Research Article

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Synthesis and biological activities of new 1*H*-1,2,4-triazole alcohol derivatives containing a ferrocenyl moiety

Jianbing Liu, Lichun Li, Hong Dai, and Jianxin Fang*

Fourteen new 1*H*-1,2,4-triazole alcohol derivatives containing a ferrocenyl moiety were synthesized. In addition, six unexpected compounds, the hydroxyls of the title compounds, methylated by methanol, were obtained. The structures of all these new compounds were confirmed using ^{1}H NMR spectra, ^{13}C NMR, MS and elemental analyses. Some compounds were also confirmed with IR spectra. The antifungal and plant growth regulatory activities of the title compounds are discussed.

Keywords: 1*H*-1,2,4-triazole; ferrocenyl moiety; antifungal activity; plant growth regulatory activity; synthesis

Introduction

A large number of heterocyclic compounds containing a 1*H*-1,2,4-triazole ring not only possess diverse pharmacological actitivities, such as antifungal, anti-inflammatory, antiviral, antimicrobial, antitumorial, anticonvulsant, analgesic and antihypotensive activities,[1] but also reveal insecticidal, herbicidal, antifungal and plant growth regulatory activities.[2] Thus, the biochemistry of these molecules has been studied for many years.[3] In addition, ferrocenyl derivatives have been reported to have antitumor, antifungal, insecticidal and plant growth regulatory activities.[4] For this reason, we are interested in exploring the biological activities of compounds that contain both ferrocenyl and 1*H*-1,2,4-triazole groups. In our previous paper,[5] we reported syntheses and biological activities of some 1*H*-1,2,4-triazole keto compounds **4** containing ferrocenyl moiety (Scheme 1). In order to compare the biological activities of the ketones **4** with their corresponding alcohol derivatives **5** (Scheme 1) and to study their structure–activity relationship (SAR), 14 title compounds were synthesized by reducing 1*H*-1,2,4-triazole ketones (Scheme 1). The structures of all these new compounds were confirmed by ^{1}H NMR spectra and elemental analysis. In some cases, the structures were also confirmed with IR spectra and MS.

Results and Discussion

Synthesis

Most 2-bromo-1-arylethanone derivatives **2** were synthesized by the reaction of ketones with bromine in acetic acid with yields of 65–70%.[6] Without being purified, the intermediates **2** could be converted to 1-aryl-2-(1*H*-1,2,4-triazol-1-yl)-ethanones **3** (scheme **1**) in the next step. Ferrocenecarboxaldehyde was synthesized according to the literature method.[7] The intermediates **4** were prepared according to Liu *et al*.[5]

The title compounds **5** were prepared by reducing intermediates **4** using $NaBH_4$ as the reducing agent in CH_3OH with yields of 70–80%. Compounds **5** were purified by silica gel column chromatography or by recrystallizing from AcOEt–petroleum ether (60–90%, 1 : 3 v/v). An unexpected compound, the hydroxyl of the compound **5i**, methylated by methanol, was obtained when we separated **5i** with silica gel column chromatography.[8] In order to investigate whether other reactions can also obtain methylated products, we studied the reaction further, and we found that, when the benzene cycle contains a donor group, the reaction can be isolated to obtain methylated product. The reason may be the formation of C^{+} under the effect of concentrated hydrochloric acid (Scheme 2). As the donor effect of the substituted group on the benzene cycle can stabilize the C^{+}, so the title compounds which contain the benzene cycle donor group can be methylated easily by the resolution of CH_3OH.

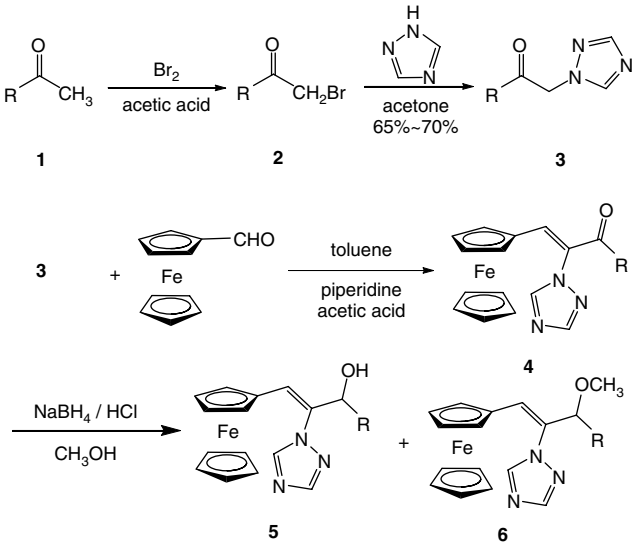
Biological activities

The title compounds **5** were screened for their biological activities *in vitro* against the *G. zeae*, *A. solani*, *C. arachidicola*, *P. piricola*, *P. asparagi*, *C. cucumerinum*, *S. sclerotiorum* and *P. oryzae* at the concentration of 50 μg l^{-1}, and the relative inhibitory ratios (%) against these fungi are listed in Table 1.

The screening data revealed that compounds **5** have some antifungal activity; among them, **5b, 5h** and **5m** showed 100% inhibitory ratios against *S. sclerotiorum*, *P. oryzae* and *C. cucumerinum*, respectively; **5h** and **5i** showed 99.5 and 95.3% inhibition against *C. cucumerinum* and *S. sclerotiorum*, respectively. Although the antibacterial activity of compounds **5** was not significant compared with known commercial agents, most of the title compounds **5** show higher antifungal activities than compounds **4**.[5] From the antifungal activity of this two series of compounds, we may speculate that converting the CO group of

* *Correspondence to: Jianxin Fang, State Key Laboratory and Institute of Elemento-Organic Chemistry, NanKai University, Weijin Road 94, Tianjin 300071, People's Republic of China. E-mail: fjx@nankai.edu.cn*

State Key Laboratory and Institute of Elemento-Organic Chemistry, NanKai University, Weijin Road 94, Tianjin 300071, People's Republic of China

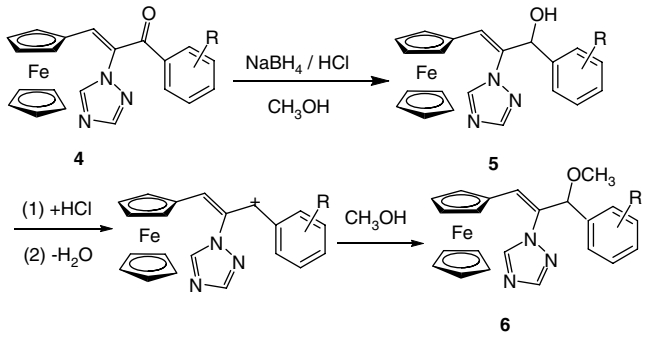


5a: R=$(CH_3)_3C$; 5b: R=C_6H_5; 5c: R=2-CH_3-C_6H_4; 5d: R=4-CH_3O-C_6H_4; 5e: R=2, 5-$(CH_3O)_2$-C_6H_3; 5f: R=4-F-C_6H_4; 5g: R=2,4-F_2-C_6H_3; 5h: R=4-Cl-C_6H_4; 5i: R=2, 4-Cl_2-C_6H_3; 5j: R=2,5-Cl_2-C_6H_3; 5k: R=3, 4-Cl_2-C_6H_3; 5l: R=3-Br-C_6H_4; 5m: R=4-Br-C_6H_4; 5n: R=3-NO_2-C_6H_4

6a: R=4-F-C_6H_4; 6b: R= 4-Cl; 6c: 4-Br; 6d: R=$_3$, 4-Cl_2-C_6H_3; 6e: R=$_2$, 4-F_2-C_6H_3; 6f: R=$_2$,5-Cl_2-C_6H_3

Scheme 1. The synthesis route of the title compound **5** and **6**.

the 1*H*-1,2,4-triazole keto compounds **4** containing a ferrocenyl unit into CHOH (compounds **5**) is useful for enhancing the antifungal activity of the compounds. Gasztonyi and Josepovits[9] 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 to be an activation process. To clarify this further, we compared the biological activities of other ferrocenyl-substituted 1*H*-1,2,4-triazole alcohol derivatives with the corresponding keto compounds, and the results will be presented in forthcoming papers.



Scheme 2. The possible reaction mechanism of the OH of the title compounds **5** methylated by methanol.

The plant growth regulatory activities of compounds **5** were tested by wheat coleoptile and cucumber cotyledon tests at the concentration of 10 μg l^{-1}. Unfortunately, these compounds showed lower plant growth regulatory activities compared with the corresponding keto compounds **4**.[5]

Experimental

The ^{1}H NMR spectra were measured on a Bruker AC 200 instrument, using tetramethylsilane (TMS) as internal standard and $CDCl_3$ as solvent. Chemical shift values (δ) are given in ppm. IR spectra were recorded on a Bruker Equinox 55 spectrometer in KBr disks. MS spectra were measured on a VG ZAB-HS spectrometer using the EI method. Elemental analysis were determined with a Yanaco CHN Corder MT-3 elemental analyzer. Melting points were measured on an X-4 digital melting point apparatus, and the thermometer was uncorrected. The biological activities of compounds **5** were assayed at the Biological Assay Centre, Nankai University according to procedures described previously.[4c]

Table 1. Fungicidal activity of the title compounds **5**

Compound	Relative inhibitory ratio (%)							
	G. zeae	*A. solani*	*C. arachidicola*	*P. piricola*	*P. asparagi*	*C. cucumerinum*	*S. sclerotiorum*	*P. oryzae*
5a	66.8	72.6	79.2	56.7	68.4	89.3	78.1	77.7
5b	33.5	48.6	65.2	78.9	40.3	80.7	100	100
5c	23.9	19.7	37.5	47.6	19.1	23.0	65.3	78.6
5d	76.2	56.7	65.9	58.7	34.9	22.8	76.3	77.9
5e	39.9	49.1	54.7	37.8	59.1	60.7	69.7	39.9
5f	15.9	37.6	21.0	67.8	25.8	56.6	66.3	76.7
5g	38.7	56.2	10.5	37.8	46.9	68.7	74.3	65.1
5h	56.7	75.1	25.6	69.8	74.4	99.5	100	100
5i	57.5	47.9	26.8	32.2	37.5	87.6	95.3	76.8
5j	37.8	78.0	47.5	39.9	57.1	65.8	87.2	79.9
5k	47.8	39.8	37.7	47.8	57.6	76.7	81.0	89.9
5l	53.1	68.8	51.9	76.3	77.1	84.3	26.8	37.5
5m	65.0	47.9	59.2	38.9	57.0	100	69.5	45.8
5n	67.8	56.9	21.6	69.7	79.8	87.9	79.5	88.8
Triadimenol[a]	95.6	100	99.5	100	100	99.8	100	100

[a] 1-(4-Chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butan-2-ol.

General procedure for the synthesis of the title compounds 5

To a stirred solution of the intermediate **4** (0.0025) in MeOH (15 ml), 0.114 g (0.003 mol) $NaBH_4$ was added in batches over a period of 20 min at room temperature. The mixtures were stirred for another 6 h at room temperature, then 0.3 ml (0.0036 mol) 12 M HCl was added. After stirring for 2 h, a solution of 0.6 g (0.0072 mol) $NaHCO_3$ in 10 ml H_2O was added dropwise. After 1 h, the sol. was extracted with three 30 ml portions of Et_2O. The extract was washed with 10 ml H_2O, and then dried with anhydrous Na_2SO_4. After evaporation of Et_2O, the remaining solid was recrystallized from AcOEt–petroleum ether (60–90%, 1 : 3 v/v) or purified by silica gel column chromatography to give a yellow solid **5** and **6** in various yields.

*1-Ferrocenyl-4,4-dimethyl-2-(1H-1,2,4-triazol-1-yl)pent-1-en-3-ol (**5a**)*

Yield: 74.2%; yellow solid; m.p. 179–180C; ^{1}H NMR δ = 8.25 (s, 1H), 7.40 (s, 1H), 6.63 (s, 1H), 4.18 (s, 5H), 3.91 (s, 2H), 3.69 (s, 2H), 3.44 (d, J = 5.94 Hz, 1H), 1.66 (s, 1H), 0.76 (s, 9H) ppm. ^{13}C NMR: δ = 21.25 (CH_3), 71.74, 76.60 (C_5H_4), 77.02 (C_5H_4), 77.44 (C_5H_4), 127.98, 128.68, 152.67, 161.32 ppm. MS (EI): *m/z* (%), 365.15 ([M]$^+$, 100). Anal. calcd for $C_{19}H_{23}N_3OFe$: C 62.47; H 6.30; N 11.51. Found: C 62.46; H 6.33; N 11.46.

*1-Ferrocenyl-3-phenyl-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5b**)*

Yield: 75.1%; yellow solid; m.p. 158–159 °C. IR (KBr): ν = 3405.5, 3295.5, 3186.0 cm^{-1}. ^{1}H NMR δ: 8.02 (s, 1H), 7.60 (s, 1H), 7.18 (s, 5H), 6.49 (s, 1H), 5.50 (s, 1H), 4.12 (d, J = 3.86 Hz, 7H), 3.68 (s, 2H), 2.14 (s, 1H) ppm. ^{13}C NMR: δ = 71.72, 76.62 (C_5H_4), 77.03 (C_5H_4), 77.47 (C_5H_4), 127.99, 128.70, 128.94, 130.75, 133.13, 133.33, 152.63, 161.28 ppm. MS (EI): *m/z* (%), 385.09 ([M]$^+$, 100). Anal. calcd for $C_{21}H_{19}N_3OFe$: C 65.45; H 4.94; N 10.91. Found: C 65.25; H 4.74; N 10.74.

*1-Ferrocenyl-3-o-tolyl-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5c**)*

Yield: 75.2%; yellow solid; m.p. 164–165 °C. ^{1}H NMR δ = 8.00 (s, 1H), 7.56 (s, 1H), 7.07 (s, 4H), 6.59 (s, 1H), 5.54 (s, 1H), 4.16 (s, 7H), 3.66 (s, 2H), 2.56 (s, 1H), 2.26 (s, 3H) ppm. ^{13}C NMR: δ = 14.42, 71.74, 76.60 (C_5H_4), 77.02 (C_5H_4), 77.43 (C_5H_4), 125.68, 127.93, 128.65, 128.91, 130.72, 133.11, 133.30, 152.61, 161.26 ppm. MS (EI): *m/z* (%), 399 ([M]$^+$, 100). Anal. calcd for $C_{22}H_{21}N_3OFe$: C 66.16; H 5.26; N 10.53. Found: C 66.10; H 5.19; N 10.42.

*1-ferrocenyl-3-(4-methoxyphenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5d**)*

Yield: 76.3%; yellow solid; m.p. 196–199 °C. ^{1}H NMR δ = 8.07 (s, 1H), 7.66 (s, 1H), 7.30 (s, 4H), 6.66 (s, 1H), 5.55 (s, 1H), 4.05 (s, 6H), 3.87 (s, 3H), 3.80 (s, 3H), 2.53 (s, 1H) ppm. ^{13}C NMR: δ = 56.42, 71.76, 76.64 (C_5H_4), 77.07 (C_5H_4), 77.48 (C_5H_4), 125.70, 127.91, 128.69, 128.95, 130.76, 133.14, 147.32, 152.64, 161.28 ppm. MS (EI): *m/z* (%), 415.12 ([M]$^+$, 100). Anal. Calcd for $C_{22}H_{21}N_3O_2Fe$: C 63.61; H 5.06; N 10.12. Found: C 63.20; H 5.05; N 10.13.

*1-ferrocenyl-3-(2,5-dimethoxyphenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5e**)*

Yield: 76.7%; yellow solid; m.p. 201–203 °C. ^{1}H NMR δ = 8.13 (s, 1H), 7.72 (s, 1H), 6.83–7.28 (m, 3H), 6.57 (s, 1H), 5.38 (s, 1H), 4.22 (s, 7H), 3.81 (s, 6H), 3.48 (s, 2H) ppm. ^{13}C NMR: δ = 56.47, 54.38, 71.70, 76.62 (C_5H_4), 77.01 (C_5H_4), 77.43 (C_5H_4), 125.68, 127.89, 128.65, 128.91, 130.72, 146.50, 147.30, 152.62, 161.26 ppm. MS (EI): *m/z* (%), 445.11 ([M]$^+$, 100). Anal. calcd for $C_{23}H_{23}N_3O_3Fe$: C 62.76; H 5.49; N 9.42. Found: C 62.20; H 5.15; N 9.25.

*1-Ferrocenyl-3-(4-fluorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5f**)*

Yield: 69.9%; yellow solid; m.p. 126–128 °C. ^{1}H NMR δ = 8.21 (s, 1H), 7.85 (s, 1H), 7.49–7.62 (m, 4H), 6.78 (s, 1H), 5.68 (s, 1H), 4.21 (s, 2H), 3.92 (s, 5H), 3.79 (s, 2H) ppm. ^{13}C NMR: δ = 71.70, 76.63 (C_5H_4), 77.05 (C_5H_4), 77.49 (C_5H_4), 127.97, 128.72, 129.04, 130.86, 133.19, 158.79, 152.65, 161.30 ppm. MS (EI): *m/z* (%), 403.05 ([M]$^+$, 100). Anal. Calcd for $C_{21}H_{18}N_3OFFe$: C 63.33; H 4.83; N 10.07. Found: C 63.20; H 5.05; N 10.13.

*1-Ferrocenyl-3-(2, 4-difluorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5g**)*

Yield: 77.9%; yellow solid; m.p. 165–166 °C. ^{1}H NMR δ: 8.31 (s, 1H), 8.04 (s, 1H), 7.27–7.62 (m, 3H), 6.79 (s, 1H), 5.59 (s, 1H), 4.36 (s, 2H), 4.25 (s, 5H), 3.84 (s, 2H), 2.86 (s, 1H) ppm. ^{13}C NMR: δ = 71.73, 76.65 (C_5H_4), 77.06 (C_5H_4), 77.47 (C_5H_4), 127.92, 128.76, 139.14, 137.76, 136.28, 139.78, 157.68, 158.67, 152.64, 161.32 ppm. MS (EI): *m/z* (%): 421.07 ([M]$^+$, 100). Anal. calcd for $C_{21}H_{17}N_3OF_2Fe$: C 59.88; H 4.07; N 9.98. Found: C 59.60; H 4.16; N 10.20.

*1-Ferrocenyl-3-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5h**)*

Yield: 73.9%; yellow solid; m.p. 164–165 °C. ^{1}H NMR δ: 8.16 (s, 1H), 7.79 (s, 1H), 7.58 (d, J = 4.20 Hz, 2H), 7.33 (d, J = 4.42 Hz, 2H), 6.69 (s, 1H), 5.56 (s, 1H), 4.59 (s, 5H), 4.15 (s, 5H), 3.86 (s, 2H), 3.67 (s, 2H) ppm. ^{13}C NMR: δ = 71.74, 76.61 (C_5H_4), 77.04 (C_5H_4), 77.47 (C_5H_4), 127.95, 128.74, 128.87, 128.99, 131.17, 148.72, 152.63, 161.28 ppm. MS (EI): *m/z* (%), 419 ([M]$^+$, 100). Anal. Calcd for $C_{21}H_{18}N_3OClFe$: C 60.07; H 4.29; N 10.01. Found: C 60.15; H 4.18; N 10.15.

*1-Ferrocenyl-3-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5i**)*

Yield: 76.8%; yellow solid; m.p. 159–160 °C. ^{1}H NMR δ = 8.05 (s, 1H), 7.75 (s, 1H), 7.07–7.43 (m, 3H), 6.62 (s, 1H), 5.47 (s, 1H), 4.22 (s, 2H), 4.13 (s, 5H), 3.72 (s, 2H), 1.83 (s, 1H) ppm. ^{13}C NMR: δ = 71.72, 76.63 (C_5H_4), 77.04 (C_5H_4), 77.45 (C_5H_4), 127.90, 128.74, 129.14, 130.79, 132.27, 136.71, 145.62, 148.65, 152.62, 161.30 ppm. MS (EI): *m/z* (%), 453.01 ([M]$^+$, 100). Anal. Calcd for $C_{21}H_{17}N_3OCl_2Fe$: C 55.54; H 3.77; N 9.25. Found: C 55.28; H 3.78; N 9.38.

*1-ferrocenyl-3-(2,5-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5j**)*

Yield: 75.7%; yellow solid; m.p. 162–164 °C. ^{1}H NMR δ = 8.01 (s, 1H), 7.68 (s, 1H), 7.00–7.36 (m, 3H), 6.48 (s, 1H), 5.36 (s, 1H), 4.18 (s, 2H), 4.09 (s, 5H), 3.63 (s, 2H), 1.96 (s, 1H) ppm. ^{13}C NMR: δ = 71.73, 76.62 (C_5H_4), 77.01 (C_5H_4), 77.43 (C_5H_4), 127.92, 128.73, 129.10, 130.71, 132.23, 136.69, 145.57, 148.61, 152.60, 161.32 ppm. MS (EI): *m/z* (%), 453.01 ([M]$^+$, 100). Anal. Calcd for $C_{21}H_{17}N_3OCl_2Fe$: C 55.54; H 3.77; N 9.25. Found: C 55.31; H 3.75; N 9.53.

1-Ferrocenyl-3-(3, 4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5k**)

Yield: 73.1%; yellow solid; m.p. 161–163 °C. ^{1}H NMR δ = 7.92 (s, 1H), 7.63 (s, 1H), 6.95–7.26 (m, 3H), 6.54 (s, 1H), 5.39 (s, 1H), 4.16 (s, 2H), 4.08 (s, 5H), 3.54 (s, 2H), 2.69 (s, 1H) ppm. ^{13}C NMR: δ = 71.75, 76.64 (C_5H_4), 77.03 (C_5H_4), 77.42 (C_5H_4), 127.90, 128.71, 129.09, 130.74, 132.21, 136.67, 145.55, 148.58, 152.62, 161.37 ppm. MS (EI): *m/z* (%): 453.01 ([M]$^+$, 100). Anal. calcd for $C_{21}H_{17}N_3OCl_2Fe$: C 55.54; H 3.77; N 9.25. Found: C 55.41; H 3.86; N 9.45.

1-Ferrocenyl-3-(3-bromophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5l**)

Yield: 76.4%; yellow solid; m.p. 154–156 °C. ^{1}H NMR δ = 8.16 (s, 1H), 7.83 (s, 1H), 7.10–7.35 (m, 4H), 6.73 (s, 1H), 5.56 (s, 1H), 4.56 (s, 1H), 4.20 (s, 5H), 3.76 (s, 2H), 3.69 (s, 2H) ppm. ^{13}C NMR: δ = 71.73, 76.62 (C_5H_4), 77.01 (C_5H_4), 77.45 (C_5H_4), 127.90, 128.76, 129.04, 130.68, 133.19, 143.37, 152.61, 161.26 ppm. MS (EI): *m/z* (%), 463 ([M]$^+$, 100). Anal. calcd for $C_{21}H_{18}N_3OBrFe$: C 54.31; H 3.88; N 9.05. Found: C 54.14; H 3.92; N 8.95.

1-Ferrocenyl-3-(4-bromophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5m**)

Yield: 73.8%; yellow solid; m.p. 175–177 °C. ^{1}H NMR δ = 8.02 (s, 1H), 7.83 (s, 1H), 7.60 (d, J = 4.16 Hz, 2H), 7.30 (d, J = 4.36 Hz, 2H), 6.69 (s, 1H), 5.54 (s, 1H), 4.57 (s, 1H), 4.16 (s, 5H), 3.80 (s, 2H), 3.64 (s, 2H) ppm. ^{13}C NMR: δ = 71.73, 76.63 (C_5H_4), 77.02 (C_5H_4), 77.43 (C_5H_4), 127.93, 128.71, 128.81, 128.92, 131.10, 143.68, 152.62, 161.26 ppm. MS (EI): *m/z* (%), 463 ([M]$^+$, 100). Anal. calcd for $C_{21}H_{18}N_3OBrFe$: C 54.31; H 3.88; N 9.05. Found: C 54.36; H 3.68; N 8.79.

1-Ferrocenyl-3-(3-nitrophenyl)-2-(1H-1,2,4-triazol-1-yl)prop-2-en-1-ol (**5n**)

Yield: 78.9%; yellow solid; m.p. 164–165 °C. IR (KBr): ν = 3402.2, 3266.0, 3091.0, cm^{-1}. ^{1}H NMR δ: 8.12 (s, 1H), 7.63 (s, 1H), 7.23–7.88 (m, 4H), 6.63 (s, 1H), 5.66 (s, 1H), 5.49 (s, 5H), 3.91 (s, 2H), 3.76 (s, 2H), 2.55 (s, 1H) ppm. ^{13}C NMR: δ = 71.71, 76.64 (C_5H_4), 77.05 (C_5H_4), 77.41 (C_5H_4), 127.92, 128.78, 133.79, 138.64, 140.62, 145.87, 147.62, 148.98, 152.63, 161.28 ppm. MS (EI): *m/z* (%), 430 ([M]$^+$, 100). Anal. Calcd for $C_{21}H_{18}N_4O_3Fe$: C 58.60; H 4.19; N 13.02. Found: C 58.50; H 4.25; N 13.07.

1-(1-Ferrocenyl-3-methoxy-3-phenylprop-1-en-2-yl)-1H-1,2,4-triazole (**6a**)

Yield: 27.1%; yellow solid; m.p. 145–147 °C; ^{1}H NMR: δ = 3.46 (s, 3H, OCH_3), 3.63 (s, 1H, FcH), 3.71 (s, 1H, FcH), 4.12 (s, 5H, FcH), 4.18 (s, 2H, FcH), 4.98 (s, 1H, CH), 6.62 (s, 1H, ═CH), 6.97–7.04 (m, 2H, PhH), 7.18–7.23 (m, 2H, PhH), 7.61 (s, 1H, TrH), 8.08 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.23 (OCH_3), 75.72, 76.63 (C_5H_4), 77.01 (C_5H_4), 77.47 (C_5H_4), 115.78, 115.49, 128.25, 128.43, 133.87, 161.03, 162.28, 164.25 ppm. MS (EI): *m/z* (%), 417.09 ([M]$^+$, 100). Anal. calcd for $C_{22}H_{20}FFeN_3O$: C, 63.33; H, 4.83; N, 10.07. Found: C, 63.33; H, 4.99; N, 10.31.

1-[1-Ferrocenyl-3-methoxy-3-(4-chlorophenyl)prop-1-en-2-yl]-1H-1,2,4-triazole (**6b**)

Yield: 25.3%; yellow solid; m.p. 161–163 °C; ^{1}H NMR δ = 3.45 (s, 3H, OCH_3), 3.65 (s, 2H, C_5H_4), 3.83 (s, 5H, C_5H_4), 4.12 (s, 2H, C_5H_4), 5.01 (s, 1H, CH), 6.60 (s, 1*H*, ═CH), 7.00 (d, J = 8.4 Hz, 2H, ArH), 7.25 (d, J = 8.7 Hz, 2H, ArH), 7.68 (s, 1H, TrH), 8.03 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.26 (OCH_3), 75.71, 76.61 (C_5H_4), 77.00 (C_5H_4), 77.45 (C_5H_4), 115.73, 115.42, 128.12, 128.40, 133.79, 159.78, 162.25, 164.17 ppm. MS (EI): *m/z* (%), 433 ([M]$^+$, 100). Anal. Calcd for $C_{22}H_{20}ClFeN_3O$: C, 60.92; H, 4.65; N, 9.69. Found: C, 60.75; H, 4.86; N, 10.03.

1-(1-Ferrocenyl-3-methoxy-3-(4-bromophenyl)prop-1-en-2-yl)-1H-1,2,4-triazole (**6c**)

Yield: 26.6%; yellow solid; m.p. 179–181 °C; ^{1}H NMR δ = 3.44 (s, 3H, OCH_3), 3.62 (s, 2H, C_5H_4), 3.83 (s, 5H, C_5H_4), 4.11 (s, 2H, C_5H_4), 5.00 (s, 1H, CH), 6.59 (s, 1*H*, ═CH), 7.68 (d, J = 8.1 Hz, 2H, ArH), 7.20 (d, J = 8.4 Hz, 2H, ArH), 7.69 (s, 1H, TrH), 8.02 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.24 (OCH_3), 75.73, 76.60 (C_5H_4), 77.00 (C_5H_4), 77.44 (C_5H_4), 115.75, 115.41, 128.10, 128.37, 133.75, 159.73, 162.24, 164.15 ppm. MS (EI): *m/z* (%), 477 ([M]$^+$, 100). Anal. Calcd for $C_{22}H_{20}BrFeN_3O$: C, 55.26; H, 4.22; N, 8.79. Found: C, 55.41; H, 4.37; N, 8.99.

1-(1-Ferrocenyl-3-methoxy-3-(3,4-dicholorophenyl)prop-1-en-2-yl)-1H-1,2,4-triazole (**6d**)

Yield: 21.9%; yellow solid; m.p. 163–165 °C; ^{1}H NMR δ = 3.47 (s, 3H, OCH_3), 3.66 (s, 2H, C_5H_4), 3.85 (s, 5H, C_5H_4), 4.14 (s, 2H, C_5H_4), 5.05 (s, 1H, CH), 6.61 (s, 1*H*, ═CH), 7.18–7.27 (m, 3H, ArH), 7.69 (s, 1H, TrH), 8.05 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.25 (OCH_3), 75.71, 76.61 (C_5H_4), 77.02 (C_5H_4), 77.45 (C_5H_4), 115.72, 115.40, 128.08, 128.36, 133.73, 159.69, 162.22, 164.11 ppm. MS (EI): *m/z* (%), 467 ([M]$^+$, 100). Anal. calcd for $C_{22}H_{19}Cl_2FeN_3O$: C, 56.44; H, 4.09; N, 8.99. Found: C, 56.21; H, 3.92; N, 9.18.

1-(1-Ferrocenyl-3-methoxy-3-(2,4-difluorophenyl)prop-1-en-2-yl)-1H-1,2,4-triazole (**6e**)

Yield: 23.2%; yellow solid; m.p. 172–174 °C; ^{1}H NMR δ = 3.52 (s, 3H, OCH_3), 3.67 (s, 2H, C_5H_4), 3.90 (s, 5H, C_5H_4), 4.18 (s, 2H, C_5H_4), 5.09 (s, 1H, CH), 6.66 (s, 1*H*, ═CH), 7.25–7.38 (m, 3H, ArH), 7.70 (s, 1H, TrH), 8.11 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.21 (OCH_3), 75.69, 76.60 (C_5H_4), 77.00 (C_5H_4), 77.42 (C_5H_4), 115.66, 115.35, 128.01, 128.32, 133.69, 159.61, 162.19, 164.07 ppm. MS (EI): *m/z* (%), 435.08 ([M]$^+$, 100). Anal. calcd for $C_{22}H_{19}F_2FeN_3O$: C, 60.71; H, 4.40; N, 9.65. Found: C, 60.83; H, 4.51; N, 9.71.

1-(1-Ferrocenyl-3-methoxy-3-(2,5-dicholorophenyl)prop-1-en-2-yl)-1H-1,2,4-triazole (**6f**)

Yield: 25.8%; yellow solid; m.p. 164–166C; ^{1}H NMR δ = 3.48 (s, 3H, OCH_3), 3.65 (s, 2H, C_5H_4), 3.87 (s, 5H, C_5H_4), 4.15 (s, 2H, C_5H_4), 5.06 (s, 1H, CH), 6.62 (s, 1*H*, ═CH), 7.19–7.29 (m, 3H, ArH), 7.68 (s, 1H, TrH), 8.06 (s, 1H, TrH) ppm. ^{13}C NMR: δ = 57.22 (OCH_3), 75.70, 76.63 (C_5H_4), 77.06 (C_5H_4), 77.45 (C_5H_4), 115.69, 115.41, 128.11, 128.37, 133.74, 159.66, 162.23, 164.12 ppm. MS (EI): *m/z* (%), 467.03 ([M]$^+$, 100). Anal. calcd for $C_{22}H_{19}Cl_2FeN_3O$: C, 56.44; H, 4.09; N, 8.99. Found: C, 56.31; H, 3.89; N, 9.01.

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References

[1] Eweiss NF, Bahajaj AA, Elsherbini EA. *J. Heterocyclic Chem.* 1986; **23**: 1451; b) Gasztonyi M, Josepovits G. *Pestic. Sci.* 1984; **15**: 48; c) Ikizler AA, Ucar F, Demirbas N, Yasa I, Ikizler A, Genzer T. *Indian J. Het. Chem.* 1999; **61**: 271; d) Walser A, Flynn T, Mason C. *J. Het. Chem.* 1991; **28**: 1121; e) Demirbs N, Demirbas AU. *Bioorg. Med. Chem.* 2002; **10**: 3717; f) Emilsson H, Salender H, Gaarder J. *Eur. J. Med. Chem. Chim. Ther.* 1985; **21**: 333; g) Manas MM, Arredondo Y, Pleixats R, Teixido M, Haga MM, Palacin C, Castello JM, Oritizz JA. *J. Heterocyclic Chem.* 1992; **29**: 1557; h) Rhaimini AE, Mornet R. *Indian. J. Heterocyclic Chem.* 1992; **29**: 1561.

[2] Chu CH, Hui XP, Sun L, Zhang Y, Zhang Z, Li ZC, Liao RA. *J. Chin. Chem. Soc.* 2001; **8**: 121; b) Takano H, Oguri Y, Kato T. *J. Pestic. Sci.* 1983; **8**: 572; c) Izumi K, Yamaguchi I, wada A, Oshio H, Takahashi N. *Plant Cell Physiol.* 1984; **25**: 611.

[3] Buchenauer H. *J. Plant. Dis. Protect.* 1979; **10**: 341; b) Buchenauer H. *Proc. Br. Crop. Protect. Conf.* 1977; **2**: 699; c) Hui XP, Zhang Y, Xu PF, Wang Q, Zhang ZY. *Chin. J. Org. Chem.* 2005; **25**: 700.

[4] Motohashi N, Meyer R, Gollapudi SR. *J. Organomet. Chem.* 1990; **398**: 205; b) Allardyce CS, Dorcier A, Scolaro C, Dyson PJ. *Appl. Organomental. Chem.* 2005; **9**: 1; c) Fang JX, Jin Z, Liu T, Liu W. *Appl. Organomental. Chem.* 2003; **17**: 145; d) Jin Z, Huo AH, Liu T, Hu Y, Liu JB, Fang JX. *J. Organomet. Chem.* 2005; **690**: 1226; e) Michelotti EL, Le DP, Carlson GR, Egan AR, *US Patent* 5075471 1991; f) Fang JX, Jin Z, Liu T, Liu W. *J. Organomet. Chem.* 2003; **674**: 1.

[5] Liu JB, Li LC, Dai H, Liu T, Fang JX. *J. Organomet. Chem.* 2006; **691**: 2686.

[6] Hill GA. *J. Am. Chem. Soc.* 1993; **55**: 2509; b) Widman O. *Ber.* 1991; **44**: 2605.

[7] Tang J. *Synthetic Commun.* 2000; **30**: 1657.

[8] Liu JB, Dai H, Li LC, Tao WF, Fang JX. *Acta Crystallogr.* 2005; **61**: m2166.

[9] Gasztonyi M, Josepovits G. *Pestic. Sci.* 1979; **10**: 57.

