Rhodium catalyzed selective hydroaminomethylation of biorenewable eugenol under aqueous biphasic condition

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Rhodium Catalyzed Selective Hydroaminomethylation of Biorenewable Eugenol Under an Aqueous Biphasic Condition

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Abstract

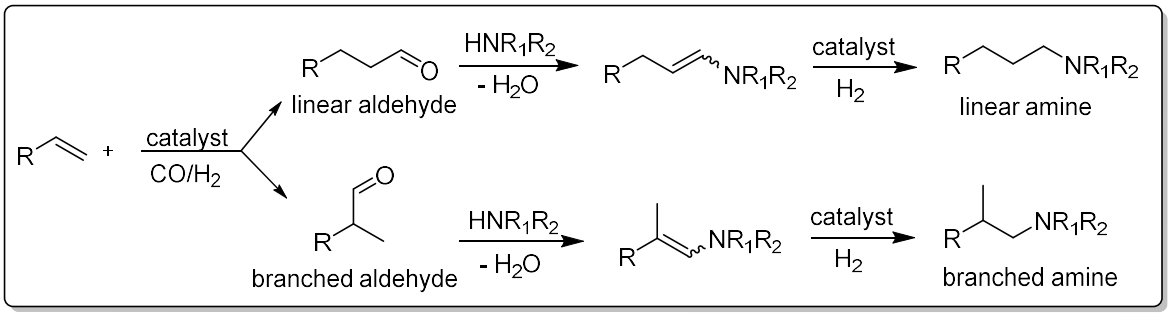
This work reports highly regioselective hydroaminomethylation of eugenol, anethole and estragole with piperidine in aqueous medium. The catalytic system was composed of rhodium complexes stabilized by the trisulfonated triphenylphosphine (TPPTS) and of a native or chemically modified cyclodextrin. Various cyclodextrins such as *α*-cyclodextrins (*α*-CD), *β*-cyclodextrin (*β*-CD), *γ*-cyclodextrin (*γ*-CD), hydroxyl propyl *β*-cyclodextrin (hp-*β*-CD) and RAndomly MEthylated *β*-cyclodextrin (RAME-*β*-CD) have been tested. The effect of different parameters such as syngas pressure, time, temperature, catalyst precursor/loading and the ratio of Metal/Ligand/Cyclodextrin were also investigated. The addition of cyclodextrins as a mass transfer agent emarkably increased the rate reaction and the selectivity of linear amines, specially in the case of RAME-β-CD. So, the Rh/TPPTS/RAME-β-CD catalytic system exhibited high conversion (99%) and selectivity (85%) towards the linear amine as major product under mild conditions. Finally, the catalytic system could be recycled five times without a significant decrease in activity and selectivity.

Keywords: Amines, Biphasic hydroaminomethylation, Rhodium, TPPTS, Cyclodextrins, Eugenol.

1. Introduction

Amines are a class of valuable organic compounds for the pharmaceutical, agrochemical and fine chemical industries [1]. Hydroaminomethylation (HAM) reaction is a highly atom-economical, homogeneous industrial process for the synthesis of linear and branched amines from olefins, amines and syngas by the use of single catalyst [2]. The HAM process is a triple sequential reaction involving hydroformylation of an alkene, condensation of the produced aldehyde with an amine, and the hydrogenation of the resulting imine or enamine, which provides a highly efficient method to construct amines **(Scheme 1)** [3]. It has high attraction in industry as well as in academics, since it was discovered by reppe in 1949 at BASF [4]. There are processes available for the production of aliphatic amines consist of hydroamination, hydrocyanation of alkenes followed by reduction, nucleophilic substitution of alkyl halides, reductive amination of carbonyl compounds etc. Despite these processes available, amine preparation often suffers from low generality, costly starting materials, side reactions and the necessity of protecting groups [5].

Scheme 1. *The general hydroaminomethylation of olefins and amines.*



In general, the hydroaminomethylation reactions are carried out in a homogeneous catalytic system, [6-9] which suffers from some shortcomings such as the difficulties of the catalyst recovery, catalyst separation from products, selectivity of desired product, to control the hydrogenation and isomerisation etc. [10]. Probable solutions to these troubles consist of making the homogeneous catalyst into heterogeneous by anchoring the metal on support or by using two-phase catalytic system. Beller and co-workers[11] reported the hydroaminomethylation of C5 olefins in aqueous-organic biphasic catalysis in 1999. The catalytic system was composed of Iridium and Rhodium complexes stabilized by trisulfonated

triphenylphosphine (TPPTS: $P(m\text{-}C_6H_4SO_3Na)_3$) or sulfonated 2,2'-bis(diphenylphosphinomethyl)-1,1'-binaphthylene (BINAS). Addition of iridium complex was required to increase the catalytic activity and amine selectivity. Indeed, the rhodium catalysts are not sufficiently active for the hydrogenation of the imine at high phosphorus to rhodium ratio.

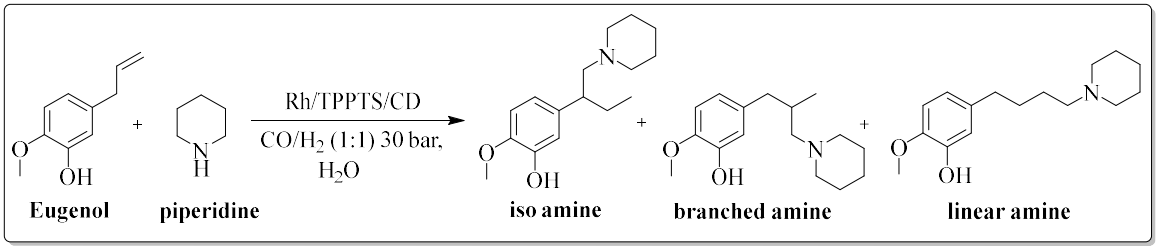
In 2004, Li group[12] reported the hydroaminomethylation of long chain olefins with poor water solubility in an aqueous-organic biphasic system using the water-soluble rhodium complex $RhCl(CO)(TPPTS)_2$ as catalyst in the presence of the cationic surfactant cetyltrimethylammonium bromide. The use of sulfonated 2,2'-bis(diphenylphosphinomethyl)-1,1'-biphenyl ligand (BISBIS) instead of TPPTS ligand significantly improved the amine selectivity (80 % vs. 46 % for the BISBIS and TPPTS, respectively) and linear/branched amines selectivities (l:b ratio: 83 vs. 15 for the BISBIS and TPPTS, respectively) [13]. Interestingly, A. Behr et al. have reported that the addition of inorganic and organic acids allowed the quantitative conversion of 1-octene with very high selectivity for the amines. For instance, the hydroaminomethylation of 1-octene with synthesis gas and di-n-butylamine gives rise to the desired amines in 96 % yield in the presence of sulfuric acid [14].

In 2005, Behr and co-workers[15] achieved also the hydroaminomethylation of 1-octene with morpholine in temperature-dependent solvent systems, in which reaction occurs in a single-phase at a higher temperature followed by splitting into two phases at a lower temperature. Furthermore, in 2006 Wang and co-workers reported the biphasic hydroaminomethylation of long chain olefins in ionic Liquids [16]. Although the catalyst could be easily separated by a simple phase separation, the catalyst recycling remained to be improved. Though the several practices have been explored for hydroaminomethylation of olefins in recent years [17], the synthesis of linear amines from internal and terminal natural olefins such as eugenol, anethole and estragole is always challenging. Such reactions are of industrially important because natural olefins such as eugenol, anethole and estragole are more cost-efficient and abundant in nature. These bio-renewable starting materials which are the derivatives of natural allyl benzenes were obtained from biomass, such as eugenol from cloves, anethole from basil and estragole from sweet basil etc.[18].

As a continuation of our research on the catalytic valorization of biomass to value-added products, [19] we hereby report the aqueous biphasic hydroaminomethylation of eugenol into linear amines using Rh/TPPTS as catalytic system and cyclodextrins (CDs) as

mass transfer promoters (**Scheme 2**). Chemically modified CDs are cyclic oligosaccharides composed of (α-1,4) -linked α-D-glucopyranose units which is obtained from the enzymatic conversion of starch [20]. These compounds allowed to achieve the catalytic fonctionalisation of numerous substrate in an aqueous organic two-phase system with high reaction rates, while avoiding the formation of an emulsion and the partition of the catalyst between the organic and aqueous phases. This outstanding result was attributed to the formation of inclusion complexes at the aqueous/organic interface [21]. The main objective of this work is to investigate the effect of the various cyclodextrins such as *α*-cyclodextrin (*α*-CD), *β*-cyclodextrin (*β*-CD), *γ*-cyclodextrin (*γ*-CD), hydroxyl propyl *β*-cyclodextrin (hp-*β*-CD) and RAndomly MEthylated *β*-cyclodextrin (RAME-*β*-CD) on the rate and selectivities of hydroaminomethylation of eugenol.

Scheme 2. *An Aqueous biphasic selective hydroaminomethylation of naturally occurring eugenol and piperidine using Rh/TPPTS/CD as greener and reusable catalytic system.*



2. Experimental

2.1 General Methods and reagents

All the reaction experiments were carried out in presence of nitrogen atmosphere. The chemicals and reagents were procured from Sigma Aldrich, Alfa Aesar, Spectrochem Pvt. Ltd., India with a purity grade of 99% and higher which are used as received. The distilled deionized water was used as solvent in all experiments. A syngas containing mixture of hydrogen (49.9%) and carbon monoxide (49.9%) were purchased from Rakhangi Gas Service, Mumbai. All experiments were performed in a 100 mL autoclave. The reaction process was monitored by gas chromatography on Perkin Elmer Clarus 400 GC equipped with flame ionization detector with a capillary column (Elite-1, 30 m x 0.32 mm x 0.25 µm). GC-MS-QP 2010 instrument (Rtx-17, 30 m × 25 mm ID, film thickness 0.25 µm df) (column flow 2 10 mLmin-1, 80 °C to 240 °C at 10°/min rise).

2.2 Typical experimental procedure for aqueous biphasic hydroaminomethylation of Eugenol

In a 100 mL volume of high pressure reactor, Eugenol (1 mmol), Piperidine (1 mmol), [Rh(acac)$(CO)_2$] (0.0015 mmol), TPPTS (0.0075 mmol), RAME-*β*-CD (0.015 mmol) and deionised distilled water (10 mL) were added. Then reactor was closed, flushed three times with syngas and pressurized with 30 bar of syngas pressure heated with 80 °C for 8 h. After the completion of the reaction, the reactor was cooled down to room temperature, remaining syngas gas was vented carefully and the reactor was opened. The organic layer containing product from aqueous layer was separated by a simple separation technique using separating funnel. The reactor vessel was thoroughly washed with ethyl acetate (3 × 5 mL) to remove traces of the product. The reaction mixture was collected in separating funnel and separates the organic layer containing product. The separated aqueous layer containing catalytic system was reused as catalyst for further recycle experiment. The organic layer containing product was passed through dry Na_2SO_4 to remove traces of water (moisture) if present and it is subjected to GC and GC-MS analysis.

2.3 Typical experimental procedure for recycling of the Catalyst (Rh/TPPTS/CD) for aqueous biphasic hydroaminomethylation of Eugenol

The procedure for the recovery and recycling of the catalytic system were carried out under inert condition that is in nitrogen atmosphere. The catalytic system was recovered by separating the aqueous layer from organic layer in the separating funnel. The reaction mixture was washed three times with 5 mL of ethyl acetate to remove the complete product from the reation mixture. Then the organic layer was separated from aqueous solution. This aqueous solution containing metal, ligand and cyclodextrin was collected and used as it is for next recycle experiment. The Rh/TPPTS/CDs as biphasic catalytic system was easily recycled up to five consecutive cycles without loosing its catalytic activity and selectivity.

3. Results and Discussion

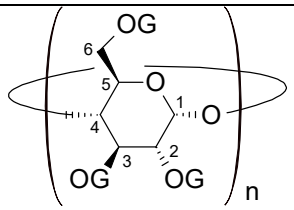
3.1 Selective hydroaminomethylation of eugenol and piperidine using Rh/TPPTS/CD an as reusable catalyst under an aqueous biphasic condition

The aqueous biphasic hydroaminomethylation of eugenol (**1a**) and piperidine (**1a***) to linear amine i.e. 2-methoxy-5-(4-(piperidin-1-yl)butyl)phenol (**4a**) was chosen as model reaction. The reaction was conducted under an aqueous media with Rhacac$(CO)_2$ as a catalyst precursor, TPPTS as water soluble phosphine lignd and cyclodextrin as mass transfer promoter. The reaction experiments was carried out under the nitrogen atmosphere.

3.2 An influence of various modified cyclodextrins and its concentration on the hydroaminomethylation of eugenol (1a) and piperidine (1a)*

The properties and chemical environment of native cyclodextrins (α-CD, β-CD and γ-CD) and modified cyclodextrins (RAME-α-CD, RAME-β-CD and hp-β-CD) were shown in table 1. Cyclodextrins are the cyclic oligosaccharides with a hydrophilic outer surface and a lipophilic central cavity. The α-CD, β-CD and γ-CD contains 6, 7 and 8 (α-1,4) linked α-D-glucopyranose units, respectively. The RAME-α-CD and RAME-β-CD were a mixture of CDs partially O-methylated with statistically 11.8 OH and 12.6 groups modified per CD, respectively. The OH groups in C-6 position are fully methylated whereas those in C-2 and C-3 positions are partially methylated (Table 1, entries 4 and 5). The hp-β-CD is a mixture of β-CDs partially O-hydroxypropylated with statistically 5.6 OH groups modified per CD. The OH groups can be in C-2, C-3 or C-6 positions (Table 1, entry 6).

Table 1. *Chemical structure and characteristic of the cyclodextrin derivatives*



G : H or R

Entry	Abbreviation	n	Substituent R	Carbons bearing the OR group	Number of R groups per CD	Molecular weight(g mol^{-1})
1	α-CD	6	(-)	(-)	0	972
2	β–CD	7	(-)	(-)	0	1134
3	γ–CD	8	(-)	(-)	0	1297
4	RAME-α-CD	6	CH_3	2, 3 and 6	10.8	1127
5	RAME-β-CD	7	CH_3	2, 3 and 6	12.6	1314
6	HP-β-CD	7	CH_2-CHOH-CH_3	2, 3 and 6	5.6	1460

Primarily, we have studied an influence of various cyclodextrins and its concentration on the hydroaminomethylation of eugenol (**1a**) and piperidine (**1a***) to the synthesis of **4a** as shown in Table 2. The first reaction was carried out in absence of cyclodextrins i.e the Rh/TPPTS/H_2O used as catalytic system which can affords 67% conversion with 62% yield of amines and 50% selectivity of **4a** (Table 2, entry 1). We tested the α-CD at various

concentrations of 0.030 mmol, 0.061 mmol and 0.102 mmol (Table 2, entries 2-4) for the hydroaminomethylation of **1a**, out of these three concentrations 0.061 mmol of α-CD provides good conversion (84%) and selectivity (66%) of **4a** (Table 2, entry 3). It was achieved the 75% yield of amines and 80% selectivity of **4a** along with 92 % conversion for 0.0052 mmol concentration of β-CD (Table 2, entry 6). As compared to the α-CD and γ-CD, superior results were obtained with 0.026 mmol and 0.088 mmol concentration of β-CD used (Table 2, entries 5-7). The fewer yield of amines and low selectivity of **4a** was observed using α-CD (Table 2, entries 2-4) and γ-CD (Table 2, entries 8-10) rather than the use of β-CD at the same rection conditions. From these results, it is indicated that the size of CDs cavity was play to be key limit to handle the catalytic activity.

Furthermore, modified CDs such as RAME-α-CD, RAME-β-CD and hp-β-CD were also evaluated. A 0.053 mmol concentration of RAME-α-CD can provides the 85% conversion of **1a**, 70% yield of amines with 62% selectivity of **4a** (Table 2, entry 12). The RAME-α-CD can provides better conversion, but selectivity was observed to be less as compared to the RAME-β-CD and hp-β-CD (Table 2, entries 11-13). Then the RAME-β-CD showed the best results at 0.0252 mmol concentration for higher conversion (99%) of **1a** and high selectivity (85%) of **4a** (Table 2, entry 15). Increase in concentration of RAME-β-CD from 0.010 mmol to 0.040 mmol resulting into the conversion increases from 94% to 99%. The yield of amine and selectivity of linear amine initially increases and then decreases finally (Table 2, entries 14-16). The high activity can likely be attributed to the surface-active properties of RAME-β-CD and selectivity towards the **4a** could be due to the steric hinderance of randomly methyl groups present in the RAME-β-CD. Finally, the hp-β-CD was also demonstrated finer results for conversion of **1a** and selectivity of **4a** (Table 2, entries 17-19). The high conversion up to 85% and yield of amines to 86% with selectivity up to 69% of **4a** can be achieved using 0.041 mmol concentration of hp-β-CD (Table 2, entry 18).

These results indicate that the presence of CD allows in every case to enhance the selectivity of linear amines. This selectivity increase can be explained by the inclusion of the substrate inside the cavity of cyclodextrins. Definitely, the CD can transitorily accommodate the substrate into its cavity restricting its conformational flexibility and masking a part of the allyl group while exposing distal position of the allyl group to Rh catalytic species. This result is noteworthy given the well-known ability of CD to interact with TPPTS to form phosphane

low-coordinated species which are expected to be less regioselective in the hydroaminomethylation reaction (**Scheme 3**) [22, 23, 24]

Scheme 3. *Plausible reaction mechanism for the selective hydroaminomethylation of eugenol using Rh/TPPTS with RAME-β-CD as greener and reusable catalytic system.*

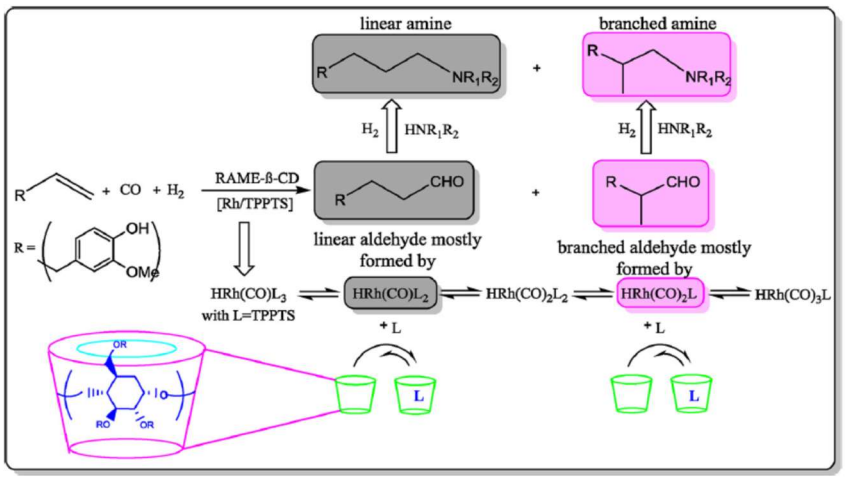
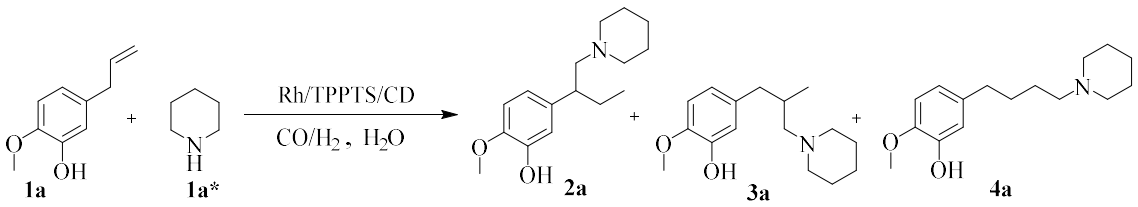


Table 2. *An influence of different cyclodextrins (CDs) and its concentration on the aqueous biphasic hydroaminomethylation of eugenol (1a) and piperidine (1a*)* [a]



Entry	CDs	Conc. in mmol	Conv. (%)[b]	Hydro:Iso: Ald. (%)[b]	Amines (%)[b]	Selec. (%)[b] 2a:3a:**4a**
1[c]	-	-	67	09:09:20	62	20:30:50
2	α-CD	0.030	82	08:10:14	68	14:24:62
3	α-CD	0.061	84	07:09:09	75	12:22:66
4	α-CD	0.102	83	08:12:10	70	10:26:64
5	β-CD	0.026	88	08:12:10	70	10:15:75
6	β-CD	0.052	92	10:10:05	75	06:14:80
7	β-CD	0.088	91	08:12:08	72	10:18:72
8	γ-CD	0.025	69	14:12:12	62	10:20:70
9	γ-CD	0.050	79	10:14:10	66	10:16:74
10	γ-CD	0.083	77	10:13:09	68	14:18:68
11	RAME-α-CD	0.028	80	09:08:15	68	21:12:67
12	RAME-α-CD	0.055	85	10:10:10	70	18:20:62
13	RAME-α-CD	0.090	84	11:10:10	69	15:20:65
14	RAME-β-CD	0.010	94	03:04:08	85	08:12:80
15	**RAME-β-CD**	**0.020**	**99**	**04:03:06**	**87**	**04:11:85**
16	RAME-β-CD	0.040	99	05:06:03	86	10:11:79
17	hp-β-CD	0.020	80	03:05:07	85	15:20:65
18	hp-β-CD	0.040	85	03:03:08	86	11:20:69
19	hp-β-CD	0.068	90	03:04:09	84	18:20:62

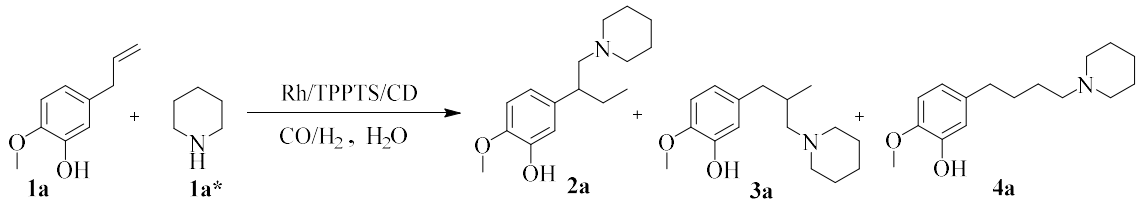
[a]**Reaction Conditions**: 1a (1 mmol), 1a* (1 mmol), [$Rhacac(CO)_2$] (0.002 mmol), TPPTS (0.008 mmol), CO/H_2 (30 bar), Distilled water (10 mL), 80 ºC, 24 h. [b]Determined by GC and GC-MS. [c]$Rh/TPPTS/H_2O$ as catalyst. RAME= RAndomly MEthylated, hp= hydroxy propyl.

3.3 An optimization of various reaction parameters for the hydroaminomethylation of eugenol (1a) and piperidine (1a)*

The different reaction parameters such as the effect of syngas (CO/H_2) pressure, time, temperature, catalyst screening and loading were studied for the regio-selective hydroaminomethylation of eugenol (**1a)** and piperidine (**1a***). These results are summarized in tables 3 and 4. Similarly the effect of metal to ligand to CDs ratio were screened and results are shown in Figure 1.

The effect of syngas pressure plays a crucial role in the hydroaminomethylation reaction using aqueous biphsic Rh/TPPTS/CDs. The use of 40 bar of syngas pressure, the conversion was almost complete but selectivity of the product (**4a**) was less about 60% (Table 3, entry 1). The 30 bar of syngas pressure was optimum pressure for reaction in which it can offer high conversion (99%) of **1a** and selectivity (78%) towards **4a** (Table 3, entry 2). After that we decreased the syngas pressure up to 20 bar, the conversion diminished to 94% and the selectivity up to 70% with less amount 10% of hydrogenation, isomerisation and aldehydes was also observed (Table 3, entry 3). Then we also studied the relative concentration ratio of carbon monoxide (CO) and hydrogen (H_2) gas by varieng the ratio of $CO:H_2$ such as 1:2 for 45 bar, 1:2 for 30 bar and 1:4 for 32 bar (Table 3, entries 4-6). At the 1:2 or 1:3 ratio of $CO:H_2$, good yields were obtained, but the results indicated that the high conversion and selectivity were achieved at 1:1 ratio of $CO:H_2$. We examine the 1:2 ratio of $CO:H_2$ at 45 bar of syngas pressure, 92% conversion and 58% selectivity of **4a** with less amount 20% of hydrogenation, isomerisation and aldehydes was detected (Table 3, entry 4). Then we reduced the pressure to 30 bar at same ratio of $CO:H_2$, slightly increase in the selectivity (62%) of **4a** and decrease in the hydrogenation and isomerisation products (Table 3, entry 5). Afterwards, we scrutinized 1:3 ratio of $CO:H_2$ for 32 bar, selectivity of expected product (**4a)** doesn't change so far, but the yield hydrogenation (20%) and isomerisation (12%) increased (Table 3, entry 6). Thus, 30 bar of $CO:H_2$ pressure with 1:1 ratio was selected as optimum pressure for the hydroaminomethylation reaction of eugenol (**1a**) and it was used for further optimization of various reaction parameters.

Table 3. *The study of various reaction parameters for an aqueous biphasic hydroaminomethylation of eugenol (1a) and piperidine (1a*)* [a]



Entry	Pressure in bar (CO:H_2)	Time (h)	Temp. (ºC)	Conv. (%)[b]	Hydro:Iso:Ald. (%)[b]	Sele. (%)[b] (2a:3a:4a)
Effect of syngas pressure						
1	40 (1:1)	12	80	100	03:06:09	16:24:60
2	**30 (1:1)**	**12**	**80**	**99**	**03:04:05**	**10:12:78**
3	20 (1:1)	12	80	94	03:03:04	14:16:70
4	45 (1:2)	12	80	92	14:06:04	14:28:58
5	30 (1:2)	12	80	90	10:05:09	12:26:62
6	32 (1:3)	12	80	96	20:12:13	15:25:60
Effect of time						
7	30 (1:1)	24	80	100	15:08:05	10:15:75
8	30 (1:1)	20	80	99	12:06:05	08:12:80
9	30 (1:1)	16	80	99	10:04:04	08:10:82
10	**30** (1:1)	**8**	**80**	**98**	**05:03:02**	**03:07:90**
11	30 (1:1)	6	80	90	05:03:05	07:15:78
Effect of temperature						
12	30 (1:1)	8	110	100	05:06:05	12:28:60
13	30 (1:1)	8	90	99	04:03:05	15:19:66
14	30 (1:1)	8	70	89	02:03:03	10:20:70
15	30 (1:1)	8	50	72	02:03:01	20:25:55

[a]**Reaction Conditions:** 1a (1 mmol), 1a* (1 mmol), $Rhacac(CO)_2$ (0.002 mmol), TPPTS (0.008 mmol), RAME-β-CD (0.020 mmol), Distilled water (10 mL), 800 rpm. [b]Confirmed by GC and GC-MS analysis.

Furthermore, we checked an effect of time within the period from 24 h to 6 h (Table 3, entries 7-11). At first, we studied the reaction performance at 24 h by keeping the constant pressure (30 bar) and temperature (80 ºC), 100% conversion of **1a** and 75% selectivity of **4a** was observed (Table 3, entry 7). Then, decrease in time from 24 h to 20 h and again from 20 h to 16 h, the conversion was almost same but selectivity of **4a** slightly increase 75% to 80% and from 80% to 82% respectively (Table 3, entries 8 and 9). Furthermore, we reduce reaction time to 8h the results describes high conversion (98%) with excellence selectivity (90%) of **4a** (Table 3, entry 10). The reaction time of 6 h was not favourable reaction time to get the best results because it can provides the 90% conversion of **1a** with 78% selectivity of **4a** (Table 3, entry 11). Later, we look at the temperature study from 110 ºC to 50 ºC to optimize the optimum temperature for an aqueous biphasic hydroaminomethylation of eugenol (**1a**) and piperidine (**1a***) (Table 3, entries 12-15). Increase in temperature up to 110 ºC conversion was almost complete, but the selectivity of **4a** decreased to 60%, the amount of branched amines (**2a** and **3a**) increased at high temperature (Table 3, entry 12). By reducing temperature to 90 ºC, conversion does not affect but slightly increase in selectivity of **4a** up to 66% (Table 3, entry 13). Best results were obtained at 80 ºC of reaction temperature affords 98% conversion of **1a** with 90% selectivity of **4a** (Table 3, entry 10). At the temperature of 70 ºC, the conversion (89%) and selectivity (70%) both decreases slightly (Table 3, entry 14). At the end, for 50 ºC of reaction temperature, 72% conversion and 55 % selectivity of **4a** was observed (Table 3, entry 15). Therefore, we keep 80 ºC constant temperature as optimum temperature for hydroaminomethylation reaction, it was used for further metallic precursors, loading study, metal-ligand-CD ratio study, substrate study and recyclability study.

3.4 Effect of metallic precursors and loading for selective hydroaminomethylation of eugenol(1a) and piperidine(1a).*

As expected, no activity was observed in the absence of catalyst confirming that the catalyst is one and only accountable for the reaction (Table 4, entry 1). The conversions with $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$ were low and the targeted product **4a** was not obtained (Table 4, entries 2 and 3). Ruthenium metal precursors such as $RuCl_3$ and $Ru_3(CO)_{12}$ gave rise to moderate conversions, 59% and 78%, with selectivity towards **4a** 70% and 72% respectively (Table 4, entries 4 and 5). The Rhodium metal precursors led to more active catalysts than other metals for this reaction. The results obtained with some important rhodium precursors such as Rhodium (III) Chloride [$RhCl_3$], Acetylacetonato dicarbonyl Rhodium (I) [$Rhacac(CO)_2$], Chloro(1,5-cyclooctadiene)Rhodium(I) dimer [$Rh(COD)Cl]_2$, Bis(1,5-

cyclooctadiene)Rhodium(I) tetrafluoroborate [$Rh(COD)_2BF_4$], and Rhodium(II) acetate dimer [$Rh_2(OAc)_4$] were presented in Table 4, entries 6-11. From all of above Rhodium precursors, $Rhacac(CO)_2$ was the most active precursor for hydroaminomethylation of **1a** and **1a***. A high conversion up to 98% and excellent selectivity of **4a** up to 90% were obtained (Table 4, entry 8). We also checked the Cobalt metal precursors such as dicobalt octacarbonyl [$Co_2(CO)_8$] and Cobalt (II) chloride hexahydrate $CoCl_2.6H_2O$. Even at high pressure (45 bar), high temperature (100 ºC) and long reaction time (24 h), moderate conversion and lower selectivity were observed (Table 4, entries 12 and 13).

Table 4. *The study of some metallic precursors on aqueous biphasic hydroaminomethylation (HAM) of eugenol (**1a**) and piperidine (**1a***).*[a]*

Entry	Metallic precursors	Conc. (mmol)	Conv. (%)[b]	Amines (%)[b]	2a:3a:4a (%)[b]
1	-	-	-	-	-
2	$PdCl_2(PPh_3)_2$	0.035	30	-	-
3	$Pd(OAc)_2$	0.044	28	-	-
4	$RuCl_3$	0.048	59	58	10:20:70
5	$Ru_3(CO)_{12}$	0.012	78	62	10:18:72
6	$RhCl_3$	0.020	68	65	15:20:65
7	$Rh(acac)(CO)_2$	0.001	90	82	06:14:80
8	**$Rh(acac)(CO)_2$**	**0.002**	**98**	**90**	**03:07:90**
9	$[Rh(COD)Cl]_2$	0.003	92	87	10:11:79
10	$Rh(COD)_2BF_4$	0.003	87	84	12:20:68
11	$Rh_2(OAc)_4$	0.002	89	89	10:18:72
12[c]	$Co_2(CO)_8$	0.025	52	67	16:28:56
13[d]	$CoCl_2.6H_2O$	0.050	49	52	16:32:52

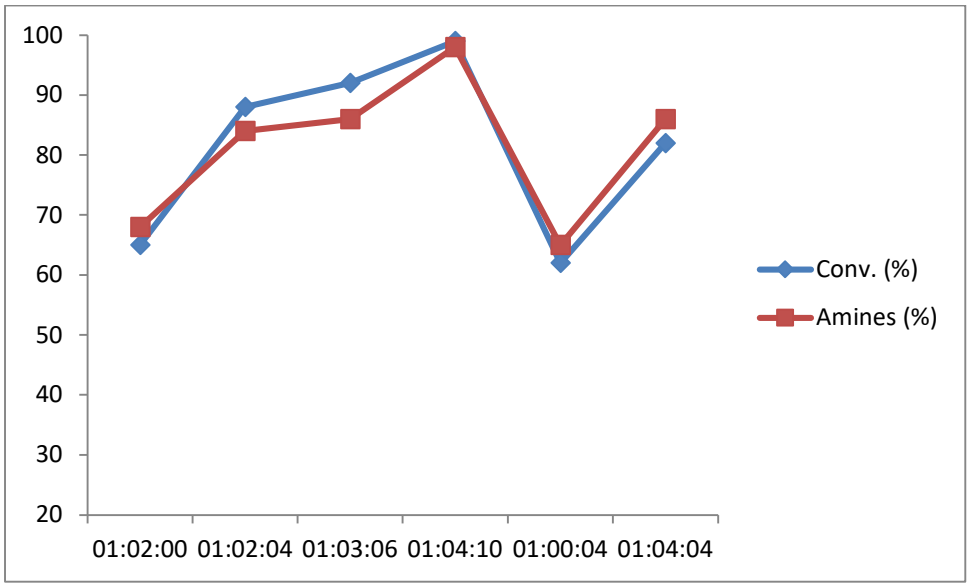
[a]**Reaction Conditions**: 1a (1 mmol), 1a* (1 mmol), TPPTS (0.008 mmol), RAME-β-CD (0.02 mmol), CO/H_2 (30 bar), Distilled water (10 mL), 800 rpm, 80 ºC, 8 h. [b]Confirmed by GC and GC-MS analysis. [c] and [d] 45 bar, 100 ºC, 24 h.

3.5 An influence of Rh/TPPTS/CDs ratio on hydroaminomethylation of eugenol(1a) and piperidine(1a)*

An influence of ratio of Rh/TPPTS/CDs as a catalyst on the conversion of **1a** and selectivity of **4a** as shown in figure 1 (**Fig. 1**). The different ratios were used as 1:2:0, 1:2:4,

1:3:6, 1:4:10, 1:0:4 and 1:4:4 with respect to Rh:TPPTS:CDs for the better conversion and selectivity of **4a**. The Rh/TPPTS was used as catalyst with 1:2 ratio, which can afforded moderate 65% conversion and 68% yield of amines with 60% selectivity of **4a** (**Fig. 1**). Addition of RAME-*β*-CD to the Rh/TPPTS catalyst the notably increase in the 88% conversion and 84% yield of amines with 75 % selectivity of **4a**. As the 1:3:6 ratio of Rh/TPPTS/RAME-*β*-CD can provides 92% conversion and 86% yield of amines with 80 % selectivity of **4a** as shown in Figure 1.

Figure 1. *Rh/TPPTS/CD ratio study for biphasic selective hydroaminomethylation of eugenol and piperidine*



[a]**Reaction Conditions**: 1a (1 mmol), 1a* (1 mmol), Rhacac$(CO)_2$ (0.001 mmol), CO/H_2 (30 bar), Distilled Water (10 mL), 80 ºC, 8 h. [b]Confirmed by GC and GC-MS analysis. [c] Rh/TPPTS as catalyst. [d]Rh/CDs as a catalyst.

The ratio as 1:4:10 of Rh/TPPTS/CDs was observed to be optimum ratio which can furnished high conversion of 99% and high 98% yield of amines with excellent selectivity of **4a** up to 90%. In absence of TPPTS, with 1:4 ratio of Rh/RAME-*β*-CD as a catalyst can provides moderate conversion up to 62%, but selectivity of **4a** fall down to 56%. It was noticed that the catalytic system was in organic phase due to absence of water soluble TPPTS ligand. The catalyst Rh/TPPTS/CDs with 1:4:4 ratio can also delivered good conversion of **1a** and better yield 86% of amines along with 79% selectivity towards **4a**. It was observed from the influence of Rh/TPPTS/CD ratio, the whole catalytic system (Rh/TPPTS/RAME-*β*-CD) with the ratio of 1:4:10 is solely responsible for high yield and excellence selectivity of **4a** in an aqueous biphasic hydroaminomethylation of **1a. [Fig. 1]**

3.6 Substrate-olefins study of hydroaminomethylation of various olefins and piperidine

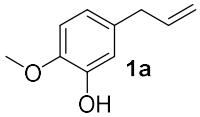
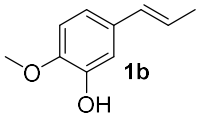
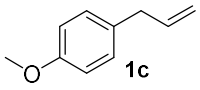
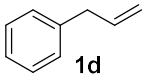
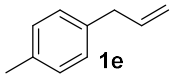
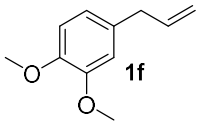
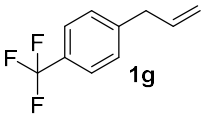
The standard optimized reaction parameters were applied for the substrate scope (Table 5). The derivatives of allyl benzenes bearing electron-donating groups (-Me, -OMe) and electron withdrawing groups (-OH, -CF_3) were smoothly transfered to the expected linear amines. An eugenol (**1a**) can provides high conversion as 99% and 87% yield of amines with 90% as an excellent selectivity of **4a** (Table 5, entry 1). Anethole (**1b**) as internal olefin also can provides 91% conversion along with 81% yield of amines, but 58% selectivity was observed to the branched amine (**3b**) as a chief product (Table 5, entry 2). Estragole (**1c**) containing electron donating -OMe group at para position of allyl benzene, which can furnished 96% conversion, 87% yield of amines with 85 % selectivity towards the linear amine (**4c**) (Table 5, entry 3). After that the simple allyl benzene can provide 98% conversion, 88% of amines with 79% selectivity of **4d** (Table 5, entry 4). The electron donating groups such as -Me (**1e**) and -OMe (**1f**) can also affected as high conversions of 98% for **1e**, 90% for **1f** with better selectivities 80% towards **4e,** 78% towards **4f** respectively (Table 5, entries 5 and 6). At last, allyl benzene containing electron withdrawing group (-CF_3) also provides 86% as good conversion, 76% yield of amines but faintly decrease to 68 % in selectivity of **4g** (Table 5, entry 7).

3.7 Substrate-amines study for selective hydroaminomethylation of eugenol under an aqueous biphasic catalysis

We investigated the reactivity of various primary and secondary amines using eugenol as substrate for the hydroaminomethylation reaction under an aqueous biphasic condition as shown in Table 6. Initially, we used the cyclohexyl amine (**A_1**), 76% yield of amines with 70% selectivity of linear amine **$4A_1$** was achieved (Table 6, entry 1). The reaction of cyclopentyl amine (**A_2**) reacted with eugenol (**1a**) resulted into 83% selectivity of **$4A_2$** was achieved (Table 6, entry 2). Dicyclohexyl amine (**A_3**) also furnished good yield and better selectivity of **$4A_3$** (Table 6, entry 3). A high conversion and excellent selectivity were achieved with cyclic secondary amines like piperidine (**A_4**) and morpholine (**A_5**) (Table 6, entries 4 and 5). Acyclic aliphatic amines such as di-iso-propylamine (A6), diallylamine (A7) and diethylamine (A8) also undergoes this transformation easily with high selectivity of linear amines (4A6, 4A7 and 4A8) (Table 6, entries 6–8). In case of diallyl amine (A7) the product was obtained with

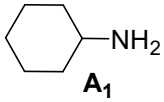
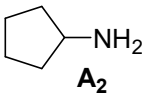
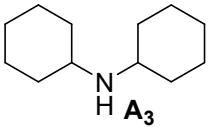
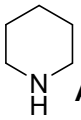
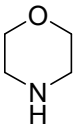
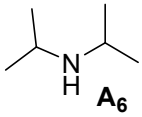
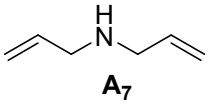
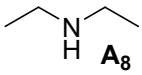
increase in molecular weight by 4 than the expected product. This was observed due to the reduction of both double bonds present in diallyl amine (Table 6, entry 8). The reaction was not proceed in case of substrates like aq. NH_3 and aq. methyl amine.

Table 5. *Substrates-olefins study for the aqueous biphasic hydroaminomethylation of natural olefins and piperidine (1a*)*[a].

Entry	Substrates(Olefins)	Conv. (%)[b]	Amine (%)[b]	Selectivity (%)[b] 2a-2g:3a-3g:4a-4g
1	 1a	99	87	03:07:90
2[c]	 1b	91	81	28:58:14
3	 1c	96	87	06:09:85
4	 1d	98	88	10:11:79
5	 1e	98	90	08:12:80
6	 1f	90	84	10:12:78
7	 1g	86	76	12:20:68

[a]**Reaction Conditions**: Olefin (1 mmol), 1a* (1 mmol), $Rhacac(CO)_2$ (0.002 mmol), TPPTS (0.008 mmol), RAME-β-CD (0.02 mmol), CO/H_2 (30 bar), Distilled water (10 mL), 80 ºC, 8 h. [b]Confirmed by GC and GC-MS analysis. [c] 90 ºC, 12 h, 40 bar.

Table 6. *Substrates-amines study for an aqueous biphasic hydroaminomethylation of eugenol (1a)[a].*

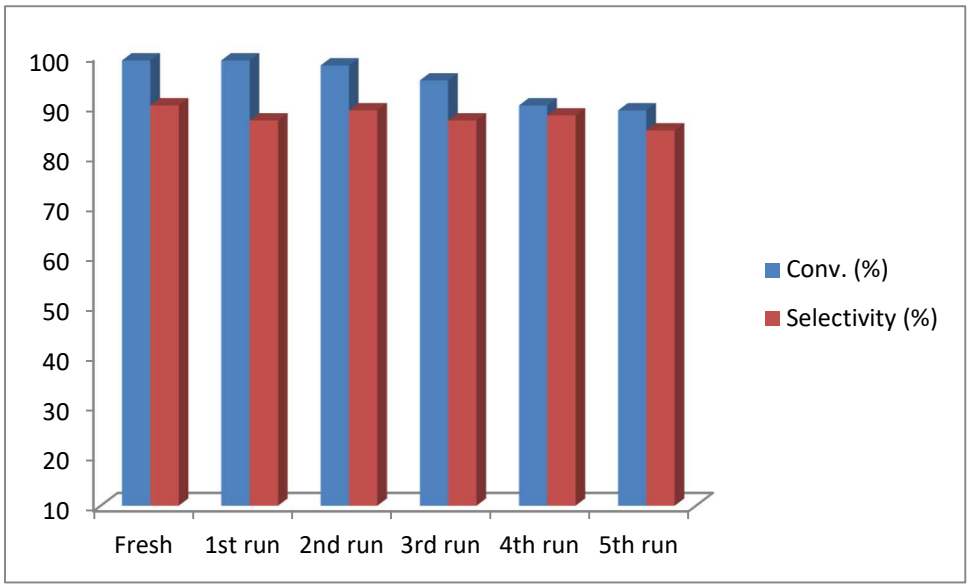
Entry	Substrates (amines)	Conv. (%)[b]	Amine (%)[b]	Selectivity (%)[b] $2A_1$-$2A_8$:$3A_1$-$3A_8$:$4A_1$-$4A_8$
1	 **A_1**	92	76	12:18:70
2	 **A_2**	87	80	09:08:83
3	 **A_3**	86	78	08:12:80
4	 **A_4**	98	90	03:07:90
5	 **A_5**	94	86	06:10:84
6	 **A_6**	90	81	08:10:82
7	 **A_7**	92	82	14:14:72
8	 **A_8**	89	83	10:10:80

[a]**Reaction Conditions**: Eugenol (1 mmol), amine (1 mmol), $Rhacac(CO)_2$ (0.002 mmol), TPPTS (0.008 mmol), RAME-β-CD (0.02 mmol), CO/H_2 (30 bar), Distilled water (10 mL), 80 ºC, 8 h. [b]Confirmed by GC and GC-MS analysis.

4. Catalyst reusability

The reusability of Rh/TPPTS/CDs catalyst was an significant feature to ensure the efficiency. We checked the reusability of Rh/TPPTS/CDs catalyst for an aqueous biphasic hydroaminomethylation of naturally occurring olefins such as eugenol, anethole and estragole. The experiments of recovery of catalysts was performed under the inert condition using nitrogen atmosphere. The catalytic system was found to be reused for five consecutive cycles with an excellent catalytic activity and selectivity towards the formation of desired product **4a** (**Figure 2**). The leaching of rhodium metal was investigated after the 1st and 5th recycle run by ICP-AES analysis and observed below detected level (≈ 0.1 ppm) of rhodium in solution which revealed that negligible leaching of rhodium metal into the solution.

Figure 2. *Recyclability study of biphasic selective hydroaminomethylation of eugenol and piperidine* [a].



5. Conclusion

In summary, we report a novel strategy for selective hydroaminomethylation of biomass derived eugenol, anethole and estragole. We have described the effect of various cyclodextrins for the aqueous biphasic hydroaminomethylation of natural olefins using Rh/TPPTS/CDs as an efficient, recyclable and greener protocol. The various cyclodextrins such as α-CD, β-CD, γ-CD, RAME-α-CD, RAME-β-CD and hp-β-CD were efficiently screened for aqueous biphasic hydroaminomethylation of eugenol. A RAME-β-CD from other cyclodextrins can provide the greatest conversion and selectivity towards the linear amines. As, hydrophobic internal cavity

of RAME-β-CD which can be directed towards fixation of eugenol benzene ring into the cavity. The terminal double bond of allyl group present in eugenol remains at outside of cavity which can be makes favourable path for the linear amines as major product instead of isomerisation and branched amines. The natural olefins like eugenol, anethole and estragole smoothly converted selectively to the linear amines with moderate to excellent yields. The derivatives of eugenol containing various functional groups likes electron withdrawing and donating groups can also be capably employed in hydroaminomethylation reaction providing greater selectivity towards amines as major products. This protocol furnished a simple and easy access for linear amines which will be very profitable in agrochemical and pharmaceutical industry. Also, the catalyst can be recycled up to five consecutive cycles with an excellent catalytic activity and selectivity towards linear amines.

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References

[1] (a) J.W. Blunt, B.R. Copp, W.P. Hu, M.H.G. Munro, P.T. Northcote, M.R. Prinsep, Nat. Prod. Rep. 26 (2009) 170-244;

(b) J.W. Blunt, B.R. Copp, R.A. Keyzers, M.H.G. Munro, M.R. Prinsep, Nat. Prod. Rep. 29 (2012) 144-222.

[2] (a) X. Jia, Z. Wang, C. Xia, K. Ding, Chem. Eur. J. 18 (2012) 15288-15295;

(b) A. Polo, C. Claver, S. Castillon, A. Ruiz, J. C. Bayon, J. Real, C. Mealli, D Masi, Organometallics 11 (1992) 3525-3533;

(c) B. Hamers, E. Kosciusko-Morizet, C. Mller, D. Vogt, ChemCatChem 1 (2009) 103-106;

(d) A. J. Sandee, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, J. Am. Chem. Soc. 123 (2001) 8468-8476;

(e) E. Zuidema, L. Escorihuela, T. Eichelsheim, J.J. Carbo, C. Bo, P.C. Kamer, P.W.N.M. van Leeuwen, Chem. Eur. J. 14 (2008) 1843-1853.

[3] (a) B.P. Bondzic, J. Mol. Catal. A:Chem. 408 (2015) 310-334;

(b) E. Petricci, E. Cini, In Hydroformylation for Organic Synthesis; M. Taddei, A. Mann, Eds.; Springer Berlin Heidelberg: Berlin, Heidelberg, 2013, p. 117;

(c) H. Alper, M. Vasylyev, Synthesis 17 (2010) 2893-2900;

(d) P. Eilbracht, A.M. Schmidt, In Catalytic Carbonylation Reactions; M. Beller, Ed.; Springer Berlin Heidelberg: Berlin, Heidelberg, 2006, p 65;

(e) P. Eilbracht, L. Barfacker, C. Buss, C. Hollmann, B.E. Kitsos-Rzychon, C.L. Kranemann, T. Rische, R. Roggenbuck, A. Schmidt, Chem. Rev. 99 (1999) 3329-3365.

[4] (a) W. Reppe, Experientia 5 (1949) 93;

(b) W. Reppe, H. Vetter, Liebigs Ann. 582 (1953) 133-161.

[5] M. Ahmed, A.M. Seayad, R. Jackstell, M. Beller, J. Am. Chem. Soc. 125 (2003) 10311-10318.

[6] (a) J. Liu, C. Kubis, R. Franke, R. Jackstell, and M. Beller; ACS Catal. 6 (2016) 907-912;

(b) M. Schulte, J. Herwig, R.W. Fischer, C.W. Kohlpaintner, J. Mol. Catal. A: Chem., 150 (1999) 147-153;

(c) T. Seidensticker, J.M. Vosberg, K.A. Ostrowski, A.J. Vorholt, Adv. Synth. Catal. 358 (2016) 610-621.

(d) T. Vanbesien, E. Monflier, F Hapiot, Green Chem. 19 (2017) 1940-1948.

(e) T. Vanbésien, J. Le Nôtre, E. Monflier, F. Hapiot, Eur. J. Lipid Sci. Technol. (2017), In Press. 10.1002/ejlt.201700190

[7] (a) S. Glak, L. Wu, Q. Liu, R. Franke, R. Jackstell, M. Beller, Angew. Chem. Int. Ed. 53 (2014) 1-5;

(b) S.R. Khan, B.M. Bhanage, Appl. Organometal. Chem. 27 (2013) 711-715;

(c) A. Seayad, M. Ahmed, H. Klein, R. Jackstell, T. Gross, M. Beller, Science 297 (2002) 1676-1678;

(d) J.R. Briggs, J. Klosin, G.T. Whiteker, Org. Lett. 7 (2005) 4795-4798.

[8] (a) S. Li, K. Huang, J. Zhang, W. Wu, X. Zhang, Org. Lett. 15 (2013) 3078-3081;

(b) C. Chen, S. Jin, Z. Zhang, B. Wei, H. Wang, K. Zhang, L. Hui, X.-Q. Dong, X. Zhang, J. Am. Chem. Soc. 138 (2016) 9017-9020.

[9] (a) D. Crozet, C.E. Kefalidis, M. Urrutigoity, L. Maron, P. Kalck, ACS Catal. 4 (2014) 435-447;

(b) J. Meng, Xing-Han Li, Z.-Y. Han, Org. Lett. 19 (2017) 1076-1079.

[10] A. Seayad, K. Selvakumar, M. Ahmed, M. Beller, Tetrahedron Lett. 44 (2003) 1679-1683.

[11] B. Zimmermann, J. Herwig, M. Beller, Angew. Chem. Int. Ed. 38 (1999) 2372-2375.

[12] Y.Y. Wang, M.M. Luo, Y.Z. Li, H. Chen, X.J. Li, Appl. Catal. A. 272 (2004) 151-155.

[13] Y.Y. Wang, J.H. Chen, M.M. Luo, H. Chen, X.J. Li, Catal. Commun. 7 (2006) 979-981.

[14] A. Behr, M. Becker, S. Reyer, Tetrahedron Lett. 51 (2010) 2438-2441.

[15] A. Behr, R. Roll, J. Mol. Catal. A: Chem. 239 (2005) 180-184.

[16] Y.Y. Wang, M.M. Luo, Q. Lin, H. Chen, X.J. Li, Green Chem. 8 (2006) 545-548.

[17] (a) F. Koc, M. Wyszogrodzka, P. Eilbracht, R. Haag, J. Org. Chem. 70 (2005) 2021-2025;
(b) M. Ahmed, C. Buch, L. Routaboul, R. Jackstell, H. Klein, A. Spannenberg, M. Beller, Chem. Eur. J. 13 (2007) 1594-1601;
(c) T.O. Vieira, H. Alper, Chem. Commun. 26 (2007) 2710-2711;
(d) B. Hamers, P.S. Bauerlein, C. Muller, D. Vogt, Adv. Synth. Catal. 350 (2008) 332-342;
(e) T.O. Vieira, H. Alper, Org. Lett. 10 (2008), 485-487;
(f) B. Hamers, E. Kosciusko-Morizet, C. Muller, D. Vogt, ChemCatChem 1 (2009) 103-106; (g) M.A. Subhani, K.S. Muller, P. Eilbracht, Adv. Synth. Catal. 351 (2009) 2113-2123;
(h) R. Kubiak, I. Prochnow, S. Doye, Angew. Chem. Int. Ed. 49 (2010) 2626-2629;
(i) G. Liu, G.; K. Huang, C. Cai, B. Cao, M. Chang, W. Wu, X. Zhang, Chem. Eur. J. 17 (2011) 14559-14563;
(j) D. Crozet, A. Gual, D. McKay, C. Dinoi, C. Godard, M. Urrutigoity, J.C. Daran, L. Maron, C. Claver, P. Kalck, Chem. Eur. J. 8 (2012) 7128-7140;
(k) K. Dong, X. Fang, R. Jackstell, M. Beller, Chem. Commun. 51 (2015) 5059-5062.

[18] G.R. Mallavarapu, S. Ramesh, R.S. Chandrasekhara, Flavour and Fragrance Journal, 10 (1995) 239-242.

[19] S.A. Jagtap, E. Monflier, A. Ponchel, B. M. Bhanage, Mol. Catal., 436 (2017) 157-163.

[20] (a) J. Szejtli, Chem. Rev. 98 (1998) 1743-1754 ;
(b) G. Crini, Chem. Rev. 114 (2014) 10940-10975.

[21] F. Hapiot, H. Bricout, S. Menuel, S. Tilloy, E. Monflier, Catal. Sci. Technol. 4 (2014) 1899-1908.

[22] T. Mathivet, C. Meliet, Y. Castanet, A. Mortreux, L. Caron, S. Tilloy, E. Monflier, J. Mol. Catal. A: Chem. 176 (2001) 105-116.

[23] M. Ferreira, H. Bricout, S. Tilloy, E. Monflier, Molecules 22 (2017) 140.

[24] E. Monflier, H. Bricout, F. Hapiot, S. Tilloy, A. Aghmiz, A.M. Masdeu-Bulto, Adv. Synth. Catal. 346 (2004) 425-431.