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SYMMETRICAL AND NON-SYMMETRICAL OLEFINIC AND ACETYLENIC DIPOLAROPHILES IN THE SYNTHESIS OF PYRROLO[1,2-b]PYRIDAZINE DERIVATIVES

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The pyrrolo[1,2-b]pyridazines **6a-j** were synthesized *via* a 1,3-dipolar cycloaddition between pyridazinium *N*-ylides and symmetrical and non-symmetrical acetylenic and olefinic dipolarophiles, by two distinct procedures. Structural assignment of the new compounds was performed on the basis of H-NMR and C-NMR spectra and elemental analysis. The regioselectivity and yields of the cycloaddition reactions remained consistent both in the case of non-symmetrical olefinic and acetylenic dipolarophiles.

INTRODUCTION

In the last decade the interest in pyrrolo[1,2-b]pyridazines has been constant. This is due to their interesting optical properties, and thus, the possibility of obtaining OLEDs and other stable light emitting organic substances.[1-5] The biological activity of pyrrolo[1,2-b]pyridazine derivatives with potential medical applications was also reported.[6-15] The high fluorescence in the solution and in the solid state of pyrrolo[1,2-b]pyridazines recommends them as new class of blue organic luminophors. Also, it was demonstrated that the optical properties are influenced by nature and number of substituents in the pyrrolopyridazine system.

The syntheses and properties of pyrrolo[1,2-b]pyridazines were reviewed in 1976 by Kuhla and Lombardino[16] and subsequently, new methods for the synthesis of these compounds were described, which can be classified into two main approaches. The first approach consists of condensation reactions[14-20] and the second is based on cycloaddition reactions.[16, 21-27]

Herein we report the synthesis and characterization of new potential blue organic luminophors pyrrolo[1,2-b]pyridazine derivatives by 1,3-dipolar cycloaddition reactions between pyridazinium *N*-ylides and symmetrical and non-symmetrical acetylenic and olefinic dipolarophiles, in the aim of obtaining a finer tuning of the optical and biological properties of these organic luminophores.

RESULTS AND DISCUSSION

The key intermediates for the synthesis of pyrrolo[1,2-b]pyridazine derivatives, pyridazinium bromides **3**, were prepared by reaction between 2-bromoacetophenones **2** and pyridazine or 3-methylpyridazine, respectively. The *N*-alkylation of pyridazines **1a,b** was performed in acetone at room temperature. The structure of bromides **3** was assigned by NMR spectroscopy. The chemical shifts for the protons of the pyridazine moiety were attributed on the basis of their multiplicity and by comparison with those of the compounds described in the literature. The C-NMR spectra showed all expected signals.

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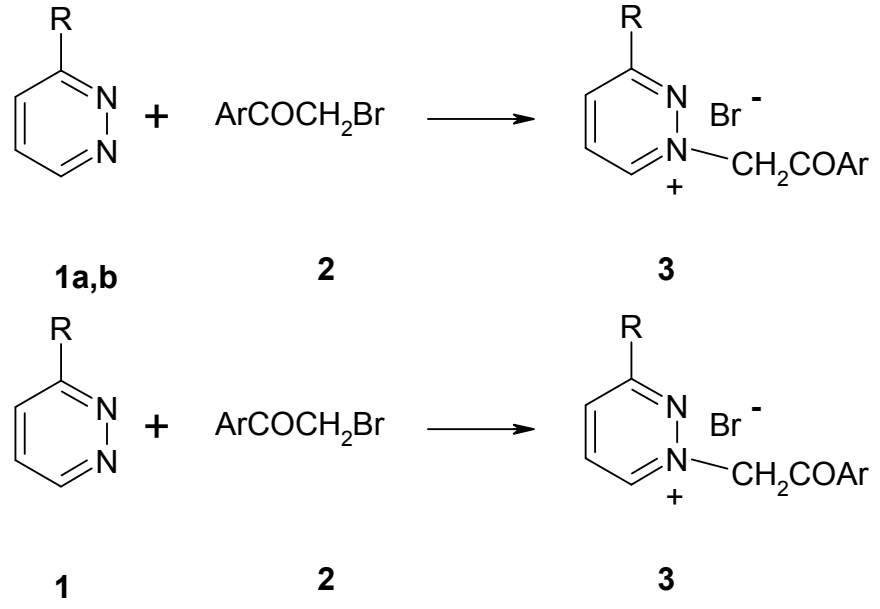
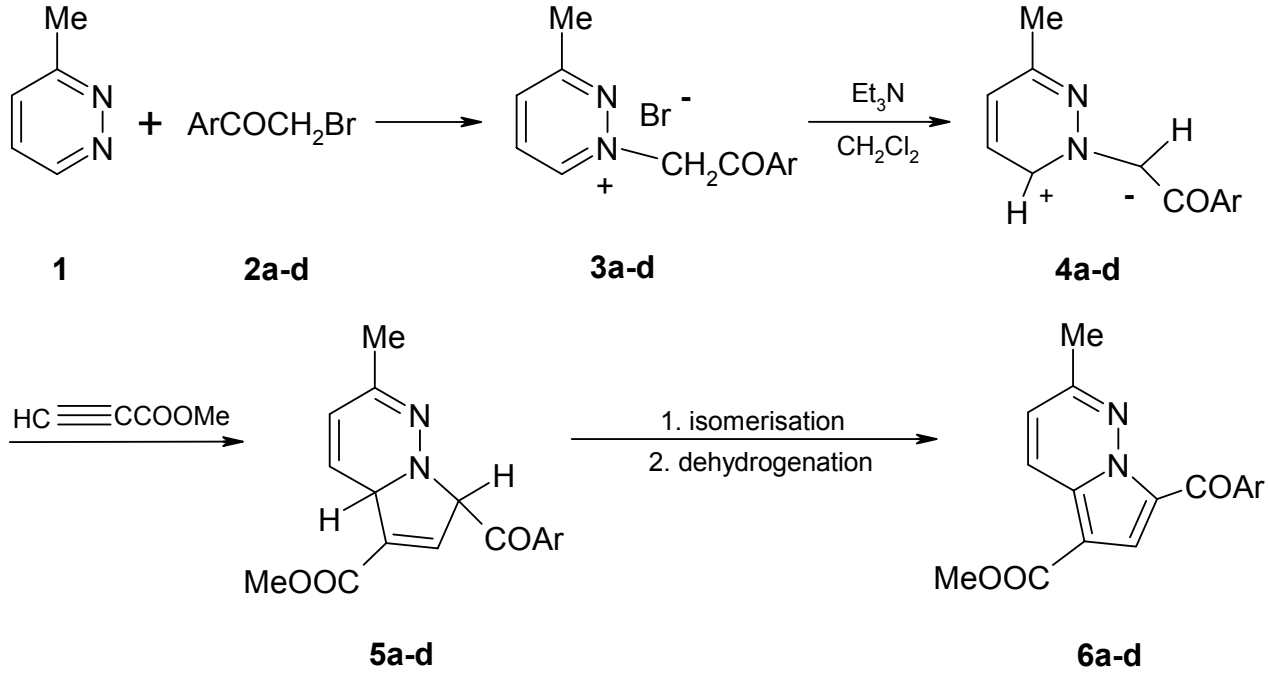


R=Me**;** a = C_6H_5; b = 4-BrC_6H_4; c = 4-$MeOC_6H_4$; d= 4-NCC_6H_4
R=H; e = 4-ClC_6H_4; f = 4-BrC_6H_4; g = 3-$O_2NC_6H_4$; h = 4-$O_2NC_6H_4$

The pyrrolopyridazines **6a-d** were obtained by 1,3-dipolar cycloaddition reactions between 3-methylpyridazinium *N*-ylides **4a-d** with methyl propiolate (Scheme 2). Usually, the pyridazinium *N*-ylides are unstable compounds and they are generated *in situ* by the reaction between *N*-alkylated pyridazinium salts and triethylamine in the presence of the dipolarophiles. The cycloaddition reactions were performed in methylene chloride at room temperature giving pyrrolopyridazines derivatives **6a-d**. As resulted from NMR data, the cycloaddition between *N*-ylides **4a-d** and non-symmetrical alkyne, methyl propiolate, is completely regioselective, as only the formation of the regioisomer with the ester attached in the 5 position of the pyrrolopyridazine moiety was observed.

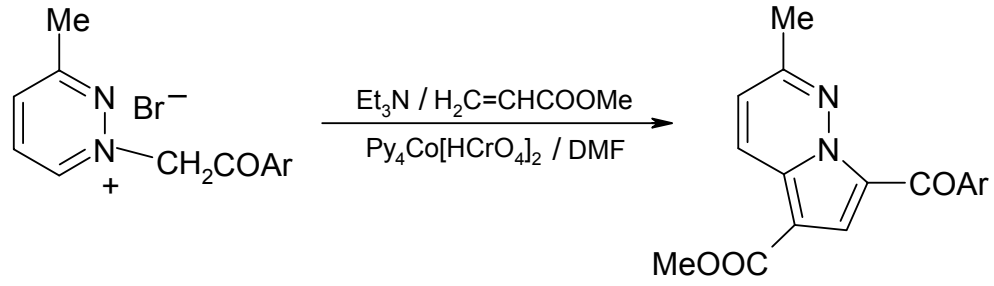


a = C_6H_5; b = 4-BrC_6H_4; c = 4-$MeOC_6H_4$; d= 4-NCC_6H_4

Scheme 1

The pyrrolopyridazine derivatives **6a-d** were also obtained from bromides **3a-d**, methyl acrylate, and triethylamine in DMF at 90 °C in the presence of - tetrakis-pyridino Co(II)dichromate (TPCD), as oxidant. This reagent was used for aromatization of cycloadducts obtained by reaction between heteroaromatics *N*-ylides and activated olefins.[28]

The formation of compounds **6** implies the generation of *N*-ylides **4** from bromide **3** by reaction with triethylamine, the cycloaddition between *N*-ylide dipole and olefinic dipolarophile, and finally the aromatization of the tetrahydroderivative by the action of tetrakis-pyridino Co(II) dichromate (TPCD).



3a-d **6a-d**

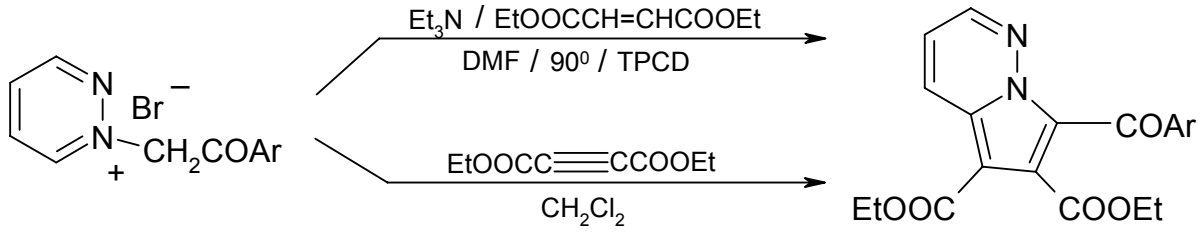
a = C_6H_5; b = 4-BrC_6H_4; c = 4-$MeOC_6H_4$; d= 4-NCC_6H_4

Scheme 2

The structures of the new compounds **6a-d** were assigned by elemental analysis and NMR spectroscopy. In the H-NMR spectra of compounds **6** the two protons H-3 and H-4 from the pyridazine moiety appear as two doublets with J = 9.2 Hz. In comparison with unsubstituted pyrrolopyridazine,[16] protons H-4 and H-6 are strongly deshielded due to the vicinity of the 5-carbomethoxy and the 7-carbonyl groups, respectivly.

The chemical shifts for the carbon atoms from pyrrolopyridazines **6** were assigned by using heteronuclear H-C correlation experiments (HETCOR). The atom C-2 (δ = 153.3-154.1 ppm) is highly deshielded in respect with the other atoms from the pyrrolopyridazine system as it is part of a C-N double bond. The strong shielding observed for C-5 (δ = 105-106 ppm) is a consequence of its relative β positions to the pyrrole nitrogen.

In a similar manner, the pyrrolopyridazines **6e-k** with three substituents grafted on the pyrrole ring were obtained by 1,3-dipolar cycloaddition from pyridazinium N-ylides generated from pyridazinium bromides **3e-k** and acetylenic or olefinic dipolarophiles. As acetylenic dipolarophile diethyl acetylenedicarboxylate was used. The generation of *N*-ylides and cycloaddition reaction was performed in methylene chloride at room temperature. The pyrrolopyridazines **6e-k** were also prepared from pyridazinium bromides **3e-k** and methyl acrylate in DMF in the presence of TPCD as oxidant agent. The yields obtained by the two distinct methods for compounds **6e-k** are not significantly different and were found to be over 50%. The main disadvantage of the method which implied the acetylenic dipolarophile in methylene chloride at at room temperature, is the formation of the dihydro-pyrrolopyridazine derivatives as by-products.



3e-h **6e-k**

e = C_6H_5; f = 4- $C_6H_4C_6H_5$; g = 4-ClC_6H_4; h = 3-BrC_6H_4; i = 4-BrC_6H_4; j = 3-$O_2NC_6H_4$; k = 4-$O_2NC_6H_4$

Scheme 3

The structure of pyrrolopyridazines **6e-k** was confirmed by NMR spectroscopy. The chemical shifts for hydrogen and carbon atoms were established on the basis of multiplicity, the magnitude of the coupling constants, as well as by classical two dimensional H/H and H/C correlations. In the NMR spectra of compounds **6e-k**, the three protons (H2, H3, H4) from the pyridazine moiety appear as an ABC system with the following coupling constants: $^{3}J_{2,3}$ = 4.5 Hz, $^{4}J_{2,4}$ = 1.9 Hz and $^{3}J_{3,4}$ = 9.2 Hz.

The chemical shifts for the carbon atoms from pyrrolopyridazines **6** were assigned by using heteronuclear H-C correlation experiments (HETCOR). The atom C-2 (δ = 144.8-145.7 ppm) from the pyrrolopyridazines **6** is highly deshielded in respect with the other atoms from the pyrrolopyridazine system, as it is part of a C-N double bond.

Additional evidence for the cyano-bearing compounds was provided by FT-IR spectroscopy. The cyano group appears at 2226 cm^{-1} in the case of the cycloadduct **6d** and at 2234 cm^{-1} for the pyridazinium salt **3d**, respectivly.

EXPERIMENTAL

Melting points were determined on a Boëtius hot plate and are uncorrected. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. Supplementary evidence was given by HETCOR and COSY experiments. FT-IR spectra were recorded on a Brucker Vertex 70 spectrometer.

Synthesis of pyridazinium bromides 3. 10 Mmol Pyridazine **1** and 11 mmol 2-bromoacetophenone **2** in 50 mL of acetone were stirred at room temperature for 5-6 hrs and then kept at room temperature until the next day. The pyridazinium bromides **3** were obtained as light brown precipitates which were collected by vacuum filtration and washed with acetone.

1-[2-(4-Cyanophenyl)-2-oxoethyl]-3-methylpyridazinium bromide (**3d**). The product was recrystallized from methanol and brown-white crystals with mp 260-1 °C were obtained; Yield 96 %. Anal. Calcd. $C_{13}H_{12}BrN_3O$: C 52.85; H 4.04; Br 25.11; N 13.21. Found C 53.18; H 4.31; Br 25.39; N 13.50. IR (ATR, cm^{-1}): 2234 (CN).

^{1}H-NMR (300 MHz, $CDCl_3$+TFA) δ: 2.88 (s, 3H, 2-Me); 6.60 (s, 2H, CH_2); 7.88 (d, 2H, *J*=8.2 Hz, H-3', H-5'); 8.17 (d, 2H, *J*=8.2 Hz, H-2', H-6'); 8.33 (d, 1H, *J* = 8.5 Hz, H-4); 8.61 (dd, 1H, *J* = 8.5, 5.7 Hz, H-5); 9.65 (d, 1H, *J* = 5.7 Hz, H-6).

^{13}C-NMR (75 MHz, $CDCl_3$+TFA) δ: 22.1 (2-Me); 71.0 (CH_2); 117.2, 117.8 (C-4', CN); 129.0 (C-2', C-6'); 133.3 (C-3', C-5'); 135.4; 137.8 (C-4, C-5); 136.3 (C-1'); 150.0 (C-6); 165.7 (C-2); 188.2 (COAr).

Method A: **Synthesis of pyrrolo[1,2-b]pyridazines 6 using acetylenic dipolarophiles**

3 Mmol pyridazinium bromide **3** were suspended in 20 mL of dichloromethane and then 4 mmol of methyl propiolate were added. Under vigorous stirring 0.45 mL (3 mmol) of triethylamine (dissolved in 10 mL of methylene chloride) were added dropwise. After 1 h the reaction mixture was washed with water and the solvent evaporated. The pyrrolopyridazine derivatives **6** were purified by recrystallization or by column chromatography on neutral Al_2O_3 using dichloromethane as eluent.

Method B: Synthesis of pyrrolo[1,2-b]pyridazines 6 using olefinic dipolarophile

5 Mmol of pyridazinium bromides **3** and 15 mmoles of methyl acrylate in 30 mL DMF were treated under stirring and at room temperature with 0.7 mL (5 mmol) triethylamine. After 30 min., 3 g TPCD were added and at the reaction mixture was heated at 80-90 ºC for 4 h. Then the mixture was cooled at room temperature and 50 mL 5% aqueous HCl were added in order to promote the precipitation of the product which was removed by vacuum filtration and air dried. The crude product was purified by chromatography on a short column (Aluminium oxide 90 standardized, chloroform).

Methyl 7-Benzoyl-2-methyl-pyrrolo[1,2-b]pyridazine-5-carboxylate (6a). The product was recrystallized from methanol and colorless crystals with mp 121-3 ºC were obtained; Yield: method A 69%; method B 64 %. Anal. Calcd. $C_{17}H_{14}N_2O_3$: C 69.38; H 4.79; N 9.52. Found C 69.67; H 5.10; N 9.76.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.60 (s, 3H, 2-Me); 3.85 (s, 3H, MeO); 7.03 (d, 1H, *J* = 9.2 Hz, H-3); 7.45-7.51 (m, 2H, H-3', H-5'); 7.52-7.58 (m, 1H, H-4'); 7.61 (s, 1H, H-6); 7.85-7.88 (m, 2H, H-2', H-6'); 8.52 (d, 1H, *J* = 9.2 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 22.4 (2-Me); 51.8 (MeO); 105.3 (C-5); 120.1 (C-3); 124.7 (C-6); 127.2 (C-7); 127.5 (C-4); 128.5 (C-3', C-5'); 129.7 (C-2', C-6'); 131.5 (C-4a); 132.4 (C-4'); 139.3 (C-1'); 153.7 (C-2); 164.2 (COO); 184.5 (COAr).

Methyl 7-(4-Bromobenzoyl)-2-methyl-pyrrolo[1,2-b]pyridazine-5-carboxylate (6b). The product was recrystallized from ethyl acetate and colorless crystals with mp 169-171 ºC were obtained; Yield: method A 68 %; method B 73 %. Anal. Calcd. $C_{17}H_{13}BrN_2O_3$: C 54.71; H 3.51; Br 21.41; N 7.51. Found: C 55.01; H 3.78; Br 21.68; N 7.67.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.65 (s, 3H, 2-Me); 3.90 (s, 3H, MeO); 7.04 (d, 1H, *J* = 9.2 Hz, H-3); 7.63 (s, 1H, H-6); 7.65, 7.76 (2d, 4H, *J* = 8.4 Hz, H-2', H-3', H-5', H-6'); 8.52 (d, 1H, *J* = 9.2 Hz, H-4).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 22.4 (2-Me); 51.7 (MeO); 105.1 (C-5); 120.2 (C-3); 124.5 (C-6); 126.5 (C-7); 127.4 (C-4'); 127.6 (C-4); 131.2, 131.8 (C-2', C-3', C-5', C-6'); 132.6 (C-4a) 138.1 (C-1'); 153.8 (C-2); 163.7 (COO); 183.3 (COAr).

Methyl 7-(4-Methoxybenzoyl)-2-methyl-pyrrolo[1,2-b]pyridazine-5-carboxylate (6c). The product was recrystallized from methanol and colorless crystals with mp 138-140 ºC were obtained; Yield: method A 77 %; method B 69 %.. Anal. Calcd. $C_{18}H_{16}N_2O_4$: C 66.66; H 4.97; N 8.64. Found: C 66.89; H 5.23; N 8.81.

^{1}H-NMR (75 MHz, $CDCl_3$) δ: 2.57 (s, 3H, 2-Me); 3.83 (s, 3H, 4-MeO); 3.91 (s, 3H, MeOO); 6.93-6.97 (m, 3H, *J* = 9.2 Hz, H-3, H-3', H-5'); 7.60 (s, 1H, H-6); 7.87 (d, 2H, *J* = 8.7 Hz, H-2', H-6'); 8.45 (d, 1H, *J* = 9.2 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 22.4 (2-Me); 51.5 (MeO); 55.7 (4-MeO); 104.5 (C-5); 113.8 (C-3', C-5'); 119.6 (C-3); 123.4 (C-6); 126.9 (C-7); 127.5 (C-4); 131.7, 132.0 (C-4a, C-1'); 132.1 (C-2', C-6'); 153.3 (C-2); 163.3 (C-4'); 163.9 (COO); 183.5 (COAr).

Methyl 7-(4-Cyanobenzoyl)-2-methyl-pyrrolo[1,2-b]pyridazine-5-carboxylate (6d). The product was recrystallized from acetonitrile and colorless crystals with mp

174-5 ºC were obtained; Yield: method A 60 %; method B 67 %. Anal. Calcd. $C_{18}H_{13}N_3O_3$: C 67.71, H 4.10; N 13.16. Found: C 68.02; H 4.25; N 13.44. IR (ATR, cm^{-1}): 2226 (CN).

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.66 (s, 3H, 2-Me); 3.91(s, 3H, MeO); 7.12 (d, 1H, *J* = 9.2 Hz, H-3); 7.63 (s, 1H, H-6); 7.80 (d, 2H, *J* = 8.4 Hz, H-3', H-5'); 7.95 (d, 2H, *J* = 8.4 Hz, H-2', H-6'); 8.56 (d, 1H, *J* = 9.2 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 22.4 (2-Me); 51.8 (MeO); 105.6 (C-5); 115.6 (CN); 118.3 (C-4'); 120.7 (C-3); 125.0 (C-6); 126.1 (C-7); 127.7 (C-4); 129.9 (C-2', C-6'); 132.4 (C-3', C-5'); 133.0 (C-4a); 143.1 (C-1'); 154.1 (C-2); 163.9 (COO); 182.6 (COAr).

Method A: Synthesis of pyrrolo[1,2-b]pyridazine 6 using acetylenic dipolarophiles

3 Mmol pyridazinium bromide **3** were suspended in 20 mL of dichloromethane and then 4 mmol of diethyl acetylenedicarboxylate were added. Under vigorous stirring 0.45 mL (3 mmol) of triethylamine (dissolved in 10 mL of methylene chloride) were added dropwise. After 1 h the reaction mixture was washed with water and the solvent evaporated. The pyrrolopyridazine derivatives **6** were purified by recrystallization or by column chromatography on neutral Al_2O_3 using dichloromethane as eluent.

Method B: Synthesis of pyrrolo[1,2-b]pyridazines 6 using olefinic dipolarophiles

5 Mmol of pyridazinium bromides **3** and 15 mmoles of olefinic dipolarophile (diethyl maleate or fumarate) in 30 mL DMF were treated under stirring and at room temperature with 0.7 mL (5 mmol) triethylamine. After 30 min. was added 3 g TPCD and at the reaction mixture was heated at 80-90 ºC for 4 h. Then the mixture was cooled at room temperature and 50 mL 5% aqueous HCl were added in order to promote the precipitation of the product which was removed by vacuum filtration and air dried. The crude product was purified by chromatography on a short column (Aluminium oxide 90 standardized, chloroform).

Diethyl 7-Benzoyl-pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6e**) The product was recrystallized from methanol and colorless crystals with mp 126-8 °C were obtained. Yield: method A 81 %; method B 79 %. Anal. Calcd. $C_{20}H_{18}N_2O_5$: C 65.57; H 4.95; N 7.65. Found: C 65.88; H 5.23; N 7.87. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.13 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.38 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.02 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.39 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.07 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.43-7.48 (m, 2H, H-3', H-5'); 7.56-7.61 (m, 1H, H-4'); 7.80-7.83 (m, 2H, H-2', H-6'); 8.33 (dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.62 (dd, 1H, *J* = 9.2, 1.9 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.0, 14.5 (2Me); 61.0, 62.0 (2OCH_2); 103.8 (C-5); 117.5 (C-3); 128.6 (C-4); 126.3, 126.8 (C-6, C-7); 128.6 (C-3', C-5',); 129.8 (C-2', C-6'); 131.2 (C-4a); 133.5 (C-4'); 138.3 (C-1'); 144.9 (C-2); 162.8, 164.3 (2COO); 185.8 (COAr).

Diethyl 7-(4-Phenylbenzoyl)-pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6f**). The product was recrystallized from isopropanol and colorless crystals with mp 129-132 °C were obtained. Yield: method A 76 %; method B 71 %. Anal. Calcd. $C_{26}H_{22}N_2O_5$: C 70.58; H 5.01, N 6.33. Found: C 70.89; H 5.32; N 6.58.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.15 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.38 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.08 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.38 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.06 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.35-7.41 (m, 1H, H-4"); 7.42-7.48 (m, 2H, H-3", H-5"); 7.60-7.64 (m, 2H, H-2", H-6"); 7.67 (d, 2H, *J* = 8.4 Hz, H-3', H-5'); 7.89 (d, 2H, *J* = 8.4 Hz, H-2', H-6'); 8.31 (dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.60(dd, 1H, *J* = 9.2, 1.9 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.2, 14.7 (2Me); 61.2, 62.2 (2OCH_2); 104.0 (C-5); 117.0 (C-3); 124.9, 125.7 (C-6, C-7); 126.2, 126.4, 128.2, 129.2 (C-2', C-6', C-3', C-5', C-2", C-3", C-5", C-6"); 127.5, 127.9 (C-4, C-4"); 129.9 (C-4a); 135.7 (C-1'); 138.9 (C-1'); 144.3 (C-2); 145.0 (C-4'); 161.6, 163.1 (2COO); 184.1 (COAr).

Diethyl 7-(4-chlorobenzoyl)pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6g**). The product was recrystallized from ethyl acetate and white crystals with mp 164-6 °C were obtained. Yield: method A 67 %; method B 71 %. Anal. Calcd. $C_{20}H_{17}ClN_2O_5$: N 6.99. Found: N 7.09.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.16 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.36 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.07 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.36 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.07 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.40 (d, 2H, *J* = 8.5 Hz, H-3', H-5'); 7.72 (d, 2H, *J* = 8.5 Hz, H-2', H-6'); 8.30 (dd, 1H, *J* = 4.5, 1.9, H-2); 8.62 (dd, 1H, *J* = 9.2, 1.9, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.7, 14.2 (2Me); 60.8, 61.9 (2OCH_2); 103.6 (C-5); 117.3 (C-3); 125.9, 126.4 (C-6, C-7); 128.6 (C-4); 128.6 130.8 (C-2', C-3', C-5', C-6'); 131.0 (C-4a); 136.2 (C-1'); 139.6 (C-4'); 144.6 (C-2); 162.4, 164.1 (2COO); 184.2 (COAr).

Diethyl 7-(3-bromobenzoyl)pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6h**). The product was recrystallized from methanol and colorless crystals with mp 98-100 °C were obtained. Yield: method A 77 %; method B 72 %. Anal. Calcd. $C_{20}H_{17}BrN_2O_5$: N 6.29. Found: N 6.41.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.21 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.39 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.10 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.39 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.11 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.34 (t, 1H, *J* = 7.8 Hz, H-5'); 7.93 (t, 1H, *J* = 1.8 Hz, H-2'); 7.69-7.73 (m, 2H, H-4', H-6'); 8.35 (dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.64 (dd, 1H, *J* = 9.2, 1.9 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.1, 14.6 (2Me); 61.1, 62.3 (2OCH_2); 104.1 (C-5); 117.8 (C-3); 122.8 (C-4'); 126.0, 126.1 (C-6, C-7); 128.3 (C-6'); 129.1 (C-4); 130.3 (C-5'); 131.5 (C-4a); 132.5 (C-2'); 136.2 (C-4'); 140.2 (C-1'); 145.1 (C-2); 162.7, 164.4 (2COO); 184.2 (COAr).

Diethyl 7-(4-bromobenzoyl)pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6i**) The product was recrystallized from acetonitrile or a mixture of methanol-ethyl acetate (1:1) and colorless crystals with mp 161-2°C were obtained. Yield: method A 78 %; method B 76 %. Anal. Calcd. $C_{20}H_{17}BrN_2O_5$: N 6.29. Found: N 6.41.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.18 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.39 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.10 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.39 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.11 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.59 (d, 2H, *J* = 8.6 Hz, H-3', H-5'); 7.67 (d, 2H, *J* = 8.6 Hz, H-2', H-6'); 8.32 (dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.62 (dd, 1H, *J* = 9.2, 1.9 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.8, 14.3 (2Me); 60.8, 61.9 (2OCH_2); 103.7 (C-5); 117.3 (C-3); 126.1, 126.4 (C-6, C-7); 128.3 (C-4'); 128.8 (C-4); 130.9, 131.3 (C-2', C-3', C-5', C-6'); 131.0 (C-4a); 136.8 (C-4'); 144.6 (C-2); 162.5, 164.1 (2COO); 184.4 (COAr).

Diethyl 7-(3-nitrobenzoyl)pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6j**) The product was recrystallized from ethanol and colorless crystals with mp 103-5 °C were obtained. Yield: method A 74 %; method B 76 %. Anal. Calcd. $C_{20}H_{17}N_3O_7$: C 58.40; H 4.17; N 10.21. Found: C 58.71; H 4.48; N 10.43.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.22 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.37 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.14 (q, 2H, *J* = 7.1 Hz,

6-CH_2O); 4.37 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.13 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.65 (t, 1H, *J* = 7.9 Hz, H-5'); 8.07-8.10 (m, 1H, H-4'); 8.27 (dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.39-8.43 (m, 1H, H-4'); 8.55 (t, 1H, 1.9, H-2'); 8.65 (dd, *J* = 1H, *J* = 9.2, 1.9, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.7, 14.2 (2Me); 60.8, 62.0 (2OCH_2); 104.1 (C-5); 117.9 (C-3); 124.5 (C-2'); 125.1, 127.9 (C-6, C-7); 127.0 (C-4'); 128.8 (C-4); 129.5 (C-5'); 131.3 (C-4a); 134.8 (C-6'); 139.3 (C-1'); 144.6 (C-2); 147.9 (C-3'); 162.1, 164.1 (2COO); 182.8 (COAr).

Diethyl 7-(4-nitrobenzoyl)pyrrolo[1,2-b]pyridazine-5,6-dicarboxylate (**6k**). The product was recrystallized from acetonitrile and pale yellow crystals with mp 183-4 °C were obtained. Yield: method A 79 %; method B 75 %. Anal. Calcd. $C_{20}H_{17}N_3O_7$: C 58.40; H 4.17; N 10.21. Found: C 58.61; H 4.40; N 10.38.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.26 (t, 3H, *J* = 7.1 Hz, 6-Me); 1.39 (t, 3H, *J* = 7.1 Hz, 5-Me); 4.15 (q, 2H, *J* = 7.1 Hz, 6-CH_2O); 4.38 (q, 2H, *J* = 7.1 Hz, 5-CH_2O); 7.13 (dd, 1H, *J* = 9.2, 4.5 Hz, H-3); 7.91 (d, 2H, *J* = 8.5 Hz, H-2', H-6'); 8.30 (d, 2H, *J* = 8.5 Hz, H-3', H-5'); 8.32(dd, 1H, *J* = 4.5, 1.9 Hz, H-2); 8.67(dd, 1H, *J* = 9.2, 1.9 Hz, H-4).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.9, 14.3 (2Me); 61.0, 62.2 (2OCH_2); 103.4 (C-5); 118.0 (C-3); 123.5 (C-3', C-5'); 125.5, 128.0 (C-6, C-7); 128.9 (C-4); 130.1 (C-2', C-6'); 131.5 (C-4a); 143.2 (C-1'); 144.7 (C-2); 150.1 (C-4'); 162.3, 164.2 (2COO); 183.5 (COAr).

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