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Polycyclic ferrocenyl-4,5-dihydropyrazoles in nucleophilic reactions with β-dicarbonyl compounds

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Abstract

Polycyclic ferrocenyldihydropyrazoles with a free –NH group react with ethyl acetoacetate and acetylacetone to give the corresponding enamino carbonyl compounds isolated as *E*-isomers. The spatial structure of (*E*)-4-[1-(ethoxycarbonyl)prop-2-en-2-yl]-3-ferrocenyl-1,4,5-triazatricyclo[5.2.2.0^{2,6}]undec-5-ene was determined using X-ray diffraction analysis. Spontaneous isomerization of (*E*)-(4-oxopent-2-en-2-yl)(ferrocenyl)dihydropyrazoles into the respective *Z*-isomers was observed.

Keywords: Ferrocenyldihydropyrazole; Ethyl acetoacetate; Acetylacetone; Enamino carbonyl compounds; *E*-/*Z*-isomerization; X-ray diffraction analysis

1. Introduction

Considerable interest in ferrocenyl-substituted heterocyclic compounds is known to be associated with both the uniqueness of the chemical behavior of the ferrocene system and unusual properties of the heterocyclic moiety due to the presence of the ferrocene substituent. This type of compounds are characterized by diverse biological activities together with other valuable properties. It is noteworthy that the ferrocenyl-containing heterocyclic compounds have acquired wide practical applications as medical products, components of silver-free light-sensitive compositions, dyestuffs, and additives enhancing principal characteristics of the rocket propellants and explosives [1].

4,5-Dihydropyrazoles with ferrocenyl substituents are studied in sufficient details [1–9]. They are prepared by the addition of hydrazines to α,β-unsaturated compounds. Ferrocenyl-substituted dihydropyrazoles with a substituent at position 1 of the heterocycle, unlike analogous dihydropyrazoles with a hydrogen atom at N(1), represent stable compounds, some of them manifest biological activities. In particular, 4-acetyl-3-ferrocenyl-1,4,5-triazatricyclo[5.2.2.0^{2,6}]undec-5-ene manifests high antiviral activity [9]. One may expect that the introduction of additional carbo- and heterocyclic fragments and various N(1)-substituents into ferrocenyldihydropyrazoles will broaden the spectrum of valuable characteristics of these products.

In the present work, we studied the reactions of polycyclic ferrocenyl-4,5-dihydropyrazoles with β-dicarbonyl compounds. The starting dihydropyrazoles **1**–**6** comprise cyclohexane, quinuclidine, and tetraline fragments (Scheme 1) and can be regarded as valuable key precursors for the construction of pharmacologically active molecules.

Compounds **1**–**6** were prepared by a standard procedure from the corresponding chalcones **7**–**12** and

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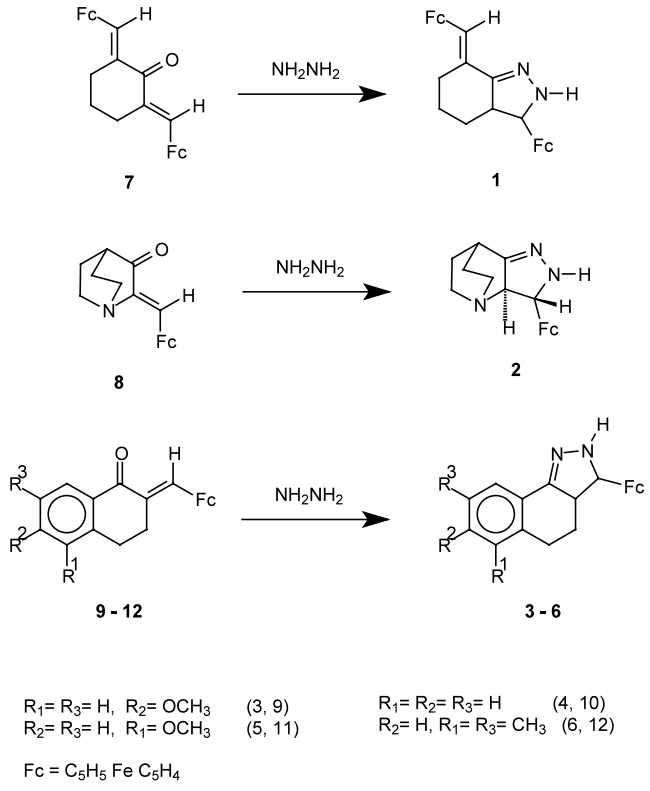


Scheme 1.

hydrazine hydrate [4,6,9]. The stereochemical outcome of these reactions is of theoretical interest.

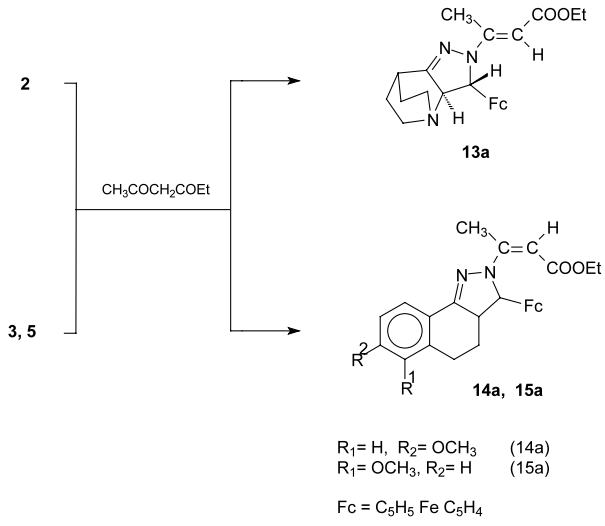
2. Results and discussion

Our investigations into the reactivity of ferrocenyl-4,5-dihydropyrazoles **2**, **3**, and **5** indicate that their reactions with β-dicarbonyl compounds, in particular, with ethyl acetoacetate, result in the corresponding enamino carbonyl compounds [10] **13a**–**15a**. Thus 3-ferrocenyl-1,4,5-triazatricyclo[5.2.2.0^{2,6}]undec-5-ene (**2**) gives one configurational istereomer of 4-[(1-ethoxycarbonyl)prop-2-en-2-yl]-3-ferrocenyl-1,4,5-triazatricyclo-[5.2.2.0^{2,6}]undec-5-ene (**13a**) (Scheme 2).

The dihydropyrazoles **3** and **5** react analogously (Scheme 2). The reaction products **13a**–**15a** represent yellow crystalline compounds stable in both solid state and solutions.

The structures of compounds **13a**–**15a** was established based on the ^{1}H- and ^{13}C-NMR spectroscopic data (Tables 1 and 2), retention of the AX-system of protons of the dihydropyrazole rings being a remarkable feature of the ^{1}H-NMR spectra. ^{1}H-NMR spectroscopic data reject also alternative structures of acetoacetic acid pyrazolides for the reaction products.

Ferrocenylmethylidene-substituted dihydropyrazoles have been identified earlier by ^{1}H-NMR and X-ray diffraction methods [11,12]. It was shown that the



Scheme 2.

chemical shift values and spin–spin coupling constants for the protons at the carbon atom bearing the ferrocenyl substituent (in our cases, H(3) for compound **13a** and H(5) for compounds **14a**, **15a**) allows one to ascribe *cis*- or *trans*-orientation of the ferrocenyl substituent relative to the bridgehead proton (here, H(2) or H(6), respectively). A comparison of the ^{1}H-NMR spectra of compounds **13a**–**15a** with those of the known compounds identified earlier [11,12] made it possible to state that the compounds under study posses the *trans*-structures. Atoms H(2) and H(3), (H(5) and H(6)), respectively, occupy pseudoaxial positions, and the ferrocenyl substituent is pseudoequatorial. However, we could not establish unambiguously the stereochemistry of the double bond of the substituent at the N(4) atom from the ^{1}H-NMR spectra.

This problem could objectively be solved by performing X-ray diffraction analysis of a single crystal of compound **13a** grown from chloroform (Fig. 1, Table 3).

The key element in the structure **13a** is the tricyclic framework. The bicyclic system of quinuclidine is fused to the five-membered ring of dihydropyrazole, which adopts a flattened envelope conformation. The ferrocenyl substituent occupies pseudoequatorial position and atoms H(2) and H(3) are *trans* arranged. The double bond in the substituent at the N(4) atom has *E*-configuration. Presumably, the same structures may be ascribed to compounds **14a** and **15a**.

The reactions of acetylacetone with ferrocenyl-4,5-dihydropyrazoles occur in the analogous manner to yield *N*-(4-oxopent-2-en-2-yl) derivatives **16a**–**21a** (Scheme 3).

The enamines obtained represent yellow crystals stable in the solid state. Their structures are established based on the data from ^{1}H- and ^{13}C-NMR spectroscopy. The ^{1}H-NMR spectra also retain the AX-system of protons of the five-membered rings and contain

Table 1
^{1}H-NMR spectral data of compounds **1**–**9** (300 MHz, $CDCl_3$,TMS); δ (ppm), J (Hz)

Compound	C_5H_5, s	C_5H_4, m	CH_3	CH	CH=	CH_2	Ar
13a	4.26	4.13 (1H), 4.19 (2H), 4.29 (1H)	1.23 t (3H), $J = 7.0$; 2.55 s (3H)	3.29 m (1H), 4.52 d (1H), $J = 8.7$; 4.60 d (1H), $J = 8.7$	4.90 s (1H)	1.94 m (4H), 2.83 m (2H), 3.07 m (2H), 4.06 q (2H), $J = 7.0$	
14a	4.16	4.20 (2H), 4.23 (2H)	1.22 t (3H), $J = 7.2$; 2.63 s (3H), 3.84 s (3H)	3.92 m (1H), 4.70 d (1H), $J = 7.3$	4.86 s (1H)	2.03 m (1H), 2.42 m (1H), 3.01 m (1H), 3.16 m (1H), 4.07 q (2H), $J = 7.2$	6.73 s (1H), 6.83 d (1H), $J = 8.5$; 7.82 d (1H), $J = 8.5$
15a	4.19	4.24 (2H), 4.45 (2H)	1.22 t (3H), $J = 6.6$; 2.64 s (3H), 3.87 s (3H)	3.65 m (1H), 4.52 d (1H), $J = 6.2$	4.90 s (1H)	1.95 m (1H), 2.48 m (1H), 2.84 m (1H), 3.13 m (1H), 4.06 q (2H), $J = 6.6$	6.86 d (1H), $J = 7.5$; 7.20 t (1H), $J = 7.5$; 7.50 d (1H), $J = 7.5$
16a	4.16, 4.17	4.14 (2H), 4.21 (2H), 4.30 (1H), 4.33 (1H), 4.41 (1H), 4.43 (1H)	2.03 s (3H), 2.69 s (3H)	3.68 m (1H), 4.45 d (1H), $J = 6.3$	5.25 s (1H), 6.86 s (1H)	1.75 m (2H), 2.31 m (3H), 3.04 m (1H)	
17a	4.28	4.08 (1H), 4.22 (2H), 4.30 (1H)	2.0 s (3H), 2.55 s (3H)	3.30 m (1H), 4.59 d (1H), 4.64 d (1H), $J = 8.4$	5.30 s (1H)	1.96 m (4H), 2.82 m (2H), 3.06 m (2H)	
17b	4.19, 4	4.17 (1H), 4.21 (1H), 4.26 (2H)	2.0 s (3H), 2.05 s (3H)	3.14 m (1H), 4.57 d (1H), 4.66 d (1H), $J = 4.8$	5.51 s (1H)	1.77–1.89 m (4H), 2.89 m (2H), 3.04 m (2H)	
18a	4.16	4.22 (4H)	2.01 s (3H), 2.69 s (3H), 3.84 s (3H)	3.98 m (1H), 4.49 d (1H), $J = 7.2$	5.28 s (1H)	2.15 m (1H), 2.48 m (1H), 3.02 m (1H), 3.17 m (1H)	6.74 d (1H), $J = 2.4$; 6.84 dd (1H), $J = 2.4$, 8.5; 7.85 d (1H), $J = 8.5$
18b	4.18	4.17 (1H), 4.19 (1H), 4.23 (2H)	2.07 s (3H), 2.23 s (3H), 3.80 s (3H)	3.94 m (1H), 4.44 d (1H), $J = 6.9$	5.51 s (1H)	2.17 m (1H), 2.49 m (1H), 2.84 m (1H), 3.20 m (1H)	6.66 d (1H), $J = 2.4$; 6.79 dd (1H), $J = 2.4$, 8.7; 7.98 d (1H), $J = 8.7$
19a	4.17	4.19 (1H), 4.23 (3H)	2.03 s (3H), 2.67 s (3H)	3.99 m (1H), 4.53 d (1H), $J = 6.9$	5.31 s (1H)	2.08 m (1H), 2.48 m (1H), 3.07 m (1H), 3.19 m (1H)	7.29 m (3H), 7.90 d (1H), $J = 6.9$
19b	4.12	4.08 (1H), 4.35 (2H), 4.61 (1H)	2.05 s (3H), 2.97 s (3H)	3.65 m (1H), 4.88 d (1H), $J = 7.8$	5.50 s (1H)	2.14 m (1H), 2.36 m (1H), 2.70 m (1H), 3.06 m (1H)	7.33 m (1H), 7.48 m (1H), 8.12 m (2H)
20a	4.15	4.12 (1H), 4.22 (2H), 4.24 (1H)	2.02 s (3H), 2.66 s (3H), 3.87 s (3H)	3.95 m (1H), 4.53 d (1H), $J = 6.3$	5.33 s (1H)	1.98 m (1H), 2.48 m (1H), 2.80 m (1H), 3.17 m (1H)	6.87 d (1H), $J = 7.8$; 7.26 t (1H), $J = 7.8$; 7.52 d (1H), $J = 7.8$
20b	4.19	4.29 (1H), 4.33 (1H), 4.45 (2H)	2.04 s (3H), 2.24 s (3H), 3.82 s (3H)	3.78 m (1H), 4.60 d (1H), $J = 7.3$	5.50 s (1H)	1.70 m (1H), 2.49 m (1H), 2.87 m (1H), 3.16 m (1H)	6.80 d (1H), $J = 7.5$; 7.19 t (1H), $J = 7.5$; 7.53 d (1H), $J = 7.5$
21a	4.16	4.12 (1H), 4.19 (1H), 4.22 (2H)	2.03 s (3H), 2.27 s (3H), 2.35 s (3H), 2.67 s (3H)	3.91 m (1H), 4.54 d (1H), $J = 6.2$	5.32 s (1H)	2.20 m (1H), 2.52 m (1H), 2.87 m (1H), 2.98 m (1H)	7.06 s (1H), 7.59 s (1H)
21b	4.21	4.28 (1H), 4.32 (1H), 4.44 (2H)	2.04 s (3H), 2.27 s (3H), 2.32 s (3H), 2.68 s (3H)	3.85 m (1H), 4.70 d (1H), $J = 7.5$	5.40 s (1H)	1.98 m (1H), 2.18 m (1H), 2.50 m (1H), 3.01 m (1H)	6.95 s (1H), 7.63 s (1H)

Table 2
^{13}C-NMR spectroscopy data for compounds **13a**, **14a**, **16a**, **17a**,**b**–**21a**,**b** (75 MHz, $CDCl_3$, TMS); δ (ppm)

Compound	C_5H_5	C_5H_4	C_{ipso}Fc	CH_2, CH_3	C	CH=	CH	C=O	C=N	Ar
13a	68.6	67.3, 68.3, 70.0, 80.3	89.4	14.6, 16.9, 22.8, 28.1, 35.1, 43.3, 48.4	158.1	88.7	58.7, 61.0, 66.8	168.7	164.2	
14a	68.4	68.5, 68.8, 69.3, 69.5	93.8	14.1, 30.1, 31.6, 36.2, 55.4	141.3, 146.8, 160.6, 161.8	113.1	50.2, 61.4	199.2	167.2	127.2, 129.9, 130.2
16a	68.6, 69.2	67.2, 67.5, 68.1, 68.2, 69.2, 69.4, 69.5, 70.5	80.5, 90.5	16.8, 24.8, 29.1, 31.4, 32.0	126.7, 157.0	97.6, 126.2	58.3, 63.4	195.6	158.3	
17a	68.6	67.1, 68.7, 70.2, 80.2	89.13	217.1, 22.6, 28.2, 35.3, 43.3	157.0	97.8	48.2, 61.0, 66.2	195.8	165.7	
17b	68.4	67.4, 67.9, 68.1, 74.8	86.8	17.2, 22.8, 24.8, 27.4, 31.8, 42.8	157.1	100.0	48.9, 63.9, 66.0	191.2	167.0	
18a	68.5	66.8, 67.2, 69.0, 69.2	90.5	24.7, 26.6, 29.6, 29.7, 55.3	140.2, 140.3, 154.2, 156.6	113.3	57.0, 63.3	191.1	160.9	125.6, 126.4, 126.5
18b	68.3	67.2, 67.4, 67.8, 68.0	97.5	24.7, 26.5, 29.5, 29.7, 55.1	136.4, 136.5, 155.7, 156.6	113.1	57.1, 65.3	195.3	160.2	120.6, 121.3, 122.0
19a	69.5	68.3, 70.7	79.1	26.9, 28.5, 31.1, 36.0	138.5, 143.0, 143.3	126.9	53.2, 63.6	191.1	186.9	127.9, 128.0, 132.8, 137.5
19b	69.3	68.6, 70.3, 70.9, 72.0	78.9	26.8, 28.5, 28.8, 35.8	133.4, 140.5, 145.0	126.7	54.0, 66.5	191.2	188.3	127.7, 131.1, 132.7, 137.3
20a	68.5	66.8, 67.3, 67.9, 69.1	90.3	23.4, 24.8, 26.1, 29.1, 55.4	127.2, 128.9, 154.5, 156.5	110.8	56.3, 63.5	191.1	157.1	116.8, 127.3, 127.35
20b	68.3	67.2, 67.7, 68.1, 68.3	87.3	22.5, 24.8, 26.2, 29.2, 55.3	126.6,129.4, 155.0, 156.4	110.0	51.7, 65.9	196.0	156.9	116.1, 126.6, 126.7
21a	69.5	68.5, 70.8	86.1	20.9, 24.5, 24.8, 26.5, 27.8, 35.5	131.2, 131.6, 133.8, 136.6, 138.8	126.1	55.9, 63.7	191.1	164.8	135.3, 136.0
21b	69.3	68.2,70.1, 70.5, 71.7	83.8	20.9, 24.5, 25.2, 26.5, 28.8, 35.5	132.1, 131.6, 134.6, 135.8, 138.6	125.2	53.0, 65.1	187.5	164.6	134.7, 135.9

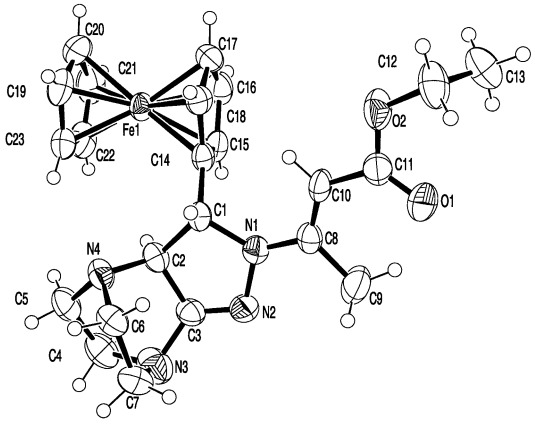


Fig. 1. Crystal structure of one of enantiomers of compound **13a**. Selected bond lengths (Å): C(3)–N(4) = 1.498(3); C(6)–N(5) = 1.267(3); C(12)–N(4) = 1.375(3); N(5)–N(4) = 1.409(3); C(12)–C(14) = 1.342(4); C(15)–C(14) = 1.444(3); C(15)–O(1) = 1.339(3); C(15)–O(2) = 1.206(3); C(3)–C(2) = 1.539(3); C(2)–C(6) = 1.492(4); C(2)–N(1) = 1.473(3). Selected bond angles (°): N(1)–C(2)–C(6) = 108.15(18); C(6)–C(2)–C(3) = 102.87(18); N(4)–C(3)–C(2) = 100.37(18); N(5)–C(6)–C(2) = 115.3(2); C(14)–C(12)–N(4) = 121.6(2); C(14)–C(12)–C(13) = 123.8(2); N(4)–C(12)–C(13) = 114.7(2); C(12)–C(14)–C(15) = 125.3(2); C(15)–C(14)–H(14) = 117.3; C(12)–C(14)–H(14) = 117.3; N(5)–N(4)–C(3) = 111.8(17); N(5)–N(4)–C(12) = 117.54(19); N(4)–N(5)–C(6) = 107.7(2).

additional singlets for the methyl groups. The reactions were also stereospecific as followed from the analysis of the ^{1}H- and ^{13}C-NMR spectra of freshly prepared solutions: the spectra demonstrated the presence of only one isomer, apparently, with the *trans*-arrangement of H(6) and H(7) (**16a**), H(2) and H(3) (**17a**), H(5) and H(6) (**18a**–**21a**) and *E*-configuration of the double bond in the substituent at the nitrogen atom of the dihydropyrazole ring.

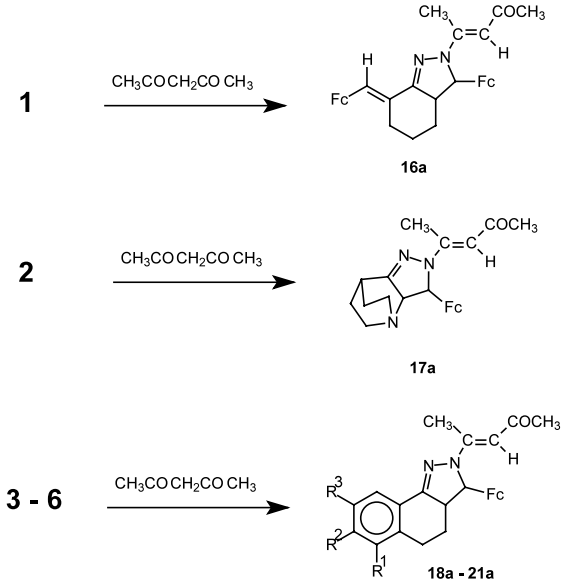
Unexpectedly, smooth isomerization of compounds **17a**–**21a** occurred at room temperature for their solutions in $CHCl_3$ and CH_2Cl_2. This followed from the observation of the ^{1}H-NMR spectra of compounds **16a**–**17a** in $CDCl_3$ at 20 °C. The spectra of compounds **17a**–**21a** isolated as single diastereomers manifested gradual appearance of a second set of signals for all the protons, which suggests their isomerization in solutions. The signal integral intensity ratios in the equilibrium mixtures were equal to ~1.3 (in favor of the starting **17a**) and ~1.5 (in favor of the starting **18a**–**21a**). No isomerization of compound **16a** occurred.

The equilibrium established seems to be dynamic in its character, and we failed to separate chromatographically the isomers **17a**–**21a** and **17b**–**21b**. The ^{1}H- and ^{13}C-NMR spectroscopic data for compounds **17b**–**21b** obtained for equilibrium mixtures are listed in Tables 2 and 3. According to the ^{1}H-NMR spectra of the isomers **17b**–**21b**, the spin–spin coupling constants $J_{H(2),H(3)}$ (**17b**), $J_{H(5),H(6)}$ (**18b**–**21b**) remain virtually unaltered, which suggests the retention of the polycyclic framework

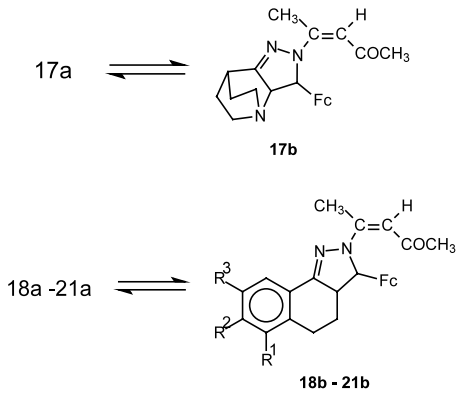
Table 3
Crystal data, data collection and refinement parameters for compound **13a**

Data	**13a**
Molecular formula	$C_{24}H_{29}FeN_3O_2$
Formula weight (g mol^{-1})	447.35
Temperature (K)	293(1)
Crystal system	Orthorhombic
Space group	$P2_1nb$
a (Å)	6.1789(12)
b (Å)	14.057(3)
c (Å)	24.324(4)
α (°)	90.0
β (°)	90.0
γ (°)	90.0
V (Å^3)	2112.7(7)
Z	4
D_{calc} (mg mm^{-3})	1.406
Absorption coefficient (mm^{-1})	0.740
$F(000)$	944
Radiation, λ (Å)	Mo–K$_\alpha$, 0.71073
Monochromator	Graphite
θ range (°)	1.67–25.15
Reflections collected	10 047
Reflections independent	3689
R_{int}	0.0277
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0305$, $wR_2 = 0.0672$
R indices (all data)	$R_1 = 0.0360$, $wR_2 = 0.0692$
Data/restraints/parameters	3689/1 [a]/274
Refinement method	Full-matrix-least-squares on F^2
Goodness-of fit	0.980
Minimum/maximum residual electron density (e Å^{-3})	−0.198/0.200
Weighting scheme	$w = 1/[\sigma^2(F_o^2)+(0.1693P)^2+10.77P]$, where $P = (F_o^2+2F_c^2)/3$

[a] The single restraint refined was an extinction parameter.



Scheme 3. $R_1 = R_3 = H$, $R_2 = OCH_3$ (**18**); $R_1 = R_2 = R_3 = H$ (**19**); $R_2 = R_3 = H$, $R_1 = OCH_3$ (**20**); $R_2 = H$, $R_1 = R_3 = CH_3$ (**21**).



Scheme 4.

of the molecules **17**–**21**. The signals for the CH(protons of the substituent at the nitrogen atom in compounds **17b**–**21b** are shifted downfield as compared with those for the original compounds **17a**–**21a** (δ 5.4–5.5 and 5.25–5.30 ppm, respectively; Table 1).

Thus, the results obtained allowed us to conclude that it is the enone fragment that is subjected to isomerization, and the double bond in compounds **17b**–**21b** has *Z*-configuration (Scheme 4).

Earlier, analogous *E*-/*Z*-isomerization has been observed for (ferrocenylmethylidene)camphor, -quinuclidone [13], -menthone [14], 2-acetyl-3-ferrocenyl-7-ferrocenylmethylidene-3,3a,4,5,6,7-hexahydro-2H-indazole [15] in an acidic medium. Spontaneous isomerization of *E*- enamines into the respective *Z*- isomers is described for the first time, its mechanism is not clear yet.

Biological assays of compounds **13a**–**21a** revealed sufficiently high anti-inflammatory activities for compounds **14a**, **15a**, **18a**–**21a** and antiviral activities for compounds **13a**, **16a**, and **17a**.

3. Experimental

The ^{1}H- and ^{13}C-NMR spectra were recorded on a Unity Inova Varian spectrometer (300 and 75 MHz) for solutions in $CDCl_3$ with Me_4Si as the internal standard. The unit cell parameters and the X-ray diffraction intensities were recorded on a Bruker CCD-Area-Detector diffractometer at 293 K. The crystallographic data, the parameters of the X-ray diffraction experiment, and refinements are listed in Table 3.

The following reagents were purchased from Aldrich: ferrocenecarbaldehyde, 98%; 3-quinuclidinone hydrochloride, 97%; α-tetralone, 98%; 5-methoxy-1-tetralone, 97%; 6-methoxy-1-tetralone, 99%; 7-methoxy-1-tetralone, 99%; 5,7-dimethyl-1-tetralone, 97%; cyclohexanone, 99.8%; pentane-2,4-dione (acetylacetone), 97%; ethyl acetocetate, 99%.

The chalcones **7**–**12** were prepared from ferrocenecarbaldehyde and the corresponding ketones in an aqueous-ethanolic alkali [4,6,9,16].

The dihydropyrazoles **1**–**6** were synthesized by a conventional method [4,16] from the chalcones **7**–**12** and hydrazine hydrate in ethanol. The dihydropyrazoles obtained were dried in vacuo and employed in subsequent transformations.

The data from elemental analysis of the compounds prepared are listed in Table 4.

3.1. Synthesis of (*E*)-*N*-[(1-ethoxycarbonyl)prop-2-en-2-yl]dihydropyrazoles (general procedure)

A mixture of ferrocenyl-4,5-dihydropyrazoles (**2**, **3**, **5**) (3.3 mmol) and ethyl acetoacetate (10 ml) was heated at 100 °C until complete dissolution of the starting materials occurred (~ 10–15 min) and cooled. Then ether (50 ml) was added to the reaction mixture, the crystals that precipitated were filtered off, washed with ether, dried in vacuo and purified by recrystallization from benzene.

Table 4
Elemental analysis data for the obtained compounds

Compound	Anal. Found (%)				Formula	Calculated (%)			
	C	H	Fe	N		C	H	Fe	N
13a	64.61	6.38	12.31	9.22	$C_{24}H_{29}FeN_3O_2$	64.44	6.53	12.48	9.40
14a	67.63	5.88	11.37	5.38	$C_{28}H_{30}FeN_2O_3$	67.47	6.07	11.21	5.62
15a	67.23	6.29	11.05	5.79	$C_{28}H_{30}FeN_2O_3$	67.47	6.07	11.21	5.62
16a	67.39	5.98	18.86	4.61	$C_{33}H_{34}Fe_2N_2O$	67.60	5.85	19.05	4.77
17a	66.31	6.28	13.46	9.84	$C_{23}H_{27}FeN_3O$	66.19	6.52	13.38	10.07
17a,b	66.02	6.69	13.19	10.20	$C_{23}H_{27}FeN_3O$	66.19	6.52	13.38	10.07
18a	69.39	5.87	12.11	5.78	$C_{27}H_{28}FeN_2O_2$	69.23	6.02	11.92	6.00
18a,b	69.48	5.79	11.76	6.12	$C_{27}H_{28}FeN_2O_2$	69.23	6.02	11.92	6.00
19a	71.11	6.16	12.58	6.23	$C_{26}H_{26}FeN_2O$	71.24	5.98	12.74	6.40
19a,b	71.42	5.74	12.97	6.60	$C_{26}H_{26}FeN_2O$	71.24	5.98	12.74	6.40
20a	69.09	5.83	12.07	5.77	$C_{27}H_{28}FeN_2O_2$	69.23	6.02	11.92	6.00
21a	72.29	6.57	12.17	5.86	$C_{28}H_{30}FeN_2O$	72.11	6.48	11.98	6.00

Compound **13a**, yield 71%, melting point (m.p.) 182–183 °C.
Compound **14a**, yield 67%, m.p. 210–211 °C.
Compound **15a**, yield 72%, m.p. 207–208 °C.

3.2. Synthesis of (*E*)-*N*-(4-oxopent-2-en-2-yl)-substituted ferrocenyldihydropyrazoles *16a–21a*

The reactions of 4,5-dihydropyrazloles **1–6** with acetylacetone were carried out analogously. The reaction products were precipitated by addition of ether and were obtained in pure state.

3-Ferrocenyl-7-ferrocenylmethylidene-2-(4-oxopent-2-en-2-yl)-3,3a,4,5,6,7-hexahydro-2*H*-indazole (**16a**), yield 63%, m.p. 192–193 °C;
3-ferrocenyl-4-(4-oxopent-2-en-2-yl)-1,4,5-triazatricyclo[5.2.2.$0^{2,6}$]undec-5-ene (**17a**), yield 73%, m.p. 174–175 °C;
3-ferrocenyl-7-methoxy-2-(4-oxopent-2-en-2-yl)-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole (**18a**), yield 71%, m.p. 189–190 °C;
3-ferrocenyl-2-(4-oxopent-2-en-2-yl)-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole (**19a**), yield 67%, m.p. 193–194 °C;
3-ferrocenyl-6-methoxy-2-(4-oxopent-2-en-2-yl)-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole (**20a**), yield 63%, m.p. 181–182 °C;
3-ferrocenyl-6,8-dimethyl-2-(4-oxopent-2-en-2-yl)-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole (**21a**), yield 66%, m.p. 222–223 °C.

3.3. Studies on the isomerization of *E*-enamino carbonyl compounds *13a–21a*

Samples of the dihydropyrazoles **13a–21a** (0.3 g) were dissolved in chloroform or dichloromethane (100 ml) and aliquots (10 ml) were withdrawn every 2 h from the solutions. The solvent was evaporated, the residues were dissolved in $CDCl_3$ (0.5 ml), and the solutions were filtered through a 1-cm layer of Al_2O_3 (Brockmann activity III) in a Pasteur pipette directly into an NMR tube. The products were eluted with an additional portion (0.5 ml) of $CDCl_3$ and the ^{1}H-NMR spectra were run immediately. It was found that compounds **13a–16a** underwent no isomerization; for compound **17a**, the equilibrium was established after 16 h (**17a**:**17b** ≈ 1.3:1); for compounds **18a–21a**, the equilibrium was established after ~6 h (**18a–21a**:**18b–21b** ≈ 1.5:1).

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Center, CCDC no. 189259 for compound **13a**. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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