



NEW SUBSTITUTED PYRROLES OBTAINED IN SEARCHING FOR PYRROLO[1,2-*a*]QUINAZOLINE FRAMEWORK

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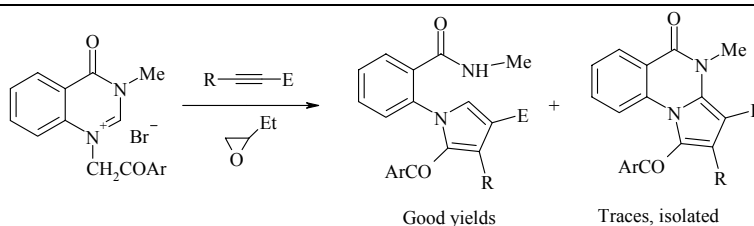
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Received April 9, 2013

The synthesis of new highly substituted N-arylpyrroles was achieved by 1,3-dipolar cycloaddition of the quinazolinium N-ylides with acetylenic dipolarophiles. The reaction was conducted as one-pot procedure in 1,2-epoxybutane as reaction medium and proton scavenger. Structural variety of compounds was conferred by the use of various symmetrical and non-symmetrical acetylenic dipolarophiles. In the case of symmetrical dipolarophiles (*i.e.* Dimethyl acetylenedicarboxylate) the pyrrolo[1,2-*a*]quinazoline framework could be isolated and characterized.



INTRODUCTION

Highly substituted pyrroles and particularly the N-substituted pyrroles are of interest due to their important biological properties.¹⁻⁴ Due to new perspectives opened by concepts such as green and sustainable chemistry efforts were directed to obtain N-arylpyrroles by one-pot procedures which are versatile and cost-effective.^{5,6} Our interest in obtaining new pyrroloazines *via* 1,3-dipolar cycloaddition⁷⁻¹⁶ of N-heteroatomic ylides conducted us to extend our studies to pyrrolo[1,2-*a*]quinazoline skeleton but surprisingly new tri- and tetra-substituted pyrroles were obtained.^{17,18}

Herein is presented the synthesis of a new library of N-arylpyrroles by one-pot procedure

starting from quinazolinium bromides in 1,2-epoxybutane acting both as solvent of the reaction and proton scavenger and also some particular features of this reaction which consist in the formation of pyrrolo[1,2-*a*]quinazoline framework as traces in the reaction mass together with the N-arylpyrroles. This gave us the opportunity to isolate and characterize this interesting tricyclic system which was rather poor investigated for example regarding its biological properties.¹⁹

RESULTS AND DISCUSSION

The main purpose of the present studies was to develop a new route to pyrrolo[1,2-*a*]quinazoline

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framework using 1,3-dipolar cycloaddition reaction as synthetic strategy. However the outcome of the reaction was unexpectedly other than we envisioned, new N-substituted pyrroles being obtained.¹⁷ Thus for the moment the opportunity of developing the reaction in this direction seemed to be very promising.

The key components for the one-pot synthesis of the pyrroles **5** were quinazolinonium bromides **1** which were previously obtained, and the acetylenic dipolarophiles **3**. The working procedure requires mild conditions and involves the mixing of the key components in 1,2-epoxybutane as reaction medium and hydrobromic acid scavenger. The structural variety of the obtained pyrroles is provided by the acetylenic dipolarophiles and the various substituted quinazolinonium bromides utilized herein. In some cases the isolation and characterization of the pyrrolo[1,2-*a*]quinazolinone derivatives was possible and thus such compounds could be characterized.

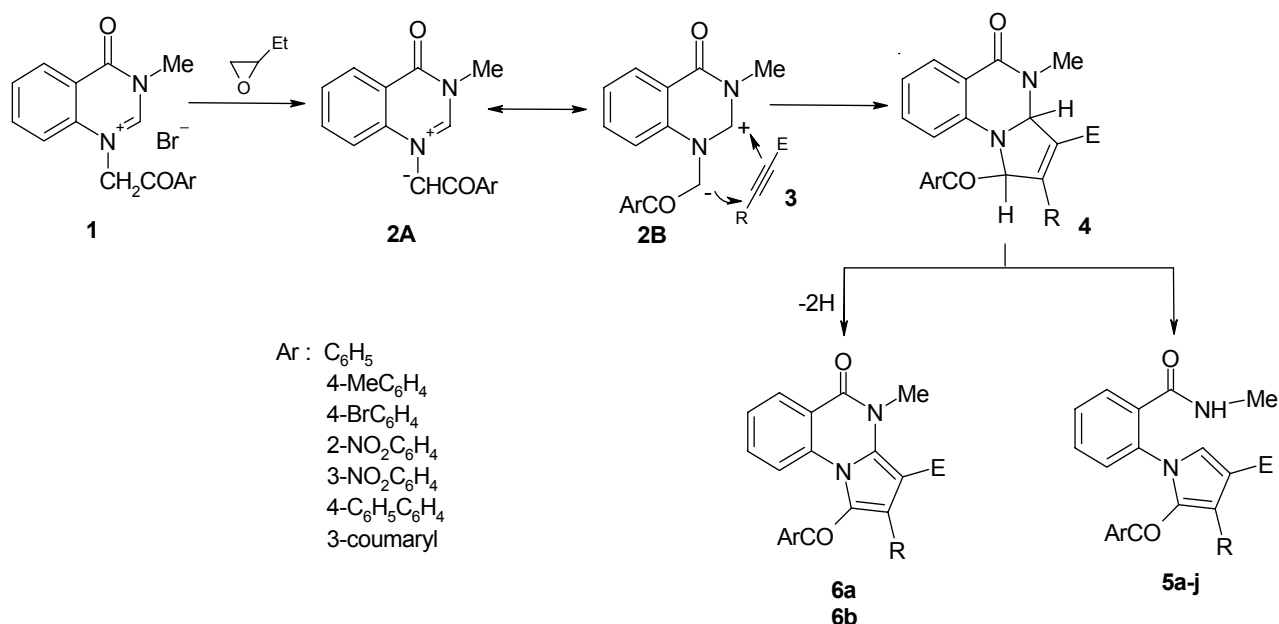
The reaction mechanism consists in the opening of the oxirane ring under the attack of the bromide anion in the salts **1**, followed by the generation of the N-ylide and subsequent cycloaddition reaction with dipolarophile **3** with formation of an unstable dihydro intermediate **4**. The reaction could proceed further in two ways: in the first one, the dehydrogenation of the intermediate could lead to the pyrrolo[1,2-*a*]quinazoline **6** and the second one

leads to the formation of N-arylpyrrole **5** by the ring opening of the dihydro derivative (Scheme 1).

The new N-arylpyrroles **5** were obtained in medium to good yields and by simple working procedures. In the case of symmetrical dipolarophiles, when investigating the reaction mass before the separation of the N-arylpyrroles we observed by means of NMR that small quantities of pyrrolo[1,2-*a*]quinazoline are formed yielding between 0-30%. Thus, the pyrrolo[1,2-*a*]quinazoline **6a** was isolated in the cycloaddition reaction of quinazolinium salt **1b** with DMAD in the presence of epoxybutane, the corresponding pyrrole derivative being reported elsewhere.¹⁷ It must be mentioned that in the same conditions the pyrrolo[1,2-*a*]quinazoline **6b** was isolated together with pyrrole **5h** in the cycloaddition reaction of quinazolinium salt **1d** with DMAD. Pyrrolo[1,2-*a*]quinazolines could be obtained within the reaction mass only in low yields maybe due to the instability of the primary cycloadduct under the influence of the epoxide which favors the rearrangement-ring opening instead of the rearrangement-aromatization path.

The new arylpyrroles **5** and pyrrolo[1,2-*a*]quinazolines **6** are presented in the Table 1.

The N-arylpyrroles **5** and the pyrrolo[1,2-*a*]quinazolines **6** were characterized by IR and NMR spectroscopy including COSY and HETCOR experiments.

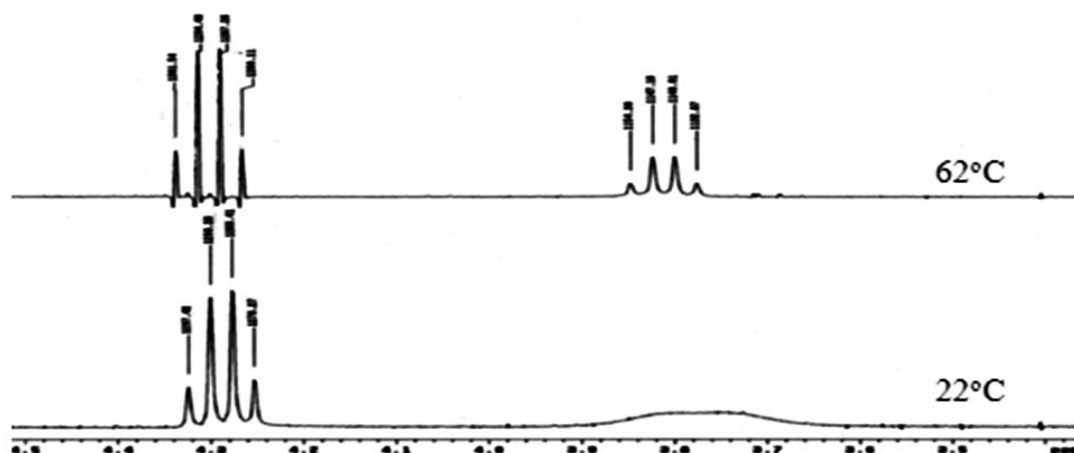


Scheme 1 – The synthetic pathway of the new compounds **5** and **6**.

Table 1

New pyrroles **5** and pyrrolo[1,2-*a*]quinazolines **6**

Nr.	R	E	Ar	mp (°C)	Yield (%)
5a	H	COMe	3-NO ₂ C ₆ H ₄	137-141	62
5b	H	CO ₂ Me	2-NO ₂ C ₆ H ₄	162-164	83
5c	H	CO ₂ Et	4-C ₆ H ₅ C ₆ H ₄	147-150	73
5d	H	CO ₂ Et	2-NO ₂ C ₆ H ₄	149-151	87
5e	H	CO ₂ Et	4-BrC ₆ H ₄	171-172	51
5f	H	CO ₂ CH(CH ₃) ₂	3-NO ₂ C ₆ H ₄	187-189	67
5g	CO ₂ Me	CO ₂ Me	4-C ₆ H ₅ C ₆ H ₄	191-193	80
5h	CO ₂ Me	CO ₂ Me	2-NO ₂ C ₆ H ₄	151-153	65
5i	CO ₂ Me	CO ₂ Me	3-coumaryl	203-204	60
5j	CO ₂ Et	CO ₂ Et	C ₆ H ₅	159-163	54
6a	CO ₂ Me	CO ₂ Me	4-MeOC ₆ H ₄	191-192	30
6b	CO ₂ Me	CO ₂ Me	2-NO ₂ C ₆ H ₄	200-203	20

Fig. 1 – Hindered rotation about C-N bond emphasized by H-NMR spectroscopy (compound **5j**).

The most characteristic bands in the IR spectra of the pyrroles **5** found at 3299-3407 cm⁻¹ corresponding to the amidic NH group. This is the proof for the quinazolinone ring opening, leading to an N-arylpyrrole derivative. The carbonyl bands of pyrroles **5** and the absorption bands of the NO₂ group in the compounds **5a,b,d,f** and **5h** appear in the expected ranges. The ¹H-NMR spectra of compounds **5** are in accordance with the proposed structures. One important evidence of the ring opening of the primary cycloadducts towards the pyrroles ring is given by the multiplicity of the signals of the NH hydrogen which appears as a quartet with $J = 4.9$ Hz and the methyl group attached to it which appears as a doublet with the same magnitude of the coupling constant. Also the hydrogens H-3 and H-5 which appear as two doublets with the coupling constant $J = 1.6$ Hz are in agreement with pyrrolic structure of the compounds. In the case of pyrroles **5g-j** obtained by replacing non-symmetrical dipolarophiles with symmetrical ones like DMAD and DEAD the hydrogen H-5 appears as a sharp singlet in the

range 7.51-7.54 ppm. In the ¹³C-NMR spectra the most characteristic signals are those of the carbon C-5 which appears at ~135 ppm, strongly deshielded due to its direct bonding to the nitrogen atom in the pyrrole moiety. In the case of the carbon atom C-4 there is a slight chemical shift observed for the pyrroles **5a-f** in comparison with pyrroles **5g-j** due to replacing of the hydrogen atom with a carboxylate group. Also for the compound **5a** C-4 appears at ~126 ppm due to the influence of acetyl group which induces a slight deshielding. All the carbon atoms in the carbonyl groups appear at expected chemical shifts.

An interesting feature of the pyrroles **5** is the hindered rotation about the C-N bond which was observed by H-NMR spectroscopy. Thus, due to the substituents from the *ortho* position (CONHMe) of the benzene ring, as well as of COAr group from the α position of pyrrole moiety the rotation about N-Ar bond is sterically hindered. In the case when enantiotopic protons are present in the molecule the free rotation could be observed in ¹H-NMR spectra.

This structural condition is present in the case of ethyl esters **5c-e** or diethyl ester **5j** when used as dipolarophiles. Indeed, the methylenic protons from ethyl group appear at room temperature as a multiplet and for **5j** (DEAD as dipolarophile) as a broad signal (Fig. 1) these clearly indicating the hindered rotation about Ar-N. When raising the temperature the broad signal resolves to the expected quartet.

The structure of the pyrrolo[1,2-*a*]quinazolines **6a,b** was assigned by IR and NMR spectroscopy. The IR spectra present the bands of the carbonyl groups in expected ranges. The ¹H-RMN spectra of the pyrrolo[1,2-*a*]quinazolines **6a,b** present as main characteristics the signals of the hydrogen atom H-9 which appears at around 8.40 ppm deshielded most probably due to the spatial influence of the carbonyl group in the aroyl moiety. The methyl groups appear as sharp singlets in the expected ranges. The ¹³C-NMR spectra provide interesting information regarding the structure of the pyrrolo[1,2-*a*]quinazolines **6**. The main characteristics are the carbon atoms of the methyl group directly bonded to the nitrogen atom which appears at ~30 ppm, and the carbon atom C-3 which appears at 99 ppm due to the shielding effect of the carboxyl groups. The carbon atoms in the carbonyl groups appear as expected.

Thus 10 new pyrroles were synthesized and characterized together with 2 pyrrolo[1,2-*a*]quinazoline derivatives. Further studies could determine the conditions to direct the reaction to go either to pyrrolo[1,2-*a*]quinazolines or to N-arylpyrroles with high efficiency.

EXPERIMENTAL

General

Melting points were determined on a Boëtius hot plate microscope. The elemental analysis was carried out on a COSTECH Instruments EAS32 apparatus the results agreed favorably with the calculated values. The IR spectra were recorded on a Fourier-transform (FT)-IR Bruker Vertex 70 spectrometer. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ¹H-NMR and 75 MHz for ¹³C-NMR. Supplementary evidence was given by HETCOR and COSY experiments.

3-Butyn-2-one, methyl propiolate, ethyl propiolate, DMAD, DEAD and 1,2-epoxybutane were purchased from Aldrich. All commercial reagents and solvents were used without further purification. Quinazolinium salts **1** were obtained according to our previous work [17].

General procedure for obtaining of compounds **5** and **6**

A mixture of 3 Mmol quaternary salt **1** and 5 mmol of acetylenic dipolarophile in 30 cm³ 1,2-epoxybutane was

heated at reflux for 40 hours. The solvent was partly removed by evaporation, 5 cm³ methanol was added and the mixture was left overnight. The solid was filtered and crystallized from a suitable solvent. The pyrrolo[1,2-*a*]quinazolines were obtained by the same procedure in mixture with the corresponding pyrrole from which was isolated by column chromatography using methylene chloride as eluent and Al₂O₃ (70-230 mesh) as stationary phase.

4-Acetyl-1-(2-methylaminocarbonylphenyl)-2-(3-nitrobenzoyl)pyrrole (5a). Colorless crystals (from methanol). Anal. Calc. C₂₁H₁₇N₃O₅: C 64.45, H 4.38, N 10.74; Found: C 64.72, H 4.60, N 10.95. IR (ATR, cm⁻¹): 1238, 1531, 1638, 1639, 2936, 3076, 3407; ¹H-NMR (300 MHz, CDCl₃) δ = 2.35 (s, 3H, COMe); 2.60 (d, 3H, *J* = 4.9 Hz, MeNH); 6.43 (q, 1H, *J* = 4.9 Hz, NH); 7.16 (d, 1H, *J* = 1.6 Hz, H-5); 7.18-7.22 (m, 1H, H-6''); 7.40-7.44, 7.51-7.54 (2m, 3H, H-3'', H-4'', H-5''); 7.58 (d, 1H, *J* = 1.6 Hz, H-3); 7.83 (t, 1H, *J* = 7.8 Hz, H-5''); 8.13-8.16, 8.34-8.37 (2m, 2H, H-4', H-6'); 8.58-8.60 (m, 1H, H-2'); ¹³C-NMR (75 MHz, CDCl₃) δ = 26.5, 27.4 (MeNH, COMe); 121.1 (C-3); 124.3 (C-2'); 126.0 (C-4'); 127.2, 128.4, 129.4, 129.8, 130.8 (C-5', C-3'', C-4'', C-5'', C-6''); 126.0, 132.2, 134.4, 136.6 (C-2, C-4, C-1'', C-2''); 135.2 (C-6'); 135.3 (C-5); 138.8 (C-1'); 148.3 (C-3'); 167.4 (CONH); 183.5 (COAr); 192.5 (COMe).

Methyl 1-(2-methylaminocarbonylphenyl)-2-(2-nitrobenzoyl)pyrrole-4-carboxylate (5b). Colorless crystals (from 2-propanol). Anal. Calc. C₂₁H₁₇N₃O₆: C 61.92, H 4.21, N 10.31; Found: C 62.02, H 4.33, N 10.54. IR (ATR, cm⁻¹): 1234, 1527, 1629, 1657, 1709, 2966, 3057, 3327; ¹H-NMR (300 MHz, CDCl₃) δ = 2.80 (d, 3H, *J* = 4.9 Hz, MeNH); 3.78 (s, 3H, Me); 6.18 (q, 1H, *J* = 4.9 Hz, NH); 6.97 (d, 1H, *J* = 1.6 Hz, H-5); 7.35-7.39 (m, 1H, H-6''); 7.50-7.55 (m, 2H, H-4'', H-5''); 7.57-7.60 (m, 1H, H-6'); 7.61 (d, 1H, *J* = 1.6 Hz, H-3); 7.65-7.69 (m, 1H, H-3''); 7.71-7.79 (m, 2H, H-4', H-5'); 8.14-8.17 (m, 1H, H-3'); ¹³C-NMR (75 MHz, CDCl₃) δ = 26.8 (MeNH); 51.7 (MeO); 117.3 (C-4); 123.0 (C-3); 124.9 (C-3'); 127.8, 128.6, 129.4, 129.7, 130.6 (C-6', C-3'', C-4'', C-5'', C-6''); 132.1, 134.9, 135.1 (C-2, C-1'', C-2''); 133.8 (C-4'); 130.7, 136.1 (C-1', C-5'); 136.4 (C-5); 147.2 (C-2'); 163.6 (COO); 167.5 (CONH); 183.0 (COAr).

Ethyl 2-(4-phenylbenzoyl)-1-(2-methylaminocarbonylphenyl)pyrrole-4-carboxylate (5c). Colorless crystals (from methanol). Anal. Calc. C₂₈H₂₄N₂O₄: C 74.32, H 5.35, N 6.19. Found: C 74.14, H 5.11 N 6.27. IR (ATR, cm⁻¹): 1626, 1664, 1711, 2934, 3065, 3393; ¹H NMR (300 MHz, CDCl₃) δ = 1.34 (t, 3H, *J* = 7.1 Hz, MeCH₂); 2.70 (d, 3H, *J* = 4.9 Hz, MeNH); 4.31 (sext, 2H, *J* = 9.5, 7.1 Hz, CH₂); 6.78 (q, 1H, *J* = 4.9 Hz, NH); 7.17(dd, 1H, *J* = 7.7, 1.4 Hz H-6''); 7.34 (d, 1H, *J* = 1.6 Hz, H-5); 7.42-7.52 (m, 5H, H-4'', H-5'', 3H-Ph); 7.61 (d, 1H, *J* = 1.6 Hz, H-3); 7.65-7.72 (m, 3H, H-3'', 2H-Ph); 7.74 (d, 2H, *J* = 8.4 Hz, H-2', H-6') 8.03 (d, 2H, *J* = 8.4 Hz, H-3', H-5'); ¹³C NMR (75 MHz, CDCl₃) δ = 14.4 (MeCH₂); 26.6 (MeNH); 60.5 (CH₂O); 117.3 (C-4); 122.1 (C-3); 127.1 (C-6''); 128.9 (C-3''); 127.2, 127.4, 128.5, 128.8, 129.0, 129.1 (C-2', C-3', C-5', C-6', 4C-Ph); 129.4, 130.7 (C-4'', C-5'', 1C-Ph); 134.9, 135.0, 135.8 (C-2, C-1'', C-2''); 133.0 (C-1'); 136.7 (C-5); 139.7 (1C-Ph); 146.2 (C-4'); 163.6 (COO); 167.8 (CONH); 185.9 (COAr).

Ethyl 1-(2-methylaminocarbonylphenyl)-2-(2-nitrobenzoyl)pyrrole-4-carboxylate (5d). Colorless crystals (from ethanol). Anal. Calc. C₂₂H₁₉N₃O₆: C 62.70, H 4.54 N 9.97. Found: C 62.87, H 4.39 N 9.76. IR (ATR, cm⁻¹): 1256, 1524, 1649, 1704, 2935, 3086, 3286; ¹H NMR (300 MHz, CDCl₃) δ = 1.30 (t, 3H, *J* = 7.1 Hz, MeCH₂); 2.81 (d, 3H, *J* = 4.9 Hz,

MeNH); 4.26 (sext, 2H, $J = 9.5, 7.1$ Hz, CH₂); 6.20 (q, 1H, $J = 4.9$ Hz, NH); 6.98 (d, 1H, $J = 1.6$ Hz, H-5); 7.34-7.37 (m, 1H, H-6''); 7.49-7.55 (m, 2H, H-4'', H-5''); 7.57-7.60 (m, 1H, H-5''); 7.61 (d, 1H, $J = 1.6$ Hz, H-3); 7.66-7.69 (m, 1H, H-3''); 7.74-7.79 (m, 2H, H-4'', H-5''); 8.15-8.18 (m, 1H, H-3''); ¹³C NMR (75 MHz, CDCl₃) $\delta = 14.4$ (MeCH₂); 26.8 (MeNH); 60.6 (CH₂O); 117.7 (C-4); 123.1 (C-3); 124.9 (C-3''); 127.8, 128.6, 129.4, 129.7, 130.6 (C-6', C-3'', C-4'', C-5'', C-6''); 132.1, 134.0, 136.1 (C-2, C-1'', C-2''); 133.8 (C-4''); 130.8, 135.1 (C-1', C-5'); 136.4 (C-5); 147.2 (C-2''); 163.2 (COO); 167.6 (CONH); 183.1 (COAr).

Ethyl 2-(4-bromobenzoyl)-1-(2-methylaminocarbonylphenyl)pyrrole-4-carboxylate (5e). Colorless crystals (from methanol). Anal. Calc. C₂₂H₁₉N₂O₄: C 58.04, H 4.21, Br 17.55, N 6.15. Found: C 58.29, H 4.43, Br 17.82, N 6.37. IR (KBr, cm⁻¹): 1238, 1675, 1707, 3402; ¹H NMR (300 MHz, CDCl₃) $\delta = 1.34$ (t, 3H, $J = 7.1$ Hz, MeCH₂); 2.79 (d, 3H, $J = 4.9$ Hz, MeNH); 4.30 (sext, 2H, $J = 9.5, 7.1$ Hz, CH₂); 6.60 (q, 1H, $J = 4.9$ Hz, NH); 7.16-7.18 (m, 1H, H-6''); 7.26 (d, 1H, $J = 1.6$ Hz, H-5); 7.42-7.53 (m, 2H, H-4'', H-5''); 7.60 (d, 1H, $J = 1.6$ Hz, H-3); 7.65-7.67 (m, 3H, H-3'', H-2', H-6''); 7.80 (d, 2H, $J = 6.6$ Hz, H-3', H-5''). ¹³C NMR (75 MHz, CDCl₃) $\delta = 14.5$ (MeCH₂); 26.6 (MeNH); 60.6 (CH₂O); 117.4 (C-4); 122.4 (C-3); 127.1 (C-6''); 128.8 (C-3''); 129.4, 130.7 (C-4''); C-5''); 131.4, 132.0 (C-2', C-3', C-5', C-6'); 134.9, 135.3, 136.7 (C-2, C-1'', C-2''); 132.4 (C-1'); 135.2 (C-5); 136.0 (C-4'); 163.5 (COO); 167.6 (CONH); 185.1 (COAr).

Isopropyl 1-(2-methylaminocarbonylphenyl)-2-(3-nitrobenzoyl)pyrrole-4-carboxylate (5f). Colorless crystals (from ethanol). Anal. Calc. C₂₃H₂₁N₃O₆: C 63.44, H 4.86, N 9.56. Found: C 63.59, H 5.03, N 9.75. IR (ATR, cm⁻¹): 1242, 1526, 1650, 1705, 2981, 3081, 3314; ¹H NMR (300 MHz, CDCl₃) $\delta = 1.30$ (d, 6H, $J = 6.3$ Hz, 2Me); 2.78 (d, 3H, $J = 4.9$ Hz, MeNH); 5.12-5.30 (m, 1H, CH); 6.42 (q, 1H, $J = 4.9$ Hz, NH); 7.20-7.26 (m, 1H, H-6''); 7.25 (d, 1H, $J = 1.6$ Hz, H-5); 7.44-7.53 (m, 2H, H-4'', H-5''); 7.62-7.64 (m, 1H, H-3''); 7.65 (d, 1H, $J = 1.6$ Hz, H-3); 7.72 (t, 1H, $J = 7.8$ Hz, H-5'); 8.23-8.25, 8.42-8.48, 8.68-8.71 (3m, 3H, H-2', H-4', H-6''); ¹³C NMR (75 MHz, CDCl₃) $\delta = 22.0$ (2Me); 26.7 (MeNH); 68.2 (CH); 118.2 (C-4); 123.0 (C-3); 124.9 (C-3''); 127.3, 128.6, 129.5, 129.8, 130.8 (C-6', C-3'', C-4'', C-5'', C-6''); 132.9, 137.8, 136.6 (C-2, C-1'', C-2''); 135.3 (C-5); 135.8 (C-4'); 134.7, 138.9 (C-1', C-5'); 148.3 (C-2''); 162.8 (COO); 167.5 (CONH); 183.5 (COAr).

Dimethyl 2-(4-phenylbenzoyl)-1-(2-methylaminocarbonylphenyl)pyrrole-3,4-dicarboxylate (5g). Colorless crystals (from methanol). Anal. Calc. C₂₉H₂₄N₂O₆: C 70.15, H 4.87, N 5.64. Found: C 70.41, H 5.12, N 5.87. IR (ATR, cm⁻¹): 1640, 1712, 2933, 3040, 3299; ¹H NMR (300 MHz, CDCl₃) $\delta = 2.84$ (d, 3H, $J = 4.9$ Hz, MeNH); 3.36, 3.83 (2s, 6H, 2MeO); 7.06-7.09 (m, 1H, H-6''); 7.10 (q, 1H, $J = 4.9$ Hz, NH); 7.35-7.52 (m, 5H, H-4'', H-5'', 3H-Ph) 7.51 (1H, s, H-5); 7.63-7.65 (m, 2H, H-3'', 1H-Ph); 7.71-7.74 (m, 3H, H-2', H-6', 1H-Ph); 7.94 (d, 2H, $J = 8.2$ Hz, H-3', H-5''); ¹³C NMR (75 MHz, CDCl₃) $\delta = 26.7$ (MeNH); 51.9, 52.0 (2MeO); 115.4, 122.7 (C-3, C-4); 127.0 (C-6''); 128.7 (C-3''); 127.3, 129.1, 129.3, 130.2 (C-2', C-3', C-5', C-6', 4C-Ph); 130.1, 130.7 (C-4'', C-5'', 1C-Ph); 134.9, 135.2, 136.0 (C-2, C-1'', C-2''); 133.0 (C-1'); 135.5 (C-5); 139.4 (1C-Ph); 146.2 (C-4'); 162.7, 163.9, 167.2 (2COO, CONH); 187.8 (COAr).

Dimethyl 1-(2-methylaminocarbonylphenyl)pyrrole-2-(2-nitrobenzoyl)-3,4-dicarboxylate (5h). Colorless crystals (from 2-propanol). Anal. Calc. C₂₃H₁₉N₃O₈: C 59.36, H 4.11, N 9.03. Found: C 59.55, H 4.33, N 9.31. ¹H NMR (300 MHz, CDCl₃) $\delta = 2.85$ (d, 3H, $J = 4.9$ Hz, MeNH); 3.30, 3.75 (2s,

6H, 2MeO); 6.25 (q, 1H, $J = 4.9$ Hz, NH); 7.38-7.41 (m, 1H, H-6''); 7.49-7.58 (m, 2H, H-4'', H-5''); 7.54 (1H, s, H-5); 7.66-7.78 (m, 4H, H-3'', H-4', H-5', H-6'); 8.17-8.20 (m, 1H, H-3') ¹³C NMR (75 MHz, CDCl₃) $\delta = 26.9$ (MeNH); 51.9, 52.5 (2MeO); 115.5, 124.1 (C-3, C-4); 124.4 (C-3''); 127.8, 128.7, 129.9, 130.1, 130.1 (C-6', C-3'', C-4'', C-5'', C-6''); 132.0, 132.3, 134.2 (C-2, C-1'', C-2''); 133.9 (C-4'); 131.6, 134.9 (C-1', C-5'); 136.1 (C-5); 146.8 (C-2''); 162.4, 164.5 (2COO); 167.4 (CONH); 183.1 (COAr).

Dimethyl 2-(3-coumaroyl)-1-(2-methylaminocarbonylphenyl)pyrrole-3,4-dicarboxylate (5i). Colorless crystals (from methanol). Anal. Calc. C₂₆H₂₀N₂O₈: C 63.93, H 4.13, N 5.74. Found: C 64.12, H 4.02, N 6.01. IR (ATR, cm⁻¹): 1224, 1405, 1659, 1728, 1747, 3387; ¹H NMR (300 MHz, CDCl₃) $\delta = 2.80$ (d, 3H, $J = 4.9$ Hz, MeNH); 3.58, 3.79 (2s, 6H, 2Me); 6.75 (q, 1H, $J = 4.9$ Hz, NH); 7.26-7.45 (m, 6H, H-4'', H-5'', H-6'', 3H Coum); 7.48 (s, 1H, H-5); 7.60-7.68 (m, 2H, H-3'', 1H Coum); 8.20 (s, 1H, Coum); ¹³C NMR (75 MHz, CDCl₃) $\delta = 26.8$ (MeNH); 51.9, 52.8 (2MeO); 115.7, 123.8 (C-3, C-4); 117.9, 125.5, 132.8, 134.8, 135.1, 154.9, 158.2 (C-2, C-1'', C-2'', 4Cq Coum); 127.9 (C-6''); 129.2 (C-3''); 129.8, 130.0 (C-4'', C-5''); 134.5 (C-5); 117.0, 125.3, 130.6 (3H Coum); 146.6 (1H Coum); 162.6, 164.7 (COO); 167.1 (CONH); 182.4 (COAr).

Diethyl 2-benzoyl-1-(2-methylaminocarbonylphenyl)pyrrole-3,4-dicarboxylate (5j). Colorless crystals (from ethanol). Anal. Calc. C₂₅H₂₄N₂O₆: C 66.95, H 5.39, N 6.25; Found: C 67.18, H 5.61, N 6.41. IR (ATR, cm⁻¹): 1651, 1661, 1703, 2936, 3059, 3369; ¹H NMR (300 MHz, CDCl₃) $\delta = 0.93, 1.31$ (2t, 6H, $J = 7.1$ Hz, 2Me); 2.79 (d, 3H, $J = 4.9$ Hz, MeNH); 3.81 (bs, 2H, CH₂); 4.30 (q, 2H, $J = 7.1$ Hz, CH₂); 7.09 (q, 1H, $J = 4.9$ Hz, NH); 7.06-7.09 (m, 1H, H-6''); 7.34-7.41 (m, 1H, H-4''); 7.45-7.51 (m, 3H, H-5'', *o*-Ph); 7.53 (s, 1H, H-5); 7.60-7.65 (m, 1H, H-4'); 7.67-7.71 (m, 1H, H-3''); 7.86-7.89 (m, 2H, *m*-Ph); ¹³C NMR (75 MHz, CDCl₃) $\delta = 13.5, 14.3$ (2Me); 26.7 (MeNH); 60.8, 61.4 (2CH₂); 115.8, 123.4 (C-3, C-4); 127.0, 129.3, 129.9, 130.7 (C-3'', C-4'', C-5'', C-6''); 128.7, 129.7, 132.5 (C-2', C-3', C-4', C-5', C-6'); 134.2 (C-5); 133.0, 135.3, 135.4, 137.4, (C-2, C-1', C-1'', C-2''); 162.4, 163.5, 167.2 (2COO, CONH); 188.3 (COAr).

*Dimethyl 1-(4-methoxybenzoyl)-pyrrolo[1,2-*a*]quinazolin-5(*H*)-one-2,3-dicarboxylate (6a)*. Colorless crystals (from ethanol). Anal. Calc. C₂₄H₂₀N₂O₇: C 64.28, H 4.50, N 6.25. Found: C 64.43, H 4.78, N 6.49. IR (KBr, cm⁻¹): 1219, 1234, 1262, 1529, 1574, 1598, 1651, 1678, 1717; ¹H NMR (300 MHz, CDCl₃) $\delta = 3.51, 3.68, 3.89, 3.92$ (4s, 12H, 4Me); 6.97 (d, 2H, $J = 9.1$ Hz, H-3', H-5'); 7.36-7.50 (m, 3H, H-6, H-7, H-8); 7.96 (d, 2H, $J = 9.1$ Hz, H-2', H-6''); 8.36-8.38 (m, 1H, H-9). ¹³C NMR (75 MHz, CDCl₃) $\delta = 31.4, 51.1, 53.0, 55.7$ (MeN, 3MeO); 99.4 (C-3); 114.5 (C-3', C-5'); 117.0 (C-6), 117.7, 119.3, 125.2, 130.5, 134.3, 135.5, 163.0 (C-1, C-2, C-3a, C-5a, C-9a, C-1', C-4'); 126.4, 130.0 (C-7, C-8); 132.3 (C-2', C-6'); 134.4 (C-9); 158.3, 164.8, 165.6 (2COO, CO); 187.8 (COAr).

*Dimethyl 1-(2-nitrobenzoyl)-pyrrolo[1,2-*a*]quinazolin-5(*H*)-one-2,3-dicarboxylate (6b)*. Colorless crystals (from ethanol). Anal. Calc. C₂₃H₁₇N₃O₈: C 59.61, H 3.70, N 9.07. Found: C 59.82, H 3.51, N 9.32. IR (ATR, cm⁻¹): 1235, 1259, 1529, 1635, 1689, 1713, 1727; ¹H NMR (300 MHz, CDCl₃) $\delta = 3.29, 3.70, 3.76$ (3s, 9H, 3Me); 7.49-7.55 (m, 1H, H-8); 7.60-7.78 (m, 3H, H-7, H-4', H-5'); 8.11-8.14 (m, 2H, H-6, H-3'). 8.37 (dd, 1H, $J = 8.00, 1.6$ Hz, H-9). ¹³C NMR (75 MHz, CDCl₃) $\delta = 34.4, 52.4, 52.5$ (MeNH, 2MeO); 99.4 (C-3); 120.2 (C-6); 124.4 (C-3'); 127.0, 129.0 (C-7, C-8); 118.0, 122.3, 130.3, 134.4, 135.6, 139.4 (C-1, C-2, C-3a, C-5a, C-9a,

C-1'); 132.0, 132.3, 133.7 (C-4', C-5', C-6'); 134.1 (C-9); 148.5 (C-2'); 159.5, 162.7, 164.1 (2COO, CO); 181.2 (COAr).

CONCLUSIONS

In conclusion, we have extended our work on the developments of libraries of N-arylpyrroles in a highly efficient way and more environmentally friendly than in classical 1,3-dipolar cycloaddition strategy which uses chlorinated solvents in most of the cases. An interesting feature is the isolation of the pyrrolo[1,2-*a*]quinazoline framework which will be a target for our future studies. The new compounds were structurally characterized by specific analytical methods. The method for obtaining highly substituted N-arylpyrroles could be successfully applied in combinatorial libraries in view of property screening and lead compound optimization.

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