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Synthesis, Controlled Release Properties, and Increased Antifungal Activities of Novel *cis*- and *trans*-Racemate Complexes of Propiconazole

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Twenty novel metal complexes M^1(*cis*-L)$_2Y_2$, M^1(*trans*-L)$_2Y_2$, M^2(*cis*-L)$_4Y_2$, and M^2(*trans*-L)$_4Y_2$ (M^1 = Zn(II), Co(II), Cu(II); M^2 = Mn(II), Ni(II); *Y* = OAc, Cl, ClO_4, and NO_3) were synthesized by reacting bivalent transitional metal salt $MY_2 \cdot nH_2O$ ($n = 0-6$) with ligands *cis*-racemate of propiconazole (*cis*-L) and *trans*-racemate of propiconazole (*trans*-L), respectively. All of these synthesized complexes were identified by atomic absorption spectrometry, elemental analysis, and IR and UV spectra. The cumulative release studies of some selected complexes in static water were performed; all determined complexes were found to exhibit attractive controlled release properties, yet the ligand release rates of *cis*-L complexes were slower than those of *trans*-L complexes. Meanwhile, it was found that the release rate of ligand *cis*-L from representative complex Zn(*cis*-L)$_2Cl_2$ was affected obviously by different conditions, such as temperature, pH, and PVA film coating. The antifungal activities of the ligands and their complexes against five selected plant pathogenic fungi were evaluated; the results demonstrated that the toxicity of *cis*-L was 3.39−5.95 times greater than that of *trans*-L, and all of the synthesized complexes showed superior activities of 1.19−6.36 times to those of their ligands, especially Zn complexes having toxicities 2.62−6.36 times greater than those of their ligands. Moreover, the *cis*-L complexes had more sensitive activities than their relevant *trans*-L complexes; for example, Zn(*cis*-L)$_2Cl_2$ appeared to be 5.00−8.67 times stronger than Zn(*trans*-L)$_2Cl_2$ complex. In addition, the mechanism of increased antifungal activities of the title complexes in comparison with their ligands was discussed preliminarily.

KEYWORDS: Metal complex; *cis*-racemate; *trans*-racemate; propiconazole; synthesis; controlled release; antifungal activity

INTRODUCTION

Structure modification of conventional pesticides can produce more multifunctional and all-purpose compounds, and it has captured the extensive interests of chemists. Thereinto, controlled release technology (*1*−*3*) presents advantages over the conventional applications of pesticides (*4*) and has become a research focus within this field. Complexation of effective pesticides with metal salt as a technique can obtain more novel compounds for controlled release (*5, 6*). For example, the reaction of the pesticides diarinon and chlorpyrifos [ligand (L)] with cobalt or copper salt [metal (M); counterion (X)] afforded complexes (*7*) having the molecular formula ML_2X_2, and the bioassay indicated that two obtained complexes showed 100% toxicity for up to 20−22 weeks, whereas the ligands diazinon or chlorpyrifos alone showed 100% toxicity for only up to 4−8 weeks. In addition, the application of mancozeb (*8*) and krecalvin (*9*) also made people realize the complexes can enhance toxicities in comparison with their ligands.

Propiconazole is a systemic fungicide (*10, 11*) for controlling harmful microorganisms and for preventing fungus attack, especially in seed dressing (*12*). Its chemical name is 1-[2-(2,4-dichlorophenyl)-4-*n*-propyl-1,3-dioxolan-2-ylmethyl]-1*H*-1,2,4-triazole. Potent bioactivity of propiconazole is related to its complicated molecular configuration. It contains two asymmetric carbon atoms on its dioxolan, which produce four pure enantiomers including *cis*-racemate and *trans*-racemate. The *cis*-racemate contains the pair of enantiomers having the 2*R*,4*S*- and 2*S*,4*R*-configurations, and the *trans*-racemate contains the pair of enantiomers having the 2*S*,4*S*- and 2*R*,4*R*-configurations (*13*). The four pure enantiomers exhibit different levels of activities as foliar fungicides and can be placed in the following order according to the degree of their activities: 2*S*,4*R* > 2*S*,4*S* > 2*R*,4*S* > 2*R*,4*R* (*12*). Reports of complexes of propiconazole are quite infrequent; only five metal complexes of general propiconazole have been studied (*14, 15*). In this study, 20 novel metal complexes of *cis*-racemate and *trans*-racemate of propiconazole were introduced. The controlled release properties and antifungicidal activities of both racemates and their complexes with various metal ions were investigated. These studies are

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Table 1. Melting Points and Yields of the Title Complexes

compd	formula	appearance	mp (°C)	yield (%)
1a	Zn(*cis*-L)$_2$Cl$_2$	white solid	163.9−164.1	84.1
1b	Zn(*cis*-L)$_2$(NO$_3$)$_2$	white solid	107.8−108.2	79.4
1c	Co(*cis*-L)$_2$Cl$_2$	blue solid	174.5−176.5	78.3
1d	Co(*cis*-L)$_2$(NO$_3$)$_2$	rosy solid	106.7−108.4	72.7
1e	Ni(*cis*-L)$_4$Cl$_2$	glaucous solid	120.1−120.7	63.9
1f	Ni(*cis*-L)$_4$(OAc)$_2$	glaucous solid	139.4−140.7	42.1
1g	Mn(*cis*-L)$_4$Cl$_2$	white solid	107.6−108.1	67.4
1h	Cu(*cis*-L)$_2$Cl$_2$	blue solid	182.3−184.4	25.2
1i	Cu(*cis*-L)$_2$(OAc)$_2$	blue solid	99.2−99.8	65.3
1j	Cu(*cis*-L)$_2$(ClO$_4$)$_2$	sky-blue solid	181.6−181.2	69.1
1k	Cu(*cis*-L)$_2$(NO$_3$)$_2$	blue solid	178.8−179.1	34.6
1m	Cu(*cis*-L)$_2$(C$_2$O$_4$)$_2$	sky-blue solid	241.2−243.3	67.4
2a	Zn(*trans*-L)$_2$Cl$_2$	white solid	124.6−125.7	80.1
2c	Co(*trans*-L)$_2$Cl$_2$	rosy solid	91.7−93.2	62.5
2e	Ni(*trans*-L)$_4$Cl$_2$	glaucous solid	115.6−116.7	58.7
2g	Mn(*trans*-L)$_4$Cl$_2$	white solid	102.0−103.8	55.9
2h	Cu(*trans*-L)$_2$Cl$_2$	blue solid	172.6−174.5	26.1
2i	Cu(*trans*-L)$_2$(OAc)$_2$	blue solid	108.2−109.0	38.9
2j	Cu(*trans*-L)$_2$(ClO$_4$)$_2$	sky-blue solid	160.0−161.7	53.6
2k	Cu(*trans*-L)$_2$(NO$_3$)$_2$	blue solid	184.8−185.2	22.5

intended to provide fundamental information for the production of environmentally friendly and more effective propiconazole complex fungicides.

MATERIALS AND METHODS

Materials. The general propiconazole was synthesized according to previously reported methods (*12*, *16*, *17*). All of the chemicals were of analytical or HPLC reagent grade and were used as received. Pressed KBr plates were used for IR measurements within the range of 400−4000 cm^{-1} with a Bruker Tensor 27 FT-IR spectrometer. Melting points were taken on a WRS-1B digital melting-point apparatus. UV spectra were recorded on a UV-160A UV spectrophotometer. C, H, N, and metal ion analyses of the title complexes were executed with an Elementar Vario III element analyzer and a Hitachi 180-80 polarized zeeman atomic absorption spectrophotometer, respectively. *cis*-Racemate and *trans*-racemate of propiconazole were determined by HPLC of Waters (2487 ultraviolet absorption detector, 515 volumetric infusion pump).

Preparation of *cis*-L and *trans*-L. The *cis*-L and *trans*-L were separated from general propiconazole by column chromatography (*12*, *18*); the preferred solvent was an isopropyl alcohol and petroleum ether mixture (1:9, v/v) (*18*). After separation, the racemates were detected by TLC and HPLC (*18*−*20*) (using an ODS C18 column; methanol/water (80:20, v/v) as mobile phase); the result showed the isomerics can be separated completely.

Synthesis of the Title Complexes. The *cis*-L complexes were prepared by adding EtOH or MeOH solution of $MY_2 \cdot nH_2O$ (M = Mn(II), Co(II), Ni(II), Cu(II) and Zn(II); Y = OAc, Cl, ClO_4, and NO_3; and n = 0−6) to EtOH or MeOH solution of *cis*-L (*21*−*25*) with stirring at refluxing temperature, and the reaction solution was further stirred under refluxing for 3−6 h. After cooling, the formed complex was filtered off, washed several times with EtOH or MeOH, and dried under vacuum. Then the solid complexes of **1a**−**1m** (**Table 1**) were obtained. The *trans*-L complexes were synthesized according to above method, but all of the *trans*-L complexes were highly viscous liquids after reaction except the complexes of $ZnCl_2$, by recrystallization from a mixture of ethyl acetate and petroleum ether (1:4, v/v) to yield solid **2a**−**2k** (**Table 1**). All of the complexes were prepared by *cis*-L or *trans*-L with metal salts in 2:1 molar ratios except the complexes of Mn(II) and Ni(II), for which the molar ratios were 4:1. From the result of the experiment, we found the reaction ability of *trans*-L and the yields of its complexes were lower than those of *cis*-L and its relevant complexes (**Table 1**); this result may be ascribed to the different binding abilities, which were caused by the difference in the steric hindrance effect between *cis*-L and *trans*-L (*26*).

Table 3. Atomic Absorption Spectrometry and Element Analysis Data of the Title Complexes

compd	C (%)	H (%)	N (%)	M (%)
1a	43.84 (43.90)[a]	4.21 (4.18)	10.46 (10.24)	8.01 (7.97)
1b	41.19 (41.23)	3.92 (3.92)	12.76 (12.82)	7.58 (7.49)
1c	44.20 (44.25)	4.22 (4.21)	10.52 (10.32)	7.31 (7.24)
1d	41.46 (41.54)	4.01 (3.95)	12.99 (12.92)	6.59 (6.79)
1e	47.91 (48.09)	4.51 (4.57)	11.31 (11.22)	4.01 (3.92)
1f	49.81 (49.73)	4.75 (4.83)	10.79 (10.87)	3.90 (3.80)
1g	48.28 (48.21)	4.48 (4.59)	11.19 (11.25)	3.76 (3.68)
1h	43.90 (44.00)	4.15 (4.18)	10.45 (10.26)	7.81 (7.76)
1i	47.23 (47.15)	4.57 (4.66)	9.79 (9.70)	7.32 (7.34)
1j	37.92 (38.05)	3.64 (3.62)	8.91 (8.88)	6.68 (6.71)
1k	41.35 (41.32)	3.81 (3.93)	12.91 (12.85)	7.34 (7.29)
1m	44.11 (44.19)	3.79 (3.71)	9.15 (9.10)	6.82 (6.88)
2a	43.85 (43.90)	4.20 (4.18)	10.44 (10.24)	8.12 (7.97)
2c	44.18 (44.25)	4.23 (4.21)	10.49 (10.32)	7.39 (7.24)
2e	48.10 (48.09)	4.41 (4.57)	11.35 (11.22)	4.11 (3.92)
2g	48.14 (48.21)	4.49 (4.59)	11.20 (11.25)	3.89 (3.80)
2h	43.85 (44.00)	4.20 (4.18)	10.43 (10.26)	7.82 (7.76)
2i	47.20 (47.15)	4.65 (4.66)	9.66 (9.70)	7.42 (7.34)
2j	37.94 (38.05)	3.51 (3.62)	8.80 (8.88)	6.70 (6.71)
2k	41.21 (41.32)	3.83 (3.93)	12.90 (12.85)	7.35 (7.29)

[a] The theoretical data are in parentheses.

Controlled Release of Title Complexes. The cumulative release of some representative *cis*-L and *trans*-L complexes in static water and the *cis*-L release rate of the complex **1a** under different conditions (influence of temperature and pH and the effect of PVA film coating) were also studied.

Release Assay for Some cis-L Complexes and Relevant trans-L Complexes. The complexes **1a**, **1c**, **1e**, **2a**, **2c**, and **2e** (25 mg every sample) were placed, respectively, in 25 mL of distilled water (pH 6, 25 °C) in a beaker with film to minimize loss of water by evaporation and then allowed to stand at room temperature (*7*). After the desired time had elapsed (6, 12, 24, 48, and 96 h), *cis*-L or *trans*-L released in each beaker was extracted with ether (25 mL). After complete ether volatilization, the extract was diluted to 100 mL in a standard flask with methanol and distilled water (80:20, v/v). The extracts were analyzed for *cis*-L or *trans*-L content by HPLC using calibration curves obtained from standard samples. All release tests were performed in triplicate.

Table 2. UV and IR Spectral Data of the Title Complexes

compd	λ_{max} (nm)	ν (cm^{-1})	compd	λ_{max} (nm)	ν (cm^{-1})
cis-L	208	3109, 2960, 1585, 1507, 1464, 1139	**1j**	204	3140, 2961, 1586, 1532, 1466, 1122
trans-L	205	3108, 2960, 1584, 1506, 1466, 1138	**1k**	205	3140, 2962, 1586, 1534, 1466, 1127
1a	205	3118, 2962, 1587, 1533, 1467, 1133	**1m**	205	3151, 2961, 1587, 1533, 1465, 1132
1b	205	3118, 2962, 1588, 1533, 1468, 1133	**2a**	203	3116, 2961, 1587, 1533, 1466, 1133
1c	204	3115, 2962, 1587, 1529, 1467, 1131	**2c**	203	3139, 2961, 1588, 1526, 1466, 1130
1d	204	3115, 2961, 1585, 1530, 1466, 1131	**2e**	202	3139, 2962, 1587, 1520, 1465, 1129
1e	205	3146, 2962, 1586, 1529, 1466, 1130	**2g**	203	3134, 2961, 1587, 1520, 1465, 1131
1f	205	3149, 2962, 1586, 1526, 1467, 1130	**2h**	203	3147, 2961, 1587, 1528, 1466, 1126
1g	205	3136, 2961, 1586, 1516, 1465, 1131	**2i**	202	3136, 2961, 1587, 1529, 1466, 1126
1h	205	3152, 2961, 1586, 1527, 1465, 1122	**2j**	202	3127, 2961, 1587, 1529, 1466, 1122
1i	204	3160, 2961, 1585, 1531, 1465, 1128	**2k**	203	3125, 2961, 1587, 1525, 1466, 1130

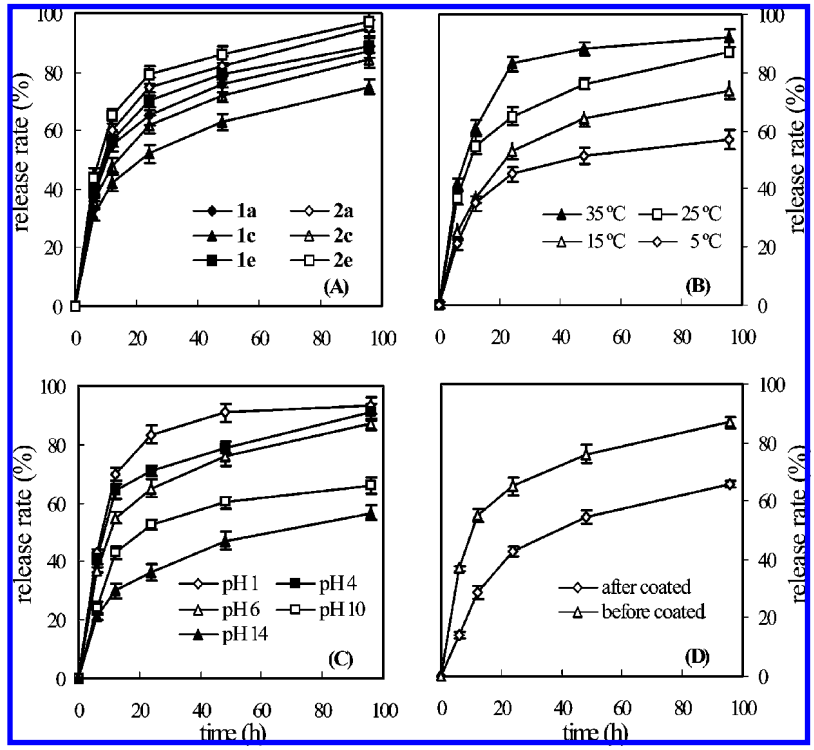

Figure 1. Release profiles of (**A**) ligands from complexes in static water (pH 6) at 25 °C, (**B**) *cis*-L from**1a** at different temperatures, (**C**) *cis*-L from **1a** at different pH values, and (**D**) *cis*-L from **1a** after coating.

Table 4. EC_{50} Values[a] of *cis*-L, *trans*-L, and Their Metal Complexes against Plant Pathogenic Fungi

compd	*R. cerealis*	*G. zeae*	*C. orbiculare*	*F. moniliforme*	*B. cinerea*
cis-L	0.936 ± 0.085	0.775 ± 0.046	0.707 ± 0.061	0.423 ± 0.018	0.889 ± 0.097
trans-L	4.124 ± 0.278	4.607 ± 0.401	3.063 ± 0.189	1.437 ± 0.143	3.359 ± 0.192
1a	0.157 ± 0.010	0.194 ± 0.014	0.106 ± 0.007	0.110 ± 0.009	0.212 ± 0.011
1b	0.147 ± 0.008	0.192 ± 0.011	0.103 ± 0.009	0.107 ± 0.004	0.218 ± 0.010
1c	0.230 ± 0.016	0.251 ± 0.022	0.151 ± 0.013	0.190 ± 0.017	0.291 ± 0.019
1e	0.425 ± 0.034	0.345 ± 0.017	0.357 ± 0.021	0.217 ± 0.016	0.329 ± 0.023
1g	0.601 ± 0.042	0.444 ± 0.028	0.306 ± 0.018	0.352 ± 0.012	0.609 ± 0.021
1h	0.424 ± 0.031	0.308 ± 0.016	0.419 ± 0.023	0.164 ± 0.011	0.433 ± 0.028
1i	0.423 ± 0.021	0.300 ± 0.019	0.417 ± 0.033	0.171 ± 0.013	0.420 ± 0.022
1j	0.423 ± 0.019	0.303 ± 0.011	0.416 ± 0.022	0.168 ± 0.009	0.430 ± 0.026
1k	0.421 ± 0.023	0.296 ± 0.015	0.411 ± 0.018	0.164 ± 0.011	0.428 ± 0.022
2a	0.946 ± 0.087	1.683 ± 0.097	0.654 ± 0.045	0.549 ± 0.024	1.156 ± 0.101
2c	1.602 ± 0.110	1.773 ± 0.078	1.319 ± 0.102	0.717 ± 0.049	1.387 ± 0.012
2e	1.898 ± 0.077	1.832 ± 0.132	1.521 ± 0.089	0.887 ± 0.042	1.787 ± 0.122
2g	2.337 ± 0.146	2.047 ± 0.109	1.707 ± 0.098	0.907 ± 0.065	2.306 ± 0.965
2h	1.965 ± 0.111	2.040 ± 0.137	1.311 ± 0.097	1.012 ± 0.069	1.639 ± 0.043

[a] Values (μg/mL) are the mean ± SD of three replicates.

Influence of Temperature on Release. The selected temperatures were in the range that is common under agricultural conditions. A similar procedure as above-described was carried out, but the release process of *cis*-L from **1a** was determined under controlled temperature (5, 15, 25, and 35 °C, respectively) in distilled water having a pH value of about 6.

Influence of pH on Release. Using the method described above, the release rate pattern of *cis*-L from **1a** was measured under controlled pH (1, 4, 6, 10, and 14, respectively) at 25 °C.

Influence of PVA Coating on Release. PVA (2.0 g) was dissolved into distilled water (38 g) with stirring at 75 °C until PVA was completely dissolved; the resulting PVA solution was then cooled to room temperature. **1a** (0.2 g) was dissolved in 10 mL of EtOH solution and then added into the PVA solution with stirring for 2 h (*27*, *28*). After coating, the mixture was dried at 50 °C in an oven to give **1a** with a film coating. The release rate data of *cis*-L from **1a** with film coating were recorded by using the above method.

Method of Bioassay. *Antifungal Activities of cis-L, trans-L, and Their Complexes.* The antifungal activities of *cis*-L, *trans*-L, and their 14 representative complexes against the plant fungi (*Gibberella zeae*, *Colletotrichum orbiculare*, *Botrytis cinerea*, *Rhizoctonia cerealis*, and *Fusarium moniliforme*) were tested using a radial growth inhibition technique according to the literature (*14*). The complexes and ligands were diluted by starch and ground into dust, then added to potato dextrose agar (PDA) medium, respectively, to obtain a range of concentrations (0.03125, 0.125, 0.5, 2, and 8 μg/mL) immediately before pouring into the Petri dishes (9.0 cm in diameter). Each concentration was tested in triplicate. Parallel controls were maintained with starch mixed with PDA medium. The disks of mycelial felt (0.5 cm diameter) of the plant pathogenic fungi were transferred aseptically to the centers of the Petri dishes. The treatments were incubated at 25 °C in the dark. Colony growth diameter was measured after the fungal growth in the control treatments had covered two-thirds of the Petri dishes (3−5 days). Percentage of mycelial growth inhibition was calculated, and the concentration of complex inhibiting fungus mycelial growth by 50% (EC_{50}) was determined by a linear regression method.

Influence of Mixture of the Ligand and Metal Salt on Biological Activities. The ligand *cis*-L diluted by starch was mixed with the $ZnCl_2$, $CoCl_2$, or $CuCl_2$ in a 2:1 molar ratio and with $MnCl_2$ or $NiCl_2$ in a 4:1 molar ratio and ground into dust, then added to PDA medium,

Table 5. Influence of Mixture of the Ligand and Metal Salt on Biological Activities

mixture composition	molar ratio	dose (μg/mL)	inhibition[a] (%)				
			G. zeae	*R. cerealis*	*B. cinerea*	*C. orbiculare*	*F. moniliforme*
cis-L		2	68 ± 0.9	68 ± 1.5	70 ± 2.2	73 ± 1.2	82 ± 1.6
cis-L		8	82 ± 1.3	91 ± 3.0	93 ± 1.7	94 ± 0.5	98 ± 0.7
$ZnCl_2$ + *cis*-L	1:2	2	67 ± 1.4	67 ± 2.1	72 ± 2.1	72 ± 2.9	82 ± 1.4
$CoCl_2$ + *cis*-L	1:2	2	68 ± 2.1	67 ± 2.4	71 ± 1.3	72 ± 2.0	84 ± 1.1
$CuCl_2$ + *cis*-L	1:2	2	67 ± 2.3	68 ± 2.9	72 ± 2.2	73 ± 2.3	81 ± 2.6
$NiCl_2$ + *cis*-L	1:4	2	67 ± 1.8	67 ± 1.6	69 ± 1.6	74 ± 1.7	81 ± 2.1
$MnCl_2$ + *cis*-L	1:4	2	66 ± 1.9	69 ± 0.9	70 ± 3.1	73 ± 1.9	80 ± 3.0
$ZnCl_2$ + *cis*-L	1:2	8	83 ± 1.8	91 ± 1.1	92 ± 1.8	93 ± 0.9	98 ± 1.1
$CoCl_2$ + *cis*-L	1:2	8	83 ± 2.6	91 ± 2.7	93 ± 2.2	93 ± 1.1	99 ± 0.6
$CuCl_2$ + *cis*-L	1:2	8	82 ± 2.2	89 ± 1.5	90 ± 2.9	94 ± 0.6	98 ± 0.2
$NiCl_2$ + *cis*-L	1:4	8	83 ± 3.5	90 ± 2.3	93 ± 1.8	95 ± 2.3	98 ± 0.9
$MnCl_2$ + *cis*-L	1:4	8	82 ± 1.4	88 ± 3.1	90 ± 0.7	95 ± 2.1	97 ± 1.4

[a] Values are the mean ± SD of three replicates.

respectively, to obtain mixtures in which the concentration of ligand was 2 or 8 μg/mL. Meanwhile, the metal salts ($ZnCl_2$, $CoCl_2$, $CuCl_2$, $MnCl_2$, and $NiCl_2$) were also diluted by starch, ground into dust, and then added to PDA medium to obtain concentrations of 2, 8, and 100 μg/mL, respectively. Their parallel controls were maintained with starch mixed with PDA medium. The antifungal activities of the above mixtures and metal salts were measured according to the same method as metal complexes and their ligands.

RESULTS AND DISCUSSION

Structure Determination of the Title Complexes. The physical properties of the title complexes are listed in **Table 1**. Some most noticeable IR spectra bands of the title complexes have provided information regarding the coordination mode in the complexes and were analyzed in comparison with the data for their free ligands (**Table 2**). There were considerable differences between the racemates and their metal complexes. For example, a sharp band at 3109 cm^{-1} in *cis*-L and at 3108 cm^{-1} in *trans*-L assigned to ν (=CH in triazole ring) was shifted at about 6−51 cm^{-1} to higher frequencies after complexation with respect to the free ligands. The triazole ring stretching frequency appeared at 1507 cm^{-1} in *cis*-L and at 1506 cm^{-1} in *trans*-L and was shifted to 1516−1534 cm^{-1} in **1a**−**1m** and 1520−1533 cm^{-1} in **2a**−**2k**, respectively. On the other hand, the C−O−C band stretching vibration at 1139 cm^{-1} in *cis*-L and at 1138 cm^{-1} in *trans*-L was shifted toward lower frequency in complexes and the $\Delta\nu$ difference ranged from 6 to 17 cm^{-1}. These values indicated the nitrogen atom in the triazole ring of the ligands had participated in coordination. Due to the steric hindrance effect (*29*), we confirmed the coordination bond formed between the fourth nitrogen atom in triazole ring and metal ion, a similar situation having been proved by the crystal structure of $Zn(DPMT)_2Cl_2$ (*30*) and $Mn(DPMT)_2Cl_2(H_2O)_2$ (*31*) (DPMT = (1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl]methyl-1*H*-1,2,4-triazole)).

The UV spectral data (**Table 2**) suggested that the maximum absorption wavelength, which appeared at 208 nm in *cis*-L and at 205 nm in *trans*-L, were shifted to 204−205 nm in *cis*-L complexes and to 202−203 nm in *trans*-L complexes. Nevertheless, the maximum absorption wavelengths in *cis*-L complexes were still 1−3 nm higher than in their relevant *trans*-L complexes.

In addition, the atomic absorption and element analysis data of the title complexes are shown in **Table 3**. The results indicated that the reaction of the ligands with metal salts afforded complexes having the molecular formulas M^1(*cis*-L)$_2Y_2$, M^1(*trans*-L)$_2Y_2$ (M^1 = Zn(II), Co(II), Cu(II)), and M^2(*cis*-L)$_4Y_2$, M^2(*trans*-L)$_4Y_2$ (M^2 = Mn(II), Ni(II)).

Controlled Release Properties. The releases of *cis*-L and *trans*-L from relevant complexes showed different rates yet similar profiles (**Figure 1A**). The release rate pattern indicated that *cis*-L was released more slowly than *trans*-L; for example, after 96 h in static water, **1a**, **1c**, and **1e** had released 87, 75, and 89% of *cis*-L, respectively, but **2a**, **2c**, and **2e** had released 95, 84, and 97% of *trans*-L, respectively. The reason for the above difference might be related to the different solubilities of the ligands: *trans*-L has a higher solubility in water, which led to its metal complexes being more unstable in water.

The gradual release profiles of *cis*-L from **1a** at different temperatures are shown in **Figure 1B**. At 5 °C, about 57% of *cis*-L was released after 96 h in comparison with 92% of *cis*-L at 35 °C. The release rate of *cis*-L from **1a** increased with rising temperature, suggesting the essential role of temperature in the controlled release experiment. As the temperature rose, the stability of the title complexes in static water decreased gradually.

Figure 1C reflects the release profile of *cis*-L from **1a** at different pH values. The release rate of *cis*-L from **1a** was faster at acidic solution. It had released only 56.7% of *cis*-L at pH 14 and 66.1% of *cis*-L at pH 10 in comparison with 93.3% of *cis*-L at pH 1. This result suggested that the title complexes were more stable in alkalescent water.

The release rate of *cis*-L from **1a** decreased dramatically when **1a** was coated by PVA, as shown in **Figure 1D**. Only 65.7% of *cis*-L from coated **1a** was released after 96 h. This result provided a favorable warrant for us to develop the title complexes to new medicament for slower controlled release, such as microcapsule, seed coating agent.

Biological Activities. *Toxicities of cis-L and trans-L against Plant Pathogenic Fungi.* Fungicidal effects of the two racemates are shown in **Table 4**. *cis*-L revealed stronger antifungal activities than *trans*-L against all five tested fungi. This difference was especially marked for *G. zeae*, to which the toxicity of *cis*-L was 5.95 times higher than that of *trans*-L. In addition, for the other four fungi, the toxicities of *cis*-L were 3.39−4.33 times greater than those of *trans*-L.

Toxicities of Some Complexes against Plant Pathogenic Fungi. It was clear from the antifungal screening data (**Table 4**) that the complexes, especially the *cis*-L complexes, were more sensitive than their ligands. Bioassays disclosed that complexes showed remarkable inhibitory effects on five plant pathogenic fungi. Zn complexes showed the best result; the toxicities of **1a** and **1b** were 3.85−6.36 times greater than those of *cis*-L, and **2a** was 2.62−4.36 times more sensitive than *trans*-L. Co-complexes also showed high inhibitory activities; the toxicities of **1c** and **2c** were 2.23−4.69 and 2.00−2.60 times stronger

than their ligands, respectively. The fungicidal activities of Ni, Mn, and Cu complexes were lower, relatively, their toxicity ratios being 1.19−2.71 in comparison with their ligands.

Discussion of Mechanism for Increasing Antifungal Activities. By the comparative study of the antifungal activities of Zn complexes **1a** and **1b** or Cu complexes **1h**, **1i**, **1j**, and **1k** (**Table 4**), we found that the fungicidal activities of the complexes with the same metal ion against the plant pathogenic fungi did not exhibit obvious diversity; this result indicated that the bioactivities of the title complexes were related to only the synergistic action of the ligand and metal ion, substantively irrelative of the anions. Moreover, the bioassay of the metal salts showed that none of the salts $ZnCl_2$, $CoCl_2$, $CuCl_2$, $MnCl_2$, and $NiCl_2$ exerted fungicide activities at all at 2, 8, and 100 μg/mL, and the experiment of influence of the mixture metal salt and *cis*-L made clear that mixing the ligand with metal salt did not enhance antifungal activities (**Table 5**). We can conclude that it was the coordinating of the ligand and the metal salt that increased the bioactivities (**Table 4**).

Propiconazole belongs to the ergosterol biosynthesis inhibitors (*32*); it can impair the pathogenic ability of plant fungi by destroying the structure of the cell membrane. Because of the complexity of biological systems, it is rather difficult to stipulate the exact mechanism for such activities. However, the increased biocidal properties after complexation can be very well explained by chelation theory; chelation can reduce the polarity of the metal ion, mainly by partial sharing of its positive charge with the donor groups and possible electron delocalization over the chelate rings (*33*−*36*). The forming of complexes made the electron density in the triazole ring change obviously (*37*, *38*), and the inductive effect caused by the coordination between the metal ion and the ligand made the change in force constant of bond, which can be proved by the molecular structure data of a complex $Zn(DPMT)_2Cl_2$ and its ligand 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl]methyl-1*H*-1,2,4-triazole (DPMT) (*30*, *39*), the bond lengths in the triazole ring were changed evidently after coordination with metal salt; the coordination resulted in a polarity change of the triazole ring and an increase of the lipophilic character of the metal, which subsequently favors the ligand or complex permeation through the lipoid layer of the micro-organism membrane. Meanwhile, as a result of the controlled release properties, the complexes release *cis*-L or *trans*-L step by step; the complexes can have a positive effect against the plant fungi in a longer residual period and show differences of bioactivities from their ligands, so we perceive the release of *cis*-L or *trans*-L as one of the factors that affect the antifungal activities of their complexes. Thereby, the controlled release properties may also be one of the reasons for the enhanced bioactivities of metal complexes (*7*).

In summary, it can be concluded from all of the results given above that *cis*-racemate and *trans*-racemate complexes presented excellent controlled release properties in static water and that their release rates were affected dramatically by the temperature, pH, and PVA coating. The antifungal activities of the metal complexes synthesized were more active than their ligands, especially Zn−*cis*-racemate. However, the exact mechanism of the increase of bioactivities after complexation needs to be researched further.

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