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Stereoselective cycloadditions of (1*Z*,4*R**,5*R**)-1-arylmethylidene-4-benzoylamino-5-phenylpyrazolidin-3-on-1-azomethine imines to maleimides

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Abstract—A library of 15 1,6,7,9-tetrasubstituted 6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-triones was prepared by combinatorial stereoselective cycloadditions of (1*Z*,4*R**,5*R**)-1-arylmethylidene-4-benzoylamino-5-phenylpyrazolidin-3-on-1-azomethine imines to *N*-substituted maleimides. Stereochemistry was controlled by the stereodirecting phenyl group at position-3 and by the *ortho*-substituents at the aromatic ring at position-1′ in azomethine imines. Consequently, two sets of diastereomeric cycloadducts were obtained, one set from the *ortho*-unsubstituted dipoles and the other set from the *ortho*-disubstituted dipoles.
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1. Introduction

1,3-Dipolar cycloadditions are useful for the preparation of five-membered heterocycles, because they enable access to polyfunctional compounds with multiple asymmetric centers, usually with excellent stereocontrol. Despite widely reported asymmetric cycloadditions in various chiral nitrone, nitrile oxide, and azomethine ylide series, few examples have been reported in the chiral azomethine imine series.[1–6] Within this context, stable chiral azomethine imines have been prepared from pyridazine-diazoalkane cycloadducts,[7–11] pyrazolidin-3-ones,[12–28] and 1,3,4-oxadiazin-2-ones.[29–32] Generally, 1,3-dipolar cycloadditions of these cyclic chiral azomethine imines to various dipolarophiles have been accompanied by high facial and *endo*/*exo*-selectivity and afforded the corresponding functionalized fused pyrazolones with a bridgehead N–N structural element.[7–32]

The importance of pyrazolidin-3-ones has increased significantly in the last decade, due to their applicability in industrial processes, and because several pyrazolidin-3-one derivatives exhibit biological activities.[33–35] Some examples of biologically active pyrazolidinone derivatives are depicted in Figure 1.

An important group of fused pyrazolidinone analogues is 2-acylamino-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-7-carboxylates, which are useful scaffolds for the preparation of conformationally constrained peptidomimetics.[13–19,36] A common method for the preparation of pyrazolo[1,2-*a*]-pyrazolones is the 1,3-dipolar cycloaddition of pyrazolidinone-1-azomethine imines to a suitable dipolarophile, first introduced by Dorn[37–39] and Oppolzer.[40,41]

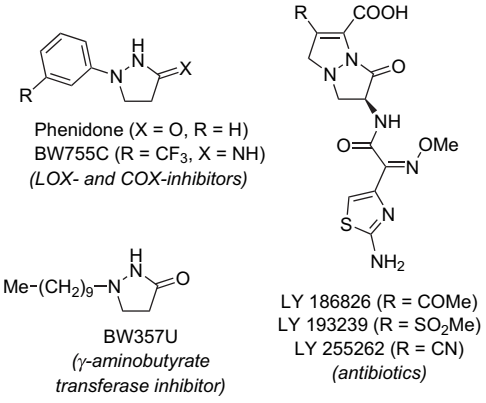

Figure 1. Some examples of biologically active pyrazolidinones.

In the last decade, a part of our research interest has also been devoted to the chemistry of pyrazolidinones and their fused analogs.[21–23,28,42–47] In connection with this, we have recently reported stereocontrol in 1,3-dipolar cycloadditions of (1Z,4*R**,5*R**)-1-arylmethylidene-4-benzoylamino-5-phenylpyrazolidin-3-on-1-azomethine imines **3** to acyclic olefinic dipolarophiles: dimethyl maleate, dimethyl fumarate, and methyl acrylate. The regiochemistry and stereoselectivity of these cycloaddition reactions were controlled

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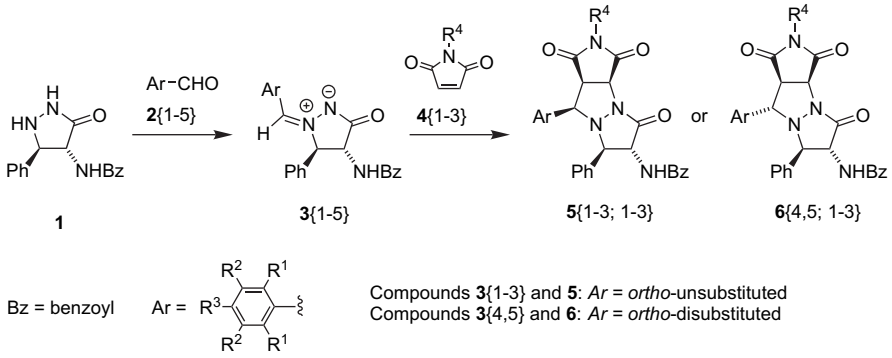


Scheme 1.

by the stereodirecting group in chiral dipole **3**, by the *ortho*-substituents at the aromatic ring, and by the structure of the dipolarophile.[28] These results prompted us to continue with further studies toward the synthesis of combinatorial libraries of fused pyrazolo[1,2-*a*]pyrazolone derivatives with variable substitution pattern and variable configuration.

Herein, we report stereoselective solution-phase combinatorial 1,3-dipolar cycloadditions of five azomethine imines **3**{1–5} (three *ortho*-unsubstituted **3**{1–3} and two *ortho*-disubstituted **3**{4,5}) to three 1-substituted maleimides **4**{1–3}, which afforded a library of 15 cycloadducts, comprising two isomeric sets of cycloadducts **5**{1–3; 1–3} and **6**{4,5; 1–3} (Scheme 1).

2. Results and discussion

The initial starting compound (4*R**,5*R**)-4-benzoylamino-5-phenylpyrazolidin-3-one (**1**) was prepared from *N*-benzoylglycine according to the literature procedure.[21] For the intended combinatorial study, five benzaldehydes **2**{1–5} were chosen as the reagents for transformation of **1** into the corresponding (1*Z*,4*R**,5*R**)-1-arylmethylidene-4-benzoylamino-5-phenylpyrazolidin-3-on-1-azomethine imines **3**{1–5}.[21,28] Three maleimides **4**{1–3} were chosen as the dipolarophiles for the subsequent 1,3-dipolar cycloaddition reactions (Fig. 2).

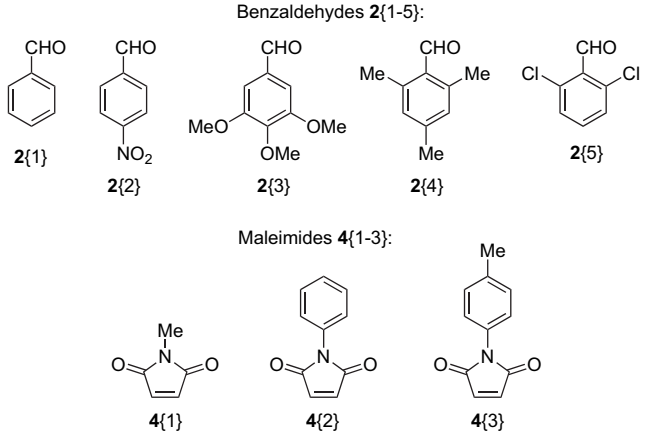
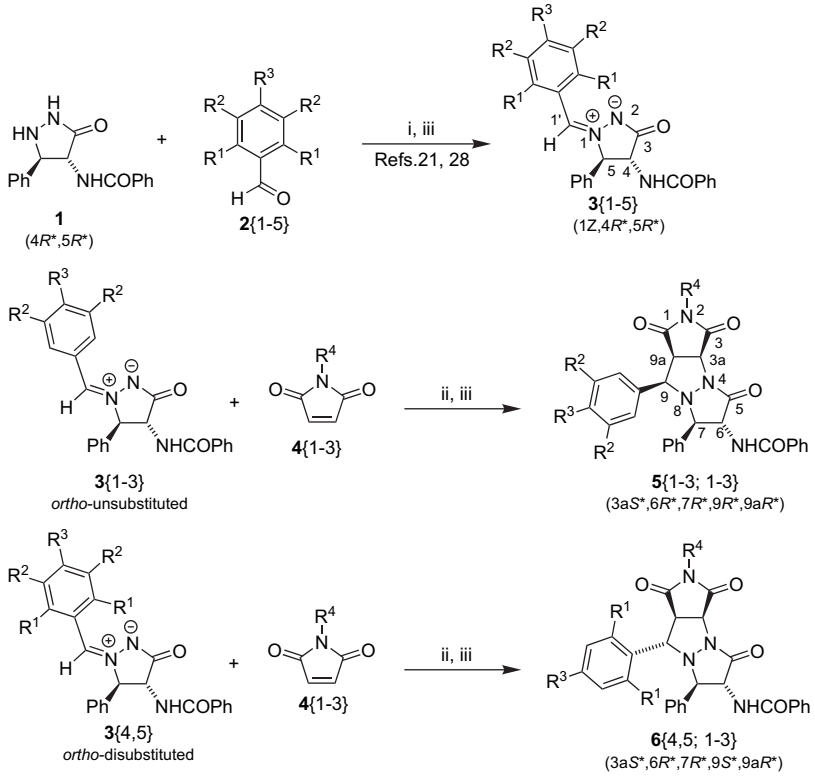


Figure 2. Sets of benzaldehydes **2**{1–5} and maleimides **4**{1–3} used in the synthesis of azomethine imines **3**{1–5} and in the synthesis of diastereomeric cycloadducts **5** and **6**.

First, stable azomethine imines **3**{1–5} were prepared in a parallel manner following the general literature procedures for conventional, single-vessel synthesis of **3**{1–5}.[21,28] Parallel heating of (4*R**,5*R**)-4-benzoylamino-5-phenyl-3-pyrazolidinone **1** with five substituted benzaldehydes **2**{1–5} in anhydrous ethanol in the presence of catalytic trifluoroacetic acid under reflux gave the corresponding dipoles **3**{1–5} in yields identical to those obtained from the previously published conventional synthesis.[21,28] These five azomethine imines **3**{1–5} were then treated combinatorially with three maleimides **4**{1–3} in refluxing anisole. Upon cooling, the precipitated cycloadducts, 9-aryl-6-benzoylamino-7-phenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione derivatives **5** and **6**, were collected by filtration, washed with ether, and dried in vacuo. In this manner, a library of 15 cycloadducts, nine (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5**{1–3; 1–3} and six (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6**{4,5; 1–3}, was obtained in 18–89% yields and in ≥90% purity. Analytical purity of 14 library members was then established by elemental analysis for C, H, and N (Scheme 2, Table 1).

In terms of selectivity, these cycloadditions proceeded according to expectations based on our previous experience with cycloadditions to dimethyl maleate:[28] (a) all products were isolated as single isomers and (b) cycloadditions afforded two isomeric sets of products, **5** and **6**, depending on the *ortho*-substitution at the aryl residue at position-1′ in dipoles **3**. Reactions of **4** with *ortho*-unsubstituted dipoles **3**{1–3} furnished cycloadducts **5**{1–3; 1–3} with (3a*S**,6*R**,7*R**,9*R**,9a*R**)-configuration, whilst reactions of **4** with *ortho*-disubstituted dipoles **3**{4,5} afforded the (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6**{4,5; 1–3} (cf. Scheme 2). The (3a*S**,6*R**,7*R**,9*S**,9a*R**)-configuration of the isomers **6** was in agreement with the expected configuration.[28] On the other hand, the relative *cis*-orientation around the C(9)–C(9a) bond in the (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5** was quite surprising, since previously published cycloadditions of **3** to acyclic dipolarophiles afforded cycloadducts with *trans*-configuration around the newly formed C–C single bond.[28]

According to the previously published cycloadditions of **3** to dimethyl maleate and related acyclic dipolarophiles, formation of (3a*S**,6*R**,7*R**,9*R**,9a*R**)-cycloadducts **5** from the *ortho*-unsubstituted dipoles **3**{1–3} might be explained by a concerted 1,3-dipolar cycloaddition mechanism, whilst formation of (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6** from the



Scheme 2. Reaction conditions: (i) Ar–CHO **2**{1–5}, EtOH, CF_3COOH (cat.), reflux; (ii) anisole, reflux; (iii) filtration, washing with Et_2O, drying in vacuo.

Table 1. Reactions of azomethine imines **3**{1–5} with maleimides **4**{1–3}. Preparation of isomeric cycloadducts **5**{1–3; 1–3} and **6**{4,5; 1–3}

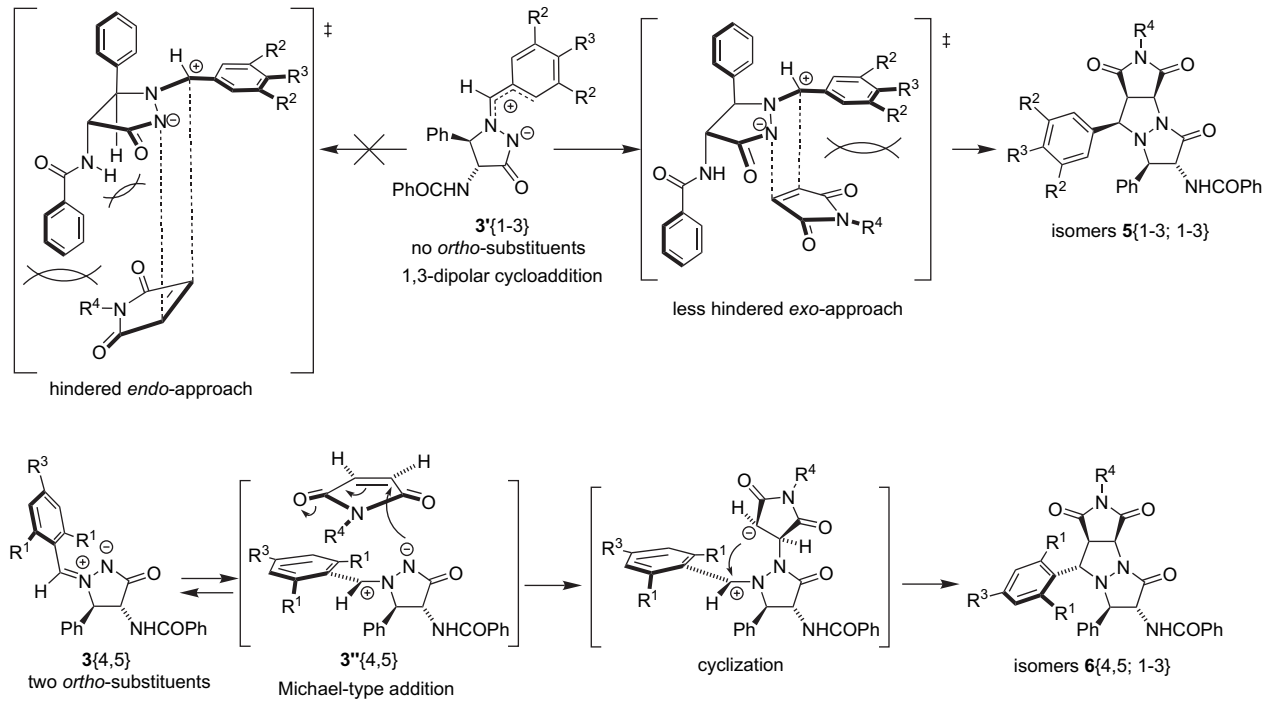
Reaction	R^1	R^2	R^3	R^4	Yield (%)	Purity (%)[a]	Configuration
3{1}+**4**{1}→**5**{1; 1}	H	H	H	Me	55	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{2}+**4**{1}→**5**{2; 1}	H	H	NO_2	Me	73	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{3}+**4**{1}→**5**{3; 1}	H	OMe	OMe	Me	85	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{1}+**4**{2}→**5**{1; 2}	H	H	H	Ph	74	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{2}+**4**{2}→**5**{2; 2}	H	H	NO_2	Ph	84	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{3}+**4**{2}→**5**{3; 2}	H	OMe	OMe	Ph	75	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{1}+**4**{3}→**5**{1; 3}	H	H	H	4-Methylphenyl	48	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{2}+**4**{3}→**5**{2; 3}	H	H	NO_2	4-Methylphenyl	57	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{3}+**4**{3}→**5**{3; 3}	H	OMe	OMe	4-Methylphenyl	76	≥95	3a*S**,6*R**,7*R**,9*R**,9a*R**
3{4}+**4**{1}→**6**{4; 1}	Me	H	Me	Me	18	≥95	3a*S**,6*R**,7*R**,9*S**,9a*R**
3{5}+**4**{1}→**6**{5; 1}	Cl	H	H	Me	84	≥95	3a*S**,6*R**,7*R**,9*S**,9a*R**
3{4}+**4**{2}→**6**{4; 2}	Me	H	Me	Ph	63	≥90[b]	3a*S**,6*R**,7*R**,9*S**,9a*R**
3{5}+**4**{3}→**6**{5; 2}	Cl	H	H	Ph	82	≥95	3a*S**,6*R**,7*R**,9*S**,9a*R**
3{4}+**4**{3}→**6**{4; 3}	Me	H	Me	4-Methylphenyl	55	≥95	3a*S**,6*R**,7*R**,9*S**,9a*R**
3{5}+**4**{3}→**6**{5; 3}	Cl	H	H	4-methylphenyl	89	≥95	3a*S**,6*R**,7*R**,9*S**,9a*R**

[a] Determined by ^1H NMR and by elemental analysis. Unless otherwise stated, the found values for C, H, and N were within ±0.4% range with respect to theoretical values.

[b] The found values for C, H, and N were outside ±0.4% range with respect to theoretical values.

ortho-disubstituted dipoles **3**{4,5} might be explained by a two-step mechanism. Dipoles **3**{1–3} with free *ortho*-positions can adopt a planar conformation **3′** allowing the transition state for the concerted 1,3-dipolar cycloaddition mechanism. On the other hand, such planar conformation **3′** is not feasible in dipoles **3**{4,5} with two *ortho*-substituents and the reaction presumably proceeds by Michael-type addition to the conformer **3″** followed by cyclization of the intermediate zwitterion (or a biradical) (Scheme 3).[28,48,49]

Stereocontrol in cycloadditions of *ortho*-disubstituted dipoles **3**{4,5} to maleimides **4** leading to (3a*S**,6*R**,7*R**,9*S**,9a*R**)-cycloadducts **6** was the same as that reported for reactions with dimethyl maleate.[28] On the other hand, cycloadditions with *ortho*-unsubstituted dipoles **3**{1–3} were *exo*-selective and gave the (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5**, in contrast to the previously published *endo*-selective cycloadditions of *ortho*-unsubstituted dipoles **3**{1–3} to dimethyl maleate.[28] A possible explanation for this unexpected *exo*-selectivity is based on the fact that maleimides **4** are cyclic and, thus, more rigid *cisoid*-dipolarophiles than dimethyl maleate. Consequently, different shapes and the presence of a (bulky) substituent at position-1 might also reflect in different steric demands. Apparently, the *exo*-approach of maleimide **4** from the less hindered face of *ortho*-unsubstituted dipoles **3′**{1–3} is less hindered than the *endo*-approach (Scheme 3).



Scheme 3.

Alternatively, different stereochemistry could also be explained by the *endo*-stereocontrol, followed by epimerization at position-9a and position-3a to furnish the final isomers **5**. In order to obtain further information on the reaction mechanism and stereocontrol, dipoles **3**{1} and **3**{5} were treated with *N*-(4-methylphenyl)maleimide (**4**{3}) in DMSO-d_6 and the reactions were monitored by ^{1}H NMR spectroscopy. The *ortho*-unsubstituted dipole **3**{1} reacted at rt, with 21% conversion into **5**{1; 3} after 6 days. In contrast, the *ortho*-disubstituted dipole **3**{5} did not react at 20–100 °C. Heating at 150 °C for 1 h was required in order to achieve a 33% conversion into **6**{5; 3}. In both cases, formation of intermediates and/or isomeric cycloadducts was not observed. The results of these two experiments supported the proposed mechanisms and stereocontrol of cycloadditions (Scheme 3).[48,49]

3. Structural determination

The structures of novel compounds **5**{1–3; 1–3} and **6**{4,5; 1–3} were determined by spectroscopic methods (IR, ^{1}H and ^{13}C NMR, NOESY spectroscopy, and MS) and by elemental analyses for C, H, and N. Isomerical purity of cycloadducts **5** and **6** was determined by ^{1}H NMR spectroscopy. Compound **6**{4; 2} was not obtained in analytically pure form. Its identity was confirmed by ^{13}C NMR spectroscopy and EI-HRMS.

The relative configurations of cycloadducts **5**{1–3; 1–3} and **6**{4,5; 1–3} were determined by ^{1}H NMR and NOESY spectroscopy. In all cycloadducts **5** and **6**, NOE supported the *cis*-orientation between *H*–C(9a)–*H* and *H*–C(3a), whilst the absence of NOE between *H*–C(6) and *H*–C(7) was in agreement with the *trans*-orientation of the corresponding protons. In the (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5**, NOE between *H*–C(7) and *H*–C(9) supported the *syn*-orientation, while the absence of NOE in the (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6** was in agreement with the *anti*-orientation between *H*–C(7) and *H*–C(9). Similarly, NOE between *H*–C(9) and *H*–C(9a) in (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5** supported their *cis*-orientation, while the absence of NOE between *H*–C(9) and *H*–C(9a) was in agreement with the *trans*-orientation of the corresponding protons in the (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6**. Finally, the configurations of both sets of isomeric compounds, **5** and **6**, were confirmed by correlation of chemical shifts for *H*–C(3a), *H*–C(6), *H*–C(7), *H*–C(9), and H–C(9a) and by correlation of vicinal coupling constants $^3J_{H6–H7}$, $^3J_{H9–H9a}$, and $^3J_{H3a–H9a}$ (Fig. 3, Table 2).

4. Conclusion

A library of 15 9-aryl-6-benzoylamino-7-phenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione derivatives **5**{1–3; 1–3} and **6**{4,5; 1–3} was prepared by solution-phase combinatorial synthesis. All 15 compounds were obtained as single isomers, 14 of them in analytical purity after simple workup and filtration. The library comprised two sets of isomers: (a) cycloadditions to *ortho*-unsubstituted dipoles **3**{1–3} gave the (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5**{1–3; 1–3} and (b) cycloadditions to *ortho*-disubstituted dipoles **3**{4,5} gave the (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6**{4,5; 1–3}.

Experimental evidence on the stereocontrol can be summarized in the following way: (a) all cycloadditions to maleimides **4** were stereoselective, regardless of the substituents at the *Ar*–C(1′) group of dipole **3**, (b) no isomeric cycloadducts were detected by monitoring the cycloaddition progress by ^{1}H NMR spectroscopy in DMSO-d_6,

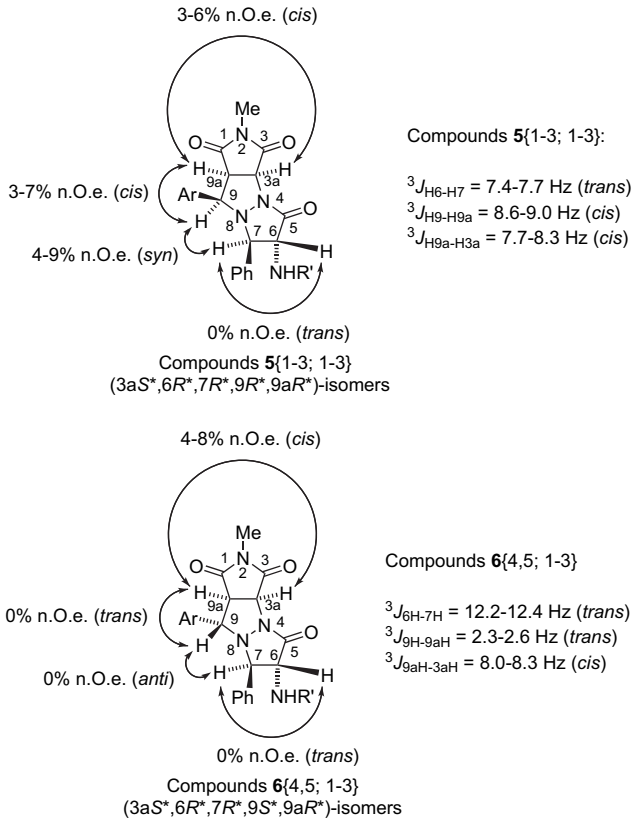


Figure 3.

(c) *ortho*-unsubstituted dipoles **3**{1–3} favored the formation of the (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5** with *syn*-oriented *H*–C(7) and *H*–C(9), (d) *ortho*-disubstituted dipoles **3**{4,5} favored the formation of the (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6** *anti*-oriented *H*–C(7) and *H*–C(9), (e) in (3a*S**,6*R**,7*R**,9*R**,9a*R**)-isomers **5** with no *ortho*-substituents at *Ar*–C(9), the *H*–C(9) and *H*–C(9a) were *cis*-oriented, and (f) in (3a*S**,6*R**,7*R**,9*S**,9a*R**)-isomers **6** with two *ortho*-substituents at *Ar*–C(9), the *H*–C(9) and *H*–C(9a) were *trans*-oriented.

In summary, stereocontrol was almost identical to that in cycloadditions to acyclic dipolarophiles. However, cycloadditions of *ortho*-unsubstituted dipoles **3**{1–3} to maleimides **4** were *exo*-selective, in contrast to the *endo*-selective cycloadditions to dimethyl maleate.[28] The *exo*-selectivity of cycloadditions of *ortho*-unsubstituted dipoles **3**{1–3} to maleimides **4** is most probably due to steric factors arising from cyclic shape of maleimides **4**.

5. Experimental

5.1. General

Melting points were determined on a Kofler micro hot stage. The NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C nucleus, using DMSO-d_6 and $CDCl_3$ with TMS as the internal standard, as solvents. Mass spectra were recorded on an AutoSpecQ spectrometer and IR spectra on a Perkin–Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin–Elmer CHN Analyser 2400 II. Parallel synthesis of azomethine imines **3**{1–5} and combinatorial synthesis of cycloadducts **5** and **6** were performed on a Radley 6 Reaction Station.

Aromatic aldehydes **2**{1–5} and maleimides **4**{1–3} are commercially available (Sigma–Aldrich). (4*R**,5*R**)-4-Benzoylamino-5-phenylpyrazolidin-3-one **1** was prepared according to the literature procedure.[21]

5.2. General procedure for the parallel preparation of azomethine imines 3{1–5}

Compounds **3**{1–5} were prepared from **1** and aldehydes **2**{1–5} according to a slightly modified literature procedure.[21] A Radley 6 Reaction Station parallel synthesizer was equipped with five 50 mL flasks. Pyrazolidinone **1** (5×1.405 g, 5×5 mmol), anhydrous ethanol (5×20 mL), and benzaldehydes **2**{1–5} (6 mmol of each) were weighed into the flasks and the mixtures were refluxed for 5 min.

Table 2. Characteristic ^{1}H NMR and NOESY data for cycloadducts **5**{1–3; 1–3} and **6**{4,5; 1–3}

Compound	δ *H* (ppm)					J_{H-H} (Hz)			NOE (%)[a]			
	9a	7	6	9	3a	6–7	9–9a	9a–3a	6–7	7–9	9–9a	9a–3a
(3a*S**,6*R**,7*R**,9*R**,9a*R**)-Isomers **5**												
5{1; 1}	4.15	4.24	4.58	4.73	5.28	7.5	8.8	7.8	0	9	7	6
5{2; 1}	4.18	4.28	4.61	4.88	5.29	7.6	8.6	8.0	0	8	6	6
5{3; 1}	4.05	4.22	4.51	4.68	5.25	7.6	8.8	7.7	0	6	7	5
5{1; 2}	4.05	~4.4[b]	~4.4[b]	5.04	5.52	[b]	8.6	8.3	0	8	5	6
5{2; 2}	4.37	4.36	4.63	5.01	5.45	7.5	8.9	7.9	0	5	5	3
5{3; 2}	4.21	4.30	4.52	4.83	5.41	7.6	8.8	7.9	0	6	5	4
5{1; 3}	4.16	4.28	4.57	4.83	5.42	7.4	9.0	7.9	0	5	6	5
5{2; 3}	4.34	4.35	4.62	5.01	5.43	7.7	8.9	8.0	0	9	3	4
5{3; 3}	4.18	4.30	4.51	4.80	5.40	7.6	8.9	7.8	0	4	3	4
(3a*S**,6*R**,7*R**,9*S**,9a*R**)-Isomers **6**												
6{4; 1}	4.12	4.05	4.89	4.92	5.35	12.3	2.6	8.2	0	0	0	5
6{5; 1}	4.33	4.02	5.03	5.42	5.41	12.4	2.3	8.0	0	0	0	4
6{4; 2}	4.29	4.16	4.98	5.04	5.48	12.2	2.6	8.3	0	0	0	4
6{5; 2}	4.52	4.08	5.09	5.56	5.56	12.4	2.2	8.2	0	0	0	8
6{4; 3}	4.27	4.10	4.98	5.03	5.46	12.2	2.5	8.3	0	0	0	4
6{5; 3}	4.50	4.07	5.09	5.53	5.53	12.4	2.3	8.3	0	0	0	6

[a] Relative intensity with respect to −100% intensity of the irradiated proton.
[b] Overlapping signals for 6-H and 7-H appeared as a multiplet.

Then, trifluoroacetic acid (5×10 drops) was added to each flask through reflux condensers, and refluxing was continued for 1 h. Upon cooling to rt, the precipitates were collected by filtration, washed with Et_2O (5×15 mL), and dried in vacuo to give the azomethine imines **3**{1–5}. The yields and physical and spectral data were identical to those reported in the literature for the conventional single-vessel synthesis of **3**{1,2,5}[21] and **3**{3,4}.[28]

The following compounds were prepared in the above manner.

5.2.1. (1*Z*,4*R,5*R**)-4-Benzoylamino-1-benzylidene-5-phenylpyrazolidin-3-on-1-azomethine imine 3{1}.** Prepared from **1** (1.405 g, 5 mmol) and benzaldehyde **2**{1} (636 mg, 6 mmol).

5.2.2. (1*Z*,4*R,5*R**)-4-Benzoylamino-1-(4-nitrobenzylidene)-5-phenylpyrazolidin-3-on-1-azomethine imine 3{2}.** Prepared from **1** (1.405 g, 5 mmol) and 4-nitrobenzaldehyde **2**{2} (906 mg, 6 mmol).

5.2.3. (1*Z*,4*R,5*R**)-4-Benzoylamino-5-phenyl-(3,4,5-trimethoxybenzylidene)pyrazolidin-3-on-1-azomethine imine 3{3}.** Prepared from **1** (1.405 g, 5 mmol) and 3,4,5-trimethoxybenzaldehyde **2**{3} (1.176 g, 6 mmol).

5.2.4. (1*Z*,4*R,5*R**)-4-Benzoylamino-5-phenyl-1-(2,4,6-trimethylbenzylidene)pyrazolidin-3-on-1-azomethine imine 3{4}.** Prepared from **1** (1.405 g, 5 mmol) and 2,4,6-trimethylbenzaldehyde **2**{4} (888 mg, 6 mmol).

5.2.5. (1*Z*,4*R,5*R**)-4-Benzoylamino-1-(2,6-dichlorobenzylidene)-5-phenylpyrazolidin-3-on-1-azomethine imine 3{5}.** Prepared from **1** (1.405 g, 5 mmol) and 2,6-dichlorobenzaldehyde **2**{5} (1.050 g, 6 mmol).

5.3. General procedure for the combinatorial preparation of cycloadducts 5 and 6

A Radley 6 Reaction Station parallel synthesizer was equipped with five 50 mL flasks. Azomethine imines **3**{1–5} (2 mmol of each) were weighed into the flasks and then *N*-methylmaleimide **4**{1} (5×2 mmol) and anhydrous anisole (5×10 mL) were added to each flask. The mixtures were heated under reflux for 6 h and then cooled to rt. The precipitates were collected by filtration, washed with Et_2O (10 mL each), and dried thoroughly in vacuo (100 °C/0.1 Torr) for 2 h to give cycloadducts **5**{1–3; 1} and **6**{4,5; 1}. Following the same procedure, azomethine imines **3**{1–5} were also reacted with *N*-phenylmaleimide **4**{2} and *N*-(4-methylphenyl)maleimide **4**{3} to give cycloadducts **5**{1–3; 2,3} and **6**{4,5; 2,3}. In summary, a library of 15 compounds, **5**{1–3; 1–3} and **6**{4,5; 1–3}, was prepared in this manner.

5.3.1. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-7,9-diphenyl-2-methyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{1; 1}.** Prepared from dipole **3**{1} (738 mg, 2 mmol) and maleimide **4**{1} (266 mg, 2.4 mmol). Yield: 524 mg (55%) of a white solid; mp 292–295 °C. ^{1}H NMR (DMSO-d_6): δ 2.87 (3H, s, Me); 4.15 (1H, dd, *J*=7.8, 8.8 Hz, 9a-H); 4.24 (1H, d, *J*=7.5 Hz, 7-H); 4.58 (1H, t, *J*=7.5 Hz, 6-H); 4.73 (1H, d, *J*=8.8 Hz, 9-H); 5.28 (1H, d, *J*=7.8 Hz, 3a-H); 7.06–7.14 (5H, m, 5H of Ph); 7.20–7.25 (5H, m, 5H of Ph); 7.50–7.60 (3H, m, 3H of Ph); 7.85–7.90 (2H, m, 2H of Ph); 9.26 (1H, d, *J*=7.5 Hz, NH). (Found: C, 70.00; H, 5.15; N, 11.63. $C_{28}H_{24}N_4O_4$ requires: C, 69.99; H, 5.03; N, 11.66.) ν_{max} (KBr) 3353 (NH); 1785, 1720, 1653 (C=O); 1535 cm^{-1}.

5.3.2. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2-methyl-9-(4-nitrophenyl)-7-phenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 5{2; 1}.** Prepared from dipole **3**{2} (828 mg, 2 mmol) and maleimide **4**{1} (266 mg, 2.4 mmol). Yield: 772 mg (73%) of a white solid; mp 287–290 °C. ^{1}H NMR (DMSO-d_6): δ 2.85 (3H, s, Me); 4.18 (1H, dd, *J*=8.0, 8.6 Hz, 9a-H); 4.28 (1H, d, *J*=7.6 Hz, 7-H); 4.61 (1H, t, *J*=7.6 Hz, 6-H); 4.88 (1H, d, *J*=8.6 Hz, 9-H); 5.29 (1H, d, *J*=8.0 Hz, 3a-H); 7.23 (4H, s, 4H of Ar); 7.40 (2H, d, *J*=8.3 Hz, 2H of Ar); 7.45–7.60 (4H, m, 4H of Ar); 7.85 (2H, d, *J*=7.2 Hz, 2H of Ar); 7.95 (2H, d, *J*=8.7 Hz, 2H of Ar); 9.25 (1H, d, *J*=7.6 Hz, NH). (Found: C, 64.17; H, 4.57; N, 13.26. $C_{28}H_{23}N_5O_6$ requires: C, 63.99; H, 4.41; N, 13.33.) ν_{max} (KBr) 3356 (NH); 1790, 1721, 1650 (C=O); 1603 cm^{-1}.

5.3.3. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2-methyl-7-phenyl-9-(3,4,5-trimethoxyphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{3; 1}.** Prepared from dipole **3**{3} (918 mg, 2 mmol) and maleimide **4**{1} (266 mg, 2.4 mmol). Yield: 973 mg (85%) of a white solid; mp 266–269 °C. EIMS: *m*/*z*=570 (M$^+$). ^{1}H NMR (DMSO-d_6): δ 2.86 (3H, s, 2-Me); 3.43, 3.55 (9H, 2s, 2:1, 3×OMe); 4.05 (1H, dd, *J*=7.7, 8.8 Hz, 9a-H); 4.22 (1H, d, *J*=7.6 Hz, 7-H); 4.51 (1H, t, *J*=7.6 Hz, 6-H); 4.68 (1H, d, *J*=8.8 Hz, 9-H); 5.25 (1H, d, *J*=7.7 Hz, 3a-H); 6.39 (2H, s, 2H of Ar); 6.90–6.98 (2H, m, 2H of Ar); 7.24–7.30 (3H, m, 3H of Ar); 7.50–7.60 (3H, m, 3H of Ar); 7.88 (2H, d, *J*=7.2 Hz, 2H of Ar); 9.24 (1H, d, *J*=7.6 Hz, NH). (Found: C, 64.95; H, 5.59; N, 9.66. $C_{31}H_{30}N_4O_7$ requires: C, 65.25; H, 5.30; N, 9.82.) ν_{max} (KBr) 3314 (NH); 1790, 1717, 1636 (C=O); 1594 cm^{-1}. EI-HRMS: *m*/*z*=570.2115 (M$^+$); $C_{31}H_{30}N_4O_7$ requires: *m*/*z*=570.2124 (M$^+$).

5.3.4. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2,7,9-triphenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo-[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{1; 2}.** Prepared from dipole **3**{1} (738 mg, 2 mmol) and maleimide **4**{2} (416 mg, 2 mmol). Yield: 800 mg (74%) of a white solid; mp 287–289 °C. ^{1}H NMR ($CDCl_3$): δ 4.05 (1H, dd, *J*=8.3, 8.6 Hz, 9a-H); 4.35–4.47 (2H, m, 6-H, 7-H); 5.04 (1H, d, *J*=8.6 Hz, 9-H); 5.52 (1H, d, *J*=8.3 Hz, 3a-H); 7.09–7.20 (7H, m, 6H of Ph, NH); 7.31–7.55 (12H, m, 12H of Ph); 7.78 (2H, d, *J*=7.2 Hz, 2H of Ph). (Found: C, 73.18; H, 4.87; N, 10.33. $C_{33}H_{26}N_4O_4$ requires: C, 73.05; H, 4.83; N, 10.33.) ν_{max} (KBr) 3395 (NH); 1790, 1725, 1656 (C=O); 1533, 1494 cm^{-1}.

5.3.5. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2,7-diphenyl-9-(4-nitrophenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{2; 2}.** Prepared from dipole **3**{2} (829 mg, 2 mmol) and maleimide **4**{2} (416 mg, 2.4 mmol). Yield: 983 mg (84%) of a white solid; mp 272–275 °C. ^{1}H NMR (DMSO-d_6): δ 4.36 (1H, d, *J*=7.5 Hz, 7-H); 4.37 (1H, dd, *J*=7.9,

8.9 Hz, 9a-H); 4.63 (1H, t, *J*=7.5 Hz, 6-H); 5.01 (1H, d, *J*=8.9 Hz, 9-H); 5.45 (1H, d, *J*=7.9 Hz, 3a-H); 7.20–7.30 (7H, m, 7H of Ar); 7.40–7.50 (8H, m, 8H of Ar); 7.88 (2H, d, *J*=8.1 Hz, 2H of Ar); 8.01 (2H, d, *J*=8.1 Hz, 2H of Ar); 9.25 (1H, d, *J*=7.5 Hz, NH). (Found: C, 67.21; H, 4.38; N, 11.79. $C_{33}H_{25}N_5O_6$ requires: C, 67.45; H, 4.29; N, 11.92.) ν_{max} (KBr) 3410 (NH); 1726, 1656 (C=O); 1602, 1524 cm^{-1}.

5.3.6. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2,7-diphenyl-9-(3,4,5-trimethoxyphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 5{3; 2}.** Prepared from dipole **3**{3} (919 mg, 2 mmol) and maleimide **4**{2} (416 mg, 2.4 mmol). Yield: 944 mg (75%) of a white solid; mp 270–272 °C. ^{1}H NMR (DMSO-d_6): δ 3.44, 3.53 (9H, 2s, 2:1, 3×OMe); 4.21 (1H, dd, *J*=7.9, 8.8 Hz, 9a-H); 4.30 (1H, d, *J*=7.6 Hz, 7-H); 4.52 (1H, t, *J*=7.6 Hz, 6-H); 4.83 (1H, d, *J*=8.8 Hz, 9-H); 5.41 (1H, d, *J*=7.9 Hz, 3a-H); 6.50 (2H, s, 2H of Ar); 7.15 (2H, d, *J*=7.2 Hz, 2H of Ar); 7.20–7.60 (11H, m, 11H of Ar); 7.90 (2H, d, *J*=7.2 Hz, 2H of Ar); 9.30 (1H, d, *J*=7.6 Hz, NH). (Found: C, 68.46; H, 5.20; N, 8.80. $C_{36}H_{32}N_4O_7$ requires: C, 68.34; H, 5.10; N, 8.86.) ν_{max} (KBr) 3366 (NH); 1793, 1726, 1665 (C=O); 1595, 1532 cm^{-1}.

5.3.7. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-7,9-diphenyl-2-(4-methylphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{1; 3}.** Prepared from dipole **3**{1} (738 mg, 2 mmol) and maleimide **4**{3} (450 mg, 2.4 mmol). Yield: 532 mg (48%) of a white solid; mp 325–326 °C. ^{1}H NMR (DMSO-d_6): δ 2.35 (3H, s, Me), 4.16 (1H, dd, *J*=7.9, 9.0 Hz, 9a-H); 4.28 (1H, d, *J*=7.4 Hz, 7-H); 4.57 (1H, t, *J*=7.4 Hz, 6-H); 4.83 (1H, d, *J*=9.0 Hz, 9-H); 5.42 (1H, d, *J*=7.9 Hz, 3a-H); 7.06 (2H, d, *J*=8.3 Hz, 2H of Ar); 7.10–7.35 (12H, m, 12H of Ar); 7.47–7.60 (3H, m, 3H of Ar); 7.90 (2H, d, *J*=6.8 Hz, 2H of Ar); 9.26 (1H, d, *J*=7.4 Hz, NH). (Found: C, 73.55; H, 5.18; N, 9.99. $C_{34}H_{28}N_4O_4$ requires: C, 73.37; H, 5.07; N, 10.07.) ν_{max} (KBr) 3351 (NH); 1798, 1721, 1650 (C=O); 1531 cm^{-1}.

5.3.8. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2-(4-methylphenyl)-9-(4-nitrophenyl)-7-phenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{2; 3}.** Prepared from dipole **3**{2} (830 mg, 2 mmol) and maleimide **4**{3} (450 mg, 2.4 mmol). Yield: 690 mg (57%) of a white solid; mp 303–305 °C. ^{1}H NMR (DMSO-d_6): δ 2.34 (3H, s, Me); 4.34 (1H, dd, *J*=8.0, 8.9 Hz, 9a-H); 4.35 (1H, d, *J*=7.7 Hz, 7-H); 4.62 (1H, t, *J*=7.7 Hz, 6-H); 5.01 (1H, d, *J*=8.9 Hz, 9-H); 5.43 (1H, d, *J*=8.0 Hz, 3a-H); 7.08 (2H, d, *J*=8.7 Hz, 2H of Ar); 7.20–7.35 (7H, m, 7H of Ar); 7.45–7.60 (5H, m, 5H of Ar); 7.88 (2H, d, *J*=7.5 Hz, 2H of Ar); 8.01 (2H, d, *J*=8.7 Hz, 2H of Ar); 9.26 (1H, d, *J*=7.7 Hz, NH). (Found: C, 68.11; H, 4.64; N, 11.63. $C_{34}H_{27}N_5O_6$ requires: C, 67.88; H, 4.52; N, 11.64.) ν_{max} (KBr) 3348 (NH); 1795, 1721, 1651 (C=O); 1524 cm^{-1}.

5.3.9. (3a*S,6*R**,7*R**,9*R**,9a*R**)-6-Benzoylamino-2-(4-methylphenyl)-7-phenyl-9-(3,4,5-trimethoxyphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 5{3; 3}.** Prepared from dipole **3**{3} (919 mg, 2 mmol) and maleimide **4**{3} (449 mg, 2.4 mmol). Yield: 982 mg (76%) of a white solid; mp 277–280 °C. ^{1}H NMR (DMSO-d_6): δ 2.34 (3H, s, 2-Me); 3.43, 3.53 (9H, 2s, 2:1, 3×OMe); 4.18 (1H, dd, *J*=7.8, 8.9 Hz, 9a-H); 4.30 (1H, d, *J*=7.6 Hz, 7-H); 4.51 (1H, t, *J*=7.6 Hz, 6-H); 4.80 (1H, d, *J*=8.9 Hz, 9-H); 5.40 (1H, d, *J*=7.8 Hz, 3-H); 6.49 (2H, s, 2H of Ar); 7.05 (2H, d, *J*=8.3 Hz, 2H of Ar); 7.22–7.35 (7H, m, 7H of Ar); 7.50–7.60 (3H, m, 3H of Ar); 7.90 (2H, dd, *J*=6.8 Hz, 2H of Ar); 9.26 (1H, d, *J*=7.6 Hz, NH). (Found: C, 69.01; H, 5.45; N, 8.64. $C_{37}H_{34}N_4O_7$ requires: C, 68.72; H, 5.30; N, 8.66.) ν_{max} (KBr) 3344 (NH); 1796, 1726, 1655, 1591 cm^{-1}.

5.3.10. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-2-methyl-7-phenyl-9-(2,4,6-trimethylphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 6{4; 1}.** Prepared from dipole **3**{4} (823 mg, 2 mmol) and maleimide **4**{1} (266 mg, 2.4 mmol). Yield: 93 mg (18%) of a white solid; mp 269–272 °C. ^{1}H NMR (DMSO-d_6): δ 1.45, 2.22, 2.40, 3.00 (12H, 4s, 1:1:1:1, 4×Me); 4.05 (1H, d, *J*=12.3 Hz, 7-H); 4.12 (1H, dd, *J*=2.6, 8.2 Hz, 9a-H); 4.89 (1H, dd, *J*=8.6, 12.3 Hz, 6-H); 4.92 (1H, d, *J*=2.6 Hz, 9-H); 5.35 (1H, d, *J*=8.2 Hz, 3a-H); 6.70 (1H, s, 1H of Ar); 7.00–7.05 (3H, m, 3H of Ar); 7.25 (3H, m, 3H of Ar); 7.40–7.55 (3H, m, 3H of Ar); 7.75 (2H, d, *J*=6.8 Hz, 2H of Ar); 8.90 (1H, d, *J*=8.6 Hz, NH). (Found: C, 71.55; H, 6.07; N, 10.62. $C_{31}H_{30}N_4O_4$ requires: C, 71.25; H, 5.79; N, 10.72.) ν_{max} (KBr) 3367 (NH); 1789, 1719, 1669 (C=O); 1604 cm^{-1}.

5.3.11. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-2-methyl-7-phenyl-9-(2,6-dichlorophenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 6{5; 1}.** Prepared from dipole **3**{5} (877 mg, 2 mmol) and maleimide **4**{1} (266 mg, 2.4 mmol). Yield: 927 mg (84%) of a white solid; mp 272–274 °C. ^{1}H NMR (DMSO-d_6): 3.02 (3H, s, Me); 4.02 (1H, d, *J*=12.4 Hz, 7-H); 4.33 (1H, dd, *J*=2.3, 8.0 Hz, 9a-H); 5.03 (1H, dd, *J*=8.9, 12.4 Hz, 6-H); 5.41 (2H, d, *J*=8.0 Hz, 3a-H); 5.42 (1H, d, *J*=2.3 Hz, 9-H); 7.07 (2H, m, 2H of Ar); 7.23 (3H, m, 3H of Ar); 7.35–7.55 (5H, m, 5H of Ar); 7.65 (1H, dd, *J*=1.1, 7.9 Hz, 1H of Ar); 7.75 (2H, dd, *J*=1.5, 7.2 Hz, 2H of Ar); 8.88 (1H, d, *J*=8.9 Hz, NH). (Found: C, 60.95; H, 4.22; N, 10.12. $C_{28}H_{22}N_4O_4Cl_2$ requires: C, 61.21; H, 4.04; N, 10.20.) ν_{max} (KBr) 3418 (NH); 1787, 1719, 1666, 1615 cm^{-1}.

5.3.12. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-2,7-diphenyl-9-(2,4,6-trimethylphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 6{4; 2}.** Prepared from dipole **3**{4} (823 mg, 2 mmol) and maleimide **4**{2} (416 mg, 2.4 mmol). Yield: 734 mg (63%) of a white solid; mp 282–284 °C. EIMS: *m*/*z*=584 (M^+). ^{1}H NMR (DMSO-d_6): 1.50, 2.22, 2.45 (9H, 3s, 1:1:1, 3×Me); 4.16 (1H, d, *J*=12.2 Hz, 7-H); 4.29 (1H, dd, *J*=2.6, 8.3 Hz, 9a-H); 4.98 (1H, dd, *J*=8.7, 12.2 Hz, 6-H); 5.04 (1H, d, *J*=2.6 Hz, 9-H); 5.48 (1H, d, *J*=8.3 Hz, 3a-H); 6.70 (1H, s, 1H of Ar); 7.00 (1H, s, 1H of Ar); 7.10 (2H, m, 2H of Ar); 7.25 (3H, m, 3H of Ar); 7.50 (8H, m, 8H of Ar); 7.75 (2H, m, 2H of Ar); 8.95 (1H, d, *J*=8.7 Hz, NH). ^{13}C NMR (DMSO-d_6): δ 20.3, 21.0, 21.2, 21.6, 22.4, 60.4, 76.6, 127.3, 127.8, 128.2, 128.3, 128.4, 128.8, 129.1, 129.2, 129.4, 130.0, 130.2, 132.5, 134.3, 137.6, 138.2, 138.7, 140.2, 167.1, 167.3, 179.9. ν_{max} (KBr) 3229 (NH); 1726,

1659, 1600, 1535 cm^{-1}. EI-HRMS: *m*/*z*=584.2424 (M^+); $C_{36}H_{32}N_4O_4$ requires: *m*/*z*=584.2435 (M^+).

5.3.13. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-9-(2,6-dichlorophenyl)-2,7-diphenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5-(2*H*,3a*H*)-trione 6{5; 2}.** From dipole **3**{5} (877 mg, 2 mmol) and maleimide **4**{2} (0.416, 2.4 mmol). Yield: 1000 mg (82%) of a white solid; mp 275–278 °C. ^{1}H NMR (DMSO-d_6): δ 4.08 (1H, d, *J*=12.4 Hz, 7-H); 4.52 (1H, dd, *J*=2.2, 8.2 Hz, 9a-H); 5.09 (1H, dd, *J*=8.8, 12.4 Hz, 6-H); 5.56 (1H, d, *J*=2.2 Hz, 9-H); 5.56 (1H, d, *J*=8.2 Hz, 3a-H); 7.15 (2H, m, 2H of Ar); 7.25 (3H, m, 3H of Ar); 7.36–7.60 (10H, m, 10H of Ar); 7.65 (1H, d, *J*=7.2 Hz, 1H of Ar); 7.76 (2H, d, *J*=7.2 Hz, 2H of Ar); 8.87 (1H, d, *J*=8.8 Hz, NH). (Found: C, 64.74; H, 4.05; N, 9.12. $C_{33}H_{24}N_4O_4Cl_2$ requires: C, 64.82; H, 3.96; N, 9.16.) ν_{max} (KBr) 3342 (NH); 1784, 1725, 1655 (C=O); 1545 cm^{-1}.

5.3.14. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-2-(4-methylphenyl)-7-phenyl-9-(2,4,6-trimethylphenyl)-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 6{4; 3}.** Prepared from dipole **3**{4} (822 mg, 2 mmol) and maleimide **4**{3} (450 mg, 2.4 mmol). Yield: 656 mg (55%) of a white solid; mp 282–283 °C. ^{1}H NMR (DMSO-d_6): δ 1.47, 2.22, 2.38, 2.45 (12H, 4s, 1:1:1:1, 4×Me); 4.10 (1H, d, *J*=12.2 Hz, 7-H); 4.27 (1H, dd, *J*=2.5, 8.3 Hz, 9a-H); 4.98 (1H, dd, *J*=8.7, 12.2 Hz, 6-H); 5.03 (1H, d, *J*=2.5 Hz, 9-H); 5.46 (1H, d, *J*=8.3 Hz, 3a-H); 6.70 (1H, s, 1H of Ar); 7.02 (1H, s, 1H of Ar); 7.10 (2H, m, 2H of Ar); 7.20–7.30 (5H, m, 5H of Ar); 7.35–7.45 (4H, m, 4H of Ar); 7.50–7.55 (1H, m, 1H of Ar); 7.75 (2H, d, *J*=7.2 Hz, 2H of Ar); 8.95 (1H, d, *J*=8.7 Hz, NH). (Found: C, 74.42; H, 5.87; N, 9.30. $C_{37}H_{34}N_4O_4$ requires: C, 74.23; H, 5.72; N, 9.36.) ν_{max} (KBr) 3282 (NH); 1796, 1725, 1634, 1549 cm^{-1}.

5.3.15. (3a*S,6*R**,7*R**,9*S**,9a*R**)-6-Benzoylamino-9-(2,6-dichlorophenyl)-2-(4-methylphenyl)-7-phenyl-6,7,9,9a-tetrahydro-5*H*-pyrazolo[1,2-*a*]pyrrolo[3,4-*c*]pyrazole-1,3,5(2*H*,3a*H*)-trione 6{5; 3}.** Prepared from dipole **3**{5} (878 mg, 2 mmol) and maleimide **4**{3} (450 mg, 2.4 mmol). Yield: 1116 mg (89%) of a white solid; mp 282–285 °C. ^{1}H NMR (DMSO-d_6): δ 2.40 (3H, s, Me); 4.07 (1H, d, *J*=12.4 Hz, 7-H); 4.50 (1H, dd, *J*=8.3, 2.3 Hz, 9a-H); 5.09 (1H, dd, *J*=8.8, 12.4 Hz, 6-H); 5.53 (1H, d, *J*=2.3 Hz, 9-H); 5.53 (1H, d, *J*=8.3 Hz, 3a-H); 7.15 (2H, m, 2H of Ar); 7.20–7.55 (12H, m, 12H of Ar); 7.65 (1H, dd, *J*=1.5, 8.3 Hz, 1H of Ar); 7.75 (2H, d, *J*=7.1 Hz, 2H of Ar); 9.02 (1H, d, *J*=8.8 Hz, NH). (Found: C, 65.18; H, 4.28; N, 8.88. $C_{34}H_{26}N_4O_4Cl_2$ requires: C, 65.29; H, 4.19; N, 8.96.) ν_{max} (KBr) 3341 (NH); 1790, 1727, 1658 (C=O); 1545 cm^{-1}.

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