ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2011, *56*(7), 691-695

PYRROLO[2,1-*a*]ISOQUINOLINE DERIVATIVES *via* 1,3-DIPOLAR CYCLOADDITION OF ISOQUINOLINIUM *N*-YLIDES (II)

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Received April 22, 2010

The reaction of *N*-isoquinolinium bromides **3** with acrylonitrile and crotononitrile as activated olefinic dipolarophiles gave in the presence of triethylamine and the oxidant tertrakis-pyridinecobalt(II) dichromate (TPCD), in DMF at 90 ºC, 1-cyanopyrrolo[2,1-*a*]isoquinoline derivatives **6** and **7**. Structural proof for the compounds was provided by elemental analysis and NMR spectroscopy, including COSY and HETCOR experiments.

INTRODUCTION

The chemistry and biological properties of the pyrrolo[2,1-*a*]isoquinoline were reviewed in 1997 by Mikhailovskii and Shklyaev.[1] After this date, new methods for the synthesis of the pyrrolo[2,1-*a*]isoquinoline and reconsiderations of already known synthetic pathways have been reported.[2] The pyrrolo[2,1-*a*]isoquinoline framework is present in a number of natural bioactive products such as lamellarins,[3] crispine,[4] telisatin.[5] The lamellarins, a group of alkaloids that were isolated from marine mollusks, exhibit a wide array of interesting and significant biological activities such as cell differentiation inhibition and cytotoxicity. For this reason the synthesis of new pyrrolo[2,1-*a*]isoquinoline derivatives related to lamellarins is a promising challenge in the area of antitumor agents.

One of the most important methods for the synthesis of pyrrolo[2,1-*a*]isoquinoline and others pyrroloazines consist in the 1,3-dipolar cycloaddition reactions of heteroaromatic *N*-ylides with activated alkynes or alkenes.[6] Our interest in the synthesis and properties of pyrroloazines[7] prompted us to synthesize new pyrrolo[2,1-*a*]isoquinoline derivatives.

Herein is reported the one-pot synthesis of pyrrolo[2,1-*a*]isoquinoline derivatives by 1,3 dipolar cycloaddition reaction between isoquinolinium *N*-ylides and acrylonitrile or crotonitrile as dipolarophile, in the presence of the oxidant reagent tetrakis-pyridine cobalt (II) dichromate (TPCD).

RESULTS AND DISCUSSION

The starting intermediates for the synthesis of 1-cyanopyrrolo[2,1-*a*]isoquinolines **6** and **7** were *N*-isoquinolinium bromides **3** (Scheme 1). The quaternary salts **3** were easily prepared by an well-known procedure consisting in *N*-alkylation of isoquinoline with activated bromo derivatives **2** in acetone at room temperature. As alkylation reagents for isoquinoline were used 2-bromoacetophenones and ethyl bromoacetate.

The 1-cyanopyrrolo[2,1-*a*]isoquinolines were obtained by 1,3-dipolar cycloaddition reaction of isoquinolinium *N*-ylides with acrylonitrile or crotononitile in the presence of tertrakis-pyridinecobalt(II) dichromate (TPCD) in DMF at 90 ºC. The tetrakis-pyridine cobalt (II) dichromate [$Py_4Co(HCrO_4)_2$] is an oxidant reagent which was

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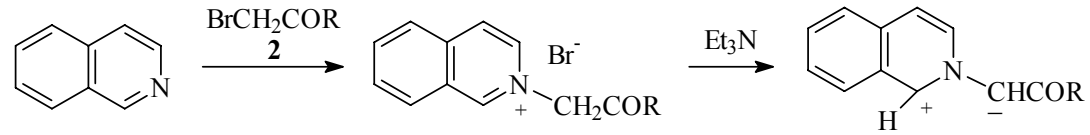
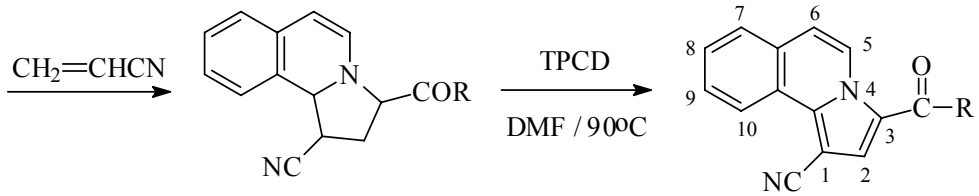
used with good results for aromatization of the cycloadducts resulted from reaction of heteroaromatic *N*-ylides and olefinic or acetylenic dipolarophiles.[8] Usually, the isoquinolinium *N*-ylides are unstable compounds and they are generated *in situ* by the reaction between *N*-alkylated isoquinolinium salts and a base such as triethylamine, aqueous solution of K_2CO_3 etc.

By heating the solution in DMF of the isoquinolium bromides **3** and acrylonitrile with triethylamine, in the presence of TPCD, 1-cyanopyrrolo[2,1-*a*]isoquinolines **6** were directly obtained with yields in the 60-85 % range (Scheme 1).

The reaction mechanism for formation of the pyrroloisoquinolines **6** implies in the first step the generation of isoquinolinium *N*-ylide **4** by the action of triethylamine on the isoquinolinium bromides **3**. Subsequently, 1,3-dipolar cycloaddition between the N-ylides **4** and acrylonitrile afforded the corresponding primary cycloadducts **5**. Finally, the 1,2,3,9a-tetrahydropyrrolo[2,1-*a*]isoquinolines **5** were aromatized to pyrroloisoquinoline **6** by the action of oxidant reagent, namely TPCD.

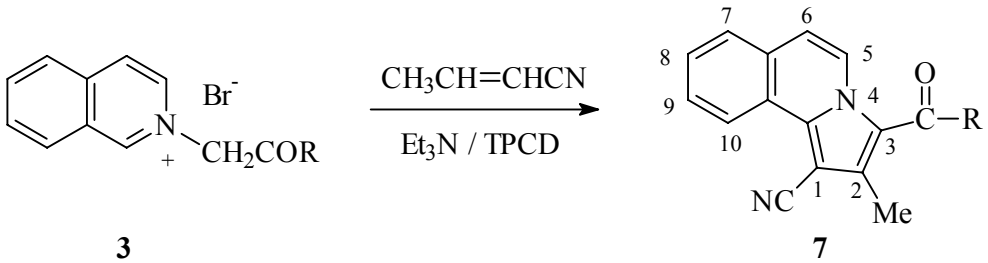
In the same way, direct reactions of *N*-isoquinolinium salts **3** with crotononitrile in DMF in the presence of triethylamine and TPCD gave 1-cyano-2-methylpyrroloisoquinolines **7** in good yields (Scheme 2).





6a: R = OEt
6b: R = 4-FC_6H_4
6c: R = 4-BrC_6H_4
6d: R = 4-$MeOC_6H_4$
6e: R = 3,4-$(MeO)_2C_6H_3$
6f: R = 1-naphthyl
6g: R = 2-naphthyl

Scheme 1



7a: R = OEt
7b: R = Ph
7c: R = 4-BrC_6H_4
7d: R = 4-$NO_2C_6H_4$
7e: R = 2-naphthyl

Scheme 2

The structures of the new pyrroloisoquinolines were assigned by elemental analysis, IR and NMR spectroscopy. On the bases of NMR data was found that the cycloaddition reaction between acrylonitrile or crotononitrile and isoquinolinium *N*-ylides is completely regioselective, as only one regioisomer was obtained.

In the IR spectra of the nitriles **6** and **7** the characteristic bands are those for carbonyl and cyano groups. The carbonyl group in the carboethoxy groups is observed as strong bands at 1700 cm^{-1} for compound **6a** and 1698 cm^{-1} for **7a**, respectively. In the case 3-aroyl-pyrrolo[2,1-*a*]isoquinolines **6b-g** and **7b-e** the wavenumbers are in the range 1618-1628 cm^{-1}. The bands for C≡N groups are distinctive for all pyrrolo[2,1-*a*]isoquinolines and are in the range 2210-2224 cm^{-1}.

In the ^{1}H-NMR spectra of compounds **6** and **7** the general characteristic feature is the chemical shifts of atoms H-5, H-6 and H-10. The two protons from the pyridine moiety, namely H-5 and H-6 appear as two doublets with a coupling constant of $^3J_{H5H6}$ = 7.5 Hz. The proton H-5 is strongly deshielded due to its vicinity with carbonyl groups. Similarly, the deshielding of H-10 could be explained by the spatial vicinity with cyano group and represents an evidence for regioselectivity of the cycloaddition reaction. In the case of pyrroloisoquinolines **6** the proton H-2 is a sharp singlet with chemical shifts in the range 7.55-7.73 ppm.

The ^{13}C-NMR spectra show all the expected signals. The most characteristic feature is strong shielding observed for C-1 with δ in the range 85.1-88.4 ppm that is a consequence of its relative β positions to the pyrrole nitrogen, as well as the effect of cyano group. The presence of the cyano group in the molecules of pyrroloisoquinolines was attributed to the signals that appear at about 117 ppm. The carbon C-2 in the compounds **6** appears in the range 124.3-131.4 ppm, whereas in compounds **7** due to the methyl group attached at the 2 position the chemical shift for C-2 is deshielded with about 8 ppm.

Table 1

Significant C-RMN data for some nitriles **6** and **7**

Compound	C-1	C-2	C-5	C-6	C-8 C-9	C-7	C-10	CO	CN
6a	85.1	124.3	124.2	115.1	128.6 129.4	127.1	123.6	160.3	117.3
6d	85.4	127.8	125.1	115.4	128.6 129.8	127.1	123.9	184.2	117.2
6e	85.4	127.8	125.1	115.5	128.7 129.8	127.2	123.9	184.2	117.2
7a	87.7	135.5	124.4	114.0	128.1 129.0	126.8,	123.0	161.0	116.8
7b	88.3	136.4	123.9	114.0	127.1 129.6	127.1	123.9	187.3	116.9
7c	88.5	136.3	124.0	114.8	127.2 129.7	127.2	124.0	186.0	116.8

EXPERIMENTAL

Melting points were determined on a Boëtius hot plate microscope and are uncorrected. The elemental analysis was carried out on a COSTECH Instruments EAS32 apparatus. The IR spectra were recorded on a Nicolet Impact 410 spectrometer, in KBr pellets. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR. Supplementary evidence was given by HETCOR and COSY experiments.

General procedure for synthesis of pyrrolo[2,1-*a*]isoquinolines 6 and 7

To a solution of 5 mmol of isoquinolinium bromide **3** and 20 mmol of nitrile derivative in 25 mL DMF 1mL of triethylamine and 1.88 g TPCD were added. The mixture was stirred at 90-95°C for 2 hours. The cooled mixture was poured under stirring in 50 mL HCl 5% and the final product was extracted with chloroform (3x25 mL). Combined extracts were washed with water, dried on Na_2SO_4 anh. and chloroform was removed by distillation. The remaining solid was recrystallised from $CHCl_3$/MeOH.

Ethyl 1-cyano-pyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**6a**). Colorless crystals with mp 166-7° C; Yield 85 %. Anal. Calcd. $C_{16}H_{12}N_2O_2$: C 72.72; H 4.58; N 10.60. Found: C 72.52; H 4.90; N 10.84. FT-IR (cm^{-1}): 1700 (C=O), 2215 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.43 (t, 3H, *J* = 7.1 Hz, $MeCH_2$); 4.41 (q, 2H, *J* = 7.1 Hz, CH_2); 7.20 (d, 1H, *J* = 7.5 Hz, H-6); 7.61-7.70 (m, 2H, H-8, H-9); 7.73 (s, 1H, H-2); 7.74 - 7.78 (m, 1H, H-7); 8.90-8.93 (m, 1H, H-10); 9.28 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.4 (Me); 60.8 (CH_2); 85.1 (C-1); 115.1 (C-6); 117.2, 117.3 124.2, 128.9, 136.9 (C-3, C-6a, C-10a, C-10b, CN); 123.6 (C-10) ; 124.2 (C-5); 124.3 (C-2); 127.1 (C-7); 128.6, 129.4 (C-8, C-9); 160.3 (COO).

1-cyano-3-(4-fluorobenzoyl)pyrrolo[2,1-*a*]isoquinoline (**6b**). Pale yellow crystals with mp 252-3º C; Yield 83 %. Anal. Calcd. $C_{20}H_{11}FN_2O$: C 76.42; H 3.53; N 8.91. Found: C 76.5, H 3.39, N 9.02. FT-IR (cm^{-1}): 1626 (C=O), 2223 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$+TFA) 7.21 (d, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.36 (d, 1H, *J* = 7.5 Hz, H-6); 7.59 (s, 1H, H-2); 7.70-7.76 (m, 2H, H-8, H-9); 7.80-7.86 (m, 3H, H-7, H-2', H-6'); 8.86-8.92 (m, 1H, H-10); 9.58 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$+TFA) δ: 85.6 (C-1); 115.9 (d, *J* = 21.9 Hz, C-3', C-5'); 116.2 (CN); 116.4 (C-6); 123.4, 125.0, 130.2, 138.9 (C-3, C-6a, C-10a, C-10b); 123.8 (C-10); 125.1 (C-5); 127.5 (C-7); 129.1 (C-2); 130.3, 130.8 (C-8, C-9); 131.2 (d, *J* = 9.0 Hz, C-2', C-6'); 134.8 (d, *J* = 3.0 Hz, C-1'); 163.6 (d, *J* = 253.5 Hz, C-4'); 185.4 (COAr).

1-cyano-3-(4-bromobenzoyl)pyrrolo[2,1-*a*]isoquinoline (**6c**). Pale yellow crystals with mp 276-7º C; Yield 61 %. Anal. Calcd. $C_{20}H_{11}BrN_2O$: C 64.02; H 2.95; Br 21.29, N 7.47. Found C 64.31; H 2.78; Br 21.60, N 7.71. FT-IR (cm^{-1}): 1627 (C=O), 2224 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$+TFA) 7.46 (d, 1H, *J* = 7.5 Hz, H-6); 7.68 (s, 1H, H-2); 7.68, 7.74 (d, 2H, *J* = 8.8 Hz, H-2', H-3', H-5', H-6'); 7.79-7.84 (m, 2H, H-7, H-9); 7.88-7.94 (m, 1H, H-8,); 8.90-8.96 (m, 1H, H-10); 9.56 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$+TFA) δ: 85.6 (C-1); 117.2 (CN); 119.9 (C-6); 123.2, 124.0, 129.2, 130.4, 136.6 (C-3, C-6a, C-10a, C-10b, C-4'); 124.2 (C-10); 125.2 (C-5); 127.6 (C-7); 129.5 (C-2); 130.7; 132.3 (C-2', C-3', C-5', C-6'); 138.8 (C-1'); 131.1, 131.8 (C-8, C-9); 186.5 (COAr).

1-cyano-3-(4-methoxybenzoyl)pyrrolo[2,1-*a*]isoquinoline (**6d**). Pale yellow crystals with mp 200-201º C; Yield 80 %. Anal. Calcd. $C_{21}H_{14}N_2O_2$: C 77.29; H 4.32; N 8.58. Found C 77.52; H 4.11; N 8.79. FT-IR (cm^{-1}): 1623 (C=O), 2220 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.91 (s, 3H, MeO); 7.03 (d, 2H, *J* = 8.8 Hz, H-3', H-5'); 7.25 (d, 1H, *J* = 7.5 Hz, H-5); 7.55 (s, 1H, H-2); 7.66-7.72 (m, 2H, H-8, H-9); 7.77-7.82 (m, 1H, H-7); 7.87 (d, 2H, *J* = 8.8 Hz, H-2', H-6'); 8.93-8.96 (m, 1H, H-10); 9.45 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 55.5 (MeO); 85.4 (C-1); 113.8 (C-3', C-5'); 115.4 (C-6); 117.2 (CN) 123.6, 124.6, 129.6, 131.3, 137.5 (C-3, C-6a, C-10a, C-10b, C-1'); 123.9 (C-10); 125.1 (C-5); 127.1 (C-7); 127.8 (C-2); 128.6, 129.8 (C-8, C-9); 131.5 (C-2', C-6'); 163.1 (C-4'); 184.2 (COAr).

1-cyano-3-(3,4-dimethoxybenzoyl)pyrrolo[2,1-*a*]isoquinoline (**6e**). Colorless crystals with mp 206-207º C; Yield 79 %. Anal. Calcd. $C_{22}H_{16}N_2O_3$: C 74.15; H 4.53; N 7.86. Found: C 74.39; H 4.19; N 8.09. FT-IR (cm^{-1}): 1619 (C=O), 2221 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.98, 4.00 (2s, 6H, 2Me); 6.98 (d, 1H, *J* = 8.4 Hz, H-5'); 7.28 (d, 1H, *J* = 7.5 Hz, H-6); 7.46 (d, 1H, *J* = 1.9 Hz, H-2'); 7.51 (dd, 1H, *J* = 1.9, 8.4 Hz, H-6'); 7.59 (s, 1H, H-2); 7.68-7.72 (m, 2H, H-8, H-9); 7.79-7.84 (m, 1H, H-7); 8.97-9.00 (m, 1H, H-10); 9.45 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 56.0, 56.1 (2 MeO); 85.4 (C-1); 110.3, 111.6 (C-2', C-5'); 115.5 (C-6); 117.2 (CN); 123.7, 124.8, 129.6, 131.5, 137.5 (C-3, C-6a, C-10a, C-10b, C-1'); 123.9 (C-10, C-6'); 125.1 (C-5); 127.2 (C-7); 127.8 (C-2); 128.7, 129.8 (C-8, C-9); 131.5 (C-2', C-6'); 163.1 (C-4'); 184.2 (COAr).

1-cyano-3-(1-napthoyl)pyrrolo[2,1-*a*]isoquinoline (**6f**). Yellow crystals with mp 209-211 ºC; Yield 83 %. Anal. Calcd. $C_{24}H_{14}N_2O$: C 83.22; H 4.07; N 8.09. Found: C 83.54; H 4.19; N 8.30. FT-IR (cm^{-1}): 1628 (C=O), 2216 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) 7.37 (d, 1H, *J* = 7.5 Hz, H-6); 7.49-7.58, 7.68-7.75, 7.81-7.87, 7.91-7.96, 8.01-8.06, 8.10-8.14 (6m, 11H, H-7, H-8, H-9, H-10, 7H-naphthyl); 7.59 (s, 1H, H-2); 8.95-8.98 (m, 1H, H-10); 9.82 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 86.1 (C-1); 115.9 (C-6); 116.7 (CN); 123.6, 125.7, 129.9, 130.7, 133.7, 136.7, 137.9 (C-3, C-6a, C-10a, C-10b, C-1', C-4a', C-8a'); 124.0, 124.3, 125.2, 125.3, 126.5, 127.0, 127.1, 127.3, 128.4, 128.8, 129.7, 130.0, 131.2 (C-2, C-5, C-7, C-8, C-9, C-10, C-2', C-3', C-4', C-5', C-6', C-7', C-8'); 186.7 (COAr).

1-cyano-3-(2-napthoyl)pyrrolo[2,1-*a*]isoquinoline (**6g**). Colorless crystals with mp 259-260 ºC; Yield 73 %. Anal. Calcd. $C_{24}H_{14}N_2O$: C 83.22; H 4.07; N 8.09. Found: C 83.02; H 4.40; N 7.91. FT-IR (cm^{-1}): 1622 (C=O), 2222 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) 7.34 (d, 1H, *J* = 7.5 Hz, H-6); 7.65 (s, 1H, H-2); 7.59-7.68, 7.72-7.78, 7.82-7.87, 7.91-7.96, 7.98-8.02 (5m, 10H, H-7, H-8, H-9, H-10, 6H-naphthyl); 8.54-8.56 (m, 1H, H-1'); 9.01-9.05 (m, 1H, H-10); 9.61 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 85.8 (C-1); 115.8 (C-6); 117.1 (CN); 123.7, 124.6, 129.8, 132.3, 135.1, 136.2, 138.1 (C-3, C-6a, C-10a, C-10b, C-2', C-4a', C-8a'); 124.1, 125.2, ,127.0, 127.2, 127.8, 128.3, 128.6, 128.8, 128.9, 129.3, 130.0, 130.4 (C-2, C-5, C-7, C-8, C-9, C-10, C-1', C-3', C-4', C-5', C-6', C-7', C-8'); 185.4 (COAr).

Ethyl 1-cyano-2-methyl-pyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**7a**). Yellow crystals with mp 171-3º C; Yield 71 %. Anal. Calcd. $C_{17}H_{14}N_2O_2$: C 73.37; H 5.07; N 10.07. Found: C 73.62; H 5.34; N 10.25. FT-IR (cm^{-1}): 1689 (C=O), 2210 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.45 (t, 3H, *J* = 7.1 Hz, **Me**CH_2); 2.65 (s, 3H, 2-Me); 4.43 (q, 2H, *J* = 7.1 Hz, CH_2); 7.10 (d, 1H, *J* = 7.5 Hz, H-6); 7.59-7.64 (m, 2H, H-8, H-9); 7.72-7.69 (m, 1H, H-7); 8.83-8.86 (m, 1H, H-10); 9.27 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.1, 14.3 (2Me); 60.5 (CH_2); 87.7 (C-1); 114.0 (C-6); 114.7, 116.8, 123.0, 128.8, 135.5, 136.6 (C-2, C-3, C-6a, C-10a, C-10b, CN); 123.0, 126.8, 128.1, 129.0 (C-7, C-8, C-9, C-10); 124.4 (C-5); 161.0 (COO).

1-cyano-3-benzoyl-2-methyl-pyrrolo[2,1-*a*]isoquinoline (**7b**). Yellow crystals with mp 221-3º C; Yield 63%. Anal. Calcd. $C_{21}H_{14}N_2O$: C 81.27; H 4.55; N 9.03. Found: C 81.49; H 4.82; N 9.31. FT-IR (cm^{-1}): 1618 (C=O), 2210 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.12 (s, 3H, 2-Me); 7.16 (d, 1H, *J* = 7.5 Hz, H-6); 7.49-7.55 (m, 2H, H-3', H-5'); 7.59-7.78 (m, 6H, H-7, H-8, H-9, 3H-Ph); 8.89-8.93 (m, 1H, H-10); 9.05 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.6 (2-Me); 88.3 (C-1); 114.0 (C-6); 116.9 (CN); 123.2, 123.5, 128.6, 136.3, 136.4, 139.9 (C-2, C-3, C-6a, C-10a, C-10b, C-1'); 123.9, 124.7, 127.1, 129.6 (C-7, C-8, C-9, C-10); 128.7 (C-2', C-3', C-5', C-6'); 132.5 (C-4'); 187.3 (COAr).

1-cyano-3-(4-bromobenzoyl)-2-methyl-pyrrolo[2,1-*a*]isoquinoline (**7c**). Pale yellow crystals with mp 210-2 ºC; Yield 67 %. Anal. Calcd. $C_{21}H_{13}BrN_2O$: C 64.80; H 3.37; Br 20.53, N 7.20. Found: C 64.59; H 3.44; Br 20.19, N 7.17. FT-IR (cm^{-1}): 1620 (C=O), 2212 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.16 (s, 3H, 2-Me); 7.19 (d, 1H, *J* = 7.5 Hz, H-6); 7.61, 7.68 (2d, 4H, H-2', H-3', H-4', H-6'); 7.67-7.72 (m, 2H, H-8, H-9); 7.76-7.81 (m, 1H, H-7); 8.92-8.96 (m, 1H, H-10); 9.01 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.8 (2-Me); 88.5 (C-1); 114.8 (C-6); 116.8 (CN); 123.0, 123.2, 127.6, 128.6, 136.3, 136.4, 138.7 (C-2, C-3, C-6a, C-10a, C-10b, C-1', C-4'); 124.0, 124.6, 127.2, 129.7 (C-7, C-8, C-9, C-10); 128.7 (C-2', C-3', C-5', C-6'); 132.5 (C-4'); 186.0 (COAr).

1-cyano-2-methyl-3-(4-nitrobenzoyl)pyrrolo[2,1-*a*]isoquinoline (**7d**). Yellow crystals with mp 262-4 ºC; Yield 60 %. Anal. Calcd. $C_{21}H_{13}N_3O_3$: C 70.98; H 3.69; N 11.82. Found: C 70.71; H 3.92; N 12.11. FT-IR (cm^{-1}): 1620 (C=O), 2210 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$+TFA) δ: 2.11 (s, 3H, 2-Me); 7.26 (d, 1H, *J* = 7.5 Hz, H-6); 7.66-7.80 (m, 5H, H-7, H-8, H-9, H-2', H-6'); 8.33 (d, 2H, *J* = 8.5 Hz, H-3', H-5'); 8.80-8.86 (m, 1H, H-10); 9.20 (d, 1H, *J* = 7.5 Hz, H-5).

1-cyano-2-methyl-3-(2-napthoyl)pyrrolo[2,1-*a*]isoquinoline (**7e**).Yellow crystals with mp 230-231 ºC; Yield 61 %. Anal. Calcd. $C_{25}H_{16}N_2O$: C 83.31; H 4.47; N 7.77. Found: C 83.70; H 4.71; N 8.04. FT-IR (cm^{-1}): 1627 (C=O), 2212 (C≡N).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.13 (s, 3H, 2-Me); 7.26 (d, 1H, *J* = 7.5 Hz, H-6); 7.55-7.70, 7.73-7.78, 7.82-7.85, 7.91-8.00 (4m, 10H, H-7, H-8, H-9, H-10, 6H-naphthyl); 8.23-8.26 (m, 1H, H-1'); 8.92-8.96 (m, 1H, H-10); 9.03 (d, 1H, *J* = 7.5 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.7 (2-Me); 88.2 (C-1); 114.6 (C-6); 117.0 (CN); 123.2, 123.5, 123.8, 132.5, 135.2, 136.1, 136.4, 137.0 (C-2, C-3, C-6a, C-10a, C-10b, C-2', C-4'a, C-8'a); 123.9, 124.6, 124.8, 127.0, 127.1, 127.9, 128.4, 128.5, 128.8, 129.2, 129.6, 130.6 (C-5, C-7, C-8, C-9, C-10, C-1', C-3', C-4', C-5', C-6', C-7', C-8'); 187.1 (COAr).

CONCLUSIONS

In conclusion, new 1-cyanopyrrolo[2,1-*a*]isoquinolines were obtained by a simple one-pot procedure and the structure of the new compounds was assigned by elemental analysis, IR and NMR spectroscopy. The regioselectivity of cycloaddition was deduced on the basis of ^{1}H-NMR data.

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