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ORIGINAL PAPER

Synthesis, UV–Vis spectra, and Hammett correlation of some novel bis(dihydropyrrolo[3,4-*c*]pyrazoles)

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Abstract Twenty-nine novel bis(dihydropyrrolo[3,4-*c*]pyrazole) derivatives were obtained by reacting C,N-phenyl-substituted nitrilimines generated in situ from corresponding hydrazonyl chlorides with bismaleimides. The structures were elucidated by physical and spectroscopic methods [m.p., R_f, infrared (IR), ^{1}H nuclear magnetic resonance (NMR), ^{13}C NMR, correlation spectroscopy (COSY), heteronuclear correlation (HETCOR), nuclear Overhauser effect (NOE), and high-resolution mass spectrometry (HRMS)]. Also, Hammett correlation graphs were obtained between Hammett constants σ_p and λ_{max} values of bis(pyrrolopyrazoles) carrying *p*-substituted phenyl-ring-bearing electron-withdrawing and electron-donating groups and discussed in terms of substituent effects.

Keywords 1,3-Dipolar cycloaddition · Nitrilimine · Bismaleimide · Heterocycles · Spectroscopy

Introduction

Nitrilimines, which were discovered by Huisgen and coworkers in 1959, are important precursors of 1,3-dipolar structure, which can be used to assemble a wide variety of five-membered heterocyclic compounds (pyrazoles, pyrazolines) with 1,3-dipolar cycloaddition reactions to various dipolarophiles [1–22]. Nitrilimines have been frequently generated in situ and used in numerous 1,3-dipolar cycloadditions. They are well known to undergo three types of reactions: 1,3-dipolar cycloaddition leading to five-membered ring heterocycles, cyclocondensation reactions leading to five-membered, six-membered or larger heterocycles, and nucleophilic addition leading to acyclic adducts, some of which were reported to show biological activities [23–26].

Experimental observations showed that the orientation observed for alkenes substituted with electron-donor, conjugating, and moderate electron-acceptor substituents is the 5-substituted regioisomer [27, 28]. Sometimes, cycloaddition of nitrilimines to very electron-deficient alkenes gives significant amounts of the 4-substituted 2-pyrazolines [29]. The rationalization of such regiochemical results became evident in terms of the frontier molecular orbital theory of Fukui [30–39].

In addition, bismaleimides have received increasing attention recently, especially in synthesis of polymeric materials [40–44], and molecules derived from the reaction of bismaleimides [45] have often been studied as DNA minor-groove-binding ligands. These types of molecules were also reported to exhibit antitumor activity [46–49].

To the best of our knowledge, based on literature search of SciFinder Scholar, Web of Knowledge, and Beilstein Crossfire databases, there is no reported study related to synthesis of bis(dihydropyrrolopyrazoles) through double cycloaddition of diaryl nitrilimines to bismaleimides. We aimed in this work to assemble bis(dihydropyrrolopyrazoles) by reacting various C,N-substituted nitrilimines bearing both electron-withdrawing and electron-donating groups on phenyl rings attached to the hydrazone azomethine carbon and hydrazone-N^2, which were produced in situ, with bis(*N*-phenylmaleimides) as dipolarophilic reagents.

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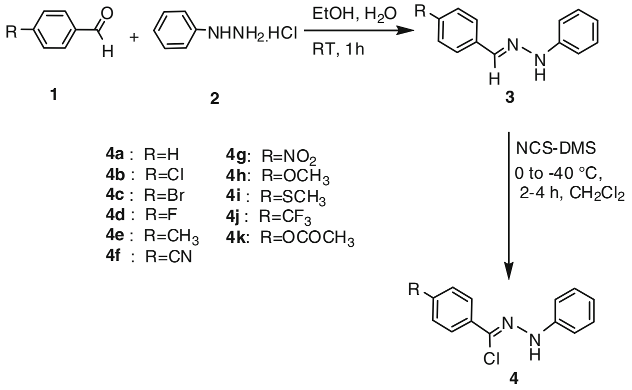
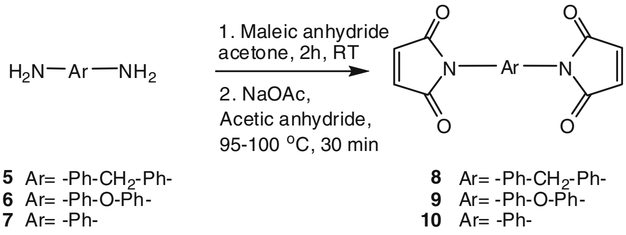
Results and discussion

Substituted hydrazones **3a**–**3k** and substituted hydrazonyl chlorides **4a**–**4k** were obtained, starting from the corresponding aldehydes and substituted hydrazines (or hydrochlorides) according to literature procedures [50–54] (Scheme 1), and bismaleimides **8**, **9**, **10** (Scheme 2) were prepared by procedures reported previously [55–59].

C,N-aryl nitrilimines generated from hydrazonyl chlorides **4** in situ cycloadded to bismaleimides **8**, **9**, **10** in dry acetonitrile at room temperature to afford bis(dihydropyrrolo[3,4-*c*]pyrazoles) **11**, **12**, **13** in excellent yields without need for chromatographic separation (Scheme 3).



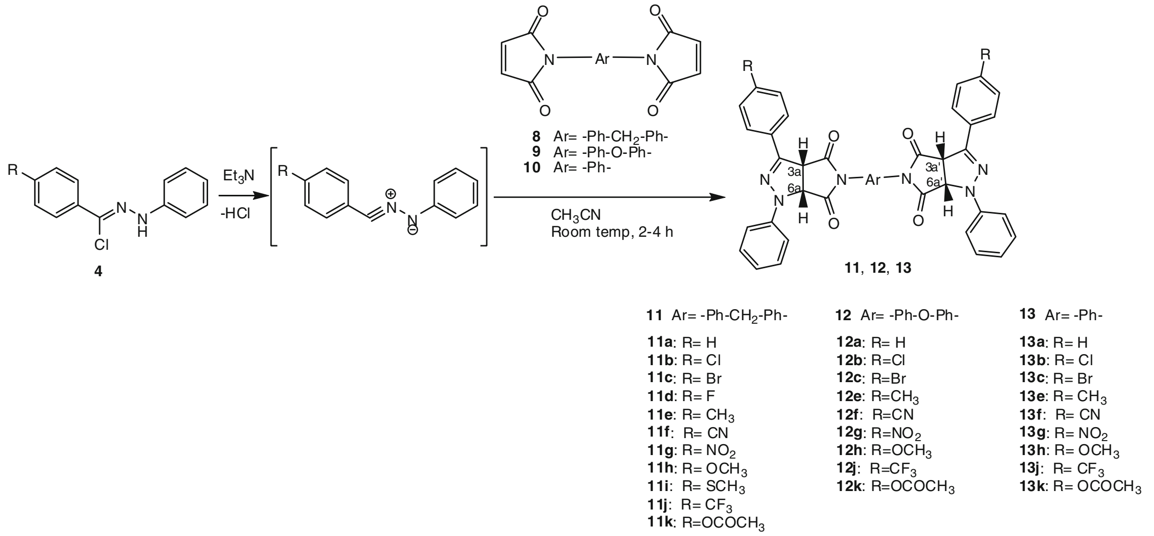
Scheme 1



Scheme 2

The reactions were monitored by thin-layer chromatography (TLC) and found to result in single diastereomers. Since the 1,3-dipolar component of the reaction is necessarily unsymmetrical, we may expect the possibility of two diastereomers due to double cycloaddition. However, no indication of another diastereomer was found upon checking the ^{1}H NMR spectra of the crude reaction mixture or upon monitoring the progress of the reaction by TLC. All of the new compounds were identified by means of spectroscopic and physical data including IR, NMR, and HRMS measurements, and CHN analyses. The cycloadducts **11**, **12**, and **13** showed strong carbonyl absorptions at around 1,720 cm^{-1} and C=N absorptions at around 1,595–1,600 cm^{-1} in the IR spectra.

Assignment of the structures **11**, **12**, and **13** was performed based on data obtained from ^{1}H NMR, ^{13}C NMR, COSY, HETCOR, and NOE spectra. Many attempts to obtain fine crystals to obtain a better view of the absolute configurations of the cycloadducts by means of X-ray diffraction were performed, but all failed. The relative stereochemistry of the cycloadducts was assigned to be all *cis* based on the coupling constants of the bridge protons (3a-H/3a′-H and 6a-H/6a′-H) resonating at around 5.20–5.50 ppm as two doublets ($J = 11.0$ Hz) and COSY, HETCOR, DEPT, and NOE experiments. The chemical shifts of 3a-H/3a′-H bridge protons showed remarkable differences compared with bridge protons 6a-H/6a′-H due to the *p*-substitution of the electron-withdrawing and electron-releasing groups on the phenyl ring attached to the azomethine carbon. In addition, NOE experiments showed strong enhancements by irradiation of the bridge protons



Scheme 3

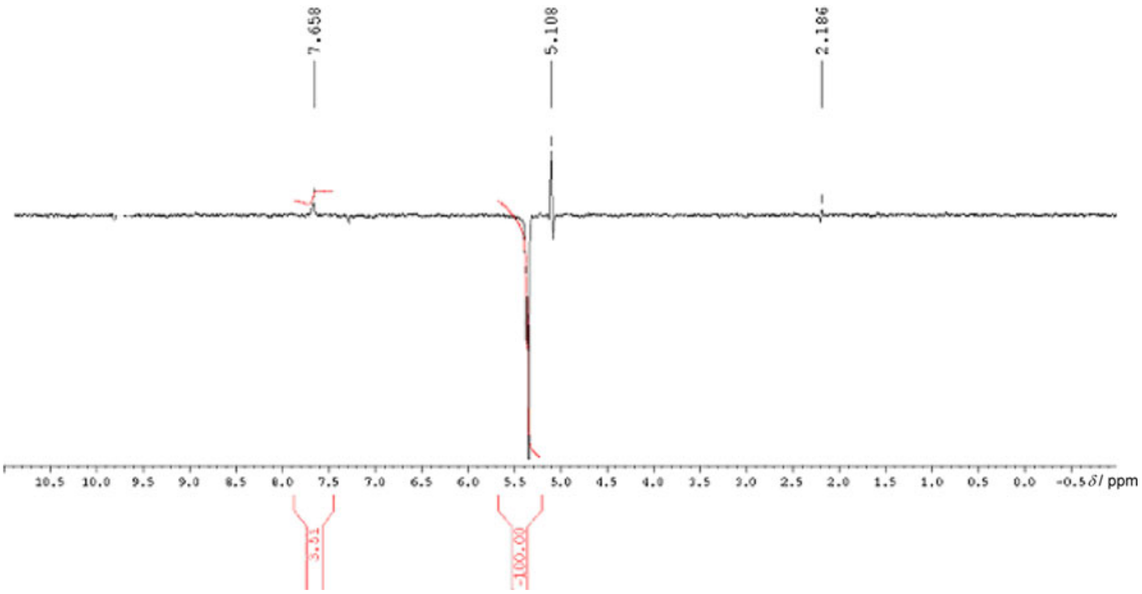


Fig. 1 Typical NOE difference spectrum of **12a**, indicating strong enhancement of 3a-H (3a′-H)

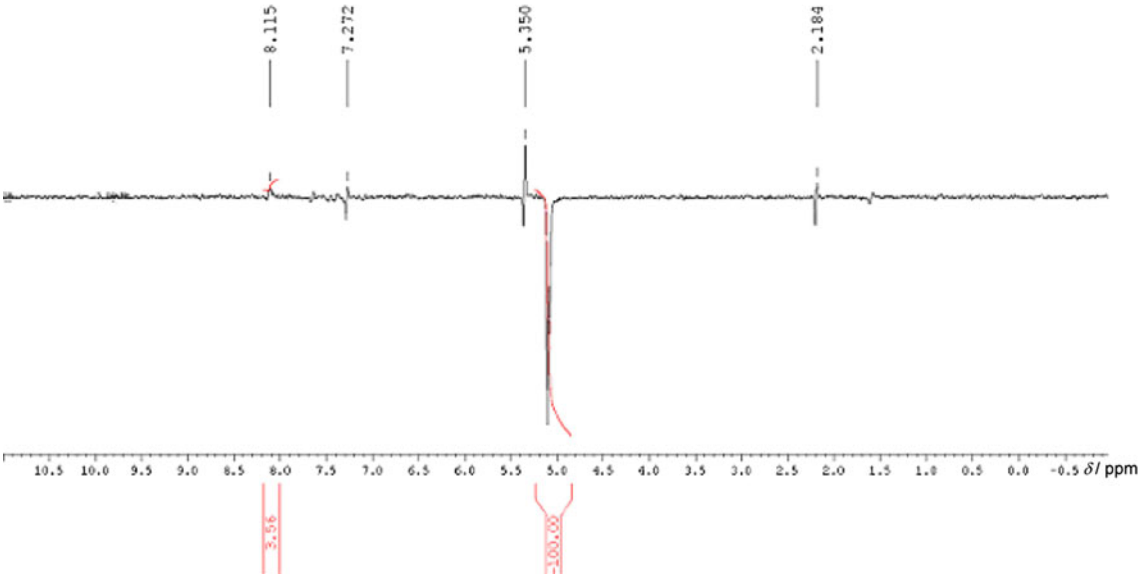


Fig. 2 Typical NOE difference spectrum of **12a**, indicating strong enhancement of 6a-H (6a′-H)

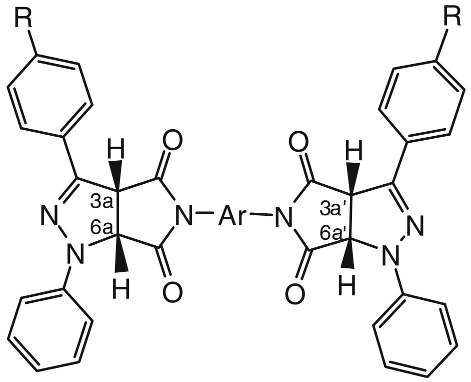
3a-H and 3a′-H, and 6a-H and 6a′-H, confirming their *cis* stereochemistry (Figs. 1, 2). This conformation is in accord with the structure reported by Noguchi et al. [60] for a similar structure.

In the case of electron-withdrawing groups in *para* position of the phenyl ring, 3a-H/3a′-H protons were found to resonate at more deshielded chemical shifts (Table 1). Due to the molecular symmetry, only two doublets regarding 3a-H and 3a′-H protons and for 6a-H and 6a′-H protons were observed in compounds **11**, **12**, and **13**. This can be attributed to strong electron delocalization through the aromatic ring due to the effect of the strong electron-withdrawing groups NO_2 and CN in *para* positions, which remarkably diminish the electron density on the azomethine carbon bonded to carbon with bridge hydrogen (3a-H/3a′-H). The distinct doublets at the specified chemical shift positions may be considered as proof of the formation of only one cycloadduct from this reaction, namely the *meso* form.

These chemical shift values are plotted against Hammett sigma constants in Fig. 3.

The carbonyl carbons appeared at around 170–175 ppm and azomethine carbons around 145–155 ppm depending on the *p*-substituents in the ^{13}C NMR spectra of the title compounds.

Table 1 3a-H/3a'-H chemical shifts of **11a–11k**



11 Ar= -Ph-CH_2-Ph-

	R	$\delta_{3a\text{-}H}$ (ppm)
a	H	5.30
b	Cl	5.30
c	Br	5.34
d	F	5.22
e	Me	5.29
f	CN	5.46
g	NO_2	5.47
h	OMe	5.20
i	SMe	5.22
j	CF_3	5.40
k	OCOMe	5.25

Upon investigation of ultraviolet (UV) absorptions of compounds **11**, **12**, and **13** it was clearly found that electron-withdrawing groups (CF_3, CN, and NO_2) on the phenyl ring attached to the azomethine carbon atom cause λ_{max} values (Table 2) to shift to longer wavelengths (towards visible region), and electron-donating groups (Me, OMe, SMe) to shorter wavelengths (Figs. 4, 5, 6).

In addition, a linear correlation between λ_{max} values and the Hammett substituent constants [61], σ_p, was obtained for compounds **11**, **12**, and **13** (Figs. 7, 8, 9). To the best of our knowledge, there are only two publications relating to correlation of UV absorption frequencies with Hammett substituent constants reported in the literature [62, 63].

Experimental

^1H and ^{13}C NMR spectra were recorded on BRUKER and VARIAN spectrometers (300 and 400 MHz for proton and 75 and 100 MHz for carbon). IR spectra were recorded on a SHIMADZU FTIR-8400S instrument (KBr pellet). Matrix-assisted laser desorption/ionization (MALDI) mass spectra were run on a Bruker FTMS 4.7-T BioAPEX II instrument, and also high-resolution mass spectra of the compounds were measured on a Bruker FTMS 4.7-T BioAPEX II and AEIMS 902 or a VG 7070E mass spectrometer. Ultraviolet spectra were recorded in 1,2-dichloroethane on a Hitachi U-2900 spectrophotometer at room temperature. Elemental analyses were performed on a Eurovector EA 3000 instrument. Melting points were determined on a MELTEMP apparatus. TLC was done using precoated plates with fluorescent indicator (Merck 5735). Stain solutions of permanganate, *p*-anisaldehyde, and iodine were used for visualization of TLC spots.

Preparation of 5,5'-substituted bis(dihydropyrrolo [3,4-c]pyrazoles) ***11–13****, typical procedure*

The corresponding hydrazonyl chloride **4** (0.5 mmol) and bismaleimide **8**, **9** or **10** (1 mmol) were dissolved in 20 cm^3 dry acetonitrile. Et_3N (0.404 g, 4 mmol) was added dropwise to the mixture with stirring, and after complete addition the reaction mixture was stirred at room temperature for 2–4 h. Progress of the reaction was monitored by TLC. After evaporating CH_3CN, the reaction mixture was

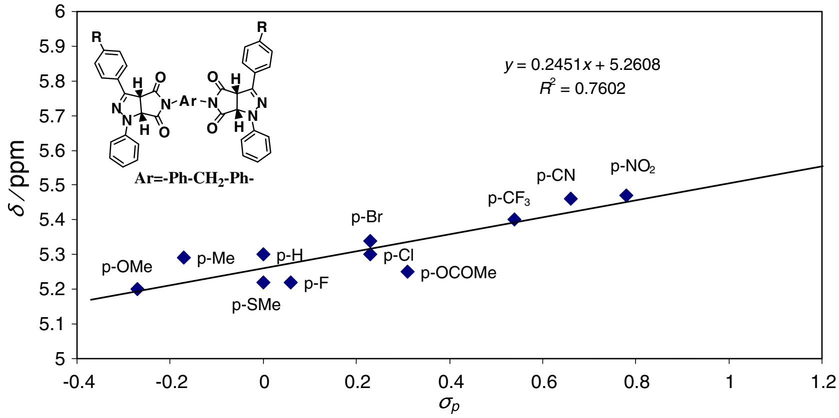


Fig. 3 Correlation of the chemical shifts of 3a-H versus Hammett σ_p constants of **11a–11k**

Table 2 UV absorption maxima (λ_{max}) and ε of compounds **11**–**13**

Compound	Substituent	λ_{max} (nm)	$\varepsilon/10^4$ ($dm^3\ mol^{-1}\ cm^{-1}$), $ClCH_2CH_2Cl$
11a	*p*-H	350.0	3.36
11b	*p*-Cl	357.0	3.72
11c	*p*-Br	358.0	3.45
11d	*p*-F	348.5	3.00
11e	*p*-Me	349.0	3.77
11f	*p*-CN	378.5	3.65
11g	*p*-NO_2	419.0	3.37
11h	*p*-OMe	349.5	3.23
11i	*p*-SMe	362.0	3.44
11j	*p*-CF_3	364.5	2.93
11k	*p*-OCOMe	353.5	3.48
12a	*p*-H	350.0	3.06
12b	*p*-Cl	357.5	3.35
12c	*p*-Br	358.0	3.44
12e	*p*-Me	349.0	3.40
12f	*p*-CN	383.0	3.49
12g	*p*-NO_2	418.5	3.20
12h	*p*-OMe	349.0	3.24
12j	*p*-CF_3	365.0	3.44
12k	*p*-OCOMe	353.0	3.42
13a	*p*–H	349.0	3.25
13b	*p*-Cl	357.0	3.12
13c	*p*-Br	358.5	3.11
13e	*p*-Me	348.5	3.45
13f	*p*-CN	378.5	4.13
13g	*p*-NO_2	417.0	3.10
13h	*p*-OMe	349.0	3.22
13j	*p*-CF_3	364.0	3.09
13k	*p*-OCOMe	353.0	3.01

poured into 50 cm^3 water to afford the crude crystalline cycloadducts. The crystals were filtered and washed with water (2 × 50 cm^3) and hexane (2 × 25 cm^3) and dried thoroughly under vacuum to yield **11**, **12** or **13**.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis(3a,6a-dihydro-1,3-diphenylpyrrolo-[3,4-c]pyrazole-4,6(1H,5H)-dione)* (**11a**, $C_{47}H_{34}N_6O_4$)

Yellow crystalline solid; yield 190 mg (quant.); m.p.: 278–280 °C; $R_f = 0.75$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,511, 1,494, 1,379, 1,193, 752, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.05$ (d, $J = 8.0$ Hz, 4H), 7.58 (d, $J = 8.0$ Hz, 4H), 7.51–7.32 (m, 18H), 7.03 (t, $J = 7.2$ Hz, 2H), 5.30 (d, $J = 11.0$ Hz, 2H), 5.05 (d, $J = 10.9$ Hz, 2H), 4.01 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.7$ (C=O), 170.8 (C=O), 144.6 (C=N), 142.9, 141.2, 130.3, 129.7, 129.6, 129.5, 129.3, 128.6, 127.2, 126.4, 121.6, 114.5, 65.6 (–CH), 53.5 (–CH), 41.0 (–CH_2–) ppm; HRMS: calculated for $C_{47}H_{34}N_6O_4$ 746.2985, found $[M + NH_4]^+$ 764.2991.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3-(4-chlorophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11b**, $C_{47}H_{32}Cl_2N_6O_4$)

Yellow–grey crystalline solid; yield 190 mg (92%); m.p.: 194–196 °C; $R_f = 0.70$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,512, 1,492, 1,379, 1,193, 752, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 8.0$ Hz, 4H), 7.62 (d, $J = 8.0$ Hz, 4H), 7.40 (t, $J = 8.1$ Hz, 8H), 7.22 (s, 8H), 7.03 (t, $J = 7.0$ Hz, 2H), 5.30 (d, $J = 10.9$ Hz, 2H), 4.97 (d, $J = 10.9$ Hz, 2H), 4.00 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.7$ (C=O), 170.9 (C=O), 144.8 (C=N), 142.0, 141.8, 135.5, 130.0, 129.7, 129.5, 129.4, 129.3, 128.7, 126.7, 121.8, 114.8, 65.8 (–CH), 53.0 (–CH), 41.0 (–CH_2) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 814 (100) $[M]^+$, 815 (51) $[M + H]^+$, 816 (70) $[M + 2]^+$, 817 (30) $[M + 3]^+$; HRMS: calculated for $C_{47}H_{32}Cl_2N_6O_4$ 814.1862, found 814.1852.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3-(4-bromophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11c**, $C_{47}H_{32}Br_2N_6O_4$)

Yellow crystalline solid; yield 230 mg (quant.); m.p.: 180–182 °C; $R_f = 0.77$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,512, 1,498, 1,375, 1,192, 750, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$ (d, $J = 8.0$ Hz, 4H), 7.64 (d, $J = 9.0$ Hz, 4H), 7.58 (d, $J = 9.0$ Hz, 4H), 7.38 (t, $J = 7.4$ Hz, 4H), 7.25–7.19 (q, $J = 8.0$ Hz, 8H), 7.04 (t, $J = 12.3$ Hz, 2H), 5.34 (d, $J = 11.1$ Hz, 2H), 5.01 (d, $J = 11.0$ Hz, 2H), 4.02 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.4$ (C=O), 170.6 (C=O), 151.5 (C=N), 144.2, 141.8, 141.3, 131.8, 129.8, 129.4, 129.3, 128.6, 126.3, 121.8, 114.6, 77.2, 65.7 (–CH), 53.4 (–CH), 41.0 (–CH_2–) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 902 (50) $[M]^+$, 904 (100) $[M + 2]^+$, 906 (60) $[M + 4]^+$; HRMS: calculated for $C_{47}H_{32}Br_2N_6O_4$ 902.0852, found 902.0849.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3-(4-fluorophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11d**, $C_{47}H_{32}F_2N_6O_4$)

Orange crystalline solid; yield 210 mg (quant.); m.p.: 183–185 °C; $R_f = 0.77$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,059$ (arom. C–H), 1,724 (C=O), 1,597 (C=N), 1,512, 1,492, 1,381, 1,193, 839, 750, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$–8.07 (q, $J = 5.4$, 2.3 Hz, 4H), 7.62 (d, $J = 9.0$ Hz, 4H), 7.37 (t, $J = 7.5$ Hz, 4H),

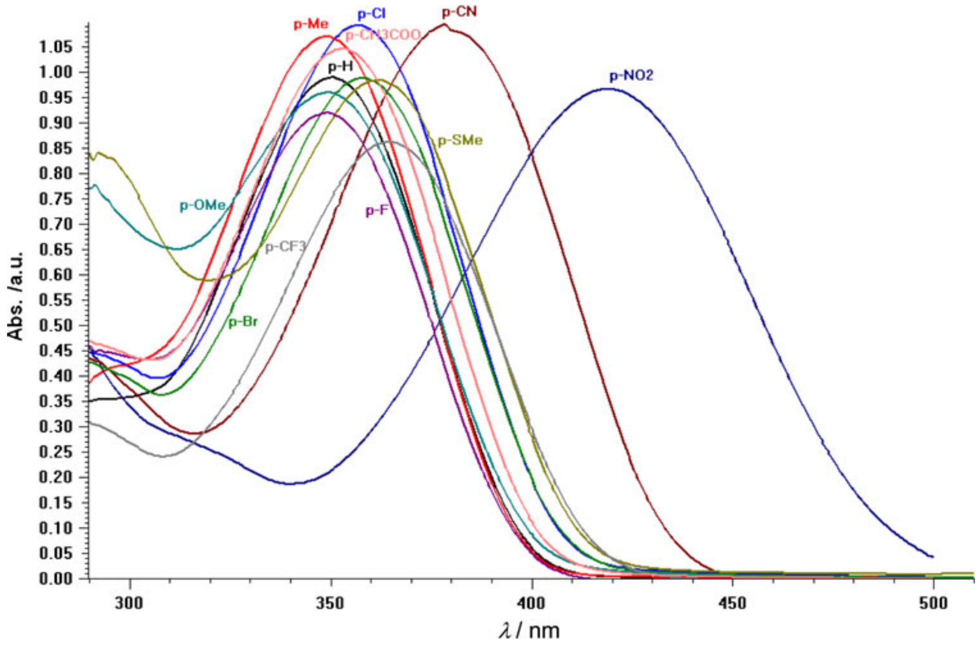


Fig. 4 UV–Vis spectra of compounds **11a**–**11k**

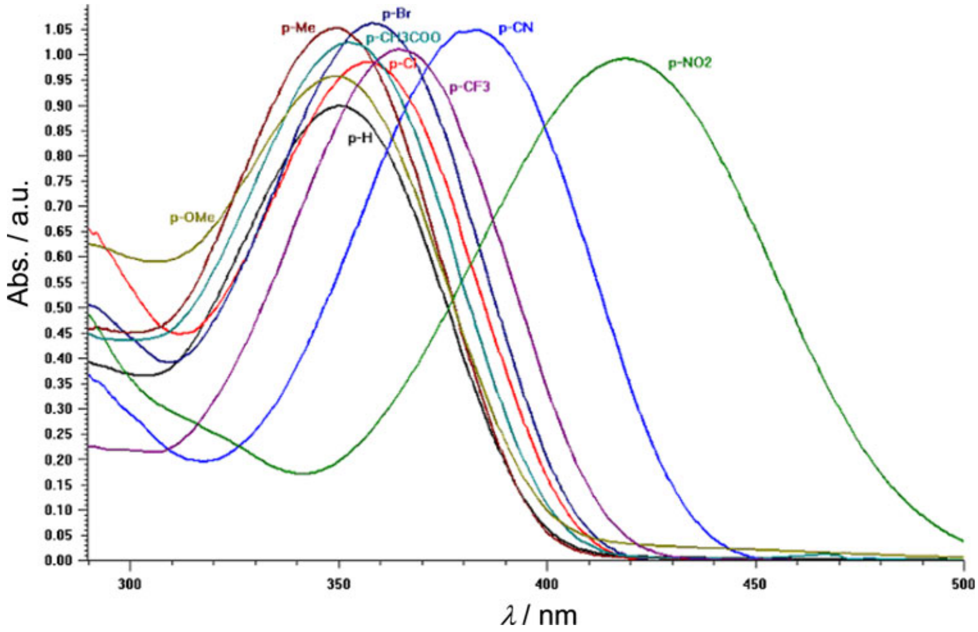


Fig. 5 UV-Vis spectra of compounds **12a**–**12k**

7.39–7.15 (m, 8H), 7.11 (t, $J = 7.8$ Hz, 4H), 7.03 (t, $J = 6.8$ Hz, 2H), 5.22 (d, $J = 11.3$ Hz, 2H), 4.92 (d, $J = 10.9$ Hz, 2H), 3.99 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.7$ (C=O), 170.8 (C=O), 165.0 (C=N), 162.5, 144.5, 142.0, 141.3, 133.9, 129.8, 129.2, 129.0, 126.4, 121.7, 115.7, 114.5, 65.7(–CH), 53.6 (–CH), 41.0 ($–CH_2–$) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 782 (100) $[M]^+$, 783 (55) $[M + H]^+$; HRMS: calculated for $C_{47}H_{32}F_2N_6O_4$ 782.2453, found 782.2441.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-methylphenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11e**, $C_{49}H_{38}N_6O_4$)

Yellow crystalline solid; yield 198 mg (quant.); m.p.: 180–182 °C; $R_f = 0.75$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}034$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,514, 1,498, 1,379, 1,184, 817, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.00$ (d, $J = 8.1$ Hz, 4H), 7.64

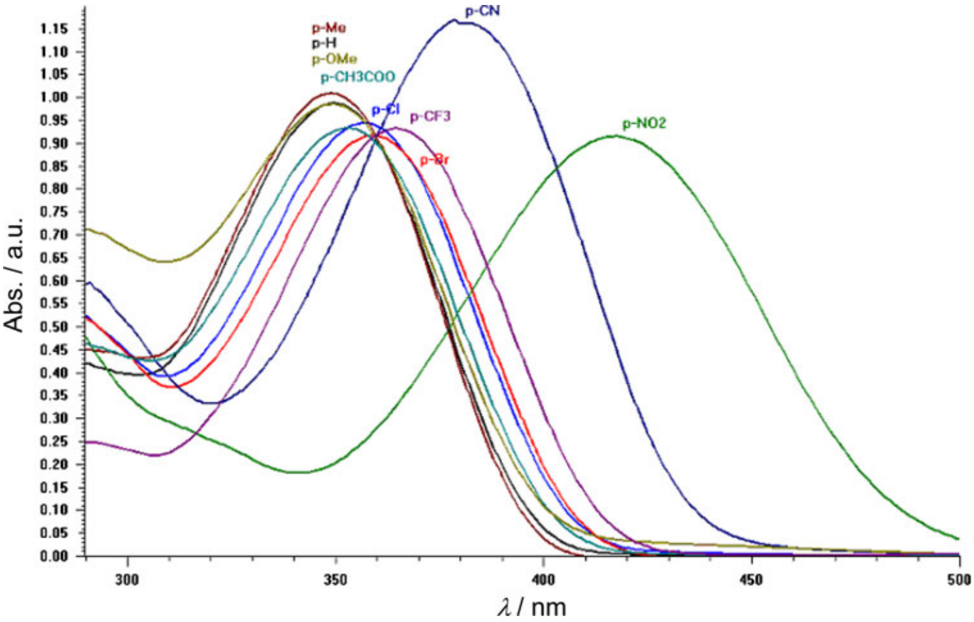


Fig. 6 UV–Vis spectra of compounds **13a–13k**

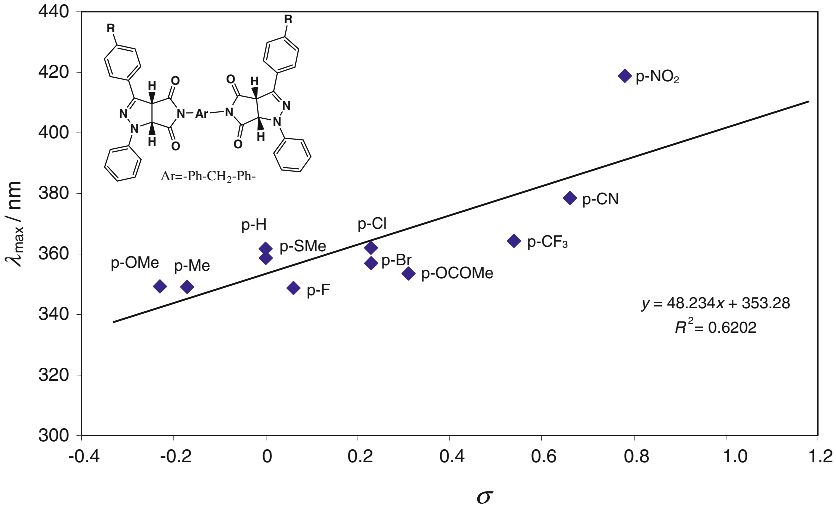


Fig. 7 Correlation between Hammett σ_p constants and λ_{max} (nm) of **11a–11k**

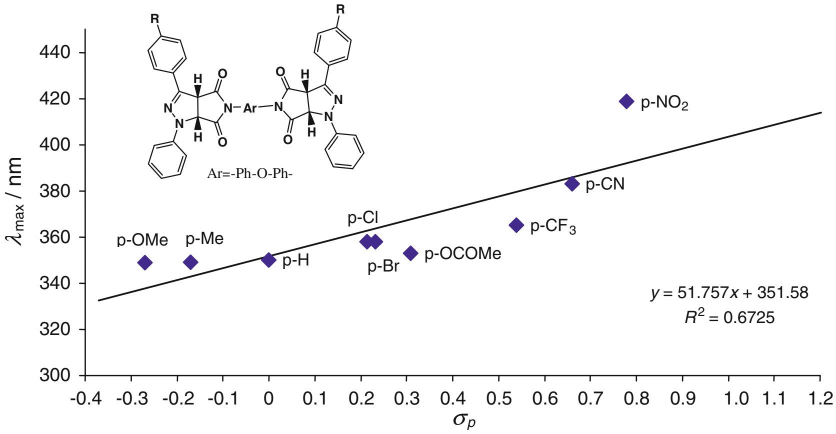


Fig. 8 Correlation between Hammett σ_p constants and λ_{max} (nm) of **12a–12k**

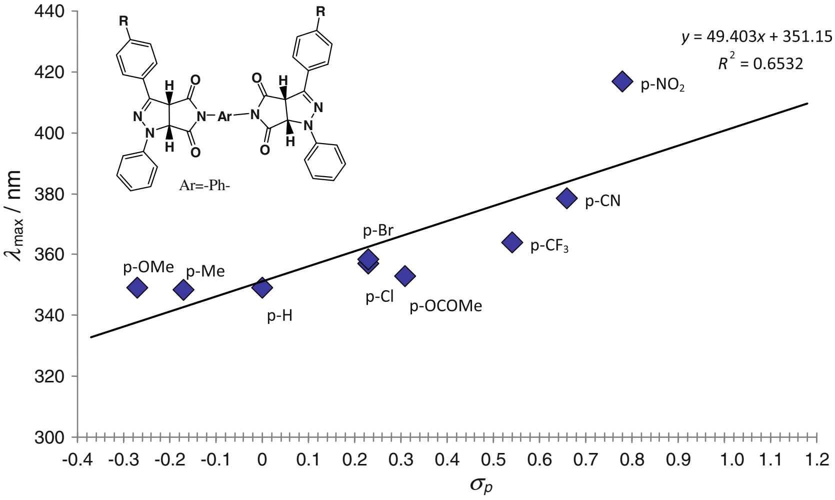


Fig. 9 Correlation between Hammett σ_p constants and λ_{max} (nm) of **13a**–**13k**

(d, $J = 7.8$ Hz, 4H), 7.37 (t, $J = 7.4$ Hz, 6H), 7.28–7.20 (m, 10H), 7.02 (t, $J = 7.3$ Hz, 2H), 5.29 (d, $J = 11.0$ Hz, 2H), 5.03 (d, $J = 10.9$ Hz, 2H), 4.02 (s, 2H), 2.42 (s, 6H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 171.8$ (C=O), 170.8 (C=O), 144.8 (C=N), 143.1, 141.2, 139.8, 129.7, 129.5, 129.3, 129.2, 127.5, 127.2, 126.4, 121.4, 114.5, 65.6 (–CH), 53.6 (–CH), 41.0 (–CH$_2$–), 21.5 (–CH$_3$) ppm; HRMS: calculated for $C_{49}H_{38}N_6O_4 + NH_4^+$ 792.3298, found 792.3296.

(3aR,6aR*,3a′S*,6a′S*)-4,4′-[Methylenebis[(4,1-phenylene)(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo-[3,4-c]pyrazole-5,3(1H)-diyl)]]bis[benzonitrile]*
(**11f**, $C_{49}H_{32}N_8O_4$)
Bright-yellow crystalline solid; yield 203 mg (quant.); m.p.: 209–211 °C; $R_f = 0.6$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{v} = 3,059$ (arom. C–H), 2,225 (C≡N), 1,720 (C=O), 1,597 (C=N), 1,512, 1,498, 1,381, 1,193, 842, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 8.20$ (d, $J = 8.4$ Hz, 4H), 7.73 (d, $J = 8.5$ Hz, 4H), 7.66 (d, $J = 8.5$ Hz, 4H), 7.40 (t, $J = 7.3$ Hz, 4H), 7.32–7.17 (m, 8H), 7.08 (t, $J = 7.3$ Hz, 2H), 5.46 (d, $J = 11.2$ Hz, 2H), 5.06 (d, $J = 11.2$ Hz, 2H), 4.04 (s, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 171.2$ (C=O), 170.6 (C=O), 143.5 (C=N), 141.4, 140.7, 134.7, 132.3, 129.8, 129.4, 129.3, 127.3, 126.3, 122.4, 118.8, 114.7, 112.2 (C≡N), 65.7 (–CH), 53.1 (–CH), 41.0 (–CH$_2$–) ppm; HRMS: calculated for $C_{49}H_{32}N_8O_4 + NH_4^+$ 814.2890, found 814.2894.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-nitrophenyl)-1-phenylpyrrolo-[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11g**, $C_{47}H_{32}N_8O_8$)
Dark-orange crystalline solid; yield 215 mg (quant.); m.p.: 208–210 °C; $R_f = 0.5$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{v} = 3,041$ (arom. C–H), 1,720 (C=O), 1,595 (C=N), 1,546, 1,512, 1,500, 1,381, 1,193, 850, 750, 690 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 8.33$–8.20 (q, $J = 9.0$ Hz, 8H), 7.67 (d, $J = 9.0$ Hz, 4H), 7.41 (t, $J = 7.5$ Hz, 4H), 7.27–7.20 (m, 8H), 7.09 (t, $J = 7.3$ Hz, 2H), 5.47 (d, $J = 11.2$ Hz, 2H), 5.08 (d, $J = 11.2$ Hz, 2H), 4.03 (s, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.9$ (C=O), 170.5 (C=O), 147.7 (C=N), 143.3, 141.4, 140.2, 136.5, 129.8, 129.7, 129.4, 127.5, 126.3, 123.9, 122.6, 114.8, 65.7 (–CH), 53.0 (–CH), 45.7(–CH$_2$–) ppm; MALDI-MS (pos. mode, DCTB): *m*/*z* (%) = 836 (100) [M]$^+$, 837 (70) [M + H]$^+$; HRMS: calculated for $C_{47}H_{32}N_8O_8$ 836.2343, found 836.2338.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-methoxyphenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]*
(**11h**, $C_{49}H_{38}N_6O_6$)
Brown crystalline solid; yield 215 mg (quant.); m.p.: 169–171 °C; $R_f = 0.37$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{v} = 3,057$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,512, 1,498, 1,379, 1,253, 1,176, 835, 750, 692 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 8.05$ (d, $J = 8.8$ Hz, 4H), 7.61 (d, $J = 7.7$ Hz, 4H), 7.36 (t, $J = 7.4$ Hz, 4H), 7.28–6.70 (m, 14H), 5.20 (d, $J = 10.9$ Hz, 2H), 4.93 (d, $J = 10.9$ Hz, 2H), 4.02 (s, 2H), 3.86 (s, 6H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 171.9$ (C=O), 170.9 (C=O), 160.8 (C=N), 145.0, 142.9, 141.2, 134.1, 129.7, 129.2, 128.9, 126.4, 123.0, 121.3, 114.4, 114.0, 65.7 (–CH), 55.4 (–O–CH$_3$), 53.7 (–CH), 41.0 (–CH$_2$–) ppm; MALDI-MS (pos. mode, DCTB): *m*/*z* (%) = 806 (100) [M]$^+$, 807 (55) [M + H]$^+$; HRMS: calculated for $C_{49}H_{38}N_6O_6$ 806.2853, found 806.2848.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3a,6a-dihydro-3-[4-(methylthio)phenyl]-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]*
(**11i**, $C_{49}H_{38}N_6O_4S_2$)
Brown crystalline solid; yield 224 mg (quant.); m.p.: 170–172 °C; $R_f = 0.50$ (ethyl acetate–*n*-hexane 1:2); IR (KBr):

$\bar{\nu} = 3,036$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,510, 1,492, 1,379, 1,188, 821, 750, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$ (d, $J = 8.3$ Hz, 4H), 7.62 (d, $J = 8.1$ Hz, 4H), 7.36 (t, $J = 7.6$ Hz, 4H), 7.30–7.10 (m, 12H), 7.03 (t, $J = 7.2$ Hz, 2H), 5.22 (d, $J = 10.9$ Hz, 2H), 4.91 (d, $J = 10.9$ Hz, 2H), 3.97 (s, 2H), 2.50 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.7$ (C=O), 170.8 (C=O), 144.6 (C=N), 142.6, 141.2, 140.8, 129.7, 129.5, 129.2, 127.5, 126.9, 126.4, 125.9, 121.5, 114.5, 65.6 (–CH), 53.5 (–CH), 41.0 (–CH_2–), 15.3 (–S–CH_3) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 838 (100) $[M]^+$, 839 (56) $[M + H]^+$; HRMS: calculated for $C_{49}H_{38}N_6O_4S_2$ 838.2396, found 838.2397.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Methylenebis(4,1-phenylene)]bis[3a,6a-dihydro-1-phenyl-3-[4-(trifluoromethyl)phenyl]pyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**11j**, $C_{49}H_{32}F_6N_6O_4$)

Bright-yellow crystalline solid; yield 223 mg (quant.); m.p.: 185–187 °C; $R_f = 0.45$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,059$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,550, 1,517, 1,498, 1,383, 1,166, 1,124, 844, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): $\delta = 8.16$ (d, $J = 8.1$ Hz, 4H), 7.65–7.59 (dd, $J = 8.3$, 7.9 Hz, 8H), 7.33 (t, $J = 7.5$ Hz, 4H), 7.18 (dd, $J = 8.6$, 4.2 Hz, 8H), 6.99 (t, $J = 7.3$ Hz, 2H), 5.40 (d, $J = 11.1$ Hz, 2H), 5.06 (d, $J = 11.1$ Hz, 2H), 3.98 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): $\delta = 176.8$ (C=O), 176.0 (C=O), 149.0 (C=N), 146.8, 146.0, 139.0, 134.6, 134.2, 134.0, 132.0, 131.5, 130.2, 129.8, 126.4, 119.5, 119.3, 71.0 (–CH), 58.5, (–CH), 50.8 (–CH_2–) ppm; HRMS: calculated for $C_{49}H_{32}F_6N_6O_4 + NH_4^+$ 900.22733, found 900.2736.

(3aR,6aR*,3a′S*,6a′S*)-4,4′-[Methylenebis[(4,1-phenylene)(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo-[3,4-c]pyrazole-5,3(1H)-diyl)]]bis[phenyl acetate]* (**11k**, $C_{51}H_{38}N_6O_8$)

Light-yellow crystalline solid; yield 203 mg (95%); m.p.: 190–192 °C; $R_f = 0.75$ (ethyl acetate); IR (KBr): $\bar{\nu} = 3,061$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,510, 1,498, 1,371, 1,199, 1,166, 848, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$ (d, $J = 8.4$ Hz, 4H), 7.62 (d, $J = 7.9$ Hz, 4H), 7.35 (t, $J = 7.3$ Hz, 4H), 7.23–7.10 (m, 12H), 7.05 (t, $J = 7.0$ Hz, 2H), 5.25 (d, $J = 11.0$ Hz, 2H), 4.90 (d, $J = 10.9$ Hz, 2H), 4.00 (s, 2H), 2.34 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.7$ (C=O), 170.8 (C=O), 169.3 (C=O), 151.5 (C=N), 144.5, 142.0, 141.3, 129.7, 129.5, 129.2, 128.4, 128.2, 126.4, 121.8, 121.6, 114.5, 65.8 (–CH), 53.5 (–CH), 41.0 (–CH_2–), 21.2 (–CH_3) ppm; HRMS: calculated for $C_{51}H_{38}N_6O_8 + NH_4^+$ 880.3095, found 880.3094.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis(3a,6a-dihydro-1,3-diphenylpyrrolo[3,4-c]-pyrazole-4,6(1H,5H)-dione)* (**12a**, $C_{46}H_{32}N_6O_5$)

Yellow–green crystalline solid; yield 177 mg (95%); m.p.: 178–180 °C (dec.); $R_f = 0.47$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,061$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,500, 1,383, 1,244, 1,193, 754, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.89$ (d, $J = 7.9$ Hz, 4H), 7.42 (d, $J = 8.2$ Hz, 4H), 7.30–7.05 (m, 14H), 6.88 (d, $J = 8.0$ Hz, 4H), 6.78 (t, $J = 7.0$ Hz, 2H), 5.22 (d, $J = 10.8$ Hz, 2H), 4.98 (d, $J = 10.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.1$ (C=O), 172.1 (C=O), 156.7 (C=N), 145.0, 144.5, 131.0, 129.7, 129.5, 129.4, 128.9, 127.8, 127.5, 121.2, 119.6, 114.4, 66.3 (–CH), 54.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 748 (100) $[M]^+$, 749 (50) $[M + H]^+$; HRMS: calculated for $C_{46}H_{32}N_6O_5$ 748.2434, found 748.2430.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3-(4-chlorophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**12b**, $C_{46}H_{30}Cl_2N_6O_5$)

Olive-green crystalline solid; yield 206 mg (quant.); m.p.: 167–169 °C (dec.); $R_f = 0.56$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,061$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,500, 1,381, 1,242, 1,193, 831, 750, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.04$ (d, $J = 8.1$ Hz, 4H), 7.54 (t, $J = 8.6$ Hz, 8H), 7.35 (d, $J = 7.9$ Hz, 8H), 7.14 (d, $J = 8.3$ Hz, 4H), 6.96 (t, $J = 7.0$ Hz, 2H), 5.55 (d, $J = 10.9$ Hz, 2H), 5.36 (d, $J = 10.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.0$ (C=O), 172.1 (C=O), 156.7 (C=N), 144.7, 143.4, 134.3, 129.9, 129.5, 129.4, 129.0, 127.8, 121.3, 119.6, 114.5, 66.4 (–CH), 54.4 (–CH) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 816 (100) $[M]^+$, 818 (70) $[M + 2]^+$, 819 (40) $[M + 3]^+$; HRMS: calculated for $C_{46}H_{30}Cl_2N_6O_5$ 816.1655, found 816.1649.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3-(4-bromophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**12c**, $C_{46}H_{30}Br_2N_6O_5$)

Light-brown crystalline solid; yield 226 mg (quant.); m.p.: 174–176 °C (dec.); $R_f = 0.63$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,045$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,500, 1,381, 1,244, 1,193, 829, 750, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 8.4$ Hz, 4H), 7.68 (d, $J = 8.4$ Hz, 4H), 7.52 (d, $J = 8.3$ Hz, 4H), 7.31 (t, $J = 8.1$ Hz, 8H), 7.10 (d, $J = 8.7$ Hz, 4H), 6.92 (t, $J = 7.3$ Hz, 2H), 5.55 (d, $J = 11.0$ Hz, 2H), 5.35 (d, $J = 10.9$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.1$ (C=O), 172.1 (C=O), 156.7 (C=N), 145.0, 143.5, 132.1, 130.5, 129.7, 129.5, 129.4, 127.8, 123.5, 121.5, 119.6, 114.5, 66.4 (–CH), 54.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): _m/z_ (%) = 904 (50) $[M]^+$, 906 (100) $[M + 2]^+$, 907 (50) $[M + 3]^+$, 908 (50) $[M + 4]^+$; HRMS: calculated for $C_{46}H_{30}Br_2N_6O_5$ 904.0644, found 904.0635.

(3aR*,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-methylphenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]
(**12e**, $C_{48}H_{36}N_6O_5$)
Bright-yellow powder; yield 188 mg (97%); m.p.: 173–175 °C (dec.); $R_f = 0.56$ (ethyl acetate–_n_-hexane 1:2); IR (KBr): $\bar{\nu} = 3,066$ (arom. C–H), 2,918 (aliph. C–H), 1,720 (C=O), 1,597 (C=N), 1,500, 1,381, 1,244, 1,194, 819, 750, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.90$ (d, $J = 7.8$ Hz, 4H), 7.50 (d, $J = 8.0$ Hz, 4H), 7.40–7.20 (m, 12H), 7.14 (d, $J = 8.5$ Hz, 4H), 6.91 (t, $J = 7.1$ Hz, 2H), 5.50 (d, $J = 10.8$ Hz, 2H), 5.34 (d, $J = 10.8$ Hz, 2H), 2.42 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.2$ (C=O), 172.1 (C=O), 156.7 (C=N), 145.2, 144.6, 139.5, 129.5, 129.5, 129.4, 128.3, 127.9, 127.5, 121.0, 119.6, 114.4, 66.3 (–CH), 54.6 (–CH), 21.4 ($-CH_3$) ppm; MALDI-MS (pos. mode, DCTB): _m/z_ (%) = 776 (100) $[M]^+$, 777 (55) $[M + H]^+$; HRMS: calculated for $C_{48}H_{36}N_6O_5$ 776.2747, found 776.2746.

(3aR*,6aR*,3a′S*,6a′S*)-4,4′-[Oxybis[(4,1-phenylene)(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo[3,4-c]pyrazole-5,3(1H)-diyl)]]bis[benzonitrile]
(**12f**, $C_{48}H_{30}N_8O_5$)
Bright-yellow crystalline solid; yield 190 mg (95%); m.p.: 288–290 °C (dec.); $R_f = 0.25$ (ethyl acetate–_n_-hexane 1:2); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 2,225 (C≡N), 1,722 (C=O), 1,599 (C=N), 1,500, 1,383, 1,242, 1,193, 839, 750, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.11$ (d, $J = 8.4$ Hz, 4H), 7.61 (d, $J = 8.3$ Hz, 4H), 7.52 (d, $J = 7.9$ Hz, 4H), 7.40 (d, $J = 12.8$ Hz, 2H), 7.25 (t, $J = 7.5$ Hz, 2H), 7.20 (d, $J = 8.8$ Hz, 4H), 7.01 (d, $J = 8.9$ Hz, 4H), 6.90 (t, $J = 7.1$ Hz, 2H), 5.45 (d, $J = 11.1$ Hz, 2H), 5.10 (d, $J = 11.1$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.6$ (C=O), 171.9 (C=O), 156.7 (C=N), 144.1, 142.4, 135.5, 132.6, 129.4, 129.4, 129.2, 127.8, 121.7, 119.5, 119.1, 114.7, 111.4 (C≡N), 66.4 (–CH), 53.9 (–CH) ppm; MALDI-MS (pos. mode, DCTB): _m/z_ (%) = 798 (90) $[M]^+$, 799 (50) $[M + H]^+$; HRMS: calculated for $C_{48}H_{30}N_8O_5$ 798.2339, found 798.2334.

(3aR*,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-nitrophenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione] (**12g**, $C_{46}H_{30}N_8O_9$)
Dark-orange crystalline solid; yield 209.5 mg (quant.); m.p.: 208–210 °C (dec.); $R_f = 0.29$ (ethyl acetate–_n_-hexane 1:2); IR (KBr): $\bar{\nu} = 3,109, 3,057$ (arom. C–H), 1,720 (C=O), 1,595 (C=N), 1,546, 1,498, 1,383, 1,340, 1,242, 1,193, 835, 750, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.32$ (d, $J = 8.9$ Hz, 4H), 8.22 (d, $J = 8.9$ Hz, 4H), 7.58 (d, $J = 7.9$ Hz, 4H), 7.40–7.30 (q, $J = 7.50$ Hz, 8H), 7.14 (d, $J = 8.8$ Hz, 4H), 7.00 (t, $J = 7.2$ Hz, 2H), 5.68 (d, $J = 11.1$ Hz, 2H), 5.42 (d, $J = 11.1$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.7$ (C=O), 172.0 (C=O), 156.7 (C=N), 147.5, 143.9, 142.3, 137.5, 129.6, 129.5, 128.1, 127.8, 124.2, 121.9, 119.5, 114.8, 66.5 (–CH), 54.0 (–CH) ppm; MALDI-MS (pos. mode, DCTB): _m/z_ (%) = 838 (100) $[M]^+$, 839 (55) $[M + H]^+$; HRMS: calculated for $C_{46}H_{30}N_8O_9$ 838.2136, found 838.2133.

(3aR*,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3a,6a-dihydro-3-(4-methoxyphenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]
(**12h**, $C_{48}H_{36}N_6O_7$)
Light-orange–brown crystalline solid; yield 202 mg (quant.); m.p.: 164–166 °C (dec.); $R_f = 0.60$ (ethyl acetate–_n_-hexane 1:3); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 1,720 (C=O), 1,597 (C=N), 1,498, 1,381, 1,247, 1,176, 833, 750, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.02$ (d, $J = 8.7$ Hz, 4H), 7.58 (t, $J = 7.9$ Hz, 4H), 7.30 (t, $J = 7.9$ Hz, 4H), 7.25–6.62 (m, 14H), 5.22 (d, $J = 10.8$ Hz, 2H), 4.96 (d, $J = 10.8$ Hz, 2H), 3.83 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.1$ (C=O), 171.1 (C=O), 161.0 (C=N), 156.9, 145.1, 143.1, 129.4, 129.0, 128.7, 128.2, 123.1, 121.6, 119.7, 114.6, 114.2, 65.8 (–CH), 55.6 ($O-CH_3$), 53.8 (–CH) ppm. Anal Calcd for $C_{48}H_{36}N_6O_7$. C, 71.28; H, 4.49; N, 10.39; found C, 70.70; H, 4.69; N, 10.43.

(3aR*,6aR*,3a′S*,6a′S*)-5,5′-[Oxybis(4,1-phenylene)]bis[3a,6a-dihydro-1-phenyl-3-[4-(trifluoromethyl)phenyl]pyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]
(**12j**, $C_{48}H_{30}F_6N_6O_5$)
Bright-yellow crystalline solid; yield 213 mg (96%); m.p.: 184–186 °C (dec.); $R_f = 0.62$ (ethyl acetate–_n_-hexane 1:3); IR (KBr): $\bar{\nu} = 3,059$ (arom. C–H), 1,724 (C=O), 1,599 (C=N), 1,500, 1,384, 1,244, 750, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.20$ (d, $J = 8.2$ Hz, 4H), 7.69–7.62 (dd, $J = 14.9$, 8.4 Hz, 8H), 7.38 (t, $J = 7.6$ Hz, 4H), 7.27–7.25 (m, 4H), 7.09–7.02 (m, 6H), 5.40 (d, $J = 11.1$ Hz, 2H), 5.07 (d, $J = 11.1$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.5$ (C=O), 170.8 (C=O), 157.0 (C=N), 144.0, 141.3, 133.8, 129.5, 128.1, 128.0, 127.4, 126.6, 125.8, 125.7, 122.4, 119.7, 114.8, 65.8 (–CH), 53.4 (–CH) ppm. Anal Calcd for $C_{48}H_{30}F_6N_6O_5$. C, 65.16; H, 3.42; N, 9.50; found C, 65.30; H, 3.73; N, 9.63.

(3aR,6aR*,3a′S*,6a′S*)-4,4′-[Oxybis[(4,1-phenylene)(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo-[3,4-c]pyrazole-5,3(1H)-diyl)]]bis[phenyl acetate]*
(**12k**, $C_{50}H_{36}N_6O_9$)
Brown crystalline solid; yield 220 mg (quant.); m.p.: 190–192 °C (dec.); $R_f = 0.25$ (ethyl acetate–*n*-hexane 1:3); IR (KBr): $\bar{\nu} = 3{,}066$ (arom. C–H), 1,720 (C=O), 1,599 (C=N), 1,500, 1,371, 1,197, 750, 690 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 8.10$ (d, $J = 8.7$ Hz, 4H), 7.60 (d, $J = 8.7$ Hz, 4H), 7.38 (t, $J = 7.3$ Hz, 4H), 7.23–6.85 (m, 14H), 5.26 (d, $J = 11.1$ Hz, 2H), 4.95 (d, $J = 10.8$ Hz, 2H), 2.30 (s, 6H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 171.9$ (C=O), 171.0 (C=O), 169.5 (C=O), 151.8 (C=N), 144.6, 142.1, 129.5, 128.6, 128.3, 128.2, 126.7, 122.1, 121.9, 119.7, 114.7, 65.9 (–CH), 53.7 (–CH), 21.4 (COCH$_3$) ppm. Anal Calcd for $C_{50}H_{36}N_6O_9$. C, 69.44; H, 4.20; N, 9.72; found C, 69.39; H, 4.48; N, 9.77.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis(3a,6a-dihydro-1,3-diphenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione)* (**13a**, $C_{40}H_{28}N_6O_4$)
Light-yellow powder; yield 158 mg (96%); m.p.: 354–356 °C (dec.); $R_f = 0.62$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}057$ (arom. C–H), 1,722 (C=O), 1,597 (C=N), 1,517, 1,498, 1,371, 1,290, 1,195, 758, 684 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.02$ (d, $J = 7.4$ Hz, 4H), 7.52 (d, $J = 8.0$ Hz, 6H), 7.49–7.38 (m, 8H), 7.33 (t, $J = 7.7$ Hz, 4H), 6.94 (t, $J = 7.0$ Hz, 2H), 5.52 (d, $J = 10.9$ Hz, 2H), 5.35 (d, $J = 10.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 172.9$ (C=O), 171.9 (C=O), 144.9 (C=N), 144.2, 132.4, 130.9, 129.7, 129.4, 128.8, 128.1, 127.9, 127.5,121.1, 114.4, 66.3 (–CH), 54.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): m/z (%) = 656 (100) [M]$^+$, 657 (45) [M + H]$^+$; HRMS: calculated for $C_{40}H_{28}N_6O_4$ 656.2172, found 656.2162.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3-(4-chlorophenyl)-3a,6a-dihydro-1-phenylpyrrolo-[3,4-c]pyrazole-4,6(1H,5H)-dione]*
(**13b**, $C_{40}H_{26}Cl_2N_6O_4$)
Light-green crystalline solid; yield 177 mg (98%); m.p.: 205–207 °C (dec.); $R_f = 0.63$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}064$ (arom. C–H), 1,722 (C=O), 1,597 (C=N), 1,514, 1,492, 1,367, 1,292, 1,190, 831, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.04$ (d, $J = 6.5$ Hz, 4H), 7.84–7.13 (m, 16H), 6.97 (s, 2H), 5.57 (d, $J = 10.1$ Hz, 2H), 5.38 (d, $J = 10.2$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 172.9$ (C=O), 171.9 (C=O), 144.7 (C=N), 143.3, 134.3, 132.5, 129.9, 129.5, 129.1, 129.0, 128.2, 126.4, 121.3, 114.4, 66.4 (–CH), 54.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): m/z (%) = 724 (100) [M]$^+$, 726 (80) [M + 2]$^+$, 727 (35) [M + 3]$^+$; HRMS: calculated for $C_{40}H_{26}Cl_2N_6O_4$ 724.1393, found 724.1388.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3-(4-bromophenyl)-3a,6a-dihydro-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**13c**, $C_{40}H_{26}Br_2N_6O_4$)
Light-brown crystalline solid; yield 182 mg (90%); m.p.: 263–265 °C (dec.); $R_f = 0.50$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}043$ (arom. C–H), 1,722 (C=O), 1,599 (C=N), 1,512, 1,492, 1,365, 1,294, 1,176, 827, 750, 690 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 7.85$ (d, $J = 8.5$ Hz, 4H), 7.54–7.39 (m, 10H), 7.28–7.2.0 (m, 4H), 6.93 (t, $J = 7.2$ Hz, 4H), 5.26 (d, $J = 11.1$ Hz, 2H), 4.94 (d, $J = 11.0$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 172.9$ (C=O), 171.9 (C=O), 144.3 (C=N), 142.0, 131.8, 131.5, 129.3, 129.2, 128.5, 126.8, 123.7, 121.8, 114.5, 65.8 (–CH), 53.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): m/z (%) = 812 (50) [M]$^+$, 814 (100) [M + 2]$^+$, 816 (50) [M + 4]$^+$; HRMS: calculated for $C_{40}H_{26}Br_2N_6O_4$ 812.0382, found 812.0379.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3a,6a-dihydro-3-(4-methylphenyl)-1-phenylpyrrolo[3,4-c]-pyrazole-4,6(1H,5H)-dione]* (**13e**, $C_{42}H_{32}N_6O_4$)
Creamy-white powder; yield 165 mg (96%); m.p.: 338–340 °C (dec.); $R_f = 0.69$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}066$ (arom. C–H), 2941 (aliph. C–H), 1,724 (C=O), 1,595 (C=N), 1,514, 1,498, 1,371, 1,288, 1,195, 819, 754, 692 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 7.86$ (d, $J = 8.1$ Hz, 4H), 7.49 (d, $J = 7.9$ Hz, 4H), 7.42 (s, 4H), 7.24 (t, $J = 7.5$ Hz, 4H), 7.15 (d, $J = 8.1$ Hz, 4H), 6.88 (t, $J = 7.2$ Hz, 2H), 5.30 (d, $J = 10.9$ Hz, 2H), 5.06 (d, $J = 10.9$ Hz, 2H), 2.30 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 173.0$ (C=O), 171.9 (C=O), 145.1 (C=N), 144.5, 139.5, 132.5, 129.6, 129.5, 129.4, 128.2, 127.5, 121.0, 114.3, 66.3 (–CH), 54.6 (–CH), 21.4 (–CH$_3$) ppm; MALDI-MS (pos. mode, DCTB): m/z (%) = 684 (100) [M]$^+$, 685 (50) [M + H]$^+$; HRMS: calculated for $C_{42}H_{32}N_6O_4$ 684.2485, found 684.2478.

(3aR,6aR*,3a′S*,6a′S*)-4,4′-[(4,1-Phenylene)bis(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo-[3,4-c]pyrazole-5,3(1H)-diyl)]bis[benzonitrile]*
(**13f**, $C_{42}H_{26}N_8O_4$)
Yellow powder; yield 168 mg (95%); m.p.: 361–363 °C (dec.); $R_f = 0.37$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3{,}063$ (arom. C–H), 2,225 (C≡N), 1,724 (C=O), 1,597 (C=N), 1,514, 1,498, 1,367, 1,255, 1,190, 837, 754, 690 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.02$ (d, $J = 8.3$ Hz, 4H), 7.77 (d, $J = 8.2$ Hz, 4H), 7.40 (d, $J = 7.8$ Hz, 4H), 7.23 (t, $J = 7.4$ Hz, 4H), 6.86 (t, $J = 7.1$ Hz, 2H), 5.51 (d, $J = 11.4$ Hz, 2H), 5.22 (d, $J = 10.9$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 172.9$ (C=O), 171.9 (C=O), 144.7 (C=N), 143.3, 134.3, 132.5,

129.9, 129.5, 129.1, 129.0, 128.2, 126.4, 121.3, 114.4 (C≡N), 66.4 (–CH), 54.5 (–CH) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 706 (100) [M]$^+$, 707 (50) [M + H]$^+$; HRMS: calculated for $C_{42}H_{26}N_8O_4$ 706.2077, found 706.2078.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3a,6a-dihydro-3-(4-nitrophenyl)-1-phenylpyrrolo[3,4-c]pyrazole-4,6(1H,5H)-dione]* (**13g**, $C_{40}H_{26}N_8O_8$)

Orange powder; yield 185 mg (99%); m.p.: 307–309 °C (dec.); $R_f = 0.43$ (ethyl acetate–*n*-hexane 1:2); IR (KBr): $\bar{\nu} = 3,074$ (arom. C–H), 1,724 (C=O), 1,595 (C=N), 1,515, 1,500, 1,340, 1,292, 1,192, 850, 750, 690 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.29$ (d, $J = 8.0$ Hz, 4H), 8.21 (d, $J = 8.3$ Hz, 4H), 7.56 (d, $J = 7.4$ Hz, 4H), 7.44 (s, 4H), 7.35 (t, $J = 7.6$ Hz, 4H), 7.00 (t, $J = 6.6$ Hz, 2H), 5.70 (d, $J = 10.9$ Hz, 2H), 5.40 (d, $J = 11.0$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 173.0$ (C=O), 171.8 (C=O), 147.8 (C=N), 144.3, 142.2, 137.4, 132.2, 129.6, 128.2, 128.0, 124.2, 122.0, 114.7, 66.3 (–CH), 53.9 (–CH) ppm; MALDI-MS (pos. mode, DCTB): *m/z* (%) = 746 (100) [M]$^+$, 747 (50) [M + H]$^+$; HRMS: calculated for $C_{40}H_{26}N_8O_8$ 746.1874, found 746.1869.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3a,6a-dihydro-3-(4-methoxyphenyl)-1-phenylpyrrolo[3,4-c]-pyrazole-4,6(1H,5H)-dione]* (**13h**, $C_{42}H_{32}N_6O_6$)

Light-orange–brown crystalline solid; yield 165 mg (92%); m.p.: 173–175 °C (dec.); $R_f = 0.25$ (ethyl acetate–*n*-hexane 1:3); IR (KBr): $\bar{\nu} = 3,057$ (arom. C–H), 1,724 (C=O), 1,597 (C=N), 1,514, 1,498, 1,367, 1,176, 835, 752, 692 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 7.95$ (d, $J = 8.2$ Hz, 4H), 7.67–6.80 (m, 18H), 5.44 (d, $J = 11.5$ Hz, 2H), 5.32 (d, $J = 10.8$ Hz, 2H), 3.79 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 172.6$ (C=O), 172.1 (C=O), 160.9 (C=N), 145.5, 144.6, 129.7, 129.4, 128.7, 128.5, 123.6, 121.0, 119.5, 114.8, 114.6, 114.4, 66.5 (–CH), 56.0 (OCH_3), 55.1 (–CH) ppm. Anal Calcd for $C_{42}H_{32}N_6O_6$. C, 70.38; H, 4.50; N, 11.73; found C, 70.11; H, 4.75; N, 11.49.

(3aR,6aR*,3a′S*,6a′S*)-5,5′-(1,4-Phenylene)bis[3a,6a-dihydro-1-phenyl-3-[4-(trifluoromethyl)phenyl]pyrrolo-[3,4-c]pyrazole-4,6(1H,5H)-dione]*
(**13j**, $C_{42}H_{26}F_6N_6O_4$)

Bright-yellow crystalline solid; yield 181 mg (91%); m.p.: 293–295 °C (dec.); $R_f = 0.62$ (ethyl acetate–*n*-hexane 1:3); IR (KBr): $\bar{\nu} = 3,063$ (arom. C–H), 1,724 (C=O), 1,599 (C=N), 1,514, 1,498, 1,327, 1,170, 840, 750, 690 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.20$ (d, $J = 8.2$ Hz, 4H), 7.84 (d, $J = 8.2$ Hz, 4H), 7.54 (d, $J = 8.2$ Hz, 4H), 7.45 (s, 4H), 7.37 (t, $J = 8.2$ Hz, 4H), 6.99 (t, $J = 8.2$ Hz, 2H), 5.63 (d, $J = 11.4$ Hz, 2H), 5.43 (d, $J = 11.1$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 173.0$ (C=O), 172.2 (C=O), 144.5 (C=N), 143.1, 135.2, 132.7, 129.8, 128.5, 128.1, 126.7, 126.1, 121.8, 114.7, 66.6 (–CH), 54.5 (–CH) ppm. Anal Calcd for $C_{42}H_{26}F_6N_6O_4$. C, 63.64; H, 3.31; N, 10.60; found C, 63.17; H, 3.74; N, 10.67.

(3aR,6aR*,3a′S*,6a′S*)-4,4′-[(4,1-Phenylene)bis(3a,4,6,6a-tetrahydro-4,6-dioxo-1-phenylpyrrolo-[3,4-c]pyrazole-5,3(1H)-diyl)]bis[phenyl acetate]*
(**13k**, $C_{44}H_{32}N_6O_8$)

Light-brown crystalline solid; yield 195 mg (quant.); m.p.: 216–218 °C (dec.); $R_f = 0.25$ (ethyl acetate–*n*-hexane 1:3); IR (KBr): $\bar{\nu} = 3,066$ (arom. C–H), 1,722 (C=O), 1,599 (C=N), 1,514, 1,498, 1,369, 1,199, 752, 692 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.05$ (d, $J = 8.7$ Hz, 4H), 7.52 (d, $J = 8.4$ Hz, 4H), 7.45 (s, 6H), 7.35 (t, $J = 7.3$ Hz, 4H), 7.26 (d, $J = 8.7$ Hz, 4H), 6.95 (t, $J = 7.3$ Hz, 2H), 5.54 (d, $J = 11.1$ Hz, 2H), 5.37 (d, $J = 11.1$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 173.3$ (C=O), 172.3 (C=O), 151.8 (C=N), 145.1, 143.9, 129.7, 128.9, 128.5, 122.7, 121.4, 114.5, 66.4 (–CH), 54.7 (–CH), 21.5 ($COCH_3$) ppm. Anal Calcd for $C_{44}H_{32}N_6O_8$. C, 68.39; H, 4.17; N, 10.88; found C, 68.23; H, 4.61; N, 10.75.

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