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Diastereoselective Synthesis of Alkylcyclopropane-Annelated Methyl 2-Iminoimidazolidinecarboxylates[‡]

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Dedicated to Professor Alain Krief

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Cyclopropane- and alkylcyclopropane-annelated methyl imidazolidinecarboxylates **5** are formed from unsubstituted **1**-H and from 2′-substituted methyl 2-chloro-2-cyclopropylideneacetates (**1**-R) and *N*,*N*′,*N*′′-triarylguanidines (**2**) in a domino process consisting of a Michael addition and an immediately ensuing ring closure by intramolecular nucleophilic substitution in moderate to very good yields (30–95 %, 8 examples). The products **5** with alkyl substituents on the spirocyclopropane moiety are formed diastereoselectively.

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Introduction

As was previously reported by our group, the highly reactive Michael acceptor methyl 2-chloro-2-cyclopropylideneacetate (**1**-H)[1,2] under basic conditions smoothly undergoes addition of carboxamides and thiocarboxamides with subsequent ring closure by intramolecular nucleophilic substitution of the chlorine atom providing a versatile synthesis of spirocyclopropane-annelated oxazoline-[3] as well as thiazolinecarboxylates.[4] In contrast, the reaction of **1**-H with amidines under similar conditions proceeded in terms of an initial Michael addition, subsequent ring-enlarging rearrangement with elimination of chloride and finally cyclization by intramolecular attack of the amidine moiety on the methoxycarbonyl group to afford cyclobutene-annelated pyrimidinones.[5] This different reaction mode of the amidines has been rationalized as occurring by way of neighboring-group participation by the amidine moiety with its enhanced nucleophilicity in the first formed intermediate to form a well-stabilized aziridinium ion which rearranges with cyclopropylcarbinyl to cyclobutyl cation ring enlargement. In view of these results, it appeared worth testing, whether *N*,*N*′,*N*′′-trisubstituted guanidines **2** would follow the reaction mode of amides and thioamides or that of amidines, because neighboring-group participation in the resulting primary Michael adduct intermediates should also be favored.

Results and Discussion

When methyl 2-chloro-2-cyclopropylideneacetate (**1**-H) in acetonitrile solution was treated with *N*,*N*′,*N*′′-triphenylguanidine (**2a**) in the presence of sodium hydride at 0 °C, and the mixture was warmed to room temperature overnight, the cyclization product methyl 5,7-diphenyl-6-phenylimino-5,7-diazaspiro[2.4]heptane-4-carboxylate (**5a**-H) resulting from Michael addition and directly ensuing cyclization by intramolecular nucleophilic substitution was isolated in 83% yield (Scheme 1). Neither rearrangement nor intramolecular nucleophilic attack on the methyl ester moiety was observed.

The analogous reactions of *N*,*N*′,*N*′′-trisubstituted guanidines with 2′-substituted methyl 2-chloro-2-cyclopropylideneacetates (**1**-R) were of special interest from a stereochemical point of view, because the resulting products contain four stereogenic elements, and thus up to four diastereomers might be formed.

Surprisingly, all reactions of four different 2′-substituted cyclopropylideneacetates (**1**-R), which were mixtures of two diastereomers each, with various *N*,*N*′,*N*′′-trisubstituted guanidines **2** each gave exclusively one diastereomer of **5**-R in yields ranging from 30 to 95% (Scheme 1, Table 1). The

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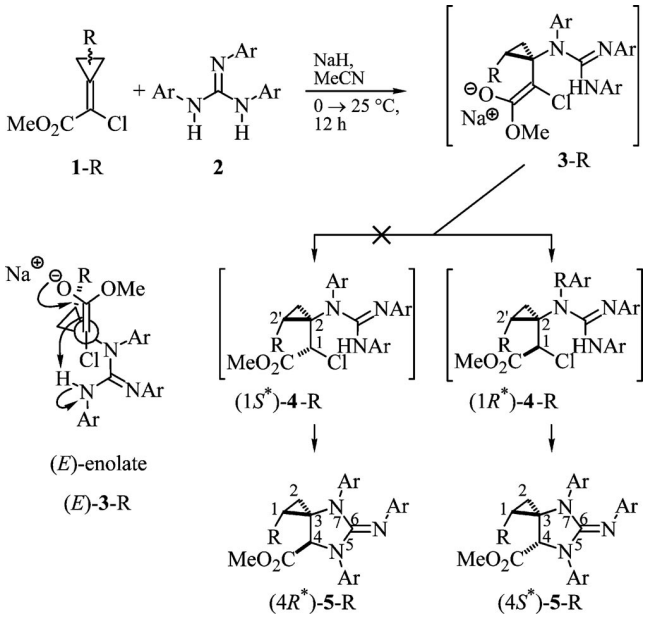

Scheme 1. Synthesis of methyl 6-imino-5,7-diazaspiro[2.4]heptane-4-carboxylates (2-imino-5-spirocyclopropaneimidazolidine-4-carboxylates) (**5**-R) from methyl 2-chloro-2-cyclopropylidenacetates (**1**-R) and *N*,*N*′,*N*′′-triarylguanidines (**2**). For details see Table 1.

relative configuration of the product **5a**-Et from **1**-Et and *N*,*N*′,*N*′′-triphenylguanidine (**2a**) was proved by an X-ray crystal-structure analysis to be (*Z*,1*R**,3*R**,4*S**) (Figure 1).[6,7] This means that the deprotonated guanidine **2a** underwent addition with complete *trans*-diastereoselectivity with respect to the substituent on the three-membered ring in **1**-Et, and the resulting enolate **3a**-Et was protonated diastereoselectively, most probably by intramolecular proton transfer from nitrogen to carbon in a six-membered-ring transition structure, to give the primary Michael adduct **4a**-Et with the relative configuration (*Z*,1*R**,2*R**,2′*R**). Intramolecular nucleophilic substitution with inversion at C-1 according to an S_N2 mechanism then gave (*Z*,1*R**,3*R**,4*S**)-**5a**-Et. It is remarkable that the phenyl group at the imino nitrogen is uniquely (*Z*)-oriented. The stereochemical assignments of all the other iminoimidazolinecarboxylates **5**-R rest on a comparison of their NMR spectra with that of (*Z*,1*R**,3*R**,4*S**)-**5a**-Et. This diastereoselectivity is unique, as the reactions of **1**-Et with oxoamides gave two of four possible diastereomers of the corresponding oxazoline-5-carboxylates with diastereomeric ratios (*dr*) of up to 17:1,[3] whereas reactions of **1**-Et with thiocarboxamides yielded up to three diastereomers of the corresponding thiazoline-4-carboxylates with rather low selectivities (*dr* up to 2:1).[4]

Table 1. Synthesis of methyl 6-imino-5,7-diazaspiro[2.5]heptane-4-carboxylates (2-iminospiro[cyclopropane-1,4′-imidazolidine]-5′-carboxylates) (**5**-R) from *N*,*N*′,*N*′′-triarylguanidines (**2**) and methyl 2-chloro-2-cyclopropylideneacetates (**1**-R) (see Scheme 1).

R in **1**-R	Ar in **2**	Product	Yield (%)
H	Ph	(4*S**)-**5a**-H	83
Et	Ph	(4*S**)-**5a**-Et	75
$(CH_2)_2OBn$	Ph	(4*S**)-**5a**-$(CH_2)_2OBn$	75
*i*Pr	Ph	(4*S**)-**5a**-*i*Pr	95
H	4-Me-C_6H_4	(4*S**)-**5b**-H	95
Me	4-Me-C_6H_4	(4*S**)-**5b**-Me	83
H	3-Cl-C_6H_4	(4*S**)-**5c**-H	30
H	4-Br-C_6H_4	(4*S**)-**5d**-H	50

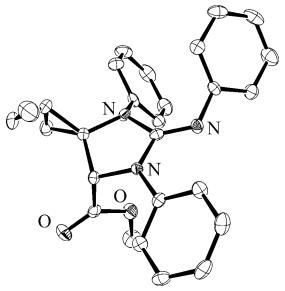

Figure 1. Structure of compound (*Z*,1*R**,3*R**,4*S**)-**5a**-Et in the crystal.[6,7]

Experimental Section

General: All reagents were used as purchased without further purification. Acetonitrile was dried prior to use with phosphorus pentoxide. ^1H and ^{13}C NMR spectra were recorded at ambient temperature with a Bruker AM 250 instrument. Chemical shifts (δ) are given in ppm relative to residual resonances of the solvents (^1H: 7.26 ppm for $CDCl_3$; ^{13}C: 77.0 ppm for $CDCl_3$). Coupling constants (*J*) are given in Hz. Multiplicities of signals are described as follows: s singlet, d doublet, t triplet, quin quintet, m multiplet, m_c multiplet centered at value given. The multiplicities of signals were determined by additional DEPT (distortionless enhancement by polarization transfer) measurements: + primary (CH_3) or tertiary (CH) (positive DEPT signal), – secondary (CH_2) (negative DEPT signal), C_{quat} quaternary C atoms. IR: Bruker IFS 66. MS: Finnigan MAT 95, 70 eV. Chromatographic separations were carried out on Merck silica gel 60 (0.063–0.200 mm, 70–230 mesh ASTM). The dimensions of the columns are given in cm as "diameter × height of the silica gel layer". TLC: Macherey–Nagel, ready to use TLC plates Alugram® Sil G/UV254. Detection under UV light at 254 nm and development with MOPS reagent (5% molybdophosphoric acid in ethanol). Melting points (uncorrected) were determined in capillaries with a Büchi 510 apparatus. Elemental analyses: Mikroanalytisches Laboratorium des Instituts für Organische und Biomolekulare Chemie der Universität Göttingen. PE stands for light petroleum (boiling range 40–50 °C).

General Procedure (GP). Methyl 5,7-Diphenyl-6-(phenylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,3*R,4*S**)-5a-H]:** A solution of methyl 2-chloro-2-cyclopropylideneacetate (**1**-H) (205 mg, 1.40 mmol) and *N*,*N*′,*N*′′-triphenylguanidine (**2a**) (402 mg, 1.40 mmol) in 20 mL of anhydrous acetonitrile was treated with NaH (56 mg, 1.40 mmol, 60% dispersion in mineral oil) at 0 °C. The suspension was subsequently stirred for 24 h and then warmed to ambient temperature. After filtration through 5 g of silica gel (column 1.5 × 3 cm), eluting with 200 mL of Et_2O, the solvent was evaporated in vacuo. The dark yellow residue was purified by column chromatography over 30 g of silica gel (column 1.5 × 30 cm) with 500 mL of Et_2O, to give (*Z*,3*R**,4*S**)-**5a**-H [R_f = 0.22 (Et_2O)] as a colorless solid, m.p. 114 °C. IR (KBr): $\tilde{\nu}$ = 3405 , 2954, 2927, 2854, 1751, 1653, 1588, 1493, 1457, 1382, 1265, 1141 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.64–1.11 (m, 4 H, *c*Pr-CH_2), 3.82

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(s, 3 H, OCH_3), 4.36 (s, 1 H, 4-H), 6.50–7.59 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 4.80 (–, *c*Pr-C), 14.50 (–, *c*Pr-C), 45.53 (C_{quat}, *c*Pr-C), 52.48 (+, OCH_3), 67.06 (+, C-4), 120.24 (+, Ph-C), 121.39 (+, Ph-C), 122.29 (+, Ph-C), 123.25 (+, Ph-C), 126.58 (+, Ph-C), 127.62 (+, Ph-C), 128.50 (+, Ph-C), 128.59 (+, Ph-C), 128.83 (+, Ph-C), 148.36 (C_{quat}, Ph-C*), 140.43 (C_{quat}, Ph-C*), 147.98 (C_{quat}, Ph-C*), 149.94 (C_{quat}, C=N*), 170.96 (C_{quat}, CO_2Me) ppm. MS (70 eV): *m*/*z* (%) = 397 (100) [M^+], 338 (62) [$M^+ - CO_2Me$], 306 (8) [$M^+ - NPh$].

Methyl 1-Ethyl-5,7-diphenyl-6-(phenylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,1*R,3*R**,4*S**)-5a-Et]:** According to the GP, (*Z*,1*R**,3*R**,4*S**)-**5a**-Et (450 mg, 75%) was obtained from **1**-Et (245 mg, 1.40 mmol), NaH (61 mg, 1.40 mmol) and **2a** (402 mg, 1.40 mmol) in acetonitrile (10 mL) as a colorless solid, R_f = 0.08 (Et_2O), m.p. 98 °C. IR (KBr): $\tilde{\nu}$ = 3061 , 2932, 2873, 1751, 1653, 1588, 1494, 1452, 1382, 1266, 1143, 1018 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.41 (t, ^3J = 7.1 Hz, 1 H, *c*Pr-CH*), 0.77 (t, ^3J = 7.1 Hz, 1 H, *c*Pr-CH_2*), 1.01 (t, ^3J = 7.1 Hz, 3 H, CH_2CH_3), 1.07–1.52 (m, 3 H, *c*Pr-CH_2, CH_2CH_3), 3.86 (s, 3 H, OCH_3), 4.38 (s, 1 H, 7-H), 6.54–7.50 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.00 (+, *c*Pr-C), 13.23 (–, *c*Pr-C), 22.29 (+, CH_2CH_3), 25.48 (–, CH_2CH_3), 49.14 (C_{quat}, *c*Pr-C), 52.48 (+, OCH_3), 62.19 (+, C-7), 120.20 (+, Ph-C), 120.67 (+, Ph-C), 122.33 (+, Ph-C), 123.34 (+, Ph-C), 126.63 (+, Ph-C), 127.64 (+, Ph-C), 128.54 (+, Ph-C), 128.61 (+, Ph-C), 129.18 (+, Ph-C), 138.33 (C_{quat}, Ph-C*), 140.50 (C_{quat}, Ph-C*), 148.60 (C_{quat}, Ph-C*), 150.17 (C_{quat}, C=N*), 171.43 (C_{quat}, CO_2Me) ppm. MS (70 eV): *m*/*z* (%) = 425 (100) [M^+], 366 (68) [$M^+ - CO_2Me$], 334 (3) [$M^+ - NPh$]. $C_{27}H_{27}N_3O_2$ (421.5): calcd. C 76.21, H 6.40, N 9.88; found C 76.40, H 6.70, N 10.03.

Methyl 1-(2′-Benzyloxyethyl)-5,7-diphenyl-6-(phenylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,1*R,3*R**,4*S**)-5a-$(CH_2)_2$OBn]:** According to the GP, (*Z*,1*R**,3*R**,4*S**)-**5a**-$(CH_2)_2$OBn (450 mg, 75%) was obtained from **1**-$(CH_2)_2$OBn (314 mg, 1.12 mmol), NaH (60 mg, 1.38 mmol) and **2a** (348 mg, 1.21 mmol) in acetonitrile (10 mL) as a colorless solid, R_f = 0.76 (PE/Et_2O, 1:1). IR (film): $\tilde{\nu}$ = 3029 , 2857, 1751, 1653, 1588, 1493, 1384, 1267, 1143 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.48 (t, ^3J = 7.2 Hz, 1 H, *c*Pr-CH*), 0.83 (dd, ^3J = 7.2, ^3J = 10.0 Hz, 1 H, *c*Pr-CH_2*), 1.27 (mc, 1 H, *c*Pr-CH_2), 1.76 (mc, 2 H, CH_2CH_2OBn), 3.55 (mc, 2 H, CH_2CH_2OBn), 3.87 (s, 3 H, OCH_3), 4.41 (s, 2 H, OCH_2Ph), 4.62 (s, 1 H, 7-H), 6.58–7.55 (m, 20 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 10.56 (–, *c*Pr-C), 21.53 (+, *c*Pr-C), 29.34 (–, CH_2CH_2OBn), 49.03 (C_{quat}, *c*Pr-C), 52.36 (+, OCH_3), 62.36 (+, C-7), 68.77 (–, CH_2CH_2OBn), 72.81 (–, OCH_2Ph), 120.11 (+, Ph-C), 120.34 (+, Ph-C), 122.27 (+, Ph-C), 123.06 (+, Ph-C), 126.56 (+, Ph-C), 127.43 (+, Ph-C), 127.49 (+, Ph-C), 127.56 (+, Ph-C), 128.22 (+, Ph-C), 128.47 (+, Ph-C), 128.60 (+, Ph-C), 129.11 (+, Ph-C), 138.07 (C_{quat}, Ph-C*), 138.29 (C_{quat}, Ph-C*), 140.52 (C_{quat}, Ph-C*), 148.58 (C_{quat}, Ph-C*), 150.49 (C_{quat}, C=N*), 171.36 (C_{quat}, CO_2Me) ppm. $C_{33}H_{33}N_3O_3$ (519.6): calcd. C 76.28, H 6.40, N 8.09; found C 76.54, H 6.03, N 7.94.

Methyl 1-Isopropyl-5,7-diphenyl-6-(phenylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,1*R,3*R**,4*S**)-5a-*i*Pr]:** According to the GP, (*Z*,1*R**,3*R**,4*S**)-**5a**-*i*Pr (330 mg, 0.75 mmol) was obtained from **1**-*i*Pr (283 mg, 1.50 mmol), NaH (60 mg, 1.50 mmol) and **2a** (283 mg, 1.50 mmol) in acetonitrile (20 mL) as a colorless solid, R_f = 0.33 (hexane/Et_2O, 15:1), m.p. 131 °C. IR (KBr): $\tilde{\nu}$ = 3060 , 2957, 2925, 2868, 1729, 1652, 1588, 1496, 1381, 1265, 1138, 1069, 1014, 763, 750, 692, 575, 507 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.44 (t, J = 6.6 Hz, 1 H, one of *c*Pr-CH_2), 0.73–0.93 (m, 2 H, *c*Pr-CH and one of *c*Pr-CH_2), 1.01 (d, J = 6.0 Hz, 6 H, CH_3), 1.17 (quin, J = 6.0 Hz, 1 H, CH), 3.85 (s, 3 H, OCH_3), 4.35 (s, 1 H, CH), 6.55 (t, J = 7.5 Hz, 1 H, Ph-CH) 6.82 (d, J = 7.5 Hz, 1 H, Ph-CH), 6.85 (d, J = 7.5 Hz, 1 H, Ph-CH), 6.95–7.14 (m, 6 H, Ph-CH), 7.23 (t, J = 7.5 Hz, 2 H, Ph-CH), 7.43 (d, J = 7.5 Hz, 2 H, Ph-CH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 10.37 (–, *c*Pr-CH_2), 21.44 (+, CH_3), 21.78 (+, CH_3), 28.92 (+, *c*Pr-CH), 49.24 (C_{quat}, *c*Pr-C), 52.33 (+, OCH_3), 62.37 (+, CH), 120.05 (+, Ph-C), 120.77 (+, Ph-C), 122.19 (+, Ph-C), 123.29 (+, Ph-C), 126.47 (+, Ph-C), 127.51 (+, Ph-C), 128.42 (+, Ph-C), 128.46 (+, Ph-C), 128.97 (+, Ph-CH), 138.13 (C_{quat}, Ph-C), 140.31 (C_{quat}, Ph-C), 148.54 (C_{quat}, Ph-C), 150.01 (C_{quat}, C=N), 171.21 (C_{quat}, CO_2Me) ppm. $C_{28}H_{29}N_3O_2$ (439.6): calcd. C 76.51, H 6.65; found C 76.34, H 6.43.

Methyl 5,7-Di(*p*-tolyl)-6-(*p*-tolylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,3*R,4*S**)-5b-H]:** According to the GP, (*Z*,3*R**,4*S**)-**5b**-H (585 mg, 1.33 mmol) was obtained from **1**-H (209 mg, 1.40 mmol), NaH (56 mg, 1.40 mmol) and **2b** (461 mg, 1.40 mmol) in acetonitrile (10 mL) as a colorless solid, R_f = 0.74 (Et_2O), m.p. 176 °C. IR (film): $\tilde{\nu}$ = 3029, 2857, 1751, 1653, 1588, 1493, 1384, 1267, 1143 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.72–1.04 (m, 4 H, *c*Pr-CH_2), 2.14 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 4.37 (s, 1 H, CH), 6.64 (d, J = 8.0 Hz, 1 H, Ar-CH), 6.70 (d, J = 8.0 Hz, 1 H, Ar-CH), 6.88 (d, J = 8.0 Hz, 1 H, Ar-CH), 6.94 (d, J = 8.0 Hz, 1 H, Ar-CH), 7.10 (d, J = 7.5 Hz, 1 H, Ar-CH), 7.44 (d, J = 7.5 Hz, 1 H, Ar-CH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 4.62 (–, *c*Pr-CH_2), 13.86 (–, *c*Pr-CH_2), 20.28 (+, CH_3), 20.43 (+, CH_3), 20.60 (+, CH_3), 45.23 (*c*Pr-C), 52.07 (+, OCH_3), 67.01 (+, CH), 120.61 (+, Ar-CH), 121.89 (+, Ar-CH), 127.85 (+, Ar-CH), 128.52 (+, Ar-CH), 128.72 (C_{quat}, Ph-C), 128.81 (+, Ar-CH), 132.42 (C_{quat}, Ph-C), 135.23 (C_{quat}, Ph-C), 135.89 (C_{quat}, Ph-C), 137.99 (C_{quat}, Ph-C), 145.73 (C_{quat}, Ph-C), 149.82 (C_{quat}, C=N), 170.83 (C_{quat}, CO_2Me) ppm. MS (70 eV): *m*/*z* (%) = 439 (76), 380 (41), 308 (25), 222 (100), 91 (27). $C_{28}H_{29}N_3O_2$ (439.6): calcd. C 76.51, H 6.65; found C 76.34, H 6.43.

Methyl 1-Methyl-5,7-diphenyl-6-(*p*-tolylimino)-5,7-diazaspiro[2.4]-heptane-4-carboxylate [(*Z*,1*R,3*R**,4*S**)-5b-Me]:** According to the GP, (*Z*,1*R**,3*R**,4*S**)-**5b**-Me (265 mg, 83%) was obtained from **1**-Me (112 mg, 0.70 mmol), NaH (28 mg, 0.70 mmol) and **2b** (229 mg, 0.70 mmol) in acetonitrile (10 mL) as a colorless solid, R_f = 0.22 (hexane/Et_2O, 4:1), m.p. 156 °C ^1H NMR (250 MHz, $CDCl_3$): δ = 0.32 (d, J = 5.5 Hz, 1 H, *c*Pr-CH_2), 0.73–0.77 (dt, J = 5.5, 6.8 Hz, 1 H, *c*Pr-CH), 1.14 (d, J = 6.8 Hz 3 H, CH_3), 1.29 (d, J = 5.5 Hz, 1 H, *c*Pr-CH_2), 2.08 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 3.83, 3.73* (s, 3 H, OCH_3), 4.37 (s, 1 H, CH), 6.51–7.50 (m, 12 H, Ar-CH) ppm. – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.12 (–, *c*Pr-CH_2), 13.80 (+, CH_3), 17.87 (–, *c*Pr-CH_2), 20.53 (+, CH_3), 20.70 (+, CH_3), 20.90 (+, CH_3), 49.04 (C_{quat}, *c*Pr-C), 52.40 (+, OCH_3), 61.90 (+, CH), 120.05 (C_{quat}, Ph-C), 120.63 (+, Ar-CH), 122.17 (+, Ar-CH), 127.55 (C_{quat}, Ph-C), 128.08 (+, Ar-CH), 129.06 (+, Ar-CH), 129.32 (C_{quat}, Ph-C), 135.86 (C_{quat}, Ph-C), 136.23 (C_{quat}, Ph-C), 138.25 (C_{quat}, Ph-C), 146.14 (C_{quat}, C=N), 171.70 (C_{quat}, CO_2Me) ppm. MS (70 eV): *m*/*z* (%) = 439 (76), 380 (41), 308 (25), 222 (100), 91 (27). *Rotamer.

Methyl 5,7-Bis(3-chlorophenyl)-6-[(3-chlorophenyl)imino]-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,3*R,4*S**)-5c-H]:** According to the GP, (*Z*,3*R**,4*S**)-**5c**-H (71 mg, 0.14 mmol) was obtained from **1**-H (75 mg, 0.51 mmol), NaH (20 mg, 0.51 mmol) and **2c** (200 mg, 0.51 mmol) in acetonitrile (10 mL) as a light yellow oil, R_f = 0.30 (hexane/Et_2O, 5:1). IR (KBr): $\tilde{\nu}$ = 3064 , 2949, 1754, 1655, 1578, 1483, 1299, 1234, 971, 800, 747 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80–1.00 (m, 4 H, *c*Pr-CH_2), 3.80 (s, 3 H,OCH_3), 4.53 (s, 1 H,

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CH), 6.88–7.33 (m, 11 H, Ar-CH), 7.70 (s, 1 H, Ar-CH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 5.24 (–, *c*Pr-CH_2), 11.47 (–, *c*Pr-CH_2), 43.21 (C_{quat}, *c*Pr-C), 52.92 (+, OCH_3), 63.46 (+, CH), 116.26 (+, Ar-CH), 116.91 (+, Ar-CH), 118.86 (+, Ar-CH), 122.48 (+, Ar-CH), 123.82 (+, Ar-CH), 127.74 (+, Ar-CH), 128.71 (+, Ar-CH), 129.57 (+, Ar-CH), 130.06 (+, Ar-CH), 130.30 (+, Ar-CH), 129.74 (+, Ar-CH), 134.17 (C_{quat}, Ar-C), 134.75 (C_{quat}, C-Cl), 134.83 (C_{quat}, C-Cl), 134.90 (C_{quat}, C-Cl), 139.88 (C_{quat}, C=N), 169.22 (C_{quat}, CO_2Me) ppm.

Methyl 5,7-Bis(4-bromophenyl)-6-[(4-bromophenyl)imino]-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,3*R,4*S**)-5d-H]:** According to the GP, (*Z*,3*R**,4*S**)-**5d**-H (410 mg, 0.65 mmol) was obtained from **1**-H (200 mg, 1.36 mmol), NaH (55 mg, 1.36 mmol) and **2d** (713 mg, 1.36 mmol) in acetonitrile (20 mL) as a colorless foam, R_f = 0.20 (hexane/Et_2O, 3:1), m.p. 124 °C. IR (KBr): $\tilde{\nu}$ = 3064 , 2949, 1731, 1653, 1575, 1483, 1380, 1282, 1192, 1136, 1068, 1009, 901, 826, 506 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.62–0.99 (m, 4 H, *c*Pr-CH_2), 3.82, 3.78* (s, 3 H, OCH_3), 4.29 (s, 1 H, CH), 6.48 (d, *J* = 8.8 Hz, 2 H, Ph-CH) 6.77 (d, *J* = 8.3 Hz, 2 H, Ph-CH), 6.97, 7.35* (d, *J* = 8.8 Hz, 2 H, Ph-CH), 7.24 (d, *J* = 8.8 Hz, 2 H, Ph-CH), 7.27–7.44 (m, 4 H, Ph-CH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 4.98 (–, *c*Pr-CH_2), 14.43 (–, *c*Pr-CH_2), 45.70 (C_{quat}, *c*Pr-C), 52.80 (+, OCH_3), 66.74 (+, CH), 113.46 (C_{quat}, C–N), 116.67 (C_{quat}, C-N), 120.96 (C_{quat}, C-N), 122.46 (+, Ph-CH), 124.01 (+, Ph-CH), 130.64 (+, Ph-CH), 130.79 (+, Ph-CH), 131.76 (+, Ph-CH), 131.88 (+, Ph-CH), 132.01 (+, Ph-CH), 136.75 (C_{quat}, C-Br), 139.11 (C_{quat}, C-Br), 147.20 (C_{quat}, C-Br), 149.78 (C_{quat}, C=N), 170.49 (C_{quat}, CO_2Me) ppm. $C_{25}H_{20}Br_3N_3O_2$ (634.2): calcd. C 47.35, H 3.18, N 6.63; found C 47.65, H 3.21, N 6.50. *Rotamer.

Crystal Structure Analysis of Methyl 1-Ethyl-5,7-diphenyl-6-(phenylimino)-5,7-diazaspiro[2.4]heptane-4-carboxylate [(*Z*,1*R,3*R**,4*S**)-5a-Et]:**[6] Crystals of **5a**-Et for the attempted X-ray crystal-structure analysis were grown by slow evaporation of a solution in Et_2O/MeOH at 0 °C. The X-ray data were collected with a Bruker SMART CCD 6000 diffractometer at 133 K. Structures were solved by using direct methods and refined by full-matrix least-squares on F^2 for all data. Non-hydrogen atoms (except for the disordered ones) were refined with anisotropic displacement parameters. Disordered atoms were refined with equal site occupation factors of 0.5. Empirical formula: $C_{27}H_{27}N_3O_2$ (425.52), crystallized in the monoclinic space group *C*2/*c*, *a* = 2733.9(5) pm α = 90°, *b* = 772.67(14) pm β = 104.348(3)°, *c* = 2230.4(4) pm γ = 90°, *V* = 4.5646(14) nm^3, *Z* = 8, ρ = 1.238 Mg/m^3, μ = 0.079 mm^{-1}. 17472 reflections collected [θ_{max} = 22.50°, *R*(int) = 0.0690]. Final R_1 [$I > 2\sigma(I)$] = 0.0795, wR_2 (all data) = 0.1392 for 291 refined parameters and 2992 independent reflections, GOF = 1.435, maximum and minimum residual electron density 0.186 and –0.261 e Å^{-3}.

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