

NaOH-Promoted Reduction of Carbonyl Compounds Assisted by Microwave

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The reduction of aldehydes and ketones based on MPV chemistry is one of the vital transformations in organic chemistry. In this study, MPV chemistry was developed in heating assistance of Microwave to synthesize a broad range of alcohol with yields up to 96 % by a simple, cheap, and safe synthetic protocol. Sodium hydroxide (NaOH) is an excellent promoter for the reduction. The method is quite cheap and straightforward while it utilized easy-to-handle chemicals and did not require strictly anhydrous reagents, transition metals, or any additional ligands. This potential method encourages a scale-up upgrading of Microwave use for alcohol production.

1. Introduction

The development of sustainable synthetic methods directed recently is due to the heightened awareness of humans and the recognition of eco-friendly and economic methodologies that minimize negative impacts on the environment (Rathi et al., 2015). Among those, microwave-assisted methods have matured and have been used safely to substitute for conventional heating techniques (Prieto et al., 2019). Microwave was applied successfully in many fields such as bioenergy recovery (Ani et al., 2020), encapsulation (Muhamad et al., 2020), phytochemical extraction (Abd Rahman et al., 2020). Also, many microwave-heated chemical transformations have been achieved (Ni et al., 2020), thereby upgrading existing protocols to form superior results compared to normal heated ones (Zhou et al., 2020). Esterification, oligolactic acid synthesis, aromatic polyester synthesis are synthetic types whose methods were developed to have scale-up applications of microwave (Nagahata and Takeuchi, 2019).

The reduction of aldehydes and ketones is one of the essential functional group transformations in organic chemistry. Meerwein Ponndorf Verley (MPV) reduction is recognized as one of such efficient transformations due to many desirable features such as high selectivity, mild conditions, and relatively cheap reagents (Cha, 2006). MPV reactions are normally catalyzed homogeneously by metal alkoxides such as aluminum isopropoxide $\text{Al}(\text{O}i\text{Pr})_3$ (Cha, 2006). The reaction proceeds a hydride transfer from alcohol to carbonyl compound, which is coordinated to the metal center of alkoxide. The catalytic activity of these alkoxides is related to their Lewis acidic character in combination with ligand exchangeability (Cohen et al., 2004). In recent years, modifications of MPV reactions have been introduced to address some of the remaining problems, including long reaction times, solvent selection, side reactions, workup issues, and catalyst effectiveness by exploring novel catalytic systems. However, the cost and toxicity of transition metals (Bruneau-Voisine et al., 2017) and the sophisticated preparation of ligands (Zheng et al., 2020) needed to enhance MPV reduction are attributed to be typical drawbacks of this reaction. Boron alkoxides $\text{B}(\text{OR})_3$, an environmentally friendly candidate, could catalyze MPV reductions as metal alkoxides but it remained long reaction time, high content of alkoxides and limited substrate scope (Uysal and Oksal, 2011).

To expand upon this trend in a different approach to build up a metal-free protocol, sodium tetraborate ($\text{Na}_2\text{B}_4\text{O}_7$) was chosen as a catalyst for the MPV reaction in initial tests of this study. However, the unnecessary presence of $\text{Na}_2\text{B}_4\text{O}_7$ in those tests led us to explore another metal-free alternative. Highly positive thermal effects of Microwave (conduction and dipolar polarization mechanism) encouraged us to use it to replace traditional heat transfer. To achieve a more sustainable alcohol synthesis that overcomes the weakness of alkoxide or metal catalytic system, an alkoxide-free and metal-free MPV method in the effective combination of the low base concentration and the crucial microwave heating was developed. The base-

promoted reduction was also upgraded in a flow reactor, followed by simple purification. This work targets to be an efficient, safe, and high-economic process for industrial alcohol production.

2. Materials and methods

Microwave reactions were carried out in 10mL microwave vials on CEM Discover – SPW/ACTIVENT 909155 or 10mL vials on Anton Paar Monowave 300. Conventional heating reactions were conducted in round bottom flasks under a positive pressure of nitrogen. Flow system used is a kit which involved: Pumps = Little Things Factory GmbH Mr. Q continuous syringe pump; Column = Omnifit®, L × I.D. 100 mm × 10 mm, bed volume 5.6 mL, fixed ends; Heat block for column = FRX volcano; Pressure regulator = Upchurch Scientific™ 100 psi. Commercially available reagents were used as purchased. Analytical thin-layer chromatography was performed using silica gel plates precoated with silica gel 60 F₂₅₄ (0.2 mm). Flash chromatography employed 230-400 mesh silica gel. Solvents used for chromatography are quoted as volume/volume ratios of hexane and ethylacetate. NMR spectroscopy was performed at 298 K using either a Bruker Avance III 300 (300.13 MHz, ¹H; 75.5 MHz, ¹³C; BBFO probe) or an Avance III 400 (400.13 MHz, ¹H; 100.6 MHz, ¹³C; BBFO probe or Prodigy cryoprobe). Data are expressed in parts per million (ppm) downfield shift from tetramethylsilane with residual solvent as an internal reference (δ 7.26 ppm for chloroform) and is reported as position (δ in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (*J* in Hz) and integration (number of protons). ¹³C NMR spectra were recorded at 298 K with complete proton decoupling. Data are expressed in parts per million (ppm) downfield shift relative to the internal reference (δ 77.2 ppm for the central peak of deuterated chloroform). Figure 1 shows the MPV reaction accelerated in microwave conditions using bases as promoters. A 10mL microwave vial was charged with base and a stirring bar. Starting ketone (1) was added to the vial at the atmosphere, followed by 2mL of isopropanol (2). Then the vial was close by a cap, and the mixture was put in a reaction chamber of Microwave reactor (ramp-up time: 2 min, holding time: 0.5-6 h, T = 150 °C), unless otherwise specified. Upon completion, the crude was evaporated to remove (2) and acetone (4), then purified by column chromatography to give pure alcohol (3).

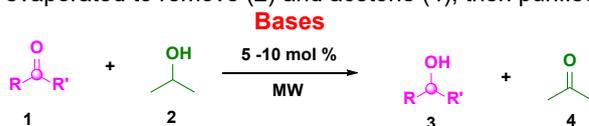


Figure 1: MPV reduction of carbonyl compounds under an optimized Microwave condition

3. Discussion

At the beginning of this work, after proving no catalytic influence of Na₂B₄O₇ on the conversion of MPV reaction, a series of cheap commercial bases were tested for MPV reduction of acetophenone 1a without any transition metal catalysts and ligands (Figure 2). Optimization of reaction conditions was conducted by the control of technical parameters such as the concentration of bases and reaction time in CEM Microwave reactor. Table 1 showed the full summary of this optimization.



Figure 2: MPV reduction of acetophenone

As shown in Table 1, acetophenone was reduced successfully in the absence of Na₂B₄O₇ (entry 3), while the reaction would not work unless there were KOH in the reaction mixture (entry 2 and 4). With a low concentration of KOH (10 mol%), the reaction still resulted in an excellent conversion (97 %). In an attempt to further understand this finding, only by applying a pool of bases, it is possible to perform MPV reduction in the Microwave without the need for adding any more metal catalyst. We are inclined to view that KOH contains a trace of metals (Al, Cu, Fe, Mg, Ni), which can catalyze the reaction in the presence of bases. This hypothesis was expanded by investigating a more extensive range of different bases (organic and inorganic bases) under similar conditions (5-20 mol% of bases, 1-6 h, 150 °C in MW). 5 mol% of strong bases such as KOH, NaOH (entry 10 and 11), LiOH (entry 12), Na-HMDS (entry 19), and NaH (entry 20) afforded excellent conversions (> 95 %) in a MW reaction time of 1.5 h, regardless of differences among their proportion of impurities on their bottle labels. Similarly, the reactions resulted in moderate conversions by employing moderate bases such as

K₃PO₄ (entry 13) and KO^t-Bu (entry 14). In contrast, the reaction did not work with weak inorganic bases such as K₂CO₃ and Na₂CO₃ (entry 14 and 15), salts such as NaCl, KI, and Na₂SO₄ (entry 16-18), and even strong organic bases (DBU in entry 22 and Et₃N in entry 23) despite having an increase of base/salt concentration applied (up to 20 mol% of base/salt). In an attempt to find a distinct mechanism for this reaction, a combination of a robust organic base (DBU) and same metal contaminants of salts (NaCl) or weaker bases (K₃PO₄) were applied (entry 24 - 26). And this combination did not improve the conversion of 1a. The catalytic role of contaminants in NaOH (entry 27) was tested as metal traces of NaOH in collaboration with DBU was utilized in the way that HCl neutralized NaOH in Dioxane before DBU was added in the reaction. However, unexpectedly, metal impurities in all kinds of those chemicals were not catalytically effective in collaboration with DBU without NaOH. Apparently, base is needed for this type of reaction, not only its metal traces.

Table 1: Investigation of different reaction conditions on MPV reduction of acetophenone

Entry	Conditions ^a	Conversion %	Entry	Conditions ^a	Conversion %
1	1 eq. KOH, 5 mol% of Na ₂ B ₄ O ₇ , 3 h in MW	99	15	20 mol% of Na ₂ CO ₃ , 6 h in MW	3
2	No base, 5 mol% of Na ₂ B ₄ O ₇ , 3h in MW	n.r	16	20 mol% of Na ₂ SO ₄ , 6 h in MW	n.r
3	1 eq. KOH, 3 h in MW	99	17	20 mol% of NaCl, 6 h in MW	n.r
4	No base, no catalyst, 3h in MW	n.r	18	20 mol% of KI, 6 h in MW	n.r
5	10 mol% of KOH, 3 h in MW	97	19	5 mol% of Na-HMDS, 1.5 h in MW	97
6	10 mol% of NaOH, 3 h in MW	99	20	5 mol% of NaH, 1.5 h in MW	97
7	5 mol% of NaOH, 3 h in MW	99	21	5 mol% of KO ^t -Bu, 1.5 h in MW	30
8 ^b	5 mol% of NaOH, normal heating	12	22	20 mol% of Et ₃ N, 6 h in MW	n.r
9 ^b	5 mol% of KOH, normal heating	48	23	5 mol% of KOH, 5 mol% of DBU, 6 h in MW	n.r
10	5 mol% of NaOH, 1.5 h in MW	95	24	5 mol% of DBU, 5 mol% of NaCl, 6 h in MW	n.r
11	5 mol% of NaOH, 0.5 h in MW	85	25	5 mol% of DBU, 5 mol% of K ₃ PO ₄ , 6 h in MW	61
12	5 mol% of LiOH, 1.5 h in MW	95	26	5 mol% of DBU, 5 mol% of Na ₂ B ₄ O ₇ , 6 h in MW	12
13	5 mol% of K ₃ PO ₄ , 6 h in MW	51	27	5 mol% of NaOH, 5 mol % of DBU, 5 mol% of HCl, 6 h in MW	trace
14	20 mol% of K ₂ CO ₃ , 6 h in MW	9	28 ^c	5 mol% of Na-HMDS, 3 h in flow	89

^aReactions were carried out in MW reactor at 150 °C with the indicated concentration of bases and reaction time. ^bReactions were carried out in round bottom flasks with 2-day reflux. ^cReaction was conducted in a flow reactor, flow rate: 0.3 mL/min, column T = 150 °C, 3 h; n.r.: no reaction

The critical heating role of microwave was confirmed by comparing it to the performance of conventional heating (Table 1). With the same concentration of bases, the reaction is not efficient under conventional heating, even after 2-day reflux (entry 8 and 9). In contrast, the reaction remained its high conversion (85 %) in only 30 min at 150 °C in a microwave reactor. The comparison, in turn, begs the question: Could the conversion be improved if the same temperature were created as in the microwave reactor? To answer the question, a reduction of acetophenone using 5 mol% of Na-HMDS was performed in a mini flow-reactor heated to 150 °C (entry 28). As expected, the conversion is much closer to the one doing in microwave (89 %) even though condition reaction of flow was not optimized. The difference between microwave and conventional heating can be attributed to simple thermal effects. One of the other benefits of this flow test was that no column chromatography needed to obtain pure alcohol 3a. The productivity of flow-chemistry in this chemical transformation, which also was confirmed by Ley group's works in different catalytic systems. Ley group also provided flow protocols for this type of reaction using zirconium oxide (Ley et al., 2013) and lithium *tert*-butoxide as catalysts (Ley et al., 2009).

In a further observation, this reaction was tested carefully with different sources of hydroxides such as Sigma-Aldrich, Ajax Finechem, and Scharlau to make clear the suspicion on the contribution of metal traces. As shown in Table 2, the performance was dependent neither on the commercial source nor on the purity given by suppliers. The reactions using NaOH with (3 wt% of metal trace) from Scharlau (entry 2) and powder LiOH (with < 2 wt% of metal trace) from Sigma-Aldrich (entry 4) did not result in the formation of 3a. One of the reasons could be that the bottle labels of those products do not show catalytic candidates (Al, Mg, Ni) which are necessary for MPV reduction. More than two samples of bases from different bottles of Chem Supply

(entry 1) and Univar Solutions (entry 5) were repeated to demonstrate that different batches of each brand did not affect the results, and this exploration was not random. An old LiOH bottle of May and Baker company without clear label information worked well with the reduction (entry 4). The suspicion was also mentioned in Ouali group's report in 2009 (Ouali et al., 2009); however, more effectively, these tests were confirmed under Microwave with shorter reaction time (1.5 h) as well as a lower concentration of alkali hydroxides (5 mol%) to achieve sustainable synthetic trend. In fact, some previous works reassessed metal-free reactions and promoted the catalytic role of contaminants of industry chemicals in some chemical transformation (Singer et al., 2004). However, it is difficult to understand the catalytic mechanism of metal trace in alkali bases, especially hydroxides bought from Suppliers such as Chem-Supply or Scharlau as the concentration and composition of metal trace in bases could not be identified precisely. Regardless of whether transformations like these, there are or are not the catalytic role of metal trace, they are still useful synthesizes (Leadbeater, 2010).

Table 2: Effect of different suppliers on reduction conversion of acetophenone.

Entry	Brand	Number of tested samples	Bases	Metal trace (%) [*]	Conversion (%)
1	Chem-supply	Ten samples from different production batches	NaOH	2	99-100
2	Scharlau	one sample	NaOH	3	Decomposed
3	Sigma-Aldrich	two samples from different bottles	LiOH	2	96
4			LiOH	<2	Decomposed
5	May and Baker	one sample	LiOH	-	96
6	Univar Solutions	Three samples from different bottles	NaOH	3	100
7		Two samples from different bottles	KOH	15	83-89

^{*}shown on bottle labels

In the next step, a wide range of carbonyl substrates was applied by the optimized procedure to demonstrate the efficiency of this method and the yields were gained as in Table 3. NaOH from Chem-Supply was used in this series instead of other strong bases because of its commercial availability and cheap price. In general, the MPV reductions occurred in 1-3 h in Microwave with using 5 mol% NaOH, affording corresponding alcohols in good to excellent yield. Functional groups of benzylic carbonyls seemed to have an insignificant effect on the outcomes of the reactions (entry 1-3, 13-14).

Not all substrates tested reacted efficiently. There was a noticeable difference in the reactivity between benzophenone and their derivative containing amino group (entry 9-10). The reduction of 2-Amino-5-Chloro benzophenone resulted in forming by-products due to the high activity of the amino group on the o-position of the aromatic ring. The reduction of aldehydes (entry 13-16) seemed to afford a slightly lower yield of isolated alcohol (< 90 %) than the reduction of ketones (> 90 %) because some side-reactions of aldehydes such as aldol condensation and decomposition occurred. The method did not work with aliphatic aldehydes and cyclic ketones while long-chain aliphatic ketone 3l (entry 12) still performed a good yield up to 70 %.

Table 3: Substrate scope 1 of MPV reaction and NMR data of products.

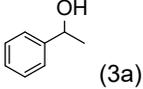
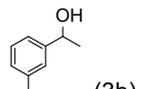
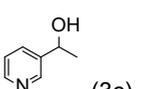
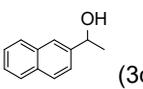
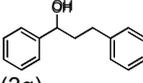
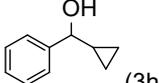
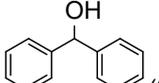
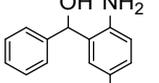
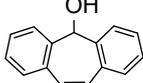
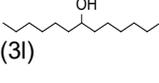
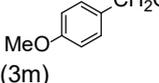
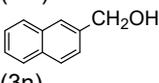
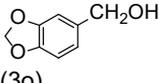
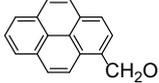
Entry	Alcohol 3	Yield (%)	NMR data
1	 (3a)	93	¹ H NMR (400 MHz, CDCl ₃) δ 7.18–7.33 (m, 5H), 4.84 (q, <i>J</i> = 6.4 Hz, 1H), 1.63 (brs, 1H), 1.43 (d, <i>J</i> = 6.5 Hz, 3H) ppm. ¹³ C NMR (75 MHz, CDCl ₃) δ 145.83, 128.54, 127.51, 125.4, 70.46, 25.19 ppm.
2	 (3b)	87	¹ H NMR (400 MHz, CDCl ₃) δ 7.21 – 7.05 (m, 3H), 7.05 – 6.98 (m, 1H), 4.79 (q, <i>J</i> = 6.5 Hz, 1H), 2.28 (d, <i>J</i> = 0.8 Hz, 3H), 1.41 (d, <i>J</i> = 6.5 Hz, 3H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 159.81, 147.61, 129.56, 117.69, 112.91, 110.91, 70.37, 55.24, 25.16 ppm.
3	 (3c)	94	¹ H NMR (400 MHz, CDCl ₃) δ 8.41 (ddd, <i>J</i> = 4.9, 1.8, 1.0 Hz, 1H), 7.59 (td, <i>J</i> = 7.7, 1.8 Hz, 1H), 7.24 (ddt, <i>J</i> = 8.9, 1.9, 1.0 Hz, 1H), 7.09 (dddd, <i>J</i> = 7.5, 4.9, 1.2, 0.5 Hz, 1H), 4.81 (q, <i>J</i> = 6.5 Hz, 1H), 1.41 (d, <i>J</i> = 6.6 Hz, 3H) ppm. ¹³ C NMR (101 MHz, CDCl ₃) δ 163.38, 148.10, 136.86, 122.19, 119.80, 69.09, 24.16 ppm.
4	 (3d)	90	¹ H NMR (400 MHz, CDCl ₃) δ 7.76 (ddd, <i>J</i> = 7.1, 4.8, 2.9 Hz, 4H), 7.48 – 7.35 (m, 3H), 5.01 (q, <i>J</i> = 6.4 Hz, 1H), 1.52 (d, <i>J</i> = 6.5 Hz, 3H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 143.22, 133.36, 132.96, 128.35, 127.96, 127.71, 126.18, 125.83, 123.85, 70.54, 25.15 ppm.

Table 3 (continue): Substrate scope 1 of MPV reaction and NMR data of products.

5	 (3e)	90	¹ H NMR (400 MHz, CDCl ₃) δ 7.28 (t, J = 1.2 Hz, 3H), 7.28 – 7.19 (m, 1H), 7.23 – 7.16 (m, 2H), 4.53 (dd, J = 7.1, 6.1 Hz, 2H), 1.82 – 1.63 (m, 5H), 0.85 (t, J = 7.4 Hz, 7H) ppm. ¹³ C NMR (101 MHz, CDCl ₃) δ 144.60, 128.42, 127.52, 125.98, 76.06, 31.91, 10.15 ppm.
6	 (3f)	88	¹ H NMR (400 MHz, CDCl ₃) δ 7.30 – 7.16 (m, 1H), 1.79 – 1.55 (m, 1H), 1.44 – 1.15 (m, 1H), 0.86 (t, J = 7.4 Hz, 1H) ppm. ¹³ C NMR (101 MHz, CDCl ₃) δ 144.94, 128.44, 127.50, 125.90, 74.46, 41.26, 19.05, 13.97 ppm.
7	 (3g)	82	¹ H NMR (400 MHz, CDCl ₃): δ 7.22-7.39 (m, 10 H), 4.72 (q, 1 H), 2.67-2.83 (m, 2 H), 2.06-2.20 (m, 2 H), 2.41 (s, 1 H) ppm. ¹³ C NMR (101 MHz, CDCl ₃): δ 144.6, 141.8, 128.5 (4 C), 128.4 (2 C), 127.7, 125.9 (2 C), 125.8, 73.9, 40.5, 32.1 ppm.
8	 (3h)	80	¹ H NMR (300 MHz, CDCl ₃) δ 7.50 – 7.33 (m, 4H), 7.38 – 7.26 (m, 1H), 4.05 (d, J = 8.3 Hz, 1H), 1.98 (s, 1H), 1.25 (dtd, J = 13.1, 8.1, 5.0 Hz, 1H), 0.74 – 0.34 (m, 5H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 143.82, 128.39, 127.57, 126.03, 78.60, 77.46, 77.03, 76.61, 19.23, 3.60, 2.84 ppm.
9	 (3i)	96	¹ H NMR (400 MHz, CDCl ₃) δ 7.35 – 7.28 (m, 4H), 7.32 – 7.25 (m, 2H), 7.28 – 7.20 (m, 3H), 7.23 – 7.17 (m, 1H), 7.18 (d, J = 3.5 Hz, 1H), 5.78 (s, 1H) ppm. ¹³ C NMR (101 MHz, CDCl ₃) δ 143.81, 128.52, 127.60, 126.56, 76.30 ppm.
10	 (3j)	70	¹ H NMR (300 MHz, CDCl ₃) δ 7.35 – 7.21 (m, 3H), 7.19 (s, 1H), 7.05 – 6.95 (m, 2H), 6.54 (d, J = 8.2 Hz, 1H), 5.74 (s, 1H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 142.98, 141.12, 129.11, 128.75, 128.65, 128.23, 128.10, 126.66, 123.36, 118.19, 74.41 ppm.
11	 (3k)	91	¹ H NMR (300 MHz, CDCl ₃) δ 7.67 (d, 2H), 7.26–7.46 (m, 6H), 7.11 (s, 2H), 5.38 (s, 1H), 2.62 (brs, 1H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 140.37, 132.60, 130.99, 128.74, 128.57, 126.83 ppm.
12	 (3l)	70	¹ H NMR (400 MHz, CDCl ₃) δ 1.39 – 1.29 (m, 2H), 1.28 – 1.18 (m, 1H), 1.21 (s, 4H), 1.12 (d, J = 6.1 Hz, 1H), 0.85 – 0.77 (m, 2H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 77.33, 77.02, 76.7, 72.03, 37.51, 31.86, 29.39, 25.63, 22.63, 14.09 ppm.
13	 (3m)	81	¹ H NMR (400 MHz, CDCl ₃) δ 7.24 (d, J = 8.4 Hz, 2 H), 6.86 (d, J = 8.4 Hz, 2 H), 4.53 (s, 2 H), 3.78 (s, 3 H), 2.63 (br., 1 H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 159.16, 133.19, 128.65, 113.94, 64.89, 55.30 ppm.
14	 (3n)	86	¹ H NMR (300 MHz, CDCl ₃) δ 7.77 – 7.64 (m, 4H), 7.44 – 7.30 (m, 3H), 4.71 (d, J = 0.8 Hz, 2H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 138.37, 133.42, 132.98, 128.37, 127.94, 127.77, 126.23, 125.94, 125.47, 125.22, 65.46 ppm.
15	 (3o)	61	¹ H NMR (400 MHz, CDCl ₃) δ 6.87 (s, 1 H), 6.76 - 6.84 (m, 2H), 5.96 (s, 2 H), 4.59 (s, 2 H), 1.68 (br.s., 1 H) ppm. ¹³ C NMR (100 MHz, CDCl ₃) δ 148.12 (C), 147.39 (C) 135.16 (C) 120.79 (CH) 108.50 (CH) 108.16 (CH) 101.29, 65.65 ppm.
16	 (3p)	77	¹ H NMR (300 MHz, CDCl ₃) δ 8.36 (d, J = 9.2 Hz, 1H), 8.24 – 8.09 (m, 4H), 8.13 – 7.95 (m, 4H), 5.39 (s, 2H) ppm. ¹³ C NMR (76 MHz, CDCl ₃) δ 133.82, 131.34, 131.30, 130.83, 128.88, 127.97, 127.53, 127.43, 126.11, 126.04, 125.35, 125.32, 124.81, 124.77, 123.06, 63.93 ppm

4. Conclusions

In summary, the simple and efficient transition metal-free transfer hydrogenation protocol conducted successfully in a microwave reactor using cheap and available bases. It is believed that metal contaminants contained in these bases might have significant catalytic effects on the reactions. The reaction is performed

using a cheap and safe reaction medium, delivering alcohol products in high yields and excellent purities in short reaction time. This reduction does not involve the hazards usually associated with other batch-mode processes, such as with hydride reagents or high-pressure hydrogenations and toxic metal catalysts. Although the mechanism of these surprising reactivities is still unclear, and it needs to be done further work, it cannot deny that cheap commercial bases from Chem-Supply or Scharlau are the best active chemicals for this type of chemistry and this protocol prompts to be a scale-up upgrading of Microwave use for alcohol production.

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