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(4+2) Dimerization of imides of arylmaleic acids in the presence of the 3,5-dimethyl-1*H*-pyrazole and 2,6-lutidine

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ABSTRACT

Imides of arylmaleic acids in the presence of 3,5-dimethyl-1*H*-pyrazole underwent (4+2) dimerization under heating in chlorobenzene within 24 h to afford 1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[*e*]pyrrolo[3,4-*g*]isoindole-1,3,4,6-tetraones in good yields. It was established that during the heating of imides of arylmaleic acid in 2,6-lutidine at 100 °C the (4+2) dimerization products containing a lutidine fragment are obtained.

1. Introduction

The Diels–Alder reaction is one of the most important transformations in organic chemistry for the construction of six-membered ring systems, and many methods of catalysis of the Diels–Alder reaction have been studied.[1–3] Arylmaleic anhydrides are often desirable as components in Diels–Alder reactions, both for synthetic purposes and as a convenient means of studying the influence of aryl substituents of varying electronic requirements on the rate of formation and stereochemistry of the adducts.[4–10] A particular point of interest is the finding that phenylmaleic anhydride can serve as both diene and dienophile.[11] The imides of arylmaleic acids have been less studied as substrates in (4+2) cycloaddition reactions. Earlier it was established that the (4+2) dimerization of *N*-methyl-3-(*p*-tolyl)imide maleic acid in hot 2,6-lutidine solution leads to the formation of corresponding *endo*-adduct. In this reaction the imide of arylmaleic acid can serve as the diene as well as the dienophile.[12] Irradiation of a solution of *N*-methyl-3-phenylmaleimide leads to the formation of three (2+2) dimers with high yield and only one (4+2) dimer (*exo*-adduct). Formation of the (4+2) dimer may involve an intermediate formed through a photochemically forbidden (4s+2s) process. The yield of the (4+2) dimer increased with an increase in the solvent polarity.[13] In this report we demonstrate the utility of 3,5-dimethyl-1*H*-pyrazole for realization of the (4+2) dimerization of imides of arylmaleic acids as a one-pot synthesis of polycyclic compounds with 1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[*e*]pyrrolo[3,4-*g*]isoindole skeleton. It should be mentioned that the compound with 1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[*e*]pyrrolo[3,4-*g*]isoindole skeleton also was prepared by the reaction of dimethyl 1-(*p*-methoxyphenyl)aziridine-2,3(*trans*)-dicarboxylate with naphthalene.[14]

2. Results and discussion

We have revealed that the reaction of imide **1a** with 3,5-dimethyl-1*H*-pyrazole in various solvents results in the formation of (4+2) dimerization products *exo*-**2a** and *endo*-**3a** with the Michael addition product **4**. The results of these studies are shown in Table 1. Application of 3,5-dimethyl-1*H*-pyrazole for the realization of (4+2) dimerization of imides of arylmaleic acids was initially studied by mixing **1a** (1 mmol) with 3,5-dimethyl-1*H*-pyrazole (1 mmol) in chloroform. The reaction proceeded at room temperature and also at 63 °C for 24 h. At room temperature in chloroform the conversion of imide **1a** is equal to 5% only (the ratio of the products **2a**/**3a**/**4** is 0:1:2, respectively), whereas at 63 °C the conversion in products is equal to 25%, the ratio of the products **2a**, **3a** and **4** was 0.12:1:2, respectively (entries 1 and 2). When the reaction performed in the benzene at 81 °C the conversion is equal to

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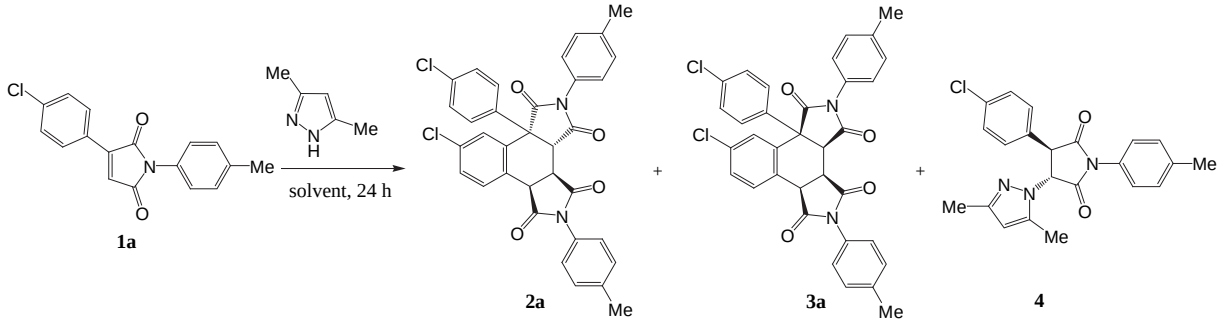
42%, the ratio of the products **2a**, **3a** and **4** was 0.14:1:1, respectively. In this case some decreasing of the amount of the Michael addition product **4** was observed (entry 3). The same reaction in dichloroethane or toluene leads to an increase of the conversion in the products, and to an increase in (4+2) dimerization products in the reaction mixture (entries 4 and 5). The interaction of **1a** (1 mmol) with 3,5-dimethyl-1*H*-pyrazole (1 mmol) in chlorobenzene at 132 °C for 24 h results in the products **2a**, **3a** and **4** in a 9:1:2 ratio (entry 7). When the reaction was performed with 1.5 equiv of 3,5-dimethyl-1*H*-pyrazole, the conversion in the products is more than 95% (entry 8). In the case of using of 0.5 equiv of 3,5-dimethyl-1*H*-pyrazole the conversion in the products is decreased to 54%, but the ratio of the reaction products is not changed almost (entry 6). In the case of using of xylene as a solvent it was revealed that the increasing amount of pyrazole results not only in an increase of conversion, but to an increase of *exo*-adduct **2a** in the reaction mixture (entries 9–11). For example, in the case of using of 0.5 equiv pyrazole the conversion is equal to 43%, and the ratio of the products **2a**/**3a**/**4** is 0.7:1:0.3, respectively. In the case of using of 1.5 equiv pyrazole the conversion is more than 95%, and the ratio of the products **2a**/**3a**/**4** is 4:1:1, respectively. As it could be seen from the data above, the best selectivity was observed in the reaction in chlorobenzene. In this case the reaction proceeds with the prevalence of the formation of *exo*-adduct **2a**, also the formation of the Michael addition byproduct **4** could be minimized. That is why the chlorobenzene was chosen as a solvent for the reactions of imides **1a**–**m** with 3,5-dimethyl-1*H*-pyrazole. Chlorobenzene and *p*-xylene have almost the same boiling temperatures (132 and 137 °C, respectively), but in chlorobenzene the reaction proceeds more selectivity, probably due to the higher media polarity.

thin layer chromatography on silica afforded the *exo*-**2a**–**m** (33–74%) and *endo*-**3a**,**f**,**h**–**j** (7–8%) adducts. The adducts *endo*-**3b**–**e**,**g**,**k** were not isolated in pure form. The pure *exo*-adducts **2a**–**k** also could be prepared by crystallization from ethanol/chloroform. The adduct *exo*-**2l** was obtained from nitro-substituted imide **1m** with low yield (Table 2, entry 13). Also the corresponding *exo*-adduct **2m** was obtained from *N*-methylimide **2n** with yield 63% (Table 2, entry 14). According to the ^{1}H NMR data the Michael addition byproducts were formed also, but in pure form they were not isolated. The use of 1*H*-pyrazole instead of 3,5-dimethyl-1*H*-pyrazole leads to the decreasing yields of (4+2) dimerization products, because of the formation of intractable byproducts. Isomerization of (*endo*)-**3** into (*exo*)-**2** by heating (*endo*)-**3** in *p*-xylene or chlorobenzene in the presence of pyrazoles did not occur. The formation of products **2** and **3** was not observed in the absence of pyrazole.

The compositions and structures of the products *exo*-**2a**–**m** and *endo*-**3a**,**f**,**h**–**j** were established by elemental and spectral analysis. The structure of compound **2j** was additionally confirmed by X-ray diffraction analysis (Fig. 1).

Earlier in Epstein's work it was observed that *N*-methyl-3-(*p*-tolyl)imide of maleic acid was transformed by the (4+2) dimerization in 2,6-lutidine (100 °C, 45 h), with the formation of the corresponding *endo*-adduct, which structure was confirmed by X-ray diffraction analysis.[12] It was interesting for us to research the reactions of 1,3-diarylimides of maleic acid in 2,6-lutidine. It was established that during the heating of imides **1a**–**c**,**e**–**h**,**m** in 2,6-lutidine at 100 °C for 45 h under an argon atmosphere the *exo*-adducts **2** and also (4+2) dimerization products **5**, containing the lutidine fragment, were obtained. Separation of the reaction mixtures by preparative thin layer chromatography on silica

Table 1
The (4+2) dimerization of imide **1a** in the presence of the 3,5-dimethyl-1*H*-pyrazole



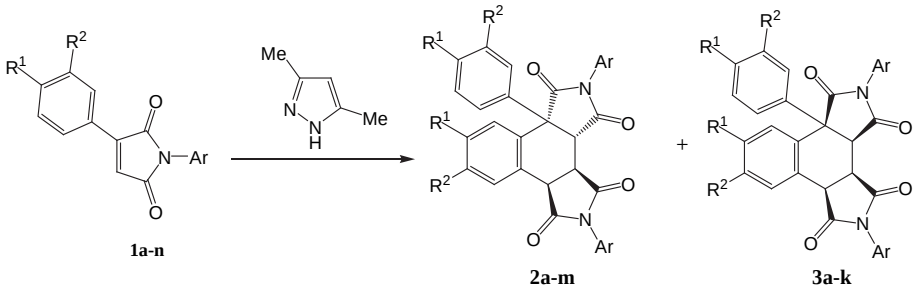
Entry	Pyrazole (equiv)	Solvent	Temperature (°C)	Conversion[a] (%)	Ratio[b] **2a**/**3a**/**4**
1	1.0	Chloroform	63	25	0.12:1:2
2	1.0	Chloroform	rt	5	0:1:2
3	1.0	Benzene	81	42	0.14:1:1
4	1.0	1,2-Dichloroethane	83	56	0.7:1:1.4
5	1.0	Toluene	110	64	1:1:0.5
6	0.5	Chlorobenzene	132	54	9:1:2.1
7	1.0	Chlorobenzene	132	90	9:1:1.8
8	1.5	Chlorobenzene	132	>95	9:1:1.6
9	0.5	*p*-Xylene	137	43	0.7:1:0.3
10	1.0	*p*-Xylene	137	90	1:1:1
11	1.5	*p*-Xylene	137	>95	4:1:1

[a] Conversion determined by ^{1}H NMR analysis.
[b] The ratio of products were determined by ^{1}H NMR analysis.

The heating of imides **1a**–**n** in boiling chlorobenzene in the presence of an equimolar amount of 3,5-dimethyl-1*H*-pyrazole leads to the formation of (4+2) dimerization products *exo*-**2a**–**m** and *endo*-**3a**–**k** with combined yields up to 82% (Table 2, entries 1–11, 13, 14). Separation of the reaction mixtures by preparative

results in the isolation of the adducts **2a**–**c**,**e**–**h**,**m** in 36–57% yields, **5a**–**g** in 13–21% yields (Table 3, entries 1–7), and also a trace of starting imides and undefined products. The *endo*-adducts **3** in the reaction mixture were not observed. The compositions and structures of the products **5a**–**g** were established by elemental

Table 2
The (4+2) dimerization of a variety of imides **1** in the presence of the 3,5-dimethyl-1*H*-pyrazole[a]



1a-n **2a-m** **3a-k**

Entry	R^1	R^2	Ar	Products (yield, %)[b]
1	Cl	H	4-MeC_6H_4 (**1a**)	**2a** (70.2), **3a** (7.7)
2	Cl	H	C_6H_5 (**1b**)	**2b** (72.5), **3b** (4.3)[c]
3	Cl	H	4-ClC_6H_4 (**1c**)	**2c** (73.8), **3c** (5.6)[c]
4	Cl	H	3,5-$Cl_2C_6H_3$ (**1d**)	**2d** (73.0), **3d** (6.1)[c]
5	H	H	4-$EtOC_6H_4$ (**1e**)	**2e** (71.4), **3e** (6.8)[c]
6	H	H	4-FC_6H_4 (**1f**)	**2f** (74.3), **3f** (8.0)
7	H	H	3-$NO_2C_6H_4$ (**1g**)	**2g** (72.2), **3g** (7.1)[c]
8	Me	H	C_6H_5 (**1h**)	**2h** (63.4), **3h** (7.2)
9	Me	H	4-MeC_6H_4 (**1i**)	**2i** (61.2), **3i** (6.7)
10	Me	H	4-ClC_6H_4 (**1j**)	**2j** (71.6), **3j** (8.3)
11	Me	H	3-Cl-4-MeC_6H_3 (**1k**)	**2k** (72.1), **3k** (5.1)[c]
12	NO_2	H	4-ClC_6H_4 (**1l**)	—[d,e,f]
13	H	NO_2	4-ClC_6H_4 (**1m**)	**2l** (33.1)[g,h]
14	Me	H	Me (**2n**)	**2m** (63.0)[h]

[a] The reactions were performed using imide (1 mmol) and 3,5-dimethyl-1*H*-pyrazole (1 mmol) in chlorobenzene (10 mL) at 132 °C for 24 h.
[b] Isolated yield of products.
[c] Spectral yield. The isomer **3** was not isolated as the pure form.
[d] The isomers **2** and **3** were not found in the reaction mixture.
[e] Starting imide **1l** (69.2%) was isolated.
[f] Michael addition byproduct (12.5%) was isolated.
[g] Starting imide **1m** (34.3%) was isolated.
[h] The isomer **3** was not found in the reaction mixture.

and spectral analysis. The structure of compound **5d** was additionally confirmed by X-ray diffraction analysis (Fig. 2). Compound **5** was not observed in the case of heating of imide **1m** in 2,6-lutidine (Table 3, entry 8).

The mechanism for these reactions has not been established yet, although it is believed that the pyrazole, like the lutidine, acts as a base to mediate the formal hydride shift after the first Diels–Alder reaction step, which is required to drive the reaction to the observed dimerization product.[12] It seems that the formation of the adduct **5** proceeds through the oxidation of the first formed product of (4+2) self-condensation and the intermediate, which results from this process

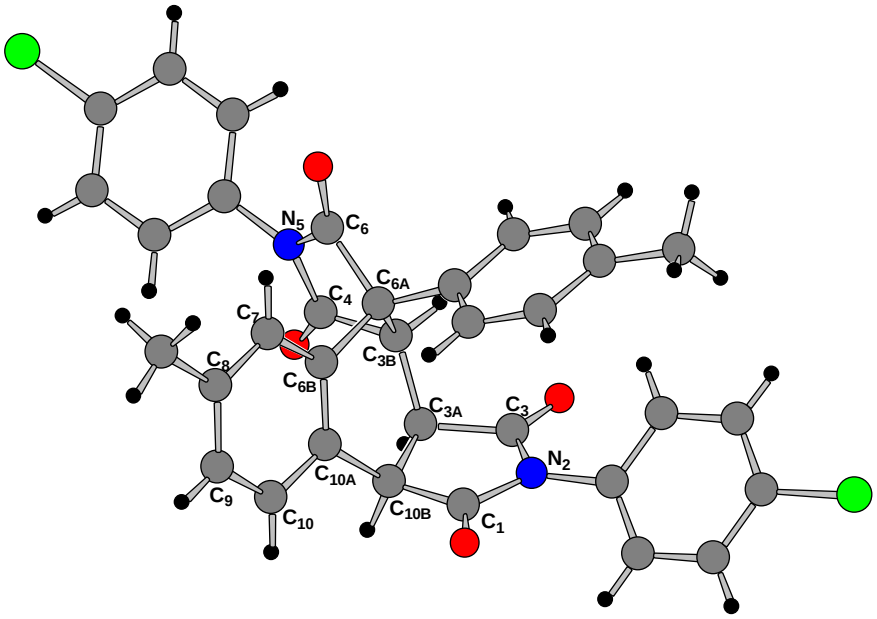
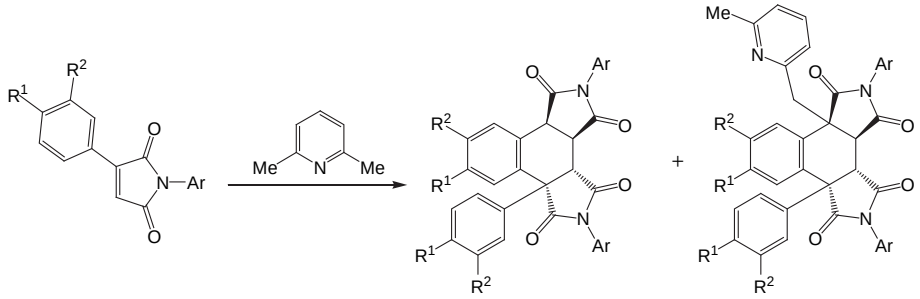


Figure 1. The X-ray crystal structure of compound **2j**.

Table 3
The reaction of imides **1a**–**c**,**e**–**h**,**m** with 2,6-lutidine[a]



1a-c, e-h, m **2a-c, e-h, m** **5a-g**

Entry	R^1	R^2	Ar	Products (yield, %)[b]
1	Cl	H	4-MeC_6H_4 (**1a**)	**2a** (38.7), **5a** (15.3)
2	Cl	H	C_6H_5 (**1b**)	**2b** (41.2), **5b** (12.8)
3	Cl	H	4-ClC_6H_4 (**1c**)	**2c** (36.4), **5c** (11.9)
4	H	H	4-$EtOC_6H_4$ (**1e**)	**2e** (43.3), **5d** (21.0)
5	H	H	4-FC_6H_4 (**1f**)	**2f** (52.3), **5e** (16.7)
6	H	H	3-$NO_2C_6H_4$ (**1g**)	**2g** (46.2), **5f** (14.3)
7	Me	H	C_6H_5 (**1h**)	**2h** (39.0), **5g** (13.1)
8	H	NO_2	4-ClC_6H_4 (**1m**)	**2m** (12.4)[c]

[a] The reactions were performed using imide (0.5 mmol) and 2,6-lutidine (3 mL) at 100 °C for 45 h under an argon atmosphere.
[b] Isolated yield of products.
[c] Compound **5** was not isolated.

reacts with a molecule of 2,6-lutidine giving adduct **5**. Probably the oxidizing reagent is the *N*-oxide, which can be present in 2,6-lutidine. Nevertheless the distillation of 2,6-lutidine before the experiments leads to the insignificant increasing of the yields of compounds **2** and decreasing of the yields of compounds **5**.

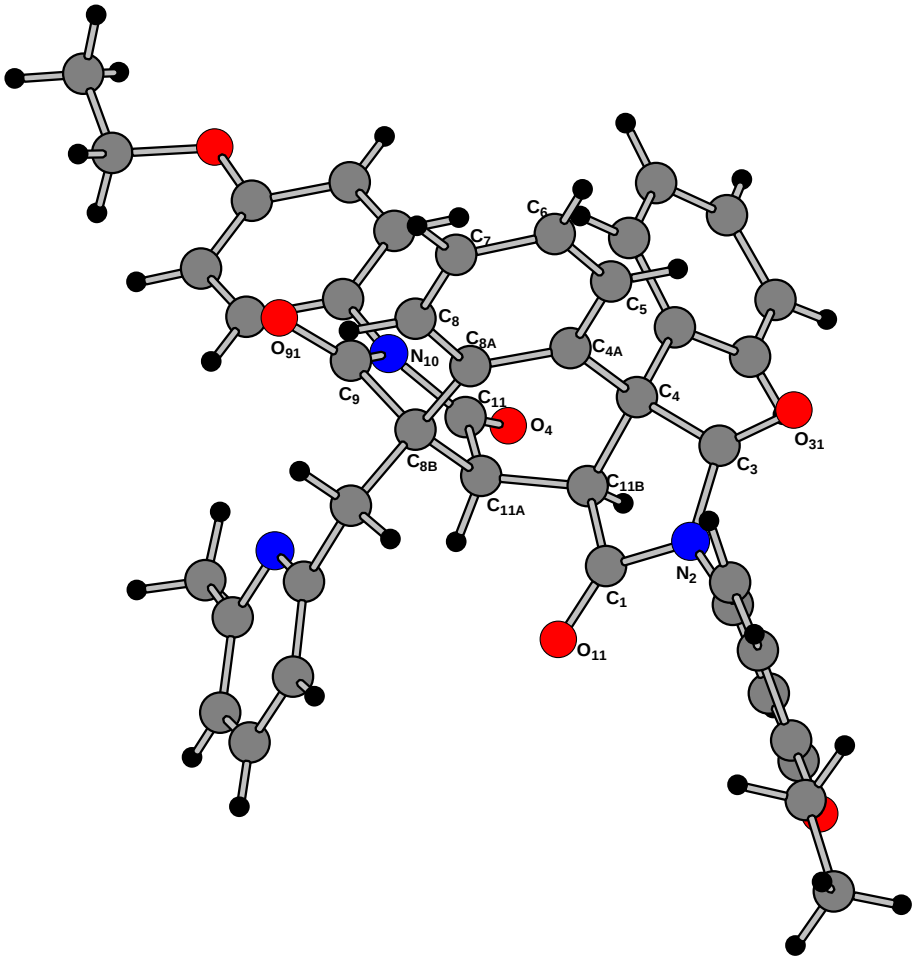


Figure 2. The X-ray crystal structure of compound **5d**.

3. Conclusion

In summary, we have presented novel results, which demonstrate the use of 3,5-dimethyl-1*H*-pyrazole for realization of (4+2) dimerization of imides of arylmaleic acid with formation of 1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[*e*]pyrrolo[3,4-*g*]isoindole-1,3,4,6-tetraones. The best yields of the reaction products and the best selectivity were arrived at using chlorobenzene as solvent. It should be note that the reactions are operationally simple and do not require temperature manipulations or an inert atmosphere. During the carrying out of this reaction in the medium of 2,6-lutidine the polycyclic products, containing a pyridine fragment, could be obtained.

4. Experimental

4.1. General methods

Infrared spectra were obtained for 2% solutions in chloroform on a Carl Zeiss UR-20 spectrometer and data are given in centimetre^{-1}. Melting points were determined on a Boetius instrument and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 as solvent using a Bruker DPX-300 (300 and 75 MHz for ^{1}H and ^{13}C, respectively). Elemental analyses were performed on a Hewlett-Packard 185B CHN analyser. Low-resolution mass spectra were measured using electron impact (EI) at 70 eV on a FinniganMAT 8340 spectrometer. The X-ray diffraction data were performed by means of an Oxford Instruments Xcalibur diffractometer with Mo Kα X-ray radiation. Reactions were monitored by TLC analysis using Silufol UV-254 plates. Thin layer chromatography was performed on silica gel 5–40 mesh eluted with hexane/ethyl acetate mixtures. Imides of arylmaleic acids were synthesized according to known procedures.[15]

4.2. Experimental procedures

*4.2.1. General procedure for the preparation of adducts **2** and **3**.* A mixture of corresponding imide **1** (1 mmol) and 3,5-dimethyl-1*H*-pyrazole (1 mmol) in dry chlorobenzene (10 mL) was stirred under reflux for 24 h. The solvent was evaporated under reduced pressure and the residue was purified by preparative thin layer chromatography eluting with hexane/ethyl acetate (2:1) or crystallized from ethanol/chloroform.

*4.2.2. General procedure for the reaction of imides **1** with 2,6-lutidine.* A mixture of corresponding imide **1** (0.5 mmol) and 2,6-lutidine (3 mL) was stirred at 100 °C for 45 h under an argon atmosphere. 2,6-Lutidine was evaporated under reduced pressure and the residue was purified by preparative thin layer chromatography eluting with hexane/ethyl acetate (2:1).

*4.2.2.1. rac-(3aS,3bR,6aS,10bR)-8-Chloro-6a-(4-chlorophenyl)-2,5-di(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2a**).* Colourless crystals; mp 234–235 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1015, 1095, 1169, 1380, 1456, 1493, 1592, 1717, 3020 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.34 (s, 3H), 2.35 (s, 3H), 4.27 (d, *J*=9.4 Hz, 1H), 4.35 (s, 1H), 4.38 (d, *J*=9.4 Hz, 1H), 6.78 (d, *J*=7.6 Hz, 2H), 6.84 (d, *J*=8.0 Hz, 2H), 7.11 (d, *J*=8.0 Hz, 2H), 7.21 (d, *J*=8.0 Hz, 2H), 7.30–7.35 (m, 3H), 7.43–7.45 (m, 3H), 7.71 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 36.2, 41.2, 50.8, 56.3, 125.9, 127.63 (2C), 127.64 (2C), 128.5 (2C), 129.3 (2C), 129.5 (2C), 129.8 (2C), 130.2 (2C), 130.5, 130.6, 131.2, 131.7, 134.90, 134.96, 136.5, 138.7, 139.6, 174.0, 175.3, 176.1, 176.9. Anal. Calcd for $C_{34}H_{24}Cl_2N_2O_4$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.51; H, 4.11; N, 4.55.

*4.2.2.2. rac-(3aS,3bR,6aS,10bR)-8-Chloro-6a-(4-chlorophenyl)-2,5-diphenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2b**).* Colourless crystals; mp 283–284 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1016, 1094, 1163, 1381, 1493, 1718, 3040 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ=4.28 (d, *J*=8.6 Hz, 1H), 4.64 (d, *J*=8.6 Hz, 1H), 4.71 (s, 1H), 6.82 (d, *J*=8.0 Hz, 2H), 7.12 (d, *J*=8.7 Hz, 2H), 7.21 (d, *J*=8.0 Hz, 2H), 7.38–7.53 (m, 9H), 7.69 (dd, *J*=8.0, 2.2 Hz, 1H), 7.83 (d, *J*=8.7 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ=36.3, 41.0, 50.1, 56.0, 127.36 (2C), 127.43 (2C), 127.9, 129.6 (2C), 129.7 (4C), 129.8, 130.0 (2C), 130.5, 131.3 (2C), 132.6 (2C), 133.90, 134.30, 134.7, 134.8, 138.9, 174.6, 175.9, 177.1, 177.2. Anal. Calcd for $C_{32}H_{20}Cl_2N_2O_4$: C, 67.74; H, 3.55; N, 4.94. Found: C, 67.77; H, 3.58; N, 4.92.

*4.2.2.3. rac-(3aS,3bR,6aS,10bR)-8-Chloro-2,5,6a-tri(4-chlorophenyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2c**).* Colourless crystals; mp 289–291 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1016, 1094, 1163, 1381, 1493, 1718, 3030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.30 (dd, *J*=10.5, 1.5 Hz, 1H), 4.34 (d, *J*=1.5 Hz, 1H), 4.39 (d, *J*=10.5 Hz, 1H), 6.81 (dd, *J*=7.0, 2.0 Hz, 2H), 6.88 (dd, *J*=6.0, 2.1 Hz, 2H), 7.22 (d, *J*=9.0 Hz, 2H), 7.30 (d, *J*=9.4 Hz, 2H), 7.37–7.48 (m, 4H), 7.59 (d, *J*=8.4 Hz, 1H), 7.67 (d, *J*=8.2 Hz, 1H), 7.84 (d, *J*=8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.0, 40.9, 50.3, 55.9, 126.4, 127.3, 127.5 (4C), 128.5 (2C), 128.9 (2C), 129.8, 129.9 (2C), 130.3 (2C), 130.9 (2C), 133.3 (2C), 135.3 (2C), 135.4 (2C), 136.1, 137.6, 138.2, 173.3, 174.4, 175.4, 175.9. Anal. Calcd for $C_{34}H_{18}Cl_4N_2O_4$: C, 60.40; H, 2.85; N, 4.40. Found: C, 60.65; H, 2.54; N, 4.09.

*4.2.2.4. rac-(3aS,3bR,6aS,10bR)-8-Chloro-6a-(4-chlorophenyl)-2,5-di(3,5-dichlorophenyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2d**).* Colourless crystals; mp 295–297 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1014, 1097, 1191, 1366, 1442, 1493, 1577, 1722, 3060 cm^{-1}; UV (1,2-dichloroethane), λ_{max}, nm (log ε): 279 (3.26); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.29 (d, *J*=10.6 Hz, 1H), 4.33 (s, 1H), 4.42 (d, *J*=10.6 Hz, 1H), 6.82 (d, *J*=2.1 Hz, 2H), 6.88 (d, *J*=8.2 Hz, 2H), 7.25 (d, *J*=2.1 Hz, 2H), 7.34–7.39 (m, 3H), 7.44 (t, *J*=2.1 Hz, 1H), 7.55 (dd, *J*=8.2, 2.1 Hz, 1H), 7.63 (d, *J*=2.1 Hz, 1H), 7.81 (d, *J*=8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.3, 41.2, 50.2, 56.4, 124.7 (2C), 124.9 (2C), 125.8, 127.8 (2C), 128.2 (2C), 129.5, 132.0 (2C), 132.5, 133.5, 133.6, 133.9, 134.7 (2C), 134.8, 135.0 (2C), 135.2, 138.5, 139.9, 173.6, 174.5, 175.7, 176.2. Anal. Calcd for $C_{32}H_{16}Cl_6N_2O_4$: C, 54.50; H, 2.29; N, 3.97. Found: C, 54.44; H, 2.31; N, 3.78.

*4.2.2.5. rac-(3aS,3bR,6aS,10bR)-2,5-Di(4-ethoxyphenyl)-6a-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2e**).* Colourless crystals; mp 265–267 °C; IR ($CHCl_3$) 1015, 1096, 1381, 1495, 1717, 3030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.39–1.46 (m, 6H), 4.00–4.06 (m, 4H), 4.29 (d, *J*=10.2 Hz, 1H), 4.39 (s, 1H), 4.41 (d, *J*=10.2 Hz, 1H), 6.77 (d, *J*=8.7 Hz, 2H), 6.85 (d, *J*=8.7 Hz, 2H), 6.93–7.32 (m, 9H), 7.43 (t, *J*=7.3 Hz, 1H), 7.54 (t, *J*=7.3 Hz, 1H), 7.72 (d, *J*=7.3 Hz, 1H), 7.85 (d, *J*=7.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.1, 15.2, 36.1, 41.2, 50.7, 56.6, 64.1, 64.2, 115.1 (2C), 115.4 (2C), 124.1, 124.4, 127.5 (2C), 127.7 (2C), 128.6 (2C), 129.3 (3C), 129.4 (2C), 129.9, 130.9, 131.9, 135.1, 139.9, 159.3, 159.4, 174.6, 175.7, 176.4, 177.5. Anal. Calcd for $C_{36}H_{30}N_2O_6$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.68; H, 5.19; N, 4.65.

*4.2.2.6. rac-(3aS,3bR,6aS,10bR)-2,5-Di(4-fluorophenyl)-6a-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2f**).* Colourless crystals; mp 271–272 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1122, 1157, 1233, 1386, 1510, 1716, 3040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.31 (d, 1H, *J*=9.4 Hz), 4.41 (s, 1H), 4.44 (d, *J*=9.4 Hz, 1H), 6.81 (d, *J*=4.4 Hz, 1H), 6.84 (d, *J*=5.1 Hz, 1H), 6.95–6.98 (m, 2H), 7.03 (d, *J*=8.0 Hz, 1H), 7.05 (d,

J=8.7 Hz, 1H), 7.12–7.24 (m, 4H), 7.29–7.33 (m, 3H), 7.44 (dd, *J*=7.5, 7.3 Hz, 1H), 7.55 (dd, *J*=7.7, 7.3 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.2, 41.3, 50.3, 56.5, 114.0 (d, *J*=23.0 Hz, 2C), 114.7 (d, *J*=23.0 Hz, 2C), 121.1, 123.2, 124.1, 125.6 (2C), 126.1, 126.6, 127.9 (2C), 128.6, 128.9 (d, *J*=8.0 Hz, 2C), 129.2 (d, *J*=8.0 Hz, 2C), 130.6, 133.7, 138.7, 142.3, 158.5 (d, *J*=134.0 Hz), 160.6 (d, *J*=134.0 Hz), 173.6, 174.5, 175.7, 176.2. Anal. Calcd for $C_{32}H_{20}F_2N_2O_4$: C, 71.91; H, 3.77; N, 5.24. Found: C, 71.90; H, 3.69; N, 5.36.

*4.2.2.7. rac-(3aS,3bR,6aS,10bR)-2,5-Di(3-nitrophenyl)-6a-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrro[3,4-g]isoindole-1,3,4,6-tetraone (**2g**).* Colourless crystals; mp 262–264 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1163, 1351, 1376, 1485, 1532, 1720, 3040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.36 (dd, *J*=10.4, 1.5 Hz, 1H), 4.49 (d, *J*=1.5 Hz, 1H), 4.53 (d, *J*=10.4 Hz, 1H), 7.00 (d, *J*=6.9 Hz, 2H), 7.33–7.71 (m, 11H), 7.87 (d, *J*=7.7 Hz, 1H), 8.21–8.29 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DMSO-d_6): δ=36.0, 41.5, 50.6, 56.4, 121.6, 121.8, 123.4 (2C), 128.4, 128.7 (3C), 129.0 (2C), 129.2, 129.3, 129.9, 130.0, 130.2, 130.7, 132.0, 132.5 (2C), 132.7, 133.2, 139.0, 148.2, 148.4, 173.6, 174.8, 175.8, 176.2; MS (EI): *m*/*z* (%)=396 (6), 205 (15), 204 (100), 203 (75), 202 (45), 164 (10), 118 (11), 90 (22). Anal. Calcd for $C_{32}H_{20}N_4O_8$: C, 65.31; H, 3.43; N, 9.52. Found: C, 65.29; H, 3.47; N, 9.43.

*4.2.2.8. rac-(3aS,3bR,6aS,10bR)-8-Methyl-2,5-diphenyl-6a-(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2h**).* Colourless crystals; mp 309–311 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1166, 1188, 1379, 1498, 1597, 1716, 3015 cm^{-1}; UV (1,2-dichloroethane), λ_{max}, nm (log ε): 276 (3.02); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.33 (s, 3H), 2.35 (s, 3H), 4.29 (d, *J*=10.1 Hz, 1H), 4.37 (s, 1H), 4.39 (d, *J*=10.1 Hz, 1H), 6.83–6.89 (m, 4H), 7.12 (d, *J*=8.0 Hz, 2H), 7.23–7.47 (m, 10H), 7.72 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.7, 36.1, 41.2, 51.0, 57.8, 126.3, 126.4 (2C), 127.3 (2C), 129.0 (2C), 129.2 (2C), 129.3, 129.4 (4C), 129.9, 130.50, 130.51, 131.6, 131.7, 131.9, 132.4, 136.8, 138.5, 139.4, 173.9, 174.8, 176.3, 177.2. Anal. Calcd for $C_{34}H_{26}N_2O_4$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.46; H, 4.98; N, 5.32.

*4.2.2.9. rac-(3aS,3bR,6aS,10bR)-8-Methyl-2,5,6a-tri(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2i**).* Colourless crystals; mp 198–199 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1022, 1162, 1188, 1382, 1514, 1715, 3029 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.33 (s, 12H), 4.27 (d, *J*=10.2 Hz, 1H), 4.35 (s, 1H), 4.37 (d, *J*=10.2 Hz, 1H), 6.72 (d, *J*=8.0 Hz, 2H), 6.87 (d, *J*=8.0 Hz, 2H), 7.12–7.17 (m, 5H), 7.25–7.33 (m, 4H), 7.48 (s, 1H), 7.73 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.46, 21.56, 21.63 (2C), 36.2, 41.2, 50.9, 56.3, 126.2 (4C), 128.5 (2C), 129.2, 129.4 (2C), 129.9 (2C), 130.1 (2C), 130.2 (2C), 130.9 (2C), 131.6 (2C), 136.9, 138.5, 139.1, 139.2, 139.3, 174.5, 175.8, 176.4, 177.4. Anal. Calcd for $C_{36}H_{30}N_2O_4$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.79; H, 5.49; N, 4.93.

*4.2.2.10. rac-(3aS,3bR,6aS,10bR)-2,5-Di(4-chlorophenyl)-8-methyl-6a-(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2j**).* Colourless crystals; mp 265–266 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1017, 1090, 1158, 1380, 1493, 1717, 3027 cm^{-1}; UV (1,2-dichloroethane), λ_{max}, nm (log ε): 275 (3.20); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.34 (6H), 4.26 (dd, *J*=10.4, 1.5 Hz, 1H), 4.35 (d, *J*=1.5 Hz, 1H), 4.38 (d, *J*=10.4 Hz, 1H), 6.77 (d, *J*=9.2 Hz, 2H), 6.84 (d, *J*=7.7 Hz, 2H), 7.10 (d, *J*=7.7 Hz, 2H), 7.21 (d, *J*=8.5 Hz, 2H), 7.31–7.44 (m, 6H), 7.70 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.7, 36.2, 41.2, 50.9, 56.4, 125.9, 127.5, 127.6 (4C), 128.5 (2C), 129.3, 129.5 (2C), 129.8 (2C), 130.2 (2C), 130.5, 130.7, 131.2, 131.7, 134.9, 135.0, 136.5, 138.7, 139.6, 174.0, 175.3, 176.0, 176.9. MS (EI): *m*/*z* (%)=594 (3) [M$^+$], 413 (12), 233 (18), 232 (100), 231 (18), 217 (33), 215 (26), 202 (25), 153 (19). Anal. Calcd for $C_{34}H_{24}Cl_2N_2O_4$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.49; H, 4.12; N, 7.61.

*4.2.2.11. rac-(3aS,3bR,6aS,10bR)-8-Methyl-2,5-di(4-methyl-3-chlorophenyl)-6a-(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2k**).* Colourless crystals; mp 291–293 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1054, 1158, 1187, 1378, 1497, 1717, 2923 cm^{-1}; UV (1,2-dichloroethane), λ_{max}, nm (log ε): 274 (3.35); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.36 (9H), 2.40 (s, 3H), 4.26 (d, *J*=10.4 Hz, 1H), 4.35 (s, 1H), 4.38 (d, *J*=10.4 Hz, 1H), 6.70 (s, 1H), 6.77 (d, *J*=8.0 Hz, 1H), 6.86 (d, *J*=8.0 Hz, 1H), 7.05–7.35 (m, 8H), 7.44 (s, 1H), 7.70 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=20.1, 20.2, 21.1, 21.2, 35.1, 41.5, 50.8, 56.6, 124.58, 124.63, 125.9, 127.0, 121.7, 128.5 (2C), 129.3, 130.3 (3C), 130.6, 130.7, 131.2, 131.4, 131.6, 131.7, 134.8, 135.1, 136.4, 137.3, 137.4, 138.9, 139.6, 174.1, 175.4, 176.2, 176.9. Anal. Calcd for $C_{36}H_{28}Cl_2N_2O_4$: C, 69.35; H, 4.53; N, 4.49. Found: C, 69.39; H, 4.46; N 4.41.

*4.2.2.12. rac-(3aS,3bR,6aS,10bR)-2,5-Di(4-chlorophenyl)-9-nitro-6a-(3-nitrophenyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2l**).* IR ($CHCl_3$) 1023, 1097, 1129, 1173, 1380, 1498, 1574, 1722, 2985 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.93 (dd, *J*=9.4, 1.5 Hz, 1H), 5.13 (d, *J*=1.5 Hz, 1H), 5.21 (d, *J*=9.4 Hz, 1H), 7.41 (d, *J*=9.7 Hz, 2H), 7.61–7.95 (m, 6H), 8.11 (s, 1H), 8.54–8.80 (m, 5H), 8.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.8, 41.7, 51.1, 56.8, 120.4, 121.9, 122.6, 123.4, 124.3 (2C), 125.1 (2C), 125.6, 126.2, 128.1 (2C), 128.6 (2C), 129.7, 131.6, 132.1 (2C), 132.4, 136.3, 139.5, 146.8, 148.7, 151.6, 174.1, 174.9, 176.2, 176.8. Anal. Calcd for $C_{32}H_{18}Cl_2N_4O_8$: C, 58.46; H, 2.76; N, 8.52. Found: C, 58.21; H, 2.90; N, 8.36.

*4.2.2.13. rac-(3aS,3bR,6aS,10bR)-2,5,8-trimethyl-6a-(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**2m**).* IR ($CHCl_3$) 1169, 1179, 1384, 1505, 1585, 1722, 3015 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.15 (s, 3H), 2.27 (s, 3H), 2.34 (s, 3H), 2.39 (s, 3H), 3.81 (d, *J*=9.8 Hz, 1H), 4.11 (s, 1H), 4.33 (d, *J*=9.8 Hz, 1H), 6.91 (d, *J*=8.0 Hz, 2H), 7.08 (d, *J*=8.0 Hz, 2H), 7.30 (s, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.63 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.41, 21.53, 24.15, 24.73, 35.7, 40.6, 50.2, 56.0, 123.7, 124.9, 125.2, 127.1 (2C), 128.8 (2C), 131.9, 133.5, 138.5, 136.8, 139.4, 173.2, 174.4, 175.7, 176.5. Anal. Calcd for $C_{24}H_{22}N_4O_4$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.44; H, 5.70; N, 6.77.

*4.2.2.14. rac-(3aS,3bS,6aR,10bR)-8-Chloro-6a-(4-chlorophenyl)-2,5-di(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**3a**).* Colourless crystals; mp 265–267 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1014, 1096, 1168, 1381, 1494, 1716, 2990 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.31 (s, 3H), 2.34 (s, 3H), 3.39 (dd, *J*=9.5, 6.5 Hz, 1H), 4.54 (d, *J*=6.5 Hz, 1H), 4.73 (d, *J*=9.5 Hz, 1H), 6.95 (d, *J*=8.0 Hz, 2H), 7.05–7.43 (m, 10H), 7.52 (d, *J*=8.0 Hz, 1H), 7.68 (d, *J*=8.0 Hz, 1H), 7.97 (d, *J*=7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 35.7, 40.2, 51.6, 56.1, 124.8, 127.7 (2C), 127.8 (2C), 128.5 (2C), 129.6 (2C), 129.5 (2C), 129.7 (2C), 129.9 (2C), 130.1 (2C), 130.9, 131.4, 135.0, 135.06, 136.10, 138.8, 139.2, 172.6, 174.8, 175.5, 176.5. Anal. Calcd for $C_{34}H_{24}Cl_2N_2O_4$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.49; H, 4.15; N, 4.61.

*4.2.2.15. rac-(3aS,3bS,6aR,10bR)-2,5-Di(4-fluorophenyl)-6a-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**3f**).* Colourless crystals; mp 265–267 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1117, 1142, 1156, 1226, 1388, 1510, 1717, 3040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.44 (dd, *J*=8.7, 6.5 Hz, 1H), 4.14 (d, *J*=6.5 Hz, 1H), 4.42 (d, *J*=8.7 Hz, 1H), 7.09–7.21 (m, 8H), 7.40–7.58 (m, 7H), 7,70 (d, *J*=8.0 Hz, 1H), 8.11 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.4, 41.8, 50.1, 56.3, 113.7 (d, *J*=23.0 Hz,

2C), 114.9 (d, *J*=23.0 Hz, 2C), 121.4, 122.7, 124.9, 125.3 (2C), 125.7, 126.2, 127.8 (2C), 128.5, 127.6 (d, *J*=8.0 Hz, 2C), 128.4 (d, *J*=8.0 Hz, 2C), 130.6, 134.2, 137.7, 142.4, 157.9 (d, *J*=134.0 Hz), 160.3 (d, *J*=134.0 Hz), 172.9, 174.3, 175.5, 176.1. Anal. Calcd for $C_{32}H_{20}F_2N_2O_4$: C, 71.91; H, 3.77; N, 5.24. Found: C, 71.89; H, 3.53; N, 5.22.

*4.2.2.16. rac-(3aS,3bS,6aR,10bR)-8-Methyl-6a-(4-methylphenyl)-2,5-diphenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**3h**).* Colourless crystals; mp 255–257 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1016, 1093, 1135, 1167, 1377, 1493, 1577, 1719, 2995 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 3H), 2.39 (s, 3H), 3.42 (dd, *J*=9.5, 6.5 Hz, 1H), 4.11 (d, *J*=6.5 Hz, 1H), 4.31 (d, *J*=9.5 Hz, 1H), 7.00 (d, *J*=8.0 Hz, 2H), 7.14 (d, *J*=7.3 Hz, 2H), 7.21 (d, *J*=7.3 Hz, 2H), 7.33–7.50 (m, 10H), 7.99 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 35.6, 40.2, 51.8, 57.7, 125.1, 126.5 (2C), 127.3 (2C), 128.7 (2C), 129.1 (2C), 129.2, 129.5 (4C), 130.1 (2C), 130.7, 131.4, 131.6, 131.8, 132.5, 136.4, 138.6, 139.0, 172.6, 175.2, 175.7, 176.8; MS (EI): *m*/*z* (%)=526 (5) [M^+], 379 (21), 233 (20), 232 (100), 231 (14), 217 (30), 216 (18), 215 (26), 202 (27), 119 (19), 91 (12). Anal. Calcd for $C_{34}H_{26}N_2O_4$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.63; H, 5.04; N, 5.21.

*4.2.2.17. rac-(3aS,3bS,6aR,10bR)-8-Methyl-2,5,6a-tri(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**3i**).* Colourless crystals; mp 248–250 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1022, 1141, 1161, 1383, 1514, 1716, 3020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.34 (s, 3H), 2.35 (s, 3H), 2.38 (s, 6H), 3.40 (dd, *J*=9.5, 5.8 Hz, 1H), 4.08 (d, *J*=5.8 Hz, 1H), 4.28 (d, *J*=9.5 Hz, 1H), 6.95–7.05 (m, 4H), 7.20–7.38 (m, 9H), 7.49 (s, 1H), 7.98 (d, *J*=7.3 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ=21.5, 21.55, 21.62, 21.70, 35.9, 41.2, 51.0, 57.6, 126.4, 127.1 (2C), 127.6 (2C), 128.5, 129.5 (2C), 129.88, 129.91 (2C), 130.3 (2C), 130.4 (2C), 130.5, 130.9, 131.8, 132.5, 137.0, 138.0, 138.1, 138.8, 139.1, 174.1, 176.2, 176.4, 177.4. Anal. Calcd for $C_{36}H_{30}N_2O_4$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.85; H, 5.41; N, 5.16.

*4.2.2.18. rac-(3aS,3bS,6aR,10bR)-2,5-Di(4-chlorophenyl)-8-methyl-6a-(4-methylphenyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**3j**).* Colourless crystals; mp 172–174 °C (EtOH/$CHCl_3$); IR ($CHCl_3$) 1017, 1091, 1158, 1379, 1493, 1717, 3020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 3H), 2.39 (s, 3H), 3.41 (dd, *J*=9.5, 5.8 Hz, 1H), 4.08 (d, *J*=5.8 Hz, 1H), 4.30 (d, *J*=9.5 Hz, 1H), 6.97 (d, *J*=7.3 Hz, 2H), 7.10 (d, *J*=7.3 Hz, 2H), 7.21 (d, *J*=7.3 Hz, 2H), 7.34–7.51 (m, 8H), 7.95 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 35.6, 40.2, 51.7, 57.7, 124.8, 127.3, 127.7 (4C), 128.56 (2C), 128.61, 129.6 (2C), 129.76, 129.81 (2C), 130.1 (2C), 130.89, 130.94, 131.4, 135.0, 135.1, 136.1, 138.8, 139.2, 172.6, 174.8, 175.4, 176.5; MS (EI): *m*/*z* (%)=594 (3) [M^+], 233 (20), 232 (100), 231 (17), 217 (40), 216 (20), 215 (32), 202 (32), 153 (31), 125 (13); Anal. Calcd for $C_{34}H_{24}Cl_2N_2O_4$: C, 68.58; H, 4.06; N, 4.70. Found: C, 68.61; H, 3.98; N, 4.59.

*4.2.2.19. 3-(4-Chlorophenyl)-4-(3,5-dimethylpyrazol-1-yl)-1-p-tolyl-pyrrolidine-2,5-dione (**4**).* Colourless crystals; ^1H NMR (300 MHz, $CDCl_3$): δ=2.15 (s, 3H), 2.29 (s, 3H), 2.37 (s, 3H), 5.05 (d, *J*=7.3 Hz, 1H), 5.16 (d, *J*=7.3 Hz, 1H), 5.90 (s, 1H), 7.22 (d, *J*=8.0 Hz, 2H), 7.36 (d, *J*=8.7 Hz, 2H), 7.42 (d, *J*=8.7 Hz, 2H), 7.78 (d, *J*=8.0 Hz, 2H). Anal. Calcd for $C_{22}H_{20}ClN_3O_2$: C, 67.09; H, 5.12; N, 10.67. Found: C, 66.97; H, 5.19; N, 10.45.

*4.2.2.20. rac-(3aS,3bS,6aS,10bR)-8-Chloro-10b-(4-chlorophenyl)-2,5-di(4-methylphenyl)-6a-(6-methyl-2-pyridylmethyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5a**).* Colourless crystals; mp 283–285 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1028, 1172, 1250, 1306, 1390, 1456, 1519, 1590, 1717, 3038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.38 (s, 3H), 2.41 (s, 3H), 2.42 (s, 3H), 3.20 (d, *J*=16.0 Hz, 1H), 4.22 (d, *J*=16.0 Hz, 1H), 4.26 (s, 1H), 4.30 (s, 1H), 6.91 (d, *J*=8.0 Hz, 2H), 7.02 (d, *J*=8.0 Hz, 2H), 7.06 (d, *J*=8.0 Hz, 2H), 7.16 (d, *J*=8.0 Hz, 2H), 7.23–7.56 (m, 8H), 7.71 (s, 1H), 8.17 (d, *J*=8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6, 21.7, 25.1, 39.5, 45.9, 46.8, 49.0, 55.3, 121.7, 122.0, 125.7 (2C), 126.1 (2C), 129.2, 129.6 (2C), 129.7, 129.9 (5C), 130.3 (2C), 130.6, 131.4, 132.8, 133.3, 134.8, 135.5, 137.5, 138.7, 139.6, 140.0, 155.8, 158.0, 174.6, 175.0, 177.2, 178.1. Anal. Calcd for $C_{41}H_{31}Cl_2N_3O_4$: C, 70.29; H, 4.46; N, 6.00. Found: C, 70.33; H, 4.41; N, 5.98.

*4.2.2.21. rac-(3aS,3bS,6aS,10bR)-8-Chloro-10b-(4-chlorophenyl)-2,5-diphenyl-6a-(6-methyl-2-pyridylmethyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5b**).* Colourless crystals; mp 233–235 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1031, 1167, 1252, 1300, 1386, 1456, 1513, 1592, 1715, 3028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.42 (s, 3H), 3.21 (d, *J*=16.9 Hz, 1H), 4.25 (d, *J*=16.9 Hz, 1H), 4.28 (s, 1H), 4.33(s, 1H), 6.92 (d, *J*=8.0 Hz, 2H), 7.03 (d, *J*=7.3 Hz, 2H), 7.19 (d, *J*=8.0 Hz, 2H), 7.30–7.57 (m, 12H), 7.72 (s, 1H), 8.18 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.1, 39.5, 45.9, 46.8, 49.1, 55.4, 116.9, 121.6, 122.0, 125.9 (2C), 126.3 (2C), 128.7, 129.3 (2C), 129.4, 129.6 (2C), 129.7 (2C), 129.9 (2C), 130.6, 131.4, 131.8, 132.4, 132.7, 133.3, 134.9, 135.6, 137.5, 139.9, 155.8, 158.1, 174.4, 174.9, 177.0, 177.9. Anal. Calcd for $C_{39}H_{27}F_2N_3O_4$: C, 73.23; H, 4.25; N, 6.57. Found: C, 73.34; H, 4.28; N, 6.49.

*4.2.2.22. rac-(3aS,3bS,6aS,10bR)-8-Chloro-10b-(4-chlorophenyl)-2,5-di(4-chlorophenyl)-6a-(6-methyl-2-pyridylmethyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5c**).* Colourless crystals; mp 224–225 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1038, 1172, 1250, 1295, 1377, 1461, 1516, 1583, 1719, 3033 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.32 (s, 3H), 3,26 (d, *J*=16.0 Hz, 1H), 4.16 (s, 1H), 4.19 (d, *J*=16.0 Hz, 1H), 4.50 (s, 1H), 7.06–7.17 (m, 5H), 7.31–7.68 (m, 12H), 8.18 (d, *J*=8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ=25.1, 40.0, 45.3, 46.7, 48.4, 54.9, 122.1, 122.3, 128.4 (2C), 129.1, 129.2 (2C), 129.3 (2C), 129.8 (5C), 130.7, 131.2 (2C), 131.3, 132.3, 133.5, 133.6, 133.8, 133.9, 134.2, 134.6, 138.2, 140.8, 156.3, 157.5, 174.4, 174.95, 177.24, 177.63. Anal. Calcd for $C_{39}H_{25}Cl_4N_3O_4$: C, 63.18; H, 3.40; N, 5.67. Found: C, 63.15; H, 3.60; N, 5.51.

*4.2.2.23. rac-(3aS,3bS,6aS,10bR)-2,5-Di(4-ethoxyphenyl)-6a-(6-methyl-2-pyridylmethyl)-10b-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5d**).* Colourless crystals; mp 238–239 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1045, 1124, 1167, 1250, 1299, 1392, 1512, 1715, 2980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=1.41 (t, *J*=6.5 Hz, 3H), 1.43 (t, *J*=6.5 Hz, 3H), 2.41 (s, 3H), 3.24 (d, *J*=16.0 Hz, 1H), 4.03 (q, *J*=6.5 Hz, 2H), 4.05 (q, *J*=6.5 Hz, 2H), 4.23 (s, 1H), 4.30 (s, 1H), 4.31 (d, *J*=16.0 Hz, 1H), 6.87–7.41 (m, 16H), 7.49–7.56 (m, 2H), 7.74 (d, *J*=8.0 Hz, 1H), 8.22 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.1, 15.2, 25.1, 39.6, 46.2, 47.0, 49.5, 56.0, 64.0, 64.2, 114.9 (2C), 115.4 (2C), 121.8, 121.9, 124.5, 125.1, 127.2 (2C), 127.6 (2C), 128.5 (2C), 128.7 (2C), 129.0, 129.2, 129.88, 129.91, 130.3, 131.1, 134.8, 137.4, 141.8, 156.3, 158.0, 158.8, 159.3, 175.3, 175.4, 178.1, 178.7. Anal. Calcd for $C_{43}H_{37}N_3O_6$: C, 74.66; H, 5.39; N, 6.07. Found: C, 74.57; H, 5.46; N, 5.93.

*4.2.2.24. rac-(3aS,3bS,6aS,10bR)-2,5-Di(4-fluorophenyl)-6a-(6-methyl-2-pyridylmethyl)-10b-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5e**).* Colourless crystals; mp 261–262 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1029, 1135, 1170, 1378, 1456, 1498, 1577, 1593, 1718, 3023 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.36 (s, 3H), 3,26 (d, *J*=16.0 Hz, 1H), 4.25 (s, 1H), 4.32 (s, 1H), 4.35(d, *J*=16.0 Hz, 1H), 6.97–7.44 (m, 16H), 7.52–7.57 (m, 2H), 7.74 (d, *J*=7.3 Hz, 1H), 8.22 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.1, 39.6, 46.2, 46.9, 56.1, 116.1 (d, J_{CF}=22.9 Hz, 2C), 116.7 (d, J_{CF}=22.9 Hz, 2C), 121.7, 122.0, 127.8 (d, J_{CF}=8.0 Hz, 2C), 128.2

(d, J_{CF}=9.0 Hz, 2C), 128.4, 128.6 (4C), 129.1, 129.3 (4C), 129.9, 130.1, 130.2, 130.8, 134.7, 137.5 (2C), 141.4, 157.1 (d, J_{CF}=132.7 Hz, 2C), 174.9, 175.1, 177.7, 178.4. Anal. Calcd for $C_{39}H_{27}F_2N_3O_4$: C, 73.23; H, 4.25; N, 6.57. Found: C, 73.34; H, 4.28; N, 6.49.

*4.2.2.25. rac-(3aS,3bS,6aS,10bR)-2,5-Di(3-nitrophenyl)-6a-(6-methyl-2-pyridylmethyl)-10b-phenyl-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5f**).* Colourless crystals; mp 170–171 °C (EtOH/CH_2Cl_2); IR ($CHCl_3$) 1093, 1158, 1350, 1376, 1485, 1532, 1721, 3040 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6): δ=2.28 (s, 3H), 3.19 (d, J=16.0 Hz, 1H), 4.08 (s, 1H), 4.32 (d, J=16.7 Hz, 1H), 4.64 (s, 1H), 7.05–7.10 (m, 2H), 7.16 (d, J=7.3 Hz, 1H), 7.35–7.43 (m, 4H), 7.48–7.83 (m, 11H), 8.17 (d, J=8.0 Hz, 1H), 8.28 (d, J=8.0 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d_6): δ=25.0, 40.0, 46.0, 46.9, 49.4, 55.9, 121.3, 122.3, 122.36, 122.42 (2C), 124.0, 124.4, 128.9, 129.4 (3C), 129.7 (2C), 130.48, 130.53, 131.4, 131.5, 132.8, 133.3, 133.5, 133.9, 134.4, 138.4, 141.7, 148.5, 148.7, 156.7, 157.5, 174.6, 175.7, 177.5, 177.6, 177.7. Anal. Calcd for $C_{39}H_{27}N_5O_8$: C, 67.53; H, 3.92; N, 10.10. Found: C, 67.43; H, 3.89; N, 9.98.

*4.2.2.26. rac-(3aS,3bS,6aS,10bR)-2,5-Diphenyl-8-methyl-6a-(6-methyl-2-pyridylmethyl)-10b-(4-tolyl)-1,2,3,3a,3b,4,5,6,6a,10b-decahydrobenzo[e]pyrrolo[3,4-g]isoindole-1,3,4,6-tetraone (**5g**).* Colourless crystals; mp 294–296 °C; IR ($CHCl_3$) 1043, 1168, 1254, 1290, 1379, 1456, 1494, 1592, 1606, 1718, 3023 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=2.33 (s, 3H), 2.36 (s, 3H), 2.42 (s, 3H), 3.15 (d, J=16.7 Hz, 1H), 4.26 (s, 1H), 4.29 (s, 1H), 4.30 (d, J=16.7 Hz, 1H), 6.88 (d, J=8.0 Hz, 2H), 7.00–7.17 (m, 6H), 7.19–7.53 (m, 10H), 8.10 (d, J=8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5, 21.6, 25.1, 39.7, 46.2, 46.8, 49.7, 55.8, 121.7, 121.8, 126.1 (2C), 126.4 (2C), 128.5, 128.6 (2C), 129.1 (3C), 129.6 (3C), 129.9 (2C), 130.4, 131.0 (2C), 131.7, 132.2, 132.7, 137.4, 138.2, 138.9, 139.0, 156.4, 158.0, 175.1, 175.4, 178.0, 178.6. Anal. Calcd for $C_{41}H_{33}N_3O_4$: C, 77.95; H, 5.27; N, 6.65. Found: C, 77.87; H, 5.34; N, 6.54.

4.3. X-ray diffraction study

Crystallographic data for the structures **2j** and **5d** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 631561 (**2j**) and CCDC 686484 (**5d**). Copies of the data can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (email: deposit@ccdc.cam.ac.uk).

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