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Synthesis of 4,*N*-Diaryl-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamides

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Abstract—Cyclohexane-1,3-dione reacted with substituted benzaldehydes and *N*-arylacetoacetamides in the presence of ammonium acetate under solvent-free conditions (150–160°C, 10–20 min) to give the corresponding 4,*N*-diaryl-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamides. The product structure was determined by IR and ^{1}H NMR spectroscopy and mass spectrometry.

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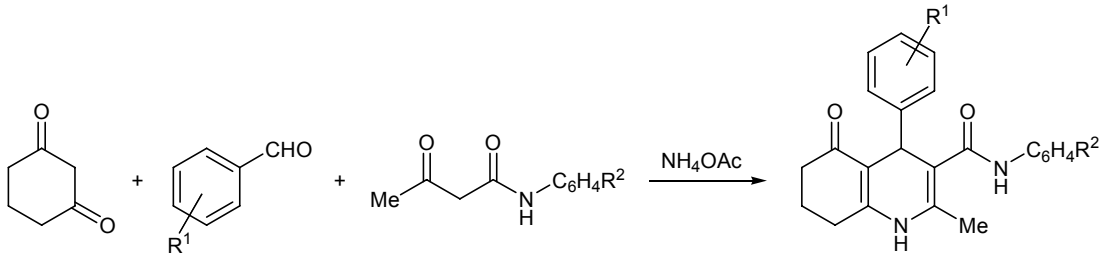
The three-component reaction of dimedone (5,5-dimethylcyclohexane-1,3-dione) with ethyl acetoacetate and benzaldehyde in the presence of ammonium acetate was reported in [1]. *N*-(4-Methylpyridin-2-yl)-3-oxobutanamide was also used in analogous reaction [2]. While continuing studies in this line, we examined three-component condensation of cyclohexane-1,3-dione with substituted benzaldehydes and *N*-arylacetoacetamides under similar conditions.

By heating a mixture of cyclohexane-1,3-dione, aromatic aldehyde, *N*-arylacetoacetamide, and ammonium acetate at 150–160°C over a period of 10–20 min in the absence of solvent we obtained the corresponding 4,*N*-diaryl-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamides **Ia**–**Ii** (Scheme 1). Compounds **Ia**–**Ii** were isolated as light yellow crystalline substances which were soluble in dimethylformamide and dimethyl sulfoxide and in ethanol on heating and insoluble in water. The ^{1}H NMR spectra of **Ia**–**Ii** contained signals from protons in the aromatic rings and substituents attached thereto, multiplets from protons in positions *7*, *8*, and *6* of the quinoline ring (δ 1.71–1.87, 1.84–1.98, and 2.11–2.35 ppm, respectively), a singlet from the 2-methyl group at δ 2.03–2.09 ppm, a singlet from 4-H at δ 4.91–5.15 ppm, and a signal from the NH proton in the heteroring at δ 8.58–9.72 ppm. Compounds **Ia**–**Ii** displayed in the IR spectra absorption bands due to stretching vibrations of the amide carbonyl group at 1638–1678 cm^{-1}, C^5=O carbonyl group at 1624–1634 cm^{-1}, and NH group at 3200–3288 cm^{-1}. In the mass spectra of **Ib** and **If** we observed the molecular ion peaks $[M - H]^+$ with *m*/*z* 386 (I_{rel} 36%) and 406 (I_{rel} 33%), respectively, as well as fragment ion peaks which were consistent with the assumed structure.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-80 spectrometer from samples dispersed in mineral oil.

Scheme 1.



Ia–Ii

$R^1 = R^2 = H$ (**a**); R^1 = 4-Cl, $R^2 = H$ (**b**); R^1 = 4-O_2N, $R^2 = H$ (**c**); R^1 = 3-O_2N, $R^2 = H$ (**d**); $R^1 = H$, R^2 = 2-Me (**e**); R^1 = 4-Cl, R^2 = 2-Me (**f**); R^1 = 3-O_2N, R^2 = 2-Me (**g**); R^1 = 4-O_2N, R^2 = 2-Me (**h**); R^1 = 4-MeO, R^2 = 2-Me (**i**).

The ^{1}H NMR spectra were measured on a Bruker DRX-500 instrument at 500.13 MHz using DMSO-d_6 as solvent and tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 mass spectrometer.

2-Methyl-5-oxo-4,*N*-diphenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ia). A mixture of 1.12 g (0.01 mol) of cyclohexane-1,3-dione, 1.06 ml (0.01 mol) of benzaldehyde, 1.70 g (0.01 mol) of acetoacetanilide, and 0.77 g (0.01 mol) of ammonium acetate was heated for 10–20 min at 150–160°C until gaseous products no longer evolved and the mixture solidified. The resulting material was cooled and treated with ethanol, and the precipitate was filtered off and recrystallized from ethanol. Yield 2.5 g (69%), mp 250–252°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1664 (C=O, amide), 1632 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.75–1.82 m (2H, 7-H), 1.87–1.95 m (2H, 8-H), 2.03 s (3H, CH_3), 2.15–2.26 m (2H, 6-H), 4.99 s (1H, 4-H), 6.97–7.56 m (10H, C_6H_5), 8.75 s (1H, NH), 9.53 s (1H, NH). Found, %: C 76.86; H 6.00; N 7.87. $C_{23}H_{22}N_2O_2$. Calculated, %: C 77.07; H 6.19; N 7.82.

Compounds **Ib**–**Ii** were synthesized in a similar way.

4-(4-Chlorophenyl)-2-methyl-5-oxo-*N*-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ib). Yield 2.1 g (53%), mp 243–245°C. IR spectrum, ν, cm^{-1}: 3208 (NH), 1663 (C=O, amide), 1632 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.73–1.85 m (2H, 7-H), 1.91–1.96 m (2H, 8-H), 2.02 s (3H, CH_3), 2.11–2.32 m (2H, 6-H), 4.96 s (1H, 4-H), 6.98–7.53 m (9H, C_6H_5, C_6H_4), 8.81 s (1H, NH), 9.58 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 392 (36) [*M* – H]$^+$, 300 (100) [*M* – NHPh]$^+$, 281 (83) [*M* – PhNH]$^+$, 272 (16) [*M* – CONHPh]$^+$. Found, %: C 70.01; H 5.69; N 7.05. $C_{23}H_{21}ClN_2O_2$. Calculated, %: C 70.31; H 5.93; N 7.13. *M* 392.

2-Methyl-4-(4-nitrophenyl)-5-oxo-*N*-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ic). Yield 2.7 g (67%), mp 239–241°C. IR spectrum, ν, cm^{-1}: 3208 (NH), 1672 (C=O, amide), 1632 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.71–1.82 m (2H, 7-H), 1.87–1.96 m (2H, 8-H), 2.06 s (3H, CH_3), 2.11–2.32 m (2H, 6-H), 5.10 s (1H, 4-H), 6.95–8.13 m (9H, C_6H_5, C_6H_4), 8.92 s (1H, NH), 9.72 s (1H, NH). Found, %: C 68.30; H 5.07; N 10.65. $C_{23}H_{21}N_3O_4$. Calculated, %: C 68.47; H 5.25; N 10.47.

2-Methyl-4-(3-nitrophenyl)-5-oxo-*N*-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Id). Yield 2.5 g (62%), mp 120–122°C. IR spectrum, ν, cm^{-1}: 3288 (NH), 1678 (C=O, amide), 1634 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.72–1.86 m (2H, 7-H), 1.87–1.92 m (2H, 8-H), 2.08 s (3H, CH_3), 2.11–2.33 m (2H, 6-H), 5.15 s (1H, 4-H), 6.97–8.10 m (9H, C_6H_5, C_6H_4), 8.97 s (1H, NH), 9.65 s (1H, NH). Found, %: C 68.30; H 5.07; N 10.65. $C_{23}H_{21}N_3O_4$. Calculated, %: C 68.47; H 5.25; N 10.47.

2-Methyl-*N*-(2-methylphenyl)-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ie). Yield 2.3 g (62%), mp 188–190°C. IR spectrum, ν, cm^{-1}: 3228 (NH), 1675 (C=O, amide), 1633 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.72–1.82 m (2H, 7-H), 1.87–1.95 m (2H, 8-H), 2.06 s (3H, CH_3), 2.11–2.32 m (2H, 6-H), 2.32 s (3H, C**H**$_3$C$_6$H$_4$), 4.95 s (1H, 4-H), 6.77–7.25 m (9H, C_6H_5, C_6H_4), 8.57 s (1H, NH), 8.85 s (1H, NH). Found, %: C 77.20; H 6.71; N 7.25. $C_{24}H_{24}N_2O_3$. Calculated, %: C 77.39; H 6.49; N 7.52.

4-(4-Chlorophenyl)-2-methyl-*N*-(2-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (If). Yield 2.0 g (50%), mp 243–245°C. IR spectrum, ν, cm^{-1}: 3236 (NH), 1670 (C=O, amide), 1624 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.73–1.84 m (2H, 7-H), 1.86–1.95 m (2H, 8-H), 2.03 s (3H, CH_3), 2.11–2.30 m (2H, 6-H), 2.32 s (3H, C**H**$_3$C$_6$H$_4$), 4.91 s (1H, 4-H), 6.67–7.31 m (8H, C_6H_4, C_6H_4), 8.53 s (1H, NH), 8.75 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 406 (33) [*M* – H]$^+$, 299 (100), 281 (3). Found, %: C 70.40; H 5.87; N 6.65. $C_{24}H_{24}ClN_2O_2$. Calculated, %: C 70.67; H 5.93; N 6.87. *M* 406.

2-Methyl-*N*-(2-methylphenyl)-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ig). Yield 3.5 g (85%), mp 165–167°C. IR spectrum, ν, cm^{-1}: 3238 (NH), 1675 (C=O, amide), 1634 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.72–1.84 m (2H, 7-H), 1.85–1.95 m (2H, 8-H), 2.03 s (3H, CH_3), 2.11–2.30 m (2H, 6-H), 2.32 s (3H, C**H**$_3$C$_6$H$_4$), 4.81 s (1H, 4-H), 6.53–7.25 m (8H, C_6H_4), 8.43 s (1H, NH), 8.75 s (1H, NH). Found, %: C 68.80; H 5.27; N 9.95. $C_{24}H_{23}N_3O_4$. Calculated, %: C 69.07; H 5.55; N 10.07. *M* 417.

2-Methyl-*N*-(2-methylphenyl)-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ih). Yield 2.8 g (68%), mp 178–180°C. IR spectrum, ν, cm^{-1}: 3288 (NH), 1638 (C=O, amide), 1631 (C^5=O). ^{1}H NMR spectrum, δ, ppm: 1.73–1.85 m (2H, 7-H), 1.86–1.97 m (2H, 8-H), 2.07 s (3H, CH_3), 2.13–2.30 m (2H, 6-H), 2.33 s (3H, C**H**$_3$C$_6$H$_4$), 5.11 s (1H, 4-H), 6.77–7.98 m (8H, C_6H_4), 8.63 s (1H, NH),

8.97 s (1H, NH). Found, %: C 68.80; H 5.37; N 10.35. $C_{24}H_{23}N_3O_4$. Calculated, %: C 69.07; H 5.55; N 10.07.

4-(4-Methoxyphenyl)-2-methyl-*N*-(2-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (Ii). Yield 2.3 g (57%), mp 154–156°C. IR spectrum, ν, cm^{-1}: 3288 (NH), 1678 (C=O, amide), 1634 (C^5=O). ^1H NMR spectrum, δ, ppm: 1.72–1.84 m (2H, 7-H), 1.85–1.95 m (2H, 8-H), 2.03 s (3H, CH_3), 2.11–2.30 m (2H, 6-H), 2.32 s (3H, C**H**$_3C_6H_4$), 3.65 s (3H, OCH_3), 4.81 s (1H, 4-H), 6.53–7.25 m (8H, C_6H_4), 8.43 s (1H, NH), 8.75 s (1H, NH). Found, %: C 74.67; H 6.71; N 7.05. $C_{25}H_{26}N_2O_3$. Calculated, %: C 74.60; H 6.51; N 6.96.

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