Efficient Synthesis of New *N*-Benzyl- or *N*-(2-Furylmethyl)cinnamamides Promoted by the 'Green' Catalyst Boric Acid, and Their Spectral Analysis

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Abstract: New *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides were prepared in good to excellent yields by amidation reactions between cinnamic acid and benzylamines or (2-furylmethyl)amine in the presence of 5 mol% boric acid. All the cinnamamides were characterized by IR and ^{1}H and ^{13}C NMR spectroscopy.

Key words: amides, amidation, catalysis, carboxylic acids, *N*-benzylamides

N-Substituted amides of carboxylic acids make up an important and interesting class of organic molecules, and have always attracted the attention of organic, bioorganic, and medicinal chemists due to their many synthetic applications as well as biological properties. That is why many procedures for the formation of carboxylic acid amides are known in the chemical literature. The treatment of acyl halides with amines is a very general reaction for the preparation of amides.[1] Different options include the use of acid anhydrides or activated esters. The same chemical procedures have been used for diverse cinnamamides, derived from substituted cinnamic acid.[2–4]

Acylation reactions of amines are frequently used in the preparation of drug candidate molecules. In a recent review of Carey et al., it was indicated that the dominance of N-acylations is expected as often as amides occur in drug molecules.[5] Despite their wide scope, these acylation reactions of amines with acyl halides ('amino-de-halogenation reactions'[6]) suffer several drawbacks, e.g. the limited stability of many acyl halides and the need for hazardous reagents for their preparation, releasing corrosive and volatile byproducts. Moreover, almost any other functional group of the starting substrate needs to be protected to ensure chemoselective amide formation. Thus, although economic amide formation reactions are available, these are not particularly atom efficient or 'green'.

It is believed that the acylation of amines by carboxylic acids ('amino-de-hydroxylation reactions'[6]) is a less convenient method than that mentioned above. However, advances in catalytic methods allow direct amide formation from carboxylic acids and amines as reaction partners. For example, Orru et al. reported the formation of an amide bond after reaction between a carboxylic acid and an amines in one pot under solvent-free microwave conditions.[7] Another example is the biocatalytic amidation studied by Prasad and co-workers, who found a novel and efficient method for the preparation of optically enriched amides, also from carboxylic acids and amines.[8] There are alternative, similar methods that permit the preparation of amides under environmentally friendly conditions from different reagents such as aldehydes and hydroxylamine hydrochloride[9] or esters and amines in aminolysis reactions.[10]

At the moment, catalytic amino-de-hydroxylation reactions present a convenient alternative to this standard protocol. Recently, during the development of catalytic, low-waste acylation methods, which would improve the environmental performance of N-substituted amide synthesis, it was found that environmentally benign boric acid, which is nontoxic, inexpensive, and readily available, acts as a highly effective catalyst for addition–elimination reactions of carboxylic carbon, for example direct amide formation[11,12] or the selective esterification of carboxylic acids.[12,13]

With these facts in mind and towards the development of our medicinal program directed at small molecules for drug delivery, we were particularly interested in diverse *N*-(hetarylmethyl)cinnamamides that could serve as useful precursors to many drug-like molecules and interesting biological models in our quest for compounds with antifungal and antiparasitic properties.[14–16] To the best of our knowledge, an efficient synthesis of *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides in which a 'green' catalyst is used has not been described before. The results of our research on the synthesis, the spectral characterization, and the preliminary biological evaluations of these new *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides are reported here.

First, we investigated the best reaction conditions for the preparation of the new *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides, studying two parameters: the catalyst amount and the stoichiometry between cinnamic acid and benzylamine. It was found that a 2:1 cinnamic acid/amine molar ratio was the most efficient, and that 5 mol% boric acid was enough to provide the new *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides in good yields (Scheme 1). All products were obtained as white solids, in yields of 60–100% (Table 1). The best yield was for cinnamamide **3a**. The introduction of electron-withdrawing or electron-do-

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Table 1 Physicochemical Properties of Substituted *N*-Benzyl- and *N*-(2-Furylmethyl)cinnamamides **3a–j**[a]

Product	Ar	R^1	R^2	Molecular formula[b]	R_f[c]	Mp (°C)	Yield (%)	IR n_{N-H} (cm^{-1})	IR $n_{NC=O}$ (cm^{-1})
3a	Ph	H	H	$C_{16}H_{15}NO$	0.51	97	100	3297	1654
3b	4-Tol	H	H	$C_{17}H_{17}NO$	0.85	119	89	3254	1649
3c	Ph	H	Me	$C_{17}H_{17}NO$	0.55	75	60[d] 93[e]	–	1648
3d	4-FC_6H_4	H	H	$C_{16}H_{14}FNO$	0.71	121	84	3265	1650
3e	4-ClC_6H_4	H	H	$C_{16}H_{14}ClNO$	0.57	155	78	3258	1656
3f	PMP	H	H	$C_{17}H_{17}NO_2$	0.33	110	87	3297	1654
3g	Ph	Me	H	$C_{17}H_{17}NO$	0.66	139	74	3263	1655
3h	Ph	(*R*)-Me	H	$C_{17}H_{17}NO$	0.66	140	78	3308	1654
3i	Ph	(*S*)-Me	H	$C_{17}H_{17}NO$	0.66	140	76	3307	1655
3j	2-furyl	H	H	$C_{14}H_{13}NO_2$	0.38	122	83[f]	3239	1655

[a] Reagents and conditions: **1** (1 equiv), **2** (2 equiv), H_3BO_3 (5 mol%), toluene, reflux, 5 h.
[b] Confirmed by elemental analysis.
[c] TLC (aluminum sheets, detection: UV 254 nm, PE–EtOAc, 2:1).
[d] Reaction time was 9 h.
[e] H_3BO_3 (10 mol%) was used.
[f] Reaction time was 6 h.

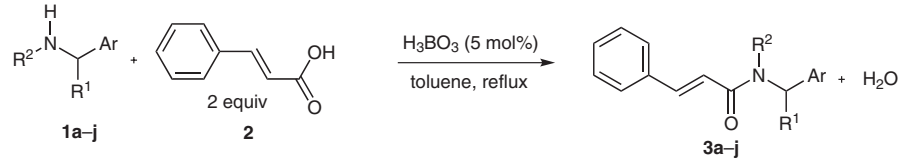
nating groups did not improve or diminish the yields considerably, which were always around or over 80%, and in all cases the reactions proceeded cleanly. To evaluate the effect of the catalyst quantity on the reaction yield, we carried out the condensation between benzylamine (**1c**) and cinnamic acid (**2**) with 10 mol% boric acid (Table 1, product **3c**). These conditions led to a 30% improvement in the yield (from 60% to 93%), and to a reduction of the reaction time (from 9 h to 5 h).

The cinnamamides are obtained by classic nucleophilic substitution at a trigonal carbon (A_N–D_N). The role of boric acid in this condensation process is to increase the electrophilic character of the carboxylic carbon (carboxyl activation step).[17] It is proposed that the boric acid reacts with the carboxylic acid to form a mixed anhydride as the proper acylating agent; in this step, water is released under azeotropic reflux conditions when less polar solvents such as toluene are used, so that the water is collected in a Dean–Stark trap to ensure the shift of the reaction to amide formation. Upon reaction with an amine, this intermediate forms the desired carboxamide and regenerates the catalytically active boric acid.[18,19]

The structures of the synthesized N-substituted cinnamamides **3a–j** were confirmed by ^1H and ^{13}C NMR spectroscopy and were supported by inverse-detected 2D NMR experiments.

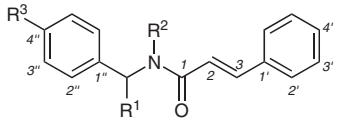
The ^1H NMR spectra of compounds **3** contain a group of general characteristic signals of this series. For example, in the spectrum of cinnamamide **3a**, the methylene protons at δ = 4.42 (d, *J* = 5.8 Hz, 2 H, CH_2) appear at low frequency. An olefinic proton appears at δ = 6.39 (d, *J* = 15.6 Hz, 1 H, =CHCO), coupling with the other *trans*-olefinic proton. The N–H signal is observed as a broad singlet at δ = 6.43. In the aromatic region (δ = 7.13–7.35), the protons on the aromatic ring of the benzylamine moiety are located together with the 3′-H and 4′-H protons. A little more displaced, the 2′-H protons appear at δ = 7.35 as a doublet of doublets with coupling constants *J* = 6.8 and 2.1 Hz. The most remote signal in the spectrum (δ = 7.55) belongs to the second olefinic proton (=CHPh) that is distinguished as a doublet, and is coupled with the *trans* form of proton 2-H (*J* = 15.6 Hz). The ^1H NMR data of all the cinnamamides are presented in Table 2.

From the conformational analysis, the tertiary cinnamamide **3c** presents an interesting case (Figure 1). Similar to *N*-methylformamide, *N*-methylacetamide, and *N*,*N*-dimethylcinnamamide [with an OC–N(H or Me)Me bond],[3,20] this amide has an OC–N(Bn)Me bond, with re-

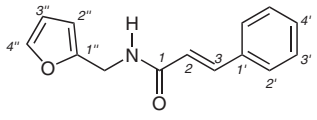


Scheme 1 Preparation of substituted *N*-benzyl- or *N*-(2-furylmethyl)cinnamamides **3a–j**

Table 2 ^{1}H NMR Spectroscopic Data of Substituted *N*-Benzyl- or *N*-(2-Furylmethyl)cinnamamides **3a–j**



3a–i



3j

^{1}H NMR Data [δ, multiplicity, *J* (Hz)]

Prod.	Me	CH_2	CH	2-H	N-H	2′-H	3′-H, 4′-H, 2″-H, 3″-H, 4″-H	3-H
3a	–	4.42 (d J = 5.8)	–	6.39 (d $J_{2,3}$ = 15.6)	6.43 (br s)	7.35 (dd $J_{2',3'}$ = 6.8 $J_{2',4'}$ = 2.1)	7.25–7.13 (m)	7.55 (d $J_{3,2}$ = 15.6)
3b	2.32 (s)	4.50 (d J = 5.7)	–	6.45 (d $J_{2,3}$ = 15.6)	6.41 (br s)	7.46 (dd $J_{2',3'}$ = 6.8 $J_{2',4'}$ = 2.3)	7.30–7.35 (m, 3′-H, 4′-H), 7.21 (d, J = 8.0, 2″-H), 7.13 (d, J = 7.8, 3″-H)	7.65 (d $J_{3,2}$ = 15.6)
s-cis-**3c**	3.06 (s)	4.71 (s)	–	6.93 (d $J_{2,3}$ = 15.6)	–	7.54 (dd $J_{2',3'}$ = 7.3 $J_{2',4'}$ = 1.9)	7.41–7.17 (m)	7.77 (d $J_{3,2}$ = 15.6)
s-trans-**3c**	3.05 (s)	4.71 (s)	–	6.88 (d $J_{2,3}$ = 15.6)	–	7.26 (dd $J_{2',3'}$ = 7.7 $J_{2',4'}$ = 3.6)	7.41–7.17 (m)	7.76 (d $J_{3,2}$ = 15.5)
3d	–	4.50 (d J = 5.9)	–	6.42 (d $J_{2,3}$ = 15.6)	6.23 (br s)	7.26 (dd $J_{2',3'}$ = 6.3 $J_{2',4'}$ = 3.2)	7.37–7.32 (m, 3′-H, 4′-H), 7.30–7.25 (m, 2″-H), 7.02 (dd, $J_{3'',19F}$ = 8.7, $J_{3'',2''}$ = 8.8, 3″-H)	7.55 (d $J_{3,2}$ = 15.6)
3e	–	4.42 (d J = 5.9)	–	6.33 (d $J_{2,3}$ = 15.6)	6.33 (br s)	7.47 (dd $J_{2',3'}$ = 7.2 $J_{2',4'}$ = 2.9)	7.30–7.23 (m, 3′-H, 4′-H), 7.21–7.12 (m, 2″-H, 3″-H)	7.56 (d $J_{3,2}$ = 15.6)
3f	3.69 (s)	4.38 (d J = 5.7)	–	6.32 (d $J_{2,3}$ = 15.6)	6.02 (br s)	7.37 (dd $J_{2',3'}$ = 6.3 $J_{2',4'}$ = 2.3)	7.28–7.21 (m, 3′-H, 4′-H), 7.15 (d, $J_{2'',3''}$ = 8.4, 2″-H), 6.76 (d, $J_{3'',2''}$ = 8.4, 3″-H)	7.56 (d $J_{3,2}$ = 15.6)
3g	1.54 (d $J_{Me,CH}$ = 6.9)	–	5.26 (dq J = 7.0, 7.1)	6.43 (d $J_{2,3}$ = 15.5)	6.21 (br d J = 7.5)	7.45 (dd $J_{2',3'}$ = 6.6 $J_{2',4'}$ = 3.0)	7.38–7.28 (m, 3′-H, 4′-H, 2″-H, 3″-H), 7.24 (tt, $J_{4'',3''}$ = 6.8, $J_{4'',2''}$ 1.7, 4″-H)	7.62 (d $J_{3,2}$ = 15.6)
3h	1.54 (d $J_{Me,CH}$ = 7.0)	–	5.26 (dq J = 7.0, 7.1)	6.43 (d $J_{2,3}$ = 15.6)	6.20 (br d J = 7.5)	7.45 (dd $J_{2',3'}$ = 6.6 $J_{2',4'}$ = 3.1)	7.38–7.28 (m, 3′-H, 4′-H, 2″-H, 3″-H), 7.25 (tt, $J_{4'',3''}$ = 6.8, $J_{4'',2''}$ 1.7, 4″-H)	7.62 (d $J_{3,2}$ = 15.6)
3i	1.53 (d $J_{Me,CH}$ = 7.0)	–	5.26 (dq J = 7.0, 7.0)	6.44 (d $J_{2,3}$ = 15.6)	6.20 (br d J = 7.5)	7.44 (dd $J_{2',3'}$ = 6.6 $J_{2',4'}$ = 3.1)	7.38–7.28 (m, 3′-H, 4′-H, 2″-H, 3″-H), 7.24 (tt, $J_{4'',3''}$ = 6.8, $J_{4'',2''}$ 1.8, 4″-H)	7.62 (d $J_{3,2}$ = 15.6)
3j	–	4.55 (d J = 5.5)	–	6.46 (d $J_{2,3}$ = 15.5)	6.46 (br s)	7.45 (m)	7.37–7.28 (m, 3′-H, 4′-H, 4″), 5.27–5.24 (m, 2″-H), 5.33–5.27 (m, 3″-H)	7.64 (d $J_{3,2}$ = 15.6)

stricted rotation around the OC–N bond.[21] From analysis of the ^{1}H and ^{13}C NMR data of amide **3c**, we concluded that the *s-cis*-/*s-trans*-conformer composition (*anti* and *syn* to CO) at room temperature was almost 1:1 (Figure 1).

The right connections to the entire nucleus were obtained from the HMBC (heteronuclear multiple-bond correlation) NMR spectra. For example, the spectrum of *N*-benzylcinnamamide **3a** contains an unambiguous cross peak for the methylene protons (–CH_2–) and the carbonyl carbon as well as the aromatic hydrocarbons 2″-C and 1″-C at δ = 127.7. The identification, differentiation, and assignment of the olefinic protons were further confirmed by the existence of an HMBC cross signal connection between the carbons 1-C, 3-C, 1′-C, and 2-C with the protons 2-H/3-H. At the same time, the HMBC measurement allowed an unequivocal assignment of all aromatic hydrocarbon atoms. Consequently, the structure of **3a** was elucidated as *N*-benzyl-3-phenylprop-2-enamide.

In summary, we have demonstrated that boric acid is a practical and useful catalyst for the amidation reaction between cinnamic acid and benzylamines. Mild and environmentally friendly reaction conditions, good yields and

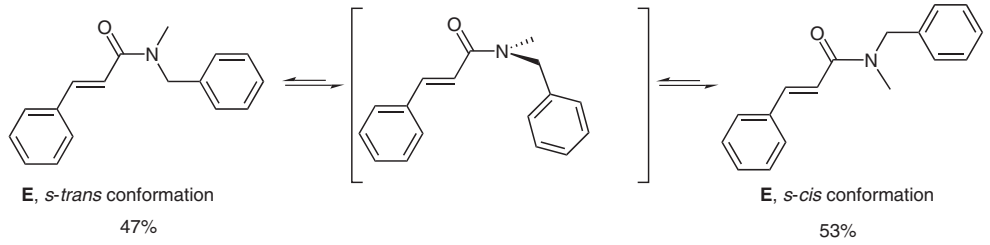


Figure 1 Conformers of *N*-benzyl-*N*-methyl-3-phenylprop-2-enamide (**3c**)

reaction rates, and cleaner reaction profiles are the notable features of this procedure.[22] The spectral data described for these *N*-benzylcinnamamides should be reliable for the structural analysis of natural cinnamamides or analogues. New N-substituted cinnamamides are interesting biological models[23] and synthetic precursors, which can be used in the synthesis of 2-benzazepine derivatives. Research toward the synthesis of 2-benzazepin-3-one derivatives is under way in our laboratory, and these results will be published in the near future.

All reagents were purchased from Aldrich and were of commercial grade. IR spectra were recorded on a Perkin Elmer Tensor 27-FT spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer. Chemical shifts are reported relative to the solvent peak ($CHCl_3$ in $CDCl_3$ at $\delta = 7.26$ for ^{1}H and at $\delta = 77.0$ for ^{13}C NMR) or TMS. For the DEPT-135 spectra reported below, the signals of the CH_3, CH_2, and CH carbons are shown as positive (+) or negative (–). Quaternary carbons are not shown. A Hewlett Packard 5890a Series II gas chromatograph interfaced to an HP 5972 mass-selective detector (MSD) with an HP MS ChemStation Data system was used for MS identification at 70 eV for which a 60-m capillary column coated with HP-5 [5%-phenylpoly(dimethylsiloxane)] was used. Melting points were measured on a Fisher Johns melting point apparatus. Column chromatography was carried out on columns packed with alumina. TLC was conducted on standard aluminum sheets precoated with a 0.2 mm layer of silica gel.

Synthesis of *N*-Benzyl- and *N*-(2-Furylmethyl)-3-phenylprop-2-enamides 3; General Procedure

H_3BO_3 (5.0 mol%) was added to a soln of *trans*-cinnamic acid (**2**; 42.2 mmol) in anhyd toluene (80 mL). Then the appropriate amine **1** (21.1 mmol) was added in one portion to the stirred colorless reaction mixture. The mixture was refluxed between 5–9 h, and after completion of the reaction (shown by the appropriate volume of H_2O collected in the Dean–Stark trap, as well as TLC), it was stopped. The mixture was allowed to cool to r.t. and was then poured into stirring hexanes; this led to the immediate precipitation of a white solid, which was collected and purified by column chromatography (alumina, EtOAc–PE). Physicochemical characteristics of the synthesized N-substituted cinnamamides **3a**–**j** are given in Tables 1 and 2.

N-Benzyl-3-phenylprop-2-enamide (3a)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.7 (–), 119.6 (+), 126.4 (+), 126.6 (+), 126.7(+), 126.8 (+), 126.9 (+), 127.6 (+), 127.7 (+), 127.8 (+), 127.9 (+), 128.6 (+), 133.8, 137.2, 140.2 (+), 164.9

COSY correlation [δ_H/δ_H]: 7.55/6.39 [3-H/2-H], 7.35/7.24–7.13 [2′-H_{Ph}/H_{Ph}], 7.24–7.13/7.35 [H_{Ph}/2′-H_{Ph}], 7.24–7.13/7.35–7.25 [H_{Bn}/H_{Bn}], 6.39/7.55 [2-H/3-H], 6.13/4.42 [H-NH/H-CH_2], 4.42/6.13 [CH_2/NH].

HMQC correlation [δ_H/δ_C]: 7.35/140.2 [3-H/3-C], 7.35/126.6 [2′-H_{Ar}/2′-C_{Ar}], 7.24–7.13/128.6–126.6 [H_{Ar}-C_{Ar}], 6.39/119.6 [2-H/2-C], 4.42/42.7 [H-CH_2/C-CH_2].

HMBC correlation [δ_H/δ_C]: 7.55/165.9/129.6/120.6 [3-H/1-C/1′-C_{Ar}/2′-C_{Ar}/2-C], 7.35/141.1/128.7 [2′-H_{Ar}/3-C/3′-C_{Ar}], 7.25–7.13/134.7/128.7 [3′H_{Ar}/1′-C_{Ar}/2′-C_{Ar}/4′-C_{Ar}], 7.25–7.13/138.2/127.8/127.7/127.4 [2″-H_{Ar}/3″-C_{Ar}/4″-C_{Ar}/1″-C_{Ar}], 7.25–7.13/134.7/129.6/128.7 [4′-H_{Ar}/1′-C_{Ar}/2′-C_{Ar}/3′-C_{Ar}], 6.39/165.9/141.1/134.7 [2-H/1-C/3-C/1′-C_{Ar}], 4.42/165.9/138.2/127.7 [H-CH_2/1-C/1″-C_{Ar}/2″-C_{Ar}].

GC-MS (EI, 70 eV): t_R = 23.8 min; *m*/*z* (%) = 237 (73) [M$^+$], 131 (100), 103 (66), 91 (22), 77 (50).

3-Phenyl-*N*-4-tolylprop-2-enamide (3b)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (+), 43.5 (–), 120.6 (+), 127.5 (+), 127.7 (+), 127.8 (+), 128.2 (+), 128.7 (+), 129.1 (+), 129.2 (+), 129.3 (+), 129.5 (+), 134.8, 135.1, 137.2, 141.0 (+), 165.8.

COSY correlation [δ_H/δ_H]: 7.65/6.45 [3-H/2-H], 7.46/7.20–7.10 [2′-H_{Ph}/H_{Ph}], 7.30–7.20/7.46 [H_{Ph}/2′-H_{Ph}], 7.20–7.10/7.20–7.10 [H_{Bn}/H_{Bn}], 6.45/7.65 [2-H/3-H], 6.41/4.50 [H-NH/H-CH_2], 4.50/6.41 [H-CH_2/H-NH].

HMQC correlation [δ_H/δ_C]: 7.65/141.0 [3-H/3-C], 7.46/128.8 [2′-H_{Ph}/2′-C_{Ph}], 7.30–7.10/128.5–126.6 [H_{Ar}-C_{Ar}], 6.45/120.6 [2-H/2-C], 4.50/43.5 [H-CH_2/C-CH_2].

HMBC correlation [δ_H/δ_C]: 7.55/165.8/135.2/129.3/120.6 [3-H/1-C/1′-C_{Ph}/2′-C_{Ph}/2-C], 7.46/141.1/135.2/128.7 [2′-H_{Ph}/3-C/1′-C_{Ph}/3′-C_{Ph}], 7.37–7.32/135.0–127.0 [3′-H_{Ph}, 4′-H_{Ph}/1′-C_{Ph}, 2′-C_{Ph}, 3′-C_{Ph}, 4′-C_{Ph}], 7.21/137.1/134.8/127.7/43.5 [2″-H_{Bn}/1″-C_{Bn}/4″-C_{Bn}/3″-C_{Bn}/C-CH_2], 7.13/137.1/134.8/129.5/43.5/21.0 [3″-H_{Bn}/C_{Bn}/C-CH_2/C-Me], 6.93/141.0/135.2 [2-H/3-C/1′-C_{Ph}], 4.50/165.8/137.1/129.5 [H-CH_2/1-C/1″-C_{Bn}/2″-C_{Bn}], 2.32/137.1/134.8/129.5/127.7 [H-Me/4″-C_{Bn}/3″-C_{Bn}/2″-C_{Bn}/1″-C_{Bn}].

GC-MS (EI, 70 eV): t_R = 24.8 min; *m*/*z* (%) = 251 (47) [M$^+$], 131 (55), 120 (42), 103 (85), 91 (38), 77 (100).

N-Benzyl-*N*-methyl-3-phenylprop-2-enamide (3c)

^{13}C NMR (100 MHz, $CDCl_3$): δ (*s-trans*-**3c**) = 34.2 (+), 53.4 (–), 117.2 (+), 126.3 (+), 127.2 (+), 127.7 (+), 128.5 (+), 128.7 (+), 129.4 (+), 135.1, 136.7, 142.9 (+), 167.0; δ (*s-cis*-**3c**) = 34.8 (+), 51.2 (–), 117.2 (+), 127.9 (+), 127.6 (+), 127.7 (+), 128.6 (+), 128.8 (+), 129.5 (+), 135.2, 137.2, 143.0 (+), 165.5.

COSY correlation [δ_H/δ_H] (*s-cis*-**3c**): 7.77/6.93 [3-H/2-H], 7.41–7.17/7.41–7.17/4.71 [H_{Ar}/H_{Ar}/CH_2], 6.93/7.77 [2-H/3-H], 4.71/7.20–7.13/3.06 [H-CH_2/ H_{Ar}/C-Me], 3.06/4.71 [H-Me/C-CH_2].

HMQC correlation [δ_H/δ_C] (*s-cis*-**3c**): 7.77/142.9 [3-H/3-C], 7.54/127.9 [2′-H_{Ph}/2′-C_{Ph}], 7.41–7.17/129.5–126.3 [H_{Ar}-C_{Ar}], 6.93/117.2 [2-H/2-C], 4.71/53.4 [H-CH_2/C-CH_2], 3.06/34.2 [H-Me/C-Me].

HMBC correlation [δ_H/δ_C]: 7.77/177.0/135.1/127.7/117.2 [3-H/1-C/1′-C_{Ph}/2′-C_{Ph}], 7.54/135.2/129.3 [2′-H_{Ph}/1′-C_{Ph}/2′-C_{Ph}], 7.17–7.41/135.1/129.5–126.3 [H_{Ar}/1′-C_{Ph}/C_{Ar}], 177.0/142.9/135.1 [2-H/

1-C/3-C/1′-H_{Ph}], 4.71/177.0/136.7/129.3–126.3 [H-CH_2/1-C/1″-C_{Bn}/C-$_{Ar}$], 3.06/177.0 [H-Me/1-C].

GC-MS (EI, 70 eV): t_R = 23.3 min; *m*/*z* (%) = 251 (48) [M$^+$], 174 (24), 131 (100), 103 (90), 91 (37), 77(55).

***N*-(4-Fluorobenzyl)-3-phenylprop-2-enamide (3d)**

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.1 (–), 115.5 (+), 115.5 (+), 115.7 (+), 120.3 (+), 127.8 (+), 128.8 (+), 129.5 (+), 129.6 (+), 129.8 (+), 134.1, 134.7 (+), 141.5 (+), 160.9, 163.4, 165.9.

GC-MS (EI, 70 eV): t_R = 23.9 min; *m*/*z* (%) = 255 (50) [M$^+$], 131 (100), 103 (58), 91 (3), 77 (47).

***N*-(4-Chlorobenzyl)-3-phenylprop-2-enamide (3e)**

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.1 (–), 120.1 (+), 127.8 (+), 128.8 (+), 129.2 (+), 129.8 (+), 133.4, 134.6, 136.8, 141.7 (+), 165.8.

GC-MS (EI, 70 eV): t_R = 26.1 min; *m*/*z* (%) = 271 (36) [M$^+$], 140 (28), 131 (100), 103 (56), 77 (50).

***N*-(4-Methoxybenzyl)-3-phenylprop-2-enamide (3f)**

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.3 (–), 55.3 (+), 114.1 (+), 120.5 (+), 127.7 (+), 128.8 (+), 129.3 (+), 129.6 (+), 130.1, 134.8, 141.2 (+), 159.0, 165.7.

GC-MS (EI, 70 eV): t_R = 26.7 min; *m*/*z* (%) = 267 (83) [M$^+$], 136 (100), 131 (93), 121 (43), 103 (63), 91 (10), 77 (65).

(±)-3-Phenyl-*N*-(1-phenylethyl)prop-2-enamide (3g)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (+), 48.8 (+), 120.8 (+), 126.2 (+), 127.3 (+), 127.7 (+), 128.6 (+), 128.7 (+), 129.5 (+), 134.8, 141.0 (+), 143.1, 164.9.

COSY correlation [δ_H/δ_H]: 7.62/6.43 [3-H/2-H], 7.45/7.38–7.28 [2′-H_{Ph}/H_{Ph}], 7.38–7.28/7.38–7.28 [H_{Bn}/H_{Bn}], 7.38–7.28/7.45 [H_{Ph}/2′-H_{Ph}], 6.43/7.62 [2-H/3-H], 6.21/5.26 [H-CH/H-NH], 5.26/6.21 [H-NH/H-CH], 5.26/1.54 [H-CH/H-Me], 1.54/5.26 [H-Me/H-CH].

HMQC correlation [δ_H/δ_C]: 7.62/141.1 [3-H/3-C], 7.45/128.6 [2′-H_{Ph}/2′-C_{Ph}], 7.38–7.28/130–125 [H_{Ar}-C_{Ar}], 7.24/129.6 [4′-H_{Ph}/4′-C_{Ph}], 6.43/120.8 [2-H/2-C], 5.26/48.9 [H-CH/C-CH], 1.54/21.7 [H-Me/C-Me].

GC-MS (EI, 70 eV): t_R = 23.5 min; *m*/*z* (%) = 251 (52) [M$^+$], 131 (100), 120 (60), 103 (62), 91 (3), 77 (54).

(*R)-3-Phenyl-*N*-(1-phenylethyl)prop-2-enamide (3h)**

$[\alpha]_D^{26}$ +83.7 (*c* 0.036, $CHCl_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (+), 48.8 (+), 120.8 (+), 126.2 (+), 127.3 (+), 127.7 (+), 128.6 (+), 128.7 (+), 129.5 (+), 134.8, 141.1 (+), 143.1, 165.0.

COSY correlation [δ_H/δ_H]: 7.62/6.43 [3-H/2-H], 7.45/7.38–7.28 [2′-H_{Ph}/H_{Ph}], 7.38–7.28/7.38–7.28 [H_{Bn}/H_{Bn}], 7.38–7.28/7.45 [H_{Ph}/2′-H_{Ph}], 6.43/7.62 [2-H/3-H], 6.21/5.26 [H-NH/H-CH], 5.26/6.21 [H-NH/H-CH], 5.26/1.54 [H-CH/H-Me], 1.54/5.26 [H-Me/H-CH].

HMQC correlation [δ_H/δ_C]: 7.62/141.1 [3-H/3-C], 7.45/128.6 [2′-H_{Ph}/2′-C_{Ph}], 7.38–7.28/130–125 [H_{Ar}-C_{Ar}], 7.24/129.6 [4′-H_{Ph}/4′-C_{Ph}], 6.43/120.8 [2-H/2-C], 5.26/48.9 [H-CH/C-CH], 1.54/21.7 [H-Me/C-Me].

HMBC correlation [δ_H/δ_C]: 7.62/164.9/134.8/127.7/120.8 [3-H/1-C/2′-C_{Ph}/1′-C_{Ph}, 2-C], 7.45/141.1/134.8/129.5 [2′-H_{Ph}/3-C/1′-C_{Ph}/3′-C_{Ph}], 7.38–7.28/143.1/134.8/135.0–129.0/48.9 [H_{Ar}/1″-C_{Bn}/1′-C_{Ar}/C_{Ar}-C_{Ar}/C-Me], 6.43/165.0/141.1/134.8/ [2-H/1-C/3-C/1′-C_{Ph}], 5.25/164.9/143.1/21.7 [H-CH/1-C/1″-C_{Bn}/C-Me], 1.54/143.1/48.8 [H-Me/1″-C_{Ph}/C-CH].

GC-MS (EI, 70 eV): t_R = 23.8 min; *m*/*z* (%) = 251 (31) [M$^+$], 131 (100), 120 (50), 103 (52), 91 (4), 77 (49).

(*S)-3-Phenyl-*N*-(1-phenylethyl)prop-2-enamide (3i)**

$[\alpha]_D^{26}$–80.9 (*c* 0.036, $CHCl_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (+), 48.9 (+), 120.8 (+), 126.2 (+), 127.3 (+), 127.7 (+), 128.6 (+), 128.6 (+), 128.7 (+), 129.5 (+), 134.8, 141.1 (+), 143.1, 164.9.

GC-MS (EI, 70 eV): t_R = 23.7 min; *m*/*z* (%) = 251 (35) [M$^+$], 131 (100), 120 (50), 103 (52), 91 (4), 77 (48).

***N*-(2-Furylmethyl)-3-phenylprop-2-enamide (3j)**

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.7 (+), 107.4 (+), 110.5 (+), 120.4 (+), 127.8 (+), 128.6 (+), 128.8 (+), 127.7 (+), 134.7, 141.4 (+), 142.2 (+), 151.1, 165.8.

GC-MS (EI, 70 eV): t_R = 21.3 min; *m*/*z* (%) = 227 (53) [M$^+$], 131 (100), 103 (95), 81 (23), 77 (92).

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(22) The boric acid promoted azeotropic reflux procedure seems not to be limited to cinnamic acid or its derivatives; see refs. 11 and 13.
(23) Compounds **3c**, **3g**, and **3j** displayed antifungal activity, especially **3c**, which showed to be a moderate antifungal agent for three different dermatophytic pathogenic fungi stumps. All the evaluated products (**3a**–**j**) possessed poor anti-AChE activity. These results will be published elsewhere.