Synthesis, Crystal Structures, and Fungicidal Activity of Novel 1,5-Diaryl-3-(glucopyranosyloxy)-1*H*-pyrazoles

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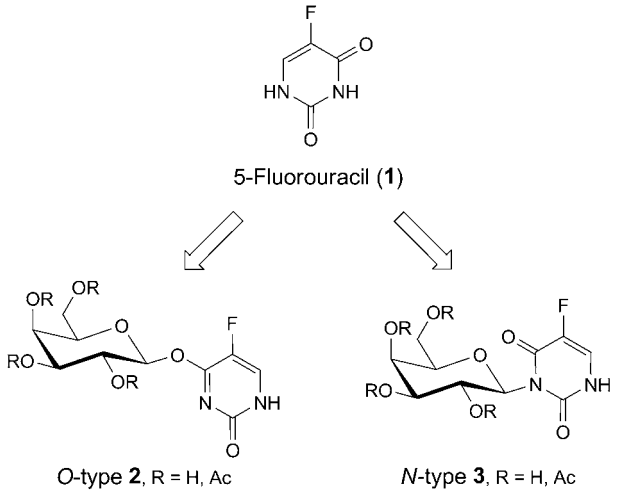
Five novel pyrazole-coupled glucosides, 1,5-diaryl-1*H*-pyrazol-3-yl 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosides **5a**–**5e**, were synthesized by the phase-transfer catalytic reaction of 1,5-diaryl-1*H*-pyrazol-3-ols **4a**–**4e** with acetobromo-*α*-D-glucose in $H_2O/CHCl_3$ under alkaline conditions, using $Bu_4N^+Br^-$ as catalyst. Then, glucosides **5a**–**5c** were deacetylated in a solution of Na_2CO_3/MeOH to yield the 1,5-diaryl-3-(*β*-D-glucopyranosyloxy)-1*H*-pyrazoles **6a**–**6c**. Their structures were characterized by ^{1}H,^{1}H-COSY, ^{1}H-, ^{13}C-, and ^{19}F-NMR spectroscopy, as well as elemental analysis. The structures of **5d** and **6c** were also determined by single-crystal X-ray diffraction analysis. A preliminary *in vitro* bioassay indicated that compounds **4e** and **5d** exhibited excellent-to-medium fungicidal activity against *Sclerotinia sclerotiorum* at the dosage of 10 μg/ml.

Introduction. – Modern crop production cannot be developed without chemical means for pathogens control, which are referred to as fungicides or pesticides [1–3]. However, as a result of the application of the same fungicide or fungicides with the same mode of action over many years, plant pathogens become resistant to these chemicals. Therefore, the design and synthesis of novel fungicides with unique structures and mechanisms of action, low mammalian toxicity, and a broad spectrum of bioactivities, are an increasingly active area of current pesticide research [4][5].

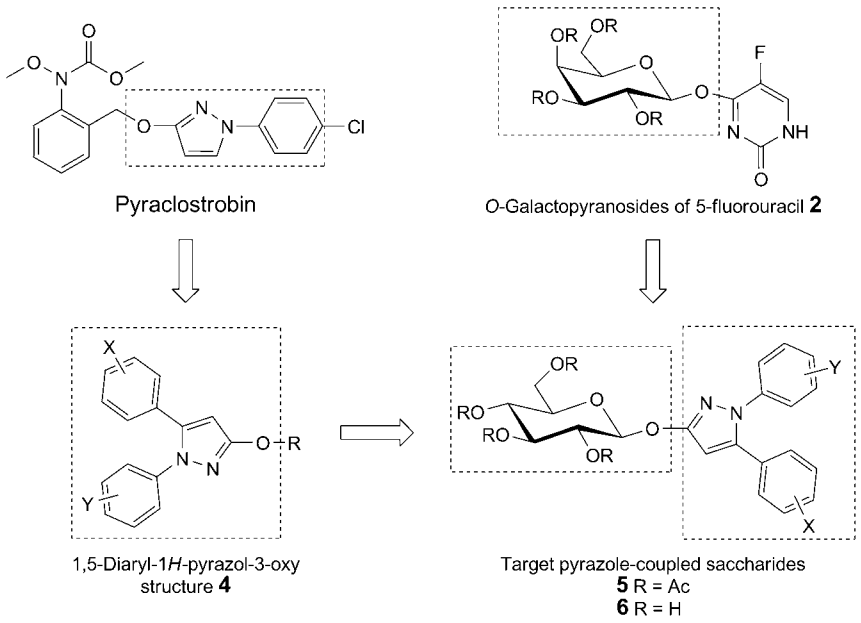
In recent years, the ever-increasing importance of glycobiology and the chemistry of glycoconjugates have gained enormous attention due to the understanding of the role played by these carbohydrates in biological events [6–9], such as inflammation, immune responses, cell growth, and adhesion [10]. Among these compounds, glycosides of heterocycles are essential and reliable platforms for the development of many anticancer and antitumor drugs [11][12], and have been regarded as good glycosyl donors, in addition to their biological activities such as the inhibition of enzyme activity [13–16]. For example, 5-fluorouracil (**1**; *Scheme 1*), an excellent representative of antimetabolic anticancer drugs in curing gastrointestinal [17] and breast cancer [18], was transferred to galactosides by the phase-transfer catalysis [19] or the *Koenigs–Knorr* reaction [20] to form *O*- or *N*-galactopyranosides of 5-fluorouracil (**2** and **3**, resp.; *Scheme 1*), which could then slowly release 5-fluorouracil *in vivo*, reduce its toxicity toward mammalian cells, and improve its inhibitory effects on tumor cells [21]. Therefore, the efficient synthesis of heterocycle-coupled glycosides is of great value, and represents a continuing challenge that is at the forefront of organic chemistry.

Scheme 1. *5-Fluorouracil* (**1**) *and its Transformation to its* O- *or* N-*Galactopyranosides*



Since the discovery of the strobilurin fungicide pyraclostrobin (= methyl {2-[1-(4-chlorophenyl)-1*H*-pyrazol-3-yloxymethyl]phenyl}methoxycarbamate) by BASF scientists in the year 2000 (*Scheme 2*) [22–24], 1*H*-pyrazol-3-oxy derivatives have attracted considerable attention in pesticide research because of their low mammalian toxicity and diverse bioactivities such as fungicidal [25–27], insecticidal [28], herbicidal [29],

Scheme 2. *Design Strategy of the Target Pyrazole-Coupled Saccharides*

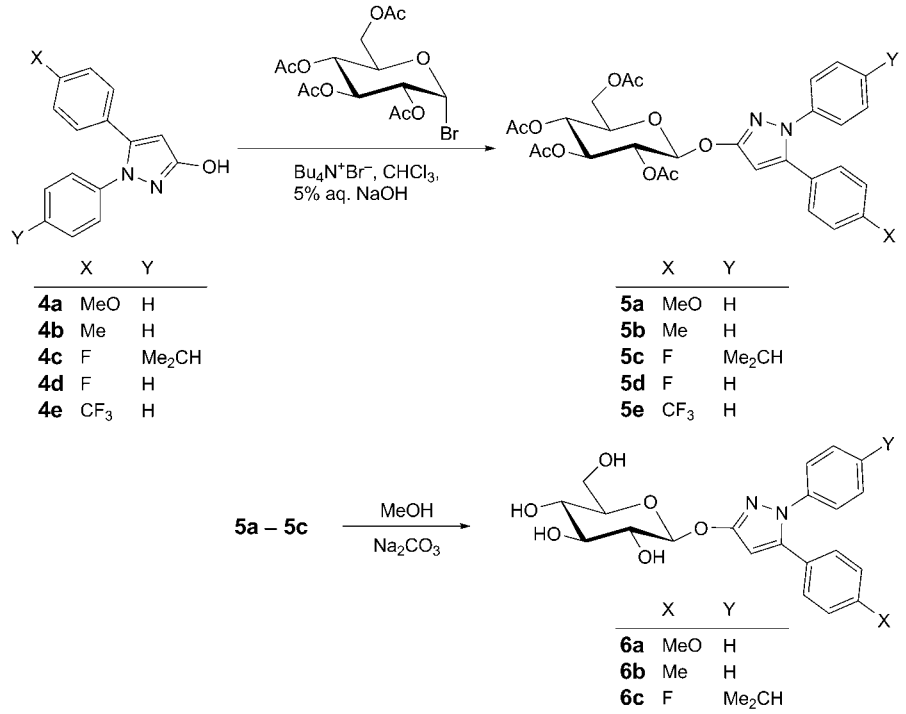


and plant-growth-regulatory activities [30]. 1,5-Diaryl-1*H*-pyrazol-3-oxy derivatives represent one of the most active classes of these compounds and can be used not only as precursors to a variety of *N*-containing heterocycles with fungicidal activity [31][32], but also as analgesic [33], anti-inflammatory [34], and enzyme inhibitory agents [35] with wide medicinal applications. Motivated by these findings, we conceived that transforming the 1,5-diaryl-1*H*-pyrazol-3-oxy structure **4** to glucosides might result in new pyrazole-coupled saccharide molecules [36] with good bioactivities (*Scheme 2*).

In this study, the synthesis of a series of novel 1,5-diaryl-3-(glucopyranosyloxy)-1*H*-pyrazole derivatives containing a per-*O*-acetylated glucopyranosyl (**5a**–**5e**) or a glucopyranosyl (**6a**–**6c**) moiety, and the crystal structures of **5d** and **6c** are reported. Meanwhile, the fungicidal activity of **4a**–**4e**, **5a**–**5e**, and **6c** has been investigated with the aim of understanding the structure–activity relationships (SAR) and developing novel fungicides. A preliminary *in vitro* bioassay indicated that some compounds displayed good fungicidal activity at the dosage of 10 μg/ml.

Results and Discussion. – *Synthesis and Characterization*. 1,5-Diaryl-1*H*-pyrazol-3-ols **4a**–**4e** (*Scheme 3*) were prepared from methyl 3-arylacrylates *via* two steps including addition-cyclization and oxidation [31]. 'Acetobromo-α-D-glucose', a significant glucosyl donor for the synthesis of heterocycle-coupled glucosides, was obtained from glucose by acylation and treatment of the pentaacetyl-β-D-glucopyranose with HBr in AcOH [37].

Scheme 3. *Synthesis of 1,5-Diaryl-3-(glucopyranosyloxy)-1*H*-pyrazole Derivatives* **5a**–**5e** *and* **6a**–**6c**



	X	Y
4a	MeO	H
4b	Me	H
4c	F	Me_2CH
4d	F	H
4e	CF_3	H

	X	Y
5a	MeO	H
5b	Me	H
5c	F	Me_2CH
5d	F	H
5e	CF_3	H

	X	Y
6a	MeO	H
6b	Me	H
6c	F	Me_2CH

Several methods are known for the formation of glycosidic bonds [19][38–40], among which the phase-transfer catalysis and the *Koenigs–Knorr* method are preferred due to the experimental simplicity and readily accessible materials. In contrast to the phase-transfer catalysis, the catalysts for the *Koenigs–Knorr* method are expensive silver salts (Ag_2CO_3 or Ag_2O) [38][41]. Therefore, in our procedure, the five novel pyrazole-glucosides, 1,5-diaryl-1*H*-pyrazol-3-yl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosides **5a**–**5e**, were prepared by the phase-transfer catalytic reaction of 'acetobromo-α-D-glucose' with **4a**–**4e** in an alkaline $H_2O/CHCl_3$ system, using tetrabutylammonium bromide ($Bu_4N^+Br^-$) as catalyst (*Scheme 3*). The crude products were recrystallized from EtOH, and no other glucoside type products were detected.

Taking some special properties of glucosides such as hygroscopicity into full consideration, the deacetylation of the glucosides **5a**–**5c** was carried out in dry MeOH in the presence of dry Na_2CO_3. Good yields of 1,5-diaryl-3-(β-D-glucopyranosyloxy)-1*H*-pyrazoles **6a**–**6c** were obtained after recrystallization from dry MeOH (*Scheme 3*).

The ^{1}H,^{1}H-COSY spectrum of product **5a** enables us to assign the chemical shifts of the anomeric H-atom from the saccharide ring (*Fig. 1*). As a result of the deshielding

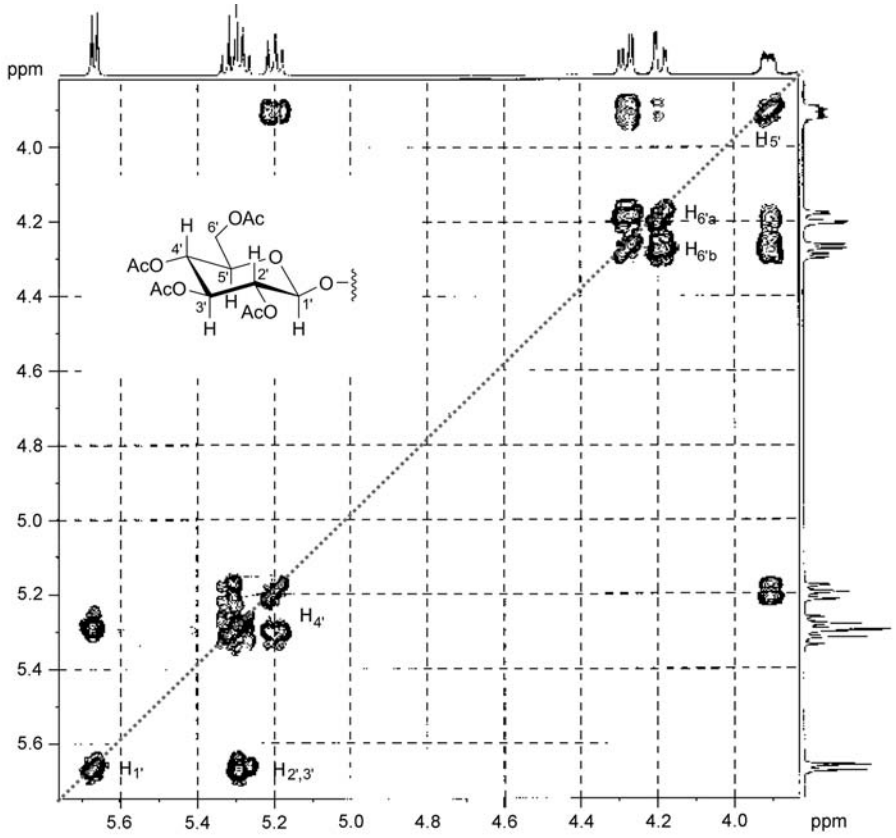


Fig. 1. *^{1}H,^{1}H-COSY Correlations of compound* **5a**

effect of C=O, the anomeric H–C(1′) appeared at low field (5.67 ppm) as a *doublet* with a coupling constant of 7.6 Hz. The coupling constant confirmed the β-anomeric form. The H-atoms H–C(2′), H–C(3′), H–C(4′), H–C(5′), and CH_2(6′) formed a coupling system. A *multiplet* appearing at 5.32 – 5.28 ppm was attributed to H–C(2′) and H–C(3′), whereas a *triplet* at 5.20 ppm ($J = 9.5$) was assigned to H–C(4′). Due to the different chemical environment, the CH_2 H-atoms H_a–C(6′) and H_b–C(6′) gave rise to two *dd*s at 4.19 ppm ($J = 2.3$, 12.3) and 4.28 ppm ($J = 4.9$, 12.3), respectively. A *multiplet* locating at high field (3.92 – 3.90 ppm) was attributed to H–C(5′). Furthermore, the ^{13}C-NMR spectra of **5a** – **5e** and **6a** – **6c** confirmed the presence of the glycoconjugated products, as the anomeric C-atom was identified at 102.7 – 97.6 ppm. The AcO groups present in the saccharide moiety of **5a** – **5e** were well resolved in both ^{1}H- and ^{13}C-NMR spectra. The AcO H-atoms of **5a** – **5e** resonated in the region of 2.06 – 2.00 ppm in ^{1}H-NMR spectra, and the ^{13}C-NMR signals were observed around 20.7 – 20.6 ppm. As expected, such signals were absent in the spectra of **6a** – **6c**. Because of the different shielding effect in *O*-acetylated glucopyranosyl (**5a** – **5e**) and glucopyranosyl groups (**6a** – **6c**), the chemical shift of the CH of the pyrazole ring displayed at 6.10 – 5.97 and 6.23 – 6.18 ppm, respectively. The ^{1}H-NMR spectra of these glucosides exhibited a *multiplet* of aromatic H-atoms in the range of 7.55 – 6.81 ppm.

Structural Discussion. To further validate the structures and understand the effect of structural factors on their interactions, the crystal structures of 5-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-3-yl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**5d**) and 5-(4-fluorophenyl)-1-[4-(propan-2-yl)phenyl]-1*H*-pyrazol-3-yl β-D-glucopyranoside (**6c**) were investigated.

Compound **5d** crystallizes in an orthorhombic space group $P2_12_12_1$. The detailed crystal and structure refinement data for **5d** are collected in *Table 1*. An ORTEP view of the molecule **5d** (*Fig. 2*) reveals that the saccharide moiety in **5d** is a glucopyranose. The glucopyranose ring is in the usual $^4C_1$ conformation, and the anomeric center of the saccharide has the β-configuration, which is also confirmed from the torsion angles O(1)–C(20)–O(2)–C(16) -174.54° and O(2)–C(20)–C(19)–O(6) -168.06°. The torsion angle C(17)–C(16)–C(21)–O(3) is 56.6°, pointing out that the AcO group attached to the primary OH group is in the *gt* position, which is known to be the favored orientation for a glucopyranose. The pyrazole ring is nearly coplanar with the anomeric C-atom C(20) by making a torsion angle of C(20)–O(1)–C(15)–C(14) 19.5°, and this orientation facilitates delocalization of electrons from the lone-pair orbitals of O(1) with the π orbitals of the pyrazole ring. The intramolecular H-bond (C–H ⋯ O) results in the formation of one planar five-membered *pseudo*-ring *A* (O(9)/C(26)/O(5)/C(18)/H(18)). The *N*-linked benzene ring *B* (C(1) to C(6)) and *C*-linked benzene ring *C* (C(7) to C(12)) are twisted 43.15° and 45.56°, respectively, from the plane of the pyrazole ring (N(1), N(2), C(13) to C(15)). Rings *B* and *C* are planar and the dihedral angle between them is 58.9°.

Compound **6c** crystallizes in a monoclinic space group $P2_1$. The detailed crystal and structure refinement data for **6c** are also listed in *Table 1*. An ORTEP view of the molecule **6c** is shown in *Fig. 3*. The saccharide adopts the $^4C_1$ conformation along with its β-anomeric form, which is further confirmed by the torsion angles O(1)–C(19)–O(2)–C(20) -179.0° and O(2)–C(19)–C(23)–O(6) -180.0°. The H_2O molecule in the crystal is linked to H–C(11) of the *N*-linked benzene ring by an

Table 1. *Crystallographic Data for Compounds* **5d** *and* **6c**

Compound		**5d**	**6c**
Empirical formula		$C_{29}H_{29}FN_2O_{10}$	$C_{24}H_{29}FN_2O_7$
CCDC No.		823219	697145
Formula weight		584.54	476.49
Temp. [K]		180(2)	291(2)
Wavelength [Å]		0.71073 Å	0.71073 Å
Crystal system		Orthorhombic	Monoclinic
Space group		$P2_12_12_1$	$P2_1$
Z		4	2
Crystal dimensions [mm]		$0.26 \times 0.29 \times 0.35$	$0.24 \times 0.26 \times 0.30$
θ Range for cell determination [°]		1.66–31.18	2.49–27.99
Unit cell parameters	a [Å]	8.222(2)	8.216(2)
	b [Å]	14.205(5)	9.149(2)
	c [Å]	24.558(7)	15.529(4)
	β [°]	90.00	94.766(3)
Volume [Å^3]		2868.2(15)	1163.3(5)
μ [mm^{-1}]		0.107	0.105
D_x [g cm^{-3}]		1.354	1.360
$F(000)$		1224	504
Index ranges		$-11 \le h \le 11$	$-10 \le h \le 8$
		$-20 \le k \le 20$	$-11 \le k \le 8$
		$-35 \le l \le 34$	$-20 \le l \le 20$
Reflections collected		60086	7263
Independent reflections (R_{int})		8743 ($R_{int} = 0.0377$)	2930 ($R_{int} = 0.0556$)
Refinement method on F^2		Full-matrix least-squares	Full-matrix least-squares
Max. and min. transmission		0.9727/0.9635	0.98/0.97
Data/restraints/parameters		8743/0/383	2930/1/309
Goodness-of-fit on F^2		1.251	1.016
Final R indices [$I > 2\sigma(I)$]; R_1, wR_2		0.0694, 0.1833	0.0658, 0.1244
R_1, wR_2 (all data)		0.0753, 0.1888	0.0852, 0.1292
Largest diff. peak and hole [eÅ^{-3}]		0.280; −0.243	0.394; −0.314

intermolecular H-bond C(11)–H(11) ··· O(7). An intramolecular O–H ··· O H-bond results in the formation of a non-planar *pseudo*-ring *D* (O(2), C(20), C(24), O(3), H(3A)). The *N*-linked benzene ring *E* (C(10) to C(15)) and *C*-linked benzene ring *F* (C(4) to C(9)) are twisted 53.66° and 39.41°, respectively, from the plane of the pyrazole ring (N(1), N(2), C(1) to C(3)). Rings *E* and *F* are planar and the dihedral angle between them is 54.92°.

Fungicidal Activity Studies. The compounds **4a**–**4e**, **5a**–**5e**, and **6c** were screened for bioactivity against three fungi, namely *Sclerotinia sclerotiorum*, *Gibberella zeae*, and *Rhizoctonia cerealis*, at a concentration of 10 μg/ml each. As can be seen in *Table 2*, most compounds have weak fungicidal activity, except **4e** (X = CF_3, Y = H, OH group at C(3) of the pyrazole ring) and **5d** (X = F, Y = H, *O*-acetylated glucopyranosyl group at C(3) of the pyrazole ring), which exhibited excellent-to-medium inhibitory activity against *Sclerotinia sclerotiorum*. This might imply that the introduction of the electron-withdrawing group or *O*-acetylated glucopyranosyl group by taking the electronic effect into full consideration was important for improving its fungicidal activity. In

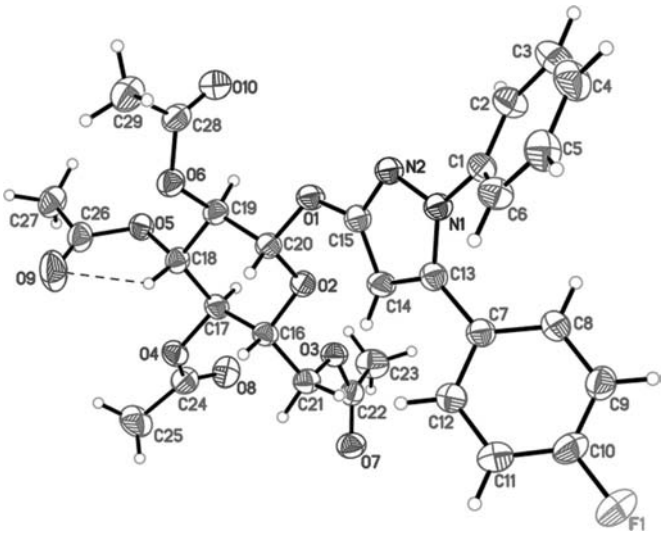


Fig. 2. *ORTEP Plot of the molecular structure of* **5d** *showing atom-numbering scheme; 50% probability thermal ellipsoids*

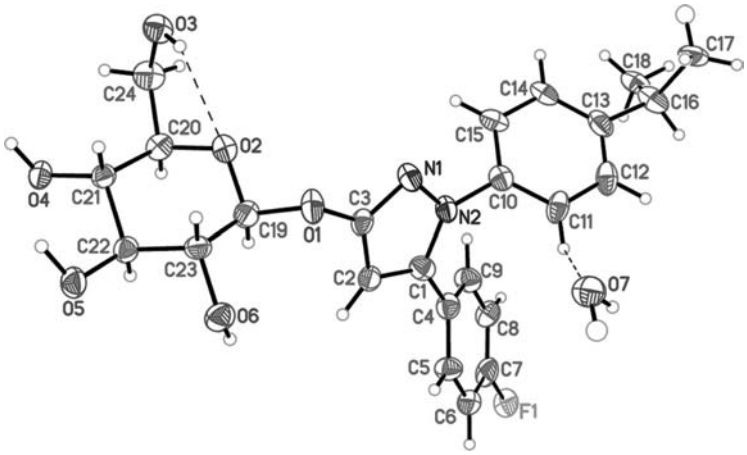


Fig. 3. *ORTEP Plot of the molecular structure of* **6c** *showing atom-numbering scheme; 50% probability thermal ellipsoids*

terms of X, compounds with electron-withdrawing groups on the 5-phenyl ring displayed higher fungicidal activity than that with electron-donating groups, as seen in the comparison of compounds **4d** (X = F) and **4e** ($X = CF_3$) *vs.* **4a** (X = MeO) and **4b** (X = Me), **5c** and **5d** (X = F) *vs.* **5a** (X = MeO) and **5b** (X = Me). However, compounds **4c** and **6c** (X = F), and **5e** ($X = CF_3$) are three exceptions: **4c** and **6c** showed no fungicidal activity against *Sclerotinia sclerotiorum* and *Rhizoctonia cerealis*, and **5e** only weak activity, which indicated switching the substituents Y from H to ^{i}Pr, or

Table 2. *Antifungal Activity of Tested Compounds* (% inhibition)

Compounds	X	Y	Effect of test compound (10 μg/ml)[a])		
			S. sclerotiorum	*G. zeae*	*R. cerealis*
4a	MeO	H	0	1	5
4b	Me	H	18	13	8
4c	F	Me_2CH	0	4	0
4d	F	H	39	30	17
4e	CF_3	H	100	23	9
5a	MeO	H	0	1	0
5b	Me	H	10	5	0
5c	F	Me_2CH	29	11	19
5d	F	H	53	8	2
5e	CF_3	H	0	1	6
6c	F	Me_2CH	0	6	0

[a]) 0 = no activity and 100 = total kill.

O-acetylated glucopyranosyl to glucopyranosyl had no effective impact on the inhibition rates. The present work indicated that **4e** and **5d** could be used as potential lead compounds for further studies of novel fungicides.

Conclusions. – In summary, a series of novel 1,5-diaryl-3-(glucopyranosyloxy)-1*H*-pyrazole derivatives containing per-*O*-acetylated glucopyranosyl (**5a**–**5e**) or glucopyranosyl (**6a**–**6c**) moieties were synthesized by the phase-transfer catalytic reaction of 1,5-diaryl-1*H*-pyrazol-3-ols **4a**–**4e** with acetobromo-α-D-glucose, followed by deacetylation with Na_2CO_3/MeOH. The fungicidal activities of **4a**–**4e**, **5a**–**5e**, and **6c** were tested *in vitro* against *Sclerotinia sclerotiorum*, *Gibberella zeae*, and *Rhizoctonia cerealis*. Only **4e** and **5d** exhibited excellent-to-medium inhibitory activity against *Sclerotinia sclerotiorum*. This implies that the introduction of the electron-withdrawing group or the *O*-acetylated glucopyranosyl residue is important for improving their fungicidal activity. The most promising compounds in this study, **4e** and **5d**, can be used as potential lead compounds for further studies of novel fungicides.

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Experimental Part

General. All starting materials were used in analytical grades, and solvents were dried by standard methods and distilled before use. Compounds **4a** [42], **4b**–**4d** [34], and **4e** [43] were prepared according to the published procedures. TLC: precoated silica-gel plates (*Merck* silica gel *60 F_{254}*); detection by UV light. M.p.: *X-4* microscope electrothermal apparatus; uncorrected. ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra: *Bruker* spectrometer at 300 or 500 MHz; in $CDCl_3$ or (D_6)DMSO; chemical shifts δ in ppm rel. to Me_4Si as internal standard, and coupling constants *J* in Hz. Elemental analyses: *Vario EL III* elemental analyzer.

Fungicidal Assays. The fungicidal activity of compounds **4a**–**4e**, **5a**–**5e**, and **6c** against fungi *Sclerotinia sclerotiorum*, *Gibberella zeae*, and *Rhizoctonia cerealis* was investigated. The fungi were

obtained from *Jiangsu Pesticide Research Institute Co., Ltd.*, P. R. China. The tested compounds were dissolved in acetone and added to a sterile agarized *Czapek-Dox* medium at 45°. In preliminary screenings, the compounds were used in a concentration of 10 μg/ml. The control sample contained only one equivalent of acetone. The media were poured onto 8-cm *Petri* dishes (10 ml for each dish) and after 2 d inoculated with 5-mm PDA discs of overgrown mycelium. In the case of *Sclerotinia sclerotiorum*, the medium was inoculated by a prick of laboratory needle containing fungus spores. The *Petri* dishes were incubated at r.t. in the dark. After 4 d, the diameters of the inoculation of the cultures were measured. The percentage inhibition of fungal growth was determined by comparison between the development of fungi colonies on media containing compounds and on the control. Three replicates of each test were carried out.

Suitable crystals of **5d** and **6c** were obtained by slow evaporation of EtOH soln. at r.t. Further details about the data collection are listed in *Table 1*. Crystal data[1]) were collected on a *Nonius CAD-4* diffractometer by using MoK_α (0.71073 Å) irradiation. The data of **5d** were collected at 180 K and those of **6c** at 291 K. The structures were solved by direct method using SHELXS-97 [44] and refined by full-matrix least-squares on F^2 for all data using SHELXL-97 [44]. The H-atoms of the H_2O molecules in **6c** were located in the difference *Fourier* map. Their thermal displacement parameters were fixed to 1.5 times the equivalent one of the parent O-atom. All other H-atoms were added at calculated positions and refined using a riding model. Their isotropic temp. factors were fixed to 1.2 times (1.5 times for Me groups) the equivalent isotropic displacement parameters of the C-atom the H-atom is attached to. Anisotropic thermal displacement parameters were used for all non-H-atoms.

*General Procedure for the Synthesis of 1,5-Diaryl-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β*-D*-glucopyranosides* **5a**–**5e**. A mixture of $CHCl_3$ (20 ml), $Bu_4N^+Br^-$ (2.3 g, 7.1 mmol), and H_2O (15 ml) was heated to 55°, and then a soln. of 1,5-diaryl-1*H*-pyrazol-3-ol (**4a**–**4e**; 10.5 mmol) in $CHCl_3$ (15 ml) and 5% aq. NaOH (15 ml) were added dropwise. The pH value was adjusted to 8–10, and acetobromo-α-D-glucose (5.4 g, 13.0 mmol) was added under vigorous stirring. The mixture was stirred at 55° for another 4 h, and then left to cool to r.t. The org. layer was separated, washed with 5% aq. NaOH, and dried ($MgSO_4$). Then, the solvent was removed *in vacuo*. The pure product **5a**–**5e** was obtained by recrystallization from dry EtOH.

*5-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β*-D*-glucopyranoside* (**5a**). Yield: 3.70 g (59%). Colorless crystals. M.p. 181–182°. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.30–7.23 (*m*, 5 arom. H); 7.12 (*d*, *J* = 8.8, 2 arom. H); 6.81 (*d*, *J* = 8.8, 2 arom. H); 5.97 (*s*, H–C(4)); 5.67 (*d*, *J* = 7.6, H–C(1′)); 5.32–5.28 (*m*, H–C(2′), H–C(3′)); 5.20 (*t*, *J* = 9.5, H–C(4′)); 4.28 (*dd*, *J* = 4.9, 12.3, H_b–C(6′)); 4.19 (*dd*, *J* = 2.3, 12.3, H_a–C(6′)); 3.92–3.90 (*m*, H–C(5′)); 3.79 (*s*, MeO); 2.05, 2.04, 2.03, 2.01 (4*s*, 4 MeCO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.6; 170.2; 169.4; 169.3; 164.8; 161.0; 142.7; 139.5; 133.8; 129.1; 128.9; 127.6; 125.5; 125.2; 97.7; 95.6; 73.0; 72.3; 71.1; 68.3; 61.9; 55.8; 20.7; 20.6. Anal. calc. for $C_{30}H_{32}N_2O_{11}$ (596.58): C 60.40, H 5.41, N 4.70; found: C 60.25, H 5.39, N 4.72.

*5-(4-Methylphenyl)-1-phenyl-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β*-D*-glucopyranoside* (**5b**). Yield: 2.93 g (48%). Colorless crystals. M.p. 147–148°. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.34–7.09 (*m*, 9 arom. H); 6.00 (*s*, H–C(4)); 5.66 (*d*, *J* = 7.7, H–C(1′)); 5.33–5.26 (*m*, H–C(2′), H–C(3′)); 5.20 (*t*, *J* = 9.5, H–C(4′)); 4.28 (*dd*, *J* = 4.9, 12.4, H_b–C(6′)); 4.18 (*dd*, *J* = 2.4, 12.4, H_a–C(6′)); 3.92–3.89 (*m*, H–C(5′)); 2.34 (*s*, Me); 2.06, 2.04, 2.03, 2.01 (4*s*, 4 MeCO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.6; 170.2; 169.4; 169.3; 162.7; 138.6; 132.3; 129.7; 129.2; 129.0; 128.6; 127.1; 125.2; 125.1; 97.7; 94.7; 77.4; 77.2; 77.0; 76.6; 61.9; 21.2; 20.7; 20.6. Anal. calc. for $C_{30}H_{32}N_2O_{10}$ (580.58): C 62.06, H 5.56, N 4.83; found: C 61.88, H 5.58, N 4.85.

*5-(4-Fluorophenyl)-1-[4-(propan-2-yl)phenyl]-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β*-D*-glucopyranoside* (**5c**). Yield: 3.03 g (46%). Colorless crystals. M.p. 151–152°. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.26–6.97 (*m*, 8 arom. H); 5.99 (*s*, H–C(4)); 5.67 (*d*, *J* = 7.7, H–C(1′)); 5.32–5.26 (*m*, H–C(2′), H–C(3′)); 5.19 (*t*, *J* = 9.5, H–C(4′)); 4.28 (*dd*, *J* = 4.7, 12.4, H_b–C(6′)); 4.18 (*dd*, *J* = 2.4, 12.4, H_a–C(6′)); 3.91–3.88 (*m*, H–C(5′)); 2.93–2.87 (*m*, Me_2CH); 2.05, 2.04, 2.03, 2.01 (4*s*, 4 MeCO); 1.23 (*d*, *J* = 6.9, Me_2CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.6; 170.2; 169.4; 164.4; 161.1; 160.8 (*J*(C,F) = 36.8); 148.2; 143.2; 137.4; 130.5 (*J*(C,F) = 8.3); 126.9 (*J*(C,F) = 5.2); 126.5; 125.0; 115.6 (*J*(C,F) = 21.0); 97.6; 94.6; 77.4; 77.2; 76.6;

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[1]) CCDC-823219 (**5d**) and 697145 (**6c**) contain the supplementary crystallographic data for this artilce. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif.

76.0; 61.9; 33.7; 23.9; 20.7; 20.6. ^{19}F-NMR ($CDCl_3$, 282 MHz): −111.3. Anal. calc. for $C_{32}H_{35}FN_2O_{10}$ (626.63): C 61.34, H 5.63, N 4.47; found: C 61.52, H 5.61, N 4.45.

*5-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β-*D*-glucopyranoside* (**5d**). Yield: 2.58 g (42%). Colorless crystals. M.p. 116–117°. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.31–7.16 (*m*, 7 arom. H); 7.00–6.98 (*m*, 2 arom. H); 6.01 (*s*, H–C(4)); 5.67 (*d*, *J* = 7.6, H–C(1′)); 5.32–5.28 (*m*, H–C(2′), H–C(3′)); 5.19 (*t*, *J* = 9.5, H–C(4′)); 4.27 (*dd*, *J* = 4.8, 12.4, H_b–C(6′)); 4.18 (*dd*, *J* = 2.4, 12.3, H_a–C(6′)); 3.91–3.90 (*m*, H–C(5′)); 2.05, 2.04, 2.03, 2.00 (4*s*, 4 MeCO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.6; 170.2; 169.4; 169.3; 164.5; 160.3 (*J*(C,F) = 84.8); 144.2; 139.9; 130.5 (*J*(C,F) = 8.3); 130.0; 128.8 (*J*(C,F) = 5.3); 127.0; 125.0; 115.6 (*J*(C,F) = 21.8); 97.6; 94.4; 76.6; 73.0; 72.2; 68.3; 61.9; 20.7; 20.6. ^{19}F-NMR ($CDCl_3$, 282 MHz): −111.0. Anal. calc. for $C_{29}H_{29}FN_2O_{10}$ (584.55): C 59.59, H 5.00, N 4.79; found: C 59.72, H 4.98, N 4.77.

*1-Phenyl-5-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-3-yl 2,3,4,6-Tetra*-O*-acetyl-β-*D*-glucopyranoside* (**5e**). Yield: 3.40 g (51%). Colorless crystals. M.p. 158–159°. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.55 (*d*, *J* = 8.2, 2 arom. H); 7.35–7.22 (*m*, 7 arom. H); 6.10 (*s*, H–C(4)); 5.69 (*d*, *J* = 7.5, H–C(1′)); 5.32–5.29 (*m*, H–C(2′), H–C(3′)); 5.20 (*t*, *J* = 9.4, H–C(4′)); 4.28 (*dd*, *J* = 4.8, 12.4, H_b–C(6′)); 4.19 (*dd*, *J* = 2.0, 12.3, H_a–C(6′)); 3.93–3.90 (*m*, H–C(5′)); 2.06, 2.05, 2.04, 2.01 (4*s*, 4 MeCO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.6; 170.2; 169.4; 169.3; 161.0; 142.7; 139.5; 133.7; 130.8; 129.1; 128.9; 127.6; 125.6; 125.5; 125.4–125.2 (*m*); 97.7; 95.6; 77.4; 77.2; 77.0; 76.6; 61.9; 20.7; 20.6. ^{19}F-NMR ((D_6)DMSO, 282 MHz): −60.2. Anal. calc. for $C_{30}H_{29}F_3N_2O_{10}$ (634.55): C 56.78, H 4.61, N 4.41; found: C 56.64, H 4.63, N 4.39.

*General Procedure for the Synthesis of 1,5-Diaryl-1*H*-pyrazol-3-yl β-*D*-Glucopyranosides* (**6a**–**6c**). To a soln. of **5a**–**5c** (1.0 mmol) in dry MeOH (10 ml) was added dry Na_2CO_3 (0.16 g, 1.5 mmol). The mixture was then stirred at r.t. until the starting material had been completely consumed as judged by TLC analysis. The solvent was then evaporated *in vacuo*, and the residue was recrystallized from dry MeOH to give the pure products **6a**–**6c**.

*5-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrazol-3-yl β-*D*-Glucopyranoside* (**6a**). Yield: 0.27 g (63%). Colorless crystals. M.p. 119–120°. ^{1}H-NMR (CD_3OD, 500 MHz): 7.37–7.32 (*m*, 3 arom. H); 7.24–7.22 (*m*, 2 arom. H); 7.14 (*d*, *J* = 8.9, 2 arom. H); 6.85 (*d*, *J* = 8.8, 2 arom. H); 6.18 (*s*, H–C(4)); 5.14 (*d*, *J* = 7.7, H–C(1′)); 3.88 (*dd*, *J* = 2.3, 12.0, H–C(2′)); 3.78 (*s*, MeO); 3.70 (*dd*, *J* = 5.8, 12.0, H–C(3′)); 3.49–3.45 (*m*, H–C(4′), CH_2(6′)); 3.41–3.39 (*m*, H–C(5′)). ^{13}C-NMR (CD_3OD, 75 MHz): 163.8; 161.6; 146.2; 141.2; 130.1; 129.5; 128.7; 126.8; 126.5; 126.2; 102.7; 94.8; 78.5; 78.0; 74.9; 71.4; 62.7; 55.7. Anal. calc. for $C_{22}H_{24}N_2O_7$ (428.44): C 61.67, H 5.65, N 6.54; found: C 61.82, H 5.63, N 6.52.

*5-(4-Methylphenyl)-1-phenyl-1*H*-pyrazol-3-yl β-*D*-Glucopyranoside* (**6b**). Yield: 0.24 g (59%). Colorless crystals. M.p. 127–128°. ^{1}H-NMR (CD_3OD, 300 MHz): 7.39–7.06 (*m*, 9 arom. H); 6.21 (*s*, H–C(4)); 5.15 (*d*, *J* = 7.5, H–C(1′)); 3.89 (*dd*, *J* = 2.2, 12.0, H–C(2′)); 3.69 (*dd*, *J* = 5.4, 12.1, H–C(3′)); 3.49–3.44 (*m*, H–C(4′), CH_2(6′)); 3.41–3.38 (*m*, H–C(5′)); 2.32 (*s*, Me). ^{13}C-NMR (CD_3OD, 75 MHz): 163.8; 146.3; 141.2; 130.2; 129.8; 129.5; 128.6; 126.8; 126.5; 126.2; 102.7; 95.0; 78.5; 78.0; 74.9; 71.4; 62.7; 21.2. Anal. calc. for $C_{22}H_{24}N_2O_6$ (412.44): C 64.07, H 5.87, N 6.79; found: C 64.18, H 5.89, N 6.76.

*5-(4-Fluorophenyl)-1-[4-(propan-2-yl)phenyl]-1*H*-pyrazol-3-yl β-*D*-Glucopyranoside* (**6c**). Yield: 0.27 g (58%). Colorless crystals. M.p. 104–105°. ^{1}H-NMR (CD_3OD, 500 MHz): 7.28–7.24 (*m*, 4 arom. H); 7.15 (*d*, *J* = 8.5, 2 arom. H); 7.06 (*d*, *J* = 8.8, 2 arom. H); 6.23 (*s*, H–C(4)); 5.13 (*d*, *J* = 7.6, H–C(1′)); 3.90 (*dd*, *J* = 2.2, 12.0, H–C(2′)); 3.70 (*dd*, *J* = 5.7, 12.1, H–C(3′)); 3.48–3.45 (*m*, H–C(4′), CH_2(6′)); 3.40–3.36 (*m*, H–C(5′)); 2.94–2.91 (*m*, Me_2CH); 1.25 (*d*, *J* = 6.9, Me_2CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 165.9; 163.1 (*J*(C,F) = 76.9); 150.2; 145.0; 138.7; 132.0 (*J*(C,F) = 8.2); 128.1; 127.9 (*J*(C,F) = 3.8); 126.8; 116.5 (*J*(C,F) = 22.0); 102.7; 95.1; 78.5; 77.9; 74.8; 71.4; 62.6; 35.0; 24.2. ^{19}F-NMR ($CDCl_3$, 282 MHz): −110.9. Anal. calc. for $C_{24}H_{27}FN_2O_6$ (458.48): C 62.87, H 5.94, N 6.11; found: C 62.72, H 5.96, N 6.13.

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