Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Simple New Synthetic Method for the Preparation of 2-Aminoquinolines

Ferenc Kóródi [a]

[a] Alkaloida Chemical Company , H-4440, Tiszavasvári, Hungary

Published online: 23 Sep 2006.

To cite this article: Ferenc Kóródi (1991) A Simple New Synthetic Method for the Preparation of 2-Aminoquinolines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 21:18-19, 1841-1846, DOI: 10.1080/00397919108021774

To link to this article: http://dx.doi.org/10.1080/00397919108021774

SYNTHETIC COMMUNICATIONS, 21(18&19), 1841-1846 (1991)

A SIMPLE NEW SYNTHETIC METHOD FOR THE PREPARATION OF 2-AMINOQUINOLINES

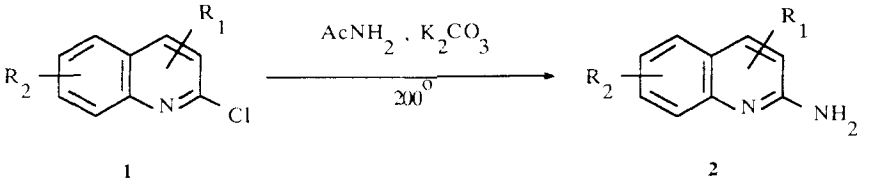
Ferenc Kóródi

Alkaloida Chemical Company, H-4440 Tiszavasvári, Hungary

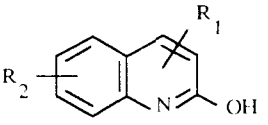
ABSTRACT: *2-Chloroquinolines (**1a** - **j**) heated in acetamide at 200° in the presence of potassium carbonate give 2-aminoquinolines (**2a** - **j**) in good yields.*

2-Aminoquinolines can be prepared starting from 2-chloroquinolines in many different ways. Heating of 2-chloroquinolines under pressure with methanolic ammonia[1], or with concentrated aqueous ammonia solution[2], or with zinc chloride - ammonia double salt in the presence of ammonium chloride in water[3] leads to the formation of 2-aminoquinolines as well as treating of 2-chloroquinolines with ammonia gas in phenol at reflux temperature[4], or with sodamide in liquid ammonia[5]. These methods are however, not generally effective[6]. Their usefulness depends on the substituents of the quinoline ring[3], and the yields are in many cases very low[3,5]. For these reasons , there is still a need for new and efficient methods for preparation of 2-aminoquinolines.

This paper reports on a new simple method for preparation of 2-aminoquinolines (**2**) starting from 2-chloroquinolines (**1**).



1 **2**



3

Halogenated heteroaromatics have been reported to give amino heteroaromatics by heating with benzamide at 180 - 230° in the presence of potassium carbonate but they give mainly acetamido derivatives with acetamide and potassium carbonate at reflux temperature[7]. According to our investigation heating 2-chloroquinolines (**1a - j**) in acetamide solution in the presence of potassium carbonate at 200° affords 2-aminoquinolines (**2a - j**) in good yields. Acetamido derivatives could not be detected in the course of the reactions by TLC monitoring. As the only byproduct, the corresponding 2-hydroxyquinoline (**3**) was detected both in the reaction mixtures and in the crude products. The formation of 2-hydroxyquinolines can be suppressed by increase of the amount of potassium carbonate, whereas, in the absence of the base the corresponding 2-hydroxyquinoline is the main product due to the autocatalytic acidic hydrolyzis of the 2-chloro group.

TABLE 1: Preparation of 2-Aminoquinolines (**2a - j**)

Compound	R_1	R_2	Time (h)	Yield[a] (%)	mp (°C)
2 a	H	H	3	58[b]	128 - 130
2 b	3-Me	H	3	66[d]	157 - 159
2 c	3-Me	6-Me	6	61[c]	185 - 187
2 d	3-Me	7-Me	5	63[b]	166 - 168
2 e	3-Me	8-Me	5	64[b]	98 - 100
2 f	3-Me	6-Cl	0.5	68[c]	210 - 212
2 g	3-Me	7-Cl	1	69[c]	206 - 208
2 h	3-Et	H	5	66[d]	130 - 132
2 i	3-Ph	H	1	63[c]	154 - 156
2 j	4-Me	7-Cl	0.5	58[d]	160 - 162

a) Yield of pure product. Purification was performed: b) by column chromatography using silica gel packing and chloroform - ethanol (9 : 1 v/v) eluent; c) by crystallization from ethanol; d) by dissolving in ethanol and precipitation with hexane.

In connection with the scope of this method we have found that the mild electron withdrawing groups (Cl, Ph) on the quinoline ring facilitate the reaction since they enhance the reactivity of the 2-chloro group toward nucleophilic substitution, but in the presence of a strong electron withdrawing nitro group we could get only a tar under these reaction conditions.

The crude 2-aminoquinolines usually were accompanied with the corresponding 2-hydroxy derivative, but they can be purified by crystallization or by column chromatography to give pure products in good yields. The structure of compounds **2a - j** and **3b** was confirmed by their ^{1}H-NMR and mass spectral data.

TABLE 2: ^{1}H-NMR and Mass Spectral Data of Compounds Prepared

Compound	^{1}H-NMR δ (ppm)	MS[a] m/e (%)
2 a	6.52 (s, 2H), 6.78 (d, 1H), 7.13 (m, 1H), 7.46 (m, 2H), 7.60 (dd, 1H), 7.87 (d, 1H).	144 (M^+, 100), 117 (41)
2 b	2.25 (s, 3H), 6.43 (s, 2H), 7.15 (m, 1H), 7.45 - 7.60 (m, 3H), 7.70 (s, 1H).	158 (M^+, 100), 141 (28)
2 c	2.22 (s, 3H), 2.37 (s, 3H), 6.35 (s, 2H), 7.27 (dd, 1H), 7.35 (d, 1H), 7.42 (d, 1H), 7.65 (s, 1H).	172 (M^+, 100), 154 (15)
2 d	2.20 (s, 3H), 2.40 (s, 3H), 6.25 (s, 2H), 6.97 (dd, 1H), 7.27 (d, 1H), 7.45 (d, 1H), 7.63 (s, 1H).	172 (M^+, 100), 154 (22)
2 e	2.22 (s, 3H), 2.53 (s, 3H), 6.20 (s, 2H), 7.02 (m, 1H), 7.30 (dd, 1H), 7.40 (dd, 1H), 7.68 (s, 1H).	172 (M^+, 100), 154 (31)
2 f	2.22 (s, 3H), 6.50 (s, 2H), 7.37 - 7.50 (m, 2H), 7.60 - 7.70 (m, 2H).	192 (M^+, 100), 175 (7)
2 g	2.20 (s, 3H), 6.60 (s, 2H), 7.12 (dd, 1H), 7.47 (d, 1H), 7.60 (d, 1H), 7.72 (s, 1H).	192 (M^+, 100), 175 (9)
2 h	1.23 (t, 3H), 2.57 (q, 2H), 6.33 (s, 2H), 7.13 (m, 1H), 7.37 - 7.50 (m, 2H), 7.62 (dd, 1H), 7.70 (s, 1H).	172 (M^+, 100), 154 (15)
2 i	6.05 (s, 2H), 7.20 (m, 1H), 7.40 - 7.60 (m, 7H), 7.70 (dd, 1H), 7.85 (s, 1H).	220 (M^+, 100), 204 (12)
2 j	2.27 (s, 3H), 6.58 (s, 2H), 6.62 (s, 1H), 7.15 (dd, 1H), 7.43 (d, 1H), 7.75 (d, 1H).	192 (M^+, 100), 164 (25)
3 b	2.12 (s, 3H), 7.15 (m, 1H), 7.30 (dd, 1H), 7.42 (m, 1H), 7.57 (dd, 1H), 7.75 (s, 1H), 11.77 (s, 1H).	159 (M^+, 100), 141 (16)

a) The elemental analyses for C, H and N were within +/- 0.4 % of the theoretical values.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Büchi apparatus and are uncorrected. The ^{1}H-NMR spectra were recorded on a Varian Gemini-200 instrument at 200 MHz in DMSO-d_6 solution using TMS as internal standard and chemical shifts are expressed in ppm. Mass spectra were scanned on a VG TRIO-2 spectrometer in EI mode at 70 eV.

*2-Aminoquinolines (**2a - j**). General procedure.*

A mixture of the 2-chloroquinoline derivative (0.01 mol), potassium carbonate (6.9 g, 0.05 mol) and acetamide (12.0 g, 0.20 mol) was heated at 200° with stirring until all the starting material had been consumed (TLC). The reaction mixture was poured into water (50 ml), the precipitate was collected by suction and dried. The crude product was purified as given in Table 1.

*2-Hydroxy-3-methylquinoline (**3b**).*

A mixture of 2-chloro-3-methylquinoline (**1b**), (1.78 g, 0.01 mol) and acetamide (12.0 g, 0.20 mol) was heated at 200° with stirring for 1 hour. The reaction mixture was poured into water (50 ml), the precipitated product was collected then was recrystallized from acetic acid to give **3b**, 1.11 g (69.8 %), mp 244-246°.

REFERENCES

1. Horner, J. K., Henry, D. W., J. Med. Chem, 1968, 11, 946.
2. Fischer, O., Guthmann, H., J. Prakt. Chem., 1916, 201, 378.
3. Backeberg, O. G., Marais, J. L. C., J. Chem. Soc., 1924, 381.

4. Bachman, G.B., Hamer, M., Proc. Indiana Acad. Sci., 1952, 61, 117.

5. Hauser, C.R., Weiss, M. J., J. Org. Chem., 1949, 14, 310.

6. Murugesan, M., Ramasamy, K., Shanmugam, P., Z. Naturforsch., 1980, 35b, 746.

7. Watanabe, M., Ohta, A., Heterocycles, 1980, 14, 287.

(Received in UK 14 May, 1991)