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Synthesis and characterization of new derivatives of cinnamic acid

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ABSTRACT

A series of new derivatives **1-11** of cinnamic acid have been synthesized by a facile procedure for esterification based on using of DCC as a coupling agent, DMAP and solvent system methylene chloride. The structures of all the newly synthesized derivatives **1-11** of cinnamic acid were assigned as 3-methyl-2-butenyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate (**1**), (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate (**2**), (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate (**3**), (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate (**4**), (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate (**5**), (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate (**6**), (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate (**7**), 3-methyl-2-butenyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate (**8**), (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate (**9**), (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate (**10**) and (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate (**11**) by extensive NMR studies

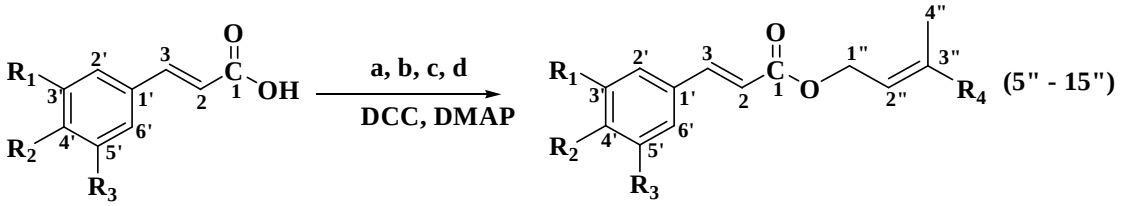
KEYWORDS

Cinnamic acid derivatives;
Alcohols;
Esterification;
NMR.

INTRODUCTION

The class of cinnamic acid derivatives, including both natural compounds and their organic analogs, is characterized by a broad spectrum of biological activity and is a promising material for creation of new drugs preparation[1-3]. Raman et al have reported that the introduction of halogen onto the benzene ring of cinnamic acid enhanced the antimicrobial activity against gram negative bacteria[4]. Certain substituted cinnamate and cinnamamide derivatives show fungitoxic and phytotoxic activities[5]. For derivatives of hydrocinnamic acid (characterized by high antioxidant activity), anti-inflammatory, analogesic and antipyretic activity has been reported[6]. Trans cinnamic acid and its derivatives were investigated for the α-glucosidase inhibitory activity[7], while some derivatives of cinnamic acid show human acyl-CoA cholesterol acyltransferase-1 and -2 inhibitory activities[8]. A cell growth inhibitory effect of Drupanin and baccharin ingredient of propoies was also found in human cancer cell lines[9].

Thus literature manifests that investigation determining the structure verses activity characteristics make a definite contribution to the development of goal-directed



1	R_1 = OH	R_2 = OH	R_3 = OH	R_4 = CH_3	**2**	R_1 = OH	R_2 = OH	R_3 = OH	R_4 = C_6H_{11}
3	R_1 = OH	R_2 = OH	R_3 = OH	R_4 = C_6H_{11}	**4**	R_1 = OH	R_2 = OH	R_3 = OH	R_4 = $C_{11}H_{19}$
5	R_1 = OMe	R_2 = OH	R_3 = H	R_4 = C_6H_{11}	**6**	R_1 = OMe	R_2 = OH	R_3 = H	R_4 = C_6H_{11}
7	R_1 = OMe	R_2 = OH	R_3 = H	R_4 = $C_{11}H_{19}$	**8**	R_1 = OMe	R_2 = OH	R_3 = OMe	R_4 = CH_3
9	R_1 = OMe	R_2 = OH	R_3 = OMe	R_4 = C_6H_{11}	**10**	R_1 = OMe	R_2 = OH	R_3 = OMe	R_4 = C_6H_{11}
11	R_1 = OMe	R_2 = OH	R_3 = OMe	R_4 = $C_{11}H_{19}$					

SCHEME 1: Route to preparation of cinnamic acid derivatives by reaction with prenol (a), nerol (b), geraniol (c) and farnesol (d)

TABLE 1: ^{1}H NMR data for 1-5 ($CDCl_3$)

	δ ^{1}H (ppm) multiplicity (J, Hz)				
H	**1**	**2**	**3**	**4**	**5**
1	-	-	-	-	-
2	6.42 d (15.2)	6.41 d (15.3)	6.42 d (15.1)	6.41 d (15.2)	6.41 d (15.4)
3	7.70 d (15.2)	7.69 d (15.3)	7.69 d (15.1)	7.70 d (15.2)	7.69 d (15.4)
1′	-	-	-	-	-
2′	6.25 d (1.08)	6.25 d (1.08)	6.25 d (1.08)	6.25 d (1.08)	6.68 d (1.09)
3′	-	-	-	-	-
4′	-	-	-	-	-
5′	-	-	-	-	6.60 d (8.41)
6′	6.25 d (1.08)	6.25 d (1.08)	6.25 d (1.08)	6.25 d (1.08)	6.72 dd (1.09, 8.41)
1″	4.87 d (7.0)	4.87 d (7.0)	4.87 d (7.0)	4.87 d (7.0)	4.84 d (7.1)
2″	5.46 m	5.46 m	5.46 m	5.46 m	5.46 m
3″	-	-	-	-	-
4″	1.80 s	2.18 m	2.18 m	2.17 m	2.17 m
5″	1.60 s	2.12 dd (7.6, 15.2)	2.12 dd (7.6, 15.2)	2.10 m	2.12 dd (7.7, 15.0)
6″	-	5.25 m	5.25 m	5.24 m	5.26 m
7″	-	-	-	-	-
8″	-	1.80 s	1.80 s	2.0 m	1.80 s
9″	-	1.60 s	1.60 s	2.05 dd (7.3, 15.1)	1.60 s
10″	-	1.80 s	1.80 s	5.24 m	1.80 s
11″	-	-	-	-	-
12″	-	-	-	1.80 s	-
13″	-	-	-	1.61 s	-
14″	-	-	-	1.80 s	-
15″	-	-	-	1.80 s	-
OMe	-	-	-	-	3.84 s

synthesis of biologically active compounds. Therefore it seemed to us that ester derivatives of cinnamic acid might also show interesting biological properties. Keeping these in mind, we synthesized new derivatives of cinnamic acid which involve first synthetic preparation by reacting with alcohols such as prenol, nerol, gernoil and farnesol in hope of their potential activity as biomarkers.

RESULTS AND DISCUSSION

Given the widespread utility and broad spectrum of biological activities of these compounds, the synthesis of more potent efficacious, new ester derivatives is of interest. All these derivatives were synthesized by following the literature procedure[10]. Cinnamic acid derivatives were coupled with various alcohols by using steglish conditions (DCC/DMAP) and methylene chloride as solvent (SCHEME 1), providing the desired products as confirmed by mass, ^{1}H NMR, ^{13}C NMR, homonuclear multiple-quantum coherence (HMQC) and heteronuclear multiple-bond connectivity (HMBC) experiments.

Compound (**1**) showed a molecular ion peak in the high-resolution mass spectrum at m/z 264.0995, corresponding to the molecular formula $C_{14}H_{16}O_5$ (calcd 264.0998 for $C_{14}H_{16}O_5$). The ^{1}H NMR spectrum (TABLE 1) showed signal for two protons at δ 7.70 (d, J = 15.2 Hz), 6.42 (d, J = 15.2 Hz) and 6.25 × 2 (d, J = 1.08 Hz) which could be assigned to the double bond adjacent to carbonyl carbon and aromatic protons. The spectrum also showed signals for the side chain protons at δ 5.46 (m), 4.87 (d, J = 7.0 Hz) and

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TABLE 2: ^{1}H NMR data for (6-11) ($CDCl_3$)

	δ ^{1}H (ppm) multiplicity (J, Hz)					
H	6	7	8	9	10	11
1	-	-	-	-	-	-
2	6.41 d (15.3)	6.40 d (15.3)	6.41 d (15.0)	6.42 d (15.2)	6.42 d (15.2)	6.41 d (15.1)
3	7.69 d (15.3)	7.70 d (15.3)	7.69 d (15.0)	7.70 d (15.2)	7.70 d (15.2)	7.69 d (15.1)
1′	-	-	-	-	-	-
2′	6.68 d (1.08)	6.68 d (1.09)	6.28 d (1.07)	6.28 d (1.08)	6.28 d (1.08)	6.28 d (1.08)
3′	-	-	-	-	-	-
4′	-	-	-	-	-	-
5′	6.60 d (8.4)	6.61 d (8.4)	-	-	-	-
6′	6.72 dd (1.08, 8.4)	6.71 dd (1.09, 8.4)	6.28 d (1.07)	6.28 d (1.08)	6.28 d (1.08)	6.28 d (1.08)
1″	4.84 d (7.1)	4.86 d (7.09)	4.87 d (7.01)	4.87 d (7.0)	4.87 d (7.0)	4.87 d (7.0)
2″	5.46 m	5.45 m	5.46 m	5.46 m	5.46 m	5.46 m
3″	-	-	-	-	-	-
4″	2.17 m	2.15 m	1.80 s	2.18 m	2.18 m	2.17 m
5″	2.12 dd (7.6, 15.2)	2.12 dd (7.6, 15.2)	1.60 s	2.12 dd (7.5, 15.2)	2.12 dd (7.5, 15.2)	2.10 dd (7.6, 15.2)
6″	5.26 m	5.26 m	-	5.25 m	5.25 m	5.24 m
7″	-	-	-	-	-	-
8″	1.80 s	2.0 m	-	1.80 s	1.80 s	2.0 m
9″	1.60 s	2.05 dd (7.2, 15.0)	-	1.60 s	1.60 s	2.05 dd (7.3, 15.1)
10″	1.80 s	5.24 m	-	1.80 s	1.80 s	5.24 m
11″	-	-	-	-	-	-
12″	-	1.80 s	-	-	-	1.80 s
13″	-	1.61 s	-	-	-	1.61 s
14″	-	1.80 s	-	-	-	1.80 s
15″	-	1.80 s	-	-	-	1.80 s
OMe	3.84 s	3.84 s	3.85 s	3.85 s	3.85 s	3.85 s
OMe	-	-	3.85 s	3.85 s	3.85 s	3.85 s

two singlets at δ 1.80 and 1.60 supporting the presence of a double bond, a methylene protons and a pair of methyl in the side chain. The ^{13}C NMR spectrum (BB and DEPT) showed 14 carbon signals (TABLE 3), two methyl, one methylene, five methine and six quaternary carbons. The low-field region of the ^{13}C NMR spectrum showed signals at δ 166.2, 147.1 x 2, 132.9, 131.0, 109.2 × 2, 143.3, 135.8, 125.0 and 120.1 which could be assigned to carbonyl carbon of the ester, aromatic ring carbons and double bond carbons of the side chain, respectively. One oxygenated methylene carbons resonated at δ 62.9 while methyl carbons appeared at δ 19.7 and 25.3. The positions of substituent could be confirmed by the homonuclear multiple-quantum coherence (HMQC) and heteronuclear multiple-bond connectivity (HMBC) experiments. Thus compound (**1**) was confirmed as 3-methyl-2-butenyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate.

Compounds (**2-4**) showed molecular ion peaks in the high-resolution mass spectrum at m/z 332.1629, 400.2255, corresponding to the molecular formulas $C_{19}H_{24}O_5$ (calcd 332.1624 for $C_{19}H_{24}O_5$) and $C_{24}H_{32}O_5$ (calcd 400.2250 for $C_{24}H_{32}O_5$), respectively. The ^{1}H NMR spectrum (TABLE 1) of compound 2-4 showed peaks similar to compound 1 with some additional peaks corresponding to the chain length. Compounds 2, 3 showed additional peaks at δ 5.25 (m), 2.18 (m), 2.12 (dd, J = 7.6, 15.2 Hz) and 1.80 (s) which indicate the presence of an additional double bond, two methylene groups and a methyl group while compound 4 showed additional peaks at δ 5.24 × 2 (m), 2.17 (m), 2.10 (m), 2.0 (m), 2.05 (dd, J = 7.3, 15.1 Hz) and 1.80 × 2 (s) which indicate the presence of an additional two double bonds, four methylene groups and two methyl groups. The ^{13}C NMR spectrum (BB and DEPT) of compounds 2, 3 showed 19 carbon signals (TABLE 3), three methyl, three methylene, six methine and seven quaternary carbons. The ^{13}C NMR spectrum of compound 2 showed the additional peaks at δ 139.9, 124.1, 40.0, 23.7 and 17.9 confirmed the structure of compound (**2**) as (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(3,4,5-trihydroxyphenyl) -2-propenoate. Similarly, compound (**3**) showed the additional peaks at δ 139.9, 124.1, 23.7 but the difference from 2 appeared in the chemical shift of the carbons adjacent to the double bond such as δ 34.5 and 22.9 indicated the presence of cis (Z) double bond at carbon 2′ and confirmed the structure of compound **3** as (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate while compound 4 showed 24 carbon signals (TABLE 3), four methyl, five methylene, seven methine and eight quaternary carbons. The additional peaks appeared at δ 139.9, 139.7, 124.1, 124.0, 40.5, 40.1, 23.9, 23.7, 18.4 and 17.8 confirmed the structure of compound 4 as (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(3,4,5-trihydroxyphenyl)-2-propenoate.

Compound (**5**) showed a molecular ion peak in the

TABLE 3 : ^{13}C NMR data for (1-5) ($CDCl_3$)

	δ ^{13}C (ppm)				
H	**1**	**2**	**3**	**4**	**5**
1	166.2	166.2	166.2	166.2	166.0
2	120.1	120.1	120.1	120.1	120.5
3	143.3	143.3	143.3	143.3	143.2
1′	131.0	131.0	131.0	131.0	129.4
2′	109.2	109.2	109.2	109.2	114.9
3′	147.1	147.1	147.1	147.1	150.2
4′	132.9	132.9	132.9	132.9	144.3
5′	147.1	147.1	147.1	147.1	118.2
6′	109.2	109.2	109.2	109.2	121.0
1″	62.9	62.9	62.9	62.9	62.8
2″	125.0	124.1	124.1	124.1	124.2
3″	135.8	139.9	139.9	139.9	139.8
4″	25.3	40.0	34.5	40.1	40.1
5″	19.7	23.7	23.7	23.9	23.8
6″	-	125.0	125.0	124.0	125.0
7″	-	135.8	135.8	139.7	135.8
8″	-	25.3	25.3	40.5	25.2
9″	-	19.6	19.6	23.7	19.5
10″	-	17.9	22.9	125.0	17.8
11″	-	-	-	135.8	-
12″	-	-	-	25.3	-
13″	-	-	-	19.7	-
14″	-	-	-	18.4	-
15″	-	-	-	17.8	-
OMe					58.0

high-resolution mass spectrum at m/z 330.1835, corresponding to the molecular formula $C_{20}H_{26}O_4$ (calcd 330.1831 for $C_{20}H_{26}O_4$). The ^{1}H NMR spectrum (TABLE 1) showed signals at δ 6.72 (dd, J = 1.09, 8.41 Hz), 6.68 (d, J = 1.09 Hz) and 6.60 (d, J = 8.41 Hz) which could be assigned to the aromatic protons. The spectrum also showed signals at δ 7.69 (d, J = 15.4 Hz), 6.41 (d, J = 15.4 Hz), 5.46 (m), 5.26 (m), 4.84 (d, J = 7.1 Hz), 2.17 (m), 2.12 (dd, J = 7.7, 15.0 Hz) and three singlets at δ 1.80 × 2 and 1.60 supporting the presence of three double bonds, three methylene protons and three methyl groups. The ^{1}H NMR spectrum also showed three protons signal at δ 3.85 (s), indicating the presence of a methoxy group. The ^{13}C NMR spectrum (BB and DEPT) showed 20 carbon signals (TABLE 3), four methyl, three methylene, seven methine and six quaternary carbons. The low-field region of the ^{13}C NMR spectrum showed signals at δ 166.0, 150.2, 144.3, 129.4, 121.0, 118.2, 114.9, 143.2, 120.5, 139.8, 124.2, 135.8 and 125.0 which could be assigned to carbonyl carbon of the ester, aromatic ring and double bonds carbons, respectively. One oxygenated methylene and one methoxy carbons resonated at δ 62.8 and 58.0 while methyl carbons appeared at δ 7.8, 19.5 and 25.2. Similarly, ^{13}C NMR spectrum also showed signals for a pair of methylene protons at 40.1 and 23.8. The positions of substituent could be confirmed by the homonuclear multiple-quantum coherence (HMQC) and heteronuclear multiple-bond connectivity (HMBC) experiments and confirmed the structure of compound (**5**) as (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate.

Compounds (**6,7**) showed molecular ion peaks in the high-resolution mass spectrum at m/z 330.1835, 398.2462, corresponding to the molecular formulas $C_{20}H_{26}O_4$ (calcd 330.1831 for $C_{20}H_{26}O_4$) and $C_{25}H_{34}O_4$ (calcd 398.2457 for $C_{25}H_{34}O_4$). The ^{1}H and ^{13}C NMR spectrum (TABLES 2 and 4) of compound 6 showed similar peaks like compound 5 with the only difference in ^{13}C NMR spectrum which showed peaks at δ 34.4 and 22.9 corresponding to the cis (Z) double bond at 2″ position and confirmed the structure of compound (**6**) as (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate. Compound 7 also showed similar ^{1}H and ^{13}C NMR spectrum (TABLE 2, 5) with some additional peaks corresponding to the chain length. ^{1}H NMR spectrum (TABLES 2 and 5) showed additional peaks at δ 5.24 (m), 2.0 (m), 2.05 (dd, J = 7.2, 15.0 Hz) and 1.8 (s) while ^{13}C NMR spectrum showed the additional peaks at δ 139.7, 124.0, 40.5, 23.7 and 18.4 confirmed the structure of compound 7 as (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(4-hydroxy-3-methoxy phenyl)-2-propenoate.

Compounds (**8-11**) showed molecular ion peaks in the high-resolution mass spectrum at m/z 292.1317, 360.1941, 428.2566, corresponding to the molecular formulas $C_{16}H_{20}O_5$ (calcd 292.1311 for $C_{16}H_{20}O_5$), $C_{21}H_{28}O_5$ (calcd 360.1937 for $C_{21}H_{28}O_5$) and $C_{26}H_{36}O_5$ (calcd 428.2563 for $C_{26}H_{36}O_5$), respectively. The ^{1}H and ^{13}C NMR spectrum (TABLE 2 and 4) of compound (**8-11**) showed peaks similar to compound 1-4, respectively, except the appearance of two methoxy proton signals at δ 3.85 × 2 (s) and 57.9 × 2 in ^{1}H and ^{13}C NMR spectrum indicates the presence of two methoxy groups at aromatic ring carbon. Further the positions of substituent could be confirmed by the homo-

TABLE 4: ^{13}C NMR data for (6-11) ($CDCl_3$)

	δ ^{13}C (ppm)					
H	**6**	**7**	**8**	**9**	**10**	**11**
1	166.0	166.2	166.1	166.1	166.1	166.1
2	120.5	120.1	120.2	120.2	120.2	120.2
3	143.2	143.3	143.2	143.2	143.2	143.2
1′	129.4	129.4	130.3	130.3	130.3	130.3
2′	114.9	114.9	107.3	107.3	107.3	107.3
3′	150.2	150.2	151.2	151.2	151.2	151.2
4′	144.3	144.3	128.9	128.9	128.9	128.9
5′	118.2	118.2	151.2	151.2	151.2	151.2
6′	121.0	121.0	107.3	107.3	107.3	107.3
1″	62.8	62.9	62.7	62.7	62.7	62.7
2″	124.2	124.1	125.1	124.0	124.0	124.2
3″	139.8	139.9	135.5	139.7	139.7	139.7
4″	34.4	40.1	25.4	40.2	34.4	40.1
5″	23.8	23.9	19.8	23.8	23.8	23.9
6″	125.0	124.0	-	125.1	125.1	124.0
7″	135.8	139.7	-	135.6	135.6	139.6
8″	25.2	40.5	-	25.4	25.4	40.4
9″	19.5	23.7	-	19.6	19.6	23.8
10″	22.9	125.0	-	17.9	22.9	125.1
11″	-	135.8	-	-	-	135.7
12″	-	25.3	-	-	-	25.3
13″	-	19.7	-	-	-	19.6
14″	-	18.4	-	-	-	18.3
15″	-	17.8	-	-	-	17.7
OMe	58.0	58.0	57.9	57.9	57.9	57.9
OMe			57.9	57.9	57.9	57.9

nuclear multiple-quantum coherence (HMQC) and heteronuclear multiple-bond connectivity (HMBC) experiments and confirmed the structures **8-11** as 3-methyl-2-butenyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl) -2-propenoate, (2E)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate, (2Z)-3,7-dimethyl-2,6-octadienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate and (2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl (E)-3-(4-hydroxy-3,5-dimethoxyphenyl)-2-propenoate, respectively.

EXPERIMENTAL

General

Column chromatography was carried out for purification of the crude materials using silica gel of 230–400 mesh (E.Merck) as stationary phase. Alumina sheets precoated with silica gel 60 F254 (20×20 cm, 0.2-mm thick; E-Merck) were used for TLC to check the purity and were visualized under UV light (254 and 365 nm) using ceric sulfate reagent. The starting materials such as trihydroxy cinnamic, sinapinic and transferullic acids were purchased from the Aldrich Chemical Company and all solvents were HPLC grade. IR spectra were recorded as KBr pellet on Jasco-320-A Infrared spectrophotometer. Mass spectra (EI and HREIMS) were measured on on Finnigan (Varian MAT) 112 and Finnigan (Varion MAT) 312 spectrometers and ions are given in *m/z* (%). The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer in $CDCl_3$. Chemical shifts (δ) were reported in ppm and coupling constants (*J*) in hertz (Hz). The chemical shift standard was internal tetramethylsilane (TMS) for both ^{1}H and ^{13}C. The following abbreviations were used: s, d, dd and m for singlet, doublet, doublet of doublet and multiplet, respectively.

General procedure for the synthesis of compounds (1-11)

The compounds (**1-11**) were synthesized by esterification of cinnamic acids (trihydroxy cinnamic, sinapinic and transferullic acids) with alcohols such as prenol, nerol, geraniol and farnesol by a synthetic procedure in which alcohols (5 mL/mmol) were added to the cinnamic acids (1.3 equiv) dissolved in anhydrous CH_2Cl_2 (10 ml). Further DMAP (0.15 equiv) and DCC (1.25 equiv) were added and stirred up to 12 h. N,N-Dicyclohexylurea was filtered and the filtrate was concentrated[10]. The crud compounds **1-11** (1.32-140 g) were subjected to flash column chromatography over silica gel, successively eluting with *n*-hexane–ethyl acetate (4 : 6 to 3 : 7) afforded **1-11** (15-20 mg).

Spectral data of compounds (1-11)

IR (KBr), υ_{max} cm$^{?1}$: 3500-3300 (OH), 2950-2860 (C-H), 1745-1735 (C=O), 1669 (trans C=C), 1658 (cis C=C), 1610-1600 (aromatic C=C) and 1200-1100 (C-O), HREIMS m/z M^+ 264.0995 (calcd 264.0998 for $C_{14}H_{16}O_5$), 332.1629 (calcd 332.1624 for $C_{19}H_{24}O_5$), 332.1629 (calcd 332.1624 for $C_{19}H_{24}O_5$), 400.2255 (calcd 400.2250 for $C_{24}H_{32}O_5$), 330.1835 (calcd 330.1831 for $C_{20}H_{26}O_4$), 330.1835 (calcd 330.1831 for $C_{20}H_{26}O_4$), 398.2462 (calcd 398.2457 for $C_{25}H_{34}O_4$), 292.1317 (calcd 292.1311 for $C_{16}H_{20}O_5$), 360.1941 (calcd 360.1937 for $C_{21}H_{28}O_5$),

360.1941 (calcd 360.1937 for $C_{21}H_{28}O_5$) and 428.2566 (calcd 428.2563 for $C_{26}H_{36}O_5$), respectively and ^{1}H and ^{13}C NMR data are given in TABLES 1-4.

REFERENCES

[1] A.V.Simonyan; Pharmaceutical Chemistry Journal, **33**, 158 **(1999)**.

[2] A.A.Avanesyan, A.V.Simonyan; Pharmaceutical Chemistry Journal, **35**, 99 **(2001)**.

[3] A.A.esyan, A.V.nyan; Pharmaceutical Chemistry Journal, **39**, 379 **(2005)**.

[4] P.N.Ramanan, M.N.A.Rao; Indian Journal of Experimental Biology, **25**, 42 **(1987)**.

[5] J.Zhu, H.Zhu, N.Kobamoto, M.Yasuda, S.Tawata, Nippon Noyaku Gakkaishi; 25, 263 **(2000)**.

[6] A.V.Simonyan; Pyatigorsk Pharmaceutical Institue, **27**, 21 **(1993)**.

[7] S.Adisakwattana, K.Sookkongwaree; S. Roengsumran, A.Petsom, N.Ngamrojnavanich, W.Chavasiri, S.Deesamerc, S.Yibchok-Anuna; Bioorg.Med. Chem.Lett., **14**, 2893 **(2004)**.

[8] S.Lee, J.M.Han, H.Kim, E.Kim, T.S.Jeong, W.S. Lee, K.H.Cho; Bioorg.Med.Chem.Lett., **14**, 4677 **(2004)**.

[9] Y.Akao, H.Maruyama, K.Matsumoto, K.Ohguchi; Biol.Pharm.Bull., **26**, 1057 **(2003)**.

[10] T.Eicher, M.Ott, A.Speicher; Synthesis, **6**, 755 **(1996)**.