Solid-Supported Green Synthesis of Substituted Hydrocinnamic Esters by Focused Microwave Irradiation[1])

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An efficient chemoselective hydrogenation protocol for substituted cinnamic esters is developed for the synthesis in quantitative yield of corresponding bioactive dihydrocinnamic esters with solid-supported palladium chloride/ammonium formate (cat.) in $HCOOH/H_2O$ 1:2 as a hydrogenating agent under focused-microwave irradiation for 10 min.

Introduction. – Environmental constrains [1] have led to the development of new chemical processes employing microwave, ultrasound, ionic liquids, recyclable catalysts and reagents, and biotransformations, etc. Catalysts and reagents on solid support under solventless (solvent-free) conditions is an especially important development of 'green' technologies which have made landmark contributions to preserve environment due to elimination of complicated workup procedures and reduction in waste effluent (more than 15 billion kg of solvent consumed worldwide annually!) [2]. Further, use of microwave irradiation on solid-supported reactions has enhanced the impact of the latter as the high heating efficiency of microwave results in remarkable rate enhancement, higher yields, greater selectivity, and ease of manipulation of such reactions [3]. In addition, the limitation of the microwave-assisted reactions in solvents enforcing development of high pressure and special sealed vessels are circumvented by this solid-support strategy [4], which enables organic reactions such as oxidation, hydrogenation, *etc*., to occur rapidly at atmospheric pressure and to upscale the reaction on a preparative scale.

A lot of hydrogenation protocols are available for the selective hydrogenation of C=C bonds of unsaturated esters which either require a special apparatus and H_2 gas (potentially explosive) [5] or else utilize expensive reagents [6] such as dithiane/Ni [6a], copper hydride [6b], YbI_2 [6c], Mg/MeOH [6d], NaSeH [6e], NaHTe [6f], organotin iodide hydride [6g], $RuCl_3/P(cy)_3$/MeOH (cy = cyclohexyl) [6h], baker's yeast [6i], rhodium/TPPTS (TPPTS = 3,3′,3″-phosphinidynetris[benzenesulfonic acid] [6j], $CoCl_2/SiHCl_3$ [6k], electrolysis [6l], SmI_2 [6m], Cl_2InH [6n], copper carbene hydride [6o], lipase [6p], $InCl_3/NaBH_4$ [6q], and $Si(OMe)_4/Pd(PPh_3)_4$ [6r], *etc*. In this regard, some catalytic transfer hydrogenation (CTH) reactions [7] including microwave-

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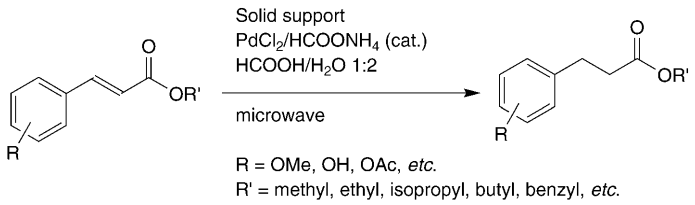
assisted hydrogenation reactions have been reported for the reduction of C=C bonds, which serve the goals of 'green' chemistry due to avoidance of hazardous H_2 gas or metal hydride donors and minimization of undesired toxic wastes. Although microwave-assisted CTH protocols [8] provide excellent yields of dihydrocinnamic ester in short time, they suffer from some limitations. These limitations include *a*) the adsorption of the hydrogen-transferring agent on either a polymeric resin [9] or an alumina support [10] before carrying out the hydrogenation reaction, *b*) the use of DMSO as solvent, *c*) the expensive *Wilkinson* catalyst, and *d*) the performance of the reaction in smaller batches (0.25 g, 0.16 mmol) [9a] in sealed tubes. In this context, it is desirable to develop a mild, simple, inexpensive and environment-friendly protocol for chemoselective manipulation of the C=C bond with extended conjugation (*e.g.*, Ar–HC=CH–COOR) on a preparative scale without use of any organic solvent. With our constant endeavor towards development of 'green' processes [11], we herein wish to report the synthesis of the bioactive dihydrocinnamic esters **1b**–**14b** *via* the chemoselective hydrogenation of the α,β-unsaturated cinnamic esters **1a**–**14a** in the presence of silica-gel-supported palladium chloride, ammonium formate (cat.), and HCOOH/H_2O 1:2 under focused-microwave irradiation (*Scheme*).

Scheme



Results and Discussion. – Dihydrocinnamic esters are common structural elements in numerous compounds of biological interest. For example, methyl 3-(2,4,5-trimethoxyphenyl)propanoate, a metabolite of *Cordia alliodora*, is reported to possess antifungal and larvicidal activities [12]. Further, ethyl dihydrocinnamic ester is used for protection of chymotrypsin from denaturation by EtOH and urea [13a], whereas methyl dihydrocinnamate is a precursor for the synthesis of 1,3,4,9-tetrahydropyrone[3,4-*b*]-indole-1-acetic acid, an analgesic and antipyretic molecule [13b]. Similarly, a natural ester, sintenin (=3-(3,4-dimethoxyphenyl)propyl 3-(3,4-dimethoxyphenyl)propanoate), is a potent cytotoxic agent [14]. Moreover, ethyl dihydrocinnamate has been used for the synthesis of HIV-1 protease inhibitor [15]. Lastly, dihydrocinnamic esters also find applications in food and flavor industries [16]. Despite their prominence, procedures for the preparation of dihydro compounds often suffer from drawbacks such as long reaction periods, harsh reaction conditions, poor chemoselectivity, expensive catalysts and reagents, and non-ecofriendly conditions.

To begin with, we decided to synthesize ethyl dihydrocinnamate (=ethyl 3-phenylpropionate=ethyl benzenepropanoate; **1b**) from ethyl cinnamate (**1a**), by using a microwave-assisted solid-supported 'green' CTH methodology. Recently, we have found a combination of palladium chloride, HCOOH, alcohol, and NaOH as an effective hydrogen source for the reduction of substituted cinnamic acids into corresponding

dihydro derivatives in a domestic microwave oven [17]. In the present case, we decided to use the combination of $PdCl_2$/HCOOH in alcohol on a solid support for the conversion of low-volatile cinnamic esters into their dihydro product under focused monomode microwaves [18]. Focused microwaves have certain inherent advantages over domestic microwaves due to homogeneous irradiation which results in a high degree of reproducibility and rapidity of results in comparison to domestic microwaves. Also, focused microwaves enable attainment of high temperatures for low-volatile compounds due to the availability of high pressure or open reflux which made such compounds ideally suited as substrates and products in our case.

In the first instance, compound **1a** was treated with silica-gel-supported palladium chloride, in MeOH/HCOOH/H_2O 1:2:3 and irradiated under *CEM*®-monomode microwaves (open reflux) for 55 min which provided 85% of product **1b**. The choice of the hydrogenation mixture was mooted by our inclined approach towards 'green' chemistry wherein beside H_2O, use of ecofriendly and inexpensive HCOOH will allow generation of CO_2 as a by-product which unhazardously eliminates into the atmosphere. In another reaction, we removed MeOH from the above hydrogenating mixture and employed HCOOH/H_2O 1:2 on silica-gel support and, surprisingly, there was no reduction in the yield of the product **1b** (86%). Although, the use of alcohol was imperative in our previous report [17], the change of substrate, in this report, may have subsided the need of organic solvent. Similarly, the reaction was also tried in HCOOH/silica gel without H_2O, however, the yield of the product drastically reduced to 56% which implied the important role played by H_2O in the above reaction. Moreover, assistance of H_2O [19] in the above reaction greatly leans the methodology towards 'green' chemistry.

After a lot of experimentation, we achieved success with silica-gel-supported $PdCl_2$ and HCOOH/H_2O 1:2 as hydrogenating mixture for reducing **1a** in 86% yield within 60 min. Our attention then moved towards reducing the reaction time. There had been reports utilizing formate salts [7c][8] such as ammonium formate as hydrogen-transfer agents resulting in short reaction time. However, the use of sealed tubes [9a][10] is one problem thwarting its applications on a large scale. Moreover, these reactions are also troublesome in a way that ammonium formate can sublime [9a] and block the reaction apparatus. Prompted by the above reports, we decided to add $HCOONH_4$ in a catalytic amount to the above reaction mixture by adsorbing a catalytic amount of $PdCl_2$ and $HCOONH_4$ on silica gel (60–120 mesh size) with HCOOH/H_2O 1:2 and irradiated under focused microwaves. To our surprise, the yield of product **1b** increased up to 95% with a remarkable reduction in time to 8 min. In the above reaction, replacement of $HCOONH_4$ with either HCOONa or HCOOK, *etc*., was found equally effective in providing **1b** in a short reaction time. However, use of ammonium formate appeared better because of its proximity to 'green' chemistry as both by-products ammonia and CO_2 are not hazardous to environment. Moreover, the problem of sublimation was not encountered as only a catalytic amount of $HCOONH_4$ was used in the above reaction.

Similarly, in the same reaction **1a** → **1b**, other solid supports such as alumina (neutral, acidic, and basic) and resin (*Amberlyst® 15* and *Amberlite® IR 120*), *etc.*, were tried in place of silica gel (see *Table 1*). It is obvious from the results that silica gel provides a maximum yield of the hydrogenated product compared to other supports. For compar-

ison purposes, the same reaction was performed under domestic-microwave, ultrasound, and conventional-heating conditions. Reactions in solid phase were not possible under conventional and ultrasound conditions, hence, $HCOOH/H_2O$ were used as solvents (excess) in the presence of silica gel/$PdCl_2$/$HCOONH_4$. In all the cases, the product **1b** was obtained in either inferior yield or after a longer reaction time in comparison to the focused-microwave conditions (see *Table 2*). Moreover, in case of conventional heating , the product **1b** was hydrolyzed into cinnamic acid, thus illustrating the superiority of the use of microwaves in this reaction (*Table 2*).

Table 1. *Effect of Solid Support on the Synthesis of Dihydrocinnamic Ester* **1b** *under Microwave Irradiation*

Support	Reaction time [min]	Product yield [%]	Support	Reaction time [min]	Product yield [%]
Silica gel	8	95	Alumina (acidic)	12	93
Alumina (neutral)	10	90	*Amberlyst 15*	>20	6
Alumina (basic)	10	81	*Amberlite IR 120*	>20	33

Table 2. *Comparative Studies of the Reduction of* **1a** *under Focused-Microwave, Domestic Microwave, Conventional, and Ultrasound-Assisted Conditions*

Substrate	Reaction conditions	Reaction time [min]	Product	Yield [%]
1a	microwave monomode	8[a])	**1b**	95
1a	microwave multimode	12[b])	**1b**	79
1a	conventional	720[c])	**1b**	15
			cinnamic acid	45
1a	ultrasound	300[d])	**1b**	68

[a]) Focused-microwave irradiation (power level 200 W, Temp. 130°). [b]) Microwave irradiation (960 W) with intermittent pauses after every 5 min. [c]) Reflux at 100°. [d]) Sonics with 75% duty, pulse length 9 s, pause of 30 s after every 10 min.

Having worked out the most successful procedure for the conversion of **1a** into **1b**, the same methodology was employed for the hydrogenation of the substituted cinnamic esters **2a**–**14a**, which successfully provided the corresponding dihydrocinnamate derivatives **2b**–**14b** in excellent yield (*Table 3*). It is worth mentioning that the reported method [6f] for the hydrogenation of dialkyl maleate (**15a**) provides only 5% yield of the hydrogenated product **15b**, but the reaction worked perfectly well with our method (*Entry 15*).

Further, to extend the applicability of the method, some conjugated alkenes **16a**–**24a** other than esters were hydrogenated, and in all the cases, the reaction showed good reproducibility and reflected a remarkable discrimination between the olefin moiety on one side and all other reducible groups like ketone (*Entries 16* and *17*), carboxylic acid (*Entry 18*), nitrile (*Entry 19*), and amide groups (*Entry 20*) on the other (*Table 4*). However, deacetylation occurred with acetylated cinnamates (*Entry 21*). In case of coumarin (*Entry 22*), hydrogenation resulted in ring opening of the lactone linkage besides reduction of the C=C bond. Similarly, hydrogenation of benzyl cinnamate

Table 3. *Chemoselective Hydrogenation of Unsaturated Cinnamic Esters* **1a**–**14a**[a]) *and* **15a**[a]) *into Their Dihydro Products* **1b**–**15b**[a])

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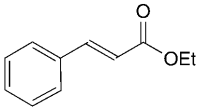
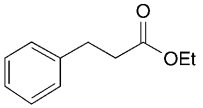
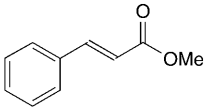
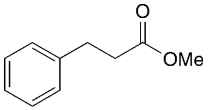
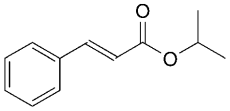
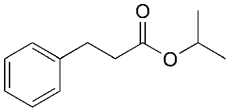
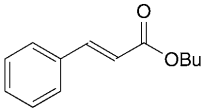
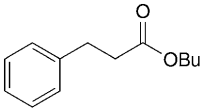
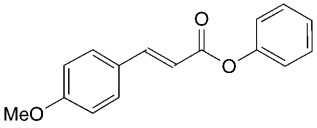
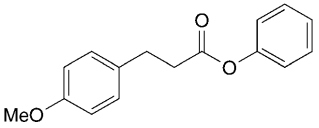
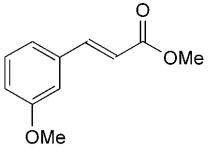
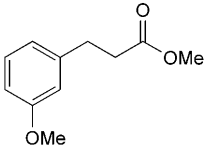
1		8		95
2		6		97
3		9		91
4		10		95
5		8		91
6		6		94

Table 3 (cont.)

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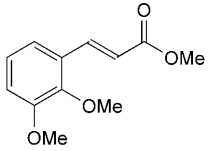
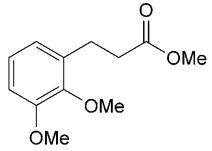
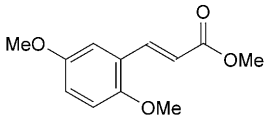
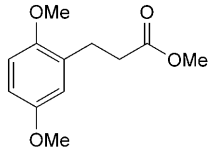
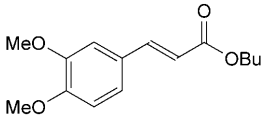
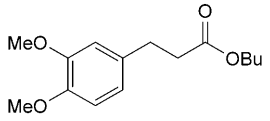
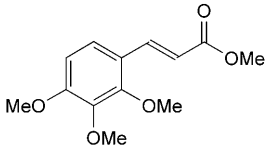
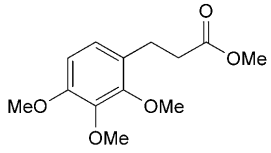
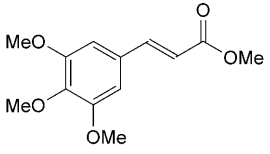
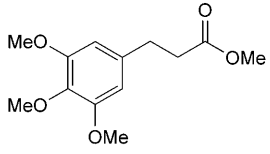
7		5		95
8		5		93
9		6		94
10		4		95
11		4		92

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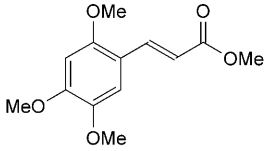
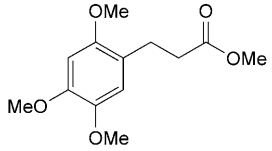
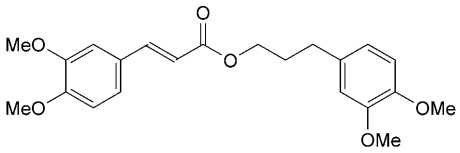
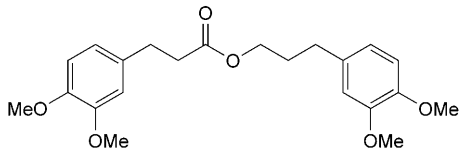
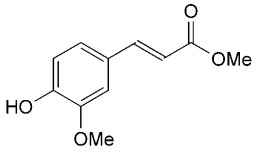
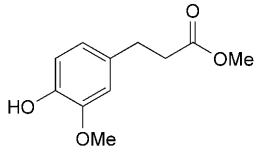
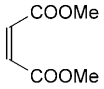
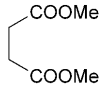
12		4		93
13		6		86
14		4		94
15		8		81

[a]) The *Entry* number corresponds to the substrate or product number.

(*Entry 23*) also resulted in hydrolysis of the ester group. Surprisingly, the C=C bond as well as the carbonyl function was reduced in case of cinnamaldehyde, and the expected dihydrocinnamaldehyde was not detected at all (*Entry 24*; *Table 4*).

All the reactions described above allowed the easy recovery of the product after a mere washing of the mixture with a solvent, and the obtained products were at least 98% pure on the basis of ^{1}H- and ^{13}C-NMR spectra which matched well with the reported values. No further purification of any of the products obtained, was performed, an important feature of the method since product separation and purification can consume a large amount of energy and plant capacity in many industrial processes. After the reaction, the remaining silica-gel or alumina-supported palladium chloride was reused, and found to be active even after three cycles of reuse, with a mere 5% loss in the activity.

Conclusion. – The described procedure is an environmentally benign, effective, mild, and chemoselective hydrogenating protocol for the synthesis of bioactive dihydrocinnamic esters on a solid support by using focused microwaves, in the absence of any toxic and hazardous H_2 gas, metal hydride donors, or organic solvents. The results shown in *Table 3* and *4* demonstrate the versatility of the process. Moreover, a considerable reaction-rate enhancement was observed by reducing the reaction time from hours to seconds with improved yield as compared to conventional heating (*Table 2*).

Two of us (*A. S.* and *V. K.*) are indebted to *CSIR* and *UGC*, Delhi, for the award of *SRF* (*A. S.*) and *JRF* (*V. K.*) respectively. The authors gratefully acknowledge the Director of I. H. B. T., Palampur, for his kind cooperation and encouragement.

Experimental Part

General. CEM-Discover© focused microwaves (2450 MHz, 300 W) and *Sonics* ultrasonicator (20 KHz, 750 W) were used wherever mentioned. M.p.: *Mettler-FP80* micromelting point apparatus; uncorrected. IR Spectra: *Perkin-Elmer-IR* spectrometer; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra ($CDCl_3$): *Bruker Avance-300* spectrometer; at 300 (^{1}H) and 75.4 MHz (^{13}C), δ in ppm, J in Hz. GC/MS and HR-EI-MS: *Shimadzu 2010* and *Micromass Q-TOF Ultima* spectrometer, resp.

Conversion of Conjugated Alkenes **1a**–**24a** *into Their Dihydro Products* **1b**–**24b***: General Procedure.* $PdCl_2$ (0.05–0.08 g), $HCOONH_4$ (0.025 mol), and silica gel (12 g, 60–120 mesh) were thoroughly mixed in a mortar and then transferred to a round bottom flask. To this powdered mixture, conjugated alkene **1a**–**24a** (0.05 mol) and $HCOOH/H_2O$ 1:2 (15 ml) were added. The mixture was then irradiated with focused monomode microwaves system for 4–10 min (depending upon the substrate). After completion of the reaction, the solid residue was washed with AcOEt (3×20 ml) and the combined org. layer washed with H_2O (3×15 ml) and brine (10 ml), dried (Na_2SO_4), and evaporated: pure **1b**–**24b** whose NMR matched well with the reported values [6–10][20].

Ethyl 3-Phenylpropanoate (**1b**) [5][6m][10]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.23–7.17 (*m*, 3 H); 7.14 (*d*, *J*=6.86, 2 H); 4.08 (*q*, *J*=6.86, 2 H); 2.90 (*t*, *J*=7.67, 2 H); 2.57 (*t*, *J*=7.67, 2 H); 1.17 (*t*, *J*=6.86, 3 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 172.9; 140.6; 128.5; 128.3; 126.5; 60.4; 35.9; 29.5; 14.5.

Methyl 3-Phenylpropanoate (**2b**) [7d][10]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.26 (*d*, *J*=7.27, 2 H); 7.15–7.09 (*m*, 3 H); 3.61 (*s*, 3 H); 2.90 (*t*, *J*=7.67, 2 H); 2.65 (*t*, *J*=7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.4; 140.5; 128.6; 126.3; 51.6; 35.7; 30.9.

Isopropyl 3-Phenylpropanoate (**3b**) [6p]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.26 (*d*, *J*=6.86, 2 H); 7.16–7.11 (*m*, 3 H); 4.96–4.93 (*m*, 1 H); 2.90 (*t*, *J*=7.67, 2 H); 2.54 (*t*, *J*=7.67, 2 H); 1.16 (*d*, *J*=6.46, 6 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 172.4; 140.6; 128.4; 128.3; 126.2; 67.7; 36.2; 31.0; 21.8.

Table 4. *Chemoselective Hydrogenation of Conjugated Alkenes* **16a**–**24a**[a]) *into Their Saturated Products* **16b**–**24b**[a])

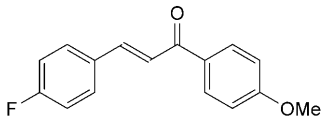
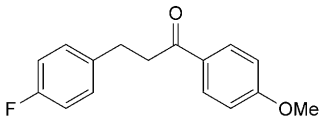
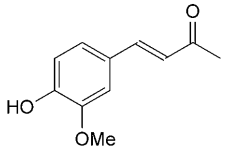
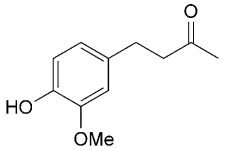
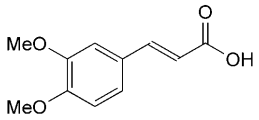
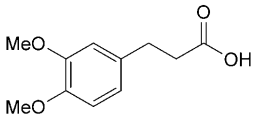
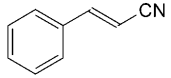
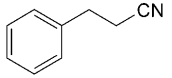
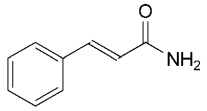
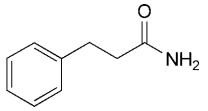
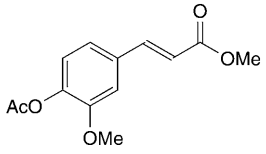
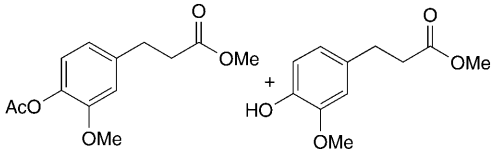
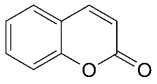
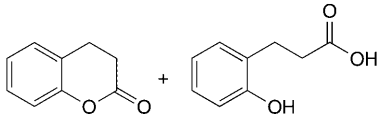
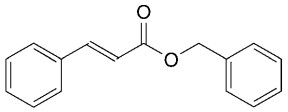
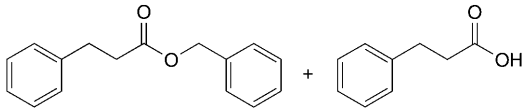
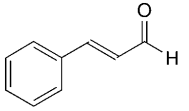
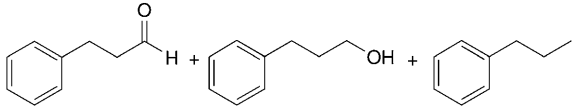
Entry	Substrate **a**[a])	Time [min]	Product **b**[a])	Yield [%]
16		9		97
17		4		96
18		9		85
19		10		82
20		10		89
21		8		52 (41)[b])

Table 4 (cont.)

Entry	Substrate **a**[a])	Time [min]	Product **b**[a])	Yield [%]
22		7		32 (47)[b])
23		8		0 (84)[b])
24		8		0 (32, 44)[b])

[a]) The *Entry* number corresponds to the substrate or product number. [b]) Numbers in the parenthesis indicate the yield of the side product(s).

Butyl 3-Phenylpropanoate (**4b**) [6l]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.21 (*d*, *J* = 6.86, 2 H); 7.11–7.05 (*m*, 3 H); 4.01 (*t*, *J* = 6.86, 2 H); 2.86 (*t*, *J* = 7.27, 2 H); 2.62 (*t*, *J* = 7.27, 2 H); 1.51–1.47 (*m*, 2 H); 1.29–1.23 (*m*, 2 H); 0.84 (*t*, *J* = 6.86, 3 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 172.7; 140.1; 128.2; 127.6; 126.4; 64.3; 36.2; 30.9; 30.3; 19.1; 13.7.

Phenyl 3-(4-Methoxyphenyl)propanoate (**5b**) [6p][21]: M.p. 88–90°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.38–7.33 (*m*, 2 H); 7.21–7.17 (*m*, 3 H); 7.21 (*d*, *J* = 8.07, 2 H); 6.79 (*d*, *J* = 8.07, 2 H); 3.72 (*s*, 3 H); 2.87 (*t*, *J* = 7.67, 2 H); 2.61 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 168.2; 158.2; 152.5; 131.4; 128.6; 128.1; 124.3; 121.6; 113.8; 55.7; 34.7; 29.2.

Methyl 3-(3-Methoxyphenyl)propanoate (**6b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.21–7.16 (*m*, 2 H); 6.73–6.68 (*m*, 2 H); 3.70 (*s*, 3 H); 3.59 (*s*, 3 H); 2.86 (*t*, *J* = 7.32, 2 H); 2.56 (*t*, *J* = 7.32, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 169.1; 155.9; 138.1; 125.4; 116.6; 110.1; 107.5; 50.9; 47.5; 31.5; 26.9.

Methyl 3-(2,3-Dimethoxyphenyl)propanoate (**7b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.90–6.86 (*m*, 1 H); 6.71–6.66 (*m*, 2 H); 3.78 (*s*, 3 H); 3.76 (*s*, 3 H); 3.60 (*s*, 3 H); 2.91 (*t*, *J* = 8.07, 2 H); 2.56 (*t*, *J* = 8.07, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.6; 152.7; 147.2; 134.3; 123.9; 121.7; 110.7; 60.6; 55.7; 51.5; 34.7; 25.6.

Methyl 3-(2,5-Dimethoxyphenyl)propanoate (**8b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.16 (*d*, *J* = 8.05, 1 H); 6.70 (*m*, 2 H); 3.70 (*s*, 3 H); 3.67 (*s*, 3 H); 3.60 (*s*, 3 H); 2.89 (*t*, *J* = 8.42, 2 H); 2.57 (*t*, *J* = 8.42, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.6; 153.5; 151.7; 128.2; 116.3; 111.5; 111.1; 55.7; 55.1; 51.4; 34.0; 26.2.

Butyl 3-(3,4-Dimethoxyphenyl)propanoate (**9b**) [6p][21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.71–6.65 (*m*, 3 H); 4.01 (*t*, *J* = 6.46, 2 H); 3.77 (*s*, 6 H); 2.81 (*t*, *J* = 7.27, 2 H); 2.59 (*t*, *J* = 7.27, 2 H); 1.49–1.44 (*m*, 2 H); 1.27–1.22 (*m*, 2 H); 0.82 (*t*, *J* = 7.27, 3 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.1; 148.8; 147.4; 133.2; 120.1; 111.6; 111.2; 64.3; 55.8; 36.2; 30.9; 30.3; 19.1; 13.7.

Methyl 3-(2,3,4-Trimethoxyphenyl)propanoate (**10b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.72 (*d*, *J* = 8.48, 1 H); 6.47 (*d*, *J* = 8.48, 1 H); 3.76 (*s*, 3 H); 3.73 (*s*, 3 H); 3.69 (*s*, 3 H); 3.53 (*s*, 3 H); 2.78 (*t*, *J* = 8.07, 2 H); 2.48 (*t*, *J* = 8.07, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.5; 152.4; 151.8; 142.2; 128.1; 123.7; 107.1; 60.7; 55.8; 51.4; 34.8; 25.4.

Methyl 3-(3,4,5-Trimethoxyphenyl)propanoate (**11b**) [6b]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.29 (*s*, 2 H); 3.70 (*s*, 6 H); 3.68 (*s*, 3 H); 3.54 (*s*, 3 H); 2.78 (*t*, *J* = 8.48, 2 H); 2.48 (*t*, *J* = 8.48, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.0; 153.1; 136.5; 136.2; 105.3; 60.6; 55.9; 51.4; 35.7; 31.2.

Methyl 3-(2,4,5-Trimethoxyphenyl)propanoate (**12b**) [12]: M.p. 49–50°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.72 (*s*, 1 H); 6.50 (*s*, 1 H); 3.88 (*s*, 3 H); 3.82 (*s*, 3 H); 3.80 (*s*, 3 H); 3.66 (*s*, 3 H); 2.87 (*t*, *J* = 7.67, 2 H); 2.58 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 174.2; 151.9; 148.5; 143.1; 120.6; 114.6; 97.9; 57.0; 56.6; 51.9; 34.9; 26.1.

3-(3,4-Dimethoxyphenyl)propyl 3-(3,4-Dimethoxyphenyl)propanoate (**13b**) [14]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.24–7.12 (*m*, 6 H); 4.07 (*t*, *J* = 6.46, 2 H); 3.77 (*s*, 12 H); 2.94 (*t*, *J* = 7.27, 2 H); 2.62–2.56 (*m*, 4 H); 1.93–1.89 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.2; 148.2; 147.5; 147.3; 133.8; 133.1; 121.6; 120.3; 112.8; 112.6; 111.9; 111.5; 63.8; 55.9; 55.7; 35.9; 32.1; 31.0; 30.2.

Methyl 3-(4-Hydroxy-3-methoxyphenyl)propanoate (**14b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.77 (*d*, *J* = 7.27, 1 H); 6.63–6.58 (*m*, 2 H); 5.47 (*s*, 1 H); 3.79 (*s*, 3 H); 3.60 (*s*, 3 H); 2.81 (*t*, *J* = 7.67, 2 H); 2.56 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 173.4; 146.4; 144.0; 132.4; 120.8; 114.3; 111.9; 55.8; 51.6; 36.1; 30.7.

Dimethyl Butanedioate (**15b**) [6f]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.72 (*s*, 6 H); 2.66 (*s*, 4 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 172.7; 51.8; 28.8.

3-(4-Fluorophenyl)-1-(4-methoxyphenyl)propan-1-one (**16b**): M.p. 71–74°. IR (KBr): 1703. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.88 (*d*, *J* = 8.88, 2 H); 7.19 (*m*, 2 H); 6.93 (*d*, *J* = 8.88, 2 H); 6.87 (*d*, *J* = 8.88, 2 H); 3.78 (*s*, 3 H); 3.18 (*t*, *J* = 7.67, 2 H); 2.98 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 197.6; 163.5; 163.0; 159.7; 137.1; 130.3; 129.9; 129.7; 115.3; 115.0; 113.7; 55.4; 40.0; 29.5. EI-MS: 258 (M^+). HR-EI-MS (pos.): 259.2928 ($[M+1]^+$, $C_{16}H_{16}FO_2^+$; calc. 259.2934).

4-(4-Hydroxy-3-methoxyphenyl)butan-2-one (**17b**) [16]: M.p. 38–41°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.75 (*d*, *J* = 7.67, 1 H); 6.61 (*s*, 1 H); 6.59 (*d*, *J* = 7.67, 1 H); 5.69 (*s*, 1 H); 3.77 (*s*, 3 H); 2.76 (*t*, *J* = 7.27, 2 H); 2.67 (*t*, *J* = 7.27, 2 H); 2.05 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 208.5; 146.5; 144.0; 132.9; 120.7; 114.4; 111.1; 55.8; 45.5; 29.7; 28.9.

3-(3,4-Dimethoxyphenyl)propanoic Acid (**18b**) [6l]: M.p. 95–98°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.03 (*d*, *J* = 8.07, 1 H); 6.41 (*s*, 1 H); 6.39 (*d*, *J* = 8.07, 1 H); 3.75 (*s*, 6 H); 2.85 (*t*, *J* = 7.67, 2 H); 2.59 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 176.8; 147.2; 144.3; 132.9; 120.8; 115.0; 114.2; 55.8; 37.2; 30.6.

3-Phenylpropanenitrile (**19b**) [5][6q][10]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.26 (*d*, *J* = 6.86, 2 H); 7.16–7.11 (*m*, 3 H); 2.89 (*t*, *J* = 7.27, 2 H); 2.55 (*t*, *J* = 7.27, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 138.1; 129.1; 128.3; 127.2; 119.2; 31.5; 19.3.

3-Phenylpropanamide (**20b**) [10]: M.p. 99–101°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.22 (*d*, *J* = 6.86, 2 H); 7.15–7.08 (*m*, 3 H); 2.92 (*t*, *J* = 7.67, 2 H); 2.48 (*t*, *J* = 7.67, 2 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 174.8; 142.3; 128.6; 128.3; 126.3; 37.5; 31.4.

Methyl 3-(4-Acetoxy-3-methoxyphenyl)propanoate (**21b**) [21]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.98 (*d*, *J* = 6.46, 1 H); 6.63–6.57 (*m*, 2 H); 3.76 (*s*, 3 H); 3.69 (*s*, 3 H); 2.88 (*t*, *J* = 7.67, 2 H); 2.59 (*t*, *J* = 7.67, 2 H); 2.05 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 172.8; 168.3; 154.9; 139.4; 136.7; 123.6; 120.8; 113.7; 55.7; 51.7; 35.2; 31.4; 17.2.

3,4-Dihydrocoumarin (= *3,4-Dihydro-2*H*-1-benzopyran-2-one*; **22b**) [7d]: Liquid. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.20–7.14 (*m*, 2 H); 7.05–7.01 (*m*, 1 H); 6.96 (*d*, *J* = 7.67, 1 H); 2.95 (*t*, *J* = 7.27, 2 H); 2.73 (*t*, *J* = 7.27, 2 H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz): 169.0; 152.1; 128.3; 128.0; 124.5; 122.9; 116.9; 29.2; 23.6.

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