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Synthesis of Diverse Fused Pyrazoles through Palladium-Mediated Heteroarylation of Heteroarene C–H Bonds[‡]

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Keywords: Palladium / Nitrogen heterocycles / Heteroarylation / Morita–Baylis–Hillman / Synthetic methods

A facile and efficient synthesis of new fused pyrazoles through the $Pd(OAc)_2$-mediated heteroarylation of heteroarene C–H bonds in Morita–Baylis–Hillman derivatives of 4-iodopyrazolecarbaldehydes is described.

Introduction

Transition-metal-catalyzed direct (hetero)arylation of heteroarene C–H bonds in an intramolecular fashion represents a powerful tool for the construction of a variety of fused-ring heteroarenes.[1] As described by Lautens et al., direct arylation of heteroarenes could be achieved through either electrophilic substitution reactions, Heck-type reactions or cross-coupling reactions.[1a] Although there are several procedures for the intramolecular direct arylation of heteroarenes, frequently the tether approach is adopted, because it is considered to be robust and proceeds with great regioselective control owing to the limited degree of freedom. Analysis of reported examples reveals that the use of halogenated benzene as the coupling partner in these reactions is common, whereas there are fewer examples illustrating the participation of halogenated heteroarenes. It is widely reported that halogenated pyrazoles are excellent building blocks for accessing new chemical entities incorporating a pyrazole nucleus.[2] As part of one of our research programs, we have also established 4-iodopyrazole derivatives to be convenient starting substrates for preparing diverse fused-pyrazoles. We have successfully demonstrated that the cross-coupling reactions of 4-iodopyrazolecarbaldehydes or their Morita–Baylis–Hillman (MBH) derivatives under different conditions results in the synthesis of pyrazolo[4,3-*b*]pyridin-5-ones, pyrazolo[4,3-*b*]pyridines, pyrazolo-fused benzodiazepines and benzoxazepines, pyrazolo[4,3-*d*]pyrimidines and pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones.[3] Fused pyrazoles are of great significance in medicinal chemistry, because compounds bearing such cores display a variety of biological activities.[4] In continuation of our work, we envisaged that palladium-promoted intramolecular heteroarylation of MBH derivatives of 4-iodopyrazolecarbaldehydes would not only allow access to several unknown fused pyrazole systems but would also enhance the scope of the intramolecular heteroarylation strategy (Figure 1). A literature survey revealed that Kim et al. have successfully accomplished the synthesis of diverse

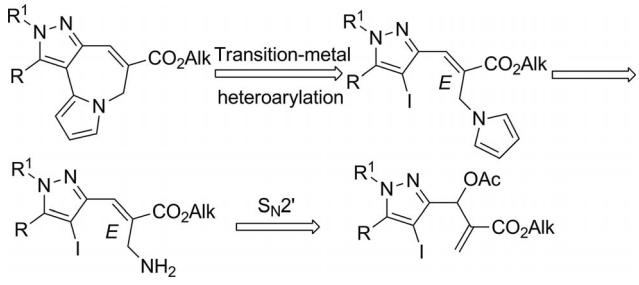

Figure 1. Retrosynthetic analysis for the synthesis of fused pyrazoles.

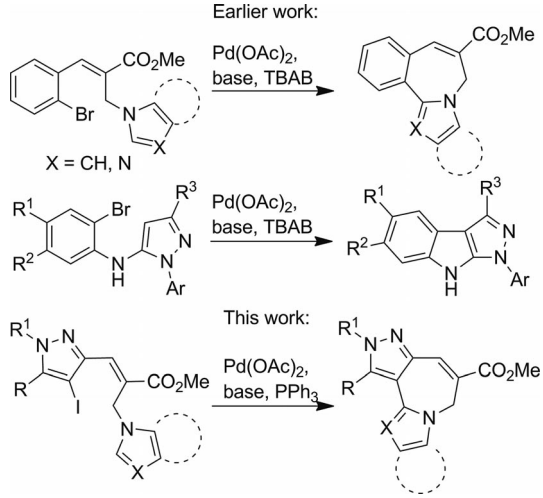

Figure 2. Different heteroarylation strategies. TBAB = tetrabutylammonium bromide.

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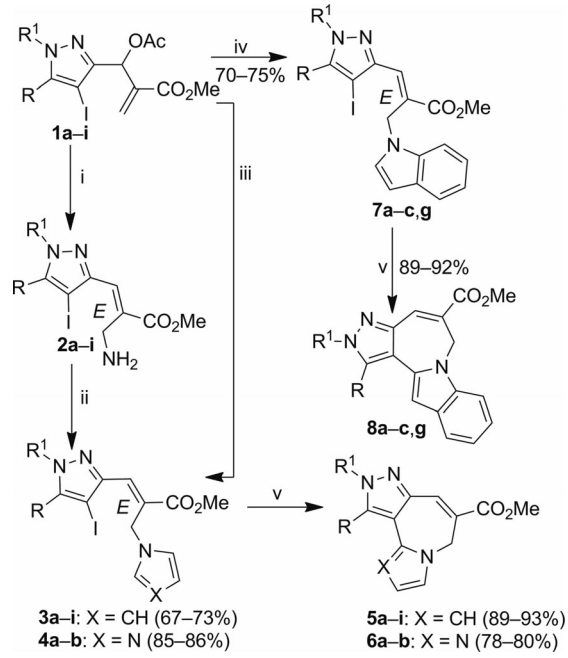
benzazepines by using a similar protocol under ligandless conditions, whereas Ila and co-workers have reported the synthesis of fused pyrazoles through intramolecular Heck heteroarylation of 1,3-disubstituted 5-(2-bromoanilino)pyrazole (Figure 2).[5,6] In both the studies 2-bromobenzene was tethered to the heterosystem, and ligandless conditions were employed. We decided to proceed to investigate the utility of iodopyrazoles for this methodology. Herein, we disclose a facile efficient synthesis of new fused pyrazole derivatives employing intramolecular palladium-mediated direct arylation of pyrrole, indole and imidazole nuclei on derivatives generated from MBH adducts of 4-iodopyrazolecarbaldehydes.

Results and Discussion

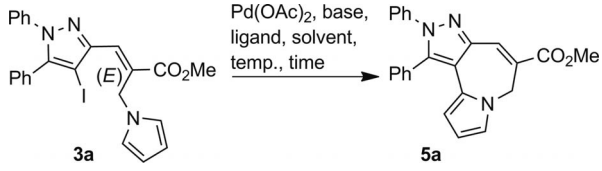
In the first phase of the study we investigated the strategy with the heteroarylation of allylpyrroles that can be readily prepared from primary allylamines. We commenced our studies with the stereoselective synthesis of primary allylamines **2a**–**i** from MBH acetates **1a**–**i** of 4-iodo-3-pyrazolecarbaldehydes according to the reported procedure.[3c] Because (*E*) stereochemistry on the substrates is required for the anticipated intramolecular heteroarylation, we performed the studies with derivatives generated from acrylates only. Treatment of these primary allylamines **2a**–**i** with 2,5-dimethoxytetrahydrofuran and AcOH/H_2O in CH_2Cl_2 at 65 °C for 4–5 h afforded allyl pyrroles **3a**–**i** in 67–73% yields stereoselectively as (*E*) isomers (Scheme 1). It is worthwhile to note that direct reaction of pyrrole with MBH acetate leads to allylpyrrole in minor yield only.[7] With the required compounds for the palladium-mediated reactions in hand, we carried out an optimization study to determine suitable conditions for the intramolecular arylation reaction (Table 1). We screened the reaction of **3a** as the model substrate under different conditions for intramolecular heteroarylation. Initially, the reaction of **3a** was performed with $Pd(OAc)_2$ (10 mol-%) and K_2CO_3 (2 equiv.) in *N*,*N*-dimethylformamide (DMF) at 90 °C for 12 h (Table 1, Entry 1), which successfully resulted in the isolation of the desired methyl 1,2-diphenyl-2,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]azepine-5-carboxylate (**5a**) in 37% yield. Next, PPh_3 (20 mol-%) was added as the ligand, and the reaction was carried out under similar conditions. In the presence of PPh_3, the reaction was complete in 2 h, and the yield of **5a** increased to 93% (Table 1, Entry 2). To investigate the effect of solvent, we performed the reaction in DMF, dimethyl sulfoxide (DMSO), acetonitrile (MeCN) and toluene and found that DMF was the most effective medium (Table 1, Entries 2–5). Amongst the different bases, K_2CO_3 performed the best, although the other bases were also successful, albeit in lower yields (Table 1, Entries 5–8).

The generality of the reaction sequence was investigated with other allylpyrrole derivatives **3b**–**i** (Table 2, Entries 1–9) prepared by making changes at position 1 and 5 of the pyrazole nucleus. Under the optimized conditions all substrates reacted efficiently to furnish respective products **5b**–**i** in excellent yields.



Scheme 1. Reagents and conditions: (i) NH_3/MeOH, room temp., 30 min. (ii) 2,5-Dimethoxytetrahydrofuran (1.5 equiv.), AcOH, H_2O, CH_2Cl_2, 60 °C, 4–5 h. (iii) Imidazole (1.2 equiv.), K_2CO_3 (1.5 equiv.), DMF, room temp., 3 h. (iv) Indole (1.2 equiv.), KOH (1.5 equiv.), DMF, 0 °C, 6–8 h. (v) $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), K_2CO_3 (2.0 equiv.), 90 °C, 2 h.

Table 1. Results of the optimization study for the heteroarylation of allylpyrrole.[a]

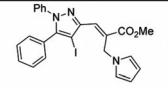
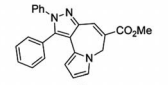
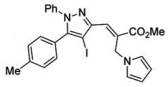
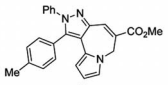
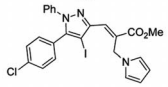
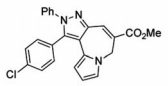
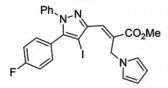
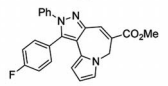
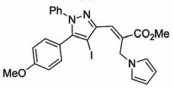
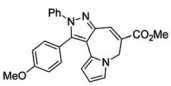
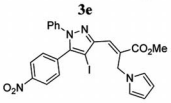
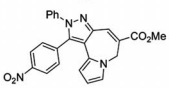
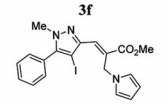
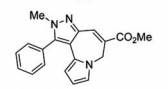
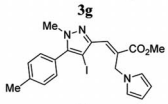
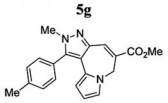
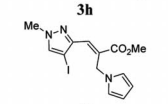
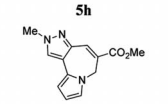
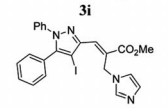
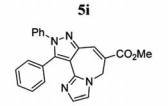
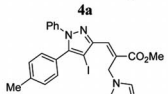
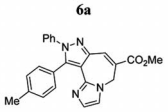
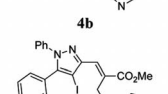
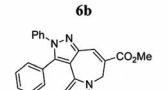
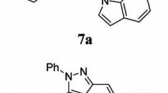
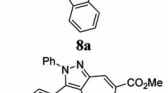
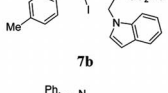
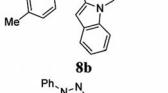
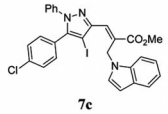
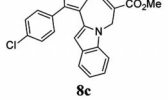


Entry	Ligand	Base	Solvent	Temp. [°C]	Time [h]	Yield[b] [%]
1	–	K_2CO_3	DMF	90	2	37
2	PPh_3	K_2CO_3	DMF	90	2	93
3	PPh_3	K_2CO_3	DMSO	90	2	78
4	PPh_3	K_2CO_3	MeCN	80	4	56
5	PPh_3	K_2CO_3	toluene	90	3	34
6	PPh_3	Na_2CO_3	DMF	90	2	67
7	PPh_3	NEt_3	DMF	90	4	72
8	PPh_3	NaOH	DMF	90	3	57

[a] Reactions were performed with $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), K_2CO_3 (2.0 equiv.). [b] Isolated yields after column chromatography.

With a successful protocol in hand, we wanted to expand the diversity of the fused pyrazoles that could be obtained by using this method. Allylimidazoles **4a**,**b** and allyl indoles **7a**–**c**,**g** were prepared from MBH acetates by using reported procedures (Scheme 1).[8] Treatment of these substrates with $Pd(OAc)_2$ in the presence of ligand and base afforded the corresponding fused pyrazoles **6a**–**b** and **8a**–**c**,**g** in excellent yields (Table 2, Entries 10–15). Theoretically, two isomeric cyclization products may arise from the coupling reaction

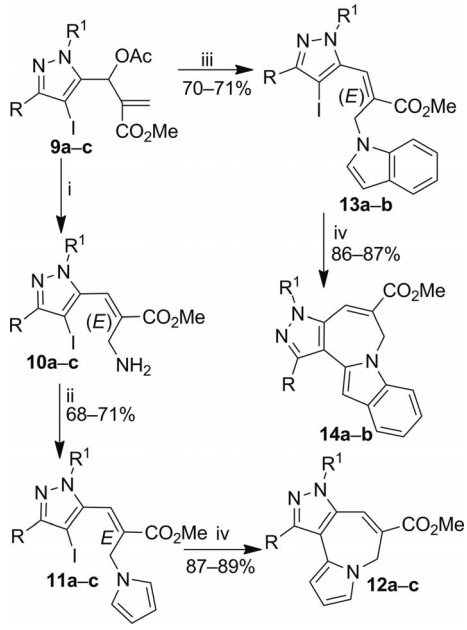
Table 2. Scope of heteroarylation[a] of the substrates derived from MBH acetates of 4-iodopyrazole-3-carbaldehydes.

Entry	Reactant	Product	Yield [%][b]
1	 **3a**	 **5a**	93
2	 **3b**	 **5b**	91
3	 **3c**	 **5c**	90
4	 **3d**	 **5d**	89
5	 **3e**	 **5e**	90
6	 **3f**	 **5f**	89
7	 **3g**	 **5g**	92
8	 **3h**	 **5h**	90
9	 **3i**	 **5i**	91
10	 **4a**	 **6a**	78
11	 **4b**	 **6b**	80
12	 **7a**	 **8a**	92
13	 **7b**	 **8b**	90
14	 **7c**	 **8c**	89
15	 **7g**	 **8g**	91

[a] Reactions were performed with $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), K_2CO_3 (2.0 equiv.), 90 °C, 2 h. [b] Isolated yields after column chromatography.

by activation of either the C–H bond at C-2 of the imidazole or the C–H bond at C-5. Interestingly, the reaction was regioselective for C-2, which was confirmed by the absence of a signal in the ^1H NMR spectrum at δ = 8.70 ppm (in **6a** from **4a**) attributed to the proton at the C-2 position.[9]

To further extend the scope of the protocol, starting allylpyrroles **11a**–**c** and allyl indoles **13a**–**b** were prepared from the MBH acetates **9a**–**c** of 4-iodo-5-pyrazolecarbaldehydes (Scheme 2). Treatment of **11a**–**c** and **13a**–**b** with $Pd(OAc)_2$ and PPh_3 in the presence of base in DMF under similar conditions resulted in **12a**–**c** and **14a**–**b** in 86–89% yields, respectively (Table 3).



Scheme 2. Reagents and conditions: (i) NH_3/MeOH, room temp., 30 min. (ii) 2,5-Dimethoxytetrahydrofuran (1.5 equiv.), AcOH, H_2O, CH_2Cl_2, 60 °C, 4–5 h. (iii) Indole (1.2 equiv.), KOH (1.5 equiv.), DMF, 0 °C, 6–8 h. (iv) $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), K_2CO_3 (2.0 equiv.), 90 °C, 2.

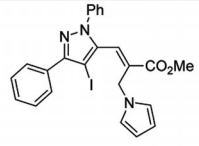
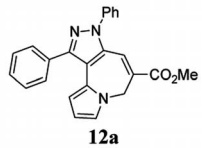
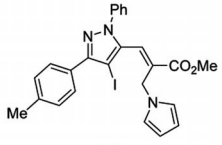
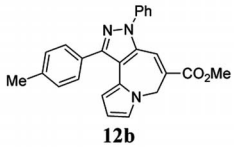
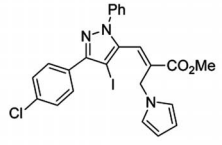
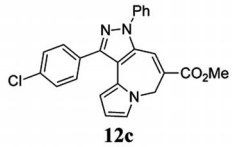
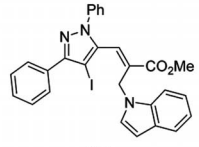
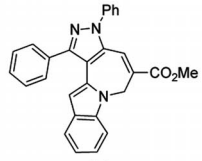
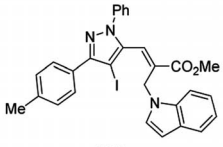
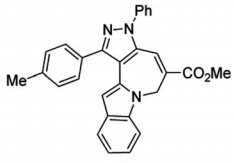
Conclusion

We have demonstrated the use of MBH derivatives of 4-iodopyrazolecarbaldehydes for the synthesis of new fused pyrazoles through heteroarylation of heteroarene C–H bonds. The protocol is attractive, because it works with a wide variety of substrates and does not require any special conditions. Excellent yields of the annulated pyrazoles are an important feature of this protocol. More work showcasing the utility of the halogenated pyrazoles for the synthesis of different fused pyrazoles through transition-metal-based reactions is underway in our laboratory, which will be reported soon.

Experimental Section

General: Melting points were determined in capillary tubes with a Precision melting point apparatus containing silicon oil. IR spectra

Table 3. Scope of heteroarylation[a] of the substrates derived from MBH acetates of 4-iodopyrazole-5-carbaldehydes.

Entry	Reactant	Product	Yield [%][b]
1	 **11a**	 **12a**	89
2	 **11b**	 **12b**	88
3	 **11c**	 **12c**	87
4	 **13a**	 **14a**	87
5	 **13b**	 **14b**	86

[a] Reactions were performed with $Pd(OAc)_2$ (0.1 equiv.), PPh_3 (0.2 equiv.), K_2CO_3 (2.0 equiv.), 90 °C, 2 h. [b] Isolated yields after column chromatography.

were recorded with a Perkin–Elmer's RX I FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded either with a Bruker DPX-200 or a Bruker Avance DRX-300 FT spectrometer with TMS as an internal standard. ESMS data were recorded with a MICROMASS Quadro-II LCMS system. HRMS data were recorded as EI-HRMS with an Agilent 6520 Q-TOF, LC-MS/MS mass spectrometer.

General Procedure for the Synthesis of Compounds 3a–i and 11a–c as Exemplified for 3a: To a solution of compound **2a** (250 mg, 0.54 mmol) in CH_2Cl_2 (10 mL), 2,5-dimethoxytetrahydrofuran (0.084 mL, 0.65 mmol), AcOH (2 mL) and water (3 mL) were added simultaneously, and the reaction mixture was heated at 60 °C for 4 h. The reaction mixture was then diluted with water (20 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL), the organic layers were combined and washed with brine (20 mL), dried with anhydrous Na_2SO_4 and concentrated under vacuum. Column chromatography of the crude product on silica gel (hexanes/EtOAc, 5:95) furnished pure **3a** as a white solid (202 mg, 73%).

Methyl (*E*)-3-(4-Iodo-1,5-diphenyl-1*H*-pyrazol-3-yl)-2-(1*H*-pyrrol-1-ylmethyl)prop-2-enoate (3a): M.p. 159–160 °C. R_f = 0.56 (hexanes/EtOAc, 90:10, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1710 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, CO_2Me), 5.52 (s, 2 H, CH_2), 6.08 (t, J = 1.9 Hz, 2 H, ArH), 6.94 (t, J = 1.9 Hz, 2 H, ArH), 7.22–7.30 (m, 7 H, ArH), 7.39–7.41 (m, 3 H, ArH), 7.73 (s, 1 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.0, 52.4, 71.2, 107.5, 121.6, 124.6, 128.1, 128.7, 129.0, 129.4, 130.2, 130.3, 131.3, 139.6, 144.8, 148.2, 167.6 ppm. MS (ES+): m/z = 509.9 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{21}IN_3O_2$ [MH]$^+$ 510.0678; found 510.0675.

Methyl (*E*)-3-(4-Iodo-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-(1*H*-pyrrol-1-ylmethyl)prop-2-enoate (11a): 71% as a colorless oil (197 mg from 250 mg). R_f = 0.61 (hexanes/EtOAc, 90:10, v/v). IR (neat): $\tilde{\nu}_{max}$ = 1722 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, CO_2Me), 4.76 (s, 2 H, CH_2), 6.03 (t, J = 2.0 Hz, 2 H, ArH), 6.43 (t, J = 1.9 Hz, 2 H, ArH), 7.38–7.49 (m, 9 H, ArH and =CH), 7.92–7.94 (m, 2 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 47.0, 53.1, 65.3, 109.0, 121.5, 124.1, 128.8, 128.88, 128.94, 129.3, 129.9, 130.5, 132.5, 135.6, 140.0, 140.2, 154.2, 166.3 ppm. MS (ES+): m/z = 510.0 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{21}IN_3O_2$ [MH]$^+$ 510.0678; found 510.0688.

General Procedure for the Synthesis of Compounds 4a–b as Exemplified for 4a: To a stirred solution of compound **1a** (500 mg, 0.99 mmol) in DMF (5 mL), imidazole (81 mg, 1.20 mmol) and K_2CO_3 (206 mg, 1.49 mmol) were added at room temperature, and the reaction was continued for 3 h. Thereafter, ethyl acetate (20 mL) and water (20 mL) were added, and the layers were separated. The aqueous layer was further extracted with ethyl acetate (2 × 15 mL), the organic layers were combined, washed with brine (20 mL), dried with anhydrous Na_2SO_4 and concentrated under vacuum. Column chromatography of the crude product on silica gel (hexanes/EtOAc, 50:50) afforded pure **4a** as a white solid (432 mg, 85%).

Methyl (E)-2-[(1*H*-Imidazol-1-yl)methyl]-3-(4-iodo-1,5-diphenyl-1*H*-pyrazol-3-yl)prop-2-enoate (4a): 85% as a white solid (432 mg from 500 mg). M.p. 210–212 °C. R_f = 0.40 (hexanes/EtOAc, 50:50, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1714 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, CO_2Me), 5.66 (s, 2 H, CH_2), 7.21–7.28 (m, 5 H, ArH), 7.37–7.42 (m, 6 H, ArH), 7.49 (s, 1 H, ArH), 7.92 (s, 1 H, =CH), 8.70 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.7, 53.2, 71.7, 119.8, 121.8, 124.9, 125.2, 128.7, 128.9, 129.1, 129.7, 129.8, 130.3, 134.6, 134.9, 139.2, 146.2, 147.4, 166.7 ppm. MS (ES+): m/z = 511.0 [M^+ + 1]. HRMS: calcd. for $C_{23}H_{20}IN_4O_2$ [MH]$^+$ 511.0631; found 511.0643.

General Procedure for the Synthesis of Compounds 7a–c,g and 13a,b as Exemplified for 7a: To a stirred solution of compound **1a** (500 mg, 0.99 mmol) in DMF (5 mL), indole (140 mg, 1.20 mmol) and KOH (84 mg, 1.49 mmol) were added, and the reaction was allowed to continue at room temperature for 6 h. After completion of the reaction, ethyl acetate (20 mL) and water (20 mL) were added, and the layers were separated. The aqueous layer was further extracted with ethyl acetate (2 × 15 mL). The organic layers were combined, washed with brine (20 mL), dried with anhydrous Na_2SO_4 and concentrated under vacuum. Column chromatography of the crude product on silica gel (hexanes/EtOAc, 5:95) furnished pure **7a** as a white solid (418 mg, 75%).

Methyl (*E*)-2-[(1*H*-Indol-1-yl)methyl]-3-(4-iodo-1,5-diphenyl-1*H*-pyrazol-3-yl)prop-2-enoate (7a): M.p. 178–180 °C. R_f = 0.49 (hexanes/EtOAc, 90:10, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1716 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, CO_2Me), 5.77 (s, 2 H, CH_2), 6.45 (d, J = 2.6 Hz, 1 H, ArH), 7.03–7.18 (m, 4 H, ArH), 7.24–7.26 (m, 3 H, ArH), 7.29–7.32 (m, 2 H, ArH), 7.37–7.42 (m, 4 H, ArH), 7.50 (d, J = 7.7 Hz, 1 H, ArH), 7.59 (d, J = 7.4 Hz, 1 H, ArH), 7.78 (s, 1 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.7, 52.5, 71.2, 101.1, 110.6, 119.2, 120.7, 121.3, 124.7, 128.2, 128.6, 128.8, 129.1, 129.2, 129.5, 129.6, 130.0, 130.1, 130.4, 131.5, 136.7, 139.6, 145.0, 148.4, 167.7 ppm. MS (ES+): m/z = 560.0 [M^+

+ 1]. HRMS: calcd. for $C_{28}H_{23}IN_3O_2$ $[MH]^+$ 560.0835; found 560.0833.

Methyl (*E*)-2-[(1*H*-Indol-1-yl)methyl]-3-(4-iodo-1,3-diphenyl-1*H*-pyrazol-5-yl)prop-2-enoate (13a): 71% as a white solid (198 mg from 250 mg). M.p. 172–174 °C. R_f = 0.48 (hexanes/EtOAc, 90:10, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1712 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, CO_2Me), 5.35 (s, 2 H, CH_2), 6.50 (s, 1 H, ArH), 7.15–7.20 (m, 3 H, ArH), 7.30–7.36 (m, 5 H, ArH), 7.51 (s, 4 H, ArH), 7.65 (d, J = 7.3 Hz, 1 H, ArH), 7.72 (s, 3 H, =CH and ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.7, 52.7, 70.3, 102.1, 109.7, 119.9, 121.3, 122.1, 125.4, 125.9, 127.3, 128.3, 128.6, 128.7, 128.9, 129.6, 130.4, 132.2, 136.3, 137.3, 139.2, 152.7, 167.0 ppm. MS (ES+): m/z = 560.0 [M^+ + 1]. HRMS: calcd. for $C_{28}H_{23}IN_3O_2$ $[MH]^+$ 560.0835; found 560.0845.

General Procedure for the Synthesis of Compounds 5a–i, 6a,b, 8a–c,g, 12a–c and 14a,b as Exemplified for 5a: To a solution of compound **3a** (250 mg, 0.49 mmol) in DMF (4 mL), $Pd(OAc)_2$ (11 mg, 0.059 mmol), PPh_3 (26 mg, 0.098 mmol) and K_2CO_3 (136 mg, 0.98 mmol) were added, and the reaction mixture was heated at 80 °C under nitrogen for 12 h. Thereafter, water (50 mL) and ethyl acetate (25 mL) were added, and the reaction mixture was filtered through a Celite pad, and the layers were separated. The aqueous layer was further extracted with ethyl acetate (2 × 20 mL), and the combined organic layers were washed with brine (25 mL), dried with anhydrous Na_2SO_4 and concentrated under vacuum. Column chromatography of the crude product on silica gel (hexanes/EtOAc, 5:95) gave pure **5a** as a yellow solid (174 mg, 93%).

Methyl 1,2-Diphenyl-2,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]-azepine-5-carboxylate (5a): 93% as a yellow solid (174 mg from 250 mg). M.p. 210–211 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1707 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, CO_2Me), 4.97 (s, 2 H, CH_2), 5.57 (d, J = 2.1 Hz, 1 H, ArH), 6.01 (t, J = 3.1 Hz, 1 H, ArH), 6.67 (s, 1 H, ArH), 7.30–7.37 (m, 10 H, ArH), 8.03 (s, 1 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.9, 52.6, 107.3, 108.5, 117.0, 121.9, 125.1, 125.7, 127.9, 128.4, 128.96, 128.99, 129.1, 130.0, 130.6, 135.7, 139.46, 139.51, 145.1, 166.4 ppm. MS (ES+): m/z = 382.1 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{20}N_3O_2$ $[MH]^+$ 382.1556; found 382.1546.

Methyl 1-(4-Methylphenyl)-2-phenyl-2,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (5b): 91% as a yellow solid (137 mg from 200 mg). M.p. 206–207 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1707 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 3.86 (s, 3 H, CO_2Me), 4.96 (s, 2 H, CH_2), 5.60 (dd, J_1 = 1.6, J_2 = 3.7 Hz, 1 H, ArH), 6.02 (dd, J_1 = 2.7, J_2 = 3.7 Hz, 1 H, ArH), 6.67 (dd, J_1 = 1.7, J_2 = 2.4 Hz, 1 H, ArH), 7.13–7.20 (m, 4 H, ArH), 7.30 (s, 5 H, ArH), 8.03 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.4, 44.8, 52.4, 107.1, 108.3, 116.8, 121.7, 125.0, 125.7, 126.7, 127.7, 128.2, 128.8, 129.5, 130.3, 135.6, 139.0, 139.5, 144.9, 166.3 ppm. MS (ES+): m/z = 396.3 [M^+ + 1]. HRMS: calcd. for $C_{25}H_{22}N_3O_2$ $[MH]^+$ 396.1712; found 396.1706.

Methyl 1-(4-Chlorophenyl)-2-phenyl-2,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (5c): 90% as a yellow solid (172 mg from 250 mg). M.p. 185–186 °C. R_f = 0.41 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1705 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, CO_2Me), 4.96 (s, 2 H, CH_2), 5.59 (d, J = 2.0 Hz, 1 H, ArH), 6.03 (t, J = 3.0 Hz, 1 H, ArH), 6.69 (s, 1 H, ArH), 7.23–7.29 (m, 4 H, ArH), 7.32–7.35 (m, 5 H, ArH), 8.01 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.9, 52.6, 107.4, 108.6, 117.1, 122.1, 125.2, 125.3, 128.2, 128.4, 128.6, 129.2, 129.4, 131.9, 135.3, 135.5, 138.1, 139.3, 145.3, 166.4 ppm. MS (ES+): m/z = 416.2 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{19}ClN_3O_2$ $[MH]^+$ 416.1166; found 416.1169.

Methyl 1-(4-Fluorophenyl)-2-phenyl-2,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (5d): 89% as a yellow solid (135 mg from 200 mg). M.p. 215–216 °C. R_f = 0.39 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1711 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, CO_2Me), 4.96 (s, 2 H, CH_2), 5.57 (dd, J_1 = 1.5, J_2 = 3.5 Hz, 1 H, ArH), 6.03 (t, J = 3.1 Hz, 1 H, ArH), 6.69 (s, 1 H, ArH), 7.06 (t, J = 8.6 Hz, 2 H, ArH), 7.27–7.32 (s, 7 H, ArH), 8.02 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.9, 52.6, 107.3, 108.5, 116.1, 116.5, 117.1, 122.1, 125.2, 125.5, 125.9, 128.2, 128.6, 129.1, 132.5, 132.6, 135.6, 138.4, 139.3, 145.2, 160.7, 166.4 ppm. MS (ES+): m/z = 400.3 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{19}FN_3O_2$ $[MH]^+$ 400.1461; found 400.1446.

Methyl 1-(4-Methoxyphenyl)-2-phenyl-2,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]azepine-5-carboxylate (5e): 90% as a yellow solid (172 mg from 250 mg). M.p. 157–158 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1712 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 3.86 (s, 3 H, CO_2Me), 4.96 (s, 2 H, CH_2), 5.61 (d, J = 1.9 Hz, 1 H, ArH), 6.02 (t, J = 2.9 Hz, 1 H, ArH), 6.67 (s, 1 H, ArH), 6.87 (d, J = 8.6 Hz, 2 H, ArH), 7.21 (d, J = 8.6 Hz, 2 H, ArH), 7.31 (s, 5 H, ArH), 8.02 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 45.0, 52.6, 55.4, 107.2, 108.4, 114.5, 116.9, 121.8, 122.0, 125.1, 126.0, 127.9, 128.3, 129.0, 131.9, 135.8, 139.4, 139.6, 145.1, 160.2, 166.5 ppm. MS (ES+): m/z = 412.3 [M^+ + 1]. HRMS: calcd. for $C_{25}H_{22}N_3O_3$ $[MH]^+$ 412.1661; found 412.1655.

Methyl 1-(4-Nitrophenyl)-2-phenyl-2,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylat (5f): 89% as a yellow solid (171 mg from 250 mg). M.p. 181–182 °C. R_f = 0.37 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1707 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, CO_2Me), 4.98 (s, 2 H, CH_2), 5.56 (dd, J_1 = 1.5, J_2 = 3.6 Hz, 1 H, ArH), 6.04 (dd, J_1 = 2.8, J_2 = 3.5 Hz, 1 H, ArH), 6.72 (t, J = 1.0 Hz, 1 H, ArH), 7.24–7.26 (m, 2 H, ArH), 7.35–7.37 (m, 3 H, ArH), 7.51 (d, J = 8.8 Hz, 2 H, ArH), 8.02 (s, 1 H, =CH), 8.20 (d, J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.9, 52.7, 107.8, 108.8, 117.7, 122.5, 124.2, 124.7, 125.3, 128.7, 129.1, 129.4, 131.6, 135.1, 136.5, 136.8, 138.9, 145.6, 148.0, 166.2 ppm. MS (ES+): m/z = 427.3 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{19}N_4O_4$ $[MH]^+$ 427.1406; found 427.1396.

Methyl 2-Methyl-1-phenyl-2,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]azepine-5-carboxylate (5g): 92% as a yellow solid (164 mg from 250 mg). M.p. 220–221 °C. R_f = 0.30 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1695 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, CO_2Me), 3.85 (s, 3 H, NCH_3), 4.89 (s, 2 H, CH_2), 5.54 (dd, J_1 = 1.5, J_2 = 3.4 Hz, 1 H, ArH), 5.98 (t, J = 3.1 Hz, 1 H, ArH), 6.63 (s, 1 H, ArH), 7.42–7.44 (m, 2 H, ArH), 7.49–7.50 (m, 3 H, ArH), 7.94 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 37.8, 44.9, 52.5, 106.5, 108.3, 115.9, 121.7, 126.2, 127.2, 129.2, 129.5, 129.8, 130.3, 135.8, 140.2, 143.3, 166.5 ppm. MS (ES+): m/z = 320.2 [M^+ + 1]. HRMS: calcd. for $C_{19}H_{18}N_3O_2$ $[MH]^+$ 320.1399; found 320.1400.

Methyl 2-Methyl-1-(4-methylphenyl)-2,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (5h): 90% as a yellow solid (163 mg from 250 mg). M.p. 243–245 °C. R_f = 0.31 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1698 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3 H, CH_3), 3.80 (s, 3 H, CO_2Me), 3.84 (s, 3 H, NCH_3), 4.88 (s, 2 H, CH_2), 5.57 (t, J = 1.7 Hz, 1 H, ArH), 5.98 (t, J = 3.0 Hz, 1 H, ArH), 6.62 (s, 1 H, ArH), 7.31 (s, 4 H, ArH), 7.93 (s, 1 H, =CH) ppm. ^{13}C NMR

(75 MHz, $CDCl_3$): δ = 21.6, 37.7, 45.0, 52.5, 106.5, 108.3, 115.9, 121.6, 126.4, 126.9, 127.1, 129.9, 130.2, 135.9, 139.5, 140.3, 143.3, 166.5 ppm. MS (ES+): *m*/*z* = 334.3 [M^+ + 1]. HRMS: calcd. for $C_{20}H_{20}N_3O_2$ [MH]$^+$ 334.1556; found 334.1558.

Methyl 2-Methyl-2,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]azepine-5-carboxylate (5i): 91% as a yellow solid (119 mg from 200 mg). M.p. 100–102 °C. R_f = 0.29 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1708 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, CO_2Me), 3.99 (s, 3 H, NCH_3), 4.83 (s, 2 H, CH_2), 6.17–6.22 (m, 2 H, ArH), 6.69 (s, 1 H, ArH), 7.58 (s, 1 H, ArH), 7.91 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 39.6, 44.9, 52.5, 105.8, 108.6, 118.2, 122.2, 126.1, 126.8, 127.1, 135.5, 143.9, 166.5 ppm. MS (ES+): *m*/*z* = 244.3 [M^+ + 1]. HRMS: calcd. for $C_{13}H_{14}N_3O_2$ [MH]$^+$ 244.1086; found 244.1076.

Methyl 9,10-Diphenyl-5,9-dihydroimidazo[1,2-*a*]pyrazolo[4,3-*c*]-azepine-6-carboxylate (6a): 78% as a yellow solid (146 mg from 250 mg). M.p. 178–180 °C. R_f = 0.28 (hexanes/EtOAc, 50:50, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1710 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, CO_2Me), 5.03 (s, 2 H, CH_2), 6.48 (s, 1 H, ArH), 7.26–7.48 (m, 11 H, ArH), 8.07 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 42.6, 52.8, 113.7, 114.2, 125.0, 126.2, 127.4, 128.2, 129.1, 129.6, 129.9, 130.2, 135.9, 139.2, 139.4, 140.3, 144.6, 166.1 ppm. MS (ES+): *m*/*z* = 383.2 [M^+ + 1]. HRMS: calcd. for $C_{23}H_{19}N_4O_2$ [MH]$^+$ 383.1508; found 383.1510.

Methyl 10-(4-Methylphenyl)-9-phenyl-5,9-dihydroimidazo[1,2-*a*]-pyrazolo[4,3-*c*]azepine-6-carboxylate (6b): 80% as a yellow solid (151 mg from 250 mg). M.p. 160–161 °C. R_f = 0.27 (hexanes/EtOAc, 50:50, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1708 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.88 (s, 3 H, CO_2Me), 5.03 (s, 2 H, CH_2), 6.49 (s, 1 H, ArH), 7.17 (s, 4 H, ArH), 7.32 (s, 5 H, ArH), 7.46 (s, 1 H, ArH), 8.06 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.5, 42.6, 52.8, 113.7, 125.0, 125.4, 126.0, 126.3, 127.3, 128.1, 129.1, 129.9, 130.0, 136.0, 136.7, 139.3, 139.6, 140.4, 144.5, 166.1 ppm. MS (ES+): *m*/*z* = 397.2 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{21}N_4O_2$ [MH]$^+$ 397.1665; found 397.1653.

Methyl 1,2-Diphenyl-2,6-dihydropyrazolo[4′,3′:3,4]azepino[1,2-*a*]-indole-5-carboxylate (8a): 92% as a yellow solid (142 mg from 200 mg). M.p. 200–201 °C. R_f = 0.41 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1710 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, CO_2Me), 5.19 (s, 2 H, CH_2), 5.87 (s, 1 H, ArH), 7.03 (t, *J* = 7.0 Hz, 1 H, ArH), 7.21 (t, *J* = 7.1 Hz, 1 H, ArH), 7.33–7.36 (m, 11 H, ArH), 7.58 (d, *J* = 7.9 Hz, 1 H, ArH), 8.07 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 40.3, 52.7, 99.7, 109.4, 119.9, 120.5, 121.8, 125.2, 128.2, 129.1, 129.5, 130.0, 130.6, 132.3, 135.1, 135.7, 136.0, 139.4, 141.3, 146.0, 166.5 ppm. MS (ES+): *m*/*z* = 432.3 [M^+ + 1]. HRMS: calcd. for $C_{28}H_{22}N_3O_2$ [MH]$^+$ 432.1712; found 432.1711.

Methyl 1-(4-Methylphenyl)-2-phenyl-2,6-dihydropyrazolo[4′,3′:3,4]-azepino[1,2-*a*]indole-5-carboxylate (8b): 90% as a yellow solid (140 mg from 200 mg). M.p. 240–241 °C. R_f = 0.41 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1704 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 3.90 (s, 3 H, CO_2Me), 5.19 (s, 2 H, CH_2), 5.91 (s, 1 H, ArH), 7.03 (t, *J* = 7.1 Hz, 1 H, ArH), 7.16–7.25 (m, 5 H, ArH), 7.33–7.41 (m, 6 H, ArH), 7.58 (d, *J* = 8.3 Hz, 1 H, ArH), 8.07 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 40.3, 52.7, 99.6, 109.4, 116.2, 119.8, 120.4, 121.7, 125.3, 126.5, 128.1, 128.5, 129.1, 129.9, 130.4, 132.5, 135.7, 136.0, 139.5, 141.5, 146.0, 166.5 ppm. MS (ES+): *m*/*z* = 446.3 [M^+ + 1]. HRMS: calcd. for $C_{29}H_{24}N_3O_2$ [MH]$^+$ 446.1869; found 446.1869.

Methyl 1-(4-Chlorophenyl)-2-phenyl-2,6-dihydropyrazolo[4′,3′:3,4]-azepino[1,2-*a*]indole-5-carboxylate (8c): 89% as a yellow solid (140 mg from 200 mg). M.p. 228–230 °C. R_f = 0.40 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1696 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, CO_2Me), 5.19 (s, 2 H, CH_2), 5.90 (s, 1 H, ArH), 7.05 (t, *J* = 7.4 Hz, 1 H, ArH), 7.21 (d, *J* = 7.3 Hz, 1 H, ArH), 7.28–7.38 (m, 9 H, ArH), 7.42 (d, *J* = 7.9 Hz, 1 H, ArH), 7.59 (d, *J* = 8.2 Hz, 1 H, ArH), 8.06 (s, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 40.3, 52.7, 99.7, 109.4, 116.4, 120.0, 120.5, 121.9, 125.3, 128.0, 128.4, 129.3, 129.5, 130.2, 132.0, 135.5, 135.6, 136.0, 139.1, 139.9, 146.2, 166.4 ppm. MS (ES+): *m*/*z* = 466.3 [M^+ + 1]. HRMS: calcd. for $C_{28}H_{21}ClN_3O_2$ [MH]$^+$ 466.1322; found 466.1300.

Methyl 2-Methyl-1-phenyl-2,6-dihydropyrazolo[4′,3′:3,4]azepino-[1,2-*a*]indole-5-carboxylate (8g): 91% as a yellow solid (135 mg from 200 mg). M.p. 195–196 °C. R_f = 0.32 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1706 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, NCH_3), 3.88 (s, 3 H, CO_2Me), 5.11 (s, 2 H, CH_2), 5.83 (s, 1 H, ArH), 7.00 (t, *J* = 7.5 Hz, 1 H, ArH), 7.18 (t, *J* = 7.1 Hz, 1 H, ArH), 7.36 (d, *J* = 7.7 Hz, 1 H, ArH), 7.48–7.55 (m, 6 H, ArH), 7.98 (s, 1 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.9, 40.4, 52.6, 98.9, 109.4, 115.3, 119.8, 120.3, 121.6, 128.5, 129.0, 129.4, 129.6, 129.8, 130.4, 132.8, 135.8, 136.1, 142.0, 144.4, 166.5 ppm. MS (ES+): *m*/*z* = 370.2 [M^+ + 1]. HRMS: calcd. for $C_{23}H_{20}N_3O_2$ [MH]$^+$ 370.1556; found 370.1541.

Methyl 1,3-Diphenyl-3,6-dihydropyrazolo[4,3-*c*]pyrrolo[1,2-*a*]-azepine-5-carboxylate (12a): 89% as a yellow solid (167 mg from 250 mg). M.p. 161–162 °C. R_f = 0.45 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1705 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, CO_2Me), 5.02 (s, 2 H, CH_2), 6.10 (d, *J* = 2.0 Hz, 1 H, ArH), 6.17 (t, *J* = 3.0 Hz, 1 H, ArH), 6.75 (s, 1 H, ArH), 7.43–7.47 (m, 4 H, ArH), 7.53–7.64 (m, 4 H, ArH), 7.70 (s, 1 H, =CH), 7.85 (d, *J* = 5.4 Hz, 2 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.9, 52.7, 108.3, 109.1, 117.7, 121.5, 124.3, 125.7, 126.6, 128.1, 128.5, 128.9, 129.6, 129.9, 132.9, 134.0, 139.1, 150.0, 165.7 ppm. MS (ES+): *m*/*z* = 382.3 [M^+ + 1]. HRMS: calcd. for $C_{24}H_{20}N_3O_2$ [MH]$^+$ 382.1556; found 382.1556.

Methyl 1-(4-Methylphenyl)-3-phenyl-3,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (12b): 88% as a yellow solid (166 mg from 250 mg). M.p. 201–202 °C. R_f = 0.44 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1714 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 3.81 (s, 3 H, CO_2Me), 4.99 (s, 2 H, CH_2), 6.10 (dd, J_1 = 1.6, J_2 = 3.7 Hz, 1 H, ArH), 6.15 (t, *J* = 3.2 Hz, 1 H, ArH), 6.72 (t, *J* = 2.1 Hz, 1 H, ArH), 7.23 (d, *J* = 8.0 Hz, 2 H, ArH), 7.42 (t, *J* = 7.2 Hz, 1 H, ArH), 7.53 (t, *J* = 7.7 Hz, 2 H, ArH), 7.58–7.61 (m, 2 H, ArH), 7.67 (s, 1 H, =CH), 7.72 (d, *J* = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 44.9, 52.6, 108.2, 109.0, 117.6, 121.4, 124.3, 125.8, 126.5, 128.0, 128.7, 129.2, 129.6, 129.90, 129.94, 133.9, 138.4, 139.2, 150.0, 165.6 ppm. MS (ES+): *m*/*z* = 396.3 [M^+ + 1]. HRMS: calcd. for $C_{25}H_{22}N_3O_2$ [MH]$^+$ 396.1712; found 396.1714.

Methyl 1-(4-Chlorophenyl)-3-phenyl-3,6-dihydropyrazolo[4,3-*c*]-pyrrolo[1,2-*a*]azepine-5-carboxylate (12c): 87% as a yellow solid (166 mg from 250 mg). M.p. 150–151 °C. R_f = 0.44 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1708 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, CO_2Me), 4.99 (s, 2 H, CH_2), 6.09 (s, 1 H, ArH), 6.17 (s, 1 H, ArH), 6.73 (s, 1 H, ArH), 7.38–7.41 (m, 3 H, ArH), 7.54–7.57 (m, 4 H, ArH), 7.66 (s, 1 H, =CH), 7.80 (d, *J* = 6.9 Hz, 2 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.9, 52.8, 108.3, 109.2, 121.2, 121.7, 124.3, 125.4, 126.9, 128.3, 128.8, 129.7, 130.1, 131.4, 134.2, 134.5, 139.1, 148.7,

165.6 ppm. MS (ES+): *m*/*z* = 416.2 [M$^+$ + 1]. HRMS: calcd. for $C_{24}H_{19}ClN_3O_2$ [MH]$^+$ 416.1166; found 416.1167.

Methyl 1,3-Diphenyl-3,6-dihydropyrazolo[4′,3′:3,4]azepino[1,2-*a*]-indole-5-carboxylate (14a): 87% as a yellow solid (134 mg from 200 mg). M.p. 211–212 °C. R_f = 0.46 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1705 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, CO_2Me), 5.24 (s, 2 H, CH_2), 6.39 (s, 1 H, ArH), 7.08 (t, *J* = 7.4 Hz, 1 H, ArH), 7.23–7.28 (m, 1 H, ArH), 7.43–7.48 (m, 5 H, ArH), 7.51–7.65 (m, 5 H, ArH), 7.72 (s, 1 H, =CH), 7.86–7.90 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.3, 52.8, 100.4, 109.4, 116.9, 120.0, 120.7, 122.0, 124.6, 128.5, 128.7, 128.9, 129.0, 129.7, 129.8, 132.0, 132.6, 135.5, 135.6, 139.0, 151.2, 165.7 ppm. MS (ES+): *m*/*z* = 432.4 [M$^+$ + 1]. HRMS: calcd. for $C_{28}H_{22}N_3O_2$ [MH]$^+$ 432.1712; found 432.1712.

Methyl 1-(4-Methylphenyl)-3-phenyl-3,6-dihydropyrazolo[4′,3′:3,4]-azepino[1,2-*a*]indole-5-carboxylate (14b): 86% as a yellow solid (134 mg from 200 mg). M.p. 197–198 °C. R_f = 0.45 (hexanes/EtOAc, 80:20, v/v). IR (KBr): $\tilde{\nu}_{max}$ = 1696 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 3.84 (s, 3 H, CO_2Me), 5.23 (s, 2 H, CH_2), 6.41 (s, 1 H, ArH), 7.08 (t, *J* = 7.5 Hz, 1 H, ArH), 7.26 (s, 2 H, ArH), 7.45–7.63 (m, 8 H, ArH), 7.70 (s, 1 H, =CH) 7.77 (d, *J* = 7.9 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 40.3, 52.8, 100.3, 109.4, 116.8, 120.0, 120.7, 121.9, 124.6, 127.5, 128.4, 128.6, 128.9, 129.4, 129.7, 129.9, 132.1, 135.4, 135.5, 138.8, 139.0, 151.3, 165.7 ppm. MS (ES+): *m*/*z* = 446.3 [M$^+$ + 1]. HRMS: calcd. for $C_{29}H_{24}N_3O_2$ [MH]$^+$ 446.1869; found 446.1859.

Supporting Information (see footnote on the first page of this article): Spectroscopic data for remaining compounds; copies of ^{1}H and ^{13}C NMR spectra of all compounds.

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