1,3-DIPOLAR CYCLOADDITION REACTIONS OF 4-HALOPHENYL-PHTHALAZINIUM YLIDES TO ACTIVATED ALKENES AND ALKYNES

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For the first time in the benzodiazinium ylide series cycloaddition of (4-halophenyl) substituted ylides to activated alkenes and alkynes was studied. The ability of these ylides to react with acrylonitrile, *N*-phenylmaleimide, ethyl propiolate and dimethyl acetylenedicarboxylate was investigated. The stereochemistry and regiochemistry involved in these reactions are also discussed. Two new salts and ten new azabicyclic compounds have been obtained.
Keywords: 1,3-Dipolar cycloadditions; Ylides; Alkenes; Alkynes; Stereoselective synthesis; Azabicyclic; Phthalazine.

The chemistry of cycloimmonium ylides has been widely discussed[1–3]. In the series of ylides with saturated carbanions, the research has focused on the ylides with (alkoxycarbonyl)alkyl or benzoylalkyl carbanions. In the case of (4-halophenyl)benzodiazinium ylides (halogen = F, Cl, Br), we are not aware of any systematic study concerning their cycloaddition reactions with activated alkenes and alkynes. Moreover, in the whole cycloimmonium ylides series, we found only one communication[4] in this respect, where only the reaction with dimethyl acetylenedicarboxylate (DMAD) is studied, and, moreover, the obtained results are uncertain.

Having in view the above considerations, we decided to study the cycloaddition reactions of 2-(4-halobenzoyl)-2-oxo-1-(phthalazin-2-ium-2-yl)-ethan-1-ylides with acrylonitrile and *N*-phenylmaleimide (NPMI) as activated alkenes and with ethyl propiolate and DMAD as activated alkynes.

In order to obtain the new ylides **3**, the Kröhnke salt method was used[5]. First we obtained the corresponding cycloimmonium salts **2**, which in alkaline medium (Et_3N) generated the ylides *in situ* (Scheme 1).

NPMI, as a symmetrical cyclic *Z*-alkene, reacts with ylides **3** giving cycloadducts **4a**–**4c**. The [3+2] cycloaddition occurs highly stereospecifically and no formation of compounds such as **5** or **6** was observed (Scheme 2).

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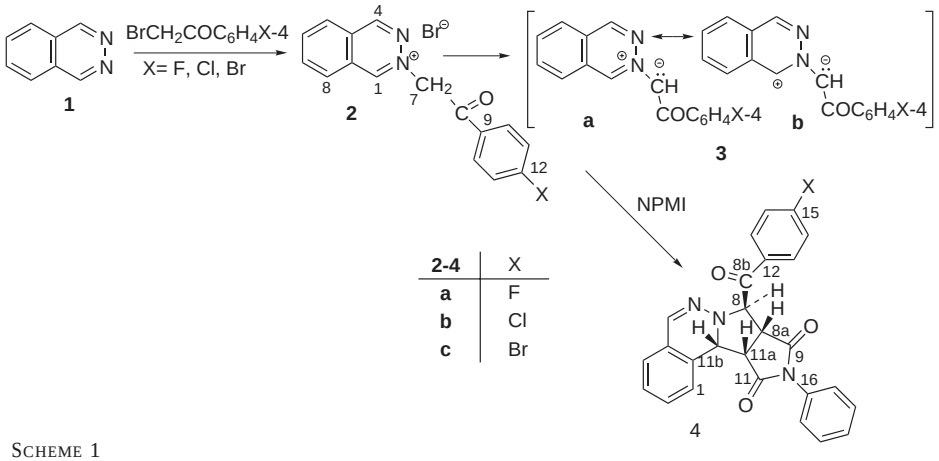
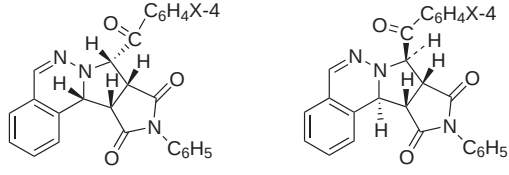
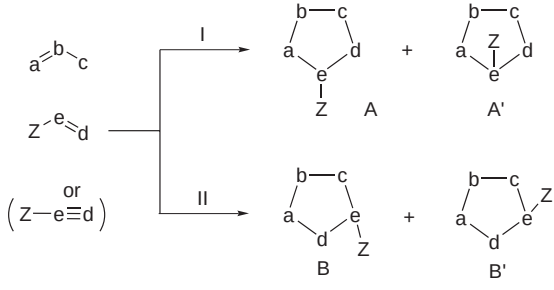


SCHEME 1

The structure of new compounds was proved by elemental and spectral analysis, as well as through comparison with analogous structures from the literature[6–13]. Following spectral methods were used: IR, ^{1}H NMR, ^{13}C NMR and two-dimensional experiments 2D-COSY, 2D-HETCOR (HMQC), long-



range 2D-HETCOR (HMBC). As the only possible manner of ring fusion at the 1- and 2-positions is *cis* geometry, H-1 (doublet of doublet) and H-2 (doublet) are *cis* to each other. This is confirmed in ^{1}H NMR by the coupling constants (8.0 Hz). The proton H-10b (d) is also in *cis* position having

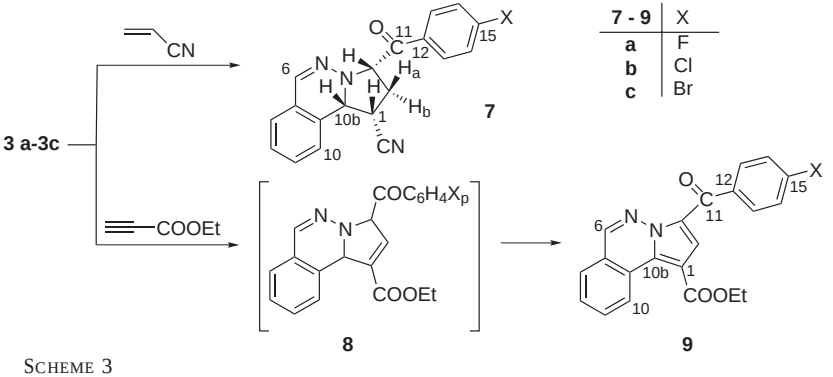


SCHEME 2

a coupling constant of 8.4 Hz with H-1. It is interesting that H-3 appears as a singlet (not as a doublet as usual) being *trans* with respect to H-2. Sterical hindrance caused by bulky neighbouring groups (4-halobenzoyl and the NPMI ring) could be responsible.

An additional evidence for the assigned structures is the extraordinarily high difference of chemical shifts between H-3 (5.90 ppm) and H-10b (4.60 ppm), H-2 (4.20 ppm), H-1 (3.70 ppm). These differences between 1.25–2.00 ppm could be explained by the fact that H-3 hydrogens are closely located to the carbonyl of the fused maleimide ring suffering from a powerful anisotropy effect (similar cases have been described[6]).

The reaction of ylides **3** with non-symmetrical dipolarophiles such as acrylonitrile and ethyl propiolate involve additional regiochemical problems[1,2,7–10] since alternative addition of dipole (ylide) to the dipolarophile has often been found (Scheme 2). No matter what conditions were used (different solvents, temperature, time), the reaction of (4-halophenyl)-phthalazinium ylides **3a**–**3c** with acrylonitrile or ethyl propiolate led to single isomers, the tetrahydropyrrolophthalazine adducts **7a**–**7c** or pyrrolophthalazine adducts **9a**–**9c** (Scheme 3). This means that one bond is formed between the ylide carbon and the non-substituted carbon atom of the dipolarophile and the second bond between positively charged carbon of the ylide and the substituted carbon of the dipolarophile (path I, regioisomer A, Scheme 2). This is in accordance with the electronic effects in dipolarophiles. Because a single regioisomer is obtained, the reaction is regiospecific being under charge control.



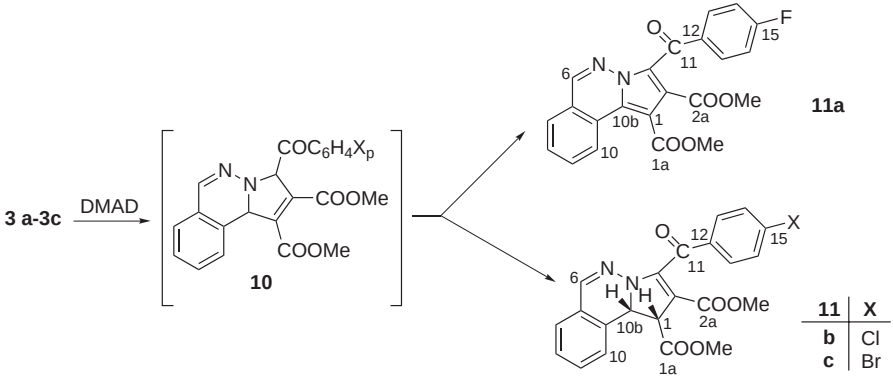
SCHEME 3

The structure of new compounds was proved by elemental and spectral analysis (IR, ^{1}H NMR, ^{13}C NMR, COSY, HMQC, HMBC). In the ^{1}H NMR spectrum of the tetrahydropyrrolophthalazine adducts **7a**–**7c**, the most important signals are those of the H-1, H-2a, H-2b, H-3 and H-10b atoms. The

H-3 atoms appear around 5.70 ppm (dd), which excludes both B and B′ structures (Scheme 2). The H-3 atoms have 2 different coupling constants (J(3,2a) = 4.4, J(3,2b) = 9.2 Hz), which prove the *trans* configuration to H-2b and *cis* to H-2a. The H-1 atoms have three different coupling constants (J(1,2a) = 7.6, J(1,2b) = 15.6, J(1,10b) = 6.4 Hz) which prove the *trans* configuration relative to H-2b and *cis* to H-2a and H-10b. An additional evidence for the assigned structures is the extraordinarily big difference of chemical shifts between H-3 (≈5.70 ppm) and H-10b (≈4.50 ppm), H-1 (≈3.40 ppm), H-2b (≈2.70 ppm), H-2a (≈2.35 ppm).

The main spectral data for pyrrolophthalazine adducts **9** confirm the proposed structure. It is of interest that H-10 protons appear at very high chemical shifts, around 10.00 ppm (in other compounds appear around 7.50–8.00 ppm). Regarding the mechanism, the formation of compounds **9** could be explained by oxidative dehydrogenation of **8**.

The reaction with DMAD proceeds differently according to the halogen nature in the *para* position of the phenacyl group. Thus, the ylide **3a** (fluoro derivative) leads to aromatized pyrrolophthalazine **11a** while ylides **3b** (chloro derivative) and **3c** (bromo derivative) lead to 1,10b-dihydropyrrolophthalazines **11b** and **11c** (for **3c** the literature[11] describes formation of the corresponding 2,3-dihydropyrrolophthalazine, but our spectroscopic data show that the correct structure of the product is **11c**) (Scheme 4).



SCHEME 4

Regarding the mechanism, the formation of compounds **11b** and **11c** could be explained by prototropic rearrangement of **10** while formation of **11a** could be explained by oxidative dehydrogenation of **10**. The structure of new compounds was proved by elemental and spectral analysis (IR, ^{1}H NMR, ^{13}C NMR, COSY, HMQC, HMBC). The lack of signals between 3.95–7.35 ppm in the proton spectra is a good evidence of the aromatized

pyrrolophthalazine **11a**. In the case of **11b** the signal of H-1 proton appears at 4.51–4.48 ppm as a doublet, having a coupling constants of 13.2 Hz, which proves the *cis* relative to H-10b (5.30–5.26 ppm, d, *J*(10b,1) = 13.2 Hz). In ^{13}C NMR spectra the corresponding carbons of these protons appear at low chemical shifts, which is also a good evidence for the proposed structure (C-1 at 52.35 and C-10b at 61.85 ppm).

Concerning the influence of the halogen in the *para* position of the phenacyl groups in cycloaddition reactions, it is hard to draw a conclusion. However, in the case of DMAD cycloaddition, it seems that the fluorine derivative leads to fully aromatized fused heterocycles while chlorine and bromine lead to partly saturated compounds.

EXPERIMENTAL

Melting points were determined on a MELTEMP II apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance instrument (400 MHz) downfield from an internal standard, $SiMe_4$ in DMSO-d_6 (for compounds **2**) or in $CDCl_3$ (for compounds **4**, **7** and **11**). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. IR spectra were recorded with a JASCO V-570 spectrometer in KBr.

2-[2-(Substituted Phenyl)-2-oxoethyl]phthalazinium Bromides **2**. General Procedure

A solution of 4-halophenacyl bromide (10 mmol) in anhydrous benzene (20 ml) was added to a stirred suspension of phthalazine (1.3 g, 10 mmol) in anhydrous benzene (30 ml). The mixture was stirred at room temperature for 2–3 h, filtered and crystallized from an appropriate solvent.

2-[2-(4-Fluorophenyl)-2-oxoethyl]phthalazinium bromide (**2a**). Yield 94%; white crystals, m.p. 108–109 °C (benzene). For $C_{16}H_{12}BrFN_2O$ (347.2) calculated: 55.35% C, 3.48% H, 8.07% N; found: 55.28% C, 3.40% H, 7.89% N. IR: 3 052, 2 980, 1696 (C=O); 1615, 1577, 1461 (C=C, C=N). ^{1}H NMR: 6.79 s, 2 H (CH_2); 7.55–7.51 t, $J_{13,12}$ = 8.4, $J_{F,13}$ = 8.8, 2 H (H-13); 8.27–8.23 q, *J* = 8.4, *J* = 5.6, 2 H (H-12); 8.52–8.48 t, *J* = 8.0, *J* = 7.2, 1 H (H-7); 8.64–8.62 t, *J* = 8.0, *J* = 7.6, 1 H (H-6); 8.69–8.67 d, *J* = 7.6, 1 H (H-5); 8.77–8.75 d, *J* = 7.2, 1 H (H-8); 10.20 s, 1 H (H-4); 10.67 s, 1 H (H-1). ^{13}C NMR: 68.80 (C-9), 116.33 (C-13), 127.27 (C-4a), 127.48 (C-8a), 128.64 (C-6), 130.27 (C-8), 131.82 (C-12), 136.63 (C-7), 139.63 (C-11), 139.95 (C-5), 153.55 (C-1), 154.90 (C-4), 167.26 (C-14), 189.38 (C-10, keto).

2-[2-(4-Chlorophenyl)-2-oxoethyl]phthalazinium bromide (**2b**). Yield 95%; white crystals, m.p. 153–154 °C (benzene). For $C_{16}H_{12}BrClN_2O$ (363.6) calculated: 52.85% C, 3.33% H, 7.70% N; found: 52.81% C, 3.30% H, 7.59% N. IR: 3054, 2980, 1691 (C=O); 1614, 1572, 1463 (C=C, C=N). ^{1}H NMR: 6.50 s, 2 H (CH_2); 7.79–7.77 d, *J* = 8.0, 2 H (H-13); 8.12–8.10 d, *J* = 8.0, 2 H (H-12); 8.49–8.46 t, *J* = 8.0, *J* = 7.2, 1 H (H-7); 8.57–8.55 t, *J* = 8.0, *J* = 7.4, 1 H (H-6); 8.61–8.59 d, *J* = 7.4, 1 H (H-5); 8.72–8.70 d, *J* = 7.2, 1 H (H-8); 9.60 s, 1 H (H-4); 9.85 s, 1 H (H-1). ^{13}C NMR: 68.86 (C-9), 127.10 (C-4a), 127.46 (C-8a), 128.60 (C-6), 129.00 (C-13), 129.97 (C-12), 130.21 (C-8), 136.54 (C-7), 139.41 (C-14), 139.65 (C-11), 139.92 (C-5), 153.52 (C-1), 154.86 (C-4), 191.02 (C-10, keto).

2-[2-(4-Bromophenyl)-2-oxoethyl]phthalazinium bromide (**2c**). Yield 95%; yellowish crystals, m.p. 166–167 °C (benzene). For $C_{16}H_{12}Br_2N_2O$ (408.1) calculated: 47.09% C, 2.69% H, 6.86% N; found: 47.00% C, 2.60% H, 6.80% N. IR: 3056, 2980, 1689 (C=O); 1612, 1570, 1497, 1458 (C=C, C=N). ^{1}H NMR: 6.52 s, 2 H (CH_2); 7.94–7.92 d, *J* = 8.0, 2 H (H-13); 8.10–8.08 d, *J* = 8.0, 2 H (H-12); 8.52–8.50 t, *J* = 8.0, *J* = 7.2, 1 H (H-7); 8.58–8.56 t, *J* = 8.0, *J* = 7.4, 1 H (H-6); 8.62–8.60 d, *J* = 7.4, 1 H (H-5); 8.76–8.74 d, *J* = 7.2, 1 H (H-8); 9.65 s, 1 H (H-4); 9.87 s, 1 H (H-1). ^{13}C NMR: 68.82 (C-9), 127.21 (C-4a), 127.47 (C-8a), 128.61 (C-6), 128.74 (C-14), 129.68 (C-13), 130.24 (C-8), 130.78 (C-12), 136.55 (C-7), 139.62 (C-11), 139.93 (C-5), 153.54 (C-1), 154.88 (C-4), 190.96 (C-10, keto).

[3+2] Cycloadducts **4**, **7** and **11**. General Procedure

The corresponding cycloimmonium salt **2** (1 mmol) was suspended in 10 ml of a solvent (chloroform for **2a** and anhydrous benzene for **2b** and **2c**). A solution of an activated alkene or alkyne (1 mmol) and triethylamine (1.1 mmol) in the same solvent (5 ml) was then added. The solution was refluxed for 2 h in the case of alkynes and for 3 h in the case of alkenes. For derivatives of salts **2b** and **2c**, the resulting mixture was filtered hot to remove triethylamine hydrobromide and the clear solution was evaporated. For derivatives of salt **2a**, the resulting mixture was washed thoroughly three times with water (50 ml), dried with sodium sulfate, filtered and evaporated. The crude product was crystallized from an appropriate solvent.

8-(4-Fluorobenzoyl)-10-phenyl-8,8a,11a,11b-tetrahydropyrrolo[3′,4′:3,4]pyrrolo[2,1-a]phthalazine-9,11-dione (**4a**). Yield 87%; white crystals, m.p. 219 °C (ethanol). For $C_{26}H_{18}FN_3O_3$ (439.5) calculated: 71.06% C, 4.13% H, 9.56% N; found: 71.0% C, 4.06% H, 9.47% N. IR: 2950, 1772, 1719 (C=O imide); 1692 (C=O keto); 1601, 1555, 1497, 1450 (C=C, C=N). ^{1}H NMR: 3.76–3.72 dd, *J* = 8.0, *J* = 8.4, 1 H (H-11a); 4.20–4.18 d, *J* = 8.0, 1 H (H-8a); 4.69–4.67 d, *J* = 8.4, 1 H (H-11b); 5.95 s, 1 H (H-8); 7.08–7.06 d, *J* = 7.2, 2 H (H-17); 7.50–7.31 m, 9 H (H-1, H-2, H-3, H-4, 2 × H-14, 2 × H-18, H-19); 7.61 s, 1 H (H-5); 8.25–8.22 q, *J* = 8.8, *J* = 8.6, 2 H (H-13). ^{13}C NMR: 46.72 (C-8a), 51.32 (C-11a), 59.75 (C-11b), 76.44 (C-8), 116.23 (C-14), 123.84 (C-4a), 126.32 (C-4), 126.81 (C-17), 128.33 (C-1a), 128.84 (C-19), 129.18 (C-1), 129.33 (C-3), 129.49 (C-18), 131.31 (C-12), 131.46 (C-2), 132.97 (C-13), 135.31 (C-16), 140.70 (C-5), 164.55 (C-15), 174.87 (C-11, keto imide), 177.50 (C-9, keto imide), 193.38 (C-8b, keto).

8-(4-Chlorobenzoyl)-10-phenyl-8,8a,11a,11b-tetrahydropyrrolo[3′,4′:3,4]pyrrolo[2,1-a]phthalazine-9,11-dione (**4b**). Yield 89%; white crystals, m.p. 230 °C (ethanol). For $C_{26}H_{18}ClN_3O_3$ (455.9) calculated: 68.50% C, 3.98% H, 9.22% N; found: 68.45% C, 3.90% H, 9.05% N. IR: 2950, 1770, 1719 (C=O imide); 1690 (CO keto); 1600, 1558, 1495, 1452 (C=C, C=N). ^{1}H NMR: 3.70–3.66 dd, *J* = 8.0, *J* = 8.4, 1 H (H-11a); 4.15–4.13 d, *J* = 8.0, 1 H (H-8a); 4.68–4.66 d, *J* = 8.4, 1 H (H-11b); 5.92 s, 1 H (H-8); 7.00–6.98 d, *J* = 7.2, 2 H (H-17); 7.48–7.27 m, 9 H (H-1, H-2, H-3, H-4, 2 × H-14, 2 × H-18, H-19); 7.50 s, 1 H (H-5); 8.20–8.18 d, *J* = 8.8, 2 H (H-13). ^{13}C NMR: 46.92 (C-8a), 51.47 (C-11a), 59.70 (C-11b), 76.45 (C-8), 123.76 (C-4a), 126.26 (C-4), 126.62 (C-17), 128.26 (C-19), 128.30 (C-1a), 129.05 (C-1), 129.16 (C-14), 129.27 (C-3), 129.37 (C-18), 130.25 (C-13), 131.29 (C-2), 133.20 (C-12), 135.10 (C-16), 140.66 (C-5), 140.96 (C-15), 174.90 (C-11, keto imide), 177.55 (C-9, keto imide), 193.47 (C-8b, keto).

8-(4-Bromobenzoyl)-10-phenyl-8,8a,11a,11b-tetrahydropyrrolo[3′,4′:3,4]pyrrolo[2,1-a]phthalazine-9,11-dione (**4c**). Yield 88%; yellowish crystals, m.p. 241 °C (ethanol). For $C_{26}H_{18}BrN_3O_3$

(500.4) calculated: 62.41% C, 3.63% H, 9.59% N; found: 62.38% C, 3.60% H, 9.40% N. IR: 2950, 1770, 1717 (C=O imide); 1688 (C=O keto); 1599, 1560, 1495, 1450 (C=C, C=N). ^{1}H NMR: 3.60–3.58 dd, *J* = 8.0, *J* = 8.4, 1 H (H-11a); 4.20–4.18 d, *J* = 8.0, 1 H (H-8a); 4.66–4.64 d, *J* = 8.4, 1 H (H-11b); 5.90 s, 1 H (H-8); 7.04–7.02 d, *J* = 7.2, 2 H (H-17); 7.40–7.11 m, 7 H (H-1, H-2, H-3, H-4, 2 × H-18, H-19); 7.49 s, 1 H (H-5); 7.78–7.76 d, *J* = 8.8, 2 H (H-13); 8.24–8.22 d, *J* = 8.8, 2 H (H-13). ^{13}C NMR: 46.90 (C-8a), 51.46 (C-11a), 59.69 (C-11b), 76.46 (C-8), 123.76 (C-4a), 126.25 (C-4), 126.65 (C-17), 128.08 (C-15), 128.28 (C-19), 128.30 (C-1a), 129.04 (C-1), 129.26 (C-3), 129.41 (C-18), 130.09 (C-14), 131.20 (C-13), 131.29 (C-2), 135.12 (C-16), 137.08 (C-12), 140.64 (C-5), 174.88 (C-11, keto imide), 177.53 (C-9, keto imide), 193.45 (C-8b, keto).

3-(4-Fluorobenzoyl)-1,2,3,10b-tetrahydropyrrolo[2,1-a]phthalazine-1-carbonitrile (**7a**). Yield 81%; white crystals, m.p. 179 °C (ethanol). For $C_{19}H_{14}FN_3O$ (319.3) calculated: 71.46% C, 4.42% H, 13.16% N; found: 71.42% C, 4.39% H, 13.00 % N. IR: 3055, 2950, 2241 (CN); 1697 (C=O keto); 1598, 1560, 1495, 1450 (C=C, C=N). ^{1}H NMR: 2.42–2.36 8 lines: dxdxd, $J_{2a,2b}$ = 19.6, $J_{2a,1}$ = 7.6, $J_{2a,3}$ = 4.4, 1 H (H-2a); 2.69–2.62 8 lines: dxdxd, *J* = 19.6, *J* = 15.6, *J* = 9.2, 1 H (H-2b); 3.79–3.74 8 lines: dxdxd, $J_{1,2a}$ = 7.6, $J_{1,2b}$ = 15.6, $J_{1,10b}$ = 7.4, 1 H (H-1); 4.54–4.52 d, *J* = 7.4, 1 H (H-10b); 5.80–5.77 dd, $J_{3,2b}$ = 9.2, $J_{3,2a}$ = 4.4, 1 H (H-3); 7.49–7.33 m, 7 H (H-6, H-7, H-8, H-9, H-10, 2 × H-14); 8.23–8.20 q, *J* = 8.8, *J* = 8.6, 2 H (H-13). ^{13}C NMR: 28.93 (C-2), 34.89 (C-1), 59.15 (C-10b), 69.77 (C-3), 116.43 (C-14), 121.59 (C-1a, CN), 124.73 (C-7), 126.25 (C-7), 127.34 (C-8), 129.05 (C-10a), 129.60 (C-9), 131.40 (C-10), 132.14 (C-12), 132.65 (C-13), 138.66 (C-6), 167.00 (C-15), 195.57 (C-11, keto).

3-(4-Chlorobenzoyl)-1,2,3,10b-tetrahydropyrrolo[2,1-a]phthalazine-1-carbonitrile (**7b**). Yield 80%; white crystals, m.p. 175 °C (ethanol). For $C_{19}H_{14}ClN_3O$ (335.8) calculated: 67.96% C, 4.20% H, 12.51% N; found: 67.89% C, 4.17% H, 12.40% N. IR: 3055, 2950, 2240 (CN); 1695 (C=O keto); 1600, 1558, 1494, 1450 (C=C, C=N). ^{1}H NMR: 2.36–2.30 8 lines: dxdxd, $J_{2a,2b}$ = 19.6, $J_{2a,1}$ = 7.6, $J_{2a,3}$ = 4.4, 1 H (H-2a); 2.98–2.91 8 lines: dxdxd, *J* = 19.6, *J* = 15.6, *J* = 9.4, 1 H (H-2b); 3.38–3.33 8 lines: dxdxd, $J_{1,2a}$ = 7.6, $J_{1,2b}$ = 15.6, $J_{1,10b}$ = 7.4, 1 H (H-1); 4.44–4.42 d, *J* = 7.4, 1 H (H-10b); 5.68–5.65 dd, $J_{3,2b}$ = 9.4, $J_{3,2a}$ = 4.4, 1 H (H-3); 7.12–7.10 d, *J* = 8.0, 1 H (H-7); 7.30–7.28 d, *J* = 8.4, 1 H (H-10); 7.42–7.39 m, 2 H (H-8, H-9); 7.44 s, 1 H (H-6); 7.47–7.45 d, *J* = 8.8, 2 H (H-14); 8.15–8.12 d, *J* = 8.8, 2 H (H-13). ^{13}C NMR: 28.57 (C-2), 35.67 (C-1), 59.07 (C-10b), 70.82 (C-3), 120.18 (C-6a), 124.19 (C-1a, CN), 126.57 (C-7), 126.68 (C-8), 128.15 (C-10a), 129.04 (C-14), 129.57 (C-9), 130.93 (C-13), 131.35 (C-10), 133.19 (C-12), 140.13 (C-6), 140.40 (C-15), 194.67 (C-11, keto).

3-(4-Bromobenzoyl)-1,2,3,10b-tetrahydropyrrolo[2,1-a]phthalazine-1-carbonitrile (**7c**). Yield 81%; white crystals, m.p. 176 °C (ethanol). For $C_{19}H_{14}BrN_3O$ (380.24) calculated: 60.02% C, 3.71% H, 11.05% N; found: 60.00% C, 3.68% H, 11.00% N. IR: 3053, 2950, 2240 (CN); 1694 (C=O keto); 1602, 1560, 1490, 1450 (C=C, C=N). ^{1}H NMR: 2.30–2.26 8 lines: dxdxd, $J_{2a,2b}$ = 19.6, $J_{2a,1}$ = 7.6, $J_{2a,3}$ = 4.4, 1 H (H-2a); 2.94–2.90 8 lines: dxdxd, *J* = 19.6, *J* = 15.6, *J* = 9.4, 1 H (H-2b); 3.32–3.29 8 lines: dxdxd, $J_{1,2a}$ = 7.6, $J_{1,2b}$ = 15.6, $J_{1,10b}$ = 7.4, 1 H (H-1); 4.40–4.38 d, *J* = 7.4, 1 H (H-10b); 5.60–5.56 dd, $J_{3,2b}$ = 9.4, $J_{3,2a}$ = 4.4, 1 H (H-3); 7.40–7.34 m, 5 H (H-6, H-7, H-8, H-9, H-10); 7.64–7.61 d, *J* = 8.8, 2 H (H-14); 7.85–7.82 d, *J* = 8.8, 2 H (H-13). ^{13}C NMR: 28.52 (C-2), 35.61 (C-1), 59.00 (C-10b), 70.76 (C-3), 120.10 (C-6a), 123.89 (C-1a, CN), 126.46 (C-7), 126.60 (C-8), 128.06 (C-15), 128.10 (C-10a), 129.52 (C-9), 130.12 (C-14), 131.21 (C-13), 131.32 (C-10), 137.10 (C-12), 140.06 (C-6), 194.60 (C-11, keto).

Ethyl 3-(4-fluorobenzoyl)pyrrolo[2,1-a]phthalazine-1-carboxylate (**9a**). Yield 79%; white crystals, m.p. 182 °C (ethanol). For $C_{21}H_{15}FN_2O_3$ (362.4) calculated: 69.61% C, 4.17% H, 7.73% N; found: 69.38% C, 4.14% H, 7.56% N. IR: 3055, 2950, 1694 (C=O ester); 1663 (C=O

keto); 1598, 1562, 1498, 1450 (C=C, C=N); 1228, 1120 (C–O–C). ^{1}H NMR: 1.37–1.15 t, J = 14.0, 3 H (CH_3); 4.39–4.33 q, J = 14.0, 2 H (CH_2); 7.43–7.38 t, $J_{F,14}$ = 8.8, $J_{14,13}$ = 8.4, 2 H (H-14); 7.59 s, 1 H (H-2); 7.96–7.87 m, 3 H (2 × H-13, H-8); 8.04–8.01 t, J = 7.6, J = 8.0, 1 H (H-9); 8.17–8.15 d, J = 8.0, 1 H (H-7); 9.04 s, 1 H (H-6); 9.70–9.68 d, J = 8.0, 1 H (H-10). ^{13}C NMR: 14.20 (CH_3), 60.46 (CH_2), 107.49 (C-2), 115.80 (C-14), 121.16 (C-6a), 121.79 (C-10a), 126.27 (C-7), 127.97 (C-1), 128.44 (C-10), 129.12 (C-10b), 130.09 (C-8), 132.25 (C-13), 133.14 (C-9), 137.12 (C-12), 137.18 (C-3), 146.64 (C-6), 163.88 (C-1a, keto ester), 170.10 (C-15), 184.92 (C-11, keto).

Ethyl 3-(4-chlorobenzoyl)pyrrolo[2,1-a]phthalazine-1-carboxylate (**9b**). Yield 80%; white crystals, m.p. 196 °C (ethanol). For $C_{21}H_{15}ClN_2O_3$ (378.8) calculated: 66.58% C, 3.99% H, 7.40% N; found 66.54% C, 3.96% H, 7.29% N. IR: 3060, 2952, 1692 (C=O ester); 1663 (C=O keto); 1597, 1565, 1500, 1457 (C=C, C=N); 1228, 1121 (C–O–C). ^{1}H NMR: 1.44–1.40 t, J = 14.0, 3 H (CH_3); 4.44–4.39 q, J = 14.0, 2 H (CH_2); 7.35 s, 1 H (H-2); 7.50–7.48 d, J = 8.4, 2 H (H-14); 7.76–7.72 t, J = 8.4, J = 8.0, 1 H (H-8); 7.92–7.98 m, 4 H (2 × H-13, H-7, H-9); 8.17–8.15 d, J = 8.0, 1 H (H-7); 8.74 s, 1 H (H-6); 9.84–9.82 d, J = 8.4, 1 H (H-10). ^{13}C NMR: 14.45 (CH_3), 60.81 (CH_2), 108.44 (C-2), 122.18 (C-10a), 124.56 (C-7), 126.76 (C-6a), 127.61 (C-10), 128.33 (C-1), 128.71 (C-14), 129.38 (C-8), 130.38 (C-10b), 131.14 (C-13), 133.01 (C-9), 136.62 (C-3), 137.36 (C-12), 138.83 (C-15), 146.53 (C-6), 164.10 (C-1a, keto ester), 183.31 (C-11, keto).

Ethyl 3-(4-bromobenzoyl)pyrrolo[2,1-a]phthalazine-1-carboxylate (**9c**). Yield 79%; white crystals, m.p. 194 °C (ethanol). For $C_{21}H_{15}BrN_2O_3$ (423.3) calculated: 59.59% C, 3.57% H, 6.62% N; found: 59.55% C, 3.53% H, 6.49% N. IR: 3061, 2948, 1690 (C=O ester); 1660 (C=O keto); 1597, 1563, 1502, 1462 (C=C, C=N); 1227, 1121 (C–O–C). ^{1}H NMR: 1.44–1.40 t, J = 14.0, 3 H (CH_3); 4.42–4.39 q, J = 14.0, 2 H (CH_2); 7.68–7.64 m, 4 H (2 × H-14, H-2, H-9); 7.76–7.72 t, J = 8.4, J = 8.0, 1 H (H-8); 7.83–7.81 d, J = 8.4, 2 H (H-13); 7.91–7.87 m, 2 H (H-7, H-9), 8.74 s, 1 H (H-6); 9.83–9.81 d, J = 8.4, 1 H (H-10). ^{13}C NMR: 14.45 (CH_3), 60.80 (CH_2), 108.44 (C-2), 122.16 (C-10a), 124.60 (C-7), 126.72 (C-6a), 127.57 (C-10), 127.43 (C-1), 128.20 (C-15), 129.80 (C-8), 130.38 (C-10b), 131.24 (C-14), 131.67 (C-13), 132.98 (C-9), 136.60 (C-3), 137.12 (C-12), 146.51 (C-6), 164.06 (C-1a, keto ester), 183.41 (C-11, keto).

Dimethyl 3-(4-fluorobenzoyl)pyrrolo[2,1-a]phthalazine-1,2-dicarboxylate (**11a**). Yield 89%; white crystals, m.p. 159 °C (ethanol). For $C_{22}H_{15}FN_2O_5$ (406.4) calculated: 65.02% C, 3.72% H, 6.89% N; found: 64.96% C, 3.69% H, 6.78% N. IR: 3053, 2956, 1742 (C=O ester-1); 1718 (C=O ester-2); 1668 (C=O keto); 1601, 1572, 1504, 1452 (C=C, C=N); 1227, 1121 (C–O–C). ^{1}H NMR: 3.63 s, 3 H (CH_3, from 1); 3.95 s, 3 H (CH_3, from 2); 7.39–7.35 t, $J_{F,14}$ = 8.8, $J_{14,13}$ = 8.6, 2 H (H-14); 7.83–7.80 t, $J_{8,9}$ = 8.0, $J_{8,7}$ = 7.6, 1 H (H-8); 7.91–7.89 q, J = 8.6, J = 5.2, 2 H (H-13); 8.01–7.97 t, J = 8.0, J = 8.0, 1 H (H-9); 8.10–8.08 d, J = 7.6, 1 H (H-7); 8.62–8.60 d, J = 8.0, 1 H (H-10); 8.90 s, 1 H (H-6). ^{13}C NMR: 68.71 (CH_3, COOMe from 2), 69.11 (CH_3, COOMe from 1), 107.58 (C-1), 116.76 (C-14), 121.52 (C-6a), 123.87 (C-2), 124.00 (C-7), 126.15 (C-10a), 128.56 (C-10b), 129.72 (C-10), 130.04 (C-8), 132.92 (C-13), 134.16 (C-12), 134.34 (C-9), 144.31 (C-3), 148.39 (C-6), 163.72 (C-1a, keto ester), 165.59(C-2a, keto ester), 167.28 (C-15), 185.77 (C-11, keto).

Dimethyl 3-(4-chlorobenzoyl)-1,10b-dihydropyrrolo[2,1-a]phthalazine-1,2-dicarboxylate (**11b**). Yield 83%; yellow crystals, m.p. 146 °C (ethanol). For $C_{22}H_{17}ClN_2O_5$ (424.8) calculated: 62.20% C, 4.03% H, 6.59% N; found: 62.16% C, 3.99% H, 6.51% N. IR: 3055, 2952, 1740 (C=O ester); 1708 (C=O ester unsaturat); 1677 (C=O keto); 1605, 1575, 1500, 1450 (C=C, C=N); 1229, 1124 (C–O–C). ^{1}H NMR: 3.52 s, 3 H (CH_3, from 1); 3.91 s, 3 H (CH_3, from 2);

4.51–4.48 d, *J* = 13.2, 1 H (H-1); 5.30–5.26 d, *J* = 13.2, 1 H (H-10b); 7.25–7.23 d, *J* = 8.0, 1 H (H-7); 7.44–7.39 m, 3 H (H-8, H-9, H-10); 7.54–7.47 m, 3 H (H-6, 2 × H-14); 7.97–7.95 d, *J* = 8.4, 2 H (H-13). ^{13}C NMR: 52.35 (C-1), 61.85 (C-10b), 68.67 (CH_3, COOMe from 2), 69.48 (CH_3, COOMe from 1), 101.83 (C-2), 123.54 (C-8), 124.80 (C-6a), 125.90 (C-7), 128.92 (C-9), 130.84 (C-10a), 130.67 (C-13), 131.86 (C-10), 133.37 (C-12), 141.09 (C-15), 142.45 (C-3), 152.55 (C-6), 164.25 (C-2a, keto ester), 176.17 (C-1a, keto ester), 187.16 (C-11, keto).

Dimethyl 3-(4-bromobenzoyl)-1,10b-dihydropyrrolo[2,1-a]phthalazine-1,2-dicarboxylate (**11c**). Yield 82%; yellow crystals, m.p. 146 °C (ethanol). For $C_{22}H_{17}BrN_2O_5$ (469.3) calculated: 56.31% C, 3.65% H, 5.97% N; found: 56.27% C, 3.60% H, 5.89% N. IR: 3053, 2950, 1740 (C=O ester), 1710 (C=O ester unsatur.), 1685 (C=O keto); 1609, 1578, 1507, 1458 (C=C, C=N); 1231, 1128 (C–O–C). ^{1}H NMR: 3.50 s, 3 H (CH_3, from 1); 3.87 s, 3 H (CH_3, from 2); 4.49–4.46 d, *J* = 13.0, 1 H (H-1); 5.27–5.22 d, *J* = 13.0, 1 H (H-10b); 7.24–7.21 d, *J* = 8.0, 1 H (H-7); 7.40–7.37 m, 3 H (H-8, H-9, H-10); 7.59–7.48 m, 3 H (H-6, 2 × H-14); 7.85–7.83 d, *J* = 8.2, 2 H (H-13). ^{13}C NMR: 52.35 (C-1), 61.85 (C-10b), 68.69 (CH_3, COOMe from 2), 69.50 (CH_3, COOMe from 1), 101.85 (C-2), 123.55 (C-8), 124.82 (C-6a), 125.90 (C-7), 128.22 (C-15), 128.94 (C-9), 130.84 (C-10a), 131.31 (C-14), 131.70 (C-13), 137.16 (C-12), 142.46 (C-3), 152.55 (C-6), 164.27 (C-2a, keto ester), 176.18 (C-1a, keto ester), 187.17 (C-11, keto).

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