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# CSJ acting as a versatile highly efficient greener resource for organic transformations†

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Simple, new, greener and efficient alternatives to the existing protocols have been developed for the reduction of aromatic aldehydes to their corresponding alcohols, decarboxylation of substituted benzoic acids (C<sub>6</sub>–C<sub>1</sub>) and substituted cinnamic acids (C<sub>6</sub>–C<sub>3</sub>) with a hydroxyl group at the *para* position with respect to the acid group to corresponding phenolic compounds and vinyl phenols respectively by using a natural feedstock, cucumber juice (CSJ), which acts as a greener solvent system, performing a substrate-selective reaction. Additionally, the hydrolysis of the acetyl as well as the benzoyl group of aromatic compounds has been carried out to afford excellent yield by CSJ.

Hydroxycinnamic acids in plants are known to be precursors of aromatic compounds such as styrenes, polymers, epoxides, alkylbenzenes, stilbenes *etc.*<sup>1</sup> Vinyl phenol (hydroxy styrene) derivatives, like 4-vinylphenol (4-VP), 4-vinylcatechol (4-VC), 4-vinylguaiacol (4-VG) and 4-vinylsyringol (4-VS) obtained from *p*-coumaric acid, caffeic acid, ferulic acid and sinapic acid subsequently, are considered as flavouring agents in perfumery, food, and beverage industries being recognized as FEMA GRAS (Flavour and Extract Manufacturer's Association; General Regarded as for the Safe).<sup>2</sup> 4-VP and *p*-acetoxystyrene (pAS) derivatives are active starting materials for the synthesis of bioactive compounds and act as versatile intermediates in the preparation of ion-exchange resins, additives in elastomers, adhesives, agents for control of germination, coatings, automotive finishes, ink, semiconductor manufacturing, UV-absorbers, photoresists, photolithography and cancer preventive agents.<sup>2,3</sup> In addition, these compounds have attracted considerable attention due to their various biological and pharmacological activities such as antioxidant, antibacterial, antifungal, hypolipidemic and antimutagenic.<sup>3a</sup> Ferulic acid,

a highly abundant naturally occurring phenolic compound, is a precursor of 4-VG, the commercial cost of which nearly 40 times more than that of ferulic acid.<sup>4a</sup> 4-VG has been chemically transformed into more biodegradable, oxygenated polystyrenes which demonstrate superior mechanical strengths over other polystyrenes.<sup>4b</sup> Moreover, catechol and pyrogallol obtained from protocatechuic acid and gallic acid are often introduced into synthesis of biologically active molecules such as flavonoids, the anti-biotic trimethoprim, and muscle relaxant gallamine triethiodide.<sup>5</sup> A burgeoning global demand, several research groups have been involved for the synthesis of the above discussed compounds to replace the chemical methods by using the green and safer technologies such as ionic liquids, microwave and bio-catalysis.<sup>6</sup> However, the development of a simple and efficient synthetic methodology has been a tedious task because of the requirement for harsh reaction conditions (such as high temperature, high pressure), protection–deprotection steps, low yield, toxic reagents, besides the susceptibility of the hydroxyl functional group towards several side reactions, including polymerization.<sup>3,6</sup>

Deprotection of functional groups is one of the most important and widely carried out synthetic transformations in preparative organic chemistry. Phenols are protected as acetates and benzoates.<sup>7</sup> The methods available for deprotection of aryl acetates involve the treatment with activated Zn in MeOH,<sup>8</sup> NaHTe in refluxing EtOH,<sup>9</sup> *n*-BuNH<sub>2</sub> in benzene,<sup>10</sup> Al<sub>2</sub>O<sub>3</sub> under microwave irradiation,<sup>11</sup> cyclodextrine in aqueous DMSO,<sup>12</sup> Yb(OTf)<sub>3</sub>,<sup>13</sup> K<sub>2</sub>CO<sub>3</sub> in *N*-methyl-2-pyrrolidone,<sup>7</sup> amberlyst-15,<sup>14</sup> metal complexes,<sup>15</sup> metalloenzymes,<sup>16</sup> and natural kaolinitic clay.<sup>17</sup> However, these methods suffer from the disadvantages of harsh reaction conditions, use of costly reagents, and not always being effective for multifunctional substrates.<sup>7,18</sup>

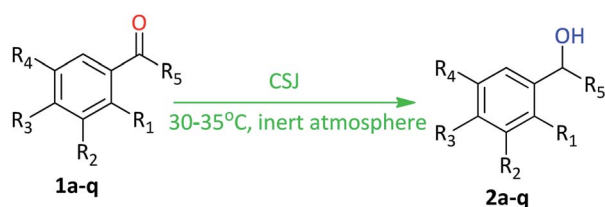
Biotransformation, a simple, environmentally friendly and useful alternative to the chemical route, is rapidly drawing interest owing to the possibility of producing compounds with high stereo-specificity and selectivity under mild reaction conditions.<sup>6a</sup> Nowadays, much attention has been paid to bioconversion of organic compounds by using plants, animal or

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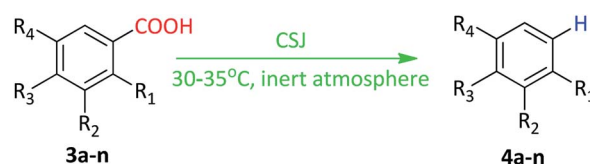
† Electronic supplementary information (ESI) available. See DOI: 10.1039/c6ra01760f

microbial cells or purified enzymes as catalyst.<sup>19</sup> The biocatalytic decarboxylation of substituted *para*-hydroxycinnamic acids were performed by *para*-hydroxycinnamic acid decarboxylase (PDC) in biphasic reaction medium,<sup>20</sup> *Sporotrichum thermophile*,<sup>1</sup> *Bacillus pumilus*,<sup>4b</sup> *Klebsiella oxytoca*,<sup>21</sup> plant cell culture (e.g. *Camellia sinensis*),<sup>22</sup> *Saccharomyces cerevisial*<sup>23</sup> etc. The development of green, safe and sustainable protocols for the use of natural feedstocks in chemical synthesis alternative to hazardous organic chemicals is extensively acknowledged.<sup>24</sup> Some plants were reported as natural resources of reductase activity with alcohol dehydrogenase systems such as *Daucus carota*, *Manihot* species and *Saccharum officinarum*.<sup>25</sup> Water Extract of Banana (WEB) at room temperature was very efficient catalyst system for Dakin reaction.<sup>24a</sup> Suzuki–Miyaura cross-coupling reaction was also developed by Water Extract of Rice Straw Ash (WERSA) as well as WEB at room temperature.<sup>24b-c</sup> The two fruits of *Cucurbita pepo* L. (marrow) and *Cucurbita maxima* L. (pumpkin) showed reducing properties towards ketones.<sup>26</sup> Nag *et al.* reported that the decarboxylation of the *para*-hydroxycinnamic acids to styrene and the reduction of some aromatic aldehydes to alcohols have been performed by the juice of *Cocos nucifera* L. and *Borassus flabellifer* L.<sup>2b</sup> Being concerned about environmental impact, we focused our attention on cucumber juice (CSJ), a highly abundant natural feedstock. Cucumber (*Cucumis sativus* L.), belongs to cucurbitaceae family which is agriculturally and economically important crop used as a fruit in worldwide and cheap, easily available throughout the year. But two fruits (*Cocos nucifera* L. and *Borassus flabellifer* L.) are expensive and collections of juices are tedious. Our present method for choosing cucumber juice over two specified juices and vegetables is more appropriate on the basis of availability, price, collection of juice, simplicity in reaction procedure and versatility. To the best of our knowledge, we first report the biotransformation of cucumber juice for the selective reduction of aromatic aldehydes to alcohols, decarboxylation of substituted aromatic acids, deacetylation and debenzoylation of substituted aromatic compounds without using any catalyst, base, hazardous reagent and organic solvent. In this communication, we report on the use of cucumber juice as an all-in-one mixture of solvent and greener alternatives.

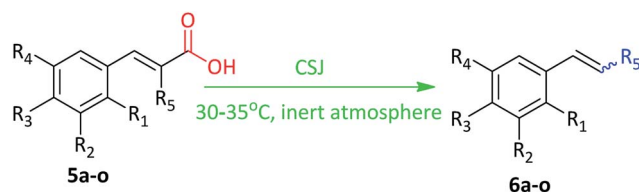
In CSJ catalysed reduction, decarboxylation and deprotection (hydrolysis) were discussed according to Schemes 1–4 where all experiments were investigated at 30–35 °C under argon atmosphere. During our study, 40 to 50 ml fruit juice was obtained from 100 g of cucumber fruit. Fresh green cucumbers collected from the local market were washed with distilled water and cut into small pieces by a metallic sharp knife. Then it was



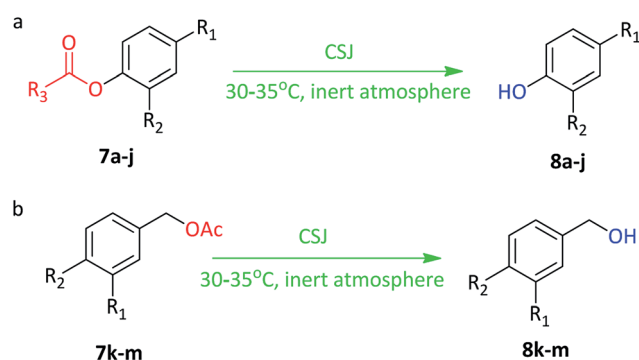
Scheme 1 Reduction of substituted aromatic aldehydes.



Scheme 2 Decarboxylation of substituted benzoic acid.



Scheme 3 Decarboxylation of substituted cinnamic acids.



Scheme 4 (a) De-acetylation and de-benzoylation of substituted aromatic compounds. (b) Deprotection of substituted benzyl acetates.

ground under the mixture grinder. Then it was filtered through Buchner funnel in vacuum using ordinary filter paper as soon as possible for the maximum elimination of residue and the filtrate was abbreviated as CSJ here. Literature reports reveal that CSJ is composed mostly of water more than 95% along with proteins, ions, fats, vitamin B1 and C, pectin, sugars, erepsin, proteolytic enzyme, rutin, oxidase, succinic and maleic dehydrogenases and so on.<sup>27</sup> In each experiment for biotransformation by CSJ, substrate (1 g) separately was added to the freshly prepared cucumber juice (200 ml). The reaction mixture was stirred at 30–35 °C temperature maximum for 72 h under argon atmosphere (Schemes 1–4). Each individual suspension was filtered, and the residue was washed with water, as well as with ethyl acetate. The filtrate was then extracted with ethyl acetate (3 × 100 ml), and the organic phase was dried over sodium sulphate and evaporated under reduced pressure. Maximum cases, column chromatography was not required for product purification due to excellent yield. Some cases, reaction mixtures were purified by column chromatography using ethyl acetate and *n*-hexane as eluents to afford the products. The structure of the products were confirmed by NMR spectroscopy. In Scheme 1, the activity of CSJ on aromatic aldehydes and ketones were shown.

From Table 1, it was seen that the reducing activity and yield of the products depended on substituents with respect to aldehyde group in benzene ring. These results indicated that the electron donating groups present either at *meta* or *para* position of aromatic aldehydes showed activity in the presence of CSJ, but *ortho* substituted aromatic aldehydes did not produce any alcohol. The methoxy group present at *para* rather than *meta* position of the phenyl ring, enhanced the rate as well as the yield of the product. That is why; it was isolated with better yield from vanillin (1i) to isovanillin (1k) to veratraldehyde (1j). CSJ did not show any activity towards chloro, nitro substituted benzaldehyde, acetophenone and benzophenone during 72 h.

Subsequently, in Tables 2 and 3 it was observed that *p*-hydroxybenzoic acids and *p*-hydroxycinnamic acids produced decarboxylated products rather than reduced products within 24 h. From Table 2, it was observed that benzoic acids containing phenolic –OH group at *para* position rather than *ortho* and *meta* position with respect to acid group, decarboxylated products were obtained. When more –OH groups are present at R<sub>2</sub> or R<sub>4</sub> position together with phenolic –OH group at R<sub>3</sub> position, the yield of decarboxylated products were increased. It was also observed that when bulky groups such as methoxy group present at R<sub>2</sub> or R<sub>4</sub> position along with phenolic –OH group at R<sub>3</sub> position the, the yield of decarboxylated products were decreased in presence of CSJ due to steric effect.

For this reason, the increasing yield was observed from syringic acid (3n) to protocatechuic acid (3i) to gallic acid (3m) with the increase of hydroxyl groups rather than methoxy groups. In case of hydroxycinnamic acids to hydroxystyrenes were formed by the removal of the carboxyl group from the C-3 side chain. The same trend of increasing yield was observed for 4-VC (6d) from caffeic acid (5d). But the isolated yield of 4-VC

**Table 1** Reduction of substituted aromatic carbonyl compounds by CSJ<sup>a</sup>

Reactant	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	Reaction time (h)	Yield <sup>b</sup> (%)
1a	H	H	H	H	H	72	50
1b	H	H	OH	H	H	72	65
1c	H	OH	H	H	H	72	60
1d	OH	H	H	H	H	72	0
1e	H	H	OMe	H	H	72	68
1f	H	OMe	H	H	H	72	63
1g	OMe	H	H	H	H	72	0
1h	H	OH	OH	H	H	72	70
1i	H	OMe	OH	H	H	72	74
1j	H	OMe	OMe	H	H	72	81
1k	H	OH	OMe	H	H	72	78
1l	H	OMe	OH	OMe	H	72	82
1m	H	OMe	OMe	OMe	H	72	86
1n	H	H	NO <sub>2</sub>	H	H	72	0
1o	H	H	Cl	H	H	72	0
1p	H	H	H	H	CH <sub>3</sub>	72	0
1q	H	H	H	H	Ph	72	0

<sup>a</sup> Reaction conditions: 1 g substrate in 200 ml CSJ stirred at 30–35 °C maximum for 72 h under argon atmosphere. <sup>b</sup> Isolated yield.

**Table 2** Decarboxylation of substituted benzoic acids by CSJ<sup>a</sup>

Reactant	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	Reaction time (h)	Yield <sup>b</sup> (%)
3a	H	H	H	H	72	0
3b	H	H	OH	H	48	75
3c	H	OH	H	H	72	0
3d	OH	H	H	H	72	0
3e	H	H	OMe	H	72	0
3f	H	H	NO <sub>2</sub>	H	72	0
3g	H	H	NH <sub>2</sub>	H	72	0
3h	H	H	SH	H	72	0
3i	H	OH	OH	H	48	85
3j	H	OMe	OH	H	48	80
3k	H	OH	OMe	H	72	0
3l	H	COOH	H	H	72	0
3m	H	OH	OH	OH	48	98
3n	H	OMe	OH	OMe	48	25

<sup>a</sup> Reaction conditions: 1 g substrate in 200 ml CSJ stirred at 30–35 °C maximum for 72 h under argon atmosphere. <sup>b</sup> Isolated yield.

**Table 3** Decarboxylation of substituted cinnamic acids by CSJ<sup>a</sup>

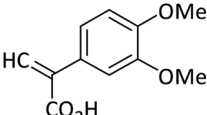
Reactant	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	Reaction time (h)	Yield <sup>b</sup> (%)
5a	H	H	H	H	H	72	0
5b	H	H	OH	H	H	24	94
5c	H	H	OMe	H	H	72	0
5d	H	H	OH	OH	H	24	98
5e	H	H	OH	OMe	H	24	92
5f	H	H	OMe	OH	H	72	0
5g	H	H	OMe	OMe	H	72	0
5h	H	OMe	OH	OMe	H	24	30
5i	H	H	H	OH	H	72	0
5j	OH	H	H	H	H	72	0
5k	H	H	NH <sub>2</sub>	H	H	72	0
5l	H	H	NO <sub>2</sub>	H	H	72	0
5m	H	H	OH	H	Me	24	15
5n	H	H	OH	OMe	Me	24	10
5o	H	H	OH	OMe	Ph	72	0

<sup>a</sup> Reaction conditions: 1 g substrate in 200 ml CSJ stirred at 30–35 °C maximum for 72 h under argon atmosphere. <sup>b</sup> Isolated yield.

(6h) from sinapic acid (5h) was low due to presence of methoxy groups at R<sub>2</sub> and R<sub>4</sub> position with respect to acid group. Both *o*-coumaric acid (5j) and *m*-coumaric acid (5i) did not undergo decarboxylation reaction in presence of CSJ. But when nitro and amino group (also contain proton source) present at the *para* position of the cinnamic acid, no decarboxylated products were obtained. So, the observation indicating that the *para* hydroxy group was essential for decarboxylation reaction both for substituted benzoic acid and substituted cinnamic acids.

In 2010, Mancheño *et al.* also exhibited that PDC catalyse the non-oxidative decarboxylation of hydroxycinnamic acids to corresponding vinyl derivatives where hydrogen atom of *p*-OH group attains a significant role.<sup>28</sup> Here, it was also examined that, cinnamic acid and benzoic acid in the absence of *p*-OH group with respect to carboxylic acid group, decarboxylation was not achieved up to 72 h due to non-participation of

Table 4 Hydrolysis of aromatic acetates or benzoates by CSJ<sup>a</sup>

Reactant	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Reaction time (h)	Yield <sup>b</sup> (%)
7a	CHO	H	Me	6	90
7b	CHO	OMe	Me	6	94
7c	CHO	OAc	Me	6	98
7d	CHO	H	Ph	6	85
7e	CH=CH <sub>2</sub>	H	Me	6	92
7f	CH=CH <sub>2</sub>	OMe	Me	6	95
7g	CH=CH <sub>2</sub>	OAc	Me	6	98
7h	CH=CH-COOH	H	Me	6	80
7i	CH=CH-COOH	OAc	Me	6	84
7j		OMe	Me	6	78

<sup>a</sup> Reaction conditions: 1 g substrate in 200 ml CSJ stirred at 30–35 °C maximum for 6 h under argon atmosphere. <sup>b</sup> Isolated yield.

Table 5 Hydrolysis of substituted benzyl acetate by CSJ<sup>a</sup>

Reactant	R <sub>1</sub>	R <sub>2</sub>	Reaction time (h)	Yield <sup>b</sup> (%)
7k	H	OMe	6	90
7l	OMe	OMe	6	92
7m	NO <sub>2</sub>	H	6	90

<sup>a</sup> Reaction conditions: 1 g substrate in 200 ml CSJ stirred at 30–35 °C maximum for 6 h under argon atmosphere. <sup>b</sup> Isolated yield.

hydrogen atom of phenolic OH group in reaction mechanism. This result indicates that mechanism of decarboxylation may be followed *via* enzymatic route.

In Scheme 4a and b, it was discussed about the hydrolysis of acetyl as well as benzoyl group of aromatic compounds. With the increase of the electron donating group and bulky group present with respect to acetate and benzoate group, the yield as well as rate of hydrolysis also increased.

From Table 4, it was seen that the rate of hydrolysis of 2-methoxy-4-vinylphenyl acetate (8f) with respect to 4-vinylphenyl acetate (8e) increased due to addition of an extra methoxy group acting as electron donor as well as sterically hindered with respect to acetoxy group in benzene ring.

The practical utility of using CSJ was deprotection of acetyl and benzoyl group of aromatic compounds in the presence of several other functional groups, such as aldehyde, vinyl, acrylic acid *etc.* Which were remain unaffected under this reaction condition (Table 4 and 5).

## Conclusions

In conclusion, we have developed a greener, simple, high-yielding and eco-friendly protocol for the bioconversion of value added products by using a cheap natural resource such as cucumber juice avoiding any chemical reagents. The present results demonstrate the novelty of CSJ that shows unique

selectivity and constitutes a useful environmentally benign alternative to commonly accepted procedures of reduction, decarboxylation, deacetylation and debenzoylation. The developed method allows the new industrial scale synthesis of vinylphenols in good yield and excellent selectivity than other conventional chemical methods. Our investigation is continuing to understand the proper mechanistic pathway by which CSJ is responsible for reduction, decarboxylation and hydrolysis reactions.

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