Lewis Acid Catalyzed Reaction of Cinnamanilides: Competition of Intramolecular and Intermolecular Friedel–Crafts Reaction[1]

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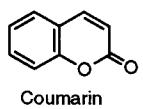
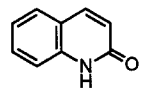
Received 12 April 1996; revised 18 July 1996

The first intermolecular Friedel–Crafts reaction of benzene leading to the formation of 3,3-diphenylpropionanilide **7** is described. 4-Methoxyaniline was reacted with cinnamoyl chloride to give 4-methoxycinnamanilide **(5a)**, the treatment of which with aluminum(III) chloride in chlorobenzene at 120 °C or in benzene at 80 °C afforded exclusively 6-hydroxyquinolin-2(1*H*)-one **(3a)** or 4′-hydroxy-3,3-diphenylpropionanilide **(7a)**, respectively. The formation of **7a** rather than **3a** in benzene indicated that an intermolecular Friedel–Crafts reaction occurred prior to the relatively more facile intramolecular ring cyclization. This intermolecular Friedel–Crafts reaction was observed during the attempted ring cyclization of cinnamanilide and its methoxy derivatives in aluminum(III) chloride/benzene. Preparation of **3a** can also be achieved in 17% overall yield via the *N*-oxidation of 6-hydroxyquinoline followed by acetylation and hydrolysis.

Coumarin [benzopyran-2(2*H*)-one] derivatives such as bishydroxycoumarin and warfarin are two of the principal anticoagulants. Recently, a number of the isomeric quinolin-2(1*H*)-one derivatives,[2–6] such as 6-[2-hydroxy-3-[(3-methoxybenzyl)amino]propoxyl]quinolin-2(1*H*)-one[2] and 3,4-dihydro-6-{3-[1-(2-tolyl)imidazol-2-yl]sulfinylpropoxyl}-quinolin-2(1*H*)-one[3] have been synthesized and proved to exhibit extensive cardiovascular activities.

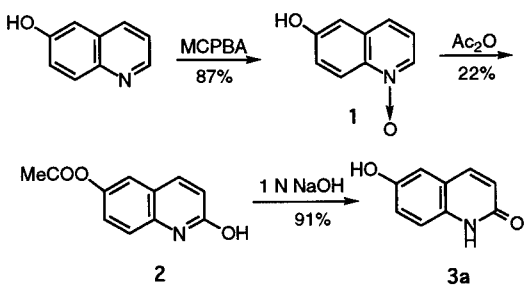


Coumarin



Quinolin-2(1*H*)-one

We have been investigating coumarin α-methylene-γ-butyrolactones as potential antiplatelet agents.[7,8] In an effort to expand these studies, i.e., to synthesize their bioisosteric isomers, we decided to prepare hydroxyquinolin-2(1*H*)-ones as the key precursors. Thus, 6-hydroxyquinoline was oxidized with 3-chloroperoxybenzoic acid (MCPBA)[9] to give 6-hydroxyquinoline 1-oxide **(1)**. Treatment of **1** with acetic anhydride afforded 6-acetoxy-2-hydroxyquinoline **(2)** which was hydrolyzed to provide the desired 6-hydroxyquinolin-2(1*H*)-one **(3a)**. Although these synthetic procedures are straightforward, the overall yield was only 17% (Scheme 1).



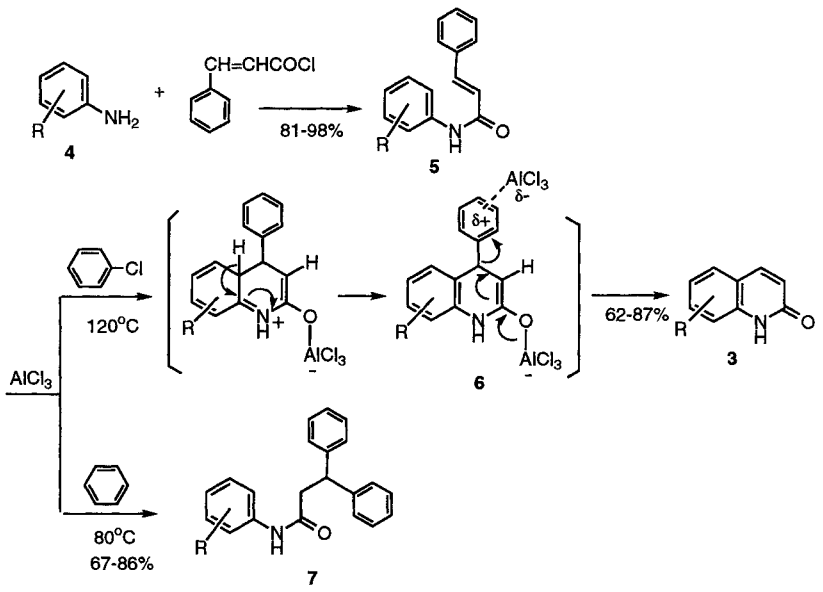
Scheme 1

An earlier report described the preparation of certain carbostyrils from the corresponding cinnamanilides.[10] Recently, Fujioka et al. also reported the preparation of 6-hydroxy-8-methylquinolin-2(1*H*)-one, a key precursor for many novel positive inotropic agents, from 4-methoxy-2-methylaniline via Schotten–Baumann reaction and an intramolecular Friedel–Crafts cyclization.[2] Although the cyclization mechanism which included an unusual dearylation was previously proposed by Manimaran et al.,[11] we believe that dearylation occurs via the enolate **6** (Scheme 2).

Following Fujioka's procedures, 4-methoxyaniline **(4a)** was reacted with cinnamoyl chloride to give 4-methoxycinnamanilide **(5a)** in 94% yield. Cyclization of **5a** with aluminum(III) chloride in chlorobenzene at 120 °C afforded the desired 6-hydroxyquinolin-2(1*H*)-one **(3a)** in 87% yield. To optimize the cyclization reaction, chlorobenzene was replaced with benzene as the reaction solvent to provide relatively mild conditions (refluxed at 80 °C). The ^{1}H NMR spectrum of the sole product isolated in this reaction showed a doublet at $\delta = 3.03$, a triplet at $\delta = 4.56$, and a multiplet at $\delta = 6.61-7.33$ corresponding to CH_2, CH, and aromatic protons, respectively. The ^{13}C NMR spectrum supported the ^{1}H NMR spectrum in confirming the presence of a methylene carbon resonance appearing at $\delta = 41.90$ and a tertiary carbon resonance at $\delta = 46.70$. The intermolecular Friedel–Crafts reaction of **5a** with benzene to give 4′-hydroxy-3,3-diphenylpropionanilide **(7a)** seems to be a reasonable deduction. In order to establish and to further confirm this novel reaction, 3-methoxyaniline **(4b)**, 2-methoxyaniline **(4c)**, and aniline **(4d)** were reacted with cinnamoyl chloride to give the respective cinnamanilides **5b–d**. Their treatment with aluminum(III) chloride in chlorobenzene (120 °C) or benzene (80 °C) gave exclusively quinolin-2(1*H*)-ones **3b–d** or 3,3-diphenylpropionanilides **7b–d**, respectively. The formation of **7b–d** in benzene indicated that an intermolecular Friedel–Crafts reaction of **5b–d** occurred prior to the relatively more facile intramolecular cyclization. A view of a single molecule of **7c** is given in the figure.

An intermolecular Friedel–Crafts reaction of **5c** occurred in aluminum(III) chloride/benzene. Accordingly, 4-methoxy-2-methylaniline was converted into 4-methoxy-2-methylcinnamanilide **(8)** which was treated with aluminum(III) chloride in refluxing benzene to give 4′-hydroxy-2′-methyl-3,3-diphenylpropionanilide **(9)** in 76% yield (Scheme 3). The structure of **9** was also established by ^{1}H NMR spectral and elemental analyses.

Melting points were determined on a YANACO micromelting point apparatus and are uncorrected. The UV absorption spectra were obtained on a Beckman UV-Visible spectrophotometer. ^{1}H and



5a R = 4-OMe **5b** R = 3-OMe **5c** R = 2-OMe **5d** R = H
7a R = 4-OH **7b** R = 3-OH **7c** R = 2-OH **7d** R = H
3a R = 6-OH **3b** R = 7-OH **3c** R = 8-OH **3d** R = H

Scheme 2

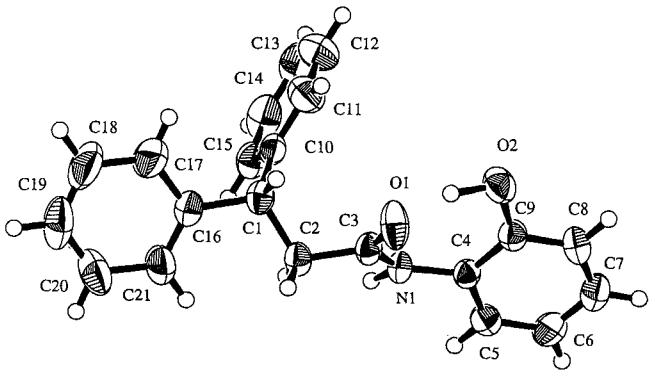
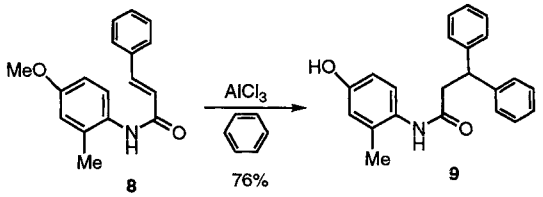


Figure. X-ray Crystallographic Structure of **7c**[12]



Scheme 3

^{13}C NMR spectra were obtained with a Varian Gemini-200 spectrometer. Chemical shifts are expressed in ppm (δ) with TMS as an internal standard. TLC was run on precoated (0.2 mm) silica gel 60 F-254 plates manufactured by EM Laboratories, Inc., and short-wave UV light (254 nm) was used to detect the UV absorbing spots. Elemental analyses were carried out on a Heraeus CHN-O-Rapid elemental analyzer and results were within +/− 0.4% of theoretical values.

6-Hydroxyquinoline 1-Oxide (1):
To a solution of 6-hydroxyquinoline (2.90 g, 20 mmol) in EtOAc (300 mL) was added MCPBA (4.48 g, 26 mmol). The mixture was stirred at r.t. for 30 min and then poured into 1.0 N $NaHCO_3$ (100 mL). The resulting precipitate was collected, crystallized from MeOH/Et_2O (1:10) to afford **1** (2.8 g, 87%) as white needle crystals; mp 229–230 °C.

^{1}H NMR (DMSO-d_6): δ = 7.25–8.43 (m, 6H, arom H), 10.44 (br s, 1H, OH).

^{13}C NMR (DMSO-d_6): δ = 109.20, 120.76, 122.02, 122.16, 123.75, 132.03, 132.60, 135.64, 157.29.

Anal. Calcd for $C_9H_7NO_2 \cdot 0.125\ H_2O$: C, 66.15; H, 4.47; N, 8.57. Found: C, 66.38; H, 4.33; N, 8.53.

6-Acetoxy-2-hydroxyquinoline (2):
A mixture of **1** (1.62 g, 10 mmol) in Ac_2O (30 mL) was heated at reflux for 2 h (monitored by TLC). After cooling, it was poured into ice-water (100 mL) and extracted with CH_2Cl_2 (4 × 60 mL). The extracts were combined, washed with water, dried (Na_2SO_4), and evaporated to give a brown solid which was crystallized from EtOAc to give **2** (0.45 g, 22%) as yellow crystals; mp 199–200 °C.

^{1}H NMR (DMSO-d_6): δ = 2.29 (s, 3H, Me), 6.55 (d, J = 9.6 Hz, 3-H), 7.30–7.47 (m, 3H, arom H), 7.90 (d, J = 9.6 Hz, 4-H), 11.85 (br s, 1H, OH).

^{13}C NMR (DMSO-d_6): δ = 20.76 (Me), 116.06, 119.36, 119.91, 122.70, 124.63, 136.65, 139.62, 144.61, 161.75,169.46.

Anal. Calcd for $C_{11}H_9NO_3 \cdot 0.125\ H_2O$: C, 64.31; H, 4.54; N, 6.82. Found: C, 64.37; H, 4.49; N, 6.86.

6-Hydroxyquinolin-2(1*H*)-one (3a):
Method A: To a stirred suspension of **2** (0.41 g, 2 mmol) in H_2O (20 mL) was added 1.0 N NaOH (5 mL). After completion of the reaction (1.5 h, monitored by TLC), the mixture was diluted with water and washed with Et_2O. The aqueous layer was acidified with 6N HCl and the resulting precipitate crystallized from MeOH to give **3a** (0.29 g, 91%) as white crystals; mp 299–300 °C.

UV: λ_{max} (log ε) = 232 (4.36) (0.1 N HCl/MeOH), 232 (4.57) (MeOH), 247 (4.53) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 6.44 (d, J = 10.0 Hz, 1H, 3-H), 6.98–7.20 (m, 3H, arom H), 7.78 (d, J = 10.0 Hz, 1H, 4-H), 9.46 (s, 1H), 11.55 (s, 1H).

^{13}C NMR (DMSO-d_6): δ = 111.43, 116.18, 119.75, 119.92, 122.00, 132.18, 139.63, 152.05 (arom C), 161.42 (C=O).

Anal. Calcd for $C_9H_7NO_2$: C, 67.07; H, 4.38; N, 8.69. Found: C, 66.68; H, 4.51; N. 8.50.

4-Methoxycinnamanilide (5a); Typical Procedure:
To a stirred solution of 4-methoxyaniline (2.46 g, 20 mmol), K_2CO_3 (4.15 g, 30 mmol), H_2O (40 mL), and acetone (20 mL) was added dropwise cinnamoyl chloride (4.10 g, 25 mmol) at 0 °C. The mixture was stirred at 0 °C for 0.5 h (monitored by TLC) and then poured into ice-water (100 mL). The resulting precipitate was collected and crystallized from CH_2Cl_2/Et_2O to give **5a** (4.76 g, 94%); mp 151–152 °C.

UV: λ_{max} (log ε) = 220 (sh) (4.31), 291 (4.35) (0.1 N HCl/MeOH), 220 (sh) (4.31), 291 (4.36) (MeOH), 291 (4.36) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.74 (s, 3 H, MeO), 6.82 (d, J = 15.7 Hz, 1 H, vinylic H), 6.90–7.67 (m, 9 H, arom H), 7.58 (d, J = 15.7 Hz, 1 H, vinylic H), 10.09 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 55.10 (MeO), 113.89, 120.64, 122.37, 127.56, 128.92, 129.56, 132.39, 134.76, 139.55, 155.26 (arom C and vinylic C), 163.00 (C=O).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.84; H, 6.00; N, 5.57.
The same reaction sequence was adopted to prepare **5b–d**.

3-Methoxycinnamanilide **(5b)**: yield: 95%; mp 111–112 °C.

UV: λ_{max} (log ε) = 220 (sh) (4.58), 294 (4.55) (0.1 N HCl/MeOH), 220 (sh) (4.56), 294 (4.54) (MeOH), 294 (4.55) 0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.76 (s, 3 H, MeO), 6.64–7.66 (m, 9 H, arom H), 6.84 (d, J = 15.7 Hz, 1 H, vinylic H), 7.61 (d, J = 15.7 Hz, 1 H, vinylic H), 10.20 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 54.95 (MeO), 105.10, 108.76, 111.57, 122.24, 127.70, 129.00, 129.56, 129.76, 134.69, 140.21, 140.40, 159.53 (arom C and vinylic C), 163.54 (C=O).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.86; H, 5.97; N, 5.51.

2-Methoxycinnamanilide **(5c)**: yield: 98%; mp 122–123 °C.

UV: λ_{max} (log ε) = 221 (sh) (5.05), 275 (4.58) (0.1 N HCl/MeOH), 224 (sh) (4.98), 275 (4.50) (MeOH), 277 (4.52) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.88 (s, 3 H, MeO), 6.90–7.67 (m, 9 H, arom H), 7.22 (d, J = 15.7 Hz, 1 H, vinylic H), 7.57 (d, J = 15.7 Hz, 1 H, vinylic H), 9.35 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 55.67 (MeO), 111.06, 120.26, 121.45, 122.73, 124.27, 127.46, 127.70, 128.90, 129.60, 134.91, 139.94, 149.30 (arom C and vinylic C), 163.66 (C=O).
Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C 75.81; H, 6.03; N, 5.53.

Cinnamanilide **(5d)**: yield: 81%; mp 150–151 °C.
UV: λ_{max} (log ε) = 221 (sh) (4.72), 293 (4.63) (0.1 N HCl/MeOH), 221 (sh) (4.73), 293 (4.64) (MeOH), 284 (4.66) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 7.04–7.75 (m, 10 H, arom H), 6.86 (d, J = 15.8 Hz, 1 H, vinylic H), 7.62 (d, J = 15.8 Hz, 1 H, vinylic H), 10.22 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 119.20, 122.27, 123.31, 127.67, 128.75, 128.97, 129.72, 134.70, 139.24, 140.10 (arom C and vinylic C), 163.48 (C=O).

Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.79; H, 5.88; N, 6.30.

6-Hydroxyquinolin-2(1*H*)-one (3a); Typical Procedure:
Method B: $AlCl_3$ (3.2 g, 24 mmol) was added portionwise to a suspension of **5a** (1.01 g, 4 mmol) in chlorobenzene (30 mL) at 0 °C. The reaction mixture was gradually warmed to 120 °C and then stirred for 2 h. After the mixture had been poured into ice-water (100 mL), the resulting precipitate was collected. The crude solid thus obtained was chromatographed (silica gel, CH_2Cl_2/MeOH, 20:1) and then crystallized from MeOH to give **3a** (0.56 g, 87%). The same procedure was used to convert each of the compounds **5b–d** to **3b–d**, respectively.

7-Hydroxyquinolin-2(1H)-one **(3b)**: yield: 70%; mp > 300 °C.

UV: λ_{max} (log ε) = 251 (4.12), 337 (4.20) (0.1 N HCl/MeOH), 251 (3.79), 337 (4.12) (MeOH), 272 (3.83), 353 (4.37) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 6.22 (d, J = 10.0 Hz, 1 H, 3-H), 6.60–7.47 (m, 3 H, arom H), 7.74 (d, J = 10.0 Hz, 1 H, 4-H), 10.13 (s, 1 H), 11.52 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 99.84, 111.55, 112.40, 117.41, 129.27, 140.13, 140.77, 159.62 (arom C), 162.33 (C=O).

Anal. Calcd for $C_9H_7NO_2 \cdot 0.125\ H_2O$: C, 66.15; H, 4.47; N, 8.57. Found: C, 66.30; H, 4.34; N, 8.55.

8-Hydroxyquinolin-2(1H)-one **(3c)**: yield: 77%; mp 277–278 °C.
UV: λ_{max} (log ε) = 257 (4.45) (0.1 N HCl/MeOH), 256 (4.34) (MeOH), 273 (4.35) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 6.50 (d, J = 10.0 Hz, 1 H, 3-H), 6.98–7.14 (m, 3 H, arom H), 7.85 (d, J = 10.0 Hz, 1 H, 4-H), 10.29 (s, 1 H), 10.50 (s,1 H).

^{13}C NMR (DMSO-d_6): δ = 114.80, 117.84, 119.97, 121.88, 121.94, 128.07, 140.58, 144.07 (arom C), 161.50 (C=O).

Anal. Calcd for $C_9H_7NO_2 \cdot 0.125\ H_2O$: C, 66.15; H, 4.47; N, 8.57. Found: C, 66.25; H, 4.56; N, 8.31.

Quinolin-2(1H)-one **(3d)**: yield: 62%; mp 198–199 °C.
UV: λ_{max} (log ε) = 277 (3.73), 317 (3.72) (0.1 N HCl/MeOH), 269 (3.84), 328 (3.78) (MeOH), 260 (3.77), 3.30 (3.72) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 6.51 (d, J = 10.0 Hz, 1 H, 3-H), 7.13–7.67 (m, 4 H, arom H), 7.91 (d, J = 10.0 Hz, 1 H, 4-H), 11.74 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 115.08, 119.07, 121.69, 121.87, 127.82, 130.30, 138.85, 140.18 (arom C), 161.89 (C=O).

Anal. Calcd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.49; H, 4.82; N, 9.56.

4′-Hydroxy-3,3-diphenylpropionanilide (7a); Typical Procedure:
$AlCl_3$ (3.2 g, 24 mmol) was added portionwise to a suspension of **5a** (1.01 g, 4 mmol) in benzene (30 mL) at 0 °C. The reaction mixture was gradually warmed to 80 °C and then stirred for 4 h (monitored by TLC). The mixture was poured into ice-water (100 mL) and the resulting precipitate collected. The crude solid thus obtained was chromatographed (silica gel, CH_2Cl_2) and then crystallized from CH_2Cl_2/Et_2O to give **7a** (0.94 g, 74%); mp 169–170 °C.

UV: λ_{max} (log ε) = 254 (4.32) (0.1 N HCl/MeOH), 254 (4.46) (MeOH), 265 (4.22) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.03 (d, J = 8.0 Hz, 2 H, CH_2), 4.56 (t, J = 8.0 Hz, 1 H, CH), 6.61–7.33 (m, 14 H, arom H), 9.12 (s, 1 H), 9.68 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 41.90 (CH_2), 46.70 (CH), 114.93, 120.83, 126.12, 127.53 , 128.35, 130.74, 144.30, 153.17 (arom C), 168.35 (C=O).

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.34; H, 6.11; N, 4.44.

The same procedure was used to convert each of the compounds **5b–d**, and **8** to the respective **7b–d** and **9**.

3′-Hydroxy-3,3-diphenylpropionanilide **(7b)**: yield: 75%; mp 183–184 °C.

UV: λ_{max} (log ε) = 274 (4.12) (0.1 N HCl/MeOH), 274 (4.17) (MeOH), 295 (3.86) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.07 (d, J = 8.0 Hz, 2 H, CH_2), 4.57 (t, J = 8.0 Hz, 1 H, CH), 6.36–7.33 (m, 14 H, arom H), 9.30 (s, 1 H), 9.81 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 42.07 (CH_2), 46.63 (CH), 106.21, 109.76, 110.16, 126.14, 127.51, 128.36, 129.21, 140.06, 144.24, 157.48 (arom C), 168.94 (C=O).

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.42; H, 6.08; N, 4.43.

2'-Hydroxy-3,3-diphenylpropionanilide **(7c)**: yield: 86%; mp 170–171 °C.

UV: λ_{max} (log ε) = 240 (sh) (4.18), 284 (3.90) (0.1 N HCl/MeOH), 238 (sh) (4.21), 284 (3.90) (MeOH), 254 (sh) (4.15), 308 (4.07) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.22 (d, J = 8.0 Hz, 2 H, CH_2), 4.56 (t, J = 8.0 Hz, 1 H, CH), 6.69–7.63 (m, 14 H, arom H), 9.27 (s, 1 H), 9.69 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 41.51 (CH_2), 46.87 (CH), 115.63, 118.86, 121.84, 124.40, 126.14, 126.29, 127.58, 128.34, 144.28, 147.50 (arom C), 169.74 (C=O).

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.21; H, 6.04; N, 4.45.

3,3-Diphenylpropionanilide **(7d)**: yield: 67%; mp 175–176 °C.

UV: λ_{max} (log ε) = 220 (sh) (4.57), 235 (4.46) (0.1 N HCl/MeOH), 220 (sh) (4.56), 235 (4.49) (MeOH), 235 (4.48) (0.1 N NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.10 (d, J = 8.0 Hz, 2 H, CH_2), 4.59 (t, J = 8.0 Hz, 1 H, CH), 6.95–7.51 (m, 15 H, arom H), 9.96 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 42.04 (CH_2), 46.63 (CH), 119.00, 123.03, 126.16, 127.51, 128.38, 128.60, 139.05, 144.22 (arom C), 169.10 (C=O).

Anal. Calcd for $C_{21}H_{19}NO \cdot 0.125\,H_2O$: C, 83.07; H, 6.39; N, 4.61. Found: C, 83.19; H, 6.31; N, 4.66.

4-Methoxy-2-methylcinnamanilide (8):
Prepared from 4-methoxy-2-methylaniline according to a known procedure.[2] Yield: 73%; mp 195–196 °C.

UV: λ_{max} (log ε) = 220 (sh) (4.49), 280 (4.55) (0.1 N HCl/MeOH), 220 (sh) (4.48), 280 (4.54) (MeOH), 280 (4.57) (0.1 N NaOH/MeOH).

^{13}C NMR (DMSO-d_6): δ = 18.10 (Me), 55.09 (MeO), 111.17, 115.37, 122.29, 126.15, 127.59, 128.94, 129.24, 129.55, 133.30, 134.85, 139.55, 156.62 (arom C and vinylic C), 163.60 (C=O).

4'-Hydroxy-2'-methyl-3,3-diphenylpropionanilide (9):
Prepared according to the procedure given for **7a**; yield: 76%; mp 164–165 °C.

UV: λ_{max} (log ε) = 220 (sh) (4.94), 273 (4.20) (0.1 N HCl/MeOH), 220 (sh) (4.97), 273 (4.17) (MeOH), 272 (4.38) (0.1 N, NaOH/MeOH).

^{1}H NMR (DMSO-d_6): δ = 1.78 (s, 3 H, Me), 3.03 (d, J = 8.0 Hz, 2 H, CH_2), 4.54 (t, J = 8.0 Hz, 1 H, CH), 6.44–7.36 (m, 13 H, arom H), 9.10 (s, 1 H), 9.15 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 17.55 (Me), 41.43 (CH_2), 47.06 (CH), 112.37, 116.39, 126.14, 126.94, 127.49, 127.60, 128.31, 134.06, 144.18, 154.85 (arom C), 168.99 (C=O).

Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.70; H, 6.42; N, 4.25.

X-ray Structural Determination of 7c:[12]
Crystallographic details: $C_{21}H_{19}NO_2$, M = 317.39, monoclinic, space group $P2_{1/c}$, a = 16.321(2) Å, b = 9.089(3) Å, c = 12.111(4) Å, β = 110.65(1)°, V = 1681.1(7) Å^3, Z = 4. $D_{calc.}$ = 1.254 g cm^{-3}. Crystal dimensions 0.33 × 0.41 × 0.50 mm. FOOO = 672.00. μ(MoKα) = 0.80 cm^{-1}. Radiation: MoKα (λ = 0.71069 Å), ω-2θ scanning technique. The crystal structure was solved by direct methods. Full-matrix least-squares refinement of atomic positional and thermal parameters (anisotropic C, N, O; fixed H contributions) converged at R = 0.041 (R_w = 0.040) for 2812 reflections.

We gratefully acknowledge the financial support from National Science Council of the Republic of China.

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(12) Selected bond lengths (Å): C1–C2 1.539(4); C1–C10 1.518(4); C1–C16 1.525(4); C2–C3 1.512(4); N1–C3 1.336(3); N1–C4 1.435(3); O1–C3 1.232(3). Selected bond angles (degree): C1–C2–C3 111.9(2); C1–C10–C11 121.1 (3); C1–C10–C15 120.9(3); C2–C1–C10 111.2(2); C2–C1–C16 112.4(2); C3–N1–C4 129.0(2); C10–C1–C16 112.0(2); N1–C3–C2 115.9(3); N1–C4–C5 115.9(2); N1–C4–C9 124.9(3); O1–C3–C2 120.1(3). Supplementary material: Atomic coordinates, bond lengths and angles, torsion angles and thermal parameters have been deposited at the Crystallographic Center of National Sun Yatsen University.