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Preparation, characterization and biological activities of novel ferrocenyl-substituted azaheterocycle compounds

Jian-Xin Fang, Zhong Jin*, Zeng-Ming Li and Wei Liu

Institute and State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China

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α-Haloacetylferrocene and α-triazolylacetylferrocene have been prepared from acetylferrocene and they have proved to be useful building blocks for the synthesis of ferrocenyl propenone. Two new types of ferrocenyl vinyl triazole compound, (*Z*,*E*)-ferrocenyl-[1-(1,2,4-triazol-1-yl)-2-phenyl]-vinyl-ones, have been synthesized and their structures characterized by crystal X-ray diffraction analysis. It has been shown for the first time that ferrocene, as an organometallic compound, has been introduced into bioactive triazole compounds in search of potent bioactive substances. Their biological activities are also discussed. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: ferrocene; 1,2,4-triazole; biological activities; fungicidal activity; plant-growth regulatory activity

INTRODUCTION

The serendipitous discovery of ferrocene caused organometallic chemistry to progress rapidly. Nowadays, ferrocene and its derivatives are also attracting much attention from the viewpoint of catalysis, organic synthesis, new materials (such as liquid crystals or polymers)[1] and supramolecular chemistry.[2] Ferrocene derivatives containing atoms with good donor abilities have attracted additional interest, since the coordination of a metal to these heteroatoms produces heteropolynuclear organometallic compounds containing ferrocene units, in which the presence of proximal metals in different environments may influence the mutual co-operation of these metals in a variety of processes.[3] In this sense, the integration of one or more ferrocene units into a heterocyclic ring system has long been recognized as an attractive way to endow a molecule functionally. This sort of compound is of considerable interest for the construction of heterobimetallic systems, which can behave either as chemical sensors[4–6] or as redox-active and photoactive molecular devices.[7–9]

There are some groups of *N*-heterocyclic compounds that have been synthesized in the search for potent and broad-spectrum fungicides, e.g. pyridines (buthilbate),[10] pyrimidines (fenarimol and nuarimol),[11] triazoles (triadimefon and propiconazole)[12,13] and imidazoles (imazalil).[14] Compounds containing the 1,2,4-triazole ring system are well known to be highly active as fungicides,[15] especially on the *Basidiomycete* and *Ascomycete* groups of fungi. These compounds are known to inhibit the biosynthesis of ergosterol in fungi.[16] It has now been found that, in addition to their fungicidal activity, they possess a very high level of plant-growth regulatory activity on a wide variety of crops.

The present work concerns the synthesis of the novel ferrocenyl-substituted azaheterocycles such as 1,2,4-triazole derivatives. We have synthesized two new series of ferrocenyl-substituted vinyl 1,2,4-triazole derivatives: (*Z*,*E*)-ferrocenyl-[1-(1,2,4-triazol-1-yl)-2-phenyl]-vinyl-ones; the biological activities of these novel triazole compounds are also evaluated.

EXPERIMENTAL

General comment

All operations were performed in an atmosphere of dry nitrogen using Schlenk and vacuum techniques. All solvents were dried by standard methods and distilled prior to use. Elemental analyses were determined on a Yanaco CHN Corder MT-3 elemental analyzer. ^{1}H NMR spectra were measured on a Bruker AC-200 spectrometer in $CDCl_3$ and DMSO-d_6 solution with tetramethylsilane (TMS) as internal standard. Mass spectra (electron impact) were recorded on an HP-5988A at 70 eV; the ionization temperature was 200 °C.

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*Correspondence to: Z. Jin, Institute and State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China.
E-mail: jinzhong2000@263.net
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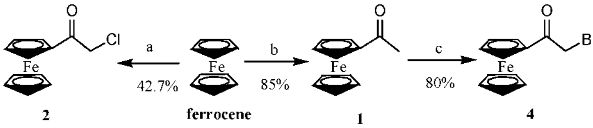


Scheme 1. Reagents and conditions: (a) $ClCH_2COCl$, $AlCl_3$; (b) acetic acid anhydride, H_3PO_4; (c) LDA, Me_3SiCl, THF −78 °C then NBS.

Synthesis of *α*-chloroacetylferrocene (2) and *α*-bromoacetylferrocene (4)

α-Chloroacetylferrocene (**2**) was synthesized as described by Schlögl and Egger[17] (Scheme 1). To a solution of ferrocene (60 mmol) in dichloromethane (60 ml) at 0 °C, a solution of chloroacetyl chloride (50 mmol) and aluminum chloride (50 mmol) in dichloromethane (80 ml) was added dropwise. After stirred for 8 h at room temperature, water was added. The organic layer was separated and washed by water and brine. The resulting solution was dried over anhydrous $MgSO_4$ and evaporated to dryness in vacuum. The residue was chromatographed on a silica gel column to give orange crystal in 42.7% yield, m.p. 94–96 °C (lit.[17] 92–93 °C). ^{1}H NMR δ ($CDCl_3$): 4.07 (s, 2H), 4.15 (s, 5H), 4.46 (m, 2H), 4.65 (m, 2H).

Bromination of acetylferrocene was achieved by using the trimethylsilylenolether of **1**. Thus, to a solution of lithium diisopropylamine (LDA) (72.3 mmol) in tetrahydrofuran (THF) (20 ml) at − 78 °C, a solution of acetylferrocene (43.8 mmol) in THF (20 ml) was added dropwise in 0.5 h. The reaction mixture was stirred at − 78 °C for 2 h and then Me_3SiCl (57 mmol) was added in one portion. After 4 h under these conditions, *N*-bromosuccinimide (NBS) (57 mmol) was added and the solution was stirred until the reaction reached room temperature (6–8 h). The reaction mixture was filtered through a short silica gel column and the resulting solution was evaporated to dryness and chromatographed on a silica gel column using dichloromethane/ethyl acetate (20/1) as eluent to give **4** ($R_f = 0.7$) in 80% yield; m.p. 70–71 °C (red prisms). Anal. Calc. for $C_{12}H_{11}BrFeO$: C, 46.95; H, 3.61. Found: C, 46.90; H, 3.57%. ^{1}H NMR δ ($CDCl_3$): 4.00 (s, 2H), 4.15 (s, 5H), 4.50 (m, 2H), 4.70 (m, 2H).

Synthesis of *α*-triazolylacetylferrocene (3)

To a suspension of α-chloroacetylferrocene (5.6 g, 21 mmol) and anhydrous potassium carbonate (3.0 g, 22 mmol) in dry acetone (100 ml), 1*H*-1,2,4-triazole (1.52 g, 22 mmol) was added under stirring. After refluxed for 8 h, the reacting mixture was filtered and washed with acetone. Evaporation of the combined solvent mixture gave a brown solid, and the residue was isolated by column chromatography on a silica gel column, to give a yellow crystal, α-triazolylferrocene (**3**, 5.6 g) in 95% yield, which was crystallized from ethyl acetate/petroleum ether. M.p. 116–118 °C. ^{1}H NMR δ ($CDCl_3$): 4.15 (s, 5H), 4.50 (m, 2H), 4.70 (m, 2H), 5.10 (s, 2H), 8.00 (s, 1H), 8.50 (s, 1H). MS (70 eV): $M^+ = 295$. Anal. Calc. for $C_{14}H_{13}FeN_3O$ (295.1): C, 56.98; H, 4.44; N, 14.24. Found: C, 56.96; H, 4.40; N, 14.09%.

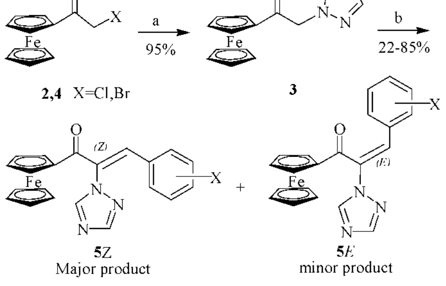
Synthesis of 3-aryl-1-ferrocenylpropenone (5)

The general procedure is as follows (Scheme 2): to a stirred solution of the α-triazolylferrocene (**3**; 2.95 g, 10 mmol), piperidine (0.1 ml) in dry toluene (30 ml) was added 4-dichlorobenzaldehyde (1.41 g, 10 mmol) at room temperature under nitrogen. The mixture was then heated to reflux and kept at this temperature until completion of the reaction, while the water generated was evaporated off. The solvent was evaporated off in vacuum and the residue was purified by chromatography on silica gel with the solvent system of ethyl acetate/petroleum ether. The *Z*-isomer **5d** was obtained as the first elute (2.95 g, 71%). The *E*-isomer **5d** was obtained as the second elute of the chromatography (0.26 g, 6%).

In all cases of this reaction, the *Z*-isomers (*Z*-**CO**) were obtained as the major products (yield: 55–71%) and the *E*-isomers (*E*-**CO**) as the minor ones (yield: below 10%). Some data on compounds **5** are listed in Table 1.

Crystallography

Diffraction data for compounds **5d** *Z*-isomer and **5d** *E*-isomer were obtained at 293 K on a Bruker Smart 1000 diffractometer (graphite-monochromatized Mo Kα radiation, $\lambda = 0.710\ 73$ Å). For the *Z*-isomer, of the total 7492 recorded reflections, 3299 reflections ($R_{int} = 0.0439$) were used for the structure determination and refinement; 3238 reflections ($R_{int} = 0.0242$) of the total 7412 recorded reflections were used for the structure determination and refinement for the *E*-isomer. The crystal class, orientation matrix and accurate unit-cell parameters were determined by standard procedures. The intensities were corrected for absorption using the SADABS program. The structures were solved by heavy atom methods and refined by a full-matrix least squares



Scheme 2. Reagents and conditions: (a) 1*H*-1,2,4-triazole, K_2CO_3, acetone, reflux, 8 h; (b) substituted benzaldehyde, piperidine, AcOH, toluene, reflux, 4–8 h.

procedure based on F^2. Non-hydrogen atoms were refined with anisotropic thermal parameters.

Crystal data for (*Z*)-**5d**: $C_{21}H_{16}ClFeN_3O$; $0.30 \times 0.25 \times 0.20\ mm^3$; monoclinic, $P2(1)/n$; $a = 11.622(3)$, $b = 7.683(2)$, $c = 21.587(6)$ Å; $\alpha = 90$, $\beta = 103.854(5)$, $\gamma = 90°$; $V = 1871.4(9)$ Å^3; $Z = 4$; $D_{calc} = 1.482\ Mg\ m^{-3}$; $F(000) = 856$; $\mu = 0.964\ mm^{-1}$; $[I > 2\sigma(I)]$ $R_1 = 0.0408$, $wR_2 = 0.0864$.

Crystal data for (*E*)-**5d**: $C_{21}H_{16}ClFeN_3O$; $0.20 \times 0.15 \times 0.05\ mm^3$; monoclinic, $P2(1)/n$; $a = 9.762(10)$, $b = 9.435(10)$, $c = 20.12(2)$ Å; $\alpha = 90$, $\beta = 98.135(17)$, $\gamma = 90°$; $V = 1835(3)$ Å^3; $Z = 4$; $D_{calc} = 1.512\ Mg\ m^{-3}$; $F(000) = 856$; $\mu = 0.9834\ mm^{-1}$; $[I > 2\sigma(I)]$ $R_1 = 0.0327$, $wR_2 = 0.0788$.

BIOLOGICAL EVALUATION

Fungicidal activity

Preventive activity against powdery mildew *on barley (foliar application)*

Barley plants were grown in a greenhouse in a plastic pot (150 ml, 6.5 cm in diameter) filled with 120 ml of sandy loam soil. When the first leaf had expanded, an aqueous suspension of the emulsifiable concentrate of each test compound was sprayed on the foliage to run-off. After drying, the seedlings were inoculated with the conidia of *Erysiphe graminis* and grown for 10 days in an air-controlled room (23 °C) under fluorescent lamps. Evaluation of the preventive activity was made by measuring the degree of fungal infection and the percentage of disease control was calculated compared with the untreated, inoculated control plants.

Preventive activity against powdery mildew *on barley (soil drench application)*

A similar evaluation was made as described above, except that the treatment was soil drench (25 ml, containing 1.25 mg a.i./pot) and the inoculation was made 4 days after the application.

Curative against brown rust *on wheat (foliar application)*

Wheat plants were grown in a greenhouse in a plastic pot (150 ml) filled with 120 ml of sandy loam soil. When the first leaf had expanded, the seedlings were inoculated with the conidia of *Puccinia recondita* and kept in a humid chamber at 23 °C for 16 h. Then an aqueous diluted suspension of the emulsifiable concentrate of each test compound was sprayed on the foliage to run-off. The seedlings were grown for 10 days in an air-controlled room (23 °C) under fluorescent lamps.

Preventive activity against brown rust *on barley (soil drench application)*

Wheat plants were grown as described in above. The treatment and the inoculation were made similarly as described for the barley soil drench application.

Plant-growth regulatory activity

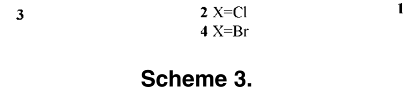
Apple seeds (var. Red delicious) were sown in John Innes Potting Compost no. 1 in pots (2.5 cm diameter) for 2 weeks, repotted into 7 cm diameter pots, and kept for 10 days in a glasshouse at about 24 °C. At the eight to ten true leaves stage, whole plants, but not the soil, were sprayed to maximum retention, twice at 3-day intervals. The assessment of plant growth was made a week after the final spray.

RESULTS AND DISCUSSION

α-Triazolylacetylferrocene **3** was prepared from α-chloroacetylferrocene **2** and α-bromoacetylferrocene **4** by Friedel–Crafts acylation (Scheme 3). The only known α-haloacetylferrocene is the α-chloro derivative, which has recently been used as a starting material for the preparation of chiral ferrocenyl-substituted β-aminocyclopentadienes.[18] However, the only method reported[17] for its preparation, which is based on the Friedel–Crafts acylation of ferrocene with chloroacetyl chloride in the presence of aluminium chloride, affords the desired α-chloroacetylferrocene in 26% yield, together with acetylferrocene. The low yield of the acylated product is due to the fact that the conventional electrophilic substitution is accompanied by an electron transfer from the ferrocene to the acylium ion to give the oxidized ferrocenium cation, usually in high yield.[19]

Therefore, our first goal was to devise a reliable method for the preparation of α-haloacetylferrocene from acetylferrocene. After several trials with various bromination reagents, which included phenyltrimethylammonium tribromide, Br_2/AcOH, CuBr/MeOH, NBS/azobis(isobutyronitrile) and NBS/HBr, we were unable to accomplish this transformation. This series of frustrating results was finally broken by using the trimethylsilylenolether of acetylferrocene. Thus, metallation of **1** with LDA at − 78 °C followed by sequential treatment with trimethylchlorosilane and an excess of NBS provided the α-bromoacetylferrocene (**4**) in 80% yield, along with a small amount of the α,α-dibromoacetylferrocene.

Conversion of **2** and **4** into α-triazolylferrocene (**3**) was achieved in complete yield by using potassium carbonate as a base. Sequentially, preparation of 3-aryl-1-ferrocenylpropenone (**5**) was achieved in good yield by condensation of **3** with substituted aldehyde under standard conditions.



Scheme 3.

Table 1. Yields and elemental analysis of the compounds **5**

Compound		X	Yield (%)	M.p. (°C)	Elemental analysis: found/calc. (%)		
					C	H	N
5a	*Z*	H	60.2	128–130	65.55/65.82	4.50/4.47	10.96/10.96
	E		11.0	140–141	65.60/65.82	4.71/4.47	10.79/10.96
5b	*Z*	2-Cl	47.6	128–129	60.30/60.39	3.70/3.86	9.95/10.06
	E		7.2	138–139	60.32/60.39	3.90/3.86	10.09/10.06
5c	*Z*	3-Cl	55.0	123–124	60.35/60.39	4.00/3.86	9.95/10.06
	E		9.2	122–123	60.40/60.39	3.76/3.86	9.85/10.06
5d	*Z*	4-Cl	71.0	149–151	60.14/60.39	3.52/3.86	9.97/10.06
	E		6.0	133–134	60.15/60.39	3.71/3.86	9.94/10.06
5e	*Z*	2,4-Cl_2	62.3	195–196	55.66/55.79	3.35/3.34	8.89/9.29
	E		10.3	173–174	55.76/55.79	3.62/3.34	9.21/9.29
5f	*Z*	2-OH	54.8	166–167	63.15/63.18	4.32/4.29	10.35/10.53
	E		8.2	161–163	63.21/63.18	4.20/4.29	10.61/10.53
5g	*Z*	4-OH	45.1	190–192	63.15/63.18	4.35/4.29	10.59/10.53
	E		8.9	178–180	63.13/63.18	4.26/4.29	10.32/10.53
5h	*Z*	4-OCH_3	66.0	159–161	63.85/63.94	4.62/4.63	10.10/10.17
	E		6.0	134–137	63.90/63.94	4.62/4.63	10.14/10.17
5i	*Z*	3-NO_2	59.8	156–157	58.62/58.79	3.82/3.76	13.12/13.05
	E		16.7	144–146	58.79/58.79	3.85/3.76	13.12/13.05
5j	*Z*	4-NO_2	18.5	191–192	58.69/58.79	3.86/3.76	12.98/13.05
	E		3.6	191–193	58.65/58.79	3.85/3.76	13.08/13.05
5k	*Z*	3,4-O—CH_2—O—	60.1	114–115	67.45/67.50	4.50/4.68	10.18/10.27
	E		8.5	108–109	67.65/67.50	4.53/4.68	10.15/10.27
5l	*Z*	3-Br	57.6	131–133	54.58/54.58	3.49/3.49	8.89/9.09
	E		8.8	129–130	54.36/54.58	3.46/3.49	8.93/9.09

^{1}H NMR

The ^{1}H NMR data of the title compounds **5** are listed in Table 2. The chemical shifts of ferrocene are in character. The chemical shifts of the unsubstituted ring appear between 4.25 and 4.35 ppm as a single peak. The chemical shifts of the substituted ring appears as two peaks, one between 4.40 and 4.60 ppm, the other between 4.60 and 4.80 ppm. The olefin proton displays an acute single peak between 7.50 and 8.10 ppm. The protons of the triazole appear as two peaks between 8.00 and 9.10 ppm.

Biological activities

The protective and curative activities of the title compounds **5** against *powdery mildew* and *brown rust* and plant-growth regulatory activity are shown in Table 3. The *E*-isomers obviously display higher fungicidal activities than the *Z*-isomers. Both of them show inhibitory activity to the growth of apple seeds and the *E*-isomer has a higher activity than *Z*-isomer.

Previously, Japanese workers reported the structure–activity relationships of the representative four types of the vinyl triazole compounds.[20] Comparing each of the ferrocenyl-substituted vinyl triazole derivatives with the corresponding vinyl triazole analogs, similar relations were also noted among them. The *Z*-isomer showed no curative activity against *brown rust* at 50 ppm. Some of the *E*-isomer was still slightly active against *powdery mildew* at 50 ppm, although many of these analogs were active against both diseases at higher concentrations. It has been shown that the reduction of the **CO** group into the **CHOH** group of these vinyl triazole derivatives, whether the geometrical configurations are *Z* or *E*, resulted in a great increase in the fungicidal activities, and the *E* configuration was favorable to excellent protective activities in the alcohol analogs.[21] Takano *et al.*[22] observed that the *E*-alcohol derivatives inhibited strongly the ergosterol biosynthesis process in *Ustilago maydis*. From a study of the inhibition of ergosterol biosynthesis by 1-*tert*-butyl-2-(1,2,4-triazol-1-yl)-3-phenylpropan-1-ols, saturated derivatives of the vinyl triazole compounds, Gadher *et al.*[23] showed that the activity depended greatly on the steric structures of the non-*N*-heterocyclic part of the molecule and gave the postulated

Table 2. ^{1}H NMR data for the compounds **5** (DMSO d_6) Q2

Compound		X	δ (PPM)					
			C_5H_5	C_5H_4	Olefin	Aryl	Triazole	X
5a	*Z*	H	4.34 (s)	4.60 (s) 4.72 (s)	7.84 (s)	7.36–7.48 (m)	8.20 (s) 8.12 (s)	–
	E		4.08 (s)	4.38 (s) 4.62 (s)	7.53 (s)	7.10–7.95 (m)	8.08 (s) 8.00 (s)	–
5b	*Z*	2-Cl	4.26 (s)	4.58 (s) 4.68 (s)	7.64 (s)	7.00–7.44 (m)	7.96 (m)	–
	E		4.20 (s)	4.36 (s) 4.49 (s)	7.23 (s)	6.50–6.66 (m)	8.09 (s) 8.32 (s)	–
5c	*Z*	3-Cl	4.31 (s)	4.53 (s) 4.70 (s)	7.93 (s)	6.80–7.60 (m)	8.39 (s) 8.77 (s)	–
	E		4.14 (s)	4.56 (s)	7.51 (s)	7.35–7.51 (m)	8.24 (s) 9.09 (s)	–
5d	*Z*	4-Cl	4.31 (s)	4.51 (s) 4.69 (s)	7.95 (s)	6.99 (d) 7.45 (d)	8.37 (s) 8.76 (s)	–
	E		4.16 (s)	4.53 (s) 4.56 (s)	7.51 (s)	7.40 (m)	8.24 (s) 9.08 (s)	–
5e	*Z*	2,4-Cl_2	4.44 (s)	4.73 (m)	8.00 (s)	7.58–6.60 (m)	8.16–8.36 (m)	–
	E		4.20 (s)	4.49 (s) 4.52 (s)	7.70 (s)	7.60–7.40 (s)	8.30 (s) 8.92 (s)	–
5f	*Z*	2-OH	4.35 (s)	4.56 (s) 4.69 (s)	8.30 (s)	7.24–6.13 (m)	8.37 (s) 8.70 (s)	2.25 (b)
	E		4.15 (s)	4.33 (m)	7.95 (s)	6.40–6.80 (m)	8.50–8.20 (m)	2.50 (b)
5g	*Z*	4-OH	4.27 (s)	4.42 (s) 4.66 (s)	7.92 (s)	6.60–6.80 (m)	8.37 (s) 8.76 (s)	1.80 (b)
	E		4.05 (s)	4.13 (m)	7.56 (s)	6.00–6.60 (m)	8.12 (s) 8.42 (s)	2.50 (b)
5h	*Z*	4-OCH_3	4.24 (s)	4.54 (d)	7.87 (s)	6.80 (m)	8.10 (s) 8.50 (s)	3.78 (s)
	E		4.06 (s)	4.45 (s) 4.63 (s)	7.37 (s)	6.75 (d) 7.24 (d)	8.08 (s) 8.62 (s)	3.74 (s)
5i	*Z*	3-NO_2	4.33 (s)	4.57 (s) 4.72 (s)	8.07 (s)	7.30–8.20 (m)	8.41 (s) 8.80 (s)	–
	E		4.14 (s)	4.55 (s)	7.68 (s)	7.60–8.30 (m)	8.28 (s) 9.10 (s)	–
5j	*Z*	4-NO_2	4.24 (s)	4.57 (s) 4.62 (s)	7.71 (s)	7.10 (d) 8.10 (d)	8.09 (s) 8.22 (s)	–
	E		4.04 (s)	4.49 (s) 4.61 (s)	7.55 (s)	7.45 (d) 8.06 (d)	8.12 (s) 8.70 (s)	–
5k	*Z*	3,4-O—CH_2—O—	4.28 (s)	4.42 (s) 4.64 (s)	7.76 (s)	6.00–7.00 (m)	8.40 (s) 8.80 (s)	6.04 (s)
	E		4.10 (s)	4.41 (s) 4.62 (s)	7.51 (s)	6.30–7.40 (m)	8.32 (s) 8.66 (s)	5.92 (s)
5l	*Z*	3-Br	4.35 (s)	4.65 (m)	7.60 (s)	6.70–7.50 (m)	7.80–7.90 (m)	–
	E		4.22 (s)	4.32 (s) 4.56 (s)	7.28 (s)	6.80–7.20 (m)	7.60 (s) 7.74 (s)	–

Table 3. Biological activities of compounds **5**

Compound		X	Fungicidal activity (%)				Plant-growth regulatory activity (%)
			Powdery mildew		*Brown rust*		
			Foliar[a]	Soil[a]	Foliar[b]	Soil[a]	
5a	*Z*	H	0	0	0	0	−17.12
	E		6.7	16.7	3.3	10.0	−49.60
5b	*Z*	2-Cl	16.7	25.0	33.3	45.0	−11.20
	E		20.0	33.3	40.0	75.0	−65.50
5c	*Z*	3-Cl	3.3	6.7	40.0	50.0	−9.90
	E		16.7	30.0	60.0	66.7	−71.40
5d	*Z*	4-Cl	6.7	14.3	30.0	50.0	−4.50
	E		16.7	21.4	50.0	75.0	−72.90
5e	*Z*	2,4-Cl_2	10.0	16.7	40.0	50.0	−16.20
	E		25.0	33.3	75.0	80.0	−77.80
5f	*Z*	2-OH	6.6	3.3	20.0	33.3	−28.60
	E		15.2	22.0	33.3	40.0	−42.10
5g	*Z*	4-OH	8.0	0	3.3	10.0	−20.50
	E		16.7	22.0	25.0	50.0	−25.42
5h	*Z*	4-OCH_3	10.0	16.7	10.0	16.7	−50.00
	E		22.0	26.7	16.7	30.0	−75.00
5i	*Z*	3-NO_2	3.3	3.3	25.0	30.0	−13.70
	E		14.8	42.8	40.0	33.3	−100.00
5j	*Z*	4-NO_2	10.0	10.0	33.3	50.0	−56.90
	E		16.7	30.0	50.0	75.0	−100.00
5k	*Z*	3,4-O—CH_2—O—	0	3.3	0	0	−2.70
	E		10.0	16.7	3.3	16.7	−64.30
5l	*Z*	3-Br	0	3.3	25.0	40.0	−7.30
	E		12.0	22.0	45.5	50.0	−60.60

[a] Preventive activity at 50 ppm.

[b] Curative activity at 50 ppm.

structure of the cytochrome P-450–fungicide complex. The *E*-configuration may be favorable to a more suitable fit in this postulated enzyme–fungicide complex. Gasztonyi and Josepovits[24] reported that triadimefon was transformed into higher fungitoxic triadimenol both in fungi and in host plants and assumed this reduction process of the **CO** group into the **CHOH** group as an activation process.

The synthesis and biological evaluation of ferrocenyl-substituted vinyl triazole alcohol derivatives (*Z*-**CHOH** and *E*-**CHOH**) will be presented in forthcoming papers.

Crystal structure

The single crystals of compounds (*Z*)-**5d** and (*E*)-**5d** were both obtained from acetone–petroleum ether (60–90 °C). Their molecular structures are shown in Figs 1 and 2. Selected bond lengths and angles are given in Table 4. Final fractional atomic coordinates for non-hydrogen atoms are listed in Table 5.

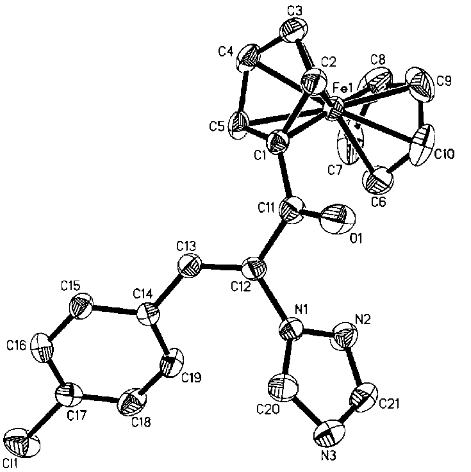


Figure 1. Molecular structure and crystallographic numbering scheme for (*Z*)-**5d**.

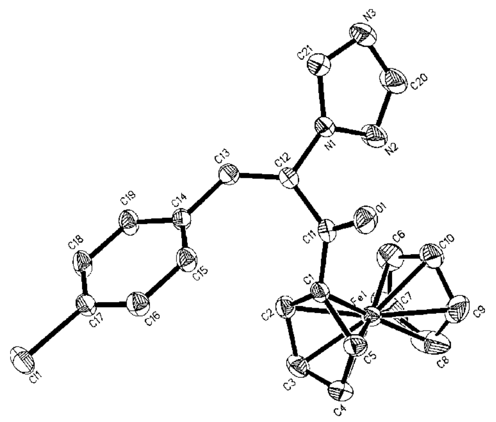


Figure 2. Molecular structure and crystallographic numbering scheme for (*E*)-**5d**.

The triazole cycle, C=C double bond and aryl group, as far as we know, are essential to their biological activities. The *E*-isomer of compound **5d** has a nearly fully extended carbon backbone in which the triazole cycle and 4-chloro-phenyl group are linear. In contrast, the backbone (N_1—C_{12}—C_{13}—C_{14}) in the *Z*-isomer is distorted.

As the *E*-isomer possesses higher activity than the *Z*-isomer, assuming that both act at the same site, it may be concluded that the *E*-isomer prefers to bind to the receptor. Alternatively, the receptor binding to molecules may be in extended conformation.

Supporting information

Crystallographic data for the structures (*E*)-**5d** and (*Z*)-**5d** have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos 190330 and 190331. 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; www: http://www.ccdc.cam.ac.uk).

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Table 4. Selected bond distances and bond angles of compounds **5d**

	Bond	Distance (Å)	Bond	Angle (°)
Z	Cl(1)—C(17)	1.733(4)	C(2)—C(1)—C(5)	107.6(3)
	N(1)—C(12)	1.426(4)	C(2)—C(1)—C(11)	122.0(3)
	O(1)—C(11)	1.218(4)	C(5)—C(1)—C(11)	129.9(3)
	C(1)—C(11)	1.476(5)	O(1)—C(11)—C(1)	120.9(3)
	C(11)—C(12)	1.496(5)	O(1)—C(11)—C(12)	119.4(3)
	C(12)—C(13)	1.334(4)	C(1)—C(11)—C(12)	119.6(3)
	C(13)—C(14)	1.462(4)	C(13)—C(12)—N(1)	122.4(3)
	C(13)—H(13A)	0.9300	C(13)—C(12)—C(11)	123.3(3)
			N(1)—C(12)—C(11)	113.7(3)
			C(12)—C(13)—C(14)	131.1(3)
			C(12)—C(13)—H(13A)	114.5
			C(14)—C(13)—H(13A)	114.5
E	Cl(1)—C(17)	1.748(3)	C(2)—C(1)—C(5)	107.4(2)
	N(1)—C(12)	1.433(3)	C(2)—C(1)—C(11)	129.1(2)
	O(1)—C(11)	1.215(3)	C(5)—C(1)—C(11)	123.1(2)
	C(1)—C(11)	1.461(3)	O(1)—C(11)—C(1)	122.2(2)
	C(11)—C(12)	1.511(3)	O(1)—C(11)—C(12)	118.2(2)
	C(12)—C(13)	1.326(3)	C(13)—C(12)—N(1)	119.7(2)
	C(13)—C(14)	1.469(3)	C(13)—C(12)—C(11)	127.4(2)
			N(1)—C(12)—C(11)	112.6(2)
			C(12)—C(13)—C(14)	128.1(2)
			C(1)—C(11)—C(12)	119.51(19)

Table 5. Fractional coordinates and thermal parameters of non-hydrogen atoms for compounds **5d**

		x	*y*	*z*	U_{eq}
Z	Fe(1)	5935(1)	1665(1)	8013(1)	44(1)
	Cl(1)	−95(1)	2539(2)	10 588(1)	87(1)
	N(1)	3753(2)	5999(4)	8887(1)	45(1)
	N(2)	4862(2)	6255(4)	9252(2)	62(1)
	N(3)	3695(3)	8534(4)	9335(2)	67(1)
	O(1)	4240(3)	5740(3)	7707(1)	74(1)
	C(1)	4291(3)	2686(4)	7710(2)	40(1)
	C(2)	4846(3)	2531(5)	7191(2)	46(1)
	C(3)	5098(3)	767(5)	7123(2)	53(1)
	C(4)	4732(3)	−190(5)	7599(2)	56(1)
	C(5)	4238(3)	986(4)	7970(2)	48(1)
	C(6)	6802(4)	2811(9)	8835(3)	90(2)
	C(7)	6956(5)	1027(10)	8885(3)	102(2)
	C(8)	7489(5)	527(8)	8417(4)	101(2)
	C(9)	7699(4)	1946(12)	8088(2)	98(2)
	C(10)	7262(4)	3360(7)	8339(3)	88(2)
	C(11)	4012(3)	4394(5)	7951(2)	48(1)
	C(12)	3449(3)	4477(4)	8505(2)	43(1)
	C(13)	2621(3)	3360(5)	8589(2)	44(1)
	C(14)	1974(3)	3240(4)	9092(1)	39(1)
	C(15)	906(3)	2335(5)	8961(2)	49(1)
	C(16)	266(3)	2139(5)	9418(2)	54(1)
	C(17)	703(3)	2802(5)	10011(2)	50(1)
	C(18)	1768(3)	3654(5)	10159(2)	63(1)
	C(19)	2397(3)	3886(5)	9699(2)	56(1)
	C(20)	3091(3)	7377(5)	8944(2)	59(1)
	C(21)	4763(4)	7787(5)	9506(2)	65(1)
E	Fe(1)	4713(1)	5624(1)	2516(1)	42(1)
	Cl(1)	1403(1)	−1279(1)	462(1)	55(1)
	O(1)	4826(2)	6070(2)	682(1)	53(1)
	C(1)	4256(2)	4736(2)	1588(1)	34(1)
	C(2)	4479(3)	3665(3)	2098(1)	43(1)
	C(3)	3488(3)	3878(3)	2541(1)	51(1)
	C(4)	2676(3)	5075(3)	2319(1)	50(1)
	C(5)	3135(2)	5602(3)	1734(1)	44(1)
	C(6)	6727(3)	5886(4)	2893(2)	71(1)
	C(7)	5908(6)	5754(6)	3421(2)	113(2)
	C(8)	4951(5)	6908(7)	3336(3)	121(2)
	C(9)	5213(4)	7676(4)	2793(3)	94(1)
	C(10)	6287(3)	7056(3)	2528(2)	63(1)
	C(11)	5068(2)	5052(2)	1050(1)	35(1)
	C(12)	6259(2)	4095(2)	943(1)	35(1)
	C(13)	6212(2)	2715(2)	816(1)	36(1)
	C(14)	4996(2)	1781(2)	727(1)	35(1)
	C(15)	3683(2)	2237(2)	454(1)	39(1)
	C(16)	2573(2)	1315(3)	375(1)	41(1)
	C(17)	2782(2)	−81(2)	569(1)	40(1)
	C(18)	4070(3)	−576(2)	824(1)	46(1)
	C(19)	5175(3)	356(2)	898(1)	44(1)
	N(1)	7520(2)	4860(2)	921(1)	40(1)
	N(2)	7945(3)	5850(3)	1394(1)	70(1)
	C(20)	9077(3)	6320(4)	1195(2)	73(1)
	N(3)	9416(3)	5740(3)	637(1)	68(1)
	C(21)	8414(3)	4825(3)	477(1)	53(1)

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