Chemistry of Heterocyclic Compounds, Vol. 38, No. 9, 2002

SYNTHESIS OF SUBSTITUTED 4,5-DIHYDRO[1,4]OXAZEPINO-[7,6-*b*]QUINOLIN-3-ONES

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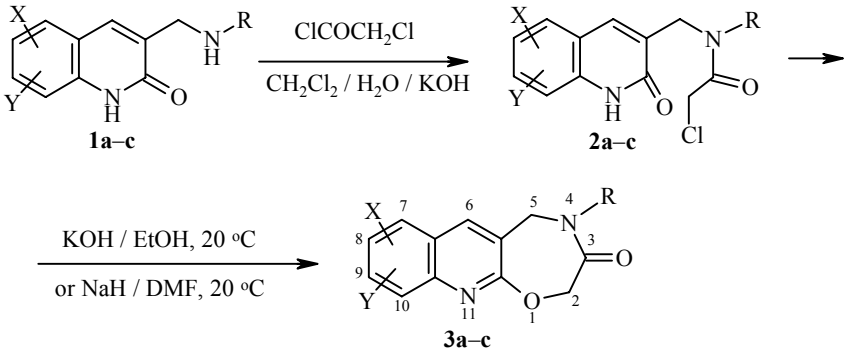
Keywords: 3-aminomethyl-2-quinolones, 4,5-dihydro[1,5]oxazepino[7,6-*b*]quinolin-3-ones, chloroacetyl chloride, O-alkylation, acylation, cyclization.

Derieg and Stembach [1] reported a synthesis for benzo-condensed 4,5-dihydro-1,4-oxazepinone systems through the acylation of *o*-anilinomethylphenols by bromoacetyl bromide and subsequent intramolecular cyclization of the resultant 2-bromo-N-(2-hydroxybenzyl)acetanilides by the action of sodium hydride [1].

We have extended this method for the preparation of previously unreported substituted 4,5-dihydro[1,4]oxazepino[7,6-*b*]quinolin-3-ones. Substituted 3-aminomethyl-2-quinolones **1a-c** are readily acylated by chloroacetyl chloride in a two-phase methylene chloride–water system in the presence of K_2CO_3 or KOH to give N-chloroacetyl derivatives **2a-c**. The action of either sodium hydride in DMF at room temperature or of ethanolic alkali, which is a weaker base, at 50°C on **2a-c** gives substituted 4,5-dihydro[1,4]oxazepino-[7,6-*b*]quinolinones **3a-c:**



1a–c **2a–c** **3a–c**

1-3 a R = *c*-C_5H_9, **b** R = (thien-2-yl)-CH_2, **c** R = CH_2Ph; **a**, **b** X = 8-Me, **c** X = OEt; **a, b** Y = 10-Me, **c** Y = H

The disappearance of the signals for the quinoline ring NH protons at δ ~10.15-10.20 ppm in the ^{1}H NMR spectrum taken on a Bruker AM-400 spectrometer at 400 MHz indicates formation of the oxazepine ring.

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 0009-3122/02/3809-1154$27.00

Thus, 1 mmol of **1a-c** was acylated with ice cooling by 1.15 mmol of chloroacetyl chloride in a system composed of methylene chloride and 20% aq. KOH (1.2 mmol) over 30 min. The course of this reaction was monitored by thin-layer chromatography using 20:1 chloroform–methanol as the eluent. The organic layer was separated, washed with aqueous sodium carbonate and, then, water, dried over Na_2SO_4, and evaporated to give **2a-c**. These products were used without further purification.

A sample of 60% NaH (50 mg, 1.1 mmol) was added to a solution of **2a-c** (1 mmol) in DMF (3 ml) and stirred for 15 min at ~20°C. Alternatively, the reaction of 1 mmol of **2a-c** was carried out with 1 mmol of KOH in 5 ml of ethanol at 50°C over 30 min. The reaction was monitored by thin-layer chromatography. The reaction mixture was diluted with water. The resultant precipitate was filtered off, washed with water, and recrystallized from ethanol to give **3a-c**.

4-Cyclopentyl-8,10-dimethyl-4,5-dihydro[1,4]oxazepino[7,6-*b*]quinolin-3-one (3a) was obtained in 70% yield; mp 188-191°C. ^{1}H NMR spectrum, δ, ppm: 1.45-1.87 (8H, m, CH_2-cyclopentyl); 2.42 and 2.57 (6H, 2s, 8- and 10-CH_3); 4.79 (3H, br. s, 5-H, 1'-H cyclopentyl); 4.99 (2H, s, 2-H); 7.39 and 7.45 (2H, 2s, 7- and 9-H); 8.21 (1H, s, 6-H). Found, %: C 73.34; H 7.26; N 9.08. $C_{19}H_{22}N_2O_2$. Calculated, %: C 73.52; H 7.14; N 9.03.

8,10-Dimethyl-4-(2-thienyl)methyl-4,5-dihydro[1,4]oxazepino[7,6-*b*]quinolin-3-one (4b) was obtained in 60% yield; mp 105-108°C. ^{1}H NMR spectrum, δ, ppm: 2.40 and 2.53 (6H, 2s, 8- and 10-CH_3); 4.82, 4.92, and 5.02 (6H, 3s, 2-, 5-CH_2, CH_2-thienyl); 6.85-7.33 (5H, m, 7-, 9-H, thienyl protons); 7.99 (1H, s, 6-H). Found, %: C 67.53; H 5.03; N 8.10. $C_{19}H_{18}N_2O_2S$. Calculated, %: C 67.43; H 5.36; N 8.28.

4-Benzyl-8-ethoxy-4,5-dihydro[1,4]oxazepino[7,6-*b*]quinolin-3-one (3c) was obtained in 68% yield; mp 148-152°C. ^{1}H NMR spectrum, δ, ppm: 1.38 (3H, t, $CH_2\underline{CH_3}$); 4.11 (2H, q, $\underline{CH_2}CH_3$); 4.67, 4.85 and 5.05 (6H, 3s, 2-, 5-CH_2, CH_2PH); 7.10-7.71 (8H, m, Ph, 7-, 9-, 10-H); 7.99 (1H, s, 6-H). Found, %: C 72.49; H 5.75; N 8.10. Calculated, %: $C_{21}H_{20}N_2O_3$. Calculated, %: C 72.40; H 5.79; N 8.04.

REFERENCES

1. M. E. Derieg and L. H. Stembach, *J. Heterocycl. Chem.*, **3**, 237 (1966).