Reductive amination of ferrocenylformylpyrazoles

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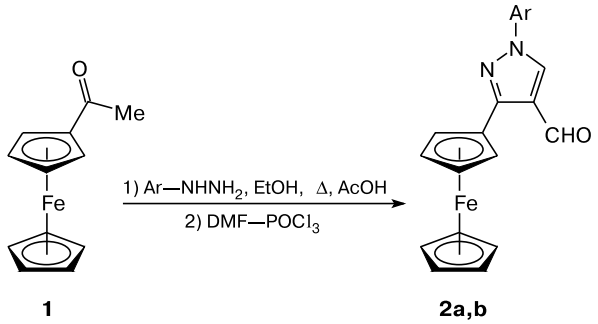
1-Aryl-3-ferrocenyl-4-formylpyrazoles were obtained from appropriate acetylferrocene arylhydrazones by the Vilsmeier—Haack reaction. Direct reductive amination of the resulting aldehydes with primary and secondary amines and amino acid esters in the presence of $NaBH(OAc)_3$ was studied.

Key words: acetylferrocene, the Vilsmeier—Haack reaction, pyrazoles, reductive amination, sodium triacetoxyborohydride.

Pyrazole derivatives exhibit a wide spectrum of pharmacological activity.[1] Introduction of a ferrocenyl fragment into a heterocyclic molecule often imparts a new biological activity to it or modifies its inherent activity. For instance, ferrocene-containing pyrazoles have antibacterial[2] and antitumor effects in combination with low toxicity[3] and are plant growth regulators.[4] In addition, optically active ferrocenylpyrazole derivatives are suitable as ligands in asymmetric catalysis and can catalyze hydrogenation, silylation, and cyanation of carbonyl compounds.[5]

In the present work, we studied direct reductive amination of 1-aryl-3-ferrocenylpyrazole-4-carbaldehydes in reactions with primary and secondary aliphatic amines.

Scheme 1



1 **2a,b**

Ar = Ph (**a**), β-$C_{10}H_7$ (**b**)
Yield (%): 84 (**2a**), 65 (**2b**)

Results and Discussion

Aryl methyl ketones are easily accessible reagents for the preparation of pyrazolecarbaldehydes. The synthesis involves condensation of ketones with arylhydrazines followed by intramolecular cyclization of the resulting hydrazones under the conditions of the Vilsmeier—Haack formylation (Scheme 1).

Reactions of acetylferrocene (**1**) with phenyl- and β-naphthylhydrazines gave the corresponding hydrazones in high yields, which were used in room-temperature reactions with three equivalents of the Vilsmeier—Haack complex (DMF—$POCl_3$) in DMF. Upon hydrolysis of the iminium salts with aqueous Na_2CO_3, the corresponding 1-aryl-3-ferrocenylpyrazole-4-carbaldehydes **2a,b** were isolated in 84 and 65% yields, respectively.

Aldehydes and ketones react with ammonia and primary and secondary amines in the presence of reducing agents to give primary, secondary, and tertiary amines, respectively. These reactions are known as reductive amination of carbonyl compounds or reductive alkylation of amines and can be effected in direct and stepwise ways. In the former case, a carbonyl compound and an amine are mixed with an appropriate reducing agent without isolating an intermediate imine or iminium salt. In the latter case, the formation of an intermediate imine is followed by its reduction. Secondary amines from pyrazolecarbaldehydes were obtained in the second way with sodium borohydride as a reducing agent,[6] while direct reductive amination of arylformylpyrazoles has not been implemented hitherto.

Using sodium borohydride as a reducing agent in direct reductive amination of 1-aryl-3-ferrocenylpyrazole-4-carbaldehydes in different solvents and at different temperatures, we isolated the corresponding alcohols only. Modification of sodium borohydride with the electron-withdrawing cyano or acetoxy group enhances the selec-

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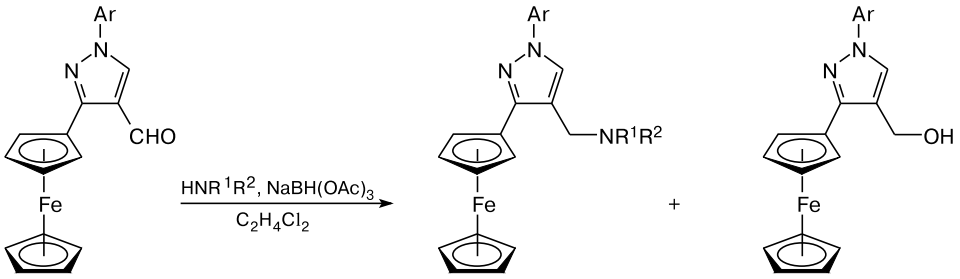
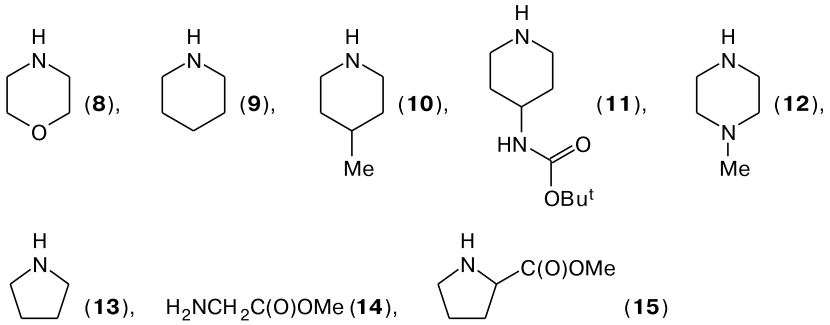
Scheme 2



2a,b **4a,b—15a,b** **3a,b**

Ar = Ph (**a**), β-$C_{10}H_7$ (**b**)

HNR^1R^2 = $HNPr^i_2$ (**3**), H_2NBu^n (**4**), H_2NBu^t (**5**), H_2NCH_2Ph (**6**), $HNPr^n_2$ (**7**),



tivity of the reducing agent. For instance, sodium triacetoxyborohydride is successfully employed in the reduction of carbonyl compounds containing multiple carbon—carbon bonds, cyano groups, and nitro groups, as well as acetals and ketals. Moreover, this reagent selectively reduces aldehydes in the presence of ketones. The selectivity of this reaction is due to steric and electron-withdrawing properties of three acetoxy groups stabilizing the B—H bond.[7] We used sodium triacetoxyborohydride as a reducing agent in reductive amination of 1-aryl-3-ferrocenylpyrazole-4-carbaldehydes. The reactions with various sterically unhindered primary and secondary (cyclic and acyclic) amines afforded the target products in 30—90% yields (Table 1, Scheme 2). Alcohols occasionally formed as by-products were separated by column chromatography. With the sterically hindered diisopropylamine, the major reaction product is the corresponding alcohol (see Scheme 2).

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer (500.13 and 125.76 MHz, respectively) in $CDCl_3$ and DMSO-d_6. Mass spectra were measured on a Finnigan Polaris Q spectrometer (electron ionizing energy 70 eV, ionization chamber temperature 250 °C). Acetylferrocene, phenylhydrazine, $NaBH(OAc)_3$, and amines (Acros Organics) were used as purchased. Amino acid methyl ester hydrochlorides were prepared from amino acids and $SOCl_2$ in methanol;[8,9] β-naphthylhydrazine hydrochloride was synthesized by diazotization of β-naphthylamine with $NaNO_2$ in conc. HCl followed by reduction with $SnCl_2 \cdot 2H_2O$ in HCl (see Ref. 10).

3-Ferrocenyl-1-phenylpyrazole-4-carbaldehyde (2a) was obtained as described earlier.[11] Yield 80%, m.p. 118 °C (*cf.* Ref. 11: m.p. 118 °C). MS, *m/z* (I_{rel} (%)): 386 $[M]^+$ (100%). ^1H NMR ($CDCl_3$, 500 MHz), δ: 4.15 (s, 5 H, Fc); 4.42, 5.96 (both s, 2 H each, Fc); 7.37 (t, 1 H, CH, J = 7.5 Hz); 7.94 (m, 2 H, CH); 7.76 (d, 2 H, CH, J = 8 Hz); 8.44 (s, 1 H, CH); 10.32 (s, 1 H, CHO). ^{13}C NMR ($CDCl_3$, 125 MHz), δ: 69.4, 69.7, 69.8, 75.7, 119.4, 122.6, 127.6, 129.6, 131.4, 138.9, 153.7, 184.5.

3-Ferrocenyl-1-(2-naphthyl)pyrazole-4-carbaldehyde (2b) Sodium methoxide (0.57 g, 10.6 mmol) was added to a solution of acetylferrocene (2.28 g, 10.00 mmol) and β-naphthylhydrazine hydrochloride (1.95 g, 10.65 mmol) in ethanol (10 mL). The reaction mixture was refluxed with stirring for 1 h and cooled to room temperature. The precipitate that formed was filtered off, washed with cold ethanol (10 mL), and dried *in vacuo* over $CaCl_2$ for 1 h. The hydrazone obtained was dissolved in DMF (15 mL), whereupon $POCl_3$ (2.25 mL, 27.22 mmol) was added under argon. The reaction mixture was stirred at room temperature for 18 h, poured onto ice (30 g) with water (30 mL), and hydrolyzed with a solution of Na_2CO_3 (40 g) in water (100 mL). The precipitate of aldehyde **2b** that formed was filtered off, washed with a large amount of water, and dried over Na_2SO_4. The product was purified by column chromatography on SiO_2 with benzene

Table 1. 4-Hydroxymethyl- (**3a,b**) and 4-aminomethyl-1-aryl-3-ferrocenylpyrazoles (**4a,b—15a,b**)

Amine	Product	Yield (%)	M.p./°C	Found / Calculated (%)			Molecular formula
				C	H	N	
Diisopropylamine	**3a**	92[a]	118—119	66.98	5.04	7.80	$C_{20}H_{18}FeN_2O$
				67.06	5.06	7.82	
	3b	90[a]	136—137	70.64	4.98	6.85	$C_{24}H_{20}FeN_2O$
				70.60	4.94	6.86	
n-Butylamine	**4a**	75[b]	147—148	—	—	—	—
	4b	60	55—56	72.63	6.30	9.10	$C_{28}H_{29}FeN_3$
				72.57	6.31	9.07	
t-Butylamine	**5a**	58	162—163	—[c]	—[c]	—[c]	—[c]
	5b	55	171—172	72.59	6.28	9.10	$C_{28}H_{29}FeN_3$
				72.57	6.31	9.07	
Benzylamine	**6a**	45	102—103	72.51	5.60	9.42	$C_{27}H_{25}FeN_3$
				72.49	5.63	9.39	
	6b	58[b]	131—132[d]	—	—	—	—
Dipropylamine	**7a**	65	Oil	70.73	7.10	9.47	$C_{26}H_{31}FeN_3$
				70.75	7.08	9.53	
	7b	65	Oil	73.27	6.73	8.50	$C_{30}H_{33}FeN_3$
				73.32	6.77	8.55	
Morpholine	**8a**	65	169—170[d]	67.52	5.94	9.75	$C_{24}H_{25}FeN_3O$
				67.46	5.90	9.83	
	8b	67	145—146	70.43	5.73	8.76	$C_{28}H_{27}FeN_3O$
				70.45	5.70	8.80	
Piperidine	**9a**	44[b]	45—46[d]	—	—	—	—
	9b	33[b]	120[d]	—	—	—	—
4-Methylpiperidine	**10a**	81	173—174	—[c]	—[c]	—[c]	—[c]
	10b	73	182—184[d]	73.73	6.43	8.54	$C_{30}H_{31}FeN_3$
				73.62	6.38	8.59	
4-*Boc*-Aminopiperidine	**11a**	54[b]	141—142	—	—	—	—
	11b	30[b]	104—105[d]	—	—	—	—
1-Methylpiperazine	**12a**	67	140—142	68.23	6.38	12.70	$C_{25}H_{28}FeN_4$
				68.19	6.41	12.72	
	12b	50	147—148[d]	71.00	6.20	11.45	$C_{29}H_{30}FeN_4$
				71.02	6.17	11.42	
Pyrrolidine	**13a**	45	78—79	70.15	6.08	10.21	$C_{24}H_{25}FeN_3$
				70.08	6.13	10.22	
	13b	64	91—92	72.96	5.95	9.04	$C_{28}H_{27}FeN_3$
				72.89	5.90	9.11	
Glycine methyl ester	**14a**	90	102	64.25	5.38	9.80	$C_{23}H_{23}FeN_3O_2$
				64.35	5.40	9.79	
	14b	36[b]	133—134[d]	—	—	—	—
Proline methyl ester	**15a**	80	140	66.51	5.85	8.90	$C_{26}H_{27}FeN_3O_2$
				66.53	5.80	8.95	
	15b	38	122—123	69.40	5.58	8.11	$C_{30}H_{29}FeN_3O_2$
				69.37	5.63	8.09	

[a] An alcohol was isolated.
[b] Isolated as hydrochloride. No satisfactory elemental analysis data were obtained. The structure was determined from NMR and mass spectra.
[c] The high-resolution mass spectrum was recorded (see Table 2).
[d] Decomposes when melting.

as an eluent. The yield was 2.63 g (65%), m.p. 190—192 °C. Found (%): C, 70.69; H, 4.44; Fe, 13.50. $C_{24}H_{18}FeN_2O$. Calculated (%): C, 70.90; H, 4.43; Fe, 13.79. MS, *m/z* (I_{rel} (%)): 406 $[M]^+$ (100%). ^1H NMR ($CDCl_3$), δ: 4.23 (s, 5 H, Fc); 4.50, 5.04 (both s, 2 H each, Fc); 7.62 (m, 2 H, Ar); 7.95 (m, 4 H, Ar); 8.28 (s, 1 H, Ar); 8.65 (s, 1 H, Pz); 10.41 (s, 1 H, CHO). ^{13}C NMR ($CDCl_3$), δ: 69.1, 69.4, 70.0, 76.2, 117.7, 118.6, 123.2, 127.0, 127.7, 128.3, 130.2, 132.1, 132.8, 133.8, 136.8, 142.4, 185.0.

Table 2. Spectroscopic data for compounds **3a—15a**

Product	MS (EI, 70 eV), m/z (I_{rel} (%))	^{1}H NMR (solvent, δ, J/Hz)	^{13}C NMR (solvent, δ)
3a	358 $[M]^+$ (100)	$CDCl_3$: 2.02 (br.s, 1 H, OH); 4.14 (s, 5 H, Fc); 4.36, 4.89 (both s, 2 H each, Fc); 4.85 (s, 2 H, CH_2); 7.29 (t, 1 H, Ar, J = 7.0); 7.47 (m, 2 H, Ar); 7.73 (d, 2 H, Ar, J = 8.0); 7.89 (s, 1 H, Pz)	$CDCl_3$: 56.1, 67.4, 68.8, 69.4, 77.6, 118.7, 120.5, 126.0, 127.0, 129.4, 140.0, 150.1
4a	413 $[M]^+$ (100)	$CDCl_3$: 0.99 (t, 3 H, CH_3, J = 7.5); 1.44 (m, 2 H, CH_2); 1.63 (m, 2 H, CH_2); 2.29 (br.s, 1 H, NH); 2.82 (t, 2 H, CH_2, J = 7.0); 3.98 (s, 2 H, CH_2); 4.15 (s, 5 H, Fc); 4.35, 4.84 (both s, 2 H each, Fc); 7.27 (t, 1 H, Ar, J = 7.0); 7.46 (m, 2 H, Ar); 7.75 (d, 2 H, Ar, J = 8.0); 7.95 (s, 1 H, Pz)	$CDCl_3$: 14.0, 20.5, 32.1, 44.2, 49.5, 67.3, 68.6, 69.4, 78.3, 118.5, 119.5, 125.7, 126.6, 129.3, 140.1, 149.7
5a	Found: 413.1498 $[M]^+$ $C_{24}H_{27}FeN_3$ Calculated: M = 413.1554	DMSO-d_6: 1.39 (s, 9 H, CH_3); 3.45 (br.s, 1 H, NH); 4.05 (s, 2 H, CH_2); 4.11 (s, 5 H, Fc); 4.31, 4.75 (both s, 2 H each, Fc); 7.26 (t, 1 H, Ar, J = 7.0); 7.47 (m, 2 H, Ar); 7.78 (d, 2 H, Ar, J = 8.0); 8.72 (s, 1 H, Pz)	DMSO-d_6: 26.7, 35.8, 39.5, 67.2, 68.1, 68.8, 77.5, 95.5, 117.6, 125.4, 128.8, 129.1, 139.4, 149.1
6a	447 $[M]^+$ (100)	$CDCl_3$: 3.85 (s, 2 H, CH_2); 3.98 (s, 2 H, CH_2); 4.04 (s, 5 H, Fc); 4.28, 4.52 (both s, 2 H each, Fc); 7.24—7.45 (m, 8 H, Ar); 7.72—7.74 (m, 2 H, Ar); 8.30 (s, 1 H, Pz)	$CDCl_3$: 40.8, 50.7, 67.6, 68.7, 69.3, 77.2, 113.1, 118.7, 126.2, 128.6, 128.8, 129.0, 129.3, 129.7, 133.0, 139.7, 150.1
7a	441 $[M]^+$ (80)	$CDCl_3$: 0.94 (m, 6 H, CH_3); 1.18 (m, 4 H, CH_2); 2.55 (m, 4 H, CH_2); 3.72 (s, 2 H, CH_2); 4.21 (s, 5 H, Fc); 4.37, 4.94 (both s, 2 H each, Fc); 7.22 (t, 1 H, Ar, J = 8.0); 7.41 (m, 2 H, Ar); 7.71 (d, 2 H, Ar, J = 8.0); 8.09 (s, 1 H, Pz)	$CDCl_3$: 12.0, 20.0, 49.5, 56.1, 67.3, 68.6, 68.9, 77.6, 118.7, 126.2, 128.6, 129.7, 137.0, 139.7, 150.5
8a	427 $[M]^+$ (100)	$CDCl_3$: 2.64 (m, 4 H, CH_2); 3.68 (s, 2 H, CH_2); 3.82 (m, 4 H, CH_2); 4.16 (s, 5 H, Fc); 4.35, 4.97 (both s, 2 H each, Fc); 7.28 (t, 1 H, Ar, J = 6.5); 7.47 (m, 2 H, Ar); 7.76 (d, 2 H, Ar, J = 7.0); 7.91 (s, 1 H, Pz)	$CDCl_3$: 52.9, 53.4, 66.7, 67.7, 68.5, 69.2, 78.1, 118.3, 125.7, 127.8, 129.2, 139.9, 150.7
9a	425 $[M]^+$ (100)	$CDCl_3$: 1.51 (m, 2 H, CH_2); 1.68 (m, 4 H, 2 CH_2); 2.56 (m, 4 H, 2 CH_2); 3.62 (s, 2 H, CH_2); 4.14 (s, 5 H, Fc); 4.32, 4.94 (both s, 2 H each, Fc); 7.26 (t, 1 H, Ar, J = 7.5); 7.45 (m, 2 H, Ar); 7.75 (d, 2 H, Ar, J = 8.0); 7.90 (s, 1 H, Pz)	$CDCl_3$: 24.9, 26.4, 53.8, 55.0, 68.3, 69.2, 69.8, 78.9, 118.9, 126.1, 128.2, 129.8, 140.6, 151.2
10a	Found: 439.1688 $[M]^+$ $C_{26}H_{29}FeN_3$ Calculated: M = 439.1711	$CDCl_3$: 0.96 (d, 3 H, CH_3, J = 6.5); 1.35 (m, 2 H, 2 CH_2(ax)); 1.44 (m, 1 H, CH); 1.67 (d, 2 H, 2 CH_2(eq), J = 12.0); 2.05 (t, 2 H, 2 CH_2(ax), J = 11.0); 3.05 (d, 2 H, 2 CH_2(eq), J = 11.5); 3.62 (s, 2 H, CH_2); 4.13 (s, 5 H, Fc); 4.32, 4.93 (both s, 2 H each, Fc); 7.24 (t, 1 H, Ar, J = 7.5); 7.45 (m, 2 H, Ar); 7.73 (d, 2 H, Ar, J = 7.5); 7.87 (s, 1 H, Pz)	$CDCl_3$: 22.3, 31.4, 34.8, 53.5, 54.5, 68.3, 69.0, 69.7, 78.9, 118.9, 119.1, 126.1, 128.1, 129.8, 140.5, 151.1
11a	540 $[M]^+$ (70)	DMSO-d_6: 1.47 (s, 9 H, 3 CH_3); 1.50 (m, 2 H, CH_2); 1.97 (d, 1 H, CH_2, J = 11.5); 2.18 (t, 1 H, CH_2, J = 11.0); 2.97—2.99 (m, 1 H, CH_2); 3.54 (m, 1 H, CH); 3.59 (s, 2 H, CH_2); 4.11 (s, 5 H, Fc); 4.31, 4.94 (both s, 2 H each, Fc); 7.25 (t, 1 H, Ar, J = 7.0); 7.45 (m, 2 H, Ar); 7.73 (d, 2 H, Ar, J = 8.0); 7.81 (s, 1 H, Pz)	DMSO-d_6: 28.4, 32.7, 47.9, 48.4, 52.3, 52.7, 67.8, 68.5, 69.2, 78.3, 118.4, 125.7, 127.6, 129.1, 129.3, 140.1, 150.1, 155.2
12a	440 $[M]^+$ (100)	$CDCl_3$: 2.36 (s, 3 H, CH_3); 2.58—2.69 (m, 8 H); 3.63 (s, 2 H, CH_2); 4.11 (s, 5 H, Fc); 4.30, 4.93 (both s, 2 H each, Fc); 7.24 (t, 1 H, Ar, J = 7.2); 7.44 (m, 2 H, Ar); 7.71 (d, 2 H, Ar, J = 7.5); 7.82 (s, 1 H, Pz)	$CDCl_3$: 45.7, 52.5, 52.7, 55.0, 67.7, 68.6, 69.2, 78.2, 117.3, 118.4, 125.7, 127.7, 129.3, 140.0, 150.8
13a	411 $[M]^+$ (100)	$CDCl_3$: 1.92 (m, 4 H, 2 CH_2); 2.76 (m, 4 H, 2 CH_2); 3.88 (s, 2 H, CH_2); 4.18 (s, 5 H, Fc); 4.37, 4.92 (both s, 2 H each, Fc); 7.30 (t, 1 H, Ar, J = 7.1); 7.50 (m, 2 H, Ar); 7.78 (d, 2 H, Ar, J = 7.8); 8.03 (s, 1 H, Pz)	$CDCl_3$: 23.6, 50.1, 54.2, 67.8, 68.6, 69.4, 78.6, 118.5, 125.8, 127.4, 129.4, 129.7, 140.1, 150.1
14a	429 $[M]^+$ (100)	$CDCl_3$: 3.64 (s, 2 H, CH_2); 3.77 (s, 3 H, CH_3); 4.13 (s, 2 H, CH_2); 4.17 (s, 5 H, Fc); 4.33, 4.82 (both s, 2 H each, Fc); 7.28 (t, 1 H, Ar, J = 7.5); 7.45 (m, 2 H, Ar); 7.75 (d, 2 H, Ar, J = 8.0); 8.12 (s, 1 H, CH)	$CDCl_3$: 42.9, 48.9, 52.1, 67.6, 68.8, 69.4, 77.9, 116.9, 118.6, 125.9, 127.6, 129.3, 139.9, 150.1, 171.4

(*to be continued*)

Table 2 (*continued*)

Product	MS (EI, 70 eV), m/z (I_{rel} (%))	^{1}H NMR (solvent, δ, J/Hz)	^{13}C NMR (solvent, δ)
15a	469 $[M]^+$ (100)	$CDCl_3$: 1.92—2.09 (m, 3 H); 2.21—2.32 (m, 1 H); 2.54—2.63 (m, 1 H); 3.22—3.27 (m, 1 H); 3.38—3.43 (m, 1 H); 3.75 (s, 3 H, CH_3); 3.81 (d, 1 H, CH_2, J = 13.5); 4.08 (d, 1 H, CH_2, J = 13.5); 4.17 (s, 5 H, Fc); 4.36 (s, 2 H, Fc); 4.95, 4.98 (both s, 1 H each, Fc); 7.28 (t, 1 H, Ar, J = 7.5); 7.48—7.53 (m, 2 H, Ar); 7.76 (d, 2 H, Ar, J = 7.8); 7.92 (s, 1 H, Pz)	$CDCl_3$: 21.9, 28.3, 47.0, 47.1, 52.8, 64.0, 66.7, 68.5, 69.2, 111.2, 118.4, 126.0, 129.0, 130.2, 139.0, 150.2, 167.0

Table 3. Spectroscopic data for compounds **3b**—**15b**

Product	MS (EI, 70 eV), m/z (I_{rel} (%))	^{1}H NMR (solvent, δ, J/Hz)	^{13}C NMR (solvent, δ)
3b	408 $[M]^+$ (100)	$CDCl_3$: 4.18 (s, 5 H, Fc); 4.38, 4.93 (both s, 2 H both, Fc); 4.89 (s, 2 H, CH_2); 7.45—7.58 (m, 2 H, Ar); 7.87—7.97 (m, 4 H, Ar); 8.05(s, 1 H, Ar); 8.12 (s, 1 H, Pz)	$CDCl_3$: 56.2, 67.4, 68.9, 69.4, 77.7, 115.6, 118.2, 121.2, 125.7, 126.9, 127.3, 127.8, 127.9, 129.4, 131.7, 133.7, 137.4, 150.6
4b	463 $[M]^+$ (100)	$CDCl_3$: 0.86 (m, 3 H, CH_3); 1.32 (m, 2 H, CH_2); 1.63 (m, 2 H, CH_2); 2.89 (m, 2 H, CH_2); 3.48 (s, 2 H, CH_2); 4.24 (s, 5 H, Fc); 4.42, 4.83 (both s, 2 H both, Fc); 7.50—7.59 (m, 2 H, Ar); 7.87—7.99 (m, 5 H, Ar); 8.15 (s, 1 H, Pz)	$CDCl_3$: 13.9, 20.6, 32.1, 44.1, 49.5, 67.3, 68.5, 69.3, 78.3, 96.4, 117.9, 118.4, 120.0, 125.7, 126.6, 127.2, 127.6, 128.1, 131.4, 133.8, 139.3, 149.2
5b	463 $[M]^+$ (100)	$CDCl_3$: 1.36 (s, 9 H, CH_3); 2.49 (br.s, 1 H, NH); 4.09 (s, 2 H, CH_2); 4.22 (s, 5 H, Fc); 4.39, 4.87 (both s, 2 H both, Fc); 7.49—7.60 (m, 2 H, Ar); 7.89—7.97 (m, 4 H, Ar); 8.17 (s, 1 H, Ar); 8.39 (s, 1 H, Pz)	$CDCl_3$: 26.6, 35.9, 39.5, 67.3, 68.1, 68.6, 77.5, 95.5, 117.6, 118.2, 120.7, 125.5, 126.5, 127.3, 127.8, 128.1, 131.4, 133.7, 139.3, 149.2
6b	497 $[M]^+$ (100)	$CDCl_3$: 1.92 (br.s, 1 H, NH); 4.01 (s, 2 H, CH_2); 4.03 (s, 2 H, CH_2); 4.10 (s, 5 H, Fc); 4.35, 4.86 (both s, 2 H both, Fc); 7.27—7.56 (m, 7 H, Ar) 7.87—7.95 (m, 4 H, Ar); 8.05 (s, 1 H, CH, Ar); 8.15 (s, 1 H, Pz)	$CDCl_3$: 43.6, 53.9, 67.3, 68.7, 69.4, 78.1, 115.3, 118.2, 119.9, 125.5, 126.9, 127.0, 127.2, 127.8, 128.2, 128.4, 128.6, 129.4, 131.5, 133.7, 137.5, 140.2, 150.1
7b	491 $[M]^+$ (84)	$CDCl_3$: 0.95 (m, 6 H, 2 CH_3); 1.16 (m, 4 H, 2 CH_2); 2.57 (m, 4 H, 2 CH_2); 3.77 (s, 2 H, CH_2); 4.17 (s, 5 H, Fc); 4.35, 4.92 (both s, 2 H both, Fc); 7.48—7.53 (m, 2 H, Ar); 7.87—8.08 (m, 5 H, Ar); 8.14 (s, 1 H, Pz)	$CDCl_3$: 12.1, 20.0, 49.6, 56.1, 67.4, 68.6, 68.9, 77.6, 115.2, 115.5, 118.2, 120.8, 125.5, 126.9, 127.3, 127.8, 128.4, 131.5, 133.6, 137.3, 150.6
8b	477 $[M]^+$ (100)	$CDCl_3$: 2.66 (m, 4 H, CH_2); 3.70 (s, 2 H, CH_2); 3.83 (m, 4 H, CH_2); 4.18 (s, 5 H, Fc); 4.38, 5.05 (both s, 2 H both, Fc); 7.48—7.59 (m, 2 H, Ar); 7.89—8.01 (m, 5 H, Ar); 8.16 (s, 1 H, Pz)	$CDCl_3$: 52.9, 53.4, 66.8, 67.7, 68.5, 69.2, 78.1, 115.3, 118.2, 125.5, 126.9, 127.8, 127.8, 128.1, 129.3, 129.5, 131.6, 133.7, 137.3, 150.1
9b	475 $[M]^+$ (100)	$CDCl_3$: 1.53 (m, 2 H, CH_2); 1.71 (m, 4 H, 4 CH); 2.61 (m, 4 H, 4 CH); 3.68 (s, 2 H, CH_2); 4.16 (s, 5 H, Fc); 4.34 (s, 2 H, Fc); 4.95 (s, 2 H, Fc); 7.47—7.55 (m, 2 H, Ar); 7.86 (d, 1 H, Ar, J = 8); 7.90 (d, 1 H, Ar, J = 8); 7.92—7.97 (m, 2 H, Ar); 8.08 (s, 1 H, Ar); 8.14 (s, 1 H, Pz)	$CDCl_3$: 22.7, 24.3, 29.4, 53.3, 54.5, 67.9, 68.7, 69.4, 78.3, 115.3, 118.2, 125.5, 126.8, 127.8, 127.9, 128.2, 129.4, 130.0, 131.5, 133.7, 137.5, 151.0
10b	489 $[M]^+$ (100)	$CDCl_3$: 0.99 (d, 3 H, CH_3, J = 6.5); 1.38 (m, 2 H, CH_2(ax)); 1.47 (m, 1 H, CH); 1.70 (d, 1 H, CH_2(eq); J = 12.5); 2.09 (t, 1 H, CH_2(ax); J = 11); 3.10 (d, 2 H, CH_2(eq); J = 11); 3.66 (s, 2 H, CH_2); 4.17 (s, 5 H, Fc); 4.35, 4.99 (both s, 2 H both, Fc); 7.47—7.57 (m, 2 H, Ar); 7.87—7.99 (m, 4 H, Ar); 8.00 (s, 1 H, Ar); 8.14 (s, 1 H, Pz)	$CDCl_3$: 21.9, 31.0, 34.5, 53.2, 54.2, 67.9, 68.6, 69.3, 78.5, 115.2, 118.3, 125.5, 126.8, 127.3, 127.8, 127.9, 129.3, 129.5, 131.6, 133.8, 137.7, 151.0
11b	590 $[M]^+$ (35)	$CDCl_3$: 1.46 (s, 9 H, 3 CH_3); 1.53 (m, 2 H, CH_2); 1.99 (d, H, CH_2, J = 11.5); 2.23 (m, 1 H, CH_2); 3.04—3.05 (m, 1 H, CH_2); 3.56—3.58 (m, 1 H, CH); 3.66 (s, 2 H, CH_2); 4.14 (s, 5 H, Fc); 4.34, 4.95 (both s, 2 H both, Fc); 7.47—7.53 (m, 1 H, Ar); 7.85 (d, 1 H, Ar, J = 8); 7.89 (d, 1 H, Ar, J = 8); 7.91—7.96 (m, 2 H, Ar); 8.00 (s, 1 H, Ar); 8.12 (s, 1 H, Pz)	$CDCl_3$: 28.5, 29.7, 32.5, 47.8, 52.4, 52.6, 67.8, 68.7, 69.3, 78.2, 115.3, 118.2, 125.5, 126.9, 127.8, 127.9, 128.1, 129.4, 129.5, 131.5, 133.7, 137.4, 151.0, 155.2

(*to be continued*)

Table 3 (*continued*)

Product	MS (EI, 70 eV), m/z (I_{rel} (%))	^{1}H NMR (solvent, δ, J/Hz)	^{13}C NMR (solvent, δ)
12b	490 $[M]^+$ (100)	$CDCl_3$: 2.40 (s, 3 H, CH_3); 2.64—2.72 (m, 8 H); 3.70 (s, 2 H, CH_2); 4.14 (s, 5 H, Fc); 4.34, 4.98 (both s, 2 H both, Fc); 7.47—7.55 (m, 2 H, Ar); 7.85—7.98 (m, 5 H, Ar); 8.12 (s, 1 H, Pz)	$CDCl_3$: 45.7, 52.6, 52.6, 55.0, 67.8, 68.6, 69.3, 78.2, 115.3, 117.5, 118.2, 125.5, 126.9, 127.8, 127.8, 128.0, 129.4, 131.5, 133.7, 137.5, 151.1
13b	461 $[M]^+$ (100)	$CDCl_3$: 1.97 (m, 4 H, CH_2); 2.98 (m, 4 H, CH_2); 3.88 (s, 2 H, CH_2); 4.09 (s, 5 H, Fc); 4.36, 4.77 (both s, 2 H both, Fc); 7.46—7.56 (m, 2 H, Ar); 7.86—8.00 (m, 5 H, Ar); 8.17 (s, 1 H, Pz)	$CDCl_3$: 23.4, 49.1, 53.2, 68.0, 68.7, 69.5, 115.7, 118.2, 125.7, 126.9, 127.8, 127.9, 128.0, 129.4, 131.8, 133.7, 149.8
14b	479 $[M]^+$ (100)	$CDCl_3$: 3.63 (s, 2 H, CH_2); 3.77 (s, 3 H, CH_3); 4.06 (s, 2 H, CH_2); 4.15 (s, 5 H, Fc); 4.36, 4.87 (both s, 2 H both, Fc); 7.47—7.53 (t, 2 H, Ar); 7.85—7.93 (m, 4 H, Ar); 8.11 (s, 1 H, Ar); 8.13 (s, 1 H, Pz)	$CDCl_3$: 43.5, 49.8, 52.0, 67.4, 68.8, 69.4, 77.9, 115.4, 118.2, 118.6, 125.6, 126.9, 127.3, 127.8, 127.9, 129.4, 131.6, 133.7, 137.4, 150.2, 172.5
15b	519 $[M]^+$ (92)	$CDCl_3$: 1.88—2.17 (m, 3 H); 2.54—2.62 (m, 1 H); 3.16—2.27 (m, 1 H); 3.38—3.42 (m, 1 H); 3.71 (s, 3 H, CH_3); 3.81 (d, 1 H, CH_2, J = 13.5); 4.08 (d, 1 H, CH_2, J = 13.5); 4.14 (s, 5 H, Fc); 4.34, 4.94 (both m, 2 H both, Fc); 7.45—7.55 (m, 2 H, Ar); 7.85—7.94 (m, 4 H, Ar); 8.02 (s, 1 H, Ar); 8.13 (s, 1 H, Pz)	$CDCl_3$: 29.4, 43.5, 49.8, 52.0, 67.3, 67.4, 67.6, 68.8, 68.9, 115.4, 118.2, 118.6, 125.6, 125.6, 126.9, 127.3, 127.8, 127.9, 129.4, 131.6, 133.7, 137.4, 150.2, 172.5

Reductive amination of ferrocenylformylpyrazoles (general procedure). A solution of ferrocenylpyrazole-4-carbaldehyde **2a** or **2b** (0.5 mmol) and an amine (0.75 mmol) in 1,2-dichloroethane (35 mL) was stirred at room temperature for 1 h. Sodium triacetoxyborohydride (0.16 g, 0.75 mmol) was added and the reaction mixture was refluxed for 30 min and decomposed with aqueous $NaHCO_3$. The product was extracted with CH_2Cl_2 (2×30 mL). The organic fractions were washed with brine and dried over Na_2SO_4. The solvent was removed in a water aspirator vacuum and the residue was chromatographed on silica gel ($CHCl_3$—MeOH, 9 : 1). The spectroscopic and elemental analysis data for the compounds obtained are given in Table 1. Their ^{1}H and ^{13}C NMR and mass spectra are given in Tables 2 and 3.

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