Chemistry of Heterocyclic Compounds, Vol. 39, No. 3, 2003

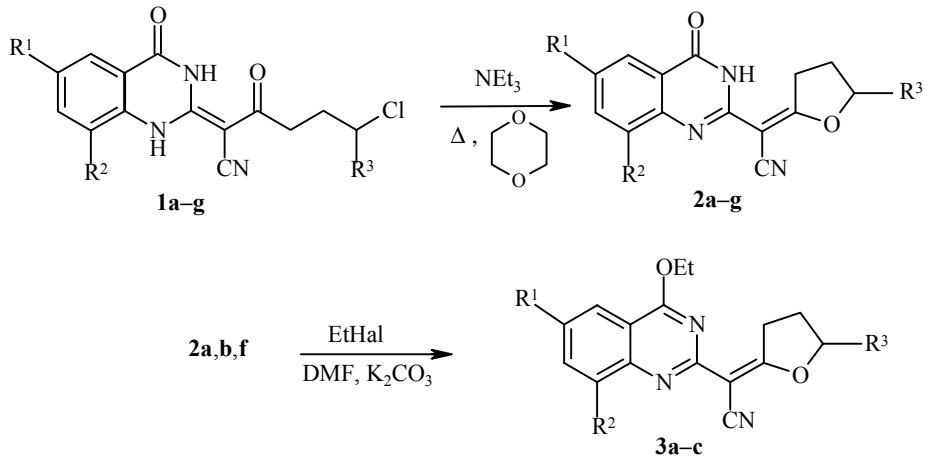
CONVENIENT METHOD FOR THE SYNTHESIS OF 2-(4-OXO-3,4-DIHYDRO-2-QUINAZOLINYL)-2-(2-TETRAHYDROFURANYLIDENE)ACETONITRILES

Yu. M. Volovenko, O. V. Khilya, and T. A. Volovenko

Keywords: 6-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)hexanenitriles, 6-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)heptanenitriles, 2-(4-oxo-3,4-dihydro-2-furanylidene)acetonitriles.

In previous work [1], we described the synthesis of 2-hetaryl-2-(pyrrolidinylidene)acetonitriles by the condensation of hetarylacetonitriles with O-methylbutyrolactine. We obtained oxygen analogs of such compounds starting from 6-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)hexanenitriles and 6-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)heptanenitriles **1**.

The nitriles have a mobile halogen atom and several nucleophilic sites, namely, the two nitrogen atoms of the quinazolone fragment, the carbonyl oxygen atom of the acyl fragment, and C(2) of the acetonitrile fragment. Thus, we would expect that intramolecular alkylation should occur upon heating these compounds. Such a reaction would probably be best carried out in the presence of triethylamine. It is remarkable, in our opinion, that of the four sites for electrophilic attack mentioned above, the acyl oxygen atom undergoes attack to give the corresponding 2-(4-oxo-3,4-dihydro-2-quinazolinyl)-2-(2-tetrahydro-2-furanylidene)acetonitriles **2**. The nitrogen atom of the 1-N-quinazolone fragment undergoes electrophilic attack in the case of 4-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)butanenitrile [2].



1, **2 a, g** R^1 = H, **b**, **d** R^1 = Me, **c** R^1 = *i*-Pr, **e** R^1 = F, **f** R^1 = Br; **a-c**, **e-g** R^2 = H, **d** R^2 = Me; **a-f** R^3 = H, **g** R^3 = Me; **3 a** R^1 = H, **b** R^1 = Me, **c** R^1 = Br, **a-c** R^2 = R^3 = H

Taras Shevchenko Kiev National University, 01033 Kiev, Ukraine; e-mail: olgakh@mail.univ.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 439-441, March, 2003. Original article submitted November 19, 2002.

 0009-3122/03/3903-0394$25.00

The ^{1}H NMR spectra of **2** and **3** feature signals for the aromatic protons at 7.4-8.2 ppm, quinazolone NH proton at low field (10.9-11.3 ppm), and tetrahydrofuran ring methylene groups at 2.2-4.7 ppm. The IR spectra show bands for the quinazolone C=O and NH groups at 1680-1660 and 3350-3340 cm^{-1}, respectively, while the band for the conjugated CN group is at 2215-2208 cm^{-1}.

The action of ethyl halides on solutions of **2** in DMF in the presence of potassium carbonate leads to alkylation at the quinazolone oxygen atom to give **3**.

2-(6-R^1-8-R^2-4-Oxo-3,4-dihydro-2-quinazolyl)-2-(5-R3-tetrahydro-2-furanylidene)acetonitriles (2a-g). A sample of triethylamine (7 mmol) was added to a suspension of 6-chloro-3-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)hexanenitrile (7 mmol) or 6-chloro-3-oxo-2-(4-oxo-1,2,3,4-tetrahydro-2-quinazolinylidene)-heptanenitrile **1** in dioxane or butanol and heated for 1-3 h. The reaction was monitored chromatographically. The reaction mixture was cooled and the precipitate of **2** was filtered off. The filtrate was evaporated and an additional amount of **2** was isolated. The precipitate was washed with water and ethanol.

Acetonitrile 2a was obtained in 73% yield; mp 242-243°C (butanol). Found, %: N 16.67. $C_{14}H_{11}N_3O_2$. Calculated, %: N 16.59.

Acetonitrile 2b was obtained in 86% yield; mp 247-249°C (butanol). Found, %: N 15.81. $C_{15}H_{13}N_3O_2$. Calculated, %: N 15.72.

Acetonitrile 2c was obtained in 75% yield; mp 229-231°C (butanol). Found, %: N 14.50. $C_{17}H_{17}N_3O_2$. Calculated, %: N 14.23.

Acetonitrile 2d was obtained in 85% yield; mp 253-255°C (butanol). Found, %: N 14.98. $C_{16}H_{15}N_3O_2$. Calculated, %: N 14.94.

Acetonitrile 2e was obtained in 81% yield; mp 273-275°C (butanol). Found, %: N 15.62. $C_{14}H_{10}FN_3O_2$. Calculated, %: N 15.49.

Acetonitrile 2f was obtained in 78% yield; mp 264-266°C (butanol). Found, %: Br 24.19; N 12.77. $C_{14}H_{10}BrN_3O_2$. Calculated, %: Br 24.06; N 12.65.

Acetonitrile 2g was obtained in 89% yield; mp 204-206°C (butanol). Found, %: N 15.86. $C_{15}H_{13}N_3O_2$. Calculated, %: N 15.72.

2-(6-R^1-4-Ethoxy-2-quinazolinyl)-2-(2-tetrahydrofuranylidene)acetonitriles (3a-3c). A sample of potassium carbonate (18 mmol) and ethyl halide (7.2 mmol) were added to a heated solution of **2** (6 mmol) in a minimal amount of DMF. The solution was heated at 60-70°C with rapid stirring for 1-2 h. The reaction was monitored chromatographically. The reaction mixture was cooled and the precipitate of **3** was filtered off. The filtrate was evaporated and an additional amount of **3** was isolated. The precipitate was washed with water and ethanol.

Acetonitrile 3a was obtained in 83% yield; mp 222-224°C (butanol). Found, %: N 15.22. $C_{16}H_{15}N_3O_2$. Calculated, %: N 14.94.

Acetonitrile 3b was obtained in 79% yield; mp 191-193°C (butanol). Found, %: N 14.53. $C_{17}H_{17}N_3O_2$. Calculated, %: N 14.23.

Acetonitrile 3c was obtained in 75% yield; mp 220-221°C (butanol). Found, %: Br 22.58; N 11.87. $C_{16}H_{14}BrN_3O_2$. Calculated, %: Br 22.18; N 11.67.

REFERENCES

1. Yu. M. Volovenko and A. V. Tverdokhlebova, *Khim. Geterotsikl. Soedin.*, 1565 (2000).
2. Yu. M. Volovenko and E. V. Resnyanskaya, *Mendeleev Commun.*, **12**, 119 (2002).