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Article

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Ru-Catalyzed Cross-Dehydrogenative Coupling between Primary Alcohols to Guerbet Alcohol Derivatives - with Relevance for Fragrance Synthesis

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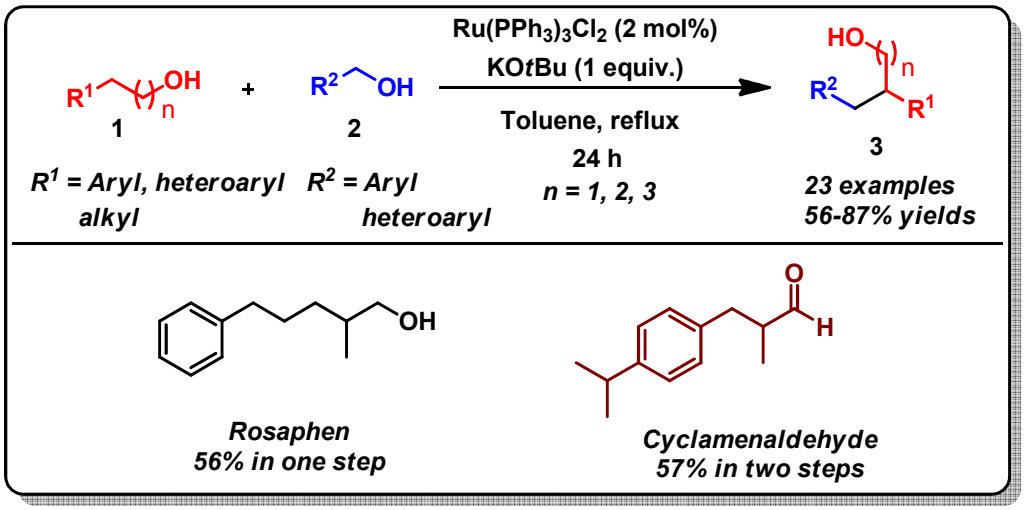
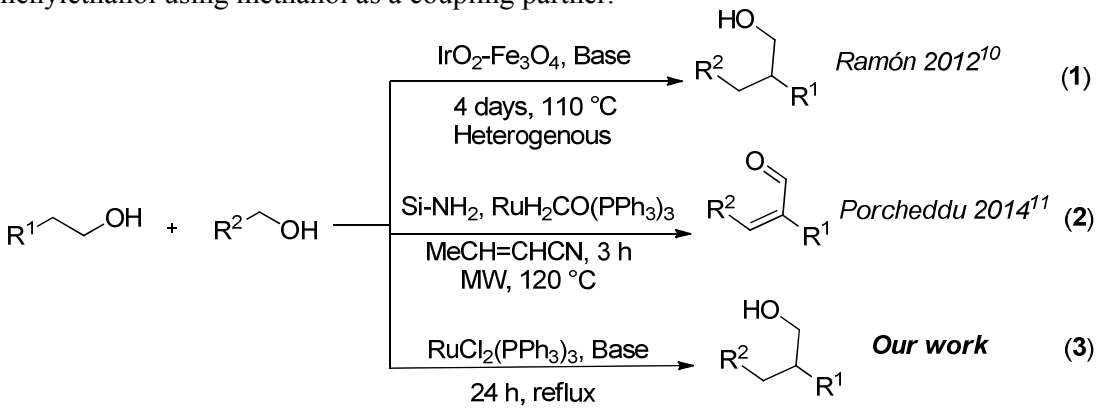


ABSTRACT

A simple method has been developed for the cross dehydrogenative coupling between two different primary alcohols using readily available $RuCl_2(PPh_3)_3$ as a precatalyst through the borrowing-hydrogen approach. The present methodology is applicable to a large variety of alcohol derivatives including long chain aliphatic alcohols and heteroaryl alcohols. In addition, the methodology was applied in a straightforward protocol to synthesize commercially available fragrances such as Rosaphen and Cyclamenaldehyde in good yields.

INTRODUCTION

The conversion of readily available and highly abundant alcohol derivatives to value added products under hydrogen-borrowing conditions has become an increasingly important concept in transition metal catalysis.[1] Classically, it is known as the Guerbet reaction which involves the conversion of primary alcohols into the corresponding *β*-alkylated dimeric alcohol with loss of water as the sole byproduct.[2] A wide variety of catalytic methods has been developed for the activation of alcohols using different transition metals in the last decades involving catalytic hydrogen transfer. The vast majority have concerned the direct alkylation of ketones[1c] and amines using alcohols as a coupling partner.[1e] The coupling between secondary and primary alcohols is significantly less frequent, but attracting increased interest.[3] In addition, the acceptorless dehydrogenative coupling (ADC) between alcohols to give esters is well known.[4] Recently, we[5] and the Obora[6] group reported the completely deoxygenative coupling of 2-arylethanol derivatives using ruthenium and iridium catalysts, respectively. Surprisingly, the selective cross coupling between two different primary alcohols such as aryl ethanol and benzylic alcohol derivatives is relatively underexplored. Beller,[7] Obora[8] and Xu[9] have developed a method for alkylation of 2-phenylethanol using methanol as a coupling partner.



Scheme 1: Cross alkylation involving two primary alcohols.

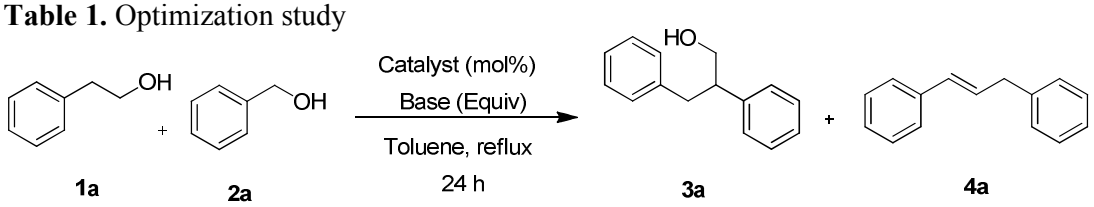
To the best of our knowledge, only two reports are available for the cross aldol reaction between aryl ethanol and aryl methanol derivatives to produce Guerbet alcohols through the borrowing-hydrogen strategy. Ramón and co-workers developed a method for cross alkylation of primary alcohols using recyclable impregnated iridium oxide on magnetite as a catalyst under heterogeneous conditions (Scheme 1, eq. 1).[10] The cross dehydrogenative coupling between two different primary alcohols to *α,β*-unsaturated aldehydes through *in situ* formation of enolates using a ruthenium catalyst, silica-grafted amine and crotononitrile as a hydrogen acceptor was demonstrated by Porcheddu *et al.* under microwave conditions (Scheme 1, eq. 2).[11] Herein, we present a simple protocol for the heterocoupling between aryl ethanol and benzyl alcohol derivatives using readily available $RuCl_2(PPh_3)_3$ catalyst under mild and convenient reaction conditions (Scheme 1, eq. 3). Linear, cyclic and heterocyclic alcohols could be used in the present method to prepare a wide variety of Guerbet alcohol derivatives. This eventually led us to develop an operationally simple method for the synthesis of Rosaphen and Cyclamenaldehyde fragrances.

RESULTS AND DISCUSSION

The reaction between 2-phenylethanol **1a** and benzyl alcohol **2a** under the previously reported reaction conditions for [Ru]-catalysed fully deoxygenative coupling of arylethanols[5] were chosen as a model reaction for optimization studies. We obtained both the hetero- **3a** and homo- **4a** products in 45% and 32% yields respectively (table 1, entry 1). The yields of products **3a** and **4a** respectively, were improved when the base was changed to KO*t*Bu (entry 2). Selectivity towards the heterocoupled alcohol **3a** was enhanced in the presence of a stoichiometric amount of base (entry 3). For the more selective formation of the cross aldol product, we turned our attention to increase both catalyst and benzyl alcohol amounts (entries 4-6). Selectivity towards the heterocoupled product was achieved when the reaction was conducted in the presence of 2.0 mol% of $Ru(PPh_3)_3Cl_2$, 3.0 equivalents of benzyl alcohol

and 1.0 equivalents of KO*t*Bu in toluene for 24 h refluxing at 120 °C (entry 6). As expected, the selective cross-coupling product was obtained, compared to when not using the benzyl alcohols which produces the homo-coupled net decarbonylative phenylethanol.[5] Then, the reaction was tested with other Ru-catalysts (entries 7 and 8), and Wilkinson's catalyst (entry 9). Different Fe-salts (entries 10-16) were also evaluated and the results were inferior to $RuCl_2(PPh_3)_3$ under otherwise identical reaction conditions.

Table 1. Optimization study



1a **2a** **3a** **4a**

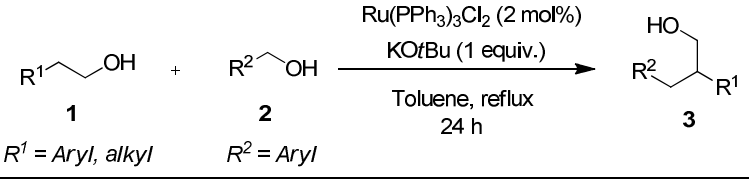
S. No.	Catalyst (mol%)	Base (equiv.)	**2a** (equiv.)	Yield (%)[a]	
				3a	**4a**
1	$RuCl_2(PPh_3)_3$ (1)	NaO*t*Bu (0.6)	1.5	45	32
2	$RuCl_2(PPh_3)_3$ (1)	KO*t*Bu (0.6)	1.5	59	38
3	$RuCl_2(PPh_3)_3$ (1)	KO*t*Bu (1.0)	1.5	61	34
4	$RuCl_2(PPh_3)_3$ (1)	KO*t*Bu (1.0)	2.0	66	17
5	$RuCl_2(PPh_3)_3$ (1)	KO*t*Bu (1.0)	3.0	83	7
6	**$RuCl_2(PPh_3)_3$ (2)**	**KO*t*Bu (1.0)**	**3.0**	**91 (84)**	**4**
7	$RuHCl(CO)(PPh_3)_3$ (2)	KO*t*Bu (1.0)	3.0	52	2
8	$[Ru(p\text{-cyemene})Cl_2]_2$ (2)	KO*t*Bu (1.0)	3.0	18	6
9	$RhCl(PPh_3)_3$ (2)	KO*t*Bu (1.0)	3.0	69	9
10	$FeCl_3.6H_2O$ (5)	KO*t*Bu (1.0)	3.0	89	6
11	$FeCl_2.4H_2O$ (5)	KO*t*Bu (1.0)	3.0	36	7
12	$Fe(acac)_3$ (5)	KO*t*Bu (1.0)	3.0	24	4
13	$FeBr_2$ (5)	KO*t*Bu (1.0)	3.0	56	4
14	$Fe(OTf)_2$ (5)	KO*t*Bu (1.0)	3.0	51	8
15	$Fe(BF_4)_2$ (5)	KO*t*Bu (1.0)	3.0	21	5
16	Ferrocene	KO*t*Bu (1.0)	3.0	27	7

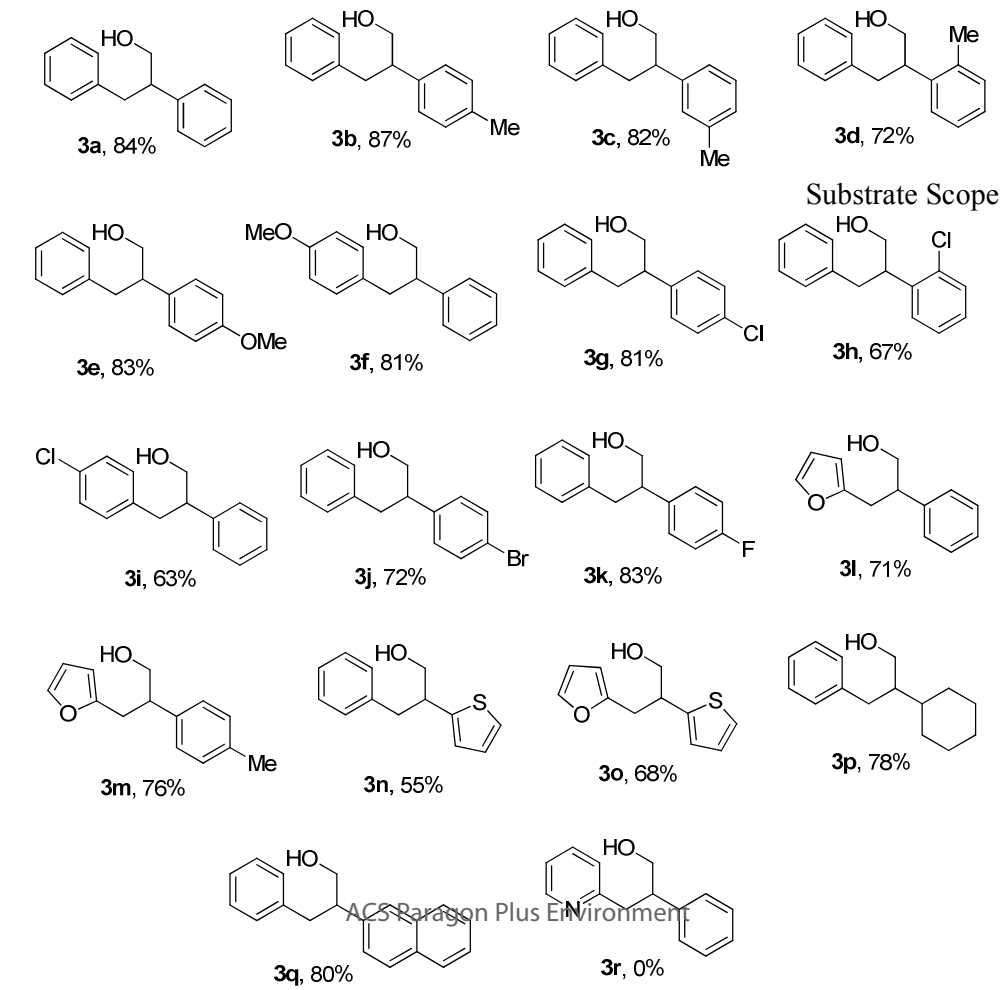
a. GC yield. Values in parentheses refers to isolated yield.

Having established the optimized reaction conditions in Table 1, entry 6, we decided to investigate the substrate scope and results are shown in Figure 1. A wide variety of aryl substituted ethanol derivatives **1** and benzyl alcohol derivatives **2** underwent selective cross coupling reaction to afford the corresponding alcohol derivatives **3** in good yields. Steric effects influence the outcome of the reaction. For instance, para substituted aryl ethanol (2-(*p*-tolyl)ethanol) **1b** gave the alcohol derivative (**3b**) with benzyl alcohol in 87% yield

whereas ortho substituted aryl ethanol derivative (2-(o-tolyl)ethanol) (**1d**) furnished the corresponding alcohol derivative (**3d**) in 72% yield. Methoxy-substituted alcohol derivatives **3e** and **3f** are obtained in 83% and 81% yields respectively under the standard reaction conditions. Cl, Br and F substituted aryl ethanol derivatives gave the respective cross aldol products (**3g-3k**) in good yields. Based on the current results, there is no significant electronic effect as the isolated yields remain within the 70-80% range when varying the substituents. To our delight, the furan moiety tolerated the present reaction conditions and products **3l** and **3m** were obtained in 71% and 76% yields respectively. As expected, sulfur functional groups appeared to act as a catalyst poisons, though product **3n** was obtained in 55% yield, indicating that the thiophene group was tolerated under these reaction conditions. In addition, both thiophene- and furan-containing

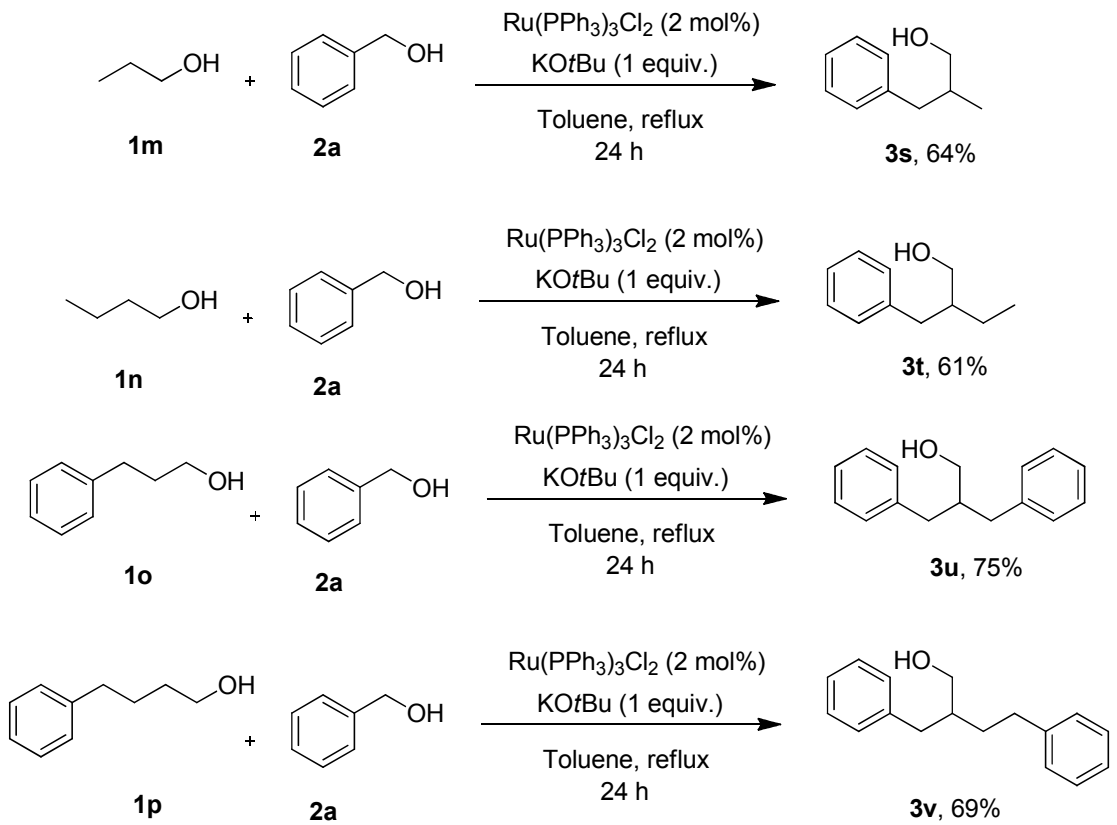
Figure 1.





compounds as **3o** could be prepared in 68% yield using the method. Interestingly, the method is not restricted to 2-aryl ethanol derivatives, as also aliphatic alcohol derivatives such as 2-cyclohexyl ethanol underwent selective cross aldol reaction with **2a** to give **3p** in 78% yield. Moreover, 80% of naphthyl substituted alcohol product **3q** was obtained under the optimized conditions. The reaction of **1a** was carried out in 5.0 mmol scale and we obtained the desired product **3a** in 79% yield along with 7% of **4a** under the present reaction conditions.

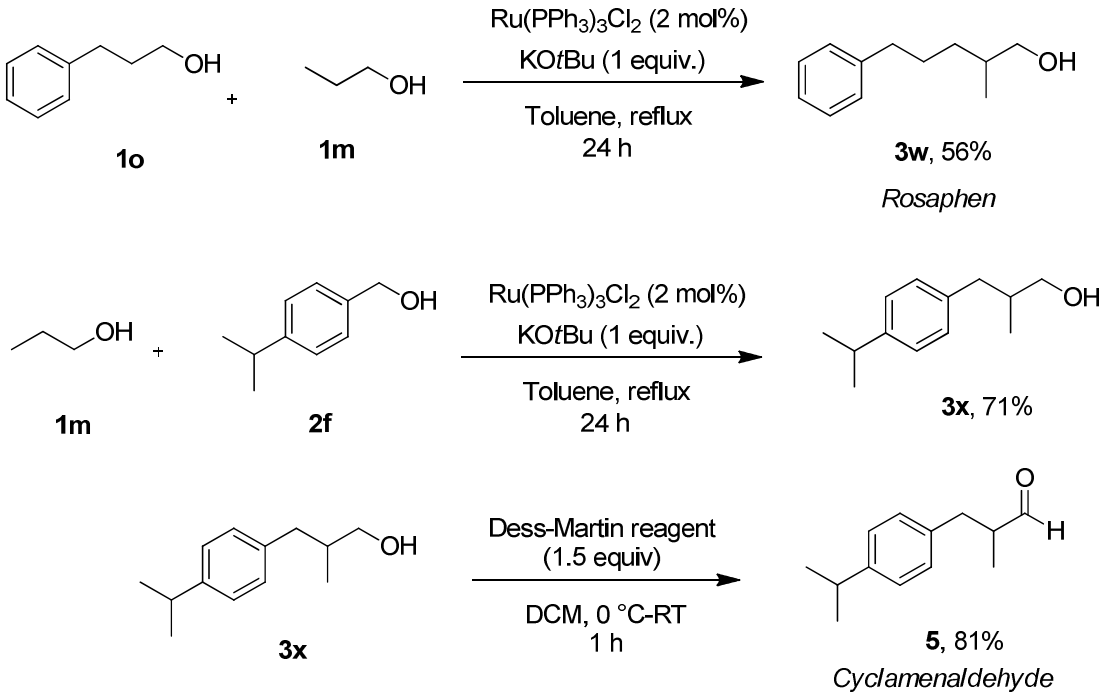
Unfortunately, the reaction of **1a** with 2-pyridinemethanol **2e** did not work to get the product **3r** and we observed only trace amounts of **2e** along with unreacted starting material **1a** in GC- and GC-MS analysis. It should be pointed out that the < 5% yield of the homo-coupled product was observed in GC-analysis from the reaction of aryl ethanol derivatives.



Scheme 2: The cross-coupling between propanol and butanol derivatives.

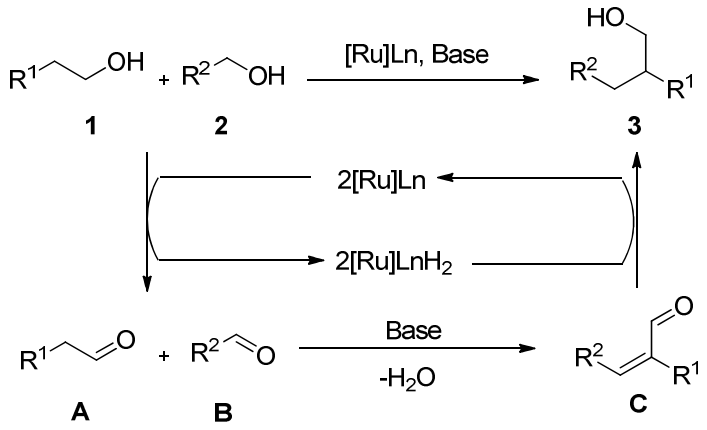
The applicability of these reaction conditions can be extended to other primary alcohols as shown in the Scheme 2. Aliphatic alcohols such as 1-propanol **1m** and 1-butanol **1n** underwent cross dehydrogenative coupling with benzyl alcohol **2a** and afforded the corresponding products **3s** and **3t** in 64% and 61% yields, respectively. Similarly, under the optimized reaction conditions ω-phenyl substituted propanol **1o** and butanol **1p** reacted with benzyl alcohol to give alcohol derivatives **3u** and **3v** in 75% and 69% yields respectively.

In order to show the applicability of our methodology, the present reaction conditions were used as a key step for the preparation of the commercially available fragrances Rosaphen and Cyclamenaledehyde from highly stable and abundant alcohol derivatives in good yields (Scheme 3). In general, the preparation method for these fragrances involves the condensation of the corresponding aldehydes followed by hydrogenation.[12,] Rosaphen (Symrise) has been used in body lotions, shampoos, detergents and soaps as rose blossom odour.[12] The coupling of 3-phenylpropan-1-ol **1o** with excess amount of 1-propanol



Scheme 3: Synthesis of Rosaphen and Cyclamenaldehyde fragrances.

1m resulted in 56% yield of Rosaphen **3w** in single step. Similarly, cyclamenaledehyde **5** can be synthesized in two steps. [13] First the cross coupling between two alcohols such as 1-propanol **1m** and 4-isopropylbenzyl alcohol (Cumic alcohol) **2f** was performed to produce compound **3x** in 71% yield under the present reaction conditions. Using Dess-Martin periodinane,[14] compound **3x** was oxidized to cyclamenaledehyde **5** in 81% yield.[15] The overall yield for the preparation of cyclamenaledehyde in two steps is 57%.



Scheme 4: Plausible mechanism

A plausible mechanism for the cross coupling between two primary alcohols has been shown in the scheme 4. Initially, alcohols **1** and **2** would undergo dehydrogenation in the presence of $Ru(PPh_3)_3Cl_2$ and base to give the respective aldehydes **A** and **B**. Base promoted aldol condensation would take place between aldehydes **A** and **B** to afford an intermediate **C** which subsequently undergoes hydrogenation reaction to give the final Guerbet alcohol derivative **3** in the presence of Ru-catalyst.

CONCLUSIONS

In summary, we have developed a simple method for the cross dehydrogenative coupling between two different primary alcohol using readily available $RuCl_2(PPh_3)_3$ catalyst through the borrowing-hydrogen approach which leads to different fragrance analogues. The present methodology is applicable to a large variety of alcohol derivatives including long

chain aliphatic alcohols and heteroaryl alcohols. In addition, we have shown a straightforward protocol to synthesize commercially available fragrances such as Rosaphen and Cyclamenaldehyde in good yields. The development of corresponding asymmetric version and further studies in this line are currently underway in our laboratory.

EXPERIMENTAL SECTION:

General information: All experiments were carried out under an atmosphere of argon or nitrogen using standard Schlenk or high vacuum line techniques unless otherwise noted. Unless stated otherwise, commercially available reagents were purchased from Sigma Aldrich or Acros Organics and used as received. NMR-spectra were recorded on Bruker Avance 400 MHz spectrometers. Multiplicities are abbreviated as follows: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, (b) broad. IR spectra were recorded on a Bruker Alpha spectrometer, with diamond ATR–FT IR detection. Gas chromatographic analyses (GC) were made using a Hewlett- Packard 5890 II instrument with a flame ionization detector (FID) and a capillary column (CP-Sil 19CB 14% cyanopropyl-phenyl/86% dimethylpolysiloxane, 0.2 μm, 0.2 mm, 25 m) with decane or dodecane as an internal standard. The retention times of different compounds in the gas chromatogram were identified using commercially available and synthesized pure compounds.

General procedure for [Ru]-Catalysis: Substituted ethanol **1** (1.0 equiv.) and benzyl alcohol **2** (3.0 equiv.) derivatives were charged into a solution of $Ru(PPh_3)_3Cl_2$ (2.0 mol%) and KO*t*Bu (1.0 equiv.) in toluene (3 mL/mmol.) at room temperature. After refluxing the reaction mixture for 24 h at 120 °C, water was added and the compound was extracted using EtOAc. Then, the crude was purified by column chromatography (silica gel, hexanes/EtOAc) to furnish the pure compound **3**.

2,3-Diphenylpropan-1-ol (**3a**):[10] It was obtained as a yellow oil in 84% yield (137 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.31 (m, 2H), 7.27-7.21 (m, 5H), 7.19-7.17 (m, 1H), 7.12-7.10 (m, 2H), 3.80-3.78 (m, 2H), 3.14-2.90 (m, 3H), 1.47 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 139.9, 129.0, 128.6, 128.2, 128.0, 126.8, 126.0, 66.3, 50.1, 38.6.

3-Phenyl-2-(*p*-tolyl)propan-1-ol (**3b**): It was obtained as a yellow oil in 87% yield (113 mg). R_f = 0.3 (in 10% EtOAc/Hexanes); IR (neat): 3355, 3024, 2920, 2862, 1603, 1513, 1495, 1453, 1378, 1183, 1113, 1018, 650, 910, 811, 751, 721, 697, 594 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.36 (m, 2H), 7.33-7.24 (m, 7H), 3.94-3.86 (m, 2H), 3.25-3.02 (m, 3H), 2.48 (s, 3H), 1.56 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 138.7, 136.3, 129.3, 129.0, 128.2, 127.9, 125.9, 66.4, 49.7, 38.7, 21.0. HRMS (ESI-TOF): $[M+NH_4]^+$ Calcd for $C_{16}H_{22}NO$ 244.1701; Found 244.1706.

3-Phenyl-2-(*m*-tolyl)propan-1-ol (**3c**): It was obtained as a yellow oil in 82% yield (133 mg). IR (neat): ^{1}H NMR (400 MHz, CDCl 3): δ 7.26-7.23 (m, 3H), 7.20-7.17 (m, 1H), 7.13-7.11 (m, 2H), 7.07-7.04 (m, 3H), 3.78-3.76 (m, 2H), 3.10-2.98, (m, 2H), 2.95-2.90 (m, 1H), 2.34 (s, 3H), 1.32 (br s, 1H); ^{13}C NMR (100 MHz, CDCl 3): δ 141.8, 140.0, 138.2, 129.0, 128.8, 128.5, 128.2, 127.6, 126.0, 125.0, 66.3, 50.0, 38.7, 21.5. HRMS (ESI-TOF): $[M+NH_4]^+$ Calcd for $C_{16}H_{22}NO$ 244.1701; Found 244.1701.

3-Phenyl-2-(*o*-tolyl)propan-1-ol (**3d**): It was obtained as a yellow oil in 72% yield (110 mg). R_f = 0.3 (in 10% EtOAc/Hexanes); IR (neat) 3324, 3027, 2921, 1494, 1453, 1380, 1206, 1014, 727, 695, 594 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 7.6 Hz, 1H), 7.25-7.21 (m, 2H), 7.19-7.17 (m, 1H), 7.14-7.12 (m, 2H), 7.09-7.07 (m, 2H), 3.81 (d, J = 6.4 Hz, 2H), 3.44 (quint, J = 7.2 Hz, 1H), 3.03 (dd, J = 13.2, 7.2 Hz, 1H), 2.86 (dd, J = 13.2, 7.2 Hz, 1H), 2.18 (s, 3H), 1.38 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 137.0, 130.5, 129.0,

128.2, 126.4, 126.3, 126.00, 125.97, 65.9, 44.8, 38.9, 19.7. HRMS (ESI-TOF): $[M+NH_4]^+$ Calcd for $C_{16}H_{22}NO$ 244.1701; Found 244.1704.

2-(4-Methoxyphenyl)-3-phenylpropan-1-ol (**3e**):[10] It was obtained as a yellow oil in 83% yield (162 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.21 (m, 2H), 7.17 (d J = 7.6 Hz, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.10-7.08 (m, 2H), 6.86 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H), 3.77-3.71 (m, 2H), 3.070-2.98 (m, 2H), 2.90-2.85 (m, 1H), 1.42 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4. 140.0. 133.7, 129.02, 128.97, 128.2, 125.9, 114.0, 66.4, 55.2, 49.3, 38.8.

3-(4-Methoxyphenyl)-2-phenylpropan-1-ol (**3f**):[10] It was obtained as a yellow oil in 81% yield (103 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, J = 6.8 Hz, 2H), 7.28-7.27 (m, 1H), 7.24-7.22 (m, 2H), 7.03 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 3.81-3.79 (m, 2H), 3.79 (s, 3H), 3.11-2.85 (m, 3H), 1.61 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 142.0, 131.9, 129.9, 128.5, 128.0, 126.7, 113.6, 66.2, 55.1, 50.3, 37.7.

2-(4-Chlorophenyl)-3-phenylpropan-1-ol (**3g**):[10] It was obtained as a yellow oil in 81% yield (128 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.21 (m, 4H), 7.19-7.16 (m, 1H), 7.13 (d, J = 8.4 Hz, 2H), 7.08-7.06 (m, 2H), 3.80-8.74 (m, 2H), 3.12-3.01 (m, 2H), 2.88-2.83 (m, 1H), 1.34 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 139.4, 132.5, 129.4, 129.0, 128.7, 126.1, 66.2, 49.6, 38.6.

2-(2-Chlorophenyl)-3-phenylpropan-1-ol (**3h**):[10] It was obtained as a yellow oil in 61% yield (101 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (dd, J = 8.0, 1.2 Hz, 1H), 7.34 (dd, J = 7.6, 1.6 Hz, 1H), 7.28-7.24 (m, 3H), 7.21-7.15 (m, 4H), 3.83-3.74 (m, 3H), 3.07 (dd, J = 14.0, 8.0 Hz, 1H), 2.97 (dd, J = 14.0, 6.8 Hz, 1H), 1.40 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 139.4, 134.6, 129.8, 129.0, 128.3, 127.7, 126.9, 126.1, 64.5, 45.1, 37.6.

3-(4-Chlorophenyl)-2-phenylpropan-1-ol (**3i**):[10] It was obtained as a yellow oil in 63% yield (102 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.30 (m, 2H), 7.25-7.23 (m, 1H), 7.18-7.16 (m, 4H), 6.98 (d, J = 8.0 Hz, 2H), 3.79 (d, J = 6.0 Hz, 2H), 3.07-3.02 (m, 2H), 2.89-2.83 (m, 1H), 1.48 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 138.3, 131.7, 130.4, 128.7, 128.3, 128.1, 127.0, 66.3, 50.1, 37.9.

2-(4-Bromophenyl)-3-phenylpropan-1-ol (**3j**):[10] It was obtained as a yellow oil in 72% yield (83 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d J = 8.4 Hz, 2H), 7.25-7.21 (m, 2H), 7.18-7.16 (m, 1H), 7.08-7.05 (m, 4H), 3.82-3.74 (m, 2H), 3.10-300 (m, 2H), 2.89-2.83 (m, 1H), 1.35 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 139.4, 131.6, 129.8, 129.0, 128.3, 126.1, 120.6, 66.1, 49.6, 38.5.

2-(4-Fluorophenyl)-3-phenylpropan-1-ol (**3k**): It was obtained as a yellow oil in 83% yield (136 mg). R_f = 0.2 (in 10% EtOAc/Hexanes); IR (neat) 3358, 3027, 2924, 1603, 1508, 1453, 1301, 1221, 1065, 1028, 1014, 830, 753, 721, 691, 593 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.21 (m, 2H), 7.19-7.14 (m, 3H), 7.08-7.06 (m, 2H), 6.99 (t, J = 8.4 Hz, 2H), 3.82-3.73 (m, 2H), 3.12-3.01 (m, 2H), 2.88-2.83 (m, 1H), 1.43 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, J = 243.0 Hz), 139.6, 137.5 (d, J = 4.0 Hz), 129.5, 129.4, 129.0, 128.2, 126.1, 115.3 (d, J = 21.0 Hz), 66.3, 49.4, 38.8. HRMS (ESI-TOF): $[M+HCO_2]^-$ Calcd for $C_{16}H_{16}FO_3$ 275.1083; Found 275.1083.

3-(Furan-2-yl)-2-phenylpropan-1-ol (**3l**): It was obtained as a yellow oil in 71% yield (101 mg). R_f = 0.35 (in 10% EtOAc/Hexanes); IR (neat): 3362, 3028, 2924, 1599, 1505, 1494, 1452, 1241, 1145, 1060, 1007, 884, 802, 731, 697, 598, 536. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.34 (m, 2H), 7.32 (dd, J = 2.0, 0.8 Hz, 1H), 7.31-7.25 (m, 3H), 6.27 (dd, J = 3.2, 2.0 Hz, 1H), 5.95 (dd, J = 3.2, 0.8 Hz, 1H), 3.87-3.79 (m, 2H), 3.25 (p, J = 6.8 Hz, 1H), 3.14-2.97 (m, 2H), 1.56 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 141.6, 141.0, 128.7,

128.6, 128.3, 127.8, 126.9, 110.1, 106.3, 66.4, 47.2, 30.7. HRMS (ESI-TOF): $[M+H]^+$ Calcd for $C_{13}H_{15}O_2$ 203.1072; Found 203.1077.

3-(Furan-2-yl)-2-(p-tolyl)propan-1-ol (**3m**): It was obtained as a yellow oil in 61% yield (101 mg). R_f = 0.3 (in 10% EtOAc/Hexanes); IR (neat) 3395, 2921, 1721, 1596, 1514, 1240, 1145, 1059, 1006, 931, 812, 727, 598, 535 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (dd, J = 2.0, 1.2 Hz, 1H), 7.15-7.10 (m, 4H), 6.23 (dd, J = 3.2, 2.0 Hz, 1H), 5.91 (dd, J = 3.2, 0.8 Hz, 1H), 3.81-3.73 (m, 2H), 3.18 (quint, J = 7.2 Hz, 1H), 3.05 (dd, J = 15.2, 7.6 Hz, 1H), 2.94 (dd, J = 15.6, 7.6 Hz, 1H), 2.33 (s, 3H), 1..46 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.9, 141.0, 138.4, 136.5, 129.3, 127.7, 110.1, 106.3, 66.5, 46.8, 30.8, 21.0. HRMS (ESI-TOF): $[M+H]^+$ Calcd for $C_{14}H_{17}O_2$ 217.1229; Found 217.1233.

3-Phenyl-2-(thiophen-2-yl)propan-1-ol (**3n**): It was obtained as a pale brown oil in 55% yield (93 mg). R_f = 0.35 (in 10% EtOAc/Hexanes); IR (neat): 3331, 3027, 2925, 2872, 1495, 1453, 1241, 1205, 1064, 1021, 911, 847, 740, 693, 594. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28-7.24 (m, 2H), 7.21-7.19 (m, 2H), 7.15-7.13 (m, 2H), 6.95 (dd, J = 5.2, 3.6 Hz, 1H), 6.84 (dq, J = 3.2, 0.8 Hz, 1H), 3.81-3.70 (m, 2H), 3.44-3.37 (m, 1H), 3.09-2.94 (m, 2H), 1.52 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 139.4, 129.0, 128.3, 126.8, 126.2, 124.9, 123.8, 66.5, 45.6, 39.6. HRMS (ESI-TOF): $[M+H]^+$ Calcd for $C_{13}H_{15}SO$ 219.0844; Found 219.0850.

3-(Furan-2-yl)-2-(thiophen-2-yl)propan-1-ol (**3o**): It was obtained as a yellow oil in 68% yield (112 mg). R_f = 0.3 (in 10% EtOAc/Hexanes); IR (neat) 3419, 3010, 2926, 1596, 1506, 1438, 1215, 1147, 1064, 1039, 1007, 827, 903, 747, 666, 598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 (dd, J = 1.6, 0.8 Hz, 1H), 7.19 (dd, J = 5.2, 1.2 Hz, 1H), 6.96 (dd, J = 5.2, 3.6 Hz, 1H), 6.88 (dq, J = 6.0, 0.8 Hz, 1H), 6.26 (dd, J = 3.2, 2.0 Hz, 1H), 5.99 (dd, J = 3.2, 0.8 Hz, 1H), 3.82-3.72 (m, 2H), 3.52 (quint, J = 7.2 Hz, 1H), 3.13-2.98 (m, 2H), 1.73 (br s, 1H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1, 144.8, 141.2, 126.8, 124.7, 123.8, 110.2, 106.7, 66.5, 42.8, 31.8. HRMS (ESI-TOF): $[M+H]^+$ Calcd for $C_{11}H_{13}SO_2$ 209.0636; Found 209.0641.

2-Cyclohexyl-3-phenylpropan-1-ol (**3p**): It was obtained as a yellow oil in 78% yield (131 mg). R_f = 0.35 (in 10% EtOAc/Hexanes); IR (neat) 3616, 2920, 1558, 1496, 1206, 1079, 1037, 1014, 975, 954, 799, 696, 639, 593, 573, 561, 543, 524, 510 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.27 (m, 2H), 7.21-7.17 (m, 3H), 3.56 (d, J = 5.6 Hz, 2H), 2.75 (dd, J = 13.6, 5.2 Hz, 1H), 2.53 (dd, J = 13.6, 9.2 Hz, 1H), 1.78-1.63 (m, 6H), 1.55-1.47 (m, 1H), 1.32-1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 129.0, 128.3, 125.7, 62.7, 48.4, 38.3, 34.7, 30.2, 30.1, 26.8, 26.73, 26.69. HRMS (ESI-TOF): $[M+NH_4]^+$ Calcd for $C_{15}H_{26}NO$ 236.2014; Found 236.2018.

2-(Naphthalen-2-yl)-3-phenylpropan-1-ol (**3q**): It was obtained as a yellow oil in 80% yield (92 mg). R_f = 0.25 (in 10% EtOAc/Hexanes); IR (neat) 3350, 3053, 3024, 2923, 1600, 1507, 1495, 1264, 1179, 1028, 1018, 962, 946, 891, 815, 735, 697, 659, 622, 590, 563 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.78 (m, 3H), 7.66 (s, 1H), 7.48-7.45 (m, 2H), 7.38 (dd, J = 8.8, 2.0 Hz, 1H), 7.24-7.20 (m, 2H), 7.17-7.12 (m, 3H), 3.88 (t, J = 5.6 Hz, 2H), 3.28 (quint, J = 7.2 Hz, 1H), 3.16-3.01 (m, 2H), 1.36 (t, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 139.3, 133.5, 132.5, 129.0, 128.35, 128.27, 127.64, 127.60, 126.9, 126.10, 126.06, 126.04, 125.6, 66.3, 50.3, 38.6. HRMS (ESI-TOF): $[M+NH_4]^+$ Calcd for $C_{19}H_{22}NO$ 280.1701; Found 280.1705.

2-Methyl-3-phenylpropan-1-ol (**3s**):[9] It was obtained as a colorless oil in 63% yield (112 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.28 (m, 2H), 7.22-7.18 (m, 3H), 3.56-3.46 (m, 2H), 2.77 (dd, J = 13.2, 6.0 Hz, 1H), 2.43 (dd, J = 13.2, 8.0 Hz, 1H), 2.00-1.91 (m, 1H), 1.60 (br s, 1H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 129.1, 128.2, 125.8, 67.6, 39.7, 37.7, 16.4.

2-Benzylbutan-1-ol (**3t**):[10] It was obtained as a colorless oil in 61% yield (96 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.28 (m, 2H), 7.22-7.19 (m, 3H), 3.55 (d, J = 5.6 Hz, 2H), 2.70-2.60 (m, 2H), 1.79-1.70 (m, 1H), 1.57 (br s, 1H), 1.47-1.34 (m, 2H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 129.1, 128.2, 125.8, 64.4, 44.1, 37.2, 23.2, 11.2.

2-Benzyl-3-phenylpropan-1-ol (**3u**):[16] It was obtained as a colorless oil in 75% yield (113 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 4H), 7.24-7.19 (m, 6H), 3.51 (d, J = 4.8 Hz, 2H), 2.75-2.65 (m, 4H), 2.17-2.13 (m, 1H), 1.39 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 129.1, 128.3, 125.9, 63.9, 44.5, 37.4.

2-Benzyl-4-phenylbutan-1-ol (**3v**):[17] It was obtained as a colorless oil in 69% yield (110 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.27 (m, 4H), 7.23-7.16 (m, 6H), 3.62-3.54 (m, 2H), 2.71 (d, J = 7.2 Hz, 2H), 2.69-2.61 (m, 2H), 1.90-1.84 (m, 1H), 1.76-1.62 (m, 2H), 1.36 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 140.5, 129.1, 128.32, 128.30, 125.9, 125.7, 64.7, 42.0, 37.5, 33.2.

2-Methyl-5-phenylpentan-1-ol (**3w**):[18] It was obtained as a colorless oil in 56% yield (66 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.28 (m, 2H), 7.19-7.17 (m, 3H), 3.50 (dd, J = 10.4, 6.0 Hz, 1H), 3.42 (dd, J = 10.4, 6.4 Hz, 1H), 2.63-2.58 (m, 2H), 1.68-1.62 (m ,3H), 1.49-1.42 (m, 3H), 1.25 (br s, 1H), 1.21-1.16 (m, 1H), 0.92 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 128.4, 128.3, 125.7, 68.3, 36.2, 35.7, 32.8, 28.9, 16.5.

3-(4-Isopropylphenyl)-2-methylpropan-1-ol (**3x**):[15] It was obtained as a colorless oil in 71% yield (160 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 3.54 (dd, J = 10.8, 6.0 Hz, 1H), 3.47 (dd, J = 10.8, 6.0 Hz, 1H), 2.88 (quin, J = 7.2 Hz, 1H), 2.71 (dd, J = 13.6, 6.8 Hz, 1H), 2.41 (dd, J = 13.2, 7.6 Hz, 1H), 1.98 -1.90 (m, 1H), 1.24 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 137.8, 129.0, 126.3, 67.7, 39.3, 37.8, 33.7, 24.0, 16.6.

3-(4-Isopropylphenyl)-2-methylpropanal (**5**):[15] It was obtained as a colorless oil in 81% yield (44 mg) by oxidation of **3x** using Dess-Martin reagent.[14] ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, J = 1.6 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 3.06 (dd, J = 13.6, 5.6 Hz, 1H), 2.88 (quin, J = 6.8 Hz, 1H), 2.69-2.24 (m, 1H), 2.58 (dd, J = 1.32, 8.0 Hz, 1H), 1.24 (d, J = 6.8 Hz, 6H), 1.09 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.6, 146.9, 136.0, 128.9, 126.5, 48.0, 36.2, 33.7, 24.0, 13.2.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website containing GC-FID calibration curves and ^{1}H- and ^{13}C-NMR spectra..

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Notes

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