SYNTHESIS OF 4-ARYL-2,7,7-TRIMETHYL-5-OXO-N-PHENYL-1,4,5,6,7,8-HEXAHYDROQUINOLINE-3-CARBOXAMIDES

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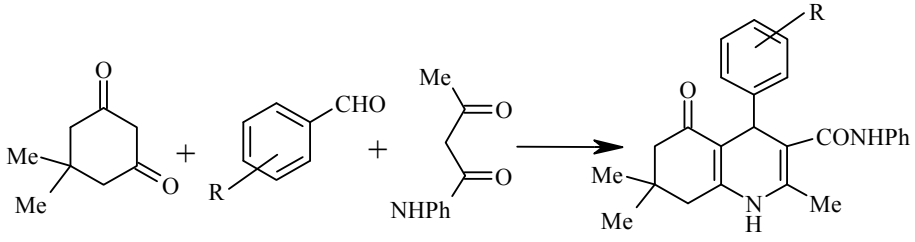
It has been found that holding a mixture of dimedone, an aryl aldehyde, acetoacetanilide, and ammonium acetate at 150-160ºC without solvent for 10-20 min gives 4-aryl-2,7,7-trimethyl-5-oxo-N-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamides.



1a–e

1 a R= H, **b** R = 4-Cl, **c** R = 4-OMe, **d** R = 3-NO_2, **e** R = 4-NO_2

The compounds **1a-e** obtained are light-yellow, crystalline materials which are soluble in DMF and DMSO, in ethanol upon heating, and insoluble in water.

Their ^{1}H NMR spectra show signals for the aromatic protons and the groups bonded to them as well as singlet signals for the protons of the two 7-CH_3 groups at 0.89-0.92 and 1.03-1.06, singlet for the protons of the 2-CH_3 group at 2.05-2.09 ppm, two doublet for the protons of H_A-8 and H_B-8 at 1.98-2.00 and 2.14-2.17 (J = 15.8-16.5 Hz), H_A-6 and H_B-6 at 2.29-2.34 and 2.38-2.42 (J = 16.5-17.4 Hz), an H-4 proton singlet at 4.96-5.10, and a signal for the heterocyclic NH proton at 8.58-8.82 ppm.

The IR spectra of compounds **1a-e** show absorption stretching bands for the amide carbonyl at 1688, a carbonyl group at 1640, C=C double bond at 1604, amide NH at 3128 and heterocyclic NH group at 3264 cm^{-1}.

The mass spectrum of compound **1a** shows the presence of a molecular ion peak $[M-H]^+$ with *m/z* 386 and fragment ion peaks for $[M-Ph]^+$ and $[M-PhNH]^+$ confirming this structure.

IR spectra were taken on a Specord M-80 spectrometer using vaseline oil. ^{1}H NMR spectra were recorded on a Bruker DRX 500 instrument (500 MHz) using DMSO-d_6 and with TMS as internal standard. Mass spectra were obtained on an Agilent 7890A/5975C spectrometer (ionization energy 70 eV).

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2,7,7-Trimethyl-5-oxo-N,4-diphenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (1a). A mixture of dimedone (1.4 g, 0.01 mol), benzaldehyde (1.06 ml, 0.01 mol), acetoacetanilide (1.7 g, 0.01 mol), and ammonium acetate (0.77 g, 0.01 mol) was held for 10-20 min at 150-160ºC until gas evolution ceased and the reaction mixture had solidified. After cooling it was treated with ethanol, filtered, and recrystallized from alcohol. Yield 2.5 g (89%); mp 243-245ºC. IR spectrum, ν, cm^{-1}: 1624 (CON), 1680 (C=O), 3264 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.90, 1.03 (6H, 2s, 7-CH_3); 2.06 (3H, s, 2-CH_3); 1.99 (1H, d, *J* = 16.1, H_A-8); 2.15 (1H, d, *J* = 16.1, H_B-8); 2.31 (1H, d, *J* = 16.8, H_A-6); 2.40 (1H, d, *J* = 16.8, H_B-6); 4.96 (1H, s, H-4); 7.16-7.54 (10H, m, 2 C_6H_5); 8.61 (1H, s, NH); 9.43 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 386 $[M]^+$ (36), 309 $[M-Ph]^+$ (100), 294 $[M-PhN]^+$ (83). Found, %: C 77.87; H 6.82; N 7.19. $C_{25}H_{26}N_2O_2$. Calculated, %: C 77.69; H 6.78; N 7.25. M = 386.

Compounds 1b-e were obtained similarly.

4-(4-Chlorophenyl)-2,7,7-trimethyl-5-oxo-N-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (1b). Yield 3.0 g (92%); mp 252-254ºC. IR spectrum, ν, cm^{-1}: 1640 (CON), 1688 (C=O), 3264 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.89, 1.03 (6H, 2s, 7-CH_3); 2.06 (3H, s, 2-CH_3); 1.99 (1H, d, *J* = 16.2, H_A-8); 2.15 (1H, d, *J* = 16.2, H_B-8); 2.30 (1H, d, *J* = 17.1, H_A-6); 2.40 (1H, d, *J* = 17.2, H_B-6); 4.96 (1H, s, H-4); 6.95-7.54 (9H, m, C_6H_5, C_6H_4Cl); 8.68 (1H, s, NH); 9.49 (1H, s, NH). Found, %: C 71.38; H 5.84; N 6.72. $C_{25}H_{25}ClN_2O_2$. Calculated, %: C 71.33; H 5.99; N 6.65.

4-(4-Methoxyphenyl)-2,7,7-trimethyl-5-oxo-N-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (1c). Yield 2.8 g (94%); mp 248-250ºC. IR spectrum, ν, cm^{-1}: 1640 (CON), 1688 (C=O), 3128 (NH), 3264 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.91, 1.03 (6H, 2 s, 7-CH_3); 2.05 (3H, s, 2-CH_3); 1.98 (1H, d, *J* = 15.8, H_A-8); 2.14 (1H, d, *J* = 15.8, H_B-8); 2.29 (1H, d, *J* = 16.5, H_A-6); 2.38 (1H, d, *J* = 16.5, H_B-6); 3.67 (3H, s, OCH_3); 4.91 (1H, s, H-4); 6.95-7.25 (9H, C_6H_5, C_6H_4OMe); 8.58 (1H, s, NH), 9.39 (1H, s, NH). Found, %: C 74.73, 75.12; H 6.57, 7.01; N 6.65, 6.91. $C_{26}H_{28}N_2O_3$. Calculated, %: C 74.98; H 6.78; N 6.73.

2,7,7-Trimethyl-4-(3-nitrophenyl)-5-oxo-N-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (1d). Yield 2.75 g (83%); mp 208-210ºC. IR spectrum, ν, cm^{-1}: 1660 (CON), 1672 (C=O), 3208 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.90, 1.04 (6H, 2s, 7-CH_3); 2.08 (3H, s, 2-CH_3); 2.00 (1H, d, *J* = 16.1, H_A-8); 2.17 (1H, d, *J* = 16.1, H_B-8); 2.34 (1H, d, *J* = 17.4, H_A-6); 2.42 (1H, d, *J* = 17.4, H_B-6); 5.10 (1H, s, H-4); 7.22-7.53 (9H, m, C_6H_5, $C_6H_4NO_2$); 8.82 (1H, s, NH); 9.57 (1H, s, NH). Found, %: C 69.81; H 5.77; N 9.55. $C_{25}H_{25}N_3O_4$. Calculated, %: C 69.59; H 5.84; N 9.74.

2,7,7-Trimethyl-4-(4-nitrophenyl)-5-oxo-N-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (1e). Yield 2.7 g (83%); mp 245-247ºC. IR spectrum, ν, cm^{-1}: 1692 (CON), 1712 (C=O), 3288 (NH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.89, 1.04 (6H, 2s, 7-CH_3); 2.08 (3H, s, 2-CH_3); 1.99 (1H, d, *J* = 16.5, H_A-8); 2.16 (1H, d, *J* = 16.5, H_B-8); 2.33 (1H, d, *J* = 17.2, H_A-6); 2.40 (1H, d, *J* = 17.2, H_B-6); 5.09 (1H, s, H-4); 7.20-7.53 (9H, m, C_6H_5, $C_6H_4NO_2$); 8.80 (1H, s, NH); 9.57 (1H, s, NH). Found, %: C 69.81; H 5.77; N 9.55. $C_{25}H_{25}N_3O_4$. Calculated, %: C 69.59; H 5.84; N 9.74.