Fused quinoline heterocycles VIII. Synthesis of polyfunctionally substituted pyrazolo[4,3-*c*]quinolin-4(5*H*)-ones

Ramadan Ahmed Mekheimer[a]*, Saeed M. Refaey[a], Kamal Usef Sadek[a], Afaf Mohamed Abdel Hameed[a], Mohamed Ashry Ibrahim[a] and Anamik Shah[b]

[a]*Department of Chemistry, Faculty of Science, El-Minia University, El-Minia 61519, Egypt*

[b]*Department of Chemistry, Saurashtra University, Rajkot-360 005, India*

Reaction of 2,4-dichloroquinoline-3-carbonitrile (**1**) with 4-methylpiperidine gave 2-chloro-4-(4-methylpiperidin-1-yl)quinoline-3-carbonitrile (**2**). Acid hydrolysis of **2** afforded the corresponding 2-quinolinones **3**, which were *N*-alkylated in DMF to form the 1-methyl, -ethyl and -phenacyl quinolinones **6a–c**. Fusion of **6a–c** with hydrazine hydrate gave the 3-aminopyrazolo[4,3-*c*]quinolin-4-ones **8a–c**. Diazotisation of **8a,b** followed by reaction with sodium azide afforded the novel 3-azidopyrazolo[4,3-*c*]quinolin-4-ones **9a,b**.

Keywords: fused pyrazoles, quinolines, azides

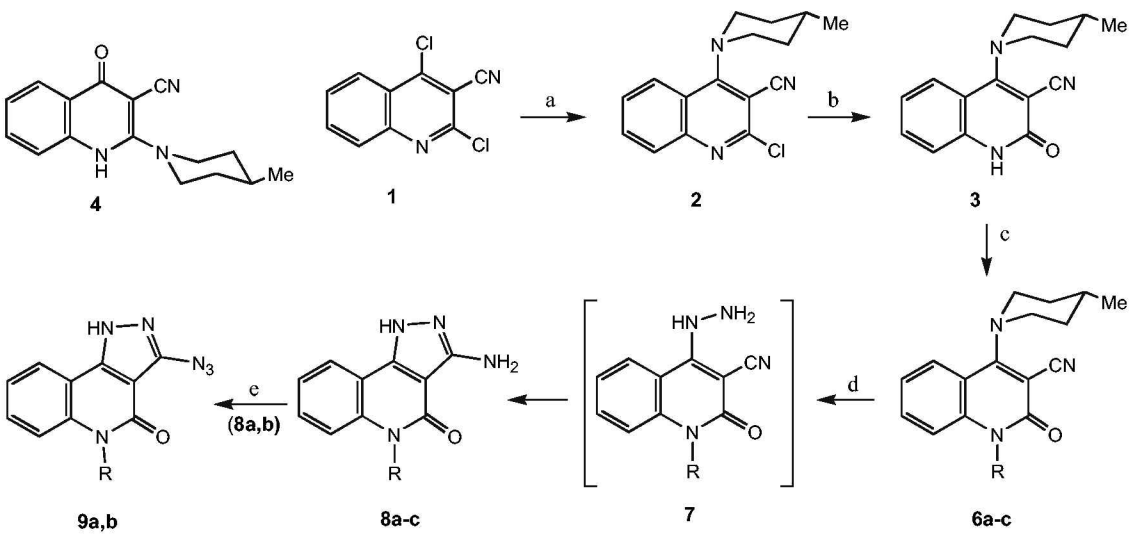
The pyrazolo[4,3-*c*]quinoline skeleton is one of the 'privileged medicinal scaffolds' that show a wide rang of pharmacological activities because of their benzodiazepine receptor affinity and activity as immunomodulating drugs.[1-4] 3-Methylamino-5-propyl-1*H*-pyrazolo[4,3-*c*]quinolin-4(5*H*)-one has been reported to show significant activity as an anti-inflammatory and liver protective agent.[5] More recently, pyrazolo[4,3-*c*]quinoline-4-one has been identified as a novel pharmacophore for selective cyclooxygenase-2 (COX-2) inhibitors that could reduce pain and inflammation without affecting the cytoprotective action of cyclooxygenase-1 (COX-1), the site of action for all the classical NSAIDS.[6]

Organic azides are well known as compounds with a high level of biological activity and have proved valuable in the treatment of cardiovascular diseases.[7] Recently, some heterocyclic azides have been synthesised as antithrombotic and blood pressure lowering agents.[8] Furthermore, they are versatile synthetic intermediates, presenting a broad range of chemical reactivity.[9]

A survey of the literature revealed that only few synthetic routes have so far been reported for the synthesis of pyrazolo[4,3-*c*]quinolin-4-ones. One of these is based on the catalytic reduction of ethyl 3-methyl-5-(2-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carboxylate.[10] Another method involves the thermal or acid-catalysed rearrangements of pyrazoloindoles.[11] Kappe *et al.*[12] have prepared pyrazolo[4,3-*c*]quinolin-4-one derivatives by the action of hydrazines on 3-acyl-4-hydroxyquinolin-2-ones.

Results and discussion

A few years ago we started a medicinal chemistry project aimed at the synthesis and the pharmacological study of new substituted pyrazolo[4,3-*c*]quinolines.[13-17] As an extension of this research, we report here a new, efficient and convenient procedure for the synthesis of hitherto unreported pyrazolo[4,3-*c*]quinolin-4-one derivatives which are often difficult to obtain by other routes, using the conveniently available 2,4-dichloroquinoline-3-carbonitrile (**1**)[18] as starting material. Kinetic studies have shown that the chlorine atom in the 4-position of **1** is about twice as reactive towards nucleophiles as that at the 2-position.[19] Consequently, the reactive chlorine atom in position 4 of **1** can readily be displaced by nucleophiles. Thus, compound **1** was reacted with 4-methylpiperidine in order to obtain the required key intermediate **3** for subsequent pyrazole ring closure. (Scheme 1)



Reagents: a, 4-methylpiperidine, DMF, R.T.; b, H_2O/AcOH, Δ; c, R-X (**5a-c**)/DMF/K_2CO_3; d, N_2H_4, Δ; e, 1) HNO_2, 2) NaN_3/H_2O

5-8: **a**, R = CH_3, X = I; **b**, R = C_2H_5, X = I; **c**, R = $C_6H_5COCH_2$, X = Br

Scheme 1

* Correspondent. E-mail: rmekh@yahoo.com

Reaction of **1** with an excess of 4-methylpiperidine in DMF solution at room temperature formed the expected kinetically more favoured product, 2-chloro-4-(4-methylpiperidin-1-yl)quinoline-3-carbonitrile (**2**), rather than the isomeric 4-chloro-2-(4-methylpiperidin-1-yl) compound. This was established by its acid hydrolysis in aqueous acetic acid, resulting in the corresponding 4-(4-methylpiperidin-1-yl)-2-oxo-1,2-dihydroquinoline-3-carbonitrile (**3**). The isomeric quinolin-4-one structure **4** could be excluded because the IR spectrum showed significantly an amide carbonyl function at 1640 cm^{-1}.[20,21] 4-Quinolinones generally have carbonyl absorptions below 1600 cm^{-1}.[22-24] Alkylation of **3** with alkyl halides **5a–c** in the presence of K_2CO_3 afforded the *N*-substituted derivatives **6a–c**. The structures of these products **6a–c** were supported by their IR, NMR and mass spectra, and elemental analysis. The IR spectra showed the absence of NH absorption at 3298 cm^{-1}. Their ^1H NMR spectra revealed the presence of the *N*-alkyl protons in addition to signals from the remainder of the molecules. Additionally, their structures were supported by the ^{13}C NMR and mass spectra, which were all compatible with the assigned structures (see Experimental).

We next investigated the reaction of **6a–c** with hydrazine hydrate in the hope of obtaining the novel pyrazolo[4,3-*c*]quinolin-4-ones **8a–c**. Indeed, it was found that refluxing the quinolinones **6a–c** with an excess of hydrazine hydrate (80%) for 12 h afforded the 5-alkyl-3-aminopyrazolo[4,3-*c*]quinolin-4-ones **8a–c** in good yields. Their structures were confirmed on the basis of consistent elemental and spectral data. The IR spectra revealed the absence of cyano absorption at 2210 cm^{-1}, but absorption bands at 3440–3136 cm^{-1} assignable to NH and NH_2 functions were observed. Furthermore, the ^1H NMR spectra showed the absence of the 4-methylpiperidino protons and the presence of signals for two amino protons at C-3 and a pyrazole NH proton in addition of signals due to aromatic and *N*-alkyl protons in their expected positions. Moreover, structures **8a–c** were supported by correct mass spectra, which were compatible with assigned structures (see Experimental). Formation of the pyrazolo[4,3-c]quinolin-4-ones **8a–c** can be rationalised as follows: the 4-methylpiperidino group at position 4 of compounds **6a–c** undergoes a nucleophilic substitution reaction with one molecule of hydrazine to give the intermediate **7**. Subsequent intramolecular cyclisation *via* the attack of the NH_2 of the hydrazino group at position 4 on the nitrile carbon in the intermediate yields the pyrazolo[4,3-*c*]quinolinones **8a–c**.

The introduction of the azido group into the pyrazolo[4,3-*c*]quinolin-4-ones **8** was next investigated. The reaction of compounds **8a,b** with sodium nitrite in 70% aqueous H_2SO_4 at –5 °C followed by reaction of the non-isolated diazonium salt with aqueous sodium azide gave the previously unreported 3-azidopyrazoloquinolines **9a,b**. The compounds **9a,b**, to the best of our knowledge, are the first examples of the 3-azido-pyrazolo[4,3-*c*]quinolin-4-one system. The IR spectra displayed no amino group absorption (NH_2) but an absorption band for the N_3 group was observed at 2130 cm^{-1}. The ^1H NMR spectra revealed no amino protons (NH_2) and the presence of a singlet at δ *ca* 13.96 ppm, assignable to the pyrazole NH. In addition, signals due to alkyl and aromatic protons were observed in their expected positions. Structures **9a,b** are also consistent with their ^{13}C NMR and mass spectra (see Experimental).

In summary: we have established a simple, and efficient method for the synthesis of the first representatives of the 3-azido-pyrazolo[4,3-*c*]quinolin-4-ones. Heterocyclic azides, in particular those with azido-azomethine substructures, are well known to cyclise spontaneously to give the fused tetrazole forms, although in certain cases, such as the present, the uncyclised azide forms are known to predominate.[25-30] Work is currently under way to prepare a new generation of novel heterocyclic compounds containing the quinoline ring, utilising 2,4-dichloroquinoline-3-carbonitrile as starting material.

Experimental

Melting points were measured on a Gallenkamp melting point apparatus. IR spectra were recorded on a Shimadzu 470 spectrophotometer (KBr pellets). ^1H and ^{13}C NMR spectra were recorded on a Bruker-Avance II (400 MHz for ^1H and 100 MHz for ^{13}C) spectrometer with DMSO as solvent and TMS as an internal standard. MS were measured on a Shimadzu GCMS-QP 2010 mass spectrometer at 70 eV. Microanalyses were performed by the Microanalytical Data Unit at Cairo University. All reagents were of commercial quality or were purified before use, and the organic solvents were of analytical grade or purified by standard procedures.

2-Chloro-4-(4-methylpiperidin-1-yl)quinoline-3-carbonitrile (**2**): To 2,4-dichloroquinoline-3-carbonitrile (**1**) (1.50 g, 6.7 mmol) in DMF (10 ml), 4-methylpiperidine (1.33 g, 13.4 mmol) was added. The reaction mixture was stirred for 30 min at room temperature and then poured into water (10 ml). The precipitated solid product was isolated by filtration and recrystallised from EtOH to give **2** as yellowish crystals; (1.85 g, 96%); m.p. 177–178 °C. IR: ν_{max} 3050 (arom CH); 2928, 2850 (aliph CH), 2210 (CN) cm^{-1}. ^1H NMR: δ_H 1.02 (d, J = 6.4 Hz, 3H, CH_3), 1.46 (m, 2H, CH_2), 1.71 (m, 1H, CH), 1.76 (m, 2H, CH_2), 3.50 (m, 2H, CH_2), 3.88 (m, 2H, CH_2), 7.65 (m, 1H, ArH), 7.86 (m, 2H, ArH), 8.04 (d, J = 8.5 Hz, 1H, ArH); δ_C 21.9 (CH_3), 30.0 (CH), 34.6 ($2CH_2$), 53.4 ($2CH_2$), 95.5 (C-3), 116.8 (CN), 122.05 (C-4a), 125.7, 127.1, 129.0 and 133.2 (Ar-C), 148.2 (C-8a), 149.8 (C-2), 162.8 (C-4). MS: *m/z* (%) 287, 285 (M^+, 36, 100), 284 (M^+-1, 98), 270 (20), 256 (37), 242 (73), 229 (28), 216 (26), 188 (12), 178 (26), 153 (54), 126 (37), 102 (12), 75 (10), 69 (11), 55 (36), 41 (47). Anal: Calcd for $C_{16}H_{16}ClN_3$ (285.77): C, 67.25; H, 5.64; Cl, 12.41; N, 14.70. Found: C, 67.44; H, 5.78; Cl, 12.26; N, 14.82%.

4-(4-Methylpiperidin-1-yl)-2-oxo-1,2-dihydroquinoline-3-carbonitrile (**3**): The amine **2** (0.5 g, 1.75 mmol) in a mixture of AcOH (5 ml) and H_2O (1 ml) was refluxed for 3 h. After concentration and cooling to room temperature, the precipitated solid product was collected by filtration, washed well with H_2O, dried and recrystallised from $CHCl_3$ to give compound **3** as yellow crystals. (0.365 g, 78%); m.p. 304–305 °C. IR: ν_{max} 3298 (NH), 3050 (arom. CH), 2944, 2848 (aliph CH), 2210 (CN), 1640 (amide CO) cm^{-1}. ^1H NMR: δ_H 1.01 (d, J = 6.3 Hz, 3H, CH_3), 1.42 (m, 2H, CH_2), 1.70 (m, 1H, CH), 1.79 (m, 2H, CH_2), 3.38 (m, 2H, CH_2), 3.75 (m, 2H, CH_2), 7.22 (t, J = 7.6 Hz, 1H, ArH), 7.29 (d, J = 8.2 Hz, 1H, ArH), 7.58 (t, J = 7.6 Hz, 1H, ArH), 7.72 (d, J = 8.2 Hz, 1H, ArH), 11.77 (s, 1H, NH); δ_C 21.9 (CH_3), 30.1 (aliph. CH), 34.5 ($2CH_2$), 52.9 ($2CH_2$), 91.1 (C-3), 115.65 (C-4a), 116.6 (CN), 117.3, 122.0, 126.25 and 133.0 (Ar-C), 140.0 (C-8a), 160.9 (C-4), 164.35 (CO). MS: *m/z* (%) 268 (M^+ + 1, 21), 267 (M^+, 100), 266 (M^+–1, 82), 252 (10), 238 (31), 224 (42), 211 (26), 196 (34), 170 (47), 155 (9), 141 (28), 114 (25), 98 (70), 55 (37), 41 (37). Anal: Calcd for $C_{16}H_{17}N_3O$ (267.30): C, 71.89; H, 6.41; N,15.72. Found: C, 71.78; H, 6.34; N, 15.89%.

1-Alkyl-1,2-dihydro-4-(4-methylpiperidin-1-yl)-2-oxoquinoline-3-carbonitriles **6a–c**, *general procedure*

To a solution of the qunolinone **3** (0.20 g, 0.75 mmole) in DMF (5 ml), anhydrous K_2CO_3 (0.311 g, 2.25 mmole) was added and then the reaction mixture was stirred for one hour at room temperature. The alkyl halide **5a,b** (1.5 mmole) was added and the reaction mixture was stirred at room temperature for 25 h. It was then poured into cold H_2O and acidified with cold dil. HCl to pH 3. The resulting solid product was collected by filtration, washed with H_2O, dried and recrystallised from MeOH to give **6a,b**. In the case of **6c**, phenacyl bromide (**5c**) (0.15 g, 0.75 mmole) was used as alkyl halide and the reaction mixture was stirred at room temperature for 52 h. Then it was worked up as described for **6a,b**.

1,2-Dihydro-1-methyl-4-(4-methylpiperidin-1-yl)-2-oxoquinoline-3-carbonitrile (**6a**): Yellowish crystals (0.185 g, 88%), m.p. 208–209 °C. IR: ν_{max} 3080 (arom. CH), 2928, 2848 (aliph CH), 2224 (CN), 1630 (amide CO) cm^{-1}. NMR: δ_H 1.01 (d, J = 6.4 Hz, 3H, CH_3), 1.47 (m, 2H, CH_2), 1.70 (m, 1H, CH), 1.78 (m, 2H, CH_2), 3.39 (m, 2H, CH_2), 3.55 (s, 3H, N-CH_3), 3.71 (m, 2H, CH_2), 7.32 (t, J = 7.3 Hz, 1H, ArH), 7.53 (d, J = 8.3 Hz, 1H, ArH), 7.72 (t, J = 7.3 Hz, 1H, ArH), 7.72 (d, J = 8.3 Hz, 1H, ArH); δ_C 21.9 (CH_3), 29.7 (aliph. CH), 30.1 (N-CH_3), 34.4 ($2CH_2$), 52.9 ($2CH_2$), 91.3 (C-3), 115.9 (C-4a), 116.6 (CN), 117.2, 122.2, 126.8 and 133.5 (Ar-C), 140.8

(C-8a), 160.3 (C-4), 163.3 (CO). MS: *m/z* (%) 282 ($M^+ + 1$, 21), 281 (M^+, 100), 266 (11), 252 (26), 238 (36), 225 (25), 212 (19), 210 (28), 184 (60), 155 (22), 128 (14), 114 (9), 98 (10), 77 (9), 55 (15), 41 (19). Anal: Calcd for $C_{17}H_{19}N_3O$ (281.35): C, 72.57; H, 6.81; N, 14.94. Found: C, 72.68; H, 6.93; N, 14.88%.

1-Ethyl-1,2-dihydro-4-(4-methylpiperidin-1-yl)-2-oxoquinoline-3-carbonitrile (**6b**): Yellow crystals (0.197 g, 89%), m.p. 173–175 °C. IR: ν_{max} 3080 (arom. CH), 2928, 2865 (aliph CH), 2210 (CN), 1630 (amide CO) cm^{-1}. NMR: δ_H 1.02 (d, J = 6.4 Hz, 3H, CH_3), 1.19 (t, J = 7 Hz, 3H, CH_3), 1.43 (m, 2H, CH_2), 1.68 (m, 1H, CH), 1.77 (m, 2H, CH_2), 3.37 (m, 2H, CH_2), 3.70 (m, 2H, CH_2), 4.23 (q, J = 7 Hz, 2H, CH_2), 7.32 (t, J = 7.6 Hz, 1H, ArH), 7.60 (d, J = 8.5 Hz, 1H, ArH), 7.72 (t, J = 7.6 Hz, 1H, ArH), 7.83 (d, J = 8.5 Hz, 1H, ArH); δ_C 12.71 (CH_3), 21.86 (CH_3), 30.07 (aliph. CH), 34.43 ($2CH_2$), 37.18 (N–CH_2), 52.90 ($2CH_2$), 91.44 (C-3), 115.65 (C-4a), 116.86 (CN), 117.20, 122.08, 127.06 and 133.60 (Ar–C), 139.71 (C-8a), 159.88 (C-4), 163.32 (CO). MS: *m/z* (%) = 296 ($M^+ + 1$, 18), 295 (M^+, 85), 294 (100), 267 (43), 266 (46), 252 (23), 238 (14), 224 (20), 198 (39), 183 (21), 170 (10), 155 (10), 141 (14), 128 (10), 114 (10), 98 (8), 77 (7), 55 (27), 41 (25). Anal: Calcd for $C_{18}H_{21}N_3O$ (295.38): C, 73.19; H, 7.17; N, 14.23. Found: C, 73.27; H, 6.95; N, 14.39%.

1,2-Dihydro-4-(4-methylpiperidin-1-yl)-2-oxo-1-phenacylquinoline-3-carbonitrile (**6c**): Yellow crystals (0.235 g, 82%), m.p. 243–244 °C. IR: ν_{max} 3090 (arom. CH), 2945, 2848 (aliph CH), 2210 (CN) 1689 (CO), 1630 (amide CO) cm^{-1}. NMR: δ_H 1.02 (d, J = 6.3 Hz, 3H, CH_3), 1.46 (m, 2H, CH_2), 1.73 (m, 1H, CH), 1.82 (m, 2H, CH_2), 3.42 (m, 2H, CH_2), 3.80 (m, 2H, CH_2), 5.86 (s, 2H, CH_2), 7.32 (t, J = 7.6 Hz, 1H, ArH), 7.40 (d, J = 8.6 Hz, 1H, ArH), 7.62 (t, J = 7.6 Hz, 3H, ArH), 7.75 (t, J = 7.6 Hz, 1H, ArH), 7.86 (d, J = 8.6 Hz, 1H, ArH), 8.13 (d, J = 7.6 Hz, 2H, ArH).; δ_C 21.86 (CH_3), 30.06 (aliph. CH), 34.5 ($2CH_2$), 49.4 (N–CH_2), 53.1 ($2CH_2$), 90.4 (C-3), 116.2 (C-4a), 116.6 (CN), 117.1, 122.35, 127.1, 128.4, 129.1, 133.5, 134.3 and 134.7 (Ar–C), 140.65 (C-8a), 160.5 (C-4), 163.7 (CO), 193.2 (CO). MS: *m/z* (%) 386 ($M^+ + 1$, 12), 385 (M^+, 47), 280 (100), 266 (13), 252 (12), 128 (14), 105 (73), 77 (36), 55 (15), 41 (10). Anal: Calcd for $C_{24}H_{23}N_3O_2$ (385.46): C, 74.78; H, 6.01; N, 10.90. Found: C, 74.93; H, 5.87; N, 11.09%.

5-Alkyl-3-amino-1H-pyrazolo[4,3-c]quinolin-4(5H)-ones (**8a–c**), *general procedure*

To a solution of the nitrile **6a–c** (0.71 mmol) in EtOH (5 ml), hydrazine hydrate (80%) (4.26 mmol) was added. The reaction mixture was refluxed for 12 h, until TLC showed the disappearance of the starting compounds. After concentration and cooling to room temperature, the resulting solid product was isolated by filtration, washed with EtOH, dried and recrystallised from EtOH to give the fused pyrazoles **8a–c**.

3-Amino-5-methyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one (**8a**): Colourless crystals, (0.10 g, 66%), m.p. 296–297 °C. IR: ν_{max} 3552, 3424, 3328, 3152 (NH, NH_2), 2928 (aliph CH), 1640 (amide CO) cm^{-1}. NMR: δ_H 3.56 (s, 3H, N-CH_3), 5.42 (br s, 2H, NH_2), 7.28–8.01 (m, 4H, ArH), 12.91 (s, 1H, pyrazole NH). MS: *m/z* (%) 215 ($M^+ + 1$, 29), 214 (M^+, 100), 213 (36), 185 (34), 170 (10), 159 (10), 142 (10), 130 (24), 116 (10), 102 (12), 89 (18), 77 (16). Anal: Calcd for $C_{11}H_{10}N_4O$ (214.22): C, 61.67; H, 4.71; N, 26.15. Found: C, 61.85; H, 4.89; N, 25.97%.

3-Amino-5-ethyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one (**8b**): Colourless crystals, (0.117 g, 72%), m.p. 228–229 °C. IR: ν_{max} 3408, 3328, 3200, 3152 (NH, NH_2), 2992, 2928 (aliph CH), 1630 (amide CO) cm^{-1}. NMR: δ_H 1.22 (t, J = 7 Hz, 3H, CH_3), 4.26 (q, J = 7 Hz, 2H, CH_2), 5.42 (br s, 2H, NH_2), 7.27–8.03 (m, 4H, ArH), 12.77 (s, 1H, pyrazole NH). MS: *m/z* (%) 229 ($M^+ + 1$, 14), 228 (M^+, 100), 227 (31), 213 (32), 200 (79), 183 (25), 171 (8), 145 (10), 128 (10), 116 (13), 102 (7), 89 (10), 77 (8). Anal: Calcd for $C_{12}H_{12}N_4O$ (228.25): C, 63.15; H, 5.30; N, 24.55. Found: C, 63.29; H, 5.16; N, 24.68%.

3-Amino-5-phenacyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one (**8c**): Yellowish crystals (0.140 g, 62%). m.p. 281–282 °C. IR: ν_{max} 3440, 3310, 3136 (NH, NH_2), 2930 (aliph CH), 1640 (amide CO) cm^{-1}. NMR: δ_H 4.34 (s, 2H, CH_2), 5.51 (br s, 2H, NH_2), 7.27 (m, 2H, ArH), 7.36 (t, J = 7.6 Hz, 2H, ArH), 7.48 (d, J = 7.5 Hz, 3H, ArH), 7.71 (d, J = 7.8 Hz, 1H, ArH), 7.99 (d, J = 7.5 Hz, 1H, ArH), 12.75 (s, 1H, pyrazole NH). MS: *m/z* (%) 320 ($M^+ + 2$, 14), 214 (100), 213 (95), 200 (38), 183 (43), 156 (9), 130 (15), 116 (12), 102 (10), 89 (9), 77 (28). Anal: Calcd for $C_{18}H_{14}N_4O_2$ (318.33): C, 67.91; H, 4.43; N, 17.60. Found: C, 68.02; H, 4.61; N, 17.47%.

5-Alkyl-3-azido-1H-pyrazolo[4,3-c]quinolin-4(5H)-ones **9a,b**: *General procedure*

A solution of the amine **8a,b** (1.87 mmol) in H_2SO_4 (4 ml, 70%) was cooled until the temperature of solution was –5 °C and treated with sodium nitrite (0.387 g, 5.61 mmol) in water (1 ml). To the resulting solution of the diazonium ion was added sodium azide (0.364 g, 5.61 mmol) in water (1 ml) and maintained between 0 and –5 °C. Stirring was continued for one h at room temperature. The resulting solid product was collected by filtration, washed with H_2O, dried and recrystallised from $CHCl_3$ to give the azide **9a,b**.

3-Azido-5-methyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one (**9a**): Colourless crystals (0.396 g, 88%), m.p. 223–224 °C (decomp.). IR: ν_{max} 3150 (NH), 3020 (arom. CH), 2900 (aliph. CH), 2130 (N_3), 1630 (amide CO) cm^{-1}. NMR: δ_H 3.57 (s, 3H, N-CH_3), 7.35 (t, J = 7.5 Hz, 1H, ArH), 7.53 (d, J = 8.5 Hz, 1H, ArH), 7.63 (t, J = 7.5 Hz, 1H, ArH), 8.06 (d, J = 8.5 Hz, 1H, ArH), 13.95 (s, 1H, pyrazole NH); δ_C 28.7 (N–CH_3), 101.8 (C-3a), 110.7 (C-9a), 116.1, 122.3, 122.6 and 130.8 (Ar–C), 138.9 (C-5a), 142.25 (C-9b), 145.7 (C-3), 156.85 (CO). MS: *m/z* (%) 241 ($M^+ + 1$, 6), 240 (M^+, 43), 214 (8), 184 (80), 155 (100), 141 (9), 129 (55), 114 (23), 102 (28), 88 (15), 77 (21), 63 (11), 51 (14). Anal: Calcd for $C_{11}H_8N_6O$ (240.22): C, 55.00; H, 3.36; N, 34.98. Found: C, 54.89; H, 3.49; N, 34.73%.

3-Azido-5-ethyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one (**9b**): Colourless crystals, (0.290 g, 87%); m.p. 227 °C (decomp.). IR: ν_{max} 3150 (NH), 3020 (arom. CH), 2970 (aliph. CH), 2130 (N_3), 1630 (amide CO) cm^{-1}. NMR: δ_H 1.22 (t, J = 7 Hz, 3H, CH_3), 4.28 (q, J = 7 Hz, 2H, CH_2), 7.35 (t, J = 7.6 Hz, 1H, ArH), 7.62 (m, 2H, ArH), 8.10 (d, J = 8 Hz, 1H, ArH), 13.97 (s, 1H, pyrazole NH); δ_C 13.0 (CH_3), 36.1 (N-CH_2), 101.8 (C-3a), 111.0 (C-9a), 116.0, 122.2, 122.9, and 130.9 (Ar-C), 137.8 (C-5a), 142.35 (C-9b), 145.7 (C-3), 156.5 (CO).Anal: Calcd for $C_{12}H_{10}N_6O$ (254.25), C, 56.69; H, 3.96; N, 33.05. Found: C, 56.53; H, 4.08; N, 33.24%.

Received 4 June 2008; accepted; 10 November 2008
Paper 08/5290 doi:10.3184/030823408X392198
Published online: 17 December 2008

References

1 G. Hojas, W. Fiala and W. Stadlbauer, *J. Heterocyclic Chem.*, 2000, **37**, 1559.
2 L. Checchi, F. Melani, G. Palazzino, G. Filacchioni and C. Martini, *Farmaco Ed. Sci*, 1985, **40**, 509.
3 F. Melani, L. Checchi, G. Palazzino, G. Filacchioni, C. Martini, E. Penacchi and A. Lucacchini, *J. Med. Chem.*, 1986, **29**, 291.
4 L. Ismaili, B. Refouvelet and J.F. Robert, *J. Heterocyclic Chem.*, 1999, **36**, 719.
5 S. Fumio, N. Yoshisuke, O. Kenji, T. Tadafumi, H. Hisashi, K. Kazuhiro and Y. Ikufumi, *Eur. Pat.* 476544 (1992); *C. A.* 1992, **116**, 255609 m.
6 B. Baruah, K. Dasu, B. Vaitilingam, A. Vanguri, S.R. Casturi and K.R. Yeleswarapu, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 445.
7 E.F.V. Scriven, *Azides and nitrenes*, Academic Press, Orlando, Florida, 1984, pp. 511-516.
8 S. Kota and R. Klaus, *Arch. Pharm.*, 1998, **331**, 207.
9 R. Castillo, J. Andrès and L.R. Domingo, *Eur. J. Org. Chem.*, 2005, 4705.
10 S. Dieter, R. Dieter, H. Siegfried, W. Horst and M. Gerhard, *Synthesis*, 1985, 331.
11 D. Boujemaa and S. Mohamed, *Tetrahedron*, 1989, **45**, 3351.
12 T. Kappe, R. Aigner, M. Joebstl, P. Hohengassner and W. Stadlbauer, *Heterocycl. Commun.*, 1995, **1**, 341.
13 R. Mekheimer, E.Kh. Ahmed and A.F. Khattab, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 2936.
14 R. Mekheimer, *Pharmazie*, 1994, **49**, 486.
15 R.A. Mekheimer and T. Kappe. *Heterocyclic Commun.*, 1998, **4**, 131.
16 R.A. Mekheimer, *Synth. Commun.*, 2001, **31**, 1971.
17 R.A. Mekheimer, E.Kh. Ahmed, H.A. El-Fahham, L.H. Kamel and D. Döpp, *J. Chem. Res. (S)*, 2003, 388.
18 R. Mekheimer, *J. Chem. Soc., Perkin Trans 1*, 1999, 2183.
19 W. Steinschifter and W. Stadlbauer, *J. Prakt. Chem.*, 1994, **336**, 311.
20 W. Stadlbauer, *Monatsh. Chem.*, 1986, **117**, 1305.
21 T. Kappe, P.F. Fitz and E. Ziegler, *Chem. Ber.*, 1973, **106**, 1927.
22 G.M. Coppola and G.E. Hardtmann, *J. Heterocycl. Chem.*, 1981, **18**, 917.
23 G.M. Coppola, A.D. Kahle and M. Shapiro, *Org. Magn. Reson.*, 1981, **17**, 242.
24 J.L. Garcia Ruano, C. Pedregal and J.H. Rodriguez, *Heterocycles*, 1991, **32**, 2151.
25 J. Elguero, R. Faure, J.P. Galy and E.J. Vincent, *Bull. Soc. Chim. Belg.*, 1975, **84**, 1189.
26 G.A. Reynolds, J.A. VanAllan and J.F. Tinker, *J. Org. Chem.*, 1959, **24**, 1205.
27 M. Tisler, *Synthesis*, 1973, 123.
28 J. Elguero, C. Marzin, A.R. Katritzky and P. Linda, *The tautomerism of heterocycles, Advances in Heterocyclic Chemistry, Suppl.*, Academic Press, New York, Vol. I., 1976.
29 R. Faure, J.P. Galy, E.J. Vincent, J.P. Fayet, P. Mauret, M.C. Vertut and J. Elguero, *Can. J. Chem.*, 1977, **55**, 1728.
30 M. Kanyalkar and E.C. Coutinho, *Tetrahedron*, 2000, **56**, 8775.