Scientific paper

1,3-Dipolar Cycloadditions of (4*R**,5*R**)-1-Arylmethylidene-4-benzamido-3-oxo-5-phenylpyrazolidin-1-ium-2-ides to Di-(–)-menthyl Maleate

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Received: 16-09-2008

Dedicated to Professor Branko Stanovnik on the occasion of his 70th birthday

Abstract

1,3-Dipolar cycloadditions of racemic (1*Z*,4*R**,5*R**)-arylmethylidene-4-benzamido-5-phenyl-3-pyrazolidinon-1-azomethine imines **3** to enantiopure di-(–)-menthyl maleate (**4**) afforded mixtures of diastereomeric cycloadducts **5/5'–7/7'**. Selectivity as well as stereochemistry of cycloadditions were dependent on the substituents at the 1'-Ar residue of dipoles **3**. Thus, reactions of dipoles **3a–j** with at least one free *ortho*-position gave either di-(–)-menthyl (1*R**,2*S**,3*R**,5*R**,6*R**)-3-aryl-6-benzamido-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylates **5/5'** (the *endo*-isomers) and/or di-(–)-menthyl (1*S**,2*R**,3*R**,5*R**,6*R**)-3-aryl-6-benzamido-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylates **6/6'** (the *exo*-isomers) with *syn*-oriented 3-H and 5-H, whilst reactions of **4** with *ortho*-disubstituted dipoles **3k**,**l** gave (1*S**,2*R**,3*S**,5*R**,6*R**)-diastereomers **7/7'k**,**l** with *anti*-oriented 3-H and 5-H. Separation of diastereomeric cycloadducts **5/5'–7/7'** by crystallization and/or MPLC furnished isomerically pure compounds **5a**,**b**,**d**,**g**, **5'b**,**d**,**h**, **6c**,**d**,**j**, and **6'c**,**d**,**f** and purified mixtures of diastereomers **5/5'e**, **6/6'e**,**h**, and **7/7'k**,**l** in 1–42% yields. The relative configuration of the pyrazolo[1,2-*a*]pyrazolone structural element in the products **5/5'–7/7'** was determined by NMR.

Keywords: 1,3-dipolar cycloadditions, (–)-menthol, pyrazolidin-3-ones, azomethine imines, pyrazolo[1,2-*a*]pyrazoles, stereochemistry

1. Introduction

1,3-Dipolar cycloadditions are powerful methods for the preparation of five-membered heterocycles, since they enable access to various polyfunctionalized chiral compounds with multiple asymmetric centres, usually with excellent stereocontrol.[1] Within this context, several examples of asymmetric cycloadditions in cyclic chiral azomethine imine series have also been reported. Generally, these reactions were accompanied by high facial and *endo/exo*-selectivity and afforded the corresponding fused pyrazolines with a bridgehead N–N structural element.[2–14]

2-Aminopyrazolo[1,2-*a*]pyrazole-7-carboxylate moiety belongs to a family of heterocyclic conformationally constrained peptide mimetics.[15] It is a constituent of biologically active compounds, such as Eli-Lilly's γ-lactam antibiotics LY 186826, LY 193239, and LY 255262 (Figure 1).[4,15]

In this context, we have previously reported preparation and synthetic utilization of (4*R**,5*R**)-4-benzamido-5-phenyl-3-pyrazolidinone (**1**) and azomethine imines **3** derived from **1** and aromatic aldehydes **2**. These studies

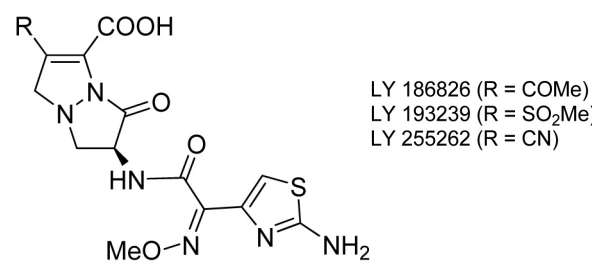
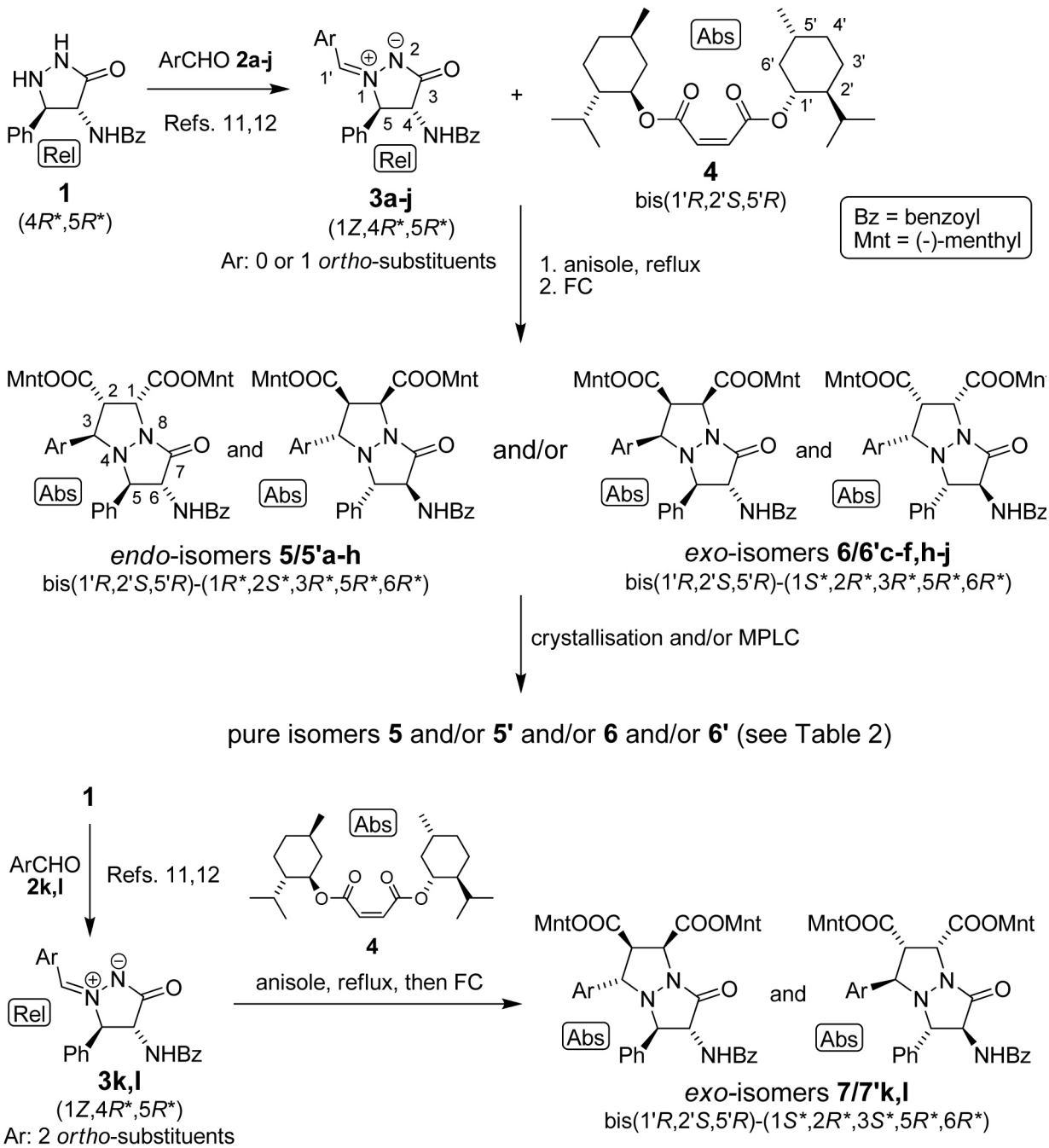


Figure 1.

were particularly focused on regioselective and stereoselective 1,3-dipolar cycloadditions of (1*Z*,4*R**,5*R**)-1-arylmethylidene-4-benzamido-5-phenyl-3-pyrazolidinon-1-azomethine imines **3** leading to polysubstituted pyrazolo[1,2-*a*]pyrazoles.[6,10–14,16,17] Generally, these cycloadditions were highly selective and stereochemistry was controlled by the stereodirecting group in the chiral dipole, by the *ortho*-substituents at the 1'-Ar group, and by the structure of the dipolarophile.[6,10–14] In extension, stereoselective combinatorial cycloadditions of these azomethine imines to maleimides[11] and β-keto esters[12] have also been reported. All these cycloadditions were carried out with racemic dipoles **3** and gave the corresponding racemic cycloadducts. In continuation, we aimed also at preparation of enantiopure pyrazolo[1,2-*a*]pyrazoles. This could be done in two ways, either by cycloaddition of enantiopure azomethine imines **3** to achiral dipolarophiles, or by cycloaddition of racemic dipoles **3** to enantiopure dipolarophiles followed by separation of the so formed diastereomeric cycloadducts. Since there is, to the best of our



Scheme 1.

knowledge, no general method for the preparation of enantiopure 4-acylamino-3-pyrazolidinone derivatives, we decided to explore cycloadditions of racemic dipoles **3** to enantiopure dipolarophiles, followed by separation of diastereomeric cycloadducts. Because previous studies showed that cycloadditions to dimethyl maleate were highly stereoselective regardless the structure of dipole,[10] di-(–)-menthyl maleate (**4**)[18] has been chosen as its chiral enantiopure analogue. Accordingly, **4** should react stereoselectively as well to furnish two diastereomeric cycloadducts, which would be then separated by crystallization or by chromatography. Herein, we report the results of this study, *i.e.* preparation of some enantiopure cycloadducts by this synthetic approach.

2. Results and Discussion

Azomethine imines **3a–l** were prepared by parallel acid-catalyzed treatment of (4*R**,5*R**)-4-benzamido-5-phenyl-3-pyrazolidinone (**1**)[6] with benzaldehydes **2a–l** according to the literature procedure.[11,12] Racemic dipoles **3a–l** were then treated with one equiv. of di-(–)-menthyl maleate (**4**)[18] in refluxing anisole followed by thorough evaporation and subsequent purification of the crude reaction mixture by flash chromatography (FC) to afford partially purified mixtures of isomeric cycloadducts **5/5'–7/7'**. On the basis of previous results[10] we expected, that all 12 dipoles **3a–l** would react stereoselectively to give two diastereomeric cycloadducts. To our surprise, however, this was the case only in reactions of seven dipoles (**3a**,**b**,**g**,**i–l**), while the other five dipoles (**3c–f**,**h**) gave mixtures of four diastereomers **5/5'/6/6'c–f**,**h** as a consequence of diminished *endo/exo*-selectivity. Thus, among azomethine imines **3a–j** with at least one free *ortho*-position at the 1'-Ar group, only dipoles **3a**,**b**,**g** gave the expected 1:1 mixtures of the *endo*-diastereomers **5/5'a**,**b**,**g**, while cycloadditions of dipoles **3c–f**,**h** gave mixtures of the major *endo*-isomers **5/5'c–f**,**h** and the minor *exo*-isomers **6/6'c–f**,**h**, and reactions of dipoles **3i** and **3j** afforded the *exo*-diastereomers **6/6'i**,**j**. On the other hand, both *ortho*-disubstituted dipoles, **3k** and **3l**, reacted selectively to afford the expected (1*S**,2*R**,3*S**,5*R**,6*R**)-diastereomers **7/7'k**,**l** (Scheme 1, Table 1).

To obtain enantiopure cycloadducts, two methods were employed for preparative separation of these mixtures of diastereomeric cycloadducts, crystallization and medium pressure liquid chromatography (MPLC). First, each mixture of diastereomers was crystallized from methanol. It has to be mentioned here, that attempts to obtain pure isomers by crystallization from other solvents were not successful. Upon crystallization from methanol, however, isomerically pure compounds **5a**,**b**, **5'b**, **6c**,**j**, and **6'f** were obtained in 1–42% yields. This method of separation was the most effective in the case of a mixture of 3-(4-nitrophenyl) substituted cycloadducts **5/5'b**, since it furnished both diastereomers, **5b** and **5'b**, in pure form. Next, the non-resolved isomeric mixtures, including filtrates obtained upon successful crystallizations, were purified by MPLC to furnish isomerically pure compounds **5d**, **5'd**,**h**, **6d**, and **6'c**,**d**, and purified mixtures of isomers **5/5'e**,**i**, **6/6'e**,**h**, and **7/7'k**,**l** (Scheme 1, Table 2).

Low *endo/exo*-electivity of cycloadditions of *ortho*-unsubstituted dipoles **3c–f**,**h** and *ortho*-monosubstituted dipoles **3i**,**j** to di-(–)-menthyl maleate (**4**) was not in agreement with high *endo*-selectivity observed previously in cycloadditions of **3a**,**b**,**d**,**e** to dimethyl maleate.[10] We do not have a firm explanation for this loss of *endo/exo*-selectivity in reactions of dipoles **3** with di-(–)-menthyl maleate (**4**), however, a similar phenomenon has already been observed previously in cycloadditions of *ortho*-unsubstituted dipoles **3a**,**b**,**e** to maleimides, which were *exo*-selective.[11] Therefore, stereocontrol in cycloadditions of dipoles **3a–j** to di-(–)-menthyl maleate (**4**) could be explained in analogous way. The dipoles **3a–j** with at least one free *ortho*-position can adopt a planar conformation **3'** where

Table 1. Selectivity of Cycloadditions.[a]

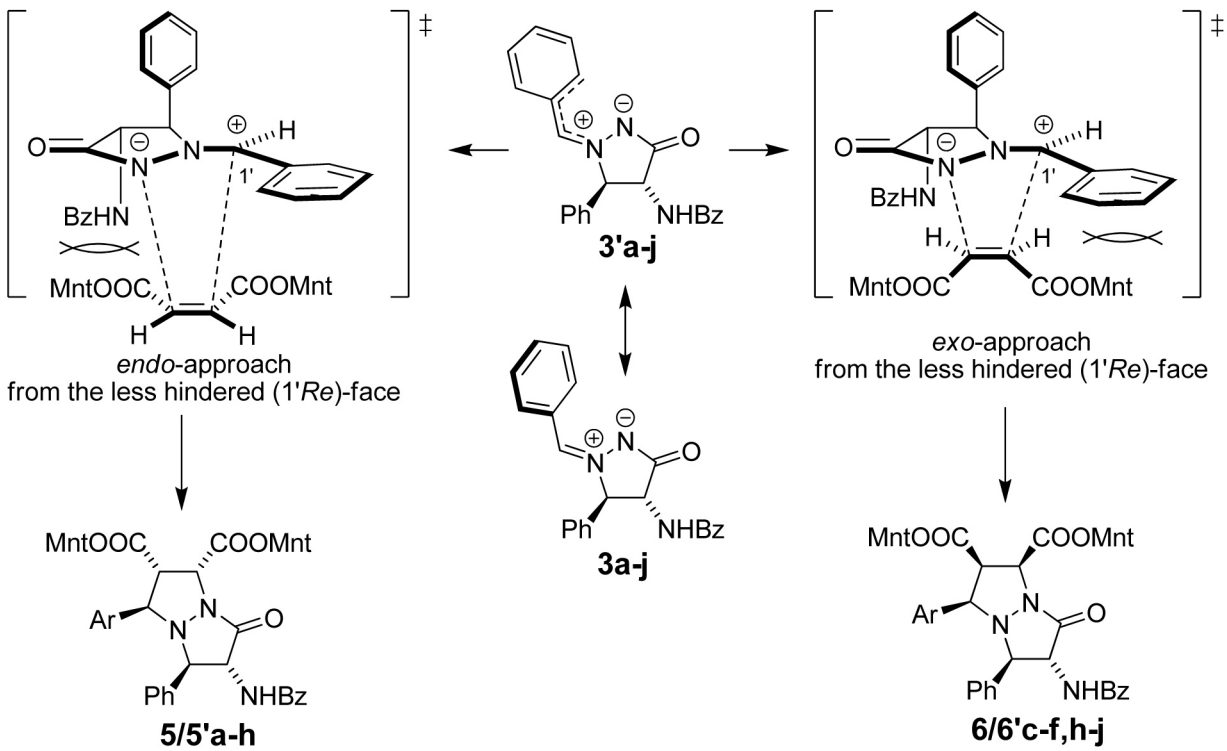
Reactants→Isomers formed	Ar	5:5':6:6'
3a+4→5a, **5a**	phenyl	56:44:0:0
3b+4→5b, **5'b**	4-nitrophenyl	54:46:0:0
3c+4→5c, **5'c**, **6c**, **6'c**	4-methylphenyl	39:37:13:11
3d+4→5d, **5'd**, **6d**, **6'd**	4-methoxyphenyl	31:29:20:20
3e+4→5e, **5'e**, **6e**, **6'e**	3,4,5-trimethoxyphenyl	39:26:18:17
3f+4→5f, **5'f**, **6f**, **6'f**	4-dimethylaminophenyl	43:27:16:14
3g+4→5g, **5'g**	2-furyl	50:50:0:0
3h+4→5h, **5'h**, **6h**, **6'h**	2-methoxyphenyl	28:25:25:22
3i+4→6i, **6'i**	3-fluorophenyl	0:0:51:49
3j+4→6j, **6'j**	2,4-dichlorophenyl	0:0:50:50
Reactants→Isomers formed	**Ar**	**7:7'**
3k+4›7k, **7'k**	2,6-dichlorophenyl	51:49
3l+4›7l, **7'l**	2,4,6-trimethylphenyl	56:44

[a] Determined by ^{1}H NMR from the spectra of the product mixtures upon FC.

Table 2. Selected Experimental Data for Compounds **5**, **5'**, **6**, **6'**, and **7/7'**.

Reactants→Isolated Isomers[a]	Ar	Separation Method[b]	Yield (%) 5	5'	6	6'	7/7'
3a+4→5a	phenyl	A	29				
3b+4→5b+5'b	4-nitrophenyl	A	32	42			
3c+4→6c+6'c	4-methylphenyl	A, B			1	2	
3d+4→5d+5'd+6d+6'd	4-methoxyphenyl	B	7	3	5	8	
3e+4→5/5'+6/6'e	3,4,5-trimethoxyphenyl	B	22[c]		11[c]		
3f+4→6f	4-dimethylaminophenyl	A				5	
3g+4→5g	2-furyl	A	6				
3h+4→5'h+6h	2-methoxyphenyl	B		6	2[c]		
3i+4→6/6'i	3-fluorophenyl	B			22[c]		
3j+4→6j	2,4-dichlorophenyl	A			21		
3k+4→7/7'k	2,6-dichlorophenyl	B					31
3l+4→7/7'l	2,4,6-trimethylphenyl	B					9

[a] Isolated isomers upon crystallization and/or chromatographic separation.
[b] A: crystallization; B: MPLC.
[c] Yield of a mixture of diastereomers **5/5'** and/or **6/6'**.



Scheme 2.

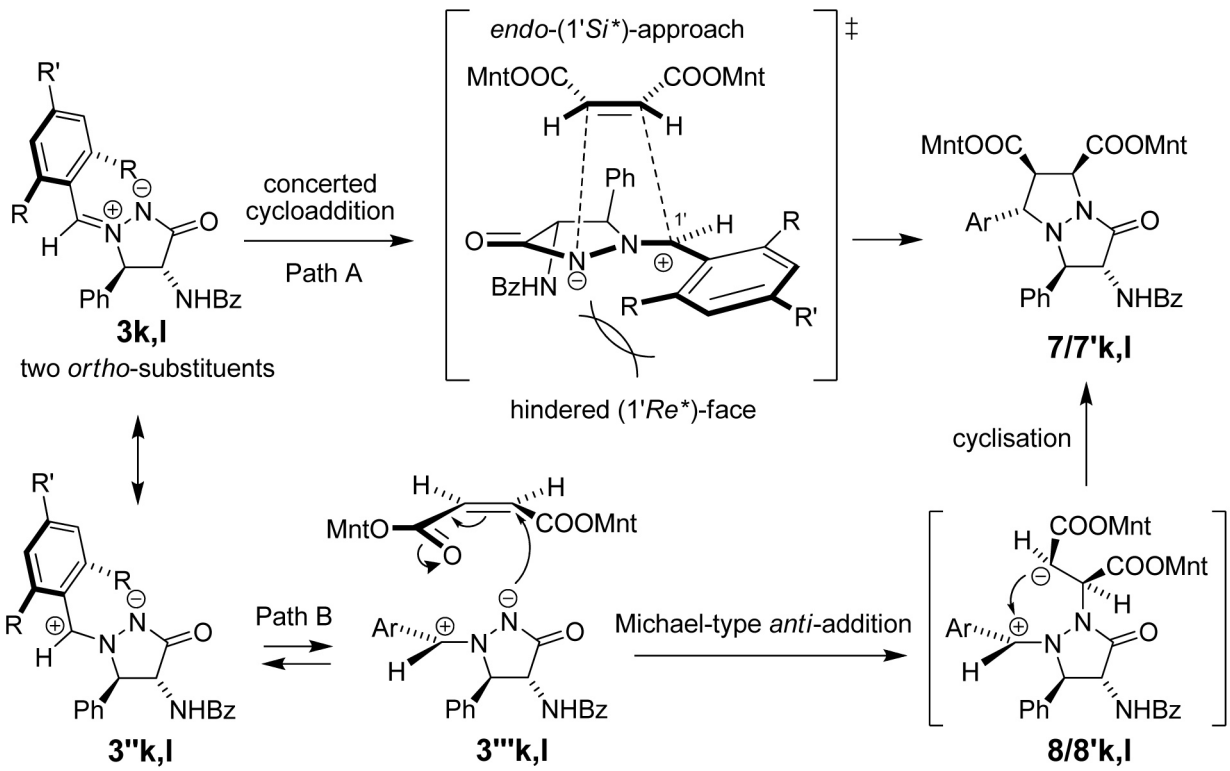
the (1'*Si*)-face is hindered by the phenyl group at position 5. In terms of facial selectivity, preferential approach of the dipolarophile from the less hindered (1'*Re*)-face is favored. In terms of *endo/exo*-selectivity, the *endo*-approach of the dipolarophile is not preferred any more, due to steric hindrance between two bulky (1'*R*,2'*S*,5'*R*)-2-isopropyl-5-methylcyclohexyl groups in the dipolarophile **4** and the benzoylamino group in the dipole **3**. Accordingly, formation of isomeric mixtures **5/5'/6/6'** is explainable by the concerted 1,3-dipolar cycloaddition mechanism *via* mixed *endo/exo*-approach of **4** from the less hindered (1'*Re*)-face of the (*Z*)-dipoles **3f**–**j** (Scheme 2).

On the other hand, selective formation of cycloadducts **7/7'k**,**l** was in agreement with stereocontrol in cycloadditions of *ortho*-disubstituted dipoles **3k**,**l** to dimethyl maleate[10] and maleimides.[11] Since *ortho*-disubstituted dipoles **3k** and **3l** cannot adopt a planar conformation **3'**, stereocontrol and mechanism of these two cycloadditions could be explained in two ways. According to the concerted 1,3-dipolar cycloaddition mechanism, the

dipoles would adopt a preferable conformation **3k**,**l**, where the (1'*Re**)-face is strongly shielded by the *ortho*-substituent facing the dipole's terminal nitrogen atom. The reaction would then proceed *via* preferential *endo*-attack of the dipolarophile from the less hindered (1'*Si**)-face of the (*Z*)-dipole (Path A, Scheme 3). Alternatively, formation of cycloadducts **7/7'k**,**l** is also explainable by a two-step addition-cyclization mechanism.[10,11] In the mesomeric structures **3"k**,**l**, rotation around the exocyclic C–N bond leads to the conformers **3'''k**,**l**, where the bulky aryl groups are twisted away from each other. Michael-type *anti*-addition of the dipolarophile **4** to the conformer **3'''** gives the zwitterion (or a biradical) **8/8'**,[19] which then cyclizes into the final product **7/7'** (Path B, Scheme 3).

while identities of **6j** and **7/7'l** were confirmed by EI-MS.

Unfortunately, we were not able to determine the absolute configuration of the isolated optically pure compounds. This should be done unambiguously by X-ray structural determination of the representative compounds **5** and/or **5'** and **6** and/or **6'**, however, all attempts to prepare suitable monocrystals failed. Nevertheless, the discrimination between the diastereomers within each diastereomeric pair **5/5'**–**7/7'** was possible by ^{1}H NMR on the basis of chemical shifts. To differentiate between the corresponding isomers **5**–**7** and **5'**–**7'**, the isomers with lower chemical shift for 2-H were assigned as the 'first' isomers **5**–**7**, while isomers with higher chemical shift for 2-H were assigned as the 'second' (adjacent) isomers **5'**–**7'**. Next,



Scheme 3.

3. Structure Determination

Structures of compounds **5/5'a**–**h**, **6/6'c**–**f**,**h**–**j**, and **7/7'k**,**l** were determined by spectroscopic methods (IR, ^{1}H NMR, ^{13}C NMR, NOESY spectroscopy, MS) and by elemental analyses for C, H, and N. Compounds **5a**,**b**,**d**, **5'b**,**d**, **6c**,**d**, and **6'c**,**d**,**f** were prepared in isomerically pure form. The isomers **5c**,**f**,**h**, **5'a**,**c**,**f**,**g**, **6f**, and **6'j** were not isolated and were characterized only by ^{1}H NMR. Compounds **5/5'e**, **6/6'e**,**h**,**i**, and **7k**,**l** were isolated and characterized as mixtures of isomers. Compounds **5b**, **6d**,**j**, and **7/7'l** were not prepared in analytically pure form. The identity of **5b** was confirmed by EI-MS and ^{13}C NMR, relative configuration at the newly formed chiral center at position 3 in compounds **5d**, **5'd**, **6d**,**j**, and **6'd** were determined by NOESY spectroscopy. A strong NOE between 3-H and 5-H was in agreement with the *syn*-orientation between these two nuclei (Figure 2).

The relative configuration at the other chiral centers were determined on the basis of chemical shifts for protons at positions 1–3, 5, and 6 and on the basis of vicinal coupling constants, $^3J_{H1–H2}$, $^3J_{H2–H3}$, and $^3J_{H5–H6}$. In cycloadducts **5/5'** and **7/7'**, the chemical shifts for protons at positions 1–3, 5, and 6, as well as coupling constants, $^3J_{H1–H2}$, $^3J_{H2–H3}$, and $^3J_{H5–H6}$ were in agreement with the data for their close dimethyl analogues.[10] Similarly, NMR

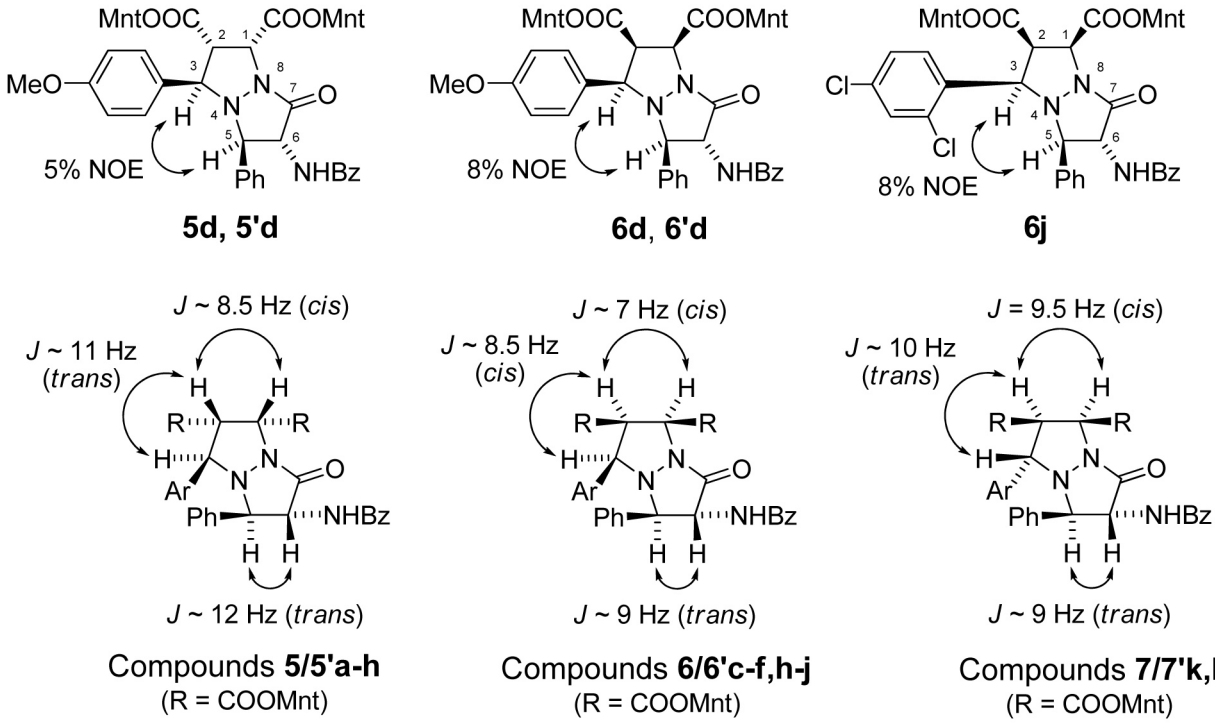


Figure 2. Structure Determination by NMR Methods.

data for the *exo*-isomers **6/6'** were in agreement with the literature data for structurally related *exo*-cycloadducts (Figure 2, Table 2).[11]

In conclusion, this study showed, that optically active di-(–)-menthyl 3-aryl-6-benzamido-7-oxo-5-phenylperhydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylates are available *via* cycloaddition of racemic (1Z,4*R**,5*R**)-1-arylmethylidene-4-benzamido-5-phenyl-3-pyrazolidinon-1-azomethine imines **3** to di-(–)-menthyl maleate (**4**) followed by separation of diastereomeric cycloadducts. From the practical point of view, this method was not very efficient, because (a) loss of *endo/exo*-selectivity often resulted in formation of four (instead of two) isomeric cycloadducts; (b) separation of diastereomers was usually complicated, and (c) the yields of the isolated optically active cycloadducts were generally low. On the other hand, this study also indicated, that the selectivity and stereocontrol in cycloadditions to azomethine imines **3** may vary significantly with increasing steric demand of the dipolarophile.

4. Experimental

4. 1. General Procedures

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 $CDCl_3$ as solvents and TMS as the internal standard. 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 Analyzer 2400. Column chromatography (CC) was performed on silica gel (Fluka, silica gel 60, 40–60 μm). Medium pressure liquid chromatography (MPLC) was performed with a Büchi isocratic system with detection on silica gel (Merck, silica gel 60, 1535 μm); column dimensions (dry filled): 15 × 460 mm; backpressure: 10–15 bar; detection: UV 254 nm; sample amount: 100–150 mg of isomeric mixture per each run. Ratio of isomers and *d.e.* were determined by ^{1}H NMR.

(4*R**,5*R**)-4-Benzamido-5-phenyl-3-pyrazolidinone (**1**),[6] azomethine imines **3a–l**[11,12] and di-(–)-menthyl maleate (**4**)[18] were prepared according to the literature procedures.

Source of chirality: (–)-Menthol (Fluka AG), product number 636600, puriss. p.a., terpene standard for GC, ≥99.0% (sum of enantiomers, GC), $[\alpha]_D^{20}$ –54.5 ± 1 (*c* = 10%, EtOH), mp ~43 °C, *e.e.* ≥98.0%.

4. 2. General Procedure for the Preparation and Separation of Isomeric Cycloadducts 5/5'–7/7'

A mixture of azomethine imine **3** (1 mmol), di-(–)-menthyl maleate (**4**) (1 mmol), and anisole (10 mL) was heated under reflux for 4 h. Volatile components were evaporated *in vacuo* (80 °C, 2–5 mbar). The residue was puri-

Table 3. Correlation of NMR data for compounds **5/5'**, **6/6'**, and **7/7'**.

(1*R**,2*S**,3*R**,5*R**,6*R**)-Isomers 5/5'								
Compound	δ [ppm]					$^3J_{H-H}$ [Hz]		
	1-H	2-H	3-H	5-H	6-H	1–2	2–3	5–6
5a	4.73	3.79	4.39	4.28	5.63	8.3	11.1	12.1
5'a	4.74	3.81	4.38	4.30	5.57	8.5	11.0	12.3
5b	4.77	3.73	4.55	4.31	5.68	8.2	11.0	12.2
5'b	4.78	3.77	4.54	4.35	5.61	8.3	11.1	12.2
5c	[a]	3.75	[a]	[a]	[a]	8.3	11.0	[a]
5'c	[a]	3.79	[a]	[a]	[a]	8.5	11.0	[a]
5d	4.71	3.74	4.34	4.26	5.61	8.3	11.1	12.0
5'd	4.72	3.76	4.33	4.27	5.56	8.5	11.1	12.0
5e	4.70	3.7[a]	4.33	4.26	5.68	8.2	11.1	12.1
5'e	4.72	3.75	4.34	4.29	5.68	8.2	11.1	12.2
5f	4.70	3.76	4.29	4.25	5.58	8.3	11.1	12.0
5'f	4.71	[a]	[a]	4.26	5.53	8.4	[a]	12.0
5g	4.75	4.14	4.51	4.31	5.48	8.4	11.1	12.1
5'g	[a]	4.17	4.54	4.39	5.36	8.5	11.1	12.0
5h	4.73	4.08	4.96	4.31	5.45	8.3	11.1	12.0
5'h	4.76	4.09	4.97	4.30	5.40	8.6	11.1	11.7
(1*S**,2*R**,3*R**,5*R**,6*R**)-Isomers 6/6'								
Compound	δ [ppm]					$^3J_{H-H}$ [Hz]		
	1-H	2-H	3-H	5-H	6-H	1–2	2–3	5–6
6c	5.04	3.47	4.17	4.69	5.67	6.4	9.2	9.2
6'c	5.12	3.56	4.17	4.39	4.86	7.1	9.3	8.6
6d	5.04	3.46	4.15	4.69	5.66	6.5	9.2	9.4
6'd	5.12	3.54	4.15	4.38	4.86	7.3	9.5	9.0
6e	5.08	3.51	4.24	4.41	4.84	7.5	9.5	9.3
6'e	5.15	3.54	4.29	4.40	4.78	6.5	8.6	8.1
6f	5.10	3.59	4.17	4.40	4.80	5.9	8.7	6.9
6'f	5.11	3.54	4.08	4.38	4.86	7.2	9.4	8.3
6h	5.10	3.65	[a]	4.47	4.93	3.9	6.8	6.6
6'h	5.11	3.69	[a]	4.43	5.00	4.8	7.4	7.0
6i	5.12	3.55	4.25	4.41	~4.8[a]	7.1	9.3	9.4
6'i	5.16	3.61	4.32	4.41	~4.8[a]	5.9	8.7	7.6
6j	5.12	3.61	4.86	4.44	5.05	4.8	7.0	7.7
6'j	5.14	3.64	[a]	4.46	4.97	4.6	6.8	6.7
(1*S**,2*R**,3*S**,5*R**,6*R**)-Isomers 7/7'								
Compound	δ [ppm]					$^3J_{H-H}$ [Hz]		
	1-H	2-H	3-H	5-H	6-H	1–2	2–3	5–6
7k	5.83	4.80	5.29	4.31	5.09	9.6	8.2	9.8
7'k	5.91	4.84	5.30	4.36	5.09	9.7	8.3	10.2
7l	č4.9[a]	4.19	5.07	4.38	~4.9[a]	9.4	10.7	4.7
7'l	5.03	4.24	~4.9[a]	4.35	~4.9[a]	8.6	10.5	6.2

[a] Overlapped by other signals.

fied by flash chromatography (FC, silica gel, EtOAc–hexanes, 1:2). Fractions containing the isomeric products were combined and evaporated *in vacuo* to give mixtures of isomeric cycloadducts **5/5'a**,**b**,**g**, **5/5'/6/6'c–f**,**h**, **6/6'i**,**j**, and **7/7'k**,**l**. These isomeric mixtures were then separated by crystallization from methanol or/and MPLC (EtOAc–hexanes) to give isomerically pure compounds **5a**,**b**,**d**,**g**, **5'b**,**d**,**h**, **6c**,**d**,**j**, and **6'c**,**d**,**f** and purified mixtures of isomers **5/5'e**,**i**, **6/6'e**,**h** and **7/7'k**,**l**.

The following compounds were prepared in this manner:

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R, 2*S**,3*R**,5*R**,6*R**)-6-benzamido-3,5-diphenyl-7-oxohexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'a.** Prepared from **4** and dipole **3a** (369 mg, 1 mmol), **5a**:**5'a** = 56:44, crystallization of **5/5'a** from methanol afforded isomerically pure compound **5a**.

Data for compound 5a. Yield: 211 mg (29%) of a white solid; mp 220–224 °C (from MeOH); $[\alpha]_D^{21}$ –61.6 (*c* = 0.1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.34, 0.47, 0.81, 0.87, 0.91, 0.95 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.55–1.85 (16H, m, 16H of menthyl); 1.93–2.04

(1H, m, 1H of menthyl); 2.26–2.35 (1H, m, 1H of menthyl); 3.79 (1H, dd, *J* = 8.3, 11.1 Hz, 2-H); 4.28 (1H, d, *J* = 12.1 Hz, 5-H); 4.39 (1H, d, *J* = 11.1 Hz, 3-H); 4.54 (1H, dt, *J* = 4.4, 10.8 Hz, 1'-H); 4.73 (1H, dd, *J* = 0.8, 8.3 Hz, 1-H); 4.81 (1H, dt, *J* = 4.3, 10.8 Hz, 1'-H); 5.63 (1H, dd, *J* = 8.5, 12.1 Hz, 6-H); 6.54 (1H, d, *J* = 8.5 Hz, NH); 6.93–7.03 (6H, m, 6H of Ph); 7.07–7.20 (4H, m, 4H of Ph); 7.34–7.41 (2H, m, 2H of Ph); 7.43–7.49 (1H, m, 1H of Ph); 7.68–7.74 (2H, m, 2H of Ph). (Found: C, 73.99; H, 7.93; N, 5.51. $C_{47}H_{59}N_3O_6$ requires: C, 74.08; H, 7.80; N, 5.51.); IR, ν_{max} (KBr): 3368 (NH), 2952, 2928, 2867, 1729 (C=O), 1648 (C=O), 1521, 1457, 1385, 1184, 960, 764, 694 cm^{-1}.

^{1}H NMR data for compound 5'a. ^{1}H NMR ($CDCl_3$): δ 0.61, 0.70, 0.78, 0.86, 0.89, 0.94 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 3.81 (1H, dd, *J* = 8.5, 11.0 Hz, 2-H); 4.30 (1H, d, *J* = 12.3 Hz, 5-H); 4.38 (1H, d, *J* = 11.0 Hz, 3-H); 4.74 (1H, dd, *J* = 0.7, 8.5 Hz, 1-H); 5.57 (1H, dd, *J* = 8.2, 12.3 Hz, 6-H); 6.55 (1H, d, *J* = 8.2 Hz, NH).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R,2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(4-nitrophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'b.** Prepared from **4** and dipole **3b** (414 mg, 1 mmol), **5b**:**5'b** = 54:46, crystallization from methanol afforded isomerically pure compound **5b**. Subsequent evaporation of the filtrate gave isomerically pure compound **5'b**.

Data for compound 5b. Yield: 224 mg (32%) of a yellowish solid; mp 207–209 °C (from MeOH); $[\alpha]_D^{23}$ –24.7 (*c* = 0.012, CH_2Cl_2). EI-MS: *m/z* = 807 (M^+). ^{1}H NMR ($CDCl_3$): δ 0.41, 0.49, 0.81, 0.87, 0.92, 0.96 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.71–1.83 (16H, m, 16H of menthyl); 1.91–2.04 (1H, m, 1H of menthyl); 2.23–2.32 (1H, m, 1H of menthyl); 3.73 (1H, dd, *J* = 8.2, 11.0 Hz, 2-H); 4.31 (1H, d, *J* = 12.2 Hz, 5-H); 4.55 (1H, d, *J* = 11.0 Hz, 3-H); 4.56 (1H, dt, *J* = 4.4, 10.9 Hz, 1'-H); 4.77 (1H, dd, *J* = 0.7, 8.2 Hz, 1-H); 4.81 (1H, dt, *J* = 4.4, 10.9 Hz, 1'-H); 5.68 (1H, dd, *J* = 8.4, 12.2 Hz, 6-H); 6.52 (1H, d, *J* = 8.4 Hz, NH); 6.96–7.03 (3H, m, 3H of Ar); 7.16–7.23 (2H, m, 2H of Ar); 7.30–7.42 (4H, m, 4H of Ar); 7.45–7.50 (1H, m, 1H of Ar); 7.66–7.73 (2H, m, 2H of Ar); 7.84–7.91 (2H, m, 2H of Ar). ^{13}C NMR ($CDCl_3$): δ 16.08, 16.14, 20.85, 21.44, 22.27, 22.42, 23.13, 25.61, 25.77, 31.91, 32.00, 34.26, 34.53, 40.89, 41.15, 47.22, 58.08, 58.26, 60.60, 70.07, 76.31, 78.59, 79.58, 123.37, 127.67, 128.51, 128.54, 128.84, 129.24, 129.48, 132.23, 133.78, 134.20, 142.74, 148.03, 164.69, 166.45, 167.62, 167.96. (Found: C, 68.85; H, 7.83; N, 7.08. $C_{47}H_{58}N_4O_8$ requires: C, 69.95; H, 7.24; N, 6.94.); IR, ν_{max} (KBr): 3433 (NH), 2957, 2929, 2868, 1724 (C=O), 1652 (C=O), 1524, 1456, 1349, 1206, 1177, 1110, 980, 954, 851, 697 cm^{-1}.

Data for compound 5'b. Yield: 297 mg (42%) of a yellowish solid; mp 120–123 °C (from MeOH); $[\alpha]_D^{23}$ –67.6 (*c* = 0.13, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.60, 0.67, 0.81, 0.86, 0.95, 0.96 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.71–1.79 (16H, m, 16H of menthyl); 2.10–2.22 (2H, m, 2H of menthyl); 3.77 (1H, dd, *J* = 8.3, 11.1 Hz, 2-H); 4.35 (1H, d, *J* = 12.2 Hz, 5-H); 4.54 (1H, d, *J* = 11.1 Hz, 3-H); 4.56 (1H, dt, *J* = 4.4, 10.9 Hz, 1'-H); 4.78 (1H, dd, *J* = 0.7, 8.3 Hz, 1-H); 4.81 (1H, dt, *J* = 4.4, 10.9 Hz, 1'-H); 5.61 (1H, dd, *J* = 8.5, 12.2 Hz, 6-H); 6.52 (1H, d, *J* = 8.5 Hz, NH); 6.96–7.03 (3H, m, 3H of Ar); 7.16–7.23 (2H, m, 2H of Ar); 7.30–7.42 (4H, m, 4H of Ar); 7.43–7.50 (1H, m, 1H of Ar); 7.66–7.73 (2H, m, 2H of Ar); 7.84–7.91 (2H, m, 2H of Ph). (Found: C, 69.93; H, 7.56; N, 6.83. $C_{47}H_{58}N_4O_8$ requires: C, 69.95; H, 7.24; N, 6.94.); IR, ν_{max} (KBr): 3429 (NH), 2955, 2929, 2868, 1735 (C=O), 1671 (C=O), 1525, 1457, 1348, 1208, 980, 953, 851, 697 cm^{-1}.

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R,2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(4-methylphenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'c and (1*S**,2*R**,3*R**,5*R**,6*R**)-isomer 6/6'c.** Prepared from **4** and dipole **3c** (383 mg, 1 mmol), **5c**:**5'c**:**6c**:**6'c** = 39:37:13:11, crystallization from methanol afforded isomerically pure compound **6c**. Evaporation of the filtrate followed by separation by MPLC afforded isomerically pure compound **6'c**.

^{1}H NMR data for compound 5c. ^{1}H NMR ($CDCl_3$): δ 3.75 (1H, dd, *J* = 8.3, 11.0 Hz, 2-H).

^{1}H NMR data for compound 5'c. ^{1}H NMR ($CDCl_3$): δ 3.79 (1H, dd, *J* = 8.5, 11.0 Hz, 2-H).

Data for compound 6c. Yield: 10 mg (1%) of a white solid; mp 200–206 °C (from MeOH); $[\alpha]_D^{23}$ –130.9 (*c* = 0.008, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.65, 0.74, 0.82 (9H, 3d, 1:1:1, *J* = 6.9 Hz, 3 × *Me*CH); 0.78–0.97 (13H, m, 3 × *Me*CH and 4H of menthyl); 0.97–1.60 (8H, m, 8H of menthyl); 1.61–1.78 (3H, m, 3H of menthyl); 1.94–2.12 (3H, m, 3H of menthyl); 2.19 (3H, s, *Me*Ar); 3.47 (1H, dd, *J* = 6.4, 9.2 Hz, 2-H); 4.17 (1H, d, *J* = 9.2 Hz, 3-H); 4.69 (1H, d, *J* = 9.2 Hz, 5-H); 4.71 and 4.89 (2H, 2dt, 1:1, *J* = 4.3, 10.7 Hz, 2 × 1'-H); 5.04 (1H, d, *J* = 6.4 Hz, 1-H); 5.67 (1H, dd, *J* = 7.9, 9.2 Hz, 6-H); 5.84 (1H, d, *J* = 7.9 Hz, NH); 7.09 (2H, d, *J* = 7.9 Hz, 2H of C_6H_4); 7.19–7.28 (5H, m, 2H of C_6H_4 and 3H of Ph); 7.30–7.38 (6H, m, 6H of Ph); 7.39–7.47 (1H, m, 1H of Ph). (Found: C, 74.49; H, 8.22; N, 5.67. $C_{48}H_{61}N_3O_6$ requires: C, 74.29; H, 7.92; N, 5.41.); IR, ν_{max} (KBr): 3423 (NH), 2954, 2928, 2866, 1732 (C=O), 1656 (C=O), 1521, 1456, 1372, 1231, 1182, 1099, 1150, 983, 819, 704 cm^{-1}.

Data for compound 6'c. Yield: 18 mg (2%) of a white solid; mp 240–242 °C; $[\alpha]_D^{23}$ –28.6 (*c* = 0.005, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.56, 0.65, 0.83, 0.90, 0.92, 0.93 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.75–1.60 (12H, m, 12H of menthyl); 1.60–1.70 (3H, m, 3H of menthyl); 1.95–2.09 (3H, m, 3H of menthyl); 2.20 (3H, s, *Me*Ar); 3.56 (1H, dd, *J* = 7.1, 9.3 Hz, 2-H); 4.17 (1H, d, *J* = 9.3 Hz, 3-H); 4.39 (1H, d, *J* = 8.6 Hz, 5-H);

4.68 and 4.84 (2H, 2dt, 1:1, J = 4.3, 10.7 Hz, 2 × 1'-H); 4.86 (1H, dd, J = 7.0, 8.6 Hz, 6-H); 5.12 (1H, d, J = 7.1 Hz, 1-H); 6.71 (1H, d, J = 7.0 Hz, NH); 6.89 (2H, d, J = 7.9 Hz, 2H of C_6H_4); 7.06 (2H, d, J = 7.9 Hz, 2H of C_6H_4); 7.11–7.19 (3H, m, 3H of Ph); 7.31–7.37 (2H, m, 2H of Ph); 7.38–7.46 (2H, m, 2H of Ph); 7.47–7.54 (1H, m, 1H of Ph); 7.75–7.81 (2H, m, 2H of Ph). (Found: C, 74.43; H, 8.17; N, 5.41. $C_{48}H_{61}N_3O_6$ requires: C, 74.29; H, 7.92; N, 5.41.); IR, ν_{max} (KBr): 3443 (NH), 2955, 2920, 2866, 1732 (C=O), 1679 (C=O), 1524, 1454, 1389, 1233, 1182, 1113, 1150, 953, 700 cm^{-1}.

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R,2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(4-methoxyphenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'd and (1*S**,2*R**,3*R**,5*R**,6*R**)-isomer 6/6'd.** Prepared from **4** and dipole **3d** (399 mg, 1 mmol), **5c**:**5'c**:**6c**:**6'c** = 31:29:20:20, separation by MPLC afforded isomerically pure compounds **5d**, **5'd**, **6d**, and **6'd**.

Data for compound 5d. Yield: 56 mg (7%) of a white solid; mp 196–200 °C; $[\alpha]_D^{26}$ –50.1 (c = 0.06, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.34, 0.48, 0.81, 0.88, 0.90, 0.95 (18H, 6d, 1:1:1:1:1:1, J = 6.7 Hz, 6 × *Me*CH); 0.75–1.64 (13H, m, 13H of menthyl); 1.65–1.85 (3H, m, 3H of menthyl); 1.90–2.06 (1H, m, 1H of menthyl); 2.25–2.36 (1H, m, 1H of menthyl); 3.65 (3H, s, OMe); 3.74 (1H, dd, J = 8.3, 11.1 Hz, 2-H); 4.26 (1H, d, J = 12.0 Hz, 5-H); 4.34 (1H, d, J = 11.1 Hz, 3-H); 4.53 (1H, dt, J = 4.4, 10.9 Hz, 1'-H); 4.71 (1H, dd, J = 0.7, 8.3 Hz, 1-H); 4.79 (1H, dt, J = 4.4, 10.9 Hz, 1'-H); 5.61 (1H, dd, J = 8.5, 12.0 Hz, 6-H); 6.53 (2H, d, J = 8.8 Hz, 2H of C_6H_4); 6.57 (1H, d, J = 8.5 Hz, NH); 6.96–7.06 (5H, m, 2H of C_6H_4 and 3H of Ph); 7.13–7.21 (2H, m, 2H of Ph); 7.33–7.41 (2H, m, 2H of Ph); 7.42–7.50 (1H, m, 1H of Ph); 7.67–7.75 (2H, m, 2H of Ph). (Found: C, 72.90; H, 8.00; N, 5.27. $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.); IR, ν_{max} (KBr): 3429 (NH), 2955, 2931, 2868, 1727 (C=O), 1647 (C=O), 1518, 1456, 1381, 1249, 1189, 1119, 1134, 957, 694 cm^{-1}.

Data for compound 5'd. Yield: 25 mg (3%) of a white solid; mp 175–178 °C; $[\alpha]_D^{26}$ –43.7 (c = 0.012, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.62, 0.72, 0.79, 0.86, 0.94, 0.95 (18H, 6d, 1:1:1:1:1:1, J = 6.7 Hz, 6 × *Me*CH); 0.69–1.64 (14H, m, 14H of menthyl); 1.65–1.77 (2H, m, 2H of menthyl); 2.10–2.22 (2H, m, 2H of menthyl); 3.65 (3H, s, OMe); 3.76 (1H, dd, J = 8.5, 11.1 Hz, 2-H); 4.27 (1H, d, J = 12.0 Hz, 5-H); 4.33 (1H, d, J = 11.1 Hz, 3-H); 4.50 (1H, dt, J = 4.4, 10.9 Hz, 1'-H); 4.72 (1H, dd, J = 0.7, 8.5 Hz, 1-H); 4.82 (1H, dt, J = 4.4, 11.1 Hz, 1'-H); 5.56 (1H, dd, J = 8.5, 12.0 Hz, 6-H); 6.54 (2H, d, J = 8.8 Hz, 2H of C_6H_4); 6.60 (1H, d, J = 8.4 Hz, NH); 6.96–7.06 (5H, m, 2H of C_6H_4 and 3H of Ph); 7.15–7.22 (2H, m, 2H of Ph); 7.33–7.41 (2H, m, 2H of Ph); 7.42–7.50 (1H, m, 1H of Ph); 7.67–7.74 (2H, m, 2H of Ph). (Found: C, 72.89; H, 7.95; N, 5.30 $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.); IR, ν_{max} (KBr): 3397 (NH), 2951, 2930, 2866, 1732 (C=O), 1642 (C=O), 1516, 1457, 1370, 1254, 1206, 1175, 1030, 959, 826, 706 cm^{-1}.

Data for compound 6d. Yield: 37 mg (5%) of a white solid; mp 91–94 °C; $[\alpha]_D^{26}$ –18.7 (c = 0.062, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.65, 0.74, 0.82, (9H, 3d, 1:1:1, J = 6.9 Hz, 3 × *Me*CH); 0.90, 0.91, 0.94, (9H, 3d, 1:1:1, J = 6.6 Hz, 3 × *Me*CH); 0.79–1.52 (12H, m, 12H of menthyl); 1.62–1.79 (3H, m, 3H of menthyl); 1.93–2.13 (3H, m, 3H of menthyl); 3.46 (1H, dd, J = 6.5, 9.2 Hz, 2-H); 3.76 (3H, s, OMe); 4.15 (1H, d, J = 9.2 Hz, 3-H); 4.69 (1H, d, J = 9.4 Hz, 5-H); 4.71 and 4.89 (2H, 2dt, 1:1, J = 4.4, 10.9 Hz, 2 × 1'-H); 5.04 (1H, d, J = 6.5 Hz, 1-H); 5.66 (1H, dd, J = 7.9, 9.4 Hz, 6-H); 5.84 (1H, d, J = 7.9 Hz, NH); 6.81 (2H, d, J = 8.8 Hz, 2H of C_6H_4); 7.19–7.38 (11H, m, 2H of C_6H_4 and 9H of Ph); 7.39–7.47 (1H, m, 1H of Ph). (Found: C, 72.29; H, 8.04; N, 5.31. $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.); IR, ν_{max} (KBr): 3441 (NH), 2955, 2928, 2868, 1734 (C=O), 1655 (C=O), 1516, 1457, 1370, 1251, 1179, 704 cm^{-1}.

Data for compound 6'd. Yield: 60 mg (8%) of a white solid; mp 215–218 °C; $[\alpha]_D^{26}$ –18.7 (c = 0.008, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.56, 0.66, 0.84, (9H, 3d, 1:1:1, J = 6.8 Hz, 3 × *Me*CH); 0.90, 0.92, 0.94, (9H, 3d, 1:1:1, J = 6.5 Hz, 3 × *Me*CH); 0.72–1.28 (9H, m, 9H of menthyl); 1.37–1.54 (3H, m, 3H of menthyl); 1.60–1.78 (3H, m, 3H of menthyl); 1.95–2.09 (3H, m, 3H of menthyl); 3.54 (1H, dd, J = 7.3, 9.5 Hz, 2-H); 3.68 (3H, s, OMe); 4.15 (1H, d, J = 9.5 Hz, 3-H); 4.38 (1H, d, J = 9.0 Hz, 5-H); 4.68 and 4.84 (2H, 2dt, 1:1, J = 4.4, 10.8 Hz, 2 × 1'-H); 4.86 (1H, dd, J = 6.8, 9.0 Hz, 6-H); 5.12 (1H, dd, J = 0.5, 7.3 Hz, 1-H); 6.62 (2H, d, J = 8.8 Hz, 2H of C_6H_4); 6.72 (1H, d, J = 6.8 Hz, NH); 7.09 (2H, d, J = 8.8 Hz, 2H of C_6H_4); 7.10–7.18 (3H, m, 3H of Ph); 7.28–7.35 (2H, m, 2H of Ph); 7.37–7.46 (2H, m, 2H of Ph); 7.47–7.54 (1H, m, 1H of Ph); 7.74–7.81 (2H, m, 2H of Ph). (Found: C, 72.97; H, 7.92; N, 5.33. $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.); IR, ν_{max} (KBr): 3447 (NH), 2957, 2928, 2868, 1731 (C=O), 1678 (C=O), 1517, 1456, 1387, 1250, 1176, 1031, 953, 829, 702 cm^{-1}.

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R,2*S**,3*R**,5*R**,6*R**)-6-benzamido-7-oxo-5-phenyl-3-(3,4,5-trimethoxyphenyl)hexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'e and (1*S**,2*R**,3*R**,5*R**,6*R**)-isomer 6/6'e.** Prepared from **4** and dipole **3e** (459 mg, 1 mmol), **5e**:**5'e**:**6e**:**6'e** = 39:26:18:17, separation by MPLC afforded purified mixtures of isomers **5/5'e** and **6/6'e**.

Data for a mixture of compounds 5/5'e. Yield: 189 mg (22%) of a white solid, **5e**:**5'e** = 50:50; mp 91–94 °C; $[\alpha]_D^{26}$ –49.6 (c = 0.082, CH_2Cl_2). (Found: C, 70.69; H, 8.02; N, 4.77 $C_{50}H_{65}N_3O_9$ requires: C, 70.48; H, 7.69; N, 4.93.); IR, ν_{max} (KBr): 3374 (NH), 2955, 2930, 2870, 1732 (C=O), 1669 (C=O), 1593, 1535, 1508, 1459, 1371, 1234, 1184, 1126, 1009, 912, 845, 698 cm^{-1}.

^{1}H NMR data for compound 5e. ^{1}H NMR ($CDCl_3$): δ 0.37–0.96 (18H, m, 6 × *Me*CH); 0.72–1.64 (10H, m, 10H of menthyl); 1.65–1.77 (4H, m, 4H of menthyl); 1.91–2.02 (1H, m, 1H of menthyl); 2.07–2.23 (2H, m, 2H of menthyl); 2.25–2.34 (1H, m, 1H of menthyl); 3.66, 3.69, 3.70 (9H, 3s, 1:1:1, 3 × OMe); 3.7 (1H, overlapped by OMe signals, 2-H); 4.26 (1H, d, *J* = 12.1 Hz, 5-H); 4.33 (1H, d, *J* = 11.1 Hz, 3-H); 4.55 (1H, dt, *J* = 4.4, 10.6 Hz, 1'-H); 4.70 (1H, dd, *J* = 0.5, 8.2 Hz, 1-H); 4.82 (1H, dt, *J* = 4.4, 10.6 Hz, 1'c-H); 5.68 (1H, dd, *J* = 8.5, 12.1 Hz, 6-H); 6.33 (2H, s, C_6H_2); 6.60 (1H, d, *J* = 8.5 Hz, NH); 6.99–7.06 (3H, m, 3H of Ar); 7.16–7.24 (2H, m, 2H of Ph); 7.32–7.42 (2H, m, 2H of Ph); 7.43–7.50 (1H, m, 1H of Ph); 7.68–7.75 (2H, m, 2H of Ph).

^{1}H NMR data for compound 5'e. ^{1}H NMR ($CDCl_3$): δ 0.37–0.96 (18H, m, 6 × *Me*CH); 0.72–1.64 (10H, m, 10H of menthyl); 1.65–1.77 (4H, m, 4H of menthyl); 1.91–2.02 (1H, m, 1H of menthyl); 2.07–2.23 (2H, m, 2H of menthyl); 2.25–2.34 (1H, m, 1H of menthyl); 3.66, 3.69, 3.70 (9H, 3s, 1:1:1, 3 × OMe); 3.75 (1H, dd, *J* = 8.2, 11.1 Hz, 2-H); 4.29 (1H, d, *J* = 12.3 Hz, 5-H); 4.34 (1H, d, *J* = 11.1 Hz, 3-H); 4.55 (1H, dt, *J* = 4.4, 10.6 Hz, 1'-H); 4.72 (1H, dd, *J* = 0.5, 8.2 Hz, 1-H); 4.82 (1H, dt, *J* = 4.4, 10.6 Hz, 1'-H); 5.68 (1H, dd, *J* = 8.5, 12.2 Hz, 6-H); 6.35 (2H, s, C_6H_2); 6.63 (1H, d, *J* = 8.5 Hz, NH); 6.99–7.06 (3H, m, 3H of Ph); 7.16–7.24 (2H, m, 2H of Ph); 7.32–7.42 (2H, m, 2H of Ph); 7.43–7.50 (1H, m, 1H of Ph); 7.68–7.75 (2H, m, 2H of Ph).

Data for a mixture of compounds 6/6'e. Yield: 96 mg (11%) of a white solid, **6e**:**6'e** = 40:60; mp 206–212 °C; $[\alpha]_D^{26}$ –31.8 (*c* = 0.06, CH_2Cl_2). (Found: C, 70.68; H, 7.99; N, 4.90 $C_{50}H_{65}N_3O_9$ requires: C, 70.48; H, 7.69; N, 4.93.); IR, ν_{max} (KBr): 3438 (NH), 3359 (NH), 2956, 2929, 2868, 1734 (C=O), 1712 (C=O), 1667 (C=O), 1597, 1537, 1509, 1462, 1427, 1371, 1327, 1236, 1204, 1128, 957, 700 cm^{-1}.

^{1}H NMR data for compound 6e. ^{1}H NMR ($CDCl_3$): δ 0.56–0.96 (18H, m, 6 × *Me*CH); 0.68–1.64 (11H, m, 11H of menthyl); 1.63–1.76 (4H, m, 4H of menthyl); 1.81–2.13 (3H, m, 3H of menthyl); 3.51 (1H, dd, *J* = 7.5, 9.5 Hz, 2-H); 3.62 and 3.69 (9H, 2s, 2:1, 3 × OMe); 4.24 (1H, d, *J* = 9.5 Hz, 3-H); 4.41 (1H, d, *J* = 9.3 Hz, 5-H); 4.72 and 4.84 (2H, 2dt, 1:1, *J* = 4.4, 10.9 Hz, 2 × 1'-H); 4.84 (1H, dd, *J* = 7.0, 9.3 Hz, 6-H); 5.08 (1H, d, *J* = 7.5 Hz, 1-H); 6.40 (2H, s, C_6H_2); 6.75 (1H, d, *J* = 7.0 Hz, NH); 7.11–7.23 (3H, m, 3H of Ph); 7.28–7.46 (4H, m, 4H of Ph); 7.47–7.55 (1H, m, 1H of Ar); 7.74–7.82 (2H, m, 2H of Ph).

^{1}H NMR data for compound 6'e. ^{1}H NMR ($CDCl_3$): δ 3.54 (1H, dd, *J* = 6.5, 8.6 Hz, 2-H); 3.61 and 3.71 (9H, 2s, 2:1, 3 × OMe); 4.29 (1H, d, *J* = 8.6 Hz, 3-H); 4.40 (1H, d, *J* = 8.1 Hz, 5-H); 5.15 (1H, d, *J* = 6.5 Hz, 1-H); 4.78 (1H, dd, *J* = 7.2, 8.1 Hz, 6-H); 6.43 (2H, s, C_6H_2); 6.82 (1H, d, *J* = 7.2 Hz, NH).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*S,2*R**,3*R**,5*R**,6*R**)-6-benzamido-3-(4-dimethylaminophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 6/6'f and (1*R**,2*S**,3*R**,5*R**,6*R**)-isomer 5/5'f**. Prepared from **4** and dipole **3f** (412 mg, 1 mmol), **5f**:**5'f**:**6f**:**6'f** = 43:27:14:16, crystallization from methanol afforded a pure isomer **6'f**.

^{1}H NMR data for compound 5f. ^{1}H NMR ($CDCl_3$): 2.79 (6H, s, NMe_2); 3.76 (1H, dd, *J* = 8.3, 11.1 Hz, 2-H); 4.25 (1H, d, *J* = 12.0 Hz, 5-H); 4.29 (1H, d, *J* = 11.1 Hz, 3-H); 4.53 (1H, dt, *J* = 4.2, 10.9 Hz, 1'-H); 4.70 (1H, dd, *J* = 0.5, 8.3 Hz, 1-H); 4.79 (1H, dt, *J* = 4.2, 10.9 Hz, 1'-H); 5.58 (1H, dd, *J* = 9.0, 12.0 Hz, 6-H); 6.35 (2H, d, *J* = 8.8 Hz, 2H of C_6H_4); 6.60 (1H, d, *J* = 9.0 Hz, NH).

^{1}H NMR data for compound 5'f. ^{1}H NMR ($CDCl_3$): δ 2.78 (6H, s, NMe_2); 4.26 (1H, d, *J* = 12.0 Hz, 5-H); 4.71 (1H, dd, *J* = 0.5, 8.4 Hz, 1-H); 5.53 (1H, dd, *J* = 8.4, 12.0 Hz, 6-H); 6.36 (2H, d, *J* = 8.8 Hz, 2H of C_6H_4); 6.59 (1H, d, *J* = 8.4 Hz, NH).

^{1}H NMR data for compound 6f. ^{1}H NMR ($CDCl_3$): δ 2.84 (6H, s, NMe_2); 3.59 (1H, dd, *J* = 5.9, 8.7 Hz, 2-H); 4.17 (1H, d, *J* = 8.7 Hz, 3-H); 4.40 (1H, d, *J* = 6.9 Hz, 5-H); 4.73 (1H, dt, *J* = 4.4, 10.67 Hz, 1'-H); 4.80 (1H, br t, *J* = 6.5 Hz, 6-H); 4.86 (1H, dt, *J* = 4.4, 10.6 Hz, 1'-H); 5.10 (1H, d, *J* = 5.8 Hz, 1-H); 6.47 (2H, d, *J* = 8.8 Hz, 2H of C_6H_4); 6.76 (1H, d, *J* = 6.3 Hz, NH).

Data for compound 6'f. Yield: 41 mg (5%) of a white solid; mp 231–234 °C (from MeOH; $[\alpha]_D^{23}$ –12.9 (*c* = 0.06, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.56, 0.65, 0.84, 0.90, 0.92, 0.93 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.78–1.64 (6H, m, 6H of menthyl); 1.37–1.78 (9H, m, 9H of menthyl); 1.96–2.09 (3H, m, 3H of menthyl); 2.82 (6H, s, NMe_2); 3.54 (1H, dd, *J* = 7.2, 9.4 Hz, 2-H); 4.08 (1H, d, *J* = 9.4 Hz, 3-H); 4.38 (1H, d, *J* = 8.3 Hz, 5-H); 4.67 (1H, dt, *J* = 4.3, 10.6 Hz, 1'-H); 4.84 (1H, dt, *J* = 4.3, 10.6 Hz, 1'-H); 4.86 (1H, dd, *J* = 6.8, 8.3 Hz, 6-H); 5.11 (1H, d, *J* = 7.2 Hz, 1-H); 6.43 (2H, d, *J* = 8.8 Hz, 2H of C_6H_4); 6.71 (1H, d, *J* = 6.8 Hz, NH); 7.01 (2H, d, *J* = 8.8 Hz, 2H of C_6H_4); 7.08–7.21 (3H, m, 3H of Ph); 7.33–7.47 (4H, m, 4H of Ph); 7.47–7.55 (1H, m, 1H of Ph); 7.74–7.84 (2H, m, 2H of Ph). (Found: C, 73.17; H, 8.14; N, 6.91 $C_{49}H_{64}N_4O_6$ requires: C, 73.10; H, 8.01; N, 6.96.); IR, ν_{max} (KBr): 3427 (NH), 2957, 2931, 2868, 1732 (C=O), 1680 (C=O), 1616, 1526, 1452, 1362, 1274, 1231, 1186, 1099, 953, 812, 704 cm^{-1}.

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R,2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(2-furyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'g.** Prepared from **4** and dipole **3g** (359 mg, 1 mmol), **5g**:**5'g** = 50:50, crystallization from methanol afforded isomerically pure compound **5g**.

Data for compound 5g. Yield: 45 mg (6%) of a white solid; mp 204–207 °C (from MeOH); $[\alpha]_D^{23}$ –41.8 (*c* = 0.08, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.47, 0.68, 0.80, 0.89, 0.92, 0.94 (18H, 6d, 1:1:1:1:1:1, *J* = 6.7 Hz, 6 × *Me*CH); 0.73–1.76 (15H, m, 15H of menthyl); 1.79–1.89 (1H, m, 1H of menthyl); 1.94–2.07 (1H, m, 1H of men-

thyl); 2.22–2.31 (1H, m, 1H of menthyl); 4.14 (1H, dd, *J* = 8.4, 11.1 Hz, 2-H); 4.31 (1H, d, *J* = 12.1 Hz, 5-H); 4.51 (1H, d, *J* = 11.1 Hz, 3-H); 4.59 (1H, dt, *J* = 4.3, 10.9 Hz, 1'-H); 4.75 (1H, dd, *J* = 0.5, 8.4 Hz, 1-H); 4.78 (1H, dt, *J* = 4.3, 10.9 Hz, 1'-H); 5.48 (1H, dd, *J* = 8.4, 12.0 Hz, 6-H); 5.86 (1H, dd, *J* = 0.6, 3.3 Hz, 1H of furan); 5.94 (1H, dd, *J* = 1.8, 3.3 Hz, 1H of furan); 6.51 (1H, d, *J* = 8.4 Hz, NH); 7.07–7.17 (4H, m, 3H of Ph, 1H of furan); 7.19–7.27 (2H, m, 2H of Ph); 7.35–7.43 (2H, m, 2H of Ph); 7.44–7.52 (1H, m, 1H of Ph); 7.68–7.76 (2H, m, 2H of Ph). (Found: C, 71.92; H, 7.81; N, 5.45. $C_{45}H_{57}N_3O_7$ requires: C, 71.88; H, 7.64; N, 5.59.); IR, ν_{max} (KBr): 3462 (NH), 2951, 2926, 2868, 1728 (C=O), 1645 (C=O), 1523, 1389, 1188, 1129, 694 cm^{-1}.

^{1}H NMR data for compound 5'g. ^{1}H NMR ($CDCsl_3$): δ 4.17 (1H, dd, *J* = 8.5, 11.1 Hz, 2-H); 4.39 (1H, d, *J* = 12.0 Hz, 5-H); 4.54 (1H, d, *J* = 8.5 Hz, 3-H); 5.36 (1H, dd, *J* = 8.4, 12.0 Hz, 6-H).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R, 2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(2-methoxyophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 5/5'h and (1*S**,2*R**,3*R**,5*R**, 6*R**)-isomer 6/6'h.** Prepared from **4** and dipole **3h** (399 mg, 1 mmol), **5h**:**5'h**:**6h**:**6'h** = 28:25:25:22, separation by MPLC afforded a pure isomer **5'h** and a purified mixture of isomers **6/6'h**.

^{1}H NMR data for compound 5h. ^{1}H NMR ($CDCl_3$): δ 0.32, 0.52, 0.81, 0.86, 0.92, 0.95 (18H, 6d, 1:1:1:1:1:1, *J* = 6.9 Hz, 6 × *Me*CH); 3.59 (3H, s, OMe); 4.08 (1H, br dd, *J* = 8.3, 11.1 Hz, 2-H); 4.31 (1H, d, *J* = 12.0 Hz, 5-H); 4.51 (1H, dt, *J* = 4.3, 10.9 Hz, 1'-H); 4.73 (1H, dd, *J* = 0.5, 8.3 Hz, 1-H); 4.78 (1H, dt, *J* = 4.3, 10.9 Hz, 1'-H); 4.96 (1H, br d, *J* = 11.1 Hz, 3-H); 5.45 (1H, dd, *J* = 8.5, 12.0 Hz, 6-H); 6.55 (1H, d, *J* = 8.5 Hz, NH).

Data for compound 5'h. Yield: 41 mg (6%) of a white solid; mp 95–97 °C; $[\alpha]_D^{28}$ –40.4 (*c* = 0.06, CH_2Cl_2). EI-MS: *m/z* = 792 (M^+). ^{1}H NMR ($CDCl_3$): δ 0.53, 0.62, 0.80, 0.87, 0.94, 0.96 (18H, 6d, 1:1:1:1:1:1, *J* = 6.9 Hz, 6 × *Me*CH); 0.67–1.60 (13H, m, 13H of menthyl); 1.62–1.79 (3H, m, 3H of menthyl); 2.14–2.28 (2H, m, 2H of menthyl); 3.61 (3H, s, OMe); 4.09 (1H, br t, *J* = 9.5 Hz, 2-H); 4.30 (1H, d, *J* = 11.7 Hz, 5-H); 4.47 (1H, dt, *J* = 4.5, 10.9 Hz, 1'-H); 4.76 (1H, dd, *J* = 0.7, 8.6 Hz, 1-H); 4.84 (1H, dt, *J* = 4.5, 10.9 Hz, 1'-H); 4.97 (1H, br d, *J* = 11.1 Hz, 3-H); 5.40 (1H, dd, *J* = 8.3, 11.7 Hz, 6-H); 6.43 (1H, d, *J* = 8.1 Hz, 1H of C_6H_4); 6.53 (1H, d, *J* = 8.3 Hz, NH); 6.69 (1H, t, *J* = 7.5 Hz, 1H of C_6H_4); 6.90–7.00 (4H, m, 4H of Ph); 7.10–7.18 (2H, m, 2H of Ph); 7.21 (1H, br d, *J* = 7.3 Hz, 1H of Ar); 7.34–7.42 (2H, m, 2H of Ar); 7.43–7.50 (1H, m, 1H of Ar); 7.67–7.75 (2H, m, 2H of Ar). (Found: C, 73.10; H, 8.13; N, 5.06 $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.); IR, ν_{max} (KBr): 3423 (NH), 1735 (C=O), 1672 (C=O) cm^{-1}.

Data for a mixture of compounds 6/6'h. Yield: 14 mg (2%) of a white solid, **6h**:**6'h** = 50:50; mp 81–84 °C. (Found: C, 72.50; H, 8.11; N, 5.22 $C_{48}H_{61}N_3O_7$ requires: C, 72.79; H, 7.76; N, 5.31.).

NMR Data for compound 6h. ^{1}H NMR ($CDCl_3$): δ 0.60–0.95 (18H, m, 6 × *Me*CH); 0.73–1.60 (13H, m, 13H of menthyl); 1.63–1.76 (3H, m, 3H of menthyl); 1.98–2.09 (2H, m, 2H of menthyl); 3.62 (3H, s, OMe); 3.65 (1H, dd, *J* = 3.9, 6.8 Hz, 2-H); 4.47 (1H, d, *J* = 6.6 Hz, 5-H); 4.69–4.87 (3H, m, 2 × 1'-H, 3-H); 4.93 (1H, dd, *J* = 5.7, 6.6 Hz, 6-H); 5.10 (1H, d, *J* = 3.9 Hz, 1-H); 6.65 (1H, dd, *J* = 0.6, 8.2 Hz, 1H of C_6H_4); 6.74–6.82 (1H, m, 1H of C_6H_4); 7.04–7.30 (5H, m, 4H of Ar and NH); 7.37–7.56 (5H, m, 5H of Ar); 7.60–7.67 (1H, m, 1H of Ar); 7.82–7.90 (2H, m, 2H of Ph).

NMR Data for compound 6'h. 0.60–0.95 (18H, m, 6 × *Me*CH); 0.73–1.60 (13H, m, 13H of menthyl); 1.63–1.76 (3H, m, 3H of menthyl); 1.98–2.09 (2H, m, 2H of menthyl); 3.64 (3H, s, OMe); 3.69 (1H, dd, *J* = 4.8, 7.4 Hz, 2-H); 4.43 (1H, d, *J* = 7.0 Hz, 5-H); 4.69–4.87 (3H, m, 2 × 1'-H, 3-H); 5.00 (1H, t, *J* = 7.0 Hz, 6-H); 5.11 (1H, d, *J* = 4.8 Hz, 1-H); 6.69 (1H, dd, *J* = 0.5, 7.6 Hz, 1H of C_6H_4); 6.74–6.82 (1H, m, 1H of C_6H_4); 7.04–7.30 (5H, m,4H of Ar and NH); 7.37–7.56 (5H, m, 5H of Ar); 7.60–7.67 (1H, m, 1H of Ar); 7.82–7.90 (2H, m, 2H of Ph).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*S, 2*R**,3*R**,5*R**,6*R**)-6-benzamido-3-(3-fluorophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 6/6'i.** Prepared from **4** and dipole **3i** (387 mg, 1 mmol), **6i**:**6'i** = 51:49, purification by MPLC afforded a purified mixture of isomers **6/6'i**.

Data for a mixture of compounds 6/6'i. Yield: 170 mg (22%) of a white solid, **6i**:**6'i** = 55:45, mp 95–99 °C; $[\alpha]_D^{23}$ –38.4 (*c* = 0.047, CH_2Cl_2). (Found: C, 72.49; H, 7.79; N, 5.34. $C_{47}H_{58}FN_3O_6$ requires: C, 72.37; H, 7.50; N, 5.39.); IR, ν_{max} (KBr): 3361 (NH), 2957, 2929, 2871, 1734 (C=O), 1656 (C=O), 1536, 1489, 1454, 1371, 1267, 1228, 1186, 1150, 982, 956, 785, 696 cm^{-1}.

^{1}H NMR Data for compound 6i. ^{1}H NMR ($CDCl_3$): δ 0.56–0.98 (22H, m, 6 × *Me*CH and 4H of menthyl); 0.99–1.56 (8H, m, 8H of menthyl); 1.61–1.78 (4H, m, 4H of menthyl); 1.93–2.13 (2H, m, 2H of menthyl); 3.55 (1H, dd, *J* = 7.1, 9.3 Hz, 2-H); 4.25 (1H, d, *J* = 9.3 Hz, 3-H); 4.41 (1H, d, *J* = 9.4 Hz, 5-H); 4.66–4.90 (3H, m, 2 × 1'-H, 6-H); 5.12 (1H, dd, *J* = 0.5, 7.1 Hz, 1-H); 6.74–6.87 (2H, m, 1H of Ar, NH); 6.87–7.10 (3H, m, 3H of Ar); 7.12–7.23 (3H, m, 3H of Ar); 7.27–7.34 (1H, m, 1H of Ar); 7.35–7.45 (3H, m, 3H of Ar); 7.46–7.55 (1H, m, 1H of Ar); 7.74–7.11 (2H, m, 2H of Ar).

^{1}H NMR data for compound 6'i. ^{1}H NMR ($CDCl_3$): δ 0.56–0.98 (22H, m, 6 × *Me*CH and 4H of menthyl); 0.99–1.56 (8H, m, 8H of menthyl); 1.61–1.78 (4H, m, 4H of menthyl); 1.93–2.13 (2H, m, 2H of menthyl); 3.61 (1H, dd, *J* = 5.9, 8.7 Hz, 2-H); 4.32 (1H, d, *J* = 8.7 Hz, 3-H); 4.41 (1H, d, *J* = 7.6 Hz, 5-H); 4.66–4.90 (3H, m, 2 × 1'-H, 6-H); 5.16 (1H, d, *J* = 5.9 Hz, 1-H); 6.74–6.87 (2H, m, 1H

of Ar, NH); 6.87–7.10 (3H, m, 3H of Ar); 7.12–7.23 (3H, m, 3H of Ar); 7.27–7.34 (1H, m, 1H of Ar); 7.35–7.45 (3H, m, 3H of Ar); 7.46–7.55 (1H, m, 1H of Ar); 7.74–7.11 (2H, m, 2H of Ar).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R, 2*S**,3*R**,5*R**,6*R**)-6-benzamido-3-(2,4-dichlorophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 6/6'j.** Prepared from **4** and dipole **3j** (438 mg, 1 mmol), **6j**:**6'j** = 50:50, crystallization from methanol afforded isomerically pure compound **6j**.

Data for compound 6j. Yield: 174 mg (21%) of a white solid; mp 210–213 °C (from MeOH); $[\alpha]_D^{21}$ –32.3 (*c* = 0.08, CH_2Cl_2). EI-MS: *m/z* = 792 (M^+). ^{1}H NMR ($CDCl_3$): δ 0.70 (3H, d, *J* = 6.9 Hz, *Me*CH); 0.75–1.15 (17H, m, 17H of menthyl); 1.22–1.60 (9H, m, 9H of menthyl); 1.61–1.76 (5H, m, 5H of menthyl); 1.83–2.17 (2H, m, 2H of menthyl); 3.61 (1H, dd, *J* = 4.8, 7.0 Hz, 2-H); 4.44 (1H, d, *J* = 7.7 Hz, 5-H); 4.70–4.84 (2H, m, 2 × 1'-H); 4.86 (1H, d, *J* = 7.0 Hz, 3-H); 5.05 (1H, t, *J* = 7.5 Hz, 6-H); 5.12 (1H, d, *J* = 4.8 Hz, 1-H); 7.01 (1H, d, *J* = 7.4 Hz, NH); 7.07 (1H, dd, *J* = 2.0, 8.5 Hz, 1H of Ar); 7.18–7.23 (3H, m, 3H of Ar); 7.36–7.57 (7H, m, 7H of Ar); 7.79–7.87 (2H, m, 2H of Ar). (Found: C, 67.46; H, 6.86; N, 5.17. $C_{47}H_{57}Cl_2N_3O_6$ requires: C, 67.94; H, 6.91; N, 5.06.); IR, ν_{max} (KBr): 3445 (NH), 2955, 2927, 2868, 1734 (C=O), 1676 (C=O), 1526, 1478, 1456, 1372, 1273, 1232, 1194, 1151, 1100, 982, 955, 793, 702 cm^{-1}.

^{1}H NMR data for compound 6'j. ^{1}H NMR ($CDCl_3$): δ 3.64 (1H, dd, *J* = 4.6, 6.8 Hz, 2-H); 4.46 (1H, d, *J* = 6.7 Hz, 5-H); 4.97 (1H, t, *J* = 7.0 Hz, 6-H); 5.14 (1H, d, *J* = 4.6 Hz, 1-H).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*S, 2*R**,3*S**,5*R**,6*R**)-6-benzamido-3-(2,6-dichlorophenyl)-7-oxo-5-phenylhexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 7/7'k.** Prepared from **4** and dipole **3k** (438 mg, 1 mmol), **7k**:**7'k** = 51:49, purification by MPLC afforded a purified mixture of compounds **7/7'k**.

Data for a mixture of compounds 7/7'k. Yield: 258 mg (31%) of a white solid, **7k**:**7'k** = 51:49, mp 109–113 °C; $[\alpha]_D^{26}$ –43.8 (*c* = 0.1, CH_2Cl_2). (Found: C, 67.64; H, 7.16; N, 5.08. $C_{47}H_{57}Cl_2N_3O_6$ requires: C, 67.94; H, 6.91; N, 5.06.); IR, ν_{max} (KBr): 3441 (NH), 2957, 2930, 2870, 1733 (C=O), 1662 (C=O), 1536, 1450, 1370, 1290, 1204, 1098, 954, 773, 697 cm^{-1}.

^{1}H NMR data for compound 7k. ^{1}H NMR ($CDCl_3$): δ 0.57–0.96 (18H, m, 6 × *Me*CH); 0.70–1.65 (13H, m, 13H of menthyl); 1.66–1.77 (2H, m, 2H of menthyl); 1.92–2.19 (3H, m, 3H of menthyl); 4.31 (1H, d, *J* = 9.8 Hz, 5-H); 4.52–4.68 (1H, m, 1'-H); 4.75–4.86 (1H, m, 1'-H); 4.80 (1H, dd, *J* = 8.2, 9.6 Hz, 2-H); 5.09 (1H, dd, *J* = 7.90, 9.8 Hz, 6-H); 5.29 (1H, d, *J* = 8.2 Hz, 3-H); 5.83 (1H, d, *J* = 9.6 Hz, 1-H); 6.45 (1H, d, *J* = 7.9 Hz, NH); 7.01–7.20 (6H, m, 6H of Ar); 7.23–7.31 (2H, m, 2H of Ar); 7.34–7.42 (2H, m, 2H of Ar); 7.43–7.52 (1H, m, 1H of Ar); 7.66–7.74 (2H, m, 2H of Ar).

^{1}H NMR data for compound 7'k. ^{1}H NMR ($CDCl_3$): δ 0.57–0.96 (18H, m, 6 × *Me*CH); 0.70–1.65 (13H, m, 13H of menthyl); 1.66–1.77 (2H, m, 2H of menthyl); 1.92–2.19 (3H, m, 3H of menthyl); 4.36 (1H, d, *J* = 10.2 Hz, 5-H); 4.52–4.68 (1H, m, 1'-H); 4.75–4.86 (1H, m, 1'-H); 4.84 (1H, dd, *J* = 8.3, 9.7 Hz, 2-H); 5.09 (1H, dd, *J* = 7.9, 10.2 Hz, 6-H); 5.30 (1H, d, *J* = 8.3 Hz, 3-H); 5.91 (1H, d, *J* = 9.7 Hz, 1-H); 6.50 (1H, d, *J* = 7.9 Hz, NH); 7.01–7.20 (6H, m, 6H of Ar); 7.23–7.31 (2H, m, 2H of Ar); 7.34–7.42 (2H, m, 2H of Ar); 7.43–7.52 (1H, m, 1H of Ar); 7.66–7.74 (2H, m, 2H of Ar).

Bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl] (1*R, 2*S**,3*R**,5*S**,6*S**)-6-benzamido-7-oxo-5-phenyl-3-(2,4,6-trimethylphenyl)hexahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate 7/7'l.** Prepared from **4** and dipole **3l** (412 mg, 1 mmol), **7k**:**7'k** = 56:44, purification by MPLC afforded a purified mixture of compounds **7/7'l**.

Data for a mixture of compounds 7/7'l. Yield: 69 mg (9%) of a white solid, **7k**:**7'k** = 47:53, mp 105–109 °C; $[\alpha]_D^{28}$ –42.2 (*c* = 0.07, CH_2Cl_2). EI-MS: *m/z* = 803 (M^+). (Found: C, 74.13; H, 8.40; N, 5.13. $C_{50}H_{65}N_3O_6$ requires: C, 74.69; H, 8.15; N, 5.23.); IR, ν_{max} (KBr): 3429 (NH), 2956, 2929, 2870, 1734 (C=O), 1665 (C=O), 1533, 1456, 1371, 1288, 1180, 1096, 955, 698 cm^{-1}.

^{1}H NMR data for compound 7l. ^{1}H NMR ($CDCl_3$): δ 0.36–0.99 (18H, m, 6 × *Me*CH); 0.63–2.30 (18H, m, 18H of menthyl); 1.38, 2.15, 2.16 (9H, 3s, 1:1:1, 3 × *Me*Ar); 4.19 (1H, dd, *J* = 9.4, 10.7 Hz, 2-H); 4.38 (1H, d, *J* = 4.7 Hz, 5-H); 4.43–4.57 (1H, m, 1'-H); 4.80–4.97 (3H, m, 1'–H, 1-H, and 6-H); 5.07 (1H, d, *J* = 10.7 Hz, 3-H); 6.66 (1H, d, *J* = 6.8 Hz, NH); 6.46 and 6.74 (2H, 2br s, 1:1, C_6H_2); 7.07–7.14 (1H, m, 1H of Ph); 7.15–7.29 (3H, m, 3H of Ph); 7.35–7.45 (3H, m, 3H of Ph); 7.45–7.55 (1H, m, 1H of Ph); 7.68–7.78 (2H, m, 2H of Ph).

^{1}H NMR data for compound 7'l. ^{1}H NMR ($CDCl_3$): δ 0.36–0.99 (18H, m, 6 × *Me*CH); 0.63–2.30 (18H, m, 18H of menthyl); 1.50, 2.56, 2.57 (9H, 3s, 1:1:1, 3 × *Me*Ar); 4.24 (1H, dd, *J* = 8.6, 10.5 Hz, 2-H); 4.35 (1H, d, *J* = 6.2 Hz, 5-H); 4.43–4.57 (1H, m, 1'-H); 4.80–4.97 (3H, m, 1'-H, 3-H, and 6-H); 5.03 (1H, d, *J* = 8.6 Hz, 1-H); 6.60 (1H, d, *J* = 6.9 Hz, NH); 6.46 and 6.74 (2H, 2br s, 1:1, C_6H_2); 7.07–7.14 (1H, m, 1H of Ph); 7.15–7.29 (3H, m, 3H of Ph); 7.35–7.45 (3H, m, 3H of Ph); 7.45–7.55 (1H, m, 1H of Ph); 7.68–7.78 (2H, m, 2H of Ph).

5. Acknowledgements

The financial support from the Ministry of Science and Technology, Slovenia through grants P0-0502-0103, P1-0179, and J1-6689-0103-04 is gratefully acknowledged. We acknowledge with thanks the financial support from pharmaceutical companies Krka d.d. (Novo mesto,

Slovenia) and Lek d.d., a new Sandoz company (Ljubljana, Slovenia).

The authors wish to express their gratitude to the Alexander von Humboldt Foundation, Germany, for the donation of a Büchi medium pressure liquid chromatograph.

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Povzetek

1.3-Dipolarne cikloadicije racemnih (1*Z*,4*R**,5*R**)-1-arilmetiliden-4-benzamido-5-fenil-3-pirazolidinon-1-azometin iminov **3** na optično aktivni dipolarofil, di-(–)-mentil maleat (**4**), so vodile do zmesi diastereomernih cikloaduktov **5/5'**–**7/7'**. Selektivnost in stereokemija cikloadicij sta bili odvisni od substituentov na arilni skupini na položaju 1' dipolov **3**. Tako so reakcije dipolov **3a**–**j** z vsaj eno prosto *orto*-pozicijo vodile do zmesi dveh ali štirih izomernih cikloaduktov, bis[(1'*R*,2'*S*,5'*R*)-2-izopropil-5-metilcikloheksil] (1*R**,2*S**,3*R**,5*R**,6*R**)-3-aril-6-benzamido-5-fenil-7-oksoheksahidropirazolo[1,2-*a*]pirazol-1,2-dikarboksilatov **5/5'** (*endo*-izomerov) in/ali bis[(1'*R*,2'*S*,5'*R*)-2-izopropil-5-metilcikloheksil] (1*S**,2*R**,3*R**,5*R**,6*R**)-3-aril-6-benzamido-5-fenil-7-oksoheksahidropirazolo[1,2-*a*]pirazol-1,2-dikarboksilatov **6/6'** (*ekso*-isomerov) s *sin*-orientacijo med protonoma na položajih 3 in 5. Pri reakcijah dipolarofila **4** z *orto*-disubstituiranima dipoloma **3k**,**l** pa so nastale zmesi (1*S**,2*R**,3*S**,5*R**,6*R**)-diastereomerov **7/7'k**,**l** z *anti*-orientiranima protonoma 3 in 5. Ločbe diastereomernih cikloaduktov **5/5'**–**7/7'** smo izvajali s kristalizacijo in/ali s preparativno tekočinsko kromatografijo (MPLC), pri čemer smo izolirali izomerno čiste spojine **5a**,**b**,**d**,**g**, **5'b**,**d**,**h**, **6c**,**d**,**j** in **6'c**,**d**,**f** ter očiščene zmesi diastereomerov **5/5'e**, **6/6'e**,**h** in **7/7'k**,**l** z nizkimi do zmernimi izkoristki. Relativno konfiguracijo na pirazolo[1,2-*a*]pirazolonskem strukturnem elementu produktov **5/5'**–**7/7'** smo določili z NMR spektroskopijo.