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STUDY ON FERROCENES, PART 6.[1] 1,3-DIPOLAR CYCLOADDITIONS OF HETEROCYCLIC HYDRAZONES OF FORMYLFERROCENE

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Abstract: 1,3-Dipolar cycloaddition reactions of ferrocenylmethylidenehydrazones containing different heterocycles (**1a-c**) with some dipolarophiles resulted a series of new cycloadducts and condensed triazoles. The reactivity of the substrates was found to be dependent on the heterocyclic moiety. The structure of the products was determined by IR, ^{1}H- and ^{13}C-NMR (1D and 2D) measurements supported by single crystal X-ray analysis.

Introduction

Huisgen recognised the general concept and scope of 1,3-dipolar cycloaddition reactions[2,3] and since then such types of conversions have become one of the most valuable methods for the synthesis of aromatic, saturated and partly saturated five-membered heterocycles. Numerous possibilities for variation are available by changing the structure of both the dipole and dipolarophile, so many examples dealing with 1,3-dipolar cycloadditions has appeared in the literature in the past decades.[4] Examples of cyclization of not obviously dipolar agents, such as oximes and hydrazones generating the actual dipolar species by 1,2-proton shift (>C=N–XH → [>C=N^{+}H–X^{-} ↔ >C^{+}–NH–X^{-}], where X = O, NAr, NCOR), have also been reported.[5] These observations and the lack of analogue experiences with appropriate metallocene derivatives prompted us to try to convert the easily available ferrocenylhydrazones **1a-c**[1] into new metallocene substituted pyrazoles with a connected heterocycle of potential pharmaceutical interest (*Scheme*).[6]

Results and discussion

The 1,3-dipolar cycloaddition reactions were performed by refluxing the appropriate hydrazones (**1a-c**) with dimethyl acetylenedicarboxylate (DMAD), dimethylmaleate (DMMA) or fumarate (DMFM) and *(E)*-ω-nitrostyrene (NTS) in freshly distilled acetonitrile, in the presence of molecular sieves under an argon atmosphere (*Scheme*). Besides a series of new pyrazole, pyrazoline and diastereomeric pyrazolidine derivatives, reactions of **1a** and **1c** also yielded condensed triazoles **5** and **6**, respectively. In the absence of the reagents these oxidative cyclizations were not observed even on prolonged treatment of **1a,c** with the boiling solvent. Probably due to its higher redox potential **1b**, the NH analogue of **1c**, was not oxidized by the applied reagents.

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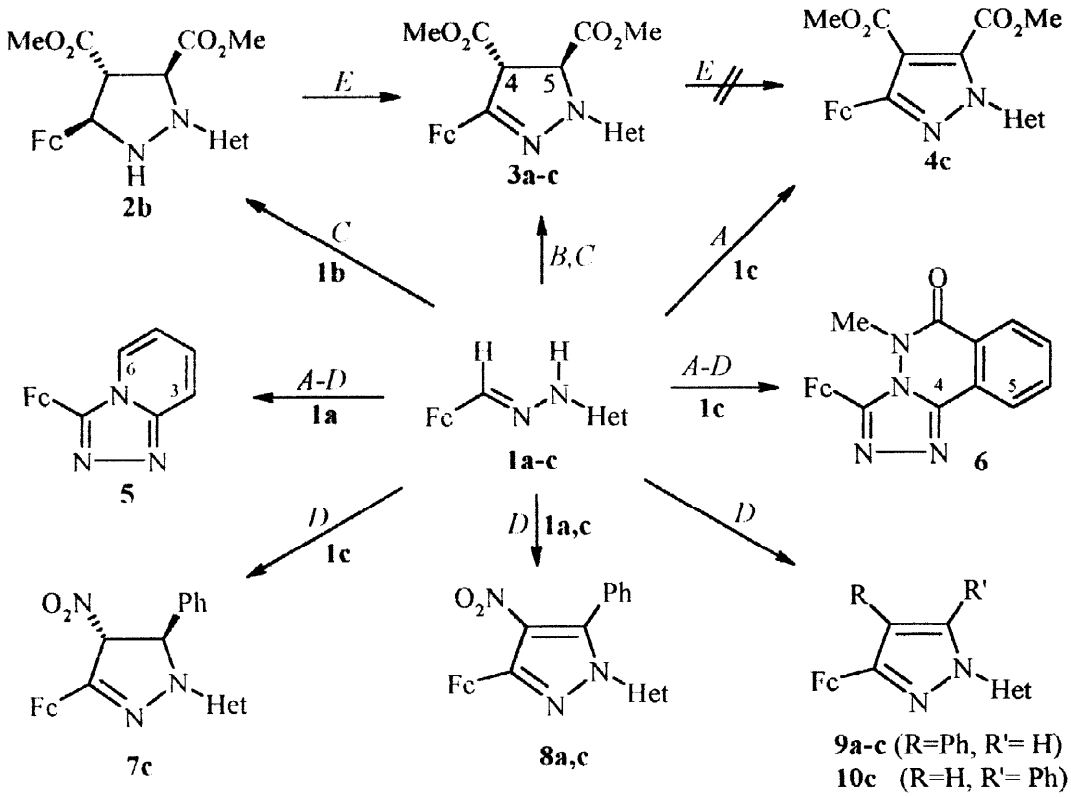
Using DMAD as dipolarophile (*Method A*), there were some difficulties in purifying the products, because some unidentifiable polymer-like substances were formed. With this reagent only **1c** gave isolable products (**6** and **4c**). The latter was formed by cycloaddition followed by aromatization.



Scheme

Fc: ferrocenyl; Het: **a**: α-pyridyl, **b**: 4-[phthalazin-1(2H)-on]-yl, **c**: 4-[2-methylphthalazin-1(2H)-on]-yl, Route of reaction; reflux in MeCN, *A*: DMAD, *B*: DMMA, *C*: DMFM, *D*: NTS; *E*: DDQ/CH_2Cl_2

Interestingly, with DMMA (*Method B*), the cycloaddition of each of the investigated models afforded pyrazoline 4,5-*trans*-dicarboxylic acid esters (**3a-c**) as final products due to fast epimerization at C-4. As expected, applying DMFM as dipolarophile (*Method C*), **1a-c** yielded **3a-c**. The formation of isolable all-*trans*-pyrazolidine **2b** points to the mechanism involving cycloaddition of dipolar intermediates resulting from the previously mentioned proton shift. On treatment with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in CH_2Cl_2 (*Method E*) **2b** was easily oxidized to the appropriate pyrazoline (**3b**), but aromatization to the pyrazole analogous to **4c** did not occur at all. Accordingly, conversion **3c** → **4c** could not be effected by DDQ. On the other hand, conversions of **1a-c** with NTS (*Method D*) gave mainly aromatic products (**8a,c**, **9a-c**, **10c**), but pyrazoline **7c** could also be isolated in low yield (4%) and identified by spectroscopic methods. The structure of pyrazoles suggest that aromatization occurs either by subsequent dehydrogenation or by elimination of nitrous acid.[7] It is worth pointing out that reaction of **1b** with NTS afforded exclusively 3-ferrocenyl-4-phenylpyrrazole (**9b**) as the isolable product (87%) indicating a pronounced regioselective cycloaddition step. It must also be noted that formation of 4-phenyl-5-nitropyrazoles, the regioisomers of **8a,c**, was not detected at all.

The structure of the novel compounds were determined by IR, ^{1}H- and ^{13}C-NMR spectroscopy (Tables 1 and 2) including DNOE measurements and 2D-techniques such as 2D-HMQC and 2D-HMBC. The most suitable way explaining the course of structure determination is to group the analogous structures.

Structures of **5** and **6** containing a condensed triazole ring are supported by the following facts: a) the ^{1}H-NMR signals of azomethine (N=CH) and NH hydrogens are absent in the ^{1}H-NMR spectrum. Accordingly, the νNH band disappears from the IR-spectra of **5** and **6**; b) IR, ^{1}H- and ^{13}C-NMR signals which would arise from incorporated dipolarophilic reagents are not observable in the spectra of these products; c) the anisotropy[8a] of the vicinal nitrogen in the condensed triazole ring causes a significant downfield shift of the H-3 and H-5 signals relative to the starting hydrazones **1a** and **1c** (by 0.51 and 0.15 ppm, resp.); d) the C-1 line in Fc is upfield shifted by 10.0 and 7.2 ppm in **5** and **6** as compared to **1a** and **1c** caused by the steric interaction of the Fc moiety with H-6 (**5**) and the N(3)Me group (**6**), respectively (steric compression shift[8b,9]) e) the presence of the electron withdrawing triazole ring is reflected on the higher amide-I IR frequency[10] of **6** relative to **1c**[1] (1673 and 1645 cm^{-1}, resp.).

Table 1. ^{1}H-NMR data[a] and the IR carbonyl frequency[b] of compounds **1a, 2b, 3a-c, 4c, 5, 6, 7c, 8a,c, 9a-c, 10c**.[c]

	NCH_3	OCH_3		H-2,5	H-3,4	H-1′-5′	H-4	H-5	H-3/5	H-4/6	H-5/7	H-6/8	νC=O
	s(3H)[d]	2x*s*	(2x3H)	~*s*(1H)	~*s*(1H)	*s* (5H)	5-Het.	ring[e]		HC-substituent[f]			band[g]
1a	8.98	–		4.59	4.32	4.17	–	7.62	7.28	7.58	6.74	8.12	–
2b	12.12[i]	3.68	3.71	4.30	4.16	4.10	3.46	5.54	8.50	7.80	7.85	8.20	1658
3a	–	3.77	3.80	4.63[h]	4.35[h]	4.16	5.38	4.23	7.38	7.55	6.70	8.11	1750
3b	11.10	3.72	3.82	4.54[h]	4.32[h]	4.12	4.19	5.34	8.78	7.22	7.80	8.36	1657
3c	3.62	3.73	3.80	4.55[h]	4.31[h]	4.12	4.16	5.30	8.80	7.69	7.74	8.40	1654
4c	3.80	3.74	3.94	4.81	4.30	4.10	–	–	7.50	7.77[j]	7.77[j]	8.45	1646
5	–	–		4.91	4.51	4.22	–	–	7.79	7.26	6.91	8.49	–
6	3.47			4.68	4.46	4.46	–	–	8.45	7.85	7.69	8.31	1673
7c	3.62	–	–	4.65[h]	4.45	4.13	5.88	6.41	8.80	7.77	7.84	8.45	
8a	–	–		4.91	4.32	4.12	–	–	7.40	7.67	7.15	8.21	–
8c	3.69			4.99	4.42	4.21	–	–	7.48	7.80[j]	7.80[j]	8.42	1669
9a	–	–		4.49	4.14	3.98	–	8.43	8.00	7.75	7.08	8.33	–
9b	10.94	–		4.57	4.23	4.07	–	8.03	8.80	7.94	7.59	8.55	1660
9c	3.88			4.57	4.23	4.07	–	8.02	8.72	7.88	7.85	8.53	1662
10c	3.76			4.79	4.33	4.15	6.68	–	7.44	7.73	7.77	8.44	1658

[a] Chemical shifts (in δ, δ_{TMS} = 0 ppm) and coupling constants (in Hz) in $CDCl_3$ solution (in DMSO-d_6 for **2b**) at 500 MHz; [b] In KBr discs (in cm^{-1}); [c] Assignments were supported by 2D-HMQC (except for **1a** and **3b**) and DNOE measurements (except for **1a**, **3b**, **4c**, **5**, **6**, and **8**). Further signals in IR: νNH: ~3195 (**1a**), 3400-2800 (**2b**, **3b**, **9b**), NO_2 1524, 1354, 824 (**7c**), 1506, 1343, 822 (**8a**), 1502, 1344, 823 (**8c**), νC–O ester bands: 1261 and 1145 (**3a**), 1206 and 1003 (**3b**), 1293 and 1171 (**3c**), 1244, 1209 and 1002 (**2b**), 1250 and 1077 (**4c**), $\gamma C_{Ar}H$ (2-pyridyl ring): 773 (**1a**): 770 (**3a**), 745 (**5**), 783 (**9a**), 775 (**8a**), $\gamma C_{Ar}H$ and $\gamma C_{Ar}C_{Ar}$ (phenyl): 764 and 699 (**7c**), 731 and 700 (**9a**), 765 and 700 (**9b**), 762 and 697 (**9c**), 737 and 698 (**8a**), 762 and 697 (**8c**), 773 and 687 (**10c**), ferrocenyl: 501-510 (522 for **6**) and 480-490; in ^{1}H-NMR, phenyl : 7.42 (**9a**), 7.50 (**9b**) *dd*(2H), H-2′,6′; 7.35 (**9a**), 7.45 (**9b,c**), ~*t* (2H), H-3′,5′; 7.30 (**9a**), 7.40 (**9b,c**), H-4′,~*t* (1H); ~7.3 (**3b**, **10c**), ~7.35 (**7c**, **10c**), *m* (5H); [d] NH, *s* (1H) for **1a**, **2b**, **3b** and **9b**; [e] CH=N group in **1a**, *s*(1H) for **1a**, **9a-c** and **10c**, 2x*d* (2x1H), *J*: 4.9 (**3a**), 7.4 (**3b**), 6.7 (**3c**, **7c**), in **2b** the H-4 signal is a *dd* (*J*: 8.5 and 7), the H-5 signal is a *d* (*J*: 7) and the H-3 signal appears at 4.04 as a *dd* (*J*: 12 and 8.5); [f] Numbering of the hydrogens in Het (α-pyridyl-/phthalazinone) ring. Multiplicities: *dd* or ~*d* (H-3/5 and H-6/8), ~*t* (H-4/6 and 5/7), except for H-5 in **1a**, **8a** and **9a**, and for H-4 in **8a** and **9a**, where it is *dd* and *dt*, resp. Couplings are in **a**-type compounds: ^3J(H-3,H-4): 8.2±0.2, ^3J(H-4,H-5): 7.7±0.1, ^3J(H-5,H-6): 4.2±0.2 and ^4J(H-4,H-6): 1.5±0.1, in **b**- and **c**-type compounds: ^3J(H-5,H-6) ≈ ^3J(H-7,H-8): 7.9±0.3; [g] Amide-I band and ester carbonyl band for **3a**. The frequencies of the latter band in **3b**, **3c**, **2b** and **4c** are 1734, 1740, 1737 and 1738; Doubled signal due to hindered rotation with the second maxima at 4.86 and 4.40 (**3a**), 4.72 and 4.35 (**3b**), 4.74 and 4.34 (**3c**) and 4.70 (**3c**), resp.; [i] Amide-NH, NH (pyrazolidine): 5.72 *d* (*J*:12); [j] Overlapping signals.

Table 2. ^{13}C NMR chemical shifts (in ppm, $\delta_{TMS} = 0$ ppm) of compounds **1a**, **2b**, **3a-c**, **4c**, **5**, **6**, **7c**, **8a,c**, **9a-c**, and **10c** in $CDCl_3$ solution[a] at 125.7 Mhz.[b]

	NCH_3	C-1'-5'	C-1	C-2,5	C-3,4	C-3	C-4	C-5	C-2/1	C3/5	C-4/6	C-5/7	C-6/8	C=O	C-4a	C-8a
		ferrocenyl				5-membered het.-ring					2-pyridyl/4-phthalazonyl ring					
1a	–	69.5	80.8	67.4	70.0	139.8	–	–	157.6	107.8	138.5	115.5	147.7	–	–	–
2b	–	69.4	84.7	68.2	68.9	62.7	57.8	65.6	146.9	126.6[d]	132.3	133.2	128.3[d]	159.8	129.6	127.6
3a	–	70.0	75.8	67.4[c]	70.4[c]	155.1	56.8	64.3	147.9	109.4	137.7	115.3	147.9	–	–	–
3b	–	69.1	74.5	66.7[c]	69.7[c]	142.4	54.7	65.1	147.8	126.1[d]	132.2	130.7	127.2[d]	159.1	128.8	125.5
3c	38.7	69.6	74.9	67.1[c]	70.1[c]	141.8	55.1	65.9	148.4	127.5	132.2	131.3	127.0	158.4	129.1	125.3
4c	39.5	69.7	74.9	68.2	69.4	151.5	115.5	136.2	138.4	127.3[e]	132.4	133.5	124.4	159.5	128.5	127.3[c]
5	–	69.4	70.8	67.7	69.8	146.1	–	–	150.3	116.9	126.3	113.5	123.2	–	–	–
6	36.5	70.5	73.2	69.2	71.7	146.1	–	–	143.0	128.7	130.7	134.3	123.1	160.1	123.3	124.4
7c	38.9	70.1	74.0	66.3[c]	70.3[c]	141.8	96.2	69.1	137.3	127.2	131.4	132.3	126.9	158.5	129.2	125.7
8a	–	69.5[e]	74.5	69.4	69.5[e]	147.4	127.4	142.1	151.2	119.4	138.4	123.5	148.5	–	–	–
8c	39.3	69.7	74.0	69.5	69.8	148.1	131.8	144.7	137.5	127.4	132.6	133.7	124.0	159.2	128.3	127.5
9a	–	69.5	78.0	68.2	68.4	150.3[d]	123.5	126.5	151.5[d]	112.3	138.5	120.9	148.0	–	–	–
9b	–	69.5	77.4	68.1	68.6	150.9	122.8	130.0	140.7	127.1	132.2	133.9	127.3	160.4	129.0	126.4
9c	39.4	69.4	77.6	68.1	68.5	150.7	122.7	129.9	139.0	127.2	132.1	133.1	126.8	159.3	129.0	126.0
10c	39.4	69.6		67.0	69.0	153.2	104.8	146.9	139.7	127.1	132.3	133.5	124.8	159.5	128.6	128.4

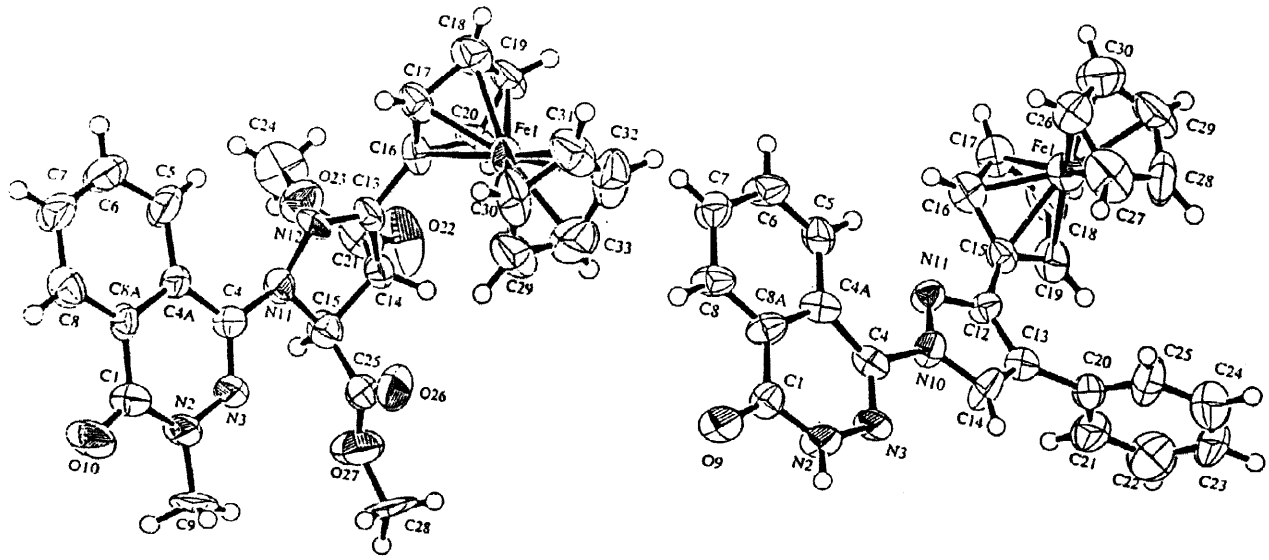
[a] and/or in DMSO-d_6 for **3a-c**, **7c**/**2b**; [b] Assignments were supported by 2D-HMQC (except for **1a** and **3b**), DEPT (except for **1a**, **2b**, **3b**, **5**, **7c** and **10c**) and for the **b**- and **c**-type compounds also by 2D-HMBC (except for **3b,c** and **4c**) measurements. Further lines: OCH_3 : 53.1 and 53.5 (**3a**), 52.2 and 52.6 (**3b**), 52.5 and 53.1 (**3c**), 53.2 and 53.3 (**2b**), 52.5 and 52.9 (**4c**); C=O (ester groups): 169.8 and 171.0 (**3a**), 168.9 and 169.3 (**3b**), 169.3 and 170.1 (**3c**), 172.1 and 172.2 (**2b**), 159.0 and 164.0 (**4c**); phenyl substituent, C-1 :144.0 (**7c**), 133.9 (**9a**), 132.8 (**9b,c**, **8a**), 126.2 (**8c**), 129.7 (**10c**), C-2,6 : 126.6 (**7c**), 129.7 (**9a-c**), 129.9 (**8a**), 126.6 (**8c**), 128.5 (**10c**), C-3,5: 129.2 (**7c**), 128.2 (**9a-c**, **8a**, **10c**), 128.4 (**8c**), C-4: 128.9 (**7c**), 127.2 (**9a**), 127.5 (**9b,c**), 129.6 (**8a**), 130.2 (**8c**), 128.6 (**10c**);[c] Due to hindered rotation of the ferrocenyl moiety doubled signal with the second line at 67.8 and 70.5 (**3a**), 68.2 and 69.8 (**3b**), 67.5 and 70.2 (**3c**), 67.5 and 70.5 (**7c**); [d] Interchangeable assignments; [e] Two coalesced lines.

Free rotation around the C–1(Cp)–C–3(triazole) bond (rotation of Fc substituent to the condensed skeleton) is proved by the chemical equivalence of H-2 and H-5 and H-3 and H-4 atoms (and similarly of C-2,5 and C-3,4 pairs). The downfield shift of the H-2,5 Fc-signal (by 0.32 ppm) in **5** supports the preference of coplanar rotamers, while in **6**, due to Fc....NMe steric hinderance the rotamers with coplanar triazole and substituted Cp-rings are unfavourable (here the shift difference is only 0.05 ppm).

The second group of new compounds are the pyrazoles **4c**, **8a,c**, **9a-c** and **10c**. In the ^{13}C-NMR spectra of these compounds besides the carbon lines of the Fc and Het moieties the C-3, C-4 and C-5 lines appear at chemical shifts characteristic[8c] for pyrazoles or substituted pyrazoles (Table 2). The characteristic IR bands and ^1H- and ^{13}C-NMR signals of the conjugated esters (**4c**), nitro (**8a,c**) and phenyl substituents (**8a,c**, **9a-c** and **10c**) are present in the appropriate spectra and, of course, the IR bands of the nitro groups are absent in the products formed by HNO_2-elimination (**9a-c** and **10c**). In these compounds the ^1H-NMR singlet of the pyrazolic hydrogen (H-5 or H-4) is observable and the protonated heteroaromatic carbon line is shifted upfield as compared to the substituted analogues.

The position of the phenyl substituent in **9a-c**, and **10c** was proved by DNOE measurements. Mutual NOEs were observed for the H-2,5 Fc-hydrogens and the *ortho*-hydrogens of the phenyl ring in **9a-c**, which demonstrates the steric proximity of these atoms (i.e. Pos. 4 for the phenyl ring). Saturating the H-4 singlet of the pyrazole ring in **10c**, the measured response of H-2,5 Fc-signal confirmed the 5-phenyl substitution. With regard to expected values of the ^{13}C-NMR chemical shifts of C-3, C-4 and C-5 pyrazole lines and the considerable downfield shift of H-2,5 Fc signal, the 3-ferrocenyl-4-nitro-5-phenyl substitution of the pyrazole ring in **8a,c** is straightforward. Free rotation of Fc moiety in all these compounds is confirmed by the chemical equivalence of C/H-2,5 and C/H-3,4 atom pairs in this substituent.

The structure of pyrazoline diesters **3a-c** are supported by the following facts: a) in the IR spectra the bands of saturated esters were detected; b) the doublets of H-4 and H-5 appear in the ^{1}H NMR spectrum in the shift interval expected for saturated CH groups; c) the corresponding ^{13}C-NMR lines of C-4 and C-5 point to sp^3 carbons (about 56 and 65 ppm); d) the ^{1}H- and ^{13}C-NMR signals of two COOMe-groups were observed; e) the *trans* arrangement of the two carbomethoxy substituents and their position (**4-*exo*-, 5-*endo*-**) relative to the fixed Fc group in **3c** are proved by X-ray measurement. The similar ^3J(H-4,H-5) coupling in **3b** and **3c** (7.4 and 6.9 Hz) and the practically identical chemical shifts of H and C atoms in Pos. 4 and 5 support analogous steric structures, for **3b**. The above shifts are also similar for **3a**, but the coupling H-4,H-5 is smaller (4.9 Hz). Nevertheless, the configuration in the pyrazoline ring is probably the same, because *cis*-arrangement would cause an opposite change in the value of this interaction.[8d] Due to a more crowded steric structure, the rotation of the Fc moiety in **3a-c** and **7c** is hindered and the H/C-2,5 and H/C-3,4 NMR signals are doubled. The barrier of rotation is high, because the separated signals did not coalesce even on heating the solution up to 130 °C. Because of the presence of a non-rotating ferrocenyl group an element of planar chirality[11] is also introduced into these pyrazolines containing the substituents on C-4 and C-5 in "*exo*" and "*endo*" positions, respectively. This is evidenced for **3c** by single crystal X-ray measurement (*Figure*). In case of **7c** the NOE between H-4 and the *ortho*-hydrogens of the phenyl ring proved unequivocally the *trans* configuration. Similarly, in pyrazolidine **2b** the *cis*-position of H-3 and H-5 is straightforward from their mutual NOE's and the response of pyrazolidine H-4 due to the irradiation of H-2,5 signal of Fc suggest the *trans* orientation of H-4 with H-3 and H-5.



3c **9b**

Figure: Structures of **3c** and **9b** determined by X-ray diffraction

An interesting NOE was observed between the H-2,5 Fc-signal and H-5 of phthalazinone in **9b**, which indicates that the ferrocenyl and the heterocyclic substituents are not coplanar with the pyrazole ring. A similar interaction was also observed for **3c**. The steric proximities of the protons involved are in good agreement with the results of single crystal X-ray analysis of these compounds (*Figure*).

The crystal structures proved all the expected structural characteristics as far as bond lengths and angles are concerned in the case of both compounds **3c** and **9b**. It is worth mentioning that the two Cp moieties are positioned exactly above each other with C-Fe distances in the 2.01-2.06 Å range in both compounds.

In **3c** (*Figure*) the 2-pyrazoline ring has an envelope conformation with C-15 being on the tip. The four coplanar atoms are also coplanar with the connected Cp moiety. Both COOMe groups on the 2-pyrazoline moiety are in *pseudo-axial* positions and on opposite sides of the mean plane of the ring. The methylphthalazonyl ring is slightly bent and the plane constituted by the C-1,4,4A,5,6,7,8,8A atoms and that formed by the C-1,4, N-2,3 atoms form an angle of 6°. This distortion might be due to the steric interaction between the neighbouring O-10 and C-9 (methyl) atoms.

In **9b** (*Figure*) the pyrazole ring is obviously flat and the plane of the ring is at an angle of 10° to that of the connected Cp moiety. Furthermore, the interplanar angles of the pyrazole ring with the connected phenyl as well as with the phthalazonyl moiety are 76° and 28°, respectively. The phthalazonyl group is completely flat.

Experimental

The ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solution in 5 mm tubes at RT, on a Bruker DRX 500 spectrometer at 500.13 (^{1}H) and 125.76 (^{13}C) MHz, with the deuterium signal of the solvent as the lock and TMS as internal standard. The standard Bruker microprogram NOEMULT.AU to generate NOE was used with a selective preirradiation time. DEPT specta were run in a standard manner, using only the Θ =135° pulse to separate CH/CH_3 and CH_2 lines phased "up" and "down", respectively. The 2D-HMQC, and 2D-HMBC spectra were obtained by using the standard Bruker pulse programs INV4GSSW and INV4GSLRNDSW, respectively.

Crystal data for **3c**. Monoclinic C2/c, a = 31.420(11) Å, b = 8.856(4) Å, c = 22.154(9) Å, β = 128.63(2)°, V = 4816(4) Å^3, Z = 8, d = 1.457 g/cm^3, μ = 5.410 mm^{-1}, F(000) = 2192, crystal size 0.2x0.1x0.1 mm, θ range for data collection 3.60 to 62.40°, index ranges: $-1 \le h \le 28$, $-10 \le k \le 10$, $-20 \le l \le 19$, reflections collected 3949, full-matrix least-squares on F^2, data/restraints/parameters 2010/0/328, goodness-of-fit on F^2 1.002, final R indices [$I > 2\sigma(I)$]: R1 = 0.0462 wR2 = 0.0657; largest diff. peak and hole: 0.197and −0.229 e.Å^{-3}

Crystal data for **9b**. Triclinic P-1, a = 10.191(5) Å, b = 11.816(6) Å, c = 9.850(3) Å, α = 99.34(3)°, β = 103.76(4) °, γ = 101.40(4)°, V = 1101.8(8) Å^3, Z = 2, d = 1.424 g/cm^3, μ = 5.707mm^{-1}, F(000) = 488, crystal size 0.8x0.2x0.1 mm, θ range for data collection 3.91 to 75.08°, index ranges: $-9 \le h \le 11$, $-14 \le k \le 14$, $-11 \le l \le 11$, reflections collected 4042, full-matrix least-squares on F^2, data/restraints/parameters 3788/0/299, goodness-of-fit on F^2 0.962, final R indices [$I > 2\sigma(I)$]: R1 = 0.0682 wR2 = 0.2468, largest diff. peak and hole: 0.329 and 0.464 e.Å^{-3}.

Compounds **1b** and **1c** are described[1] and *ferrocenylmethylidenehydrazino-2-pyridine* (**1a**) was prepared by condensation of formylferrocene (1.07 g, 5 mmol) with a slight excess of 2-hydrazinopyridine (0.6 g, 5.5 mmol). This mixture was boiled for 2 h in dry ethanol (20 mL) in the presence of 0.5 g of molecular sieves (3Å). The hot solution was filtered and cooled to RT. After 1 h the precipitated orange crystals were collected (Yield: 86%).

1,3-Dipolar cycloaddition reactions of hydrazones **1a-c** *with dipolarophiles, (general procedure for Methods A-D).* A reaction mixture containing stoichiometric amounts (2.5 mmol) of hydrazone and the appropriate dipolarophile reagent (DMAD, DMMA or DMFM, NTS) was refluxed for 15 h in 20 mL of acetonitrile in the presence of 0.5 g molecular sieves (3 Å) under an argon atmosphere. The solvent was evaporated *in vacuo* to dryness. The residue was always contaminated by paramagnetic substances. The separation by chromatography on silica (Kieselgel type 9385; eluent: $CHCl_3$) and subsequent recrystallization from ethanol gave the pure products (see Tables 1-3): *4-[(3R_p*,4S*,5S*)-4,5-bis-carbomethoxy-3-ferrocenyl-2,3,4,5-tetrahydropyrazol-1-yl]-phthalazin-1(2H)-one* (**2b**) (32%); *2-[(3R_p*,4R*,5S*)-4,5-bis-carbomethoxy-3-ferrocenyl-4,5-dihydro-pyrazol-1-yl]-pyridine* (**3a**) (59% and 57% by Methods *B* and *C*, resp.); *4-[(3R_p*,4R*,5S*)-4,5-bis-carbomethoxy-3-ferrocenyl-4,5-dihydropyrazol-1-yl]-phthalazin-1(2H)-one* (**3b**) (65% and 60% by Methods *B* and *C*, resp.); *4-[(3R_p*,4R*,5S*)-4,5-bis-carbomethoxy-3-ferrocenyl-4,5-dihydropyrazol-1-yl]-2-methylphthalazin-1(2H)-one* (**3c**) (75% and 79% by Methods *B* and *C*, resp.); *4-(4,5-bis-carbomethoxy-3-ferrocenylpyrazol-1-yl)-2-methylphthalazin-1(2H)-one* (**4c**) (62%); *3-ferrocenyl-[1,2,4]-triazolo[3,4-a]pyridine* (**5**) (18%, 11% and 28% by Methods *B*, *C* and *D*); *3-ferrocenyl-5-methyl-[1,2,4]-triazolo[3,4-a]phthalazin-6(5H)-one* (**6**) (17%, 16%, 10% and 24% by Methods *A*, *B*, *C* and *D*); *4-[(3R_p*,4R*,5S*)-3-ferrocenyl-4,5-dihydro-4-nitro-5-phenylpyrazol-1-yl)]-2-methylphthalazin-1(2H)-one* (**7c**) (4%); *2-(3-ferrocenyl-4-nitro-5-phenylpyrazol-1-yl)-pyridine* (**8a**) (30%); *4-(3-ferrocenyl-4-nitro-5-phenylpyrazol-1-yl)-2-methylphthalazin-1(2H)-one* (**8c**) (28%); *2-(3-ferrocenyl-4-phenylpyrazol-1-yl)-pyridine* (**9a**) (34%), *4-(3-ferrocenyl-4-phenylpyrazol-1-yl)-phthalazin-1(2H)-one* (**9b**) (87%), *4-(3-ferrocenyl-4-phenylpyrazol-1-yl)-2-methylphthalazin-1(2H)-one* (**9c**) (38%); *4-(3-ferrocenyl-5-phenyl-pyrazol-1-yl)-2-methylphthalazin-1(2H)-one* (**10c**) (34%).

Oxidation of pyrazolidine ***2b*** *to pyrazoline* ***3b.***

A mixture of **2b** (0.516 g; 1 mmol) and DDQ (0.227 g; 1 mmol) was dissolved in CH_2Cl_2 (5 mL). The reaction mixture was stirred at RT for 6 h then evaporated to dryness. The solid residue was recrystallized from ethanol (4 mL) to obtain 0.442 g (86%) of **3b**.

Table 3. Physical and analytical data on compounds **1a**, **2b**, **3a-c**, **4c**, **5**, **6**, **7c**, **8a,c**, **9a-c**, and **10c**.

Comp.	Appearance	Mp °C	Formula	Calcd%			Found%		
				C	H	N	C	H	N
1a	red needles	158-160	$C_{16}H_{15}FeN_3$	62.92	4.95	13.77	62.91	4.90	13.80
2b	yellow powder	164-168	$C_{25}H_{24}FeN_4O_5$	58.15	4.68	10.85	58.21	4.65	10.78
3a	red powder	154-157	$C_{22}H_{21}FeN_3O_4$	59.07	4.73	9.40	59.10	4.72	9.47
3b	orange powder	208-209	$C_{25}H_{22}FeN_4O_5$	58.38	4.31	10.83	58.44	4.35	10.93
3c	orange cubes	163-165	$C_{26}H_{24}FeN_4O_5$	59.11	4.57	10.60	59.15	4.63	10.54
4c	orange powder	150-152	$C_{26}H_{22}FeN_4O_5$	59.33	4.21	10.64	59.38	4.17	10.60
5	yellow powder	203-205	$C_{16}H_{13}FeN_3$	63.40	4.32	13.86	63.34	4.39	13.85
6	yellow powder	154-155	$C_{20}H_{18}FeN_4$	62.51	4.72	14.58	62.47	4.78	14.61
7c	purple powder	171-174	$C_{28}H_{23}FeN_5O_3$	63.05	4.34	13.13	63.10	4.35	13.18
8a	purple powder	163-165	$C_{27}H_{19}FeN_5O_3$	65.10	3.84	14..05	65.08	3.90	14.08
8c	purple powder	174-175	$C_{28}H_{21}FeN_5O_3$	63.30	3.98	13.18	63.25	4.00	13.18
9a	orange powder	184-186	$C_{24}H_{19}FeN_3$	71.13	4.72	10.37	71.19	4.71	10.42
9b	yellow cubes	235-238	$C_{27}H_{20}FeN_4O$	68.66	4.26	11.86	68.70	4.21	11.85
9c	yellow powder	166-169	$C_{28}H_{22}FeN_4O$	69.15	4.56	11.52	68.09	4.55	11.56
10c	yellow powder	149-151	$C_{28}H_{20}FeN_4O$	69.43	4.16	11.56	69.50	4.14	11.61

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