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Selective Synthesis of 3,4-Dihydrocoumarins and Chalcones from Substituted Aryl Cinnamic Esters

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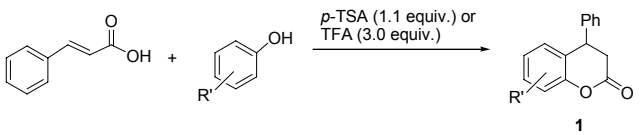
Coumarins are ubiquitous in plant kingdom and have been used as antitumor, antifungals, anticoagulants, insecticides. Chalcones are also widespread in plant kingdom and have been known to possess diverse biological activities; antibacterial, antifungal, antitumor and anti-inflammatory, *etc*. As they are considered as important natural products, numerous synthetic approaches have been reported up to the present. We devise a new selective method of preparing dihydrocoumarins and chalcones from aryl cinnamates by the selection of reagents. Dihydrocoumarin derivatives were prepared selectively by using intramolecular cyclization catalyzed by *p*-toluene sulfonic acid. Also, chalcones were prepared by Fries-rearrangement catalyzed by $TiCl_4$. This method can be used for preparing various coumarin & chalcone compounds.

Key Words: Dihydrocoumarin, Chalcone, Aryl cinnamate, Fries rearrangement, Pechmann condensation

Introduction

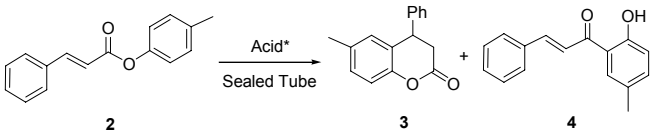
Coumarins are naturally occurring benzopyrene derivatives. They are widely distributed in plant kingdom and have been used as antitumor agents,[1] antifungals,[2] anticoagulants[3] and insecticides.[4] Recently, carbohydrate linked coumarins were also prepared[5] due to their promising role as an antibacterial (inhibitor of gyrase B[6]) and even as fluorescent probes for ultrafast DNA dynamics.[7] Dihydrocoumarins are also widely distributed and have shown so many biological activities such as aldose reductase inhibition,[8] antiherpetic,[9] protein kinases,[10] flavoring agent to a variety of foods (soft drinks, yogurt, muffins).[11]

The conventional methods for the synthesis of dihydrocoumarins were reported as follows: 1) the hydroarylation of cinnamic acids with phenols in strong acidic media[12] 2) the catalytic hydrogenation of coumarins[13] 3) Lewis acid promoted reaction of activated phenols with arylonitrile[14] 4) reaction of Fischer carbene complexes with ketene acetals[15] 5) *p*-TSA mediated hydroarylation of cinnamic acids with anisols or phenols[16] 6) $AlCl_3$-mediated C-C coupling reaction between hydroxyketene *S*,*S*-acetals and arenes[17] 7) [4+2] cycloaddition reaction of *o*-quinone methides with silyl ketene acetals[18] 8) biotransformation of coumarins by microorganisms.[19] Another type of intramolecular ring formation for coumarins was known as Pechmann condensation[20] which is the most widely employed method for coumarin synthesis. It is the reaction of phenols with β-keto esters catalyzed by strong Brönsted acid (CH_3SO_3H) or a Lewis acid ($AlCl_3$).



Scheme 1. Dihydrocoumarin synthesis from hydroarylation of cinnamic acids with anisols or phenols

Of these dihydrocoumarin forming reactions, we focussed on the trifluoroacetic acid[12c] and *p*-TSA[16] mediated hydroarylation of cinnamic acid (Scheme 1). The trifluoroacetic acid afforded dihydrocoumarins through inter-molecular reaction type. The results were remarkable, but the disadvantage of this is the using expensive TFA with excessive amount (3 equiv.). The *p*-TSA mediated hydroarylation method[16] is also beneficial



Scheme 2. Dihydrocoumarin or chalcone formation from aryl cinnamates

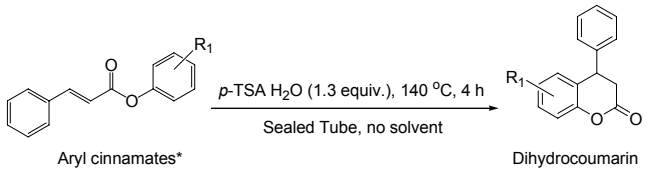
Table 1. Acid screening for dihydrocoumarin or chalcone formation

Entry	Acid*	Equiv.	Solvent	Temp (°C)	Reaction Time (h)	Product Selectivity (3:4)	Yield[a] (%)
1	*p*-TSA	1.5	neat	160	24	100:0	81
2	*p*-TSA	1.5	CH_2Cl_2	160	24	100:0	50
3	*p*-TSA	1.5	benzene	160	24	100:0	65
4	*p*-TSA	1.5	toluene	160	24	100:0	70
5	*p*-TSA	1.5	neat	140	4	100:0	83
6	$MeSO_3H$	8	neat	160	24	100:0	40
7	$MeSO_3H$	8	CH_2Cl_2	160	24	100:0	27
8	$MeSO_3H$	8	benzene	160	24	100:0	55
9	$MeSO_3H$	8	toluene	160	24	100:0	55
10	$TiCl_4$	2	neat	160	24	0:100	68
11	$TiCl_4$	2	CH_2Cl_2	160	24	0:100	60
12	$TiCl_4$	2	benzene	160	24	0:100	71
13	$TiCl_4$	2	neat	130	0.3	0:100	74
14	$InCl_3$	1.5	neat	160	24	100:0	50
15	$SnCl_4$	1.5	neat	160	24	100:0	60

[a]*Silica* gel column purified isolated yield.

due to its simplicity and generally high isolated yield. This also was reported as an inter-molecular reaction type. It is widely accepted principle that the benefit of the intramolecular reaction is less demand for the decrease of entropy, so it has drawn much attention from the view points of both efficiency and selectivity.[22] It is our research goal to devise this dihydrocoumarin forming reaction to extend for the intra-molecular version to find I) better efficiency and selectivity II) the optimum condition for wide functional group tolerance and substrate scope. The aryl cinnamates were easily prepared by the well known DCC coupling[21] from cinnamic acid and substituted phenols or reaction from cinnamoyl chloride and substituted phenols.

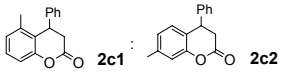
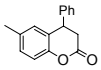
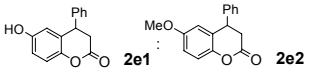
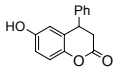
First, we screened the acid which can effectively induce this reaction. *p*-TSA, $MeSO_3H$, $TiCl_4$, $InCl_4$ and $SnCl_4$ were tested



*Easily prepared from corresponding substituted alcohol & cinnamoyl chloride

Scheme 3. Dihydrocoumarin synthesis from aryl cinnamates

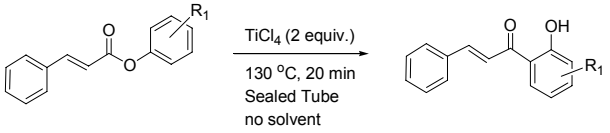
Table 2. Synthesis of dihydrocoumarin derivatives

Entry	R_1	Dihydrocoumarin	Yield (%)
1	H **1a**	 **2a**	36[a] (84[b])
2	2-Me **1b**	 **2b**	33[a] (67[b])
3	3-Me **1c**	 **2c1** : **2c2**	38:38[a]
4	4-Me **1d**	 **2d**	83[a]
5	4-OMe **1e**	 **2e1** : **2e2**	40:20[a]
6	2-OH **1f**	 **2f**	20[a] (99[b])
7	4-OH **1g**	 **2e1**	23[a] (93[b])
8	2-NO_2 **1h**	-	-
9	3-NO_2 **1i**	-	-
10	4-NO_2 **1j**	-	-
11	2-NO_2, 4-OMe **1k**	-	-
12	3-NO_2, 4-Cl **1l**	-	-
13	4-CHO **1m**	-	-

[a]*Silica* gel column purified yield. [b]GC yield.

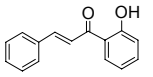
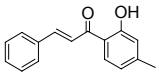
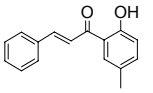
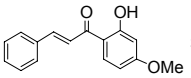
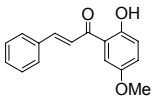
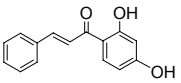
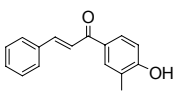
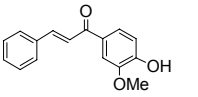
(Scheme 2, Table 1). Dihydrocoumarin **3** was produced selectively when we used *p*-TSA, $MeSO_3H$, $InCl_3$, $SnCl_4$ (entries 1-9, 13-14). Whereas $TiCl_4$ produced only chalcone **4** (entries 10-12). As *p*-TSA showed the best yield for dihydrocoumarin formation at 160 °C for 24 h (entry1), we were focusing how to optimize the reaction condition. So, we modified the reaction temperature and time. The optimized condition was 140 °C for 4 h (entry 5) for dihydrocoumarin formation. For chalcone's case, the optimized condition was 130°C for 0.3 h (entry 13).

As *p*-TSA showed the best result for dihydrocoumarin selectivity (entry 5), we further studied substituent effects during dihydrocoumarin synthesis (Scheme 3, Table 2). It is noteworthy that when R_1 = 3-Me, two isomeric dihydrocoumarins were observed almost 1:1 ratio (entry 3). The unsymmetrical methyl group attached to the phenyl ring caused the mixture of regioisomer (compare this with entries 2-4). For 4-OMe case (entry 5), the ether cleaved product was observed. This is because of the rather harsh reaction condition. For phenol case (entries 6-7), the reactions were proceeded well without protection, however, it was not clear that we observed only the low separation yield even though the reaction showed clean one-spot TLC and excellent GC yield. But for strong electron withdraw-



Scheme 4. $TiCl_4$ mediated chalcone synthesis

Table 3. Synthesis of chalcone derivatives

Entry	R_1	Chalcone	Yield (%)[a]
1	H **1a**	 **3a**	37
2	3-Me **1c**	 **3c**	57
3	4-Me **1d**	 **3d**	74
4	3-OMe **1n**	 **3n**	58
5	4-OMe **1e**	 **3e**	67
6	3-OH **1o**	 **3o**	65
7	2-Me **1b**	 **3b**	60
8	2-OMe **1p**	 **3p**	70

[a]*Silica* gel column purified yield.

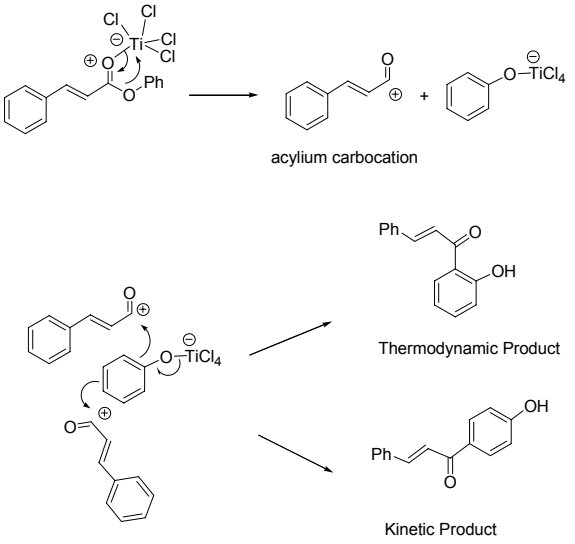


Figure 1. Mechanism of $TiCl_4$ mediated rearrangement.

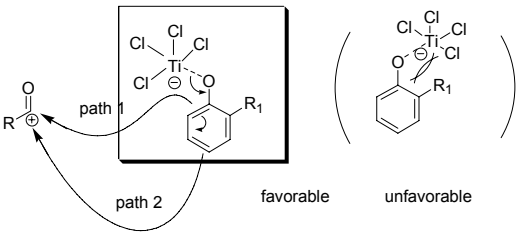


Figure 2. Mechanism of para-oriented products.

ing nitro or formyl substituent case (entries 8-13), the reaction did not proceeded at all. We now guess that the starting cinnamates may revert to cinnamic acid and the corresponding substituted phenols for these strongly electron withdrawing substrates judged by TLC pattern.

We also tried to devise a method to prepare chalcone derivatives using $TiCl_4$ (Scheme 4, Table 3). As the optimized condition was at 130 °C for 20 min, we applied this optimized condition (entry 13, Table 1).

A widely accepted mechanism of this rearrangement is involving an acylium carbocation intermediate (Fig. 1).[23]

Presumably, $TiCl_4$ first coordinates to acyl oxygen atom, then it polarizes the bond between phenolic oxygen atom and the acyl residue. This may generate free acylium carbocation ($TiCl_4$ rearranges to phenolic bond) and it underwent classical aromatic substitution. It is known that the para-product is kinetic, whereas ortho-isomer is thermodynamic product.

Normally, thermodynamic products were observed in our reaction condition (entries 1-6). For 3-Me case, no other isomer was found except thermodynamic product (entry 2). For 3-OMe case, no ether cleaved product was observed (entries 4-5). For rather electron donating substituent (R_1 = 3-OH; entry 6), the reaction was proceeded well. It is noteworthy that the kinetic products were observed at ortho-substituted case (entries 7-8). The orientation of para-substituted product can be explained on the basis of reaction mechanism (Fig. 2). Bulky $TiCl_4$ will place the other side of R_1 substituent, and will hinder the approach of the acylium carbocation on its ortho- position (path 2 is more favorable).

In summary, the selective one-pot synthesis of dihydrocoumarins or chalcones is obtained from aryl cinnamate by using *p*-TSA or $TiCl_4$, respectively. The advantage of our method is the use of rather inexpensive agent and wide versatility of this reaction to be used for the dihydrocoumarin natural product synthesis.

Experimental Section

Representative Synthetic Method for Starting Aryl Cinnamates. To a solution of corresponding alcohol in THF were added triethylamine (1.2 equiv.) and cinnamoyl chloride (1.2 equiv.) at 0 °C. The reaction mixture was stirred for 2 hr at room temperature, then was quenched with 1 N HCl. The organic layer was separated and the aqueous phase was extracted with EtOAc. After concentration of combined extracts, the resulting residue was purified by flash column chromatography on *silica* gel to give the corresponding esters.

Phenyl Cinnamate (1a): Yield 96%. R_f 0.78 (EtOAc:Hexane = 1:4); mp 70 - 71°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 15.6 Hz, 1H), 7.61-7.55 (m, 2H), 7.43-7.36 (m, 6H), 7.15 (d, J = 7.8 Hz, 2H), 6.62 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 151.0, 146.7, 134.4, 130.9, 129.6, 129.2, 128.5, 125.9, 121.8, 117.6.

2-Methylphenyl Cinnamate (1b): Yield 97%. R_f 0.69 (EtOAc: Hexane = 1:4); mp 78 - 81°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 16.6 Hz, 1H), 7.58 (m, 2H), 7.42-7.40 (m, 3H), 7.26-7.13 (m, 3H), 7.07 (d, J = 7.8 Hz, 1H), 6.65 (d, J = 16.6 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 149.5, 146.6, 134.4, 131.3, 130.8, 130.4, 129.2, 128.5, 127.1, 126.2, 122.1, 117.3, 16.6.

3-Methylphenyl Cinnamate (1c): Yield 93%. R_f 0.71 (EtOAc: Hexane = 1:3); mp 58 - 62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 15.9 Hz, 1H), 7.59-7.56 (m, 2H), 7.43-7.40 (m, 3H), 7.28 (t, J = 7.7 Hz, 1H), 7.05 (d, J = 7.7 Hz, 1H), 6.97 (s, 1H), 6.96 (d, J = 7.7 Hz, 1H), 6.62 (d, J = 15.9 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 150.6, 146.3, 139.5, 134.1, 130.5, 129.0, 128.9, 128.2, 126.5, 122.1, 118.5, 117.3, 21.4.

4-Methylphenyl Cinnamate (1d): Yield 98%. R_f 0.78 (EtOAc: Hexane = 1:4); mp 90 - 93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 16.1 Hz, 1H), 7.61-7.57 (m, 2H), 7.45-7.41 (m, 3H), 7.21 (d, J = 8.5 Hz, 2H), 7.06 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 16.1 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 148.7, 146.6, 135.6, 134.4, 130.8, 130.1, 129.2, 128.5, 121.6, 117.6, 21.3.

4-Methoxyphenyl Cinnamate (1e): Yield 93%. R_f 0.69 (EtOAc:Hexane = 1:3); mp 92 - 94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, J = 16.6 Hz, 1H), 7.59-7.55 (m, 2H), 7.43-7.40 (m, 3H), 7.07 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 9.8 Hz, 2H), 6.61 (d, J = 16.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 157.4, 146.5, 144.4, 134.4, 130.8, 129.1, 128.4, 122.5, 117.6, 114.7, 55.9.

2-Hydroxyphenyl Cinnamate (1f): Yield 35%. R_f 0.34 (EtOAc: Hexane = 1:2); mp 140 - 143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 15.6 Hz, 1H), 7.61-7.57 (m, 2H), 7.44-7.42 (m, 3H), 7.17-7.13 (m, 2H), 7.05-7.02 (m, 1H), 6.97-6.92 (m, 1H),

6.66 (d, J = 1.56 Hz, 1H), 5.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 148.0, 147.3, 138.9, 134.1, 131.2, 129.2, 128.6, 127.2, 122.6, 121.3, 118.3, 116.5.

4-Hydroxyphenyl Cinnamate (1g): Yield 31%. R_f 0.43 (EtOAc:Hexane = 1:2); mp 170 - 173 °C; ^{1}H NMR (300 MHz, Acetone-D_6) δ 8.01 (s, 1H), 7.51 (d, J = 15.6 Hz, 1H), 7.31-7.30 (m, 2H), 7.12-7.10 (m, 3H), 6.67 (d, J = 8.8 Hz, 2H), 6.56 (d, J = 8.8 Hz, 2H), 6.32 (d, J = 16.6 Hz, 1H) ; ^{13}C NMR (75 MHz, acetone-d_6) δ 165.8, 155.7, 146.5, 144.3, 135.1, 131.3, 129.7, 129.1, 123.1, 118.3, 116.3.

2-Nitrophenyl Cinnamate (1h): Yield 83%. R_f 0.64 (EtOAc:Hexane = 1:2); mp 75 - 77 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (dd, J = 8.0, 2.0 Hz, 1H), 7.90 (d, J = 15.6 Hz, 1H), 7.66 (td, J = 7.8, 2.0 Hz, 1H), 7.60 (d, J = 2.0 Hz, 1H), 7.57 (d, J = 3.9 Hz, 1H), 7.42-7.37 (m, 4H), 7.32 (d, J = 7.8 Hz, 1H), 6.65 (d, J = 16.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 148.0, 144.0, 142.0, 134.4, 133.8, 130.9, 128.9, 128.4, 126.4, 125.6, 125.2, 115.9.

3-Nitrophenyl Cinnamate (1i): Yield 89%. R_f 0.60 (EtOAc:Hexane = 1:2); mp 108 - 111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (dt, J = 7.8, 2.0 Hz, 1H), 8.07 (t, J = 2.0 Hz, 1H), 7.90 (d, J = 15.6 Hz, 1H), 7.61-7.51 (m, 5H), 7.46-7.41 (m, 3H), 6.62 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 151.0, 148.7, 147.7, 133.7, 131.0, 130.0, 129.0, 128.3, 128.0, 120.6, 117.3, 116.1.

4-Nitrophenyl Cinnamate (1j): Yield 90%. R_f 0.70 (EtOAc:Hexane = 1:2); mp 142 - 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 2H), 7.90 (d, J = 15.9 Hz, 1H), 7.61-7.58 (m, 2H), 7.46-7.43 (m, 3H), 7.37 (d, J = 9.3 Hz, 2H), 6.62 (d, J = 15.9 Hz, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 155.7, 148.2, 145.4, 133.9, 131.4, 129.3, 128.6, 125.4, 122.7, 116.3.

4-Methoxy-2-nitrophenyl Cinnamate (1k): Yield 90%. R_f 0.50 (EtOAc:Hexane = 1:2); mp 109 - 112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.89 (3H, s), 6.65 (d, J = 16.3 Hz, 1H), 7.21 (m, 2H), 7.43 (m, 3H), 7.59 (m, 3H) and 7.89 (d, J = 16.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 157.1, 147.8, 141.9, 137.4, 133.8, 130.9, 128.9, 128.4, 125.9, 121.0, 116.0, 109.7, 56.2.

4-Chloro-3-nitrophenyl Cinnamate (1l): Yield 89%. R_f 0.62 (EtOAc:Hexane = 1:2); mp 79 - 81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 15.6 Hz, 1H), 7.78 (d, J = 2.93 Hz, 1H), 7.60-7.55 (m, 3H), 7.47-7.36 (m, 4H), 6.59 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 149.5, 148.4, 148.0, 133.9, 132.6, 131.4, 129.3, 128.7, 127.1, 124.1, 119.6, 116.0.

4-Formylphenyl Cinnamate (1m): Yield 90%. R_f 0.53 (EtOAc:Hexane = 1:4); mp 87 - 90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7,93 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 15.6 Hz, 1H), 7.60-7.57 (m, 2H), 7.43-7.41 (m, 3H), 7.35 (d, J = 8.8 Hz, 2H), 6.62 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0, 164.7, 155.7, 147.7, 134.11, 134.07, 131.4, 131.2, 129.3, 128.6, 122.6, 116.8.

3-Methoxyphenyl Cinnamate (1n): Yield 93%. colorless liquid, R_f 0.63 (EtOAc:Hexane = 1:4); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 16.1 Hz, 1H), 7.58 (m, 2H), 7.42 (m, 3H), 7.29 (t, 1H), 6.78 (m, 2H), 6.72 (m, 1H), 6.62 (d, J = 15.9 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 160.6, 151.9, 146.8, 134.3, 130.9, 130.0, 129.2, 128.5, 117.5, 114.1, 111.9, 107.8, 55.7.

3-Hydroxyphenyl Cinnamate (1o): Yield 31%. R_f 0.39 (EtOAc:Hexane = 1:4); mp 105 - 107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 15.6 Hz, 1H), 7.59-7.56 (m, 2H), 7.44-7.40 (m, 3H), 6.76-6.72 (m, 2H), 6.70-6.66 (m, 2H), 6.61 (d, J = 15.6 Hz, 1H), 5.00 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 156.9, 151.7, 147.2, 134.2, 131.0, 130.3, 129.2, 128.5, 117.3, 113.7, 113.5, 109.5.

2-Methoxylphenyl Cinnamate (1p): Yield 84%. R_f 0.56 (EtOAc:Hexane = 1:3); mp 139 - 142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 15.6 Hz, 1H), 7.60-7.55 (m, 2H), 7.42-7.39 (m, 3H), 7.22 (m, 1H), 7.11 (dd, J = 7.8, 2.0 Hz, 1H), 7.00-6.94 (m, 2H), 6.67 (d, J = 15.6 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 151.4, 146.6, 134.5, 103.7, 129.1, 128.5, 127.0, 123.1, 121.0, 117.3, 112.7, 56.2.

Representative Synthetic Method for Dihydrocoumarin derivatives. To a dried thick-walled pressure tube were placed aryl cinnamates (**1a-1m**) and *p*-toluenesulfonic acid monohydrate (1.3 equiv.) under nitrogen atmosphere. The reaction mixture was heated to 140 °C in electronic furnace for 4 hr. After the reaction is over, the mixture is gradually cooled to rt and quenched with 3 N HCl. The product is dissolved in ether and the ether layer is washed successively with 3 N HCl, water, saturated $NaHCO_3$, and brine. The ether layer is dried over anhydrous sodium sulfate (Na_2SO_4), filtered and evaporated. After concentration of combined extracts, the resulting residue was chromatographed on *silica* gel to give the corresponding dihydrocoumarins.

3,4-Dihydro-4-phenyl-2*H*-1-benzopyran-2-one (1): Yield 36%. yellowish liquid, GC yield 84% (retention time: 23.34 min.) R_f 0.75 (EtOAc: Hexane = 1:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.26 (m, 4H), 7.16-7.11 (m, 3H), 7.07 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 6.84 Hz, 1H), 4.34 (t, J = 7.8 Hz, 1H), 3.13-2.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 151.8, 140.4, 129.3, 129.0, 128.5, 127.9, 127.8, 126.0, 124.8, 117.3, 41.0, 37.4.

3,4-Dihydro-8-methyl-4-phenyl-2*H*-1-benzopyran-2-one (2b): Yield 33%. GC yield 67% (retention time: 24.18 min.) R_f 0.63 (EtOAc:Hexane = 1:3); mp 104 - 106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.26 (m, 3H), 7.15-7.12 (m, 3H), 6.96 (t, J = 7.8 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 4.32 (t, J = 6.8 Hz, 1H), 3.10-2.97 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 150.1, 140.6, 130.5, 129.3, 127.7, 126.7, 126.0, 125.7, 124.33, 124.30, 41.1, 37.3, 16.3.

3,4-Dihydro-5-methyl-4-phenyl-2*H*-1-benzopyran-2-one (2c1): Yield 38%. R_f 0.51 (EtOAc:Hexane = 1:3); mp 110 - 113 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.20 (m, 4H), 7.04-6.97 (m, 4H), 4.40 (dd, J = 5.7, 2.9 Hz, 1H), 3.11-2.98 (m, 2H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 152.4, 140.2, 137.2, 129.3, 128.8, 127.7, 127.1, 126.6, 123.4, 115.3, 38.6, 38.0, 19.1.

3,4-Dihydro-7-methyl-4-phenyl-2*H*-1-benzopyran-2-one (2c2): Yield 38%. R_f 0.71 (EtOAc:Hexane = 1:3); mp 71 - 73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.26 (m, 3H), 7.14-7.11 (m, 2H), 6.93 (sd, J = 1.0 Hz, 1H), 6.88 (dd, J = 7.8, 1.0 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 4.30 (t, J = 6.8 Hz, 1H), 3.10-2.94 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 151.7, 140.7, 139.3, 129.3, 128.2, 127.7, 125.6, 122.8, 117.7, 117.6, 40.7, 37.6, 21.5.

3,4-Dihydro-6-methyl-4-phenyl-2*H*-1-benzopyran-2-one

(2d): Yield 83%. R_f 0.73 (EtOAc:Hexane = 1:2); mp 71 - 74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.25 (m, 3H), 7.16-7.13 (m, 2H), 7.08 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.77 (sd, *J* = 1.1 Hz, 1H), 4.29 (t, *J* = 6.6 Hz, 1H), 3.10-2.94 (m, 2H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 149.8, 140.7, 134.5, 129.5, 129.3, 128.9, 127.8, 127.7, 125.5, 117.1, 41.1, 37.5, 21.2.

3,4-Dihydro-6-hydroxy-4-phenyl-2*H*-1-benzopyran-2-one (2e1) from 4-methoxy phenyl cinnamates (1e): Yield 40%. R_f 0.34 (EtOAc:Hexane = 1:2); mp 128 - 131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.25 (m, 3H), 7.16-7.13 (m, 2H), 6.99 (d, *J* = 8.8, 1H), 6.73 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.39 (sd, *J* = 2.9 Hz, 1H), 4.80 (bs, 1H), 4.28- 4.23 (m, 1H), 3.08-2.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 152.4, 145.8, 140.1, 129.3, 127.9, 127.8, 127.3, 118.3, 115.6, 114.9, 41.1, 37.2.

3,4-Dihydro-6-methoxy-4-phenyl-2*H*-1-benzopyran-2-one (2e2): Yield 20%. brownish liquid, R_f 0.63 (EtOAc:Hexane = 1:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.25 (m, 3H), 7.16-7.13 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.48 (dd, *J* = 2.9, 1.0 Hz, 1H), 4.29 (t, *J* = 6.8, 1H), 3.40 (s, 3H), 3.09-2.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.4, 145.8, 140.3, 129.3, 128.2, 127.7, 126.9, 118.1, 113.9, 113.6, 55.9, 41.3, 37.3.

3,4-Dihydro-8-hydroxy-4-phenyl-2*H*-1-benzopyran-2-one (2f): Yield 20%. GC yield 99% (retention time: 28.21 min.) R_f 0.71 (EtOAc:Hexane = 1:1); mp 120 - 124 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.25 (m, 3H), 7.16-7.13 (m, 2H), 6.99-6.92 (m, 2H), 6.49 (dd, *J* = 6.8, 2.0, 1H), 5.71 (bs, 1H), 4.35 (t, *J* = 6.8 Hz, 1H), 3.15-3.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 144.1, 140.1, 139.3, 129.3, 127.9, 127.7, 126.5, 125.2, 119.5, 115.6, 41.1, 37.4.

6-Hydroxy-4-phenyldihydrocoumarin (2e1) from 4-hydroxy phenyl cinnamates (1g): Yield 23%. GC yield 93% (retention time: 28.21 min.).

Representative Synthetic Method for Chalcone. To a thick-walled pressure tube were placed aryl cinnamates (**1a-1p**) and $TiCl_4$ under dry nitrogen atmosphere. The reaction mixture was heated up to 130 °C in electric furnace for 20 minutes. After the reaction, the crude reaction mixture is gradually cooled to room temperature and quenched with 3 N HCl. The product is dissolved in ethyl acetate and the organic layer is washed successively with 3 N HCl, saturated $NaHCO_3$, brine. The organic layer is dried over anhydrous Na_2SO_4, filtered and evaporated. After concentration of combined extracts, residue was chromatographed on *silica* gel to give the corresponding chalcones.

2'-Hydroxychalcone (3a): Yield 37%. R_f 0.78 (EtOAc:Hexane = 1:4); mp 75-78°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94-7.89 (m, 2H), 7.68-7.63 (m, 3H), 7.52-7.42 (m, 4H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.94 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 163.7, 145.6, 136.5, 134.8, 131.1, 129.8, 129.2, 128.8, 120.4, 120.2, 119.0, 118.8.

2'-Hydroxy-4'-methylchalcone (3c): Yield 57%. R_f 0.81 (EtOAc:Hexane = 1:3); mp 72 - 74 °C; ^{1}H NMR (300 MHz, Acetone-d_6) δ 7.88 (d, *J* = 15.6 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.65-7.58 (m, 3H), 7.42-7.40 (m, 3H), 6.82 (s, 1H), 6.73 (dd, *J* = 8.7, 2.0 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 193.2, 163.9, 148.2, 145.1, 134.9, 130.9, 129.7, 129.2, 128.7, 120.5, 120.3, 118.9, 118.1, 22.3.

2'-Hydroxy-5'-methylchalcone (3d): Yield 74%. R_f 0.70 (EtOAc:Hexane = 1:3); mp 106 - 109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 15.6, 1H), 7.66-7.61 (m, 4H), 7.43-7.41 (m, 3H), 7.30 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 161.6, 145.4, 137.7, 134.9, 131.0, 129.5, 129.2, 128.8, 128.1, 120.5, 119.9, 118.6, 21.0.

2'-Hydroxy-4'-methoxychalcone (3n): Yield 58%. R_f 0.67 (EtOAc:Hexane = 1:3); mp 96 - 99 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 15.6 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.64-7.61 (m, 2H), 7.55 (d, *J* = 15.6 Hz, 1H), 7.41-7.40 (m, 3H), 6.49-6.45 (m, 2H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.9, 166.8, 166.3, 144.5, 135.0, 131.4, 130.8, 129.2, 128.7, 120.5, 114.3, 107.9, 101.3, 55.9.

2'-Hydroxy-5'-methoxychalcone (3e): Yield 67%. brownish liquid, R_f 0.69 (EtOAc:Hexane = 1:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 15.6 Hz, 1H), 7.66-7.63 (m, 2H), 7.58 (d, *J* = 15.6 Hz, 1H), 7.44-7.42 (m, 3H), 7.34 (d, *J* = 2.9 Hz, 1H), 7.13 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.96 (d, *J* = 9.8 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 158.1, 151.9, 145.7, 134.8, 131.1, 129.2, 128.8, 124.1, 120.4, 119.8, 119.6, 113.2, 56.5.

2',4'-Dihydroxychalcone (3o): Yield 65%. R_f 0.37 (EtOAc:Hexane = 1:3); mp 138 - 142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.64 (bs, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 15.6 Hz, 1H), 7.75 (d, *J* = 15.6 Hz, 1H), 7.75 (d, *J* = 15.6 Hz, 1H), 7.75-7.71 (m, 2H), 7.35-7.33 (m, 3H), 6.37 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.27 (d, *J* = 2.0 Hz, 1H), 1.17 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.9, 166.9, 165.1, 144.0, 135.2, 132.9, 130.7, 129.1, 128.9, 121.0, 113.8, 108.2, 103.1.

4'-Hydroxy-3'-methylchalcone (3b): Yield 60%. R_f 0.22 (EtOAc:Hexane = 1:3); mp 152 - 154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (sd, *J* = 1.95 Hz, 1H), 7.82 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.79 (d, *J* = 15.6 Hz, 1H), 7.64-7.61 (m, 2H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.40-7.38 (m, 3H), 6.89 (d, *J* = 8.8 Hz, 1H), 6.58 (bs, 1H), 2.33 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.6, 159.0, 144.4, 135.2, 132.3, 131.0, 130.5, 129.1, 129.0, 128.6, 124.7, 122.2, 115.1, 16.2.

4'-Hydroxy-3'-methoxychalcone (3p): Yield 70%. R_f 0.36 yellowish liquid, (EtOAc:Hexane = 1:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 15.6 Hz, 1H), 7.66-7.62 (m, 4H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.41-7.38 (m, 3H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.24 (bs, 1H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.4, 150.3, 146.8, 143.9, 135.0, 130.9, 130.2, 128.8, 128.2, 123.6, 121.6, 113.7, 110.5, 56.1.

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