Applications of Aziridinium Ions: Selective Syntheses of Pyrazolidin-3-ones and Pyrazolo[1,2-*a*]pyrazoles

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Dedicated to our colleague Professor *Albert Eschenmoser* on the occasion of his 75th birthday

Reaction of ethyl (2*S**,3*R**)-3-chloro-2-(dialkylamino)-3-phenylpropanoates (**4**) with hydrazine monohydrate gave pyrazolidin-3-ones (**5**) *via* selective opening of the *in situ* generated aziridinium ions, followed by intramolecular amidation. (1*Z*,4*S**,5*S**)-1-Arylmethylidene-4-(dialkylamino)-3-oxo-5-phenylpyrazolidinium-1-ide (**6**), prepared from pyrazolidin-3-ones (**5**) and aromatic aldehydes under acid catalysis, reacted with a variety of 1,3-dipolarophiles to afford good yields of pure cycloadducts **7**–**11**. The cycloaddition regio- and/or stereoselectivities, in all relevant cases, were also high.

Introduction. – Aziridinium ions have received considerable attention in biological studies [1], but in contrast to epoxides, aziridines and, particularly, aziridinium ions, have been underutilized in organic synthesis. However, thanks to outstanding efforts by several groups, the popularity of these reactive intermediates in synthetic schemes is growing rapidly [2]. The beauty of *N*,*N*-dialkylated aziridinium ions is that they can be generated *in situ* under mild conditions and then captured irreversibly by a wide range of nucleophiles, whereas simple *N*-H or *N*-alkyl aziridines require activation by an acidic agent. For simple aziridines then, the latter requirement precludes many of the most useful reagents, since nucleophiles by nature tend to be 'basic'.

1,3-Dipolar cycloadditions are widely recognized as being among the most powerful methods for the elaboration of complex molecules [3]. The stereospecific nature of these concerted processes is one of their most appreciated attributes. A first-rate manifestation of the power of these transformations is provided by the azomethine cycloadditions that create the skeleton of pyrazolo[1,2-*a*]pyrazoles [4]. These heterocycles have shown excellent activity against penicillin-binding proteins [4][5].

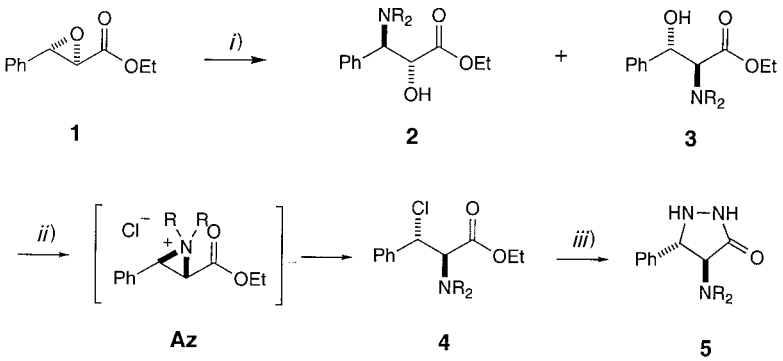
In the course of our endeavors to develop synthetic applications of aziridinium ions, we encountered a very efficient aziridinium-ion-based amine-opening route to α,β-diamino esters, with the analogous α,β-epoxy esters as the starting materials [6]. When hydrazine hydrate was used in place of the amine, the initial aziridinium ring-opening step was followed by immediate cyclization to create unusual pyrazolidin-3-ones, which are ideal precursors of azomethines. The present study was undertaken to connect this fast and reliable aziridinium-ion route to azomethines with the latter's aforementioned 1,3-cycloaddition processes, already the method of choice for constructing pyrazolo[1,2-*a*]pyrazoles.

Results and Discussion. – The transformation of racemic *trans*-oxiranecarboxylate **1** to pyrazolidin-3-ones **5** is outlined in *Scheme 1*, and the details are given in *Table 1*. Treatment of *trans*-oxiranecarboxylate **1** with morpholine or diallylamine in refluxing EtOH gave a mixture of amino hydroxy esters **2** and **3** (*ca.* 87:13). The major regioisomers **2a** and **2b** can be obtained by recrystallization from Et_2O in 72 and 62% yield, respectively. However, it is the crude mixture of regioisomers **2** and **3** that is subjected to mesylation, since, in both the morpholine (**a**) and diallylamine (**b**) series, the regioisomers **2** and **3** converge to the rearranged amino chloro ester **4** in almost quantitative yield. We previously established the structure of chloro ester **4a** as that predicted *via* the expected two-step rearrangement sequence, following mesylation of either regioisomer of **2** [6]. In the preceeding paper, we described the stereospecific and regioselective substitution reactions of chloro ester **4a**, *via* its aziridinium ion **Az**, with a variety of amines (for the synthesis and reactions of isolable aziridinium ions, see [7]).

In the present case, with hydrazine hydrate as 'the amine', chloro esters **4** furnished pyrazolidin-3-ones **5** (*Scheme 1* and *Table 1*). The reaction sequence starts with ring opening of the aziridinium ion at the benzylic site by hydrazine, followed by intramolecular conversion to the cyclic hydrazide. Several methods for the synthesis of pyrazolidin-3-ones have been reported [4a][4b][8], but they do not enable the preparation of pyrazolidin-3-ones in enantiomerically pure form. The present approach would be easily adapted to produce either enantiomer, since aryl oxiranecarboxylates such as **1** are now easily obtained in 2 or 3 steps, beginning with an osmium-catalyzed asymmetric dihydroxylation of the (*E*)-cinnamate [9]. Therefore, this new route allows one to prepare pyrazolidin-3-ones in either racemic or enantiomerically pure form.

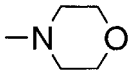
Synthesis of the azomethines (pyrazolidin-1-ium-2-ides) **6a**–**6d**, the 1,3-dipoles for the cycloadditions, was achieved in good yield, by refluxing the pyrazolidin-3-ones **5a**–**5b** and aromatic aldehydes for 1 h in absolute EtOH with catalytic CF_3COOH (*Scheme 2* and *Table 2*). With **6a**–**6d** in hand, we first examined the diastereoselectivity of the cycloadditions. Reaction of **6a** with dimethyl acetylenedicarboxylate (DMAD) in anisole at reflux for 2 h produced a 16:1 mixture of cycloadduct **7a** and its

Scheme 1



i) NHR_2, EtOH, reflux, 12 h. *ii*) MsCl, Et_3N, CH_2Cl_2, 0° to r.t., 3 h. *iii*) $NH_2NH_2 \cdot H_2O$ (4 equiv.), K_2CO_3, MeCN, 60°, 12 h.

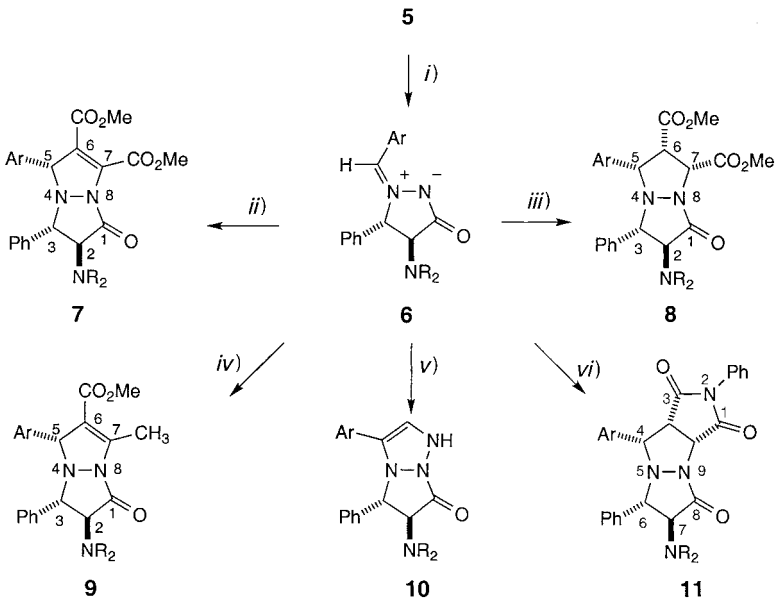
Table 1. *Synthesis of Pyrazolidin-3-ones* **5**

$-NR_2$	Amino alcohols **2** and **3**		Amino chloro ester	Pyrazolidin-3-one
	Yield [%] [a])	**2**/**3** [b])	**4**; Yield [%] [a])	**5**; Yield [%] [a])
	96	**2a**/**3a** (87 : 13)	**4a**; 96	**5a**; 73
$-N(allyl)_2$	94	**2b**/**3b** (88 : 12)	**4b**; 99	**5b**; 97

[a]) Isolated yield. [b]) Analysis by HPLC (*Zorbax SB-C18* reverse anal. column, 150 × 4.6 mm; gradient eluent H_2O/MeCN 80 : 20 to 0 : 100, containing 0.1% TFA, 0.5 ml/min for 15 min) by integration of absorption at 254 nm.

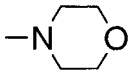
diastereoisomer. Pure isomer **7a** was obtained in 63% yield after recrystallization from AcOEt and hexane. The sense of diastereofacial selectivity indicated for **7a** was established for it, as well as for analogs **7b**–**d** by NMR techniques (HMQC, HMBC, and NOE). For instance, the stereochemical outcome is supported in all cases by the NOE enhancement observed between the protons H–C(3) and H–C(5), and is also consonant with the assignments for related pyrazolo[1,2-*a*]pyrazoles reported earlier [4a]. In all cases, the cycloaddition is strongly directed to the less hindered face of the azomethines **6**.

Scheme 2



i) ArCHO, cat. CF_3CO_2H, EtOH, reflux, 1 h. *ii*) Dimethyl acetylenedicarboxylate, toluene or anisole, 110°, 12–24 h. *iii*) Dimethyl maleate, toluene or anisole, 110°, 12–24 h. *iv*) Methyl acetoacetate, cat. CF_3CO_2H, toluene or anisole, 110°, 12–24 h. *v*) NaCN, AcOH, MeOH, r.t., 3 h. *vi*) *N*-Phenylmaleimide, toluene or anisole, 110°, 12–24 h.

Table 2. *Synthesis of Pyrazolo[1,2-a]pyrazoles* **7**–**11**

NR_2	Ar	**6** (Yield [%]) [a])	Pyrazolo[1,2-*a*]pyrazole (Yield [%]) [a])				
			7	**8**	**9**	**10**	**11**
	Ph	**6a** (88)	**7a** (63)	**8a** (62)	**9a** (65)	**10a** (84)	**11a** (41)
	4 MeO–C_6H_4	**6b** (88)	**7b** (83)	**8b** (82)	**9b** (67)	**10b** (64)	**11b** (67)
–N(allyl)$_2$	Ph	**6c** (71)	**7c** (62)	**8c** (49)	**9c** (90)	**10c** (81)	**11c** (53)
	4 MeO–C_6H_4	**6d** (61)	**7d** (79)	**8d** (55)	**9d** (82)	**10d** (63)	**11d** (50)

[a]) Isolated yield.

Finally, we examined the cycloaddition's scope regarding variations in the dipolarophile, including symmetrical dipolarophiles (dimethyl maleate, *N*-phenylmaleimide), and unsymmetrical dipolarophiles (methyl acetoacetate, HCN) (*Scheme 2*). As shown in *Table 2*, 1,3-dipolar cycloaddition of azomethines **6a**–**6d** with dimethyl maleate or *N*-phenylmaleimide afforded the eight pyrazolo[1,2-*a*]pyrazoles **8** or **11**, the structures of which were also verified by NMR techniques. In particular, the indicated stereochemical relationship fits the NOE enhancement observed between the protons H–C(3) and H–C(5) of **8a**, and among the protons H–C(3a), H–C(4), H–C(6), and H–C(7) of **11d**. Cycloaddition of azomethines **6a**–**6d** with methyl acetoacetate and HCN gave pyrazolo[1,2-*a*]pyrazoles **9a**–**9d** and pyrazo[1,2-*a*][1,2,3]triazoles **10a**–**10d**, respectively, both in a highly diastereo- and regioselective manner. Under acid catalysis, methyl acetoacetate as its enol tautomer reacted regioselectively with **6a**–**6d**, which, after elimination of H_2O, afforded pyrazolo[1,2-*a*]pyrazoles **9a**–**9d**. A positive NOE interaction between the protons H–C(3) and H–C(5) of **9c** supported the anticipated facial selectivities for this cycloaddition. The reaction of azomethines **6a**–**6d** with HCN (NaCN, AcOH in MeOH) gave pyrazolo[1,2-*a*]triazoles **10a**–**10d** with good yields and selectivities, by prototropic rearrangement of the initial cycloaddition in each case.

In summary, a highly efficient route to pyrazolidin-3-ones **5** has been developed from the reaction of amino-chloro esters **4** with hydrazine monohydrate. 1,3-Dipolar cycloaddition of the derived azomethines **6** with various dipolarophiles afforded the 20 cycloadducts **7**–**11** (*Table 2*) with high diastereofacial- and regioselectivities. These unusual, yet easily prepared nonplanar heterocyclic networks offer novel 3D shapes along with good prospects for highly modular and predictable display of functional substituents (in collaboration here at TSRI and elsewhere, they are being screened for possible biological functions).

We thank the *National Institutes of General Medical Sciences*, *National Institutes of Health* (GM-28384), the *National Science Foundation* (CHE-9531152), and the *W. M. Keck Foundation* for financial support, and are very grateful to Dr. *Laura Pasternack* for assistance with the NMR-based stereochemical assignments.

Experimental Part

General. All commercially available chemicals were used without further purification. Unless otherwise stated, the EtOH used for reactions and recrystallization was abs. EtOH. Reactions were monitored by TLC on pre-coated plates with a 0.2-mm layer of silica containing a fluorescent indicator (*Merck*, Art. 5714-3). M.p.: on a *Thomas Hoover* cap. melting-point apparatus; uncorrected. ^{1}H- and ^{13}C-NMR spectra: on *Bruker AMX-400* or *DRX-500* spectrometers; chemical shifts relative to $CHCl_3$ (δ(H) 7.25, δ(C) (central line) 77.0) or DMSO (δ(H) (central line) 2.49, δ(C) (central line) 39.5). MS: *m*/*z* (rel. intensity). High-resolution mass spectra (HR-MS): by fast-atom-bombardment (FAB) method in a 3-nitrobenzyl-alcohol matrix doped with NaI or CsI.

*Ethyl (2*R**,3*S**)-2-Hydroxy-3-morpholino-3-phenylpropanoate* (**2a**). The epoxy ester (**1**; 15.3 g, 80.0 mmol) and morpholine (7.3 ml, 7.3 g, 80.0 mmol) were dissolved in EtOH (80 ml), and the mixture was heated at reflux (open to the atmosphere) for 12 h. The resulting mixture was cooled to r.t. and concentrated *in vacuo* to afford the crude product (21.4 g, 96%; an 87:13 mixture of **2a** and **3a**). Recrystallization from Et_2O furnished the pure regioisomer **2a** (16.0 g, 72%) as a colorless crystalline solid. *Data of* **2a**: M.p. 89–91° ([11]: m.p. 88°). TLC (AcOEt/hexane 1:2): R_f 0.1. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.14 (*t*, *J* = 7.2, 3 H); 2.40–2.45 (*m*, 2 H); 2.52–2.55 (*m*, 2 H); 3.09 (br. *s*, 1 H); 3.54 (*d*, *J* = 4.4, 1 H); 3.67–3.69 (*m*, 4 H); 3.98–4.08 (*m*, 2 H); 4.72 (*d*, *J* = 4.4, 1 H); 7.24–7.29 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.0; 51.4 (2 C); 61.4; 66.8 (2 C); 69.9; 72.1; 128.1 (2 C); 128.2; 129.1 (2 C); 135.4; 172.6. FAB-MS: 280 (35, $[M+1]^+$), 176 (100).

*Ethyl (2*R**,3*S**)-3-(Diallylamino)-2-hydroxy-3-phenylpropanoate* (**2b**). According to the procedure for the preparation of **2a** described above, a mixture **2b**/**3b** (88:12) was obtained by reaction of **1** (19.2 g, 100.0 mmol) and diallylamine (12.9 ml, 10.2 g, 105.0 mmol) in EtOH (50 ml). Recrystallization from Et_2O gave pure regioisomer **2b** (18.0 g, 62%). *Data of* **2b**: M.p. 72–73°. TLC (AcOEt/Hexane 2:1): R_f 0.5. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.19 (*t*, *J* = 7.2, 3 H); 2.82 (br. *s*, 1 H); 2.94 (*dd*, *J* = 14.4, 7.5, 2 H); 3.32 (*dd*, *J* = 14.4, 5.2, 2 H); 4.04 (*d*, *J* = 5.9, 1 H); 4.06–4.12 (*m*, 2 H); 4.74 (*d*, *J* = 5.9, 1 H); 5.12–5.16 (*m*, 4 H); 5.76–5.86 (*m*, 2 H); 7.28–7.31 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.0; 52.8 (2 C); 61.3; 66.5; 71.3; 117.7 (2 C); 127.9; 128.1 (3 C); 129.2 (2 C); 135.4 (2 C); 173.1. MS: 312 (5, $[M+Na]^+$), 290 (100, $[M+1]^+$), 186 (7), 119 (18). HR-MS: 290.1745 ($C_{17}H_{24}NO_3^+$, $[M+H]^+$; calc. 290.1751).

*Ethyl (2*S**,3*R**)-3-Chloro-2-morpholino-3-phenylpropanoate* (**4a**). To a cold (0°) stirred soln. of **2** (15.6 g, 55.9 mmol) and Et_3N (8.5 ml, 6.2 g, 61.5 mmol) in CH_2Cl_2 (60 ml), MsCl (4.7 ml, 7.1 g, 61.5 mmol) was added dropwise. After the addition was completed, the reaction was allowed to warm to r.t. (ice-bath removal) and stirred for 3 h. The resulting crude mixture was filtered through a short pad of silica gel. The filtrate was concentrated and recrystallized from CH_2Cl_2/hexane to give **4a** (16.0 g, 96%). Colorless solid. M.p. 66–67°. TLC (AcOEt/hexane 1:2): R_f 0.4. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.34 (*t*, *J* = 7.2, 3 H); 2.36–2.41 (*m*, 2 H); 2.58–2.63 (*m*, 2 H); 3.28–3.40 (*m*, 4 H); 3.69 (*d*, *J* = 10.8, 1 H); 4.00–4.33 (*m*, 2 H); 5.14 (*d*, *J* = 10.8, 1 H); 7.30–7.39 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.5; 50.0 (2 C); 59.1; 60.8; 67.0 (2 C); 73.5; 127.7 (2 C); 128.3 (2 C); 128.5; 138.4; 168.5. FAB-MS: 298 (40, $[M+1]^+$), 262 (40, $[M-Cl]^+$), 172 (81).

*Ethyl (2*R**,3*R**)-3-Chloro-2-(diallylamino)-3-phenylpropanoate* (**4b**). According to the procedure for the preparation of **4a** described above, **4b** was obtained by reaction of **2b** (11.6 g, 40.0 mmol), Et_3N (4.5 g, 6.1 ml, 44.0 mmol), and MsCl (5.5 g, 3.7 ml, 48.0 mmol) in CH_2Cl_2 (40 ml). Recrystallization of the mixture from CH_2Cl_2/hexane gave pure **4b** (12.3 g, 99%). Solid. M.p. 50–51°. TLC (AcOEt/hexane 1:2): R_f 0.5. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.34 (*t*, *J* = 7.0, 3 H); 2.85 (*dd*, *J* = 12.9, 7.8, 2 H); 3.26 (br. *d*, *J* = 12.9, 2 H); 3.98 (*d*, *J* = 10.5, 1 H); 4.24–4.33 (*m*, 2 H); 4.98–5.04 (*m*, 4 H); 5.17 (*d*, *J* = 10.5, 1 H); 5.20–5.40 (*m*, 2 H); 7.29–7.33 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.4; 53.3 (2 C); 59.9; 60.6; 67.5; 117.9 (2 C); 128.1; 128.2 (2 C); 128.4 (2 C); 135.1; 138.6 (2 C); 172.0. MS: 272 (100, $[M-Cl]^+$).

*(4*S**,5*S**)-4-Morpholino-5-phenylpyrazolidin-3-one* (**5a**). To a stirred suspension of **4a** (1.1 g, 4.0 mmol) and K_2CO_3 (560.0 mg, 4.0 mmol) in MeCN (4 ml), $NH_2NH_2 \cdot H_2O$ (0.4 g, 0.4 ml, 8.0 mmol) was added at r.t., and the mixture was heated at 60° (open to air) for 12 h. The resulting mixture was then cooled to r.t. and filtered through a short plug of *Celite*, which was washed with 60 ml of CH_2Cl_2. The combined filtrates were concentrated to give a crude solid. Recrystallization of the crude product from EtOH gave **5a** (0.7 g, 73%). Solid. M.p. 195–197°. TLC (AcOEt/hexane 2:1): R_f 0.1. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.57–2.58 (*m*, 2 H); 2.83–2.85 (*m*, 2 H); 3.53 (br. *s*, 4 H); 4.53 (*t*, *J* = 8.3, 1 H); 5.39 (*d*, *J* = 8.3, 1 H); 7.28–7.49 (*m*, 5 H); 9.46 (br. *s*, 1 H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 49.6 (2 C); 61.1; 66.5 (2 C); 71.6; 127.0 (2 C); 127.4; 128.4 (2 C); 140.1; 172.3. FAB-MS: 245 (16, $[M-2]^+$), 215 (100).

*(4*S**,5*S**)-4-(Diallylamino)-5-phenylpyrazolidin-3-one* (**5b**). As described for **5a**, reaction of **4b** (1.2 g, 4.0 mmol), K_2CO_3 (560.0 mg, 4.0 mmol), and $NH_2NH_2 \cdot H_2O$ (0.8 g, 0.8 ml, 16.0 mmol) in MeCN (8 ml)

afforded **5b** (1.0 g, 97%). Oil. TLC (AcOEt/hexane 1:2): R_f 0.05. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.28 (*dd*, *J* = 14.7, 5.9, 2 H); 3.45 (*dd*, *J* = 14.7, 6.6, 2 H); 3.98 (*d*, *J* = 9.9, 1 H); 4.59 (*d*, *J* = 9.9, 1 H); 5.04–5.09 (*m*, 4 H); 5.71–5.79 (*m*, 2 H); 7.30–7.41 (*m*, 5 H); 8.21 (br. *s*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 54.1 (2 C); 63.7; 66.7; 117.4 (2 C); 127.0 (2 C); 128.3; 128.7 (2 C); 136.1 (2 C); 137.9; 175.2. MS: 258 (100, $[M+1]^+$), 226 (13), 153 (12).

(4S,5S*)-4-Morpholino-5-phenyl-1-(phenylmethylidene)-3-oxopyrazolidin-1-ium-2-ide* (**6a**). A mixture of **5a** (2.1 g, 8.5 mmol), PhCHO (1.1 g, 1.1 ml, 10.2 mmol), and CF_3CO_2H (3 drops) in EtOH (10 ml) was heated at reflux for 1 h. The resulting mixture was then cooled to r.t. and concentrated to give a crude solid. Recrystallization of the crude product from EtOH gave **6a** (2.5 g, 88%). Solid. M.p. 200–202°. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.72 (br. *s*, 2 H); 2.91 (br. *s*, 2 H); 3.72 (br. *s*, 2 H); 3.72 (br. *s*, 4 H); 6.04 (*s*, 1 H); 7.36–7.54 (*m*, 10 H); 8.31 (*s*, 1 H); 8.32 (*s*, 1 H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 49.2 (2 C); 65.6 (2 C); 71.7; 73.4; 126.3 (2 C); 128.8 (2 C); 129.0; 129.2; 129.5 (2 C); 131.7 (2 C); 132.1; 135.2; 138.2; 178. FAB-MS: 336 (100, $[M+1]^+$). HR-MS: 336.1710 ($C_{20}H_{22}N_3O_2$, $[M+H]^+$; calc. 336.1712).

(4S,5S*)-1-[4-(Methoxyphenyl)methylidene]-4-morpholino-5-phenyl-3-oxopyrazolidin-1-ium-2-ide* (**6b**). As described for **6a**, reaction of **5a** (1.6 g, 6.5 mmol), 4-methoxybenzaldehyde (1.1 g, 0.9 ml, 7.7 mmol) and CF_3CO_2H (3 drops) in EtOH (24 ml) yielded, after recrystallization from $Et_2O/CHCl_3$, **6b** (2.1 g, 88%). Solid. M.p. 199–200°. TLC ($Et_2O/CHCl_3$ 1:1): R_f 0.05. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.70–2.80 (*m*, 4 H); 3.70–3.80 (*m*, 5 H); 3.85 (*s*, 3 H); 5.47 (br. *s*, 1 H); 6.83 (*s*, 1 H); 6.93 (*d*, *J* = 8.6 Hz, 2 H); 7.32–7.41 (*m*, 5 H); 8.26 (*d*, *J* = 8.6, 2 H). MS: 366 (100, $[M+1]$), 190 (6). HR-MS: 366.1798 ($C_{21}H_{24}N_3O_3$, $[M+H]^+$; calc. 366.1812).

(4S,5S*)-4-(Diallylamino)-5-phenyl-1-(phenylmethylidene)-3-pyrazolidin-1-ium-2-ide* (**6c**). As described for **6a**, reaction of **5b** (1.0 g, 3.9 mmol), PhCHO (0.5 g, 0.5 ml, 4.7 mmol), and CF_3CO_2H (2 drops) in EtOH (10 ml) afforded, after recrystallization from $EtOH/Et_2O$, **6c** (350 mg, 71%). Solid. M.p. 182–183°. ^{1}H-NMR (500 MHz, (D_6)DMSO): 3.24 (*dd*, *J* = 14.3, 6.1, 2 H); 3.35 (*dd*, *J* = 14.3, 6.0, 2 H); 3.72 (*d*, *J* = 4.2, 1 H); 5.00–5.08 (*m*, 4 H); 5.70–5.78 (*m*, 3 H); 7.33–7.52 (*m*, 9 H); 8.36–8.38 (*m*, 2 H). ^{13}C-NMR (125 MHz, (D_6)DMSO): 53.2 (2 C); 68.6; 74.5; 117.5 (2 C); 119.8; 126.3 (2 C); 128.7 (2 C); 129.4 (2 C); 129.5; 131.4 (2 C); 131.8; 134.2; 135.8 (2 C); 138.7; 181.1. MS: 366 (100, $[M+1]^+$), 190 (6). HR-MS: 346.1901 ($C_{22}H_{24}N_3O$, $[M+H]^+$; calc. 346.1914).

(4S,5S*)-4-(Diallylamino)-1-[(4-methoxyphenyl)methylidene]-5-phenyl-3-oxopyrazolidin-1-ium-2-ide* (**6d**). As described for **6a**, reaction of **5b** (2.8 g, 11.0 mmol), 4-methoxybenzaldehyde (1.6 g, 1.5 ml, 12.0 mmol), and CF_3CO_2H (3 drops) in EtOH (20 ml) afforded, after recrystallization from $EtOH/Et_2O$, **6d** (2.5 g, 61%). Solid. M.p. 172–173°. TLC (EtOAc): R_f 0.5. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.28 (*dd*, *J* = 13.9, 5.5, 2 H); 3.54 (*dd*, *J* = 13.9, 4.0, 2 H); 3.89 (*s*, 3 H); 4.10 (br. *s*, 1 H); 5.05–5.13 (*m*, 4 H); 5.32 (*d*, *J* = 5.1, 1 H); 5.81–5.88 (*m*, 2 H); 6.84 (*s*, 1 H); 6.96–6.98 (*m*, 2 H); 7.35–7.45 (*m*, 5 H); 8.31 (*d*, *J* = 7.3, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 54.1 (2 C); 55.4; 69.3; 75.6; 114.1 (2 C); 117.5; 121.8 (2 C); 126.6 (2 C); 129.0; 129.4 (2 C); 129.9; 134.1 (2 C); 135.7 (2 C); 137.6; 162.5; 181.7. MS: 376 (100, $[M+1]^+$), 200 (8). HR-MS: 376.2036 ($C_{23}H_{26}N_3O_2$, $[M+H]^+$; calc. 376.2020).

Dimethyl (2S,3S*,5R*)-2,3-Dihydro-3,5-diphenyl-2-morpholino-1-oxo-1*H,5H*-pyrazolo[1,2-a]pyrazole-6,7-dicarboxylate* (**7a**). A mixture of **6a** (167.5 mg, 0.5 mmol) and dimethyl acetylenedicarboxylate (DMAD, 71.0 mg, 61.0 µl, 0.5 mmol) in anisole (3 ml) was heated at reflux for 2 h. The resulting mixture was then cooled to r.t. and concentrated. The residue was filtered through a short plug of silica gel (3 cm in a pipette), which was washed with 10 ml of AcOEt. The combined filtrates were concentrated to give a crude solid. Recrystallization of the crude product from AcOEt/hexane gave **7a** (150.0 mg, 63%). Solid. M.p. 74–76°. TLC (AcOEt/hexane 1:1): R_f 0.2. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.61–2.64 (*m*, 2 H); 2.80–2.85 (*m*, 2 H); 3.53 (*s*, 3 H); 3.57–3.90 (*m*, 5 H); 3.98 (*s*, 3 H); 4.42 (*d*, *J* = 11.6, 1 H); 5.22 (*s*, 1 H); 7.04–7.39 (*m*, 10 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 49.7 (2 C); 51.8; 53.5; 66.8 (2 C); 72.2; 74.0; 74.7; 114.6; 127.6 (2 C); 127.8; 127.9 (2 C); 128.3 (2 C); 128.6; 133.7; 135.0; 139.0; 162.5; 164.6. FAB-MS: 478 (61, $[M+1]^+$), 189 (100). HR-MS: 478.1988 ($C_{26}H_{28}N_3O_6$, $[M+H]^+$; calc. 478.1978).

Dimethyl (2S,3S*,5R*)-2,3-Dihydro-5-(4-methoxyphenyl)-1-oxo-3-phenyl-1*H,5H*-pyrazolo[1,2-a]pyrazole-6,7-dicarboxylate* (**7b**). As described for **7a**, reaction of **6b** (365.0 mg, 1.0 mmol) and dimethyl acetylenedicarboxylate (142.1 mg, 123.0 µl, 1.0 mmol) in anisole (3 ml) for 2 h (at reflux) afforded **7b** (420.0 mg, 83%). Oil. TLC (AcOEt/hexane 1:2): R_f 0.1. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.61–2.64 (*m*, 2 H); 2.83–2.86 (*m*, 2 H); 3.55 (*s*, 3 H); 3.58–3.61 (*m*, 4 H); 3.69 (*s*, 3 H); 3.88 (*d*, *J* = 11.4, 1 H); 4.02 (*s*, 3 H); 4.43 (*d*, *J* = 11.4, 1 H); 5.22 (*s*, 1 H); 6.65 (*d*, *J* = 8.4, 2 H); 6.98 (*d*, *J* = 8.4, 2 H); 7.16–7.24 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 49.6 (2 C); 51.7; 53.3; 54.8; 66.8 (2 C); 72.1; 73.4; 74.7; 113.2 (2 C); 114.6; 127.8; 128.2 (2 C); 128.3 (2 C); 128.6 (2 C); 131.2; 133.5; 135.2; 158.9; 159.4; 162.5; 164.7. MS: 508 (12, $[M+1]^+$), 480 (100). HR-MS: 530.1915 ($C_{27}H_{29}N_3O_7$, $[M+Na]^+$; calc. 530.1898).

Dimethyl (2S,3S*,5R*)-2-(Diallylamino)-2,3-dihydro-3,5-diphenyl-1-oxo-1*H,5H*-pyrazolo[1,2-a]pyrazole-6,7-dicarboxylate* (**7c**). As described for **7a**, reaction of **6c** (172.5 mg, 0.5 mmol) and dimethyl

acetylenedicarboxylate (71.0 mg, 61.0 µl, 0.5 mmol) in anisole (3 ml) for 2 h (90°) afforded, after recrystallization from AcOEt/hexane, **7c** (151.0 mg, 62%). Solid. M.p. 100–102°. TLC (AcOEt/hexane 1:1): R_f 0.6. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.22 (*dd*, *J* = 14.6, 5.5, 2 H); 3.48 (*dd*, *J* = 14.6, 6.6, 2 H); 3.63 (*s*, 3 H); 4.08 (*s*, 3 H); 4.16 (*d*, *J* = 11.4, 1 H); 4.37 (*d*, *J* = 11.4, 1 H); 5.05–5.09 (*m*, 4 H); 5.31 (*s*, 1 H); 5.62–5.69 (*m*, 2 H); 7.17–7.23 (*m*, 10 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 51.8; 53.5; 53.9 (2 C); 70.6; 74.1; 74.3; 114.2; 117.4 (2 C); 127.7 (2 C); 127.8 (2 C); 127.9 (4 C); 128.0 (2 C); 128.2; 133.8; 135.0; 136.0; 139.3; 159.6; 162.7; 166.3. MS: 488 (100, $[M+1]^+$), 460 (35). HR-MS: 488.2197 ($C_{28}H_{30}N_3O_5$, $[M+H]^+$; calc. 488.2180).

Dimethyl (2S,3S*,5R*)-2-(Diallylamino)-2,3-dihydro-5-(4-methoxyphenyl)-1-oxo-3-phenyl-1*H,5H-*pyrazolo[1,2-*a*]pyrazole-6,7-dicarboxylate* (**7d**). As described for **7a**, reaction of **6d** (375.0 mg, 1.0 mmol) and dimethyl acetylenedicarboxylate (142.1 mg, 122.0 µl, 1.0 mmol) in toluene (3 ml) for 2 h (110°) yielded, after recrystallization from AcOEt/hexane, **7d** (410.0 mg, 79%). Solid. M.p. 110–111°. TLC (AcOEt/hexane 2:1): R_f 0.8. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.26 (*dd*, *J* = 14.6, 5.5, 2 H); 3.40 (*dd*, *J* = 14.6, 6.6, 2 H); 3.56 (*s*, 3 H); 3.72 (*s*, 3 H); 4.00 (*s*, 3 H); 4.07 (*d*, *J* = 11.4, 1 H); 4.27 (*d*, *J* = 11.4, 1 H); 4.98–5.01 (*m*, 4 H); 5.19 (*s*, 1 H); 5.53–5.61 (*m*, 2 H); 6.67 (*d*, *J* = 6.9, 2 H); 7.01 (*d*, *J* = 6.9, 2 H); 7.14–7.19 (*m*, 5 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 51.8; 53.5 (2 C); 53.9; 55.1; 70.8; 73.9; 74.2; 113.4 (2 C); 114.4; 117.3; 128.0 (2 C); 128.1 (2 C); 128.2 (2 C); 128.8 (2 C); 131.6; 133.8; 135.2; 135.7 (2 C); 159.1; 159.7; 162.8; 166.4. MS: 518 (40, $[M+1]^+$), 490 (100). HR-MS: 518.2279 ($C_{29}H_{32}N_3O_6$, $[M+H]^+$; calc. 518.2286).

Dimethyl (2S,3S*,5R*,6S*,7R*)-2,3,6,7-Tetrahydro-2-morpholino-1-oxo-3,5-diphenyl-1*H,5H-*pyrazolo[1,2-*a*]pyrazole-6,7-dicarboxylate* (**8a**). As described for **7a**, reaction of **6a** (335.0 mg, 1.0 mmol) and dimethyl maleate (144.1 mg, 125.0 µl, 1.0 mmol) in anisole (3 ml) for 23 h (110°), followed by recrystallization from Et_2O/hexane, afforded **8a** (295.0 mg, 62%). Solid. M.p. 111–113°. TLC (AcOEt/hexane 1:1): R_f 0.1. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.63–2.67 (*m*, 2 H); 2.74–2.77 (*m*, 2 H); 3.56 (*s*, 3 H); 3.58–3.70 (*m*, 4 H); 3.74 (*dd*, *J* = 11.0, 9.0, 1 H); 3.81 (*s*, 3 H); 4.17 (*d*, *J* = 11.4, 1 H); 4.26 (*d*, *J* = 11.0, 1 H); 4.48 (*d*, *J* = 11.4, 1 H); 4.77 (*d*, *J* = 9.0, 1 H); 6.97–7.15 (*m*, 10 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 49.7 (2 C); 52.3; 53.1; 56.3; 56.9; 67.1 (2 C); 70.5; 71.4; 76.4; 127.7; 127.8 (2 C); 127.9 (4 C); 128.0 (2 C); 128.1; 134.0; 137.4; 163.6; 167.6 (2 C). MS: 480 (100, $[M+1]^+$), 190 (5). HR-MS: 480.2128 ($C_{26}H_{30}N_3O_6$, $[M+H]^+$; calc. 480.2129).

Dimethyl (2S,3S*,5R*,6S*,7R*)-2,3,6,7-Tetrahydro-5-(4-methoxyphenyl)-2-morpholino-1-oxo-3-phenyl-1*H,5H-*pyrazolo[1,2-*a*]pyrazole-6,7-dicarboxylate* (**8b**). As described for **7a**, reaction of **6b** (348.0 mg, 0.9 mmol) and dimethyl maleate (136.9 mg, 119.0 µl, 0.9 mmol) in toluene (3 ml) for 23 h (110°) afforded **8b** (420.0 mg, 82%). Oil. TLC (AcOEt/hexane 2:1): R_f 0.1. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.50–2.66 (*m*, 2 H); 2.75–2.82 (*m*, 2 H); 3.56 (*s*, 3 H); 3.60–3.65 (*m*, 5 H); 3.69 (*s*, 3 H); 3.81 (*s*, 3 H); 4.16 (*d*, *J* = 11.4, 1 H); 4.22 (*d*, *J* = 11.0, 1 H); 4.45 (*d*, *J* = 11.4, 1 H); 4.76 (*d*, *J* = 8.8, 1 H); 6.51 (*d*, *J* = 8.0, 2 H); 7.00–7.17 (*m*, 7 H). MS: 510 (100, $[M+1]^+$). HR-MS: 532.2052 ($C_{27}H_{31}N_3O_7Na$, $[M+Na]^+$; calc. 532.2054).

Dimethyl (2S,3S*,5R*,6S*,7R*)-2-(Diallylamino)-2,3,6,7-tetrahydro-1-oxo-3,5-diphenyl-1*H,5H-*pyrazolo[1,2-*a*]-pyrazole-6,7-dicarboxylate* (**8c**). As described for **7a**, reaction of **6c** (172.5 mg, 0.5 mmol) and dimethyl maleate (72.0 mg, 64.0 µl, 0.5 mmol) in anisole (3 ml) for 15 h (120°) afforded, after recrystallization from AcOEt/hexane, **8c** (120.0 mg, 49%). Solid. M.p. 173–175°. TLC (EtOAc/hexane 1:2): R_f 0.1. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.29 (*dd*, *J* = 14.6, 5.5, 2 H); 3.44 (*dd*, *J* = 14.6, 6.4, 2 H); 3.56 (*s*, 3 H); 3.75 (*dd*, *J* = 10.9, 9.2, 1 H); 3.82 (*s*, 3 H); 4.23–4.27 (*m*, 3 H); 4.74 (*d*, *J* = 8.8, 1 H); 4.92–4.97 (*m*, 4 H); 5.57–5.67 (*m*, 2 H); 6.98–7.13 (*m*, 10 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 52.3; 53.0; 53.7 (2 C); 56.2; 56.9; 70.6; 72.0; 74.4; 116.7 (2 C); 127.4; 127.5 (2 C); 127.8 (2 C); 127.9 (2 C); 128.1 (3 C); 134.1; 136.4 (2 C); 136.9; 165.0; 167.6; 167.7. MS: 512 (5, $[M+Na]^+$), 490 (100, $[M+1]^+$). HR-MS: 490.2346 ($C_{28}H_{32}N_3O_5$, $[M+H]^+$; calc. 490.2336).

Dimethyl (2S,3S*,5R*,6S*,7R*)-2-(Diallylamino)-2,3,6,7-tetrahydro-5-(4-methoxyphenyl)-1-oxo-3-phenyl-1*H,5H-*pyrazolo[1,2-*a*]pyrazole-6,7-dicarboxylate* (**8d**). As described for **7a**, reaction of **6d** (375.0 mg, 1.0 mmol) and dimethyl maleate (144.1 mg, 125.0 µl, 1.0 mmol) in toluene (3 ml) for 18 h (110°), followed by recrystallization from Et_2O, afforded **8d** (285.0 mg, 55%). Solid. M.p. 122–123°. TLC (AcOEt/hexane 1:2): R_f 0.1. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.30 (*dd*, *J* = 14.6, 5.5, 2 H); 3.44 (*dd*, *J* = 14.6, 6.2, 2 H); 3.55 (*s*, 3 H); 3.62 (*s*, 3 H); 3.71 (*dd*, *J* = 10.9, 9.1, 1 H); 3.81 (*s*, 3 H); 4.19–4.23 (*m*, 3 H); 4.72 (*d*, *J* = 9.1, 1 H); 4.94–4.97 (*m*, 4 H); 5.58–5.66 (*m*, 2 H); 6.51 (*d*, *J* = 8.8, 2 H); 7.01–7.12 (*m*, 7 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 52.2; 52.9 (2 C); 53.7; 54.9; 56.1; 56.7; 70.2; 72.1; 74.2; 113.3 (2 C); 114.1; 116.6; 125.9 (2 C); 127.5 (2 C); 128.0 (2 C); 129.0 (2 C); 130.0; 136.4 (2 C); 137.1; 159.2; 164.8; 167.8. MS: 520 (100, $[M+1]^+$). HR-MS: 520.2445 ($C_{29}H_{34}N_3O_6$, $[M+H]^+$; calc. 520.2442).

Methyl (2S,3S*,5R*)-2,3-Dihydro-7-methyl-2-morpholino-1-oxo-3,5-diphenyl-1*H,5H-*pyrazolo[1,2-*a*]pyrazole-6-carboxylate* (**9a**). A mixture of **6a** (335.0 mg, 1.0 mmol) and methyl acetoacetate (116.1 mg, 0.1 ml, 1.0 mmol) in MeOH (3 ml) was heated at reflux for 15–30 min, and CF_3CO_2H (3 drops) was added. The

resulting soln. was kept at reflux for 23 h, then cooled to r.t. and concentrated. The residue was filtered through a short plug of silica gel (3 cm in a pipette), which was washed with 10 ml of AcOEt. The combined filtrates were concentrated to give a crude solid. Recrystallization of the crude product from Et_2O/hexane gave **9a** (280.0 mg, 65%). Solid. M.p. 140–141°. TLC (AcOEt/hexane 1:1): R_f 0.3. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.63–2.67 (*m*, 2 H); 2.71 (*d*, *J* = 1.1, 3 H); 2.84–2.86 (*m*, 2 H); 3.51 (*s*, 3 H); 3.58–3.67 (*m*, 4 H); 3.84 (*dd*, *J* = 11.4, 1 H); 4.32 (*d*, *J* = 11.4, 1 H); 5.04 (*d*, *J* = 1.1, 1 H); 6.97–7.10 (*m*, 10 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 11.7; 49.9 (2 C); 51.0; 67.1 (2 C); 71.8; 73.6; 75.9; 111.8; 127.3; 127.7 (2 C); 127.8 (2 C); 128.0; 128.2 (2 C); 128.3 (2 C); 135.8; 140.7; 144.0; 164.5; 164.9. MS: 434 (100, $[M+1]^+$), 406 (40). HR-MS: 434.2083 ($C_{25}H_{28}N_3O_4$, $[M+H]^+$; calc. 434.2074).

Methyl (2S,3S*,5R*)-2,3-Dihydro-5-(4-methoxyphenyl)-7-methyl-2-morpholino-1-oxo-3-phenyl-1*H,*5*H-*pyrazolo[1,2-*a*]pyrazole-6-carboxylate* (**9b**). As described for **9a**, reaction of **6b** (365.0 mg, 1.0 mmol), methyl acetoacetate (116.1 mg, 0.1 ml, 1.0 mmol) and CF_3CO_2H (3 drops) in MeOH (3 ml) for 12 h afforded **9b** (310.0 mg, 67%). Oil. TLC (AcOEt/hexane 1:2): R_f 0.2. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.62–2.67 (*m*, 2 H); 2.70 (*d*, *J* = 1.4, 3 H); 2.82–2.85 (*m*, 2 H); 3.52 (*s*, 3 H); 3.58–3.65 (*m*, 4 H); 3.70 (*s*, 3 H); 3.83 (*d*, *J* = 11.4, 1 H); 4.31 (*d*, *J* = 11.4, 1 H); 5.01 (*d*, *J* = 1.4, 1 H); 6.60 (*d*, *J* = 8.8, 2 H); 6.88 (*d*, *J* = 8.8, 2 H); 7.12–7.18 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.7; 49.8 (2 C); 51.0; 55.0; 67.0 (2 C); 71.7; 73.0; 75.8; 111.9; 113.0 (2 C); 128.0 (2 C); 128.1 (2 C); 128.2; 128.7 (2 C); 132.9; 135.8; 143.8; 158.6; 164.5; 164.9. MS: 464 (92, $[M+1]^+$), 436 (100). HR-MS: 486.1979 ($C_{26}H_{29}N_3O_5Na$, $[M+Na]^+$; calc. 486.1999).

Methyl (2S,3S*,5R*)-2-(Diallylamino)-2,3-dihydro-7-methyl-1-oxo-3,5-diphenyl-7-1*H,*5*H-*pyrazolo[1,2-*a*]pyrazole-6-carboxylate* (**9c**). As described for **9a**, reaction of **6c** (172.5 mg, 0.5 mmol), methyl acetoacetate (59.2 mg, 55.0 µl, 0.5 mmol) and CF_3CO_2H (3 drops) in MeOH (3 ml) for 12 h yielded **9c** (200.0 mg, 90%). Oil. TLC (AcOEt/hexane 1:1): R_f 0.7. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.78 (*d*, *J* = 1.4, 3 H); 3.34 (*dd*, *J* = 14.7, 5.5, 2 H); 3.50 (*dd*, *J* = 14.7, 6.9, 2 H); 3.58 (*s*, 3 H); 4.10 (*d*, *J* = 11.3, 1 H); 4.26 (*d*, *J* = 11.3, 1 H); 5.05–5.08 (*m*, 4 H); 5.11 (*d*, *J* = 1.4, 1 H); 5.64–5.72 (*m*, 2 H); 7.08–7.17 (*m*, 10 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.6; 50.9; 54.0 (2 C); 71.5; 73.7 (2 C); 111.4; 117.2 (2 C); 127.2; 127.6 (2 C); 127.8 (4 C); 128.0; 128.1 (2 C); 135.5; 135.9 (2 C); 140.9; 144.1; 165.0; 166.2. MS: 444 (100, $[M+1]^+$), 416 (30). HR-MS: 444.2283 ($C_{27}H_{30}N_3O_3$, $[M+H]^+$; calc. 444.2282).

Methyl (2S,3S*,5R*)-2-(Diallylamino)-2,3-dihydro-5-(4-methoxyphenyl)-7-methyl-1-oxo-3-phenyl-1*H,*5*H-*pyrazolo[1,2-*a*]pyrazole-6-carboxylate* (**9d**). As described for **9a**, reaction of **6d** (154.7 mg, 0.4 mmol), methyl acetoacetate (46.5 mg, 44.0 µl, 0.4 mmol) and CF_3CO_2H (3 drops) in MeOH (3 ml) for 18 h afforded **9d** (160.0 mg, 82%). Oil. TLC (AcOEt/hexane 1:2): R_f 0.5. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.69 (*d*, *J* = 1.2, 3 H); 3.25 (*dd*, *J* = 14.4, 5.2, 2 H); 3.42 (*dd*, *J* = 14.4, 6.7, 2 H); 3.52 (*s*, 3 H); 3.7 (*s*, 3 H); 4.01 (*d*, *J* = 11.4, 1 H); 4.15 (*d*, *J* = 11.4, 1 H); 4.96–5.00 (*m*, 5 H); 5.55–5.65 (*m*, 2 H); 6.62 (*d*, *J* = 8.8, 2 H); 6.92 (*d*, *J* = 8.8, 2 H); 7.10–7.15 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.7; 51.0; 54.0 (2 C); 55.0; 71.5; 73.2; 73.7; 111.5; 113.0 (2 C); 117.2 (2 C); 127.8 (2 C); 128.0 (2 C); 128.1; 128.8 (2 C); 133.2; 135.6; 135.9 (2 C); 144.0; 158.6; 165.1; 166.2. MS: 474 (100, $[M+1]^+$), 446 (80). HR-MS: 474.2376 ($C_{28}H_{32}N_3O_4$, $[M+H]^+$; calc. 474.2387).

(5S,6S*)-5,6-Dihydro-6-morpholino-3,5-diphenyl-1*H,*7*H-*pyrazolo[1,2-*a*][1,2,3]triazol-7-one* (**10a**). A mixture of **6a** (335.0 mg, 1.0 mmol) and NaCN (73.5 mg, 1.5 mmol) in MeOH (3 ml) was stirred at r.t. for 15–30 min, and AcOH (3 drops) was added. The resulting soln. was kept stirring at r.t. for 23 h. The precipitate was collected, and the filtrates were concentrated. The residue was filtered through a short plug of silica gel (3 cm in a pipette), which was washed with 10 ml of AcOEt. The filtrates were concentrated to give a crude solid. Recrystallization of the combined solids from Et_2O/MeOH gave **10a** (304.0 mg, 84%). Solid. M.p. 161–163°. TLC (AcOEt): R_f 0.7. ^{1}H-NMR (500 MHz, (D_6)DMSO): 2.47–2.51 (*m*, 2 H); 2.78–2.82 (*m*, 2 H); 3.42–3.49 (*m*, 4 H); 3.93 (*d*, *J* = 9.9, 1 H); 5.39 (*d*, *J* = 9.9, 1 H); 7.27–7.45 (*m*, 8 H); 7.94 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (125 MHz, (D_6)DMSO): 51.9 (2 C); 68.4 (2 C); 72.0; 73.8; 110.9; 128.6 (2 C); 128.9; 129.4 (2 C); 129.5 (2 C); 130.0 (2 C); 133.6; 134.9; 141.1; 143.6; 172.9. MS: 363 (30, $[M+1]^+$), 143 (100). HR-MS: 363.1822 ($C_{21}H_{23}N_4O_2$, $[M+H]^+$; calc. 363.1816).

(5S,6S*)-5,6-Dihydro-3-(4-methoxyphenyl)-6-morpholino-5-phenyl-1*H,*7*H-*pyrazolo[1,2-*a*] *[1,2,3]triazol-7-one* (**10b**). As described for **10a**, reaction of **6b** (365.0 mg, 1.0 mmol), NaCN (73.5 mg, 1.5 mmol), and AcOH (72.0 mg, 69.0 µl, 1.2 mmol) in MeOH (6 ml) for 10 h afforded **10b** (250.0 mg, 64%). Oil. TLC (AcOEt): R_f 0.4. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.50–2.55 (*m*, 2 H); 2.69–2.74 (*m*, 2 H); 3.50–3.52 (*m*, 4 H); 3.64 (*d*, *J* = 7.3, 1 H); 3.82 (*s*, 3 H); 5.41 (*d*, *J* = 7.3, 1 H); 6.30 (br. *s*, 1 H); 6.47 (br. *s*, 1 H); 6.93 (*d*, *J* = 8.8, 2 H); 7.26–7.39 (*m*, 5 H); 7.90 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 50.9 (2 C); 55.4; 67.0 (2 C); 69.9; 74.3; 109.8; 114.2 (2 C); 126.1; 127.7; 127.8 (2 C); 128.3 (2 C); 129.5 (2 C); 139.1; 141.8; 163.0; 171.1. MS: 393 (100, $[M+1]^+$), 233 (65). HR-MS: 393.1934 ($C_{22}H_{25}N_4O_3$, $[M+H]^+$; calc. 393.1921).

(5S,6S*)-6-(Diallylamino)-5,6-dihydro-3,5-diphenyl-1H,7H-pyrazolo[1,2-a][1,2,3]triazol-7-one* (**10c**). As described for **10a**, reaction of **6c** (172.5 mg, 0.5 mmol), NaCN (36.7 mg, 0.75 mmol), and AcOH (36.0 mg, 34.5 µl, 0.6 mmol) in MeOH (3 ml) for 20 h afforded, after recrystallization from MeOH, **10c** (150 mg, 81%). Solid. M.p. 162–163°. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.11 (*dd*, *J* = 13.9, 7.0, 2 H); 3.48 (br. *d*, *J* = 13.9, 2 H); 3.56 (br. *s*, 1 H); 4.11 (*d*, *J* = 8.4, 1 H); 5.16–5.19 (*m*, 4 H); 5.56 (*d*, *J* = 8.4, 1 H); 5.61–5.68 (*m*, 2 H); 5.92 (br. *s*, 1 H); 7.34–7.51 (*m*, 8 H); 8.04 (*d*, *J* = 7.7, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 53.7 (2 C); 67.0; 71.5; 109.9; 117.3 (2 C); 127.8 (2 C); 127.9; 128.3 (2 C); 128.4 (2 C); 128.7 (2 C); 132.3; 133.5; 136.3 (2 C); 139.3; 142.6; 171.7. MS: 373 (26, $[M+1]^+$), 153 (100). HR-MS: 373.2022 ($C_{23}H_{25}N_4O$, $[M+H]^+$; calc. 373.2023).

(5S,6S*)-6-(Diallylamino)-5,6-dihydro-3-(4-methoxyphenyl)-5-phenyl-1H,7H-pyrazolo[1,2-a][1,2,3]triazol-7-one* (**10d**). As described for **10a**, reaction of **6d** (375.0 mg, 1.0 mmol), NaCN (73.5 mg, 1.5 mmol), and AcOH (72.0 mg, 69.0 µl, 1.2 mmol) in MeOH (3 ml) for 2 h afforded, after recrystallization from AcOEt/hexane, **10d** (252.0 mg, 63%). Solid. M.p. 148–150°. TLC (AcOEt/hexane 1:1): R_f 0.4. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.01 (*dd*, *J* = 14.6, 7.6, 2 H); 3.40 (*dd*, *J* = 14.6, 4.6, 2 H); 3.83 (*s*, 3 H); 4.00 (*d*, *J* = 8.5, 1 H); 5.06–5.10 (*m*, 4 H); 5.42 (*d*, *J* = 8.5, 1 H); 5.50–5.60 (*m*, 2 H); 5.87 (br. *s*, 2 H); 6.91 (*d*, *J* = 8.8, 2 H); 7.25–7.42 (*m*, 5 H); 7.91 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 53.7 (2 C); 55.4; 67.2; 71.3; 110.0; 114.1 (2 C); 117.2 (2 C); 126.4; 127.7 (2 C); 128.2; 128.3 (2 C); 129.5 (2 C); 136.3 (2 C); 139.6; 141.8; 162.9; 171.8. MS: 403 (70, $[M+1]^+$), 243 (12). HR-MS: 403.2146 ($C_{24}H_{27}N_4O_2$, $[M+H]^+$; calc. 403.2129).

(3aS,4R*,6S*,7S*,9aR*)-7-Morpholino-2,4,6-triphenylperhydropyrrolo[4′,5′:3,4]pyrazolo[1,2-a]pyrazole-1,3,8-trione* (**11a**). A mixture of **6a** (335.0 mg, 1.0 mmol) and *N*-phenylmaleimide (173.1 mg, 1.0 mmol) in anisole (3 ml) was heated at 110° for 23 h. The resulting mixture was then cooled to r.t. and concentrated. The residue was filtered through a short plug of silica gel (3 cm in a pipette), which was washed with 10 ml of AcOEt. The combined filtrates were concentrated to give a crude solid, which was recrystallized from AcOEt/hexane to yield **11a** (210.0 mg, 41%). Solid. M.p. 144–146°. TLC (AcOEt/hexane 2:1): R_f 0.1. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.63–2.67 (*m*, 2 H); 2.79–2.81 (*m*, 2 H); 3.71–3.74 (*m*, 4 H); 3.84–3.88 (*m*, 2 H); 4.14 (*d*, *J* = 6.6, 1 H); 4.25 (*d*, *J* = 8.4, 1 H); 5.43 (*d*, *J* = 7.7, 1 H); 7.13–7.45 (*m*, 15 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 50.3 (2 C); 50.8; 55.2; 64.2; 66.8 (2 C); 74.2; 75.7; 126.0 (2 C); 126.6 (2 C); 127.7; 127.9; 128.4 (2 C); 128.6 (2 C); 128.8; 128.9 (2 C); 129.1 (2 C); 131.1; 132.1; 140.5; 168.3; 171.2; 171.3. MS: 509 (100, $[M+1]^+$). HR-MS: 509.2159 ($C_{31}H_{29}N_4O_4$, $[M+H]^+$; calc. 509.2183).

(3aS,4R*,6S*,7S*,3aR*)-4-(4-Methoxyphenyl)-7-morpholino-2,6-diphenylperhydropyrrolo[4′,5′:3,4]pyrazolo[1,2-a]pyrazole-1,3,8-trione* (**11b**). As described for **11a**, reaction of **6b** (365.0 mg, 1.0 mmol) and *N*-phenylmaleimide (173.1 mg, 1.0 mmol) in toluene (3 ml) for 23 h (110°), followed by recrystallization from Et_2O, yielded **11b** (360.0 mg, 67%). Solid. M.p. 149–151°. TLC (AcOEt/hexane 2:1): R_f 0.2. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.62–2.64 (*m*, 2 H); 2.77–2.79 (*m*, 2 H); 3.60–3.70 (*m*, 8 H); 3.86 (*d*, *J* = 6.8, 1 H); 4.07 (*d*, *J* = 6.8, 1 H); 4.13 (*d*, *J* = 8.6, 1 H); 5.35 (*d*, *J* = 7.8, 1 H); 6.68 (*d*, *J* = 8.6, 2 H); 7.03 (*d*, *J* = 8.6, 2 H); 7.14–7.40 (*m*, 10 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 50.2 (2 C); 50.7; 55.0; 55.3; 64.1; 66.8 (2 C); 73.7; 75.7; 113.7 (2 C); 123.8 (2 C); 126.0 (2 C); 126.6 (2 C); 127.5; 128.5 (2 C); 128.6; 129.0; 129.1; 131.2 (2 C); 140.6; 159.6; 167.9; 171.5; 171.6. MS: 539 (100, $[M+1]^+$), 524 (25). HR-MS: 539.2280 ($C_{31}H_{31}N_4O_5$, $[M+H]^+$; calc. 539.2289).

(3aS,4R*,6S*,7S*,9aR*)-7-(Diallylamino)-2,4,6-triphenylperhydropyrrolo[4′,5′:3,4]pyrazolo[1,2-a]pyrazole-1,3,8-trione* (**11c**). As described for **11a**, reaction of **6c** (345.0 mg, 1.0 mmol), *N*-phenylmaleimide (173.1 mg, 1.0 mmol) in toluene (3 ml) for 12 h (110°), followed by recrystallization from AcOEt/hexane, provided **11c** (275.0 mg, 53%). Solid. M.p. 237–239°. TLC (AcOEt/hexane 1:1): R_f 0.3. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.24 (*dd*, *J* = 14.0, 5.6, 2 H); 3.44 (*dd*, *J* = 14.0, 6.1, 2 H); 3.84–3.91 (*m*, 2 H); 4.13 (*d*, *J* = 7.9, 1 H); 4.29 (*d*, *J* = 9.4, 1 H); 4.97–5.02 (*m*, 4 H); 5.40 (*d*, *J* = 7.9, 1 H); 5.63–5.70 (*m*, 2 H); 7.08–7.19 (*m*, 12 H); 7.30–7.50 (*m*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 51.1; 54.0 (2 C); 54.4; 69.7; 71.9; 75.4; 117.7 (2 C); 126.0 (2 C); 127.3 (2 C); 127.6; 128.1 (3 C); 128.2 (2 C); 128.7; 128.8; 129.1 (2 C); 131.1; 132.1; 135.7 (2 C); 139.2 (2 C); 166.0; 171.2; 171.6. MS: 519 (100, $[M+1]^+$). HR-MS: 519.2408 ($C_{32}H_{31}N_4O_3$, $[M+H]^+$; calc. 519.2391).

(3aS,4R*,6S*,7S*,9aR*)-7-(Diallylamino)-4-(4-methoxyphenyl)-2,6-diphenylperhydropyrrolo[4′,5′:3,4]pyrazolo[1,2-a]pyrazole-1,3,8-trione* (**11d**). As described for **11a**, reaction of **6d** (375.0 mg, 1.0 mmol) and *N*-phenylmaleimide (173.1 mg, 1.0 mmol) in anisole (3 ml) for 24 h (110°), followed by recrystallization from Et_2O, yielded **11d**. Solid. M.p. 208–209°. TLC (AcOEt/hexane 1:1): R_f 0.1. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.23 (*dd*, *J* = 14.0, 5.2, 2 H); 3.44 (*dd*, *J* = 14.0, 6.1, 2 H); 3.67 (*s*, 3 H); 3.82 (*dd*, *J* = 8.5, 7.9, 1 H); 3.88 (*d*, *J* = 9.1, 1 H); 4.09 (*d*, *J* = 8.5, 1 H); 4.27 (*d*, *J* = 9.1, 1 H); 4.97–5.02 (*m*, 4 H); 5.39 (*d*, *J* = 7.9, 1 H); 5.62–5.72 (*m*, 2 H); 6.62 (*d*, *J* = 8.8, 2 H); 6.99 (*d*, *J* = 8.4, 2 H); 7.12–7.40 (*m*, 10 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 51.0; 53.9 (2 C); 54.4; 55.0; 69.3; 71.9; 74.9; 113.4 (2 C); 117.7 (2 C); 123.8; 126.0 (2 C); 127.3 (2 C); 127.5; 128.1 (2 C); 128.7; 129.1

(2 C); 129.2 (2 C); 131.2; 135.7 (2 C); 139.4; 159.5; 166.2; 171.3; 171.6. MS: 549 (100, $[M+1]^+$). HR-MS: 549.2496 ($C_{33}H_{33}N_4O_4$, $[M+H]^+$; calc. 549.2496).

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Received April 28, 2000