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ON THE STEREOCHEMISTRY OF PYRAZOLINES: 1-ACETYL-3,5-DISUBSTITUTED PYRAZOLINES-2

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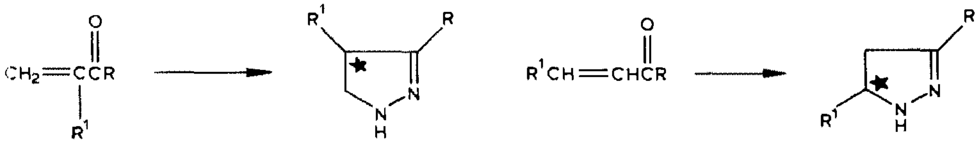
Summary

The geometries of the molecules of the isomeric *N*-acetyl derivatives of 3-ferrocenyl-5-*p*-bromophenyl- and 3-*p*-bromophenyl-5-ferrocenylpyrazolines-2 with a chiral centre in position 5 of pyrazoline have been determined by an X-ray study.

The reaction of α,β-unsaturated ketones with hydrazines gives rise to the formation of pyrazolines-2. The stereochemical result of the generally accepted reaction scheme [1] may, in principle, vary depending on the number and position of substituents in the prochiral ketone molecule.

Thus, $CH_2{=}CHCOR$ vinylketones in the reaction with hydrazines form 3-substituted pyrazolines-2 with the molecular symmetry group C_s, if R is considered a point ligand and the pyrazoline ring planar. The absence of the σ_h symmetry plane in isomeric 5-substituted pyrazoline-2, as well as the possibility of tautomeric transformations of pyrazolines depending on the solvent and the nature of a substituent in the ring, makes the pyrazoline molecule chiral.

The introduction of the second substituent in position 2 or 3 of the unsaturated ketone gives rise to enantiomeric 3,4- or, respectively, 3,5-disubstituted pyrazolines-2 with the chiral centre in position 4 or 5.



(1) (2)

The third substituent in position 2 of the unsaturated ketone leads to 1,2-asymmetric induction relative to position 4 and 5 of the pyrazoline formed, i.e. to the diastereomeric transition state and the formation of diastereomers of 3,4,5-trisub-

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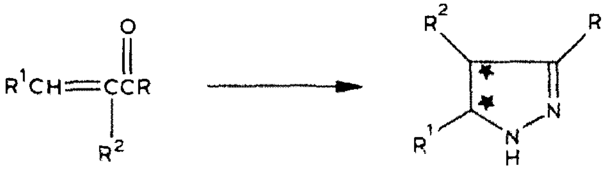
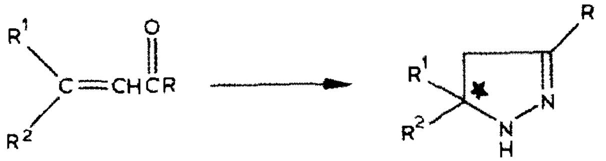
stituted pyrazolines-2:



(3)

1,3,3-Trisubstituted α,β-unsaturated ketones form enantiomeric 3,5,5-trisubstituted pyrazolines-2:



(4)

Here the transition state as well as that in cases **1** and **2** is enantiomeric with a chiral centre in position 5 of pyrazoline.

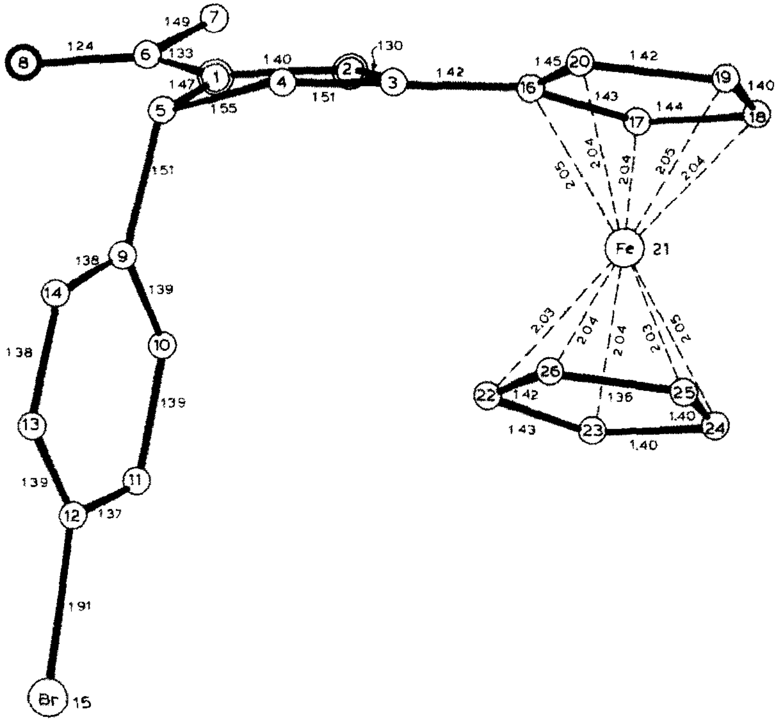


Fig. 1. Molecular geometry of I.

Finally, the formation of diastereomeric pyrazolines is also characteristic of 1,2,3,3-tetrasubstituted α,β-unsaturated ketones.

It should be noted that the configuration of the initial α,β-unsaturated ketone and subsequent acylation at the nitrogen atom in position 1 do not affect the stereochemical result of the reaction of pyrazoline formation. With any chiral elements present in the initial α,β-unsaturated ketones the stereochemistry of pyrazoline formation becomes much more complicated, as we have noted recently for unsaturated ketones with planar chirality [2].

All the pyrazolines of the metallocene series were obtained by us from 1,3-disubstituted α,β-unsaturated ketones, i.e. according to **2**. To establish unequivocally the structures of 3,5-disubstituted pyrazolines-2 with a ferrocenyl substituent, we performed an X-ray diffraction study of the *N*-acetyl derivatives of isomeric 3-ferrocenyl-5-*p*-bromophenyl- and 3-*p*-bromophenyl-5-ferrocenylpyrazolines-2 (I and II, respectively). The molecular geometries with bond lengths are shown in Figs. 1 and 2 (standard deviations in bond lengths are 0.01 Å); the bond angles are given in Tables 1 and 2.

An X-ray experiment was carried out with a four-circle automatic Syntex P2 diffractometer (λMo, graphite monochromator) at room temperature.

The crystals of I are triclinic, a 10.342(5), b 10.604(5), c 10.637(6) Å, α 65.04(4), β 63.20(4), γ 75.68(4)°, V 941.7(8) Å^3, $M = 293.95$, d_{calc} 1.60 g · cm^{-3}, $Z = 2$, space group $P\bar{1}$.

The crystals of II are monoclinic, a 17.042 (12), b 8.304(6), c 13.108(6) Å, β 93.01(5)°, V 1852(3) Å^3, $M = 451.17$, d_{calc} 1.62 g · cm^{-3}, $Z = 4$, space group $P2_1/n$.

The intensities of 2965 (I) and 3495 (II) reflections with $I \geqslant 2\sigma$ were measured by a $\theta/2\theta$ scan in the $2 \leqslant 2\theta \leqslant 56$° range, absorption being neglected. The structures of

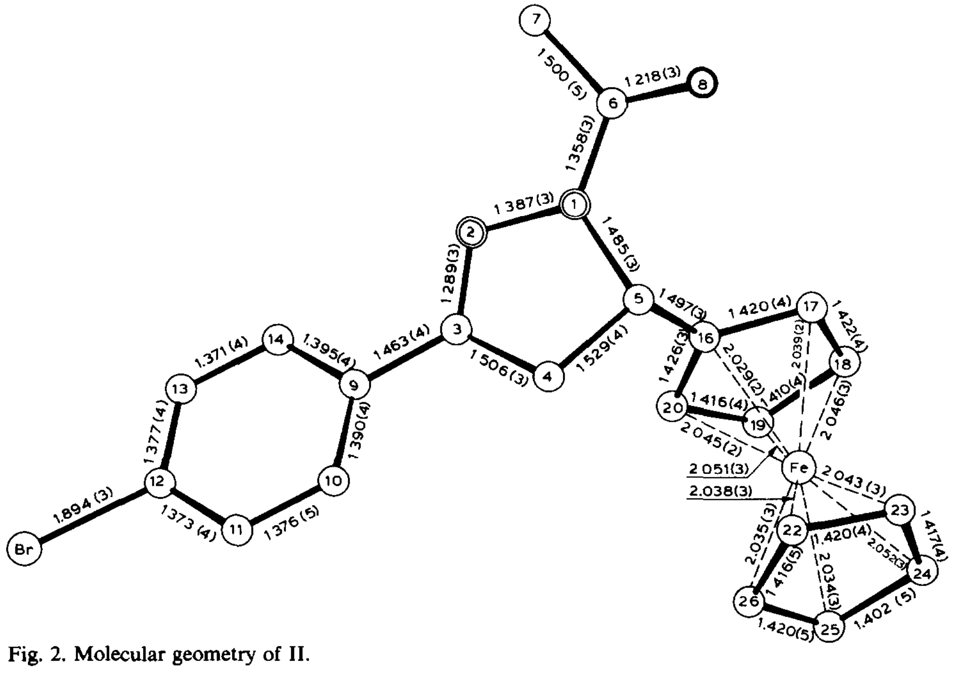


Fig. 2. Molecular geometry of II.

TABLE 1
BOND ANGLES (°) FOR STRUCTURE I

Angle	ω	Angle	ω	Angle	ω
N(2)N(1)C(5)	112.0(6)	N(1)C(6)O(8)	118.8(8)	C(3)C(16)C(17)	128.5(7)
N(2)N(1)C(6)	122.9(6)	C(7)C(6)O(8)	122.4(8)	C(3)C(16)C(20)	124.6(7)
C(5)N(1)C(6)	125.1(7)	C(5)C(9)C(10)	122.6(7)	C(17)C(16)C(20)	106.8(7)
N(1)N(2)C(3)	108.1(6)	C(5)C(9)C(14)	118.7(7)	C(16)C(17)C(18)	107.6(8)
N(2)C(3)C(4)	113.1(7)	C(10)C(9)C(14)	118.6(7)	C(17)C(18)C(19)	108.9(9)
N(2)C(3)C(16)	121.9(7)	C(9)C(10)C(11)	121.8(8)	C(18)C(19)C(20)	108.3(9)
C(4)C(3)C(16)	125.0(7)	C(10)C(11)C(12)	118.0(8)	C(16)C(20)C(19)	108.4(7)
C(3)C(4)C(5)	101.6(6)	C(11)C(12)C(13)	121.7(8)	C(23)C(22)C(26)	106.0(9)
N(1)C(5)C(4)	100.6(6)	C(11)C(12)Br(15)	119.0(7)	C(22)C(23)C(24)	108.0(9)
N(1)C(5)C(9)	112.5(6)	C(13)C(12)Br(15)	119.3(7)	C(23)C(24)C(25)	107.5(9)
C(4)C(5)C(9)	110.8(6)	C(12)C(13)C(14)	119.1(8)	C(24)C(25)C(26)	109.8(9)
N(1)C(6)C(7)	118.8(7)	C(9)C(14)C(13)	120.9(8)	C(22)C(26)C(25)	108.7(9)

I and II were solved by the standard heavy atom method and refined by the full-matrix anisotropic (isotropic for H atoms found in difference syntheses) least squares procedure. The final discrepancy factors were $R = 0.052$, $R_W = 0.056$ (I) and $R = 0.040$, $R_W = 0.046$ (II). The atomic coordinates and temperature factors of the non-hydrogen atoms are given in Tables 3 and 4; the parameters of some of the planar fragments of molecules I and II are presented in Tables 5 and 6.

The pyrazoline cycle in both isomers I and II is non-planar with an envelope conformation; folding along the N(1)–C(4) line is 20.4 and 21.9°, respectively. The orientation of the ferrocenyl substituent is pseudo-axial. The almost ideal co-planarity of the cyclopentadienyl ferrocene ring in I (respectively the phenyl ring in II) and of the acetyl substituent with the planar four-atom fragment of the heterocycle should be noted. The corresponding bond length distribution (Figs. 1 and 2) indicates conjugation between these fragments of the molecules.

The C–Br bond length is somewhat longer than the standard value [3] which is in agreement with a considerable deviation of the Br atom from the benzene ring plane.

It should be noted that both the ferrocenyl and *p*-bromophenyl substituents in I

(Continued on p. 87)

TABLE 2
BOND ANGLES (°) FOR STRUCTURE II

Angle	ω	Angle	ω	Angle	ω
N(2)N(1)C(5)	112.1(2)	N(1)C(6)O(8)	120.5(2)	C(5)C(16)C(17)	126.7(2)
N(2)N(1)C(6)	122.8(2)	C(7)C(6)O(8)	123.1(3)	C(5)C(16)C(20)	125.9(2)
C(5)N(1)C(6)	125.0(2)	C(3)C(9)C(10)	120.2(2)	C(17)C(16)C(20)	107.4(2)
N(1)N(2)C(3)	107.2(2)	C(3)C(9)C(14)	121.2(2)	C(16)C(17)C(18)	108.3(2)
N(2)C(3)C(4)	113.8(2)	C(10)C(9)C(14)	118.7(2)	C(17)C(18)C(19)	107.9(2)
N(2)C(3)C(9)	121.2(2)	C(9)C(10)C(11)	120.6(3)	C(18)C(19)C(20)	108.3(2)
C(4)C(3)C(9)	124.9(2)	C(10)C(11)C(12)	119.4(3)	C(16)C(20)C(19)	108.1(2)
C(3)C(4)C(5)	101.5(2)	C(11)C(12)C(13)	121.2(3)	C(23)C(22)C(26)	107.0(3)
N(1)C(5)C(4)	100.0(2)	C(11)C(12)Br(15)	119.5(2)	C(22)C(23)C(24)	108 9(3)
N(1)C(5)C(16)	109.8(2)	C(13)C(12)Br(15)	119.3(2)	C(23)C(24)C(25)	107.4(3)
C(4)C(5)C(16)	113.2(2)	C(12)C(13)C(14)	119.3(3)	C(24)C(25)C(26)	108.6(3)
N(1)C(6)C(7)	116.5(3)	C(9)C(14)C(13)	120.7(3)	C(22)C(26)C(25)	108.1(3)

TABLE 3
ATOMIC COORDINATES ($\times 10^4$) AND PARAMETERS OF THE ANISOTROPIC TEMPERATURE FACTORS $T = \exp[-0.25(B_{11}h^2a^{*2} + \ldots + 2B_{23}klb^*c^*)]$ FOR STRUCTURE I

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	5747(6)	3592(6)	3070(6)	2.4(3)	4.2(3)	3.1(3)	−0.7(2)	−0.8(2)	−1.4(2)
N(2)	5815(6)	2494(6)	2633(6)	3.2(3)	3.6(3)	3.0(3)	0.0(2)	−1.7(2)	−1.0(2)
C(3)	4647(7)	1830(7)	3547(8)	3.0(3)	3.2(3)	3.0(3)	−0.2(3)	−1.6(3)	−0.7(3)
C(4)	3672(8)	2394(7)	4790(8)	3.0(3)	3.5(3)	2.5(3)	0.1(3)	−0.9(3)	−0.6(3)
C(5)	4294(7)	3823(7)	4175(8)	2.9(3)	3.8(3)	2.8(3)	−0.4(3)	−1.2(3)	−1.1(3)
C(6)	6872(8)	4332(8)	2520(8)	3.4(4)	4.7(4)	2.9(4)	−0.6(3)	−1.8(3)	−1.2(3)
C(7)	8293(8)	3939(8)	1450(9)	2.9(3)	5.4(5)	4.4(4)	−1.1(3)	−1.0(3)	−1.0(4)
O(8)	6707(6)	5316(6)	2933(6)	5.3(3)	6.9(3)	3.5(3)	−2.5(3)	−1.1(2)	−1.6(3)
C(9)	3382(7)	4988(7)	3446(8)	3.0(3)	2.8(3)	2.5(3)	−0.6(3)	−0.9(3)	−1.2(3)
C(10)	3765(8)	5551(7)	1898(8)	3.0(4)	4.1(4)	3.1(4)	−0.2(3)	−0.9(3)	−1.3(3)
C(11)	2857(9)	6339(8)	1257(9)	4.4(4)	3.9(4)	3.6(4)	−0.4(3)	−1.8(4)	−0.8(3)
C(12)	1536(9)	6922(7)	2207(10)	4.9(5)	2.9(3)	5.2(5)	−0.5(3)	−3.1(4)	−0.9(3)
C(13)	1127(8)	6393(8)	3759(9)	3.4(4)	4.0(4)	4.0(4)	0.0(3)	−1.3(3)	−1.5(5)
C(14)	2066(7)	5435(7)	4362(8)	4.0(3)	3.5(3)	3.3(4)	−0.2(3)	−1.5(3)	−1.5(3)
Br(15)	201(1)	8163(1)	1375(1)	7.48(7)	5.66(6)	8.07(7)	1.79(5)	−5.36(6)	−2.06(5)
C(16)	4364(7)	684(7)	3370(8)	2.6(3)	3.2(3)	3.5(4)	−0.2(3)	−1.4(3)	−0.6(3)
C(17)	5021(8)	284(8)	2073(9)	3.5(4)	4.9(4)	4.4(4)	0.8(3)	−1.4(3)	−2.1(4)
C(18)	4334(10)	−917(8)	2432(11)	5.6(5)	4.1(4)	7.6(6)	0.3(3)	−3.6(5)	−3.0(4)
C(19)	3276(9)	−1258(8)	3908(11)	4.8(5)	3.1(4)	6.8(6)	−0.6(3)	−3.2(4)	−0.7(4)
C(20)	3266(8)	−284(7)	4506(9)	3.8(4)	2.8(3)	4.3(4)	0.1(3)	−2.3(3)	0.1(3)
Fe(21)	2840(1)	735(1)	2612(1)	3.80(6)	3.41(5)	4.12(6)	−0.10(4)	−2.20(5)	−0.82(5)
C(22)	1848(11)	2689(8)	2194(12)	7.0(5)	3.5(4)	8.2(6)	1.1(4)	−5.6(5)	−1.0(4)
C(23)	2540(10)	2379(10)	837(11)	5.2(5)	7.6(6)	4.2(5)	0.2(4)	−2.5(4)	0.7(5)
C(24)	1935(11)	1204(10)	1090(11)	6.5(6)	6.0(5)	6.1(6)	0.1(4)	−4.5(5)	−2.3(5)
C(25)	879(9)	801(9)	2567(10)	3.7(4)	5.8(5)	5.1(5)	−0.6(3)	−2.1(4)	−1.4(4)
C(26)	801(9)	1684(9)	3234(10)	4.8(5)	5.6(5)	5.1(5)	1.6(4)	−2.9(4)	−2.0(4)

TABLE 4

ATOMIC COORDINATES ($\times 10^5$ for Br and Fe and $\times 10^4$ for the other atoms) AND PARAMETERS OF THE ANISOTROPIC TEMPERATURE FACTORS $T = \exp[-0.25(B_{11}h^2a^{*2} + \ldots + 2B_{23}klb^*c^*)$ FOR STRUCTURE II

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	8667(1)	5144(3)	3837(2)	3.25(9)	3.19(8)	3.15(8)	−0.23(7)	0.26(7)	0.61(7)
N(2)	7932(1)	5786(2)	3578(2)	3.39(9)	2.85(8)	3.27(8)	−0.02(7)	0.15(7)	0.50(6)
C(3)	7316(2)	5642(3)	4366(2)	3.7(1)	2.32(8)	2.70(8)	−0.3(8)	−0.06(8)	0.01(7)
C(4)	7959(2)	4943(3)	5286(2)	4.2(1)	2.88(9)	2.55(9)	0.46(9)	−0.03(8)	−0.24(8)
C(5)	8674(1)	4208(3)	4803(2)	2.81(9)	2.96(9)	2.63(8)	−0.20(7)	−0.30(7)	−0.05(7)
C(6)	9292(2)	5331(3)	3247(2)	3.6(1)	3.7(1)	3.02(9)	−1.13(9)	0.27(8)	−0.47(8)
C(7)	9151(2)	6281(5)	2281(3)	5.1(2)	5.4(2)	3.9(1)	−1.0(1)	0.9(1)	1.0(1)
O(8)	9926(1)	4747(3)	3506(1)	3.10(8)	6.7(1)	3.79(8)	−0.65(8)	−0.03(7)	−0.76(8)
C(9)	6698(2)	6188(3)	4345(2)	3.7(1)	2.48(8)	2.77(9)	0.12(8)	0.04(8)	−0.06(7)
C(10)	6300(2)	6253(4)	5242(2)	4.3(1)	4.4(1)	2.62(9)	1.1(1)	0.07(9)	−0.07(9)
C(11)	5545(2)	6845(4)	5238(2)	4.6(1)	5.8(2)	3.1(1)	1.4(1)	0.64(9)	−0.3(1)
C(12)	5179(2)	7335(4)	4333(2)	3.5(1)	3.8(1)	4.0(1)	0.45(9)	0.03(9)	−0.30(9)
C(13)	5549(2)	7224(4)	3426(2)	3.9(1)	4.0(1)	3.11(9)	−0.07(9)	−0.37(9)	0.57(9)
C(14)	6304(2)	6652(3)	3432(2)	3.9(1)	4.0(1)	2.69(9)	−0.08(9)	0.26(8)	0.33(8)
Br(15)	41539(2)	82155(5)	43313(3)	4.03(2)	7.49(2)	5.60(2)	1.76(1)	0.03(1)	−0.45(1)
C(16)	8578(1)	2453(3)	4567(2)	2.61(9)	2.83(9)	0.30(7)	0.07(7)	0.05(6)	0.20(7)
C(17)	9189(2)	1307(3)	4476(2)	3.2(1)	2.54(9)	0.63(9)	0.63(9)	0.63(8)	0.16(8)
C(18)	8840(2)	−217(3)	4253(2)	5.0(1)	3.3(1)	2.88(9)	0.78(9)	0.46(9)	−0.50(8)
C(19)	8017(2)	−10(3)	4190(2)	4.9(1)	3.1(1)	3.15(9)	−0.46(9)	−0.58(9)	−0.39(8)
C(20)	7851(2)	1630(3)	4377(2)	3.0(1)	3.26(9)	2.62(9)	−0.16(8)	−0.45(7)	0.17(7)
Fe(21)	84730(2)	6630(4)	56053(2)	2.92(2)	2.71(1)	2.34(1)	0.22(1)	0.198(9)	0.170(9)
C(22)	8617(2)	1704(4)	7011(2)	4.9(1)	4.4(1)	2.11(9)	0.5(1)	0.19(8)	−0.04(8)
C(23)	9155(2)	413(4)	6925(2)	3.8(1)	4.6(1)	2.68(9)	0.5(1)	−0.20(8)	0.55(9)
C(24)	8729(2)	−1024(4)	6717(2)	5.3(1)	3.8(1)	3.6(1)	0.6(1)	0.2(1)	1.19(9)
C(25)	7928(2)	−631(4)	6680(2)	4.6(1)	5.5(2)	3.9(1)	−1.4(1)	0.5(1)	1.4(1)
C(26)	7852(2)	1045(4)	6867(2)	4.1(1)	6.3(2)	2.70(9)	1.2(1)	0.83(9)	0.5(1)

TABLE 5
PLANAR FRAGMENTS OF MOLECULE I

(a) Deviations Δ (Å) of atoms from the mean planes

Plane 1	Δ	Δ/σ	Plane 4	Δ	Δ/σ
N(1)	0.007	1.1	C(9)	−0.008	1.1
N(2)	−0.012	1.9	C(10)	−0.002	0.2
C(3)	0.018	2.3	C(11)	0.014	1.6
C(4)	−0.010	1.3	C(12)	−0.014	1.4
C(5)[a]	0.336	43.3	C(13)	−0.002	0.2
C(6)[a]	−0.229	26.8	C(14)	0.012	1.4
C(16)[a]	0.056	7.1	Br(15)[a]	−0.136	110.8
			C(5)[a]	−0.147	18.3
Plane 2			**Plane 5**		
N(1)	0	0	C(16)	−0.003	0.3
C(4)	0	0	C(17)	0.002	0.2
C(5)	0	0	C(18)	0.001	0.1
			C(19)	−0.004	0.3
			C(20)	0.004	0.4
			C(3)[a]	0.036	4.4
Plane 3			**Plane 6**		
N(1)	−0.001	0.2	C(22)	−0.009	0.7
C(6)	0.006	0.7	C(23)	0.005	0.4
C(7)	−0.002	0.2	C(24)	0	0
O(8)	−0.001	0.2	C(25)	−0.004	0.4
C(5)[a]	0.043	5.8	C(26)	−0.007	0.7
N(2)[a]	0.051	8.4			

(b) Coefficients of planes equations $AX + BY + CZ - D = 0$ in the orthogonal coordinate system

Plane	A	B	C	D
1	−0.6961	0.4241	−0.5792	−5.3932
2	−0.6982	0.0940	−0.7097	−7.3214
3	−0.5279	0.3681	−0.7654	−4.7505
4	0.6402	0.7652	−0.0681	8.7549
5	−0.7881	0.5073	−0.3486	−5.0716
6	−0.7915	0.5121	−0.3337	−1.7414

(c) Some dihedral angles (°)

Planes	τ	Planes	τ
1–2	20.4	1–4	97.4
1–3	14.8	1–5	15.0
		5–6	0.9

[a] Atoms not included in the mean squares plane equations.

are situated on one side of the pyrazoline cycle. The cisoid conformation found is quite natural since it corresponds to the most compact form of molecule I in the absence of steric hindrance.

The H atoms in position 4 of pyrazolines I and II are diastereotopic; however, the diastereotopic effect manifests itself differently in the ^{1}H NMR spectra of the

TABLE 6

PLANAR FRAGMENTS OF MOLECULE II

(a) Deviations Δ (Å) of atoms from the mean planes

Plane 1	Δ	Δ/σ	Plane 4	Δ	Δ/σ
N(1)	0.008	3.68	C(9)	−0.016	6.33
N(2)	−0.014	6.75	C(10)	0.018	5.64
C(3)	0.017	7.67	C(11)	0.001	0.27
C(4)	−0.012	4.47	C(12)	−0.013	4.48
C(5)[a]	0.360	152.57	C(13)	0.008	2.81
C(6)[a]	−0.233	85.79	C(14)	0.008	2.98
C(9)[a]	0.024	9.80	Br(15)[a]	−0.095	224.70
C(16)[a]	0	0	C(3)[a]	−0.074	32.61
Plane 2			Plane 5		
N(1)	0	0	C(16)	−0.005	2.57
C(4)	0	0	C(17)	0.007	2.99
C(5)	0	0	C(18)	−0.004	1.74
			C(19)	−0.001	0.41
			C(20)	0.005	1.98
			C(5)[a]	−0.007	2.89
Plane 3			Plane 6		
N(1)	−0.000	0.00	C(22)	0.004	1.85
C(6)	0.000	0.02	C(23)	−0.003	1.22
C(7)	−0.000	0.01	C(24)	0.001	0.23
O(8)	−0.000	0.01	C(25)	0.003	0.98
C(5)[a]	0.042	17.81	C(26)	−0.005	1.84
N(2)[a]	−0.001	0.68			

(b) Coefficients of planes equations $AX + BY + CZ - D = 0$ in the orthogonal coordinate system

Plane	*A*	*B*	*C*	*D*
1	−0.2949	−0.9095	−0.2931	−9.6426
2	−0.5650	−0.6918	−0.4496	−13.4092
3	−0.2264	−0.8400	−0.4931	−9.3492
4	−0.3417	−0.9285	−0.1451	−9.3795
5	0.0797	0.1978	−0.9770	−4.2929
6	0.0755	0.1750	−0.9817	−7.6928

(c) Some dihedral angles (°)

Planes	τ	Planes	τ
1–2	21.9	1–4	9.0
1–3	12.8	1–5	85.2
		5–6	1.4

[a] Atoms not included in the mean squares plane equations.

three-spin system of the pyrazoline ring (in *N*-acetyl- or *N*-phenyl derivatives) depending on the isomeric position of the ferrocenyl group [4].

The proximity of the carbonyl oxygen to the iron atom in *N*-acetylpyrazolines accounts for their specific fragmentation when the ferrocenyl substituent is in position 5 of pyrazoline [5].

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