

SHORT
COMMUNICATIONS

Convenient Preparation Procedure for 3-Alkyl-4-imino-3,4-dihydro-1*H*-quinazolin-2-ones

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3-Substituted 4-iminoquinazolin-2-ones are valuable building blocks for preparation of important for pharmacology derivatives of 2,4-dioxoquinazoline [1–3] and imidazo[1,2-*c*]quinazoline [4–6]. Syntheses of 3-aryl and 3-allyl-4-iminoquinazolinones are performed commonly by the reaction between anthranylonitriles and isocyanates involving formation of the corresponding ureas which further undergo cyclization under conditions of alkaline [7, 8] or enzymatic [9, 10] catalysis. However due to the limited range of aliphatic isocyanates this method is not applied to preparation of 3-alkyl-4-iminoquinazolinones. Nomoto *et al.* [11] and Ohshima *et al.* [12] for the synthesis of some heteryl-substituted 3-methyl- and fused 3-benzyl-4-iminoquinazolinones tried to apply high-temperature (150°C) condensation of the corresponding *N*-ethoxycarbonylanthranylonitriles with methyl- or benzylamine.

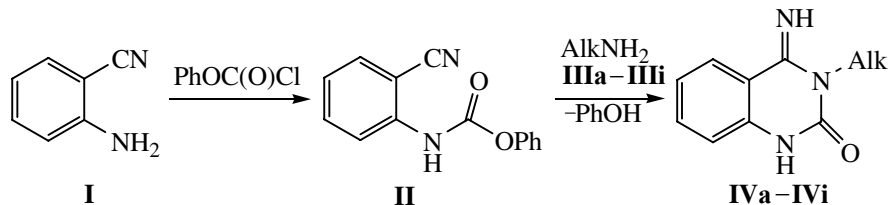
We report here on a preparatively convenient procedure avoiding isocyanate application for the synthesis of 3-alkyl-substituted 4-iminoquinazolinones, in particular, those containing functional substituents in the aliphatic chain. The method is based on a preliminary modification of the amino group in anthranylonitrile (**I**) with phenyl

chloroformate followed by treating the nearly quantitatively formed carbamate **II** with alkylamines **IIIa–IIIi**. We found that heating for two hours of reagents **II** and **III** in acetonitrile at reflux made it possible omitting the isolation of intermediate ureas to obtain analytically pure target compounds **IVa–IVi** in 76–85% yields (see scheme).

***N*-(2-Cyanophenyl)-O-phenylcarbamate (II).** To a dispersion of 11.8 g (0.1 mol) of anthranylonitrile (**I**) in 60 ml of toluene was added while stirring and cooling with ice water a solution of 17.2 g (0.11 mol) of phenyl chloroformate in 20 ml of toluene, and the mixture was heated at reflux for 2 h. On cooling the separated precipitate was filtered off, washed with 40 ml of ethyl ether, and dried. Yield 96%, mp 141–142°C. IR spectrum, ν , cm⁻¹: 1720 (C=O), 2245 (C=N), 3330 (NH). ¹H NMR spectrum, δ , ppm: 7.19–7.42 m (6H_{arom}), 7.64 d.d (2H_{arom}), 7.76 s (1H_{arom}), 10.28 s (1H, NH). Found, %: C 70.78; H 4.05; N 11.59. C₁₄H₁₀N₂O₂. Calculated, %: C 70.58; H 4.23; N 11.76.

3-Alkyl-4-imino-3,4-dihydro-1*H*-quinazolin-2-ones IVa–IVi. A mixture of 0.6 g (2.5 mmol) of

Scheme.



Alk=HOCH₂CH₂ (**a**), Me₂NCH₂CH₂ (**b**), 2-morpholinoethyl (**c**), HOCH₂CH₂CH₂ (**d**), Me₂NCH₂CH₂CH₂ (**e**), C₄H₉ (**f**), (CH₃)₂CHCH₂CH₂ (**g**), C₆H₁₃ (**h**), (1-ethylpyrrolidin-2-yl)methyl (**i**).

carbamate **II** and 2.5 mmol of amine **IIIa–IIIi** in 10 ml of acetonitrile was heated at reflux for 3 h. On cooling the separated precipitate was filtered off, washed with 10 ml of ethyl ether, and dried.

3-(2-Hydroxyethyl)-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVa). Yield 82%, mp 195–196°C. IR spectrum, ν , cm^{-1} : 1700 (C=O), 3320 (NH), 3490 (OH). ^1H NMR spectrum, δ , ppm: 3.58 t (2H, CH_2), 4.11 t (2H, CH_2), 4.87 br.s (1H, OH), 7.03–7.08 m (2H_{arom}), 7.44 t (1H_{arom}), 8.02 d (1H_{arom}), 8.89 s (1H, NH), 10.70 br.s (1H, NH). Found, %: C 58.31; H 5.59; N 20.65. $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_2$. Calculated, %: C 58.53; H 5.40; N 20.48.

3-(2-Dimethylaminoethyl)-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVb). Yield 80%, mp 206–207°C. IR spectrum, ν , cm^{-1} : 1700 (C=O), 3340 (NH). ^1H NMR spectrum, δ , ppm: 2.58 t (2H, CH_2), 4.13 t (2H, CH_2), 7.01–7.12 m (2H_{arom}), 7.42 t (1H_{arom}), 8.03 d (1H_{arom}), 8.92 s (1H, NH), 10.83 br.s (1H, NH). Found, %: C 61.79; H 7.03; N 24.24. $\text{C}_{12}\text{H}_{16}\text{N}_4\text{O}$. Calculated, %: C 62.05; H 6.94; N 24.12.

4-Imino-3-(2-morpholinoethyl)-3,4-dihydro-1H-quinazolin-2-one (IVc). Yield 85%, mp 207–208°C. IR spectrum, ν , cm^{-1} : 1695 (C=O), 3330 (NH). ^1H NMR spectrum, δ , ppm: 2.47–2.51 m (4H, 2CH_2), 3.31–3.34 m (2H, CH_2), 3.52–3.55 m (4H, CH_2), 4.11–4.16 m (2H, CH_2), 7.05–7.12 m (2H_{arom}), 7.47 t (1H_{arom}), 8.06 d (1H_{arom}), 8.89 s (1H, NH), 10.73 s (1H, NH). Found, %: C 61.17; H 6.70; N 20.20. $\text{C}_{14}\text{H}_{18}\text{N}_4\text{O}_2$. Calculated, %: C 61.30; H 6.61; N 20.42.

3-(3-Hydroxypropyl)-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVd). Yield 85%, mp 172–173°C. IR spectrum, ν , cm^{-1} : 1695 (C=O), 3305, 3390 (NH), 3530 (OH). ^1H NMR spectrum, δ , ppm: 1.74–1.78 m (2H, CH_2), 3.42 t (2H, CH_2), 4.08 t (2H, CH_2), 7.05–7.10 m (2H_{arom}), 7.44 d (1H_{arom}), 8.03 d (1H_{arom}), 8.86 br.s (1H, NH), 10.76 br.s (1H, NH). Found, %: C 60.39; H 6.09; N 19.26. $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_2$. Calculated, %: C 60.26; H 5.98; N 19.17.

3-(3-Dimethylaminopropyl)-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVe). Yield 83%, mp 146–147°C. IR spectrum, ν , cm^{-1} : 1695 (C=O), 3295, 3360 (NH). ^1H NMR spectrum, δ , ppm: 1.72–1.77 m (2H, CH_2), 2.19 s (6H, 2CH_3), 2.31 t (2H, CH_2), 3.99 t (2H, CH_2), 7.01–7.08 m (2H_{arom}), 7.41 t (1H_{arom}), 8.03 d (1H_{arom}), 8.82 br.s (1H, NH), 10.80 br.s (1H, NH). Found, %: C 63.61; H 7.25; N 22.91. $\text{C}_{13}\text{H}_{18}\text{N}_4\text{O}$. Calculated, %: C 63.39; H 7.37; N 22.75.

3-Butyl-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVf). Yield 78%, mp 209–210°C. IR spectrum, ν , cm^{-1} : 1700 (C=O), 3295, 3310 (NH). ^1H NMR spectrum, δ , ppm: 0.94 t (3H, CH_3), 1.10–1.15 m (2H, CH_2), 1.56–1.60 m (2H, CH_2), 3.99 t (2H, CH_2), 7.01–7.06 m (2H_{arom}), 7.98 d (1H_{arom}), 8.74 br.s (1H, NH), 10.66 br.s (1H, NH). Found, %: C 66.20; H 6.88; N 19.47. $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}$. Calculated, %: C 66.34; H 6.96; N 19.34.

4-Imino-3-(3-methylbutyl)-3,4-dihydro-1H-quinazolin-2-one (IVg). Yield 77%, mp 204–205°C. IR spectrum, ν , cm^{-1} : 1700 (C=O), 3300 (NH). ^1H NMR spectrum, δ , ppm: 0.96 d (6H, 2CH_3), 1.49–1.63 m (3H, $\text{CH}_2 + \text{CH}$), 4.01 t (2H, CH_2), 7.02–7.06 m (2H_{arom}), 7.42 t (1H_{arom}), 8.00 d (1H_{arom}), 8.74 br.s (1H, NH), 10.67 br.s (1H, NH). Found, %: C 67.77; H 7.39; N 18.12. $\text{C}_{13}\text{H}_{17}\text{N}_3\text{O}$. Calculated, %: C 67.51; H 7.41; N 18.17.

3-Hexyl-4-imino-3,4-dihydro-1H-quinazolin-2-one (IVh). Yield 75%, mp 161–162°C. IR spectrum, ν , cm^{-1} : 1695 (C=O), 3330 (NH). ^1H NMR spectrum, δ , ppm: 0.86 t (3H, CH_3), 1.23–1.28 m (6H, 3CH_2), 1.56–1.59 m (2H, CH_2), 3.99 t (2H, CH_2), 7.03–7.10 m (2H_{arom}), 7.47 t (1H_{arom}), 8.05 d (1H_{arom}), 8.86 s (1H, NH), 10.71 s (1H, NH). Found, %: C 68.68; H 7.64; N 16.98. $\text{C}_{14}\text{H}_{19}\text{N}_3\text{O}$. Calculated, %: C 68.54; H 7.81; N 17.13.

4-Imino-3-[(1-pyrrolidin-2-yl)methyl]-3,4-dihydro-1H-quinazolin-2-one (IVi). Yield 83%, mp 217–218°C. IR spectrum, ν , cm^{-1} : 1690 (C=O), 3290 (NH). ^1H NMR spectrum, δ , ppm: 1.04 m (3H, CH_3), 1.60–1.68 m (4H, 2CH_2), 2.12–2.32 m (2H, 2CH), 2.92–3.03 m (3H, CH_2 , CH), 3.96–4.04 m (2H, 2CH), 7.04–7.12 m (2H_{arom}), 7.40–7.45 m (1H_{arom}), 8.03–8.07 m (1H_{arom}), 8.74 br.s (1H, NH), 10.87 br.s (1H, NH). Found, %: C 66.37; H 7.23; N 20.41. $\text{C}_{15}\text{H}_{20}\text{N}_4\text{O}$. Calculated, %: C 66.15; H 7.40; N 20.57.

IR spectra of compounds were recorded on UR-20 instrument from KBr pellets. ^1H NMR spectra were registered on a spectrometer Varian-Gemini (300 MHz) from solutions in $(\text{CD}_3)_2\text{SO}$, internal reference w TMS.

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