Electronic Supplementary Information (ESI)

[4-(3,4-Dimethoxyphenyl)-3,6-dimethyl-2-phenyl-3,4-dihydroquinolin-1(2H)-yl](furan-2-yl)methanone

Sandra-Milena Bonilla-Castañeda, Andrés-Felipe Villamizar-Mogotocoro and Vladimir V. Kouznetsov*

Laboratorio de Química Orgánica y Biomolecular, CMN, Universidad Industrial de Santander, Parque Tecnológico Guatiguará, Km 2 vía refugio, Piedecuesta, A.A. 681011, Colombia.

*E-mail: kouznet@uis.edu.co

Contents

1 General information ........................................................................................................................................2
2 Experimental procedures .............................................................................................................................2
3 Characterization data of products ..............................................................................................................4
4 Copies of IR and NMR spectra of products .............................................................................................6
1   General information

The reagents and solvents used in the synthesis of the intermediate and final compounds were of purity grade for synthesis. The composition and monitoring of the reactions, as well as the preliminary analysis of the purity of the synthesized compounds, were carried out by thin-layer chromatography (TLC) on Silufol UV254 plates of 0.25 mm thickness, revealed in a UV light chamber of 254 nm or in an ethanolic solution of phosphomolybdic-sulfuric acids.

The melting points of the products were determined in a Fisher–Jöns melting point apparatus, the values were not corrected, reporting the average of three measurements; the elucidation of molecular structures was performed by instrumental methods.

The acquisition of nuclear magnetic resonance spectra $^1$H, $^{13}$C-APT, and 2D variants was performed on a Bruker Avance–400 spectrometer (400 MHz for $^1$H and 100 MHz for $^{13}$C) using deuterated chloroform (CDCl$_3$, 99.8% Merck®) as a solvent. Chemical shift values ($\delta$) are expressed in ppm. In some $^1$H NMR spectra, tetramethylsilane, TMS, was used as the internal standard, and in others, the scale was adjusted from the residual chloroform signal (7.26 ppm). Similarly, the $^{13}$C-APT spectra are scaled from the signal characteristic of the solvent (CDCl$_3$) and the phase of the signals is assigned as (+) positive phase, (-) negative phase. Coupling constants ($^n$J) are described at $n$ bonds and are given in Hz; the multiplicity of signals is expressed by the following abbreviations: (s) singlet, (br s) broad singlet, (d) doublet, (dd) doublet of doublets, (ddd) doublet of doublet of doublets, ($td$ ap) apparent triplet of doublets, ($t$ ap) apparent triplet and (m) multiplet.

2   Experimental procedures

Step. 1 Synthesis of 4-(3,4-dimethoxyphenyl)-3,6-dimethyl-2-phenyl-1,2,3,4-tetrahydroquinoline 4.

![Chemical Diagram]
In clean dry, 10 mL vial, choline chloride (ChCl, 8 mmol) and zinc chloride (ZnCl₂, 16 mmol) were added as eutectic mixture. The mixture was heated at 110 °C to obtain a liquid media. Then, p-toluidine 1 (1 mmol), trans-methyl-isoeugenol 2 (1.5 mmol) and benzaldehyde 3 (1.5 mmol) were added. Before 3 h of reaction time, the formation of 2,4-diaryl-tetrahydroquinoline 4 was confirmed by TLC. The reaction mixture was diluted with ethyl acetate and was washed with distilled water (50 mL). The reaction crude was placed in an Erlenmeyer flask over anhydrous sodium sulfate. Finally, the solvent was removed by distillation and the organic residue that remained was purified by column chromatography on silica gel, using an isocratic mixture of ethyl acetate–petroleum ether at 20 % as eluent.

**Step. 2 Synthesis of** [4-(3,4-dimethoxyphenyl)-3,6-dimethyl-2-phenyl-3,4-dihydroquinolin-1(2H)-yl](furan-2-yl)methanone 6.

![Chemical diagram]

In a clean dry, 20 mL vial, THQ 4 (1 mmol), 2-furoyl chloride 5 (2 mmol), triethylamine (2 mmol), and 5 mL of dichloromethane were added. The reaction was carried out at room temperature for 1 h. The reaction was carried out at room temperature for 1 h. The solvent was removed by distillation and crude was purified by column chromatography on silica gel using an isocratic mixture of ethyl acetate–petroleum ether at 30 % as eluent.
3 Characterization data of products

4-(3,4-Dimethoxyphenyl)-3,6-dimethyl-2-phenyl-1,2,3,4-tetrahydroquinoline 4.

Yield. 79 % (0.083 g, 0.222 mmol). C_{29}H_{27}NO_2 (373.50 g/mol) as a white solid, Mp = 157-159 °C, R_f = 0.44 (20% ethyl acetate–petroleum ether). IR [ATR, v (cm^{-1})] = 3389, 3010, 2958, 2936, 2902, 2834, 1509, 1469, 1258, 1136, 1025, 866, 817, 694, 553. ^1H-NMR (400 MHz, CDCl_3) δ ppm = 7.44 (dd, J = 8.1, 1.2 Hz, 2H), 7.40 - 7.31 (m, 3H), 6.86 - 6.79 (m, 3H), 6.70 (d, J = 1.7 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 6.41 (s, 1H), 4.10 (d, J = 9.9 Hz, 1H), 3.96 (s, 1H), 3.90 (s, 3H), 3.85 (s, 3H), 3.71 (d, J = 10.9 Hz, 1H), 2.25 - 2.14 (m, 1H), 2.10 (s, 3H), 0.58 (d, J = 6.5 Hz, 3H).

^13C-APT (100 MHz, CDCl_3) δ ppm = 149.16 (+), 147.70 (+), 143.06 (+), 142.83 (+), 137.23 (+), 130.49 (-), 128.65 (-), 128.04 (-), 127.98 (-), 127.70 (-), 126.85 (+), 125.68 (+), 122.18 (-), 113.82 (-), 112.04 (-), 110.96 (-), 64.28 (-), 56.09 (-), 55.95 (-), 52.42 (-), 41.86 (-), 20.67 (-), 16.66 (-). Anal. Calcd. (%) for [C_{29}H_{27}NO_2]: C, 80.40; H, 7.29; N, 3.75; found (%): C, 80.23; H, 7.37; N, 3.58.

[4-(3,4-Dimethoxyphenyl)-3,6-dimethyl-2-phenyl-3,4-dihydroquinolin-1(2H)-yl](furan-2-yl)methanone 6.

Yield. 92 % (0.103 g, 0.220 mmol). C_{30}H_{30}NO_4 (467.57 g/mol), as a white solid, Mp = 194-195 °C, R_f = 0.19 (30% ethyl acetate–petroleum ether). IR [ATR, v (cm^{-1})] = 3105, 2979, 2944, 2926, 2896, 2831, 1638, 1578, 1515, 1493, 1348, 1251, 1165, 1029, 751, 707. ^1H-NMR (400 MHz, CDCl_3) δ ppm = 7.32 - 7.25 (m, 6H, p-H, 7-H, 8-H, 5'-H, 6'-H, 5''-H), 6.93 (t, J = 8.3 Hz, 2H, m-H, m'-H), 6.82 (t, J = 7.0 Hz, 2H, o-H, o'-H), 6.74 (s, 1H, 5-H), 6.60 (s, 1H, 2'-H), 6.39 (d, J = 3.5 Hz, 1H, 3''-H), 6.29 (dd, J = 3.5, 1.7 Hz, 1H, 4''-H), 5.13 (d, J = 8.7 Hz, 1H, 2-H), 3.95 (s, 3H, 3'-OCH_3), 3.87 (s, 3H, 4'-OCH_3), 3.63 (d, J = 11.6 Hz, 1H, 4'-H), 2.27 (s, 3H, 6-CH_3), 2.21 (ddd, J = 11.6, 8.6, 6.5 Hz, 1H, 1'-H), 0.97 (d, J = 6.5 Hz, 3H, 3'-CH_3). ^13C-APT (100 MHz, CDCl_3) δ ppm = 159.39 (+), 149.30 (+), 148.11 (+), 147.71 (+), 143.91 (-), 143.73 (+), 138.60 (+), 135.90 (+), 135.60 (+), 131.47 (+), 128.43 (-), 127.69 (-), 127.22 (-), 127.18 (-), 126.78 (-), 125.31 (-), 116.1 (-), 111.46 (-), 111.02 (-), 65.73 (-), 56.10 (-), 55.98 (-), 49.52 (-), 47.48 (-), 21.46 (-), 18.21 (-). Anal. Calcd. (%) for [C_{30}H_{30}NO_4]: C, 77.07; H, 6.25; N, 3.00; found (%): C, 77.35; H, 6.12; N, 3.11. X-ray diffraction analysis data of furan-2-carboxamide (6) with the (2S,3S,4R)-configuration: Colorless crystal obtained from a slow chloroform evaporation, C_{30}H_{30}NO_4 (MW = 467.57 g/mol), triclinic space
group P–1, unit cell dimensions: $a = 9.9318(3)$, $b = 12.1531(5)$, $c = 12.3695(7)$ Å, $\alpha = 64.515(5)^\circ$, $\beta = 79.358(4)^\circ$, $\gamma = 70.990(3)^\circ$, $V = 272.51(11)$ Å³, $Z = 2$, $T = 293$ K.
4 Copies of IR and NMR spectra of products

Figure S1. FT–IR spectrum of compound 4.
Figure S2. $^1$H NMR spectrum of compound 4 (400 MHz, CDCl$_3$).
Figure S3. $^{13}$C NMR spectrum of compound 4 (100 MHz, CDCl$_3$).
Figure S4. $^{13}$C-APT NMR spectrum of compound 4 (100 MHz, CDCl₃).
Figure S5. FT–IR spectrum of compound 6.
Figure S6. $^1$H NMR spectrum of compound 6 (400 MHz, CDCl$_3$).
Figure S7. $^{13}$C NMR spectrum of compound 6 (100 MHz, CDCl$_3$).
Figure S8. $^{13}$C-APT NMR spectrum of compound 6 (100 MHz, CDCl$_3$).