as efficient initiators for both olefin metathesis and non-metathetic transformation reactions.²⁷⁻²⁹ The potential of Grubbs catalysts in non-metathetic reactions including hydrogenation, carboxylic acid addition and cyclotrimerization reactions has been investigated in our research group.³⁰⁻³⁴ Within this study, we have investigated the performance of Grubbs type ruthenium catalysts on dehydrogenative alcohol coupling reactions. Furthermore, sequential cross-metathesis/dehydrogenative alcohol coupling reactions were performed in a one-pot procedure for the synthesis of functional ester derivatives for the first time in literature. The selectivity of dehydrogenative alcohol coupling reactions of primary alcohols towards the formation of ester or β-alkylated dimeric alcohol strictly depends on catalyst type and reaction conditions.35 Our first attempts were focused on the optimization of dehydrogenative alcohol coupling reactions of 1-octanol in the presence of Grubbs first generation catalyst (G1) (Scheme 1).

As can be seen in literature examples, ruthenium hydride species play a key role in dehydrogenative alcohol coupling reactions.³⁶ Ruthenium hydride complexes decorated with Pincer ligands can selectively catalyze coupling of alcohols



Scheme 1 Ruthenium based metathesis catalysts that are used in this study.

and amines to form esters, imines and amides based on their donating groups.^{37,38} The idea of using Grubbs type catalysts in dehydrogenative alcohol coupling reactions was evolved from the study of Fogg *et al.* which describes the decomposition pathways of Grubbs type catalysts with primary alcohols, followed by subsequent formation of ruthenium hydride species.^{39,40} Dehydrogenative alcohol coupling reactions can be catalyzed by *in situ* generated ruthenium hydride species from Grubbs catalysts. Moreover, olefin metathesis reactions can be combined with dehydrogenative coupling reactions in a one-pot procedure for the transformation of olefinic alcohols into complex structures.

1-Octanol was chosen as the model substrate for the optimization of dehydrogenative alcohol coupling reactions using a variety of metathesis catalysts and bases. A toluene solution of 1-octanol (**1a**, 0.244 M) in the presence of KOH (50% mol) and G1 (5% mol) was reacted at 110 °C under a nitrogen atmosphere. After 6 h, 1-octanol was completely consumed and Guerbet alcohol; 2-hexyl-1-decanol (**2a**) was formed in quantitative yield instead of ester product. At the early stages of the reactions, 1-octanal was observed as an intermediate product but then rapidly consumed to form corresponding Guerbet alcohol (**2a**) in 95% yield.

A variety of different bases (Cs₂CO₃, Na₂CO₃, KOtBu, NaOMe, NaOH and KOH) were tested under identical reaction conditions and results are given in Table 1. The reaction favored the formation of the corresponding ester product; octyl octanoate (**3a**), through the dehydrogenative coupling of 1-octanol in the presence of weak bases (Na₂CO₃ and Cs₂CO₃). However, the overall yield of the reaction was only 48% even after 48 h. In comparison to the weak base assisted G1 catalyzed dehydrogenative coupling reactions, the formation of Guerbet alcohol was predominant when strong bases (KOH, NaOH, KOtBu and NaOMe) were employed under optimized reaction conditions.

To promote the ester formation in G1 catalyzed coupling reactions, 10 mol% PCy_3 was added to stabilize the catalytic intermediates and the reactions were repeated under identical reaction conditions. However, the addition of PCy_3 didn't improve the yield and the selectivity of the reaction.

Ho $1a^7$ Toluene, 110 °C $2a$ CH CH CH CH CH CH CH CH						
Entry	Base	Time (h)	Conv. ^{<i>a</i>} (%)	$2a^{b}$ (%)	3a (%)	
1	КОН	6	99	98	_	
2	KOtBu	6	99	94	_	
3	NaOMe	8	95	90	_	
4	Cs_2CO_3	48	50	_	48	
5	Na_2CO_3	48	25	_	24	
6	K_2CO_3	48	23	_	20	
7	_	24	5	_	_	
8 ^c	Cs_2CO_3/PCy_3	48	60	—	55	

 Table 1
 G1 catalyzed dehydrogenative alcohol coupling reactions of 1octanol

 a Conversion was determined by GC-MS using *n*-tetradecane as internal standard. b GC yield. c 10% (mol%) PCy₃ in 0.5 mL toluene was added to the reaction medium.

On the next trial, the performance of HG2 was tested on coupling reactions of 1-octanol using identical reaction conditions and results are given in Table 2. Unlike G1/KOH and G1/KOH/ PCy₃ catalyzed dehydrogenative alcohol coupling reactions, the addition of 10 mol% PCy₃ in HG2 catalyzed coupling reactions drastically increased the yield of the ester product (**3a**) up to 95% (Table 2, entry 8). When compared to the phosphine-free catalytic process, the addition of 10 mol% PCy₃ to the reaction media improved the reaction yield and shortened the reaction time to 8 hours for the complete consumption of the starting materials. In some cases, potassium octanoate was formed as the side-product and isolated as octanoic acid in 17% yield after acidification of the reaction mixture with 3 N HCl. More detailed experimental results were provided in Tables 3 and 4. The carboxylic acid formation mechanism was given in ESI,† section (Scheme S3, ESI†).

Alcohol coupling reactions can follow two different catalytic pathways. The first pathway includes Tishchenko reactions through the coupling of two aldehyde molecules to generate ester derivatives in the presence of transition metals, alkali alkoxides and lanthanide alkoxides.^{41–43} The second pathway utilizes hemiacetal intermediates through the reaction of aldehydes with alcohols, followed by dehydrogenation reaction to form the final ester product.¹⁶ To determine the plausible mechanism for the coupling reactions, control experiments were carried out using 1-octanal and 1-octanal/1-octanol mixture in the presence of Cs₂CO₃ (Scheme 2).

The reaction of 1-octanal in the absence of G1 didn't give any ester product even after 48 h. The reaction was repeated using 5% mol G1 under identical reaction conditions and only a trace amount of ester product (**3a**) was observed after 48 h. This result isn't surprising since alcohol derivatives are needed to generate ruthenium hydride species from Grubbs type catalysts.^{39,40} These observations showed us that reaction doesn't follow Tishchenko coupling mechanism. To prove that the reaction mechanism involves the hemiacetal pathway, 1-octanol and 1-octanal were reacted in the absence of G1.

 Table 2
 HG2 catalyzed dehydrogenative alcohol coupling reactions of 1-octanol

HO 1a	50 mol % 5 mol % H 10 mol% 7 Toluen	base HG2 PCy ₃ e, 110 °C	2a OH		+ HO′	o 4a	6
					Yiel	d^{b} (%))
Entry	Base	Additive	Time (h)	Conv. ^{<i>a</i>} (%)	2a	3a	4a
1	КОН		24	65	_	55	10
2	KOH	PCy ₃	8	99	—	82	17
3	KO <i>t</i> Bu	_	48	50	—	50	
4	KO <i>t</i> Bu	PCy ₃	12	63	—	63	
5	NaOMe	_	48	40	—	38	
6	NaOMe	PCy ₃	24	94	—	94	—
7	Cs_2CO_3	_	48	47	—	47	—
8	Cs_2CO_3	PCy ₃	12	95	—	95	—
9	_	PCy ₃	48	0	—	—	—

 a Conversion was determined by GC-MS using n-tetradecane as the internal standard. b GC yield.

 Table 3
 Dehydrogenative alcohol coupling of 1-octanol in the presence of various metathesis catalysts

HO (1) 1a	50 mol % Base <u>5 mol % G1</u> Toluene, 110 ℃	2a	(16 +)		γ_6
Catalyst	Base	Time (h)	$\operatorname{Conv.}^{a}(\%)$	$2\mathbf{a}^{b}$	3a
G1	КОН	6	99	98	_
G1	Cs_2CO_3	48	50		48
M1	КОН	6	99	98	_
M1	Cs_2CO_3	48	46	10	35
G2	КОН	12	99	90	
G2	Cs_2CO_3	48	48	25	20
HG2	КОН	48	65		55
HG2	Cs_2CO_3	48	50		47
Aquamet	КОН	48	64	4	58
Aquamet	Cs_2CO_3	48	52	3	26

 a Determined by GC-MS using $n\text{-}{\rm tetradecane}$ as the internal standard. b GC yield.

 Table 4
 The effect of different bases on the selectivity of dehydrogenative coupling of benzyl alcohol

HO Ph $\xrightarrow{50\%}$ base 5% HG2 $\xrightarrow{0}$ Ph $\xrightarrow{0}$ Ph $\xrightarrow{+}$ HO {\xrightarrow{+} HO $\xrightarrow{+}$ HO {\xrightarrow{+} HO $\xrightarrow{+}$ HO {\xrightarrow{+} HO {\longrightarrow{+}				
Entry	Base	3b %	4b %	Conversion ^b (%)
1	KOH ^a	82	8	90
2	K_2CO_3	29	_	36
3	CS_2CO_3	93	—	96
4	KO <i>t</i> Bu	94	—	94
5	$NaOCH_3$	81	19^c	100

^{*a*} Benzoic acid (4b) was formed at the early stages of the reaction as determined by GC-MS analysis. However, benzoic acid was consumed after 12 h of reaction time. ^{*b*} Determined by GC-MS. ^{*c*} Methyl benzoate was formed in this reaction.

Ester product (3a) was obtained in 36% yield after 24 h. The yield of 3a was increased up to 46% when the same reaction of equal amounts of 1-octanol/1-octanal was carried out in the presence of 5% mol G1.

These results suggested that the G1/Cs₂CO₃ catalyzed dehydrogenative coupling of alcohols proceeds through the reaction of aldehyde with alcohol to form a hemiacetal derivative, followed by catalytic dehydrogenation to give ester compound. Similar mechanistic observations regarding the ruthenium catalyzed dehydrogenative alcohol coupling reactions were also reported in the literature.^{16,44} It is important to note that the addition of G1 in 1-octanol/1-octanal mixture didn't significantly increase the reaction yield. These results suggested that the catalytic intermediate that was formed upon reaction of alcohol/base with G1 doesn't exhibit high activity. The tuning of the ligand environment of the catalytic intermediate is necessary to obtain reasonable reaction rates. The substitution of PCy₃ ligand with better σ -donor NHC ligands in the case of HG2 improved the yield of the same reaction up to 90%



Scheme 2 Mechanistic control experiments.



Scheme 3 Reactions of 1-octanol and 1-octanal in the presence of G1 and HG2.

(Scheme 3) Similar results were also obtained with the mechanistic studies regarding HG2 (Schemes S2 and S3, ESI[†])

The proposed reaction mechanism for ester formation reaction was given in Scheme 4. The ruthenium hydride species were formed upon exchange of chloride ligands in Grubbs type complexes with alkoxide ligands. The decomposition of G1 and G2 to yield well-defined ruthenium monocarbonyl hydride species in the presence of primary alcohols was first described by Mol in 2003.^{44,45} Similar ruthenium hydride generation mechanisms were also proposed by Madsen¹⁶ and Fogg.^{39,40}

The alcohol was coordinated to the ruthenium center as the alkoxide ligand. Aldehyde substituted complex was formed through rearrangement of alkoxide ligand by β -hydride elimination. The nucleophilic attack of second alcohol to carbonyl carbon yielded hemiacetal intermediate. The ester formation proceeded simultaneously with β -hydride elimination.



Scheme 4 The proposed reaction mechanism for dehydrogenative coupling of alcohols.

To gain more insight into the in situ formation of ruthenium hydride species from Grubbs catalysts, a mechanistic study was carried out using ¹H and ³¹P NMR in toluene-d₈. Dehydrogenative coupling of 1-octanol in the presence of G1/KOH in deuterated toluene (toluene-d₈) was chosen as the representative reaction. Samples were withdrawn from the reaction mixture at regular intervals and analyzed by ¹H and ³¹P NMR. After 10 minutes of reaction time, ruthenium alkylidene proton signal appearing at 20.00 ppm disappeared and three different ruthenium hydride signals were observed at -8.14 (t, 22.3 Hz, major), -10.62 (d, 32.1 Hz, minor) and -15.82 (s, minor) ppm (Scheme 5). Similar observations regarding the formation of ruthenium hydride species from Grubbs catalysts were also reported in the literature.^{39,40} The mechanistic NMR studies of G1/Cs₂CO₃ mixture yielded the same ruthenium hydride intermediate as confirmed by the proton signal appearing at -8.16(t, J = 22.5 Hz) ppm in ¹H NMR. The minor hydride signals



Scheme 5 $~^{1}\text{H}$ NMR spectrums of in situ formed ruthenium hydride species in toluene-d_8.

(-10.62 and -15.82 ppm) were not observed in the G1/Cs₂CO₃ mixture even after 8 h. An alternative ruthenium hydride formation mechanism from second generation Grubbs catalyst analogs through dissociation of asymmetric NHC ligand was reported by Maudit *et al.*⁴⁶ However, no sign of NHC ligand dissociation was observed in our mechanistic studies.

The reaction of G1/KOH with 1-octanol after 5 minutes vielded four different phosphine species as confirmed by in situ ³¹P NMR analysis. The major phosphine peak appearing at 68.98 ppm can be related to the major ruthenium hydride species decorated with tricyclohexylphosphine ligand.^{39,40} The other peaks appearing at 75.98 and 48.66 ppm indicated the presence of possible phosphine decorated ruthenium hydride species. The presence of free tricyclohexylphosphine was observed at 9.83 ppm (Scheme 6). In the case of G1/Cs₂CO₃, two similar peaks were observed at 68.97 and 49.96 ppm and two additional peaks appeared at 64.25 and 42.39 ppm. G1/Cs₂CO₃ and G1/KOH promoted dehydrogenation reactions showed us that similar catalytic intermediates take role in dehydrogenation reactions and the base strength has a substantial effect on product selectivity on dehydrogenative alcohol coupling reactions. According to the mechanistic studies, the quantitative formation of ruthenium hydride species requires an excess of alcohol and base.

Guerbet alcohol formation is favored when KOH or other strong bases are used instead of Cs_2CO_3 in G1 catalyzed 1-octanol coupling reactions. As previously reported by Fogg *et al.*, the reaction of G1 with methanol/methoxide which involves the formation of ruthenium-aldehyde intermediate proceeds faster than that of G2.⁴⁰ The rapid formation of aldehyde derivatives in G1 catalyzed dehydrogenation reactions. Therefore, aldol condensation reactions may proceed faster than hemiacetal formation/dehydrogenation reactions in the presence of strong bases (KOH, KOtBu and NaOMe). In line



Scheme 6 ^{31}P NMR spectrum of G1/KOH and G1/Cs2CO3 mixture in toluene-d8.



Scheme 7 Guerbet alcohol formation mechanism

with this mechanism, ruthenium hydride formation in HG2/ base system proceeds slower than G1/base systems as confirmed by mechanistic ¹H NMR studies. We believe that as a result of this slow initiation step, no Guerbet alcohol was observed during the reaction of 1-octanol and KOH in the presence HG2 bearing a chelating isopropoxyphenyl based ligand. In line with our observations, free 1-octanal was also observed in G1/KOH catalyzed coupling reactions of 1-octanol.

The mechanism for Guerbet alcohol formation reactions is outlined in Scheme 7. Ruthenium catalyst involves in dehydrogenation of alcohol to aldehydes. In the presence of strong bases, two molecules of aldehyde undergo Aldol condensation to yield an unsaturated aldehyde intermediate.⁴⁷ This intermediate then undergoes ruthenium catalyzed hydrogenation reaction to yield Guerbet alcohol product.

HG2/KOH/PCy₃ (5/50/10%; mol/mol/mol%) system was chosen for the selective formation of ester derivatives through dehydrogenative alcohol coupling reactions of various alcohols. A variety of alcohol derivatives; 1-hexanol (1c), isoamyl alcohol (1d), 10-undecen-1-ol (1e), 1,4-butanediol (1f), cinnamyl alcohol (1g) were used in further reactions and results are given in Scheme 8. 1-Hexanol (1c) and isoamyl alcohol (1d) were rapidly converted to the corresponding ester derivatives (2c and 2d) in 88% and 90% yields after 12 h of reaction time using 10% PCy₃, 50% KOH and 5% HG2 in toluene. In the absence of PCy₃, the reaction proceeded ineffectively, giving only 2c (55%) and 2d (55%) after 48 h of reaction time under identical reaction conditions. The dehydrogenative coupling of olefinic alcohols; 1-cinnamyl alcohol (1g) and 10-undecen-1-ol (1e) were



Scheme 8 HG2 catalyzed dehydrogenative coupling of various alcohols.

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performed using HG2/KOH/PCy₃ under a constant flow of nitrogen for the removal of evolved hydrogen gas to prevent undesired hydrogenation of double bonds. The reaction was completed within 12 h yielding corresponding unsaturated ester derivatives 2e and 2g in 92% and 95% yield. Corresponding carboxylic acids were formed in 8% and 5% yield in 2e and 2g. It is important to note that no metathesis side reaction was observed during dehydrogenative coupling of unsaturated alcohol derivatives.

1,4-Butanediol yielded γ -butyrolactone in higher yields in the both presence and absence of PCy₃ (yields: 98% and 95%) through the coupling of alcohol groups in an intramolecular fashion. It is interesting to note that 1,6-hexanediol yielded oligomeric unidentified product mixture instead of caprolactone under both reaction conditions (HG2/KOH/PCy₃; mol/mol/ mol%, 5/50/10 and 5/50/–).

Cross-metathesis of olefinic alcohol derivatives were intensively studied by several research groups.²⁴⁻²⁶ G1 was reported as an inefficient initiator for cross-metathesis of olefinic alcohols in terms of reaction yield and selectivity. In most cases, aldehydes and undefined side-products were obtained in G1 catalyzed metathesis reactions. On the other hand, HG2 performed cross-metathesis and self-metathesis of olefinic alcohols in quantitative yields in a short amount of time without any side products. Considering the above-mentioned facts, HG2 was chosen as the initiator for sequential cross-metathesis/dehydrogenative coupling reactions. Cross-metathesis of various olefinic alcohol derivatives such as olevl alcohol, cinnamyl alcohol, allyl alcohol were studied intensively using HG2 as the metathesis initiators. HG2 (5%) catalyzed cross-metathesis of allyl alcohol and 1-octene (10 fold excess) at 30 °C yielded 2-nonen-1-ol as the major product along with self-metathesis product of 1-octene; 7-tetradecene after 2 h. (Scheme 9). An excess of 1-octene was used to suppress the self-metathesis of allyl alcohol. Following the complete consumption of allyl alcohol and subsequent formation of 2-nonel-1-ol, KOH (50%) and PCy₃ (10%) in toluene were added to the reactor and the temperature of the reaction mixture was increased to 110 °C to initiate the dehydrogenative alcohol coupling reactions under constant nitrogen flow. Despite

5 mol % HG2 ⁵ 1i Toluene 30 °C 1h OH /5 2h-i (Not isolated) 50 mol % KOH Toluene 10 mol % PCy₃ 110 °C 0 \mathbb{N}_{5} $()_{5}$ 3h-i Overall yield: 85 %

Scheme 9 One-pot cross-metathesis/dehydrogenative alcohol coupling of allyl alcohol/1-octene.

the constant nitrogen flow, at the early stages of the reaction, nonalal and hydrogenation product; 1-nonanol were formed and then rapidly consumed to form nonyl nonanoate.

After 24 h, the conversion of nonalal and 1-nonanol was reached a plateau and corresponding saturated ester product; nonyl nonanoate was obtained in 85% yield. Although the reactions were carried out under static nitrogen flow, all double bonds were hydrogenated very rapidly after the metathesis reaction. Despite our countless efforts, the isomerization reactions of double bonds couldn't be suppressed.

As it can be seen in Scheme 8, dehydrogenative coupling of 1,4-butanediol yields γ -butyrolactone. We have foreseen that sequential self-metathesis of allyl alcohol followed by subsequent dehydrogenative coupling reactions can be a model reaction to build lactone derivatives efficiently (Scheme 10). For this purpose, the self-metathesis of allyl alcohol was studied under ambient reaction conditions. A Schlenk reactor was charged with allyl alcohol (0.25 M) in toluene and HG2 (5%) and reacted at 30 °C. After one hour, allyl alcohol was completely consumed and self-metathesis product; 2-butene-1,4-diol was obtained as the major product and a trace amount of 1,4-butanediol was observed. A suspension of KOH (50%) in toluene was added to the reactor and the reaction temperature was increased to 110 °C. At the early stages of the reaction, 2-butene-1,4-diol was hydrogenated to 1,4-butanediol. After 24 h, γ -butyrolactone was obtained with an overall yield of 88%.

The compatibility of dehydrogenative coupling reactions with ethenolysis reactions was investigated using cinnamyl alcohol and oleyl alcohol as the model substrates under an ethylene atmosphere. Ethenolysis of cinnamyl alcohol was performed in toluene under ethylene atmosphere (1 atm) at 80 °C (Scheme 11). Cinnamyl alcohol was completely converted to ethenolysis products; styrene and allyl alcohol within 30 minutes of reaction time. The reactor was charged with 50% KOH and 10% PCy₃ and the reaction temperature was increased to 110 °C under a nitrogen atmosphere to initiate the dehydrogenative coupling reactions. Although hydrogenation



Scheme 10 One-pot self-metathesis/dehydrogenative coupling of allyl alcohol.



Scheme 11 One-pot ethenolysis/dehydrogenative coupling of cinnamyl alcohol and oleyl alcohol.

products; ethylbenzene and *n*-propanol were observed in GC analysis, no dehydrogenative coupling products were formed even after 48 h of reaction time.

Oleyl alcohol is a more challenging substrate than cinnamyl alcohol in ethenolysis reactions due to its isomerization tendency (Scheme 11). Ethenolysis of oleyl alcohol under ethylene atmosphere (1 atm) yielded an isomeric mixture of both starting material and ethenolysis products (50% conversion, 80% isomerization). On the next trial, ethylene gas was continuously bubbled throughout the reaction to suppress isomerization reactions, however, a significant amount of isomerization product was obtained again (65% isomerization). The pressure of ethylene gas was increased to 4 atm to increase the reaction yield and suppress isomerization. However, all our efforts to suppress undesired olefin isomerization have failed. One of the known methods for suppressing olefin isomerization during the metathesis reaction is to use 1,4-benzoquinone as the hydride scavenger.^{48,49} However, ruthenium hydride is the key species in our sequential cross-metathesis/dehydrogenative coupling reactions, therefore we didn't employ benzoquinone as the isomerization suppressor. The addition of solely 50% KOH or KOH/PCy₃ (50/10; mol/mol) to the above-mentioned reaction mediums triggered the formation of isomerization reactions however no dehydrogenative coupling product was formed.

Conclusion

In summary, Grubbs catalysts performed the dehydrogenative alcohol coupling and one-pot cross-metathesis/dehydrogenative coupling reactions of various alcohol derivatives selectively for the first time in literature. The selectivity of G1 was tuned by varying base in the dehydrogenative coupling of 1-octanol to produce β-alkylated alcohols (Guerbet) with strong bases (up to 95% yield) and ester derivatives with weak bases (up to 95% yield). The in situ formation of ruthenium hydride species during G1 and HG2 catalyzed coupling reaction was confirmed by ¹H NMR mechanistic studies. Following the optimization of reaction conditions, one-pot cross-metathesis/dehydrogenative alcohol coupling reaction were investigated using allyl alcohol,cinnamyl alcohol and oleyl alcohol as the olefinic substrates. The one-pot dehydrogenative coupling/self-metathesis of allyl alcohol gave γ -butyrolactone in excellent yield using 5% HG2, 50% KOH and 10% PCy3. The sequential cross-metathesis of 1-octene with allyl alcohol and dehydrogenative coupling reactions gave nonyl nonanoate in 85% yield. It is noteworthy that all double bonds of olefinic alcohols were saturated during dehydrogenative coupling reactions. Although ethenolysis of cinnamyl alcohol and oleyl alcohol proceeded rapidly with HG2 under ethylene atmosphere, in situ formed allyl alcohol and 9-decen-1-ol didn't undergo dehydrogenative coupling reactions.

Experimental section

Otherwise noted all chemicals were purchased from Sigma-Aldrich and used as received. Toluene and *p*-xylene were dried over CaH₂ and distilled under nitrogen atmosphere. Gas chromatography-mass spectrometry (GC-MS) analyses were performed with a Shimadzu GC-MS 2010Plus using a Restek Rxi-5Sil column (30 m × 0.25 mm × 0.25 µm) and temperature range of 50–320 °C with a constant helium flow rate of 1 mL min⁻¹. ¹H, ¹³C and ³¹P NMR spectra were recorded at 25 °C with a Bruker GmbH 400 MHz high performance digital FT-NMR spectrometer using CDCl₃ and toluene-d₈ as NMR solvents.

Representative procedure for Ru-catalyzed dehydrogenative alcohol coupling reactions

Ruthenium catalyst (0.0122 mmol), KOH (0.122 mmol, 0.0068 g) and 1-octanol (0.244 mmol, 38 µL) in dry toluene (1 mL) were added to a glass Schlenk reactor under nitrogen atmosphere. The reactor was heated to 110 °C in a preheated oil bath and magnetically stirred. Samples regularly were withdrawn from the reaction mixture, diluted with methanol and analyzed by GC/MS. Once the conversion of 1-octanol has reached a plateau, toluene was removed by a high vacuum and the residual content was dissolved in CH2Cl2 and acidified with 3 N HCl to pH 2-3 for the isolation of carboxylic acid side products. The organic phase was extracted with water (5 mL \times 3) to remove the excess KOH. The organic phase of the solution was passed through a plug of silica gel to remove any catalytic impurities and then the organic phase was dried by the addition of MgSO₄. CH₂Cl₂ was removed under high vacuum and reaction product was analyzed by GC-MS and ¹H NMR in CDCl₃. Products were isolated using dry column vacuum chromatography (DCVC) starting from 100% *n*-hexane as the non-polar phase, followed by increasing the polarity of the mobile phase (5% for each addition) with ethyl acetate.

Representative procedure for HG2/PCy₃-catalyzed dehydrogenative alcohol coupling reactions

HG2 (0.01 g, 0.0122 mmol), KOH (0.122 mmol, 0.0068 g), PCy₃ (0.068 g, 0.0244 mmol) and 1-octanol (0.244 mmol, 38 µL) in dry toluene (1 mL) were added to a glass Schlenk reactor under nitrogen atmosphere. The reactor was heated to 110 °C in a preheated oil bath and magnetically stirred. Samples regularly were withdrawn from the reaction mixture, diluted with methanol and analyzed by GC/MS. Once the conversion of 1-octanol has reached a plateau, toluene was removed by a high vacuum and the residual content was dissolved in CH₂Cl₂ and the organic phase was extracted with water (5 mL \times 3) to remove the excess KOH. The organic phase of the solution was passed through a plug of silica gel to remove any catalytic impurities and then the organic phase was dried by the addition of MgSO₄. CH₂Cl₂ was removed under high vacuum and reaction product was analyzed by GC-MS and ¹H NMR in CDCl₃. Products were isolated using dry column vacuum chromatography (DCVC) starting from *n*-hexane as the non-polar phase, followed by increasing the polarity of the mobile phase gradually (5% for each addition) with ethyl acetate.

Representative procedure for the ruthenium-catalyzed dehydrogenative alcohol coupling reactions

1-Octanol (0.244 mmol, 38 μ L) and benzyl alcohol (0.488 mmol, 51 μ L) were added to a glass Schlenk reactor under a nitrogen atmosphere and magnetically stirred for five minutes at room temperature. KOH (0.122 mmol, 0.0068 g), PCy₃ (0.068 g, 0.0244 mmol) and G1 (0.01 g, 0.0122 mmol) were added in one portion to the reactor and the reaction mixture was stirred at 110 °C under nitrogen atmosphere. Samples were regularly withdrawn from the reaction mixture, diluted with methanol and analyzed by GC-MS. Products were isolated using dry column vacuum chromatography (DCVC) starting from *n*-hexane as the non-polar phase, followed by increasing the polarity of the mobile phase (5% for each addition) with ethyl acetate.

Representative procedure for the metathesis and cross-metathesis/ dehydrogenative alcohol coupling reactions

Cross-metathesis of 1-octene and allyl alcohol. Allyl alcohol (0.500 mmol, 34 μ L), 1-octene (0.955 mmol, 150 μ L) and dry toluene (1.5 mL) were mixed in a glass Schlenk reactor and stirred for five minutes at 30 °C. HG2 (0.0160 mmol, 0.010 g) in toluene (0.5 mL) was added to the reactor in one portion and the reaction mixture was magnetically stirred for 1 h at 30 °C. Samples were regularly withdrawn from the reaction mixture and analyzed by GC-MS.

One-pot cross-metathesis/dehydrogenative alcohol coupling reactions of allyl alcohol and 1-octene. Allyl alcohol (0.500 mmol, 34 μ L), 1-octene (0.955 mmol, 150 μ L) and dry toluene (1.5 mL) were mixed in a glass Schlenk reactor and stirred for five minutes at 30 °C. HG2 (0.0160 mmol, 0.010 g) in toluene (0.5 mL) was added to the reactor in one portion and the reaction mixture was magnetically stirred. Following the complete consumption of allyl alcohol after 1 h, a suspension of KOH (0.250 mmol, 0.014 g) and PCy₃ (0.050 mmol) in 0.5 mL toluene was added to the reactor and the temperature was increased to 110 °C. Samples were regularly withdrawn from the reaction mixture and analyzed by GC-MS.

Self-metathesis of allyl alcohol. Allyl alcohol (0.320 mmol, 22 μ L) and dry toluene (2.0 mL) were mixed in a glass Schlenk reactor and stirred for five minutes at 30 °C. HG2 (0.0160 mmol, 0.010 g) in toluene (0.5 mL) was added to the reactor in one portion and the reaction mixture was magnetically stirred for 1 h at 30 °C. Samples were regularly withdrawn from the reaction mixture and analyzed by GC-MS.

One-pot self-metathesis/dehydrogenative alcohol coupling reactions of allyl alcohol. Allyl alcohol (0.32 mmol, 22 μ L) and dry toluene (2.0 mL) were mixed in a glass Schlenk reactor and stirred for five minutes at 30 °C. HG2 (0.0160 mmol, 0.010 g) in toluene (0.5 mL) was added to the reactor in one portion and reaction mixture was magnetically stirred for 1 h at 30 °C. Following the complete consumption of allyl alcohol after 1 h, a suspension of KOH (0.160 mmol, 0.0090 g) and PCy₃ (0.0320 mmol, 0.0090 g) in 0.5 mL toluene was added to the reactor and the temperature was increased to 110 °C. Samples were regularly withdrawn from the reaction mixture and analyzed by GC-MS.

Representative procedure for ethenolysis and one-pot ethenolysis/ dehydrogenative coupling of cinnamyl alcohol and oleyl alcohol

A Schlenk reactor was charged with cinnamyl alcohol (0.320 mmol, 0.043 g) in dry toluene (2.0 mL). Ethylene gas (1 atm) was bubbled through the reaction mixture for 5 minutes before the introduction of HG2 (0.0160 mmol, 0.010 g) in toluene (0.5 mL). The reaction mixture was then taken to a pre-heated oil bath at 80 °C to initiate the ethenolysis reactions. After 2 h, cinnamyl alcohol was completely converted to the desired ethenolysis products; styrene and allyl alcohol as confirmed by GC-MS analysis. After that, the reaction of the temperature was increased to 110 °C and KOH (0.160 mmol, 0.0090 g) and PCy₃ (0.0320 mmol, 0.0090 g) was added to the reactor. Samples were regularly withdrawn from the reaction mixture and analyzed by GC-MS.

Representative procedure for NMR mechanistic studies

G1 (0.01 g, 0.0122 mmol), KOH (0.122 mmol, 0.0068 g) and 1-octanol (0.244 mmol, 38 μ L) in toluene-d₈ (1 mL) were added to a glass Schlenk reactor under nitrogen atmosphere. The reactor was heated to 110 °C in a preheated oil bath and magnetically stirred. Samples regularly were withdrawn from the reaction mixture and the samples were diluted with toluene-d₈ and analyzed by ¹H and ³¹P NMR.

Conflicts of interest

There are no conflicts to declare.

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