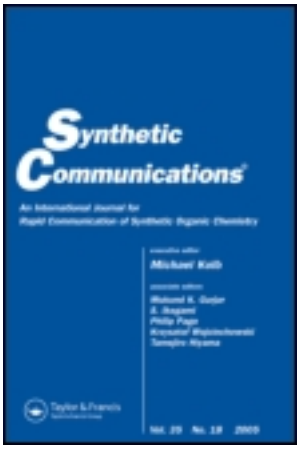

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Synthesis, Characterization, and Fungicidal Activity of New Thienopyridopyrimidine Derivatives

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SYNTHESIS, CHARACTERIZATION, AND FUNGICIDAL ACTIVITY OF NEW THIENOPYRIDOPYRIMIDINE DERIVATIVES

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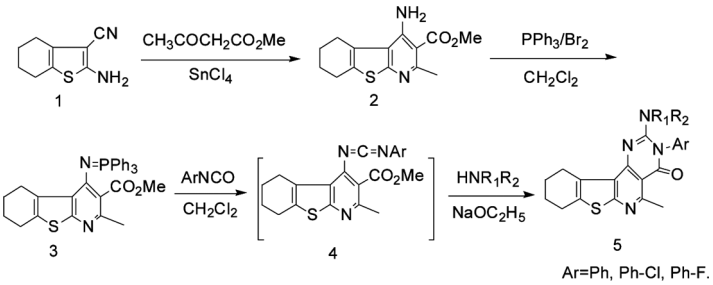
GRAPHICAL ABSTRACT



Abstract *Iminophosphorane **3** is a important intermediate in organic synthesis. A series of new 2-substituted tetrahydrobenzo[4′,5′]thieno[3′,2′:5,6]pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones **5** have been designed and synthesized via the tandem aza-Wittig reaction in 58–92% yields. Iminophosphorane 3 reacted with phenyl isocyanate (or 4-chlorophenyl isocyanate, 4-fluorophenyl isocyanate) to give carbodiimide **4**, which was further treated with amines to cyclize in the presence of a catalytic amount of EtONa. The structures of compounds **5** have been confirmed by ^{1}H NMR, electron-impact mass spectrometry, infrared spectroscopy, and elemental analyses. The results of preliminary bioassay indicated that some compounds possess inhibition activities against* Rhizoctonia solani *and* Botrytis cinereapers *at a dosage of 50 mg/L.*

Keywords Aza-Wittig reaction; carbodiimide; fungicidal activity; iminophosphorane; pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones

INTRODUCTION

The derivatives of pyrido[4,3-*d*]pyrimidine have attracted the interest of pharmaceutical companies recently. Many pyrido[4,3-*d*]pyrimidines have been synthesized as EGFR-TK (epidermal growth factor receptor–tyrosine kinase) and DHFR (dihydrofolate reductase) inhibitors. Some reports have showed that these compounds exhibited a wide range of biological activities such as antitumor,

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antiviral, anti-inflammatory, and antimicrobial properties.[1,2] However, few reports so far are available on the pesticidal activities of pyrido[4,3-*d*]pyrimidine derivatives.

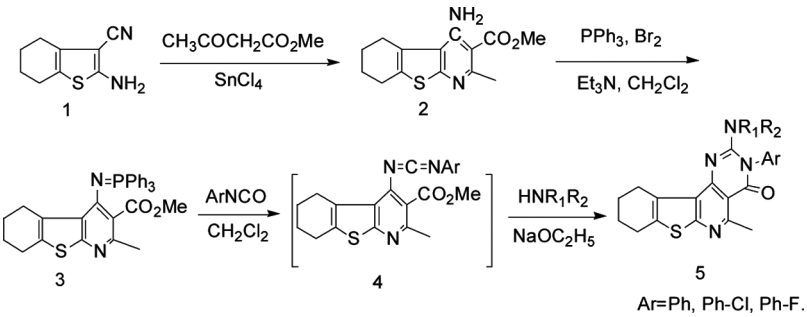
The methods described so far to prepare pyrido[4,3-*d*]pyrimidines mainly involve the formation of pyrimidine ring by cyclization of suitable substitutents of pyridine ring, but the yields are very poor in most cases. For example, pyrido[4,3-*d*]-pyrimidine was constructed by condensing 4-amino- 2,6-dichloronicotinamide with triethylorthoacetate, but pyrido[4,3-*d*]pyrimidine derivative could be isolated in only a 38% yield.[3]

The aza-Wittig reactions of iminophosphoranes have received increasing attention in view of their utility in the synthesis of N-heterocyclic compounds.[4,5] Recently, we focused our attention on the synthesis of pyrazolopyrimidinones, thienopyrimidinones, and pyridopyrimidinones from various iminophosphoranes, with the aim of evaluating their biological activities.[6,7] Here we report a facile synthesis of pyrido[4,3-*d*]pyrimidine derivatives from the easily accessible iminophosphorane **3** in good yields. The structures of the prepared compounds, 2-substituted tetrahydrobenzo[4′,5′]thieno[3′,2′:5,6] pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones **5,** have been comfirmed by ^{1}H NMR, electron-impact mass spectrometry (EI-MS), infrared (IR) spectroscopy, and elemental analyses. The preliminary bioassay showed that some of them have fungicidal activities.

RESULTS AND DISCUSSION

The tetrahydrobenzo[4,5]thieno[2,3-*b*]pyridine **2**, easily obtained from tetrahydrobenzo[*b*] thiophene-3-carbonitrile **1** and methyl acetoacetate in the presence of $SnCl_4$, was converted to iminophosphorane **3** via reaction with Ph_3P in CH_2Cl_2, Br_2, and Et_3N (Scheme 1).

The iminophosphorane **3** reacted with phenyl isocyanate (or 4-chlorophenyl isocyanate,4-fluorophenyl isocyanate) to give carbodiimide **4**. Even in refluxing toluene, **4** did not react with alkylamines to give the target compounds. However, in CH_2Cl_2 in the presence of a catalytic amount of NaOEt, compounds **4** were converted smoothly to 2-alkylamino-8,9,10,11-tetrahydrobenzo[4′,5′]thieno[3′,2′:5,6]-pyrido[4, 3-*d*]pyrimidin-4(3*H*)-ones **5a–5r** in satisfactory yields at room temperature. Irrespective of the fact of whether primary or secondary alkylamines were used, the cyclization was completed in good yields (Table 1).



Scheme 1. Reaction pathway to 2-substituted tetrahydrobenzo[4′,5′]thieno[3′,2′:5,6] pyrido[4,3-*d*]-pyrimidin-4(3*H*)-ones.

Table 1. Physical constants of 2-substituted 5-methyl-8,9,10,11-tetrahydrobenzo[4′,5′]thieno[3′,2′:5,6]pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones **5**

Compound	R_1R_2NH	Ar	Formula	Color	Mp (°)	Reaction time [h]	Yield (%)[a]
5a	Morpholin	Ph	$C_{24}H_{24}N_4O_2S$	White crystals	186–187	5	76
5b	Imidazole	Ph	$C_{23}H_{19}N_5OS$	White crystals	185–186	8	67
5c	β-ph-Ethylamine	Ph	$C_{28}H_{26}N_4OS$	White crystals	232–233	9	58
5d	$NH_2CH(CH_3)CH_2CH_3$	4-ClPh	$C_{24}H_{25}ClN_4OS$	White crystals	286–288	7	91
5e	$NH_2C(CH_3)_3$	4-ClPh	$C_{24}H_{25}ClN_4OS$	White crystals	>300	7	87
5f	$NH(CH_2CH_3)_2$	4-ClPh	$C_{24}H_{25}ClN_4OS$	White crystals	>300	9	65
5g	furfuryl amine	4-ClPh	$C_{25}H_{21}ClN_4O_2S$	White crystals	244–246	6	89
5h	hexahydropyridine	4-ClPh	$C_{25}H_{25}ClN_4OS$	White crystals	250–252	5	73
5i	Tert-amylamine	4-ClPh	$C_{25}H_{27}ClN_4OS$	White crystals	263–265	6	90
5j	$NH((CH_2)_3CH_3)_2$	4-ClPh	$C_{28}H_{33}ClN_4OS$	White crystals	168–170	10	71
5k	$NH((CH_2)_2CH_3)_2$	4-ClPh	$C_{26}H_{29}ClN_4OS$	White crystals	>300	10	83
5l	Morpholin	4-ClPh	$C_{24}H_{23}ClN_4OS$	White crystals	>300	5	75
5m	Imidazole	4-ClPh	$C_{23}H_{18}ClN_5OS$	White crystals	268–270	8	68
5n	β-ph-ethylamine	4-ClPh	$C_{28}H_{25}ClN_4OS$	White crystals	299–300	9	64
5o	β-ph-ethylamine	4-FPh	$C_{28}H_{25}FN_4OS$	White crystals	>300	9	69
5p	Morpholin	4-FPh	$C_{24}H_{23}FN_4O_2S$	White crystals	>300	5	84
5q	$NH_2CH_2CH_2CH_3$	4-FPh	$C_{23}H_{23}FN_4OS$	White crystals	251–252	7	88
5r	NH_2 $(CH_2)_3CH_3$	4-FPh	$C_{24}H_{25}FN_4OS$	White crystals	244–245	7	92

[a]Yields of isolateded products based on iminophosphorane **3**.

Table 2. Elemental analyses and IR spectral data of compounds **5**

Compound	Calcd. (found) (%)			IR (KBr, cm^{-1})
	C	H	N	
5a	66.64 (66.83)	5.59 (5.49)	12.95 (12.99)	3178 (Ph-H), 2985, 2924 (C-H), 1710 (C=O), 1587, 1495, 1195, 1108, 963.
5b	66.81 (66.60)	4.63 (4.48)	16.94 (17.06)	3135 (Ph-H), 2934, 2857 (C-H), 1700 (C=O), 1582, 1490, 1257, 1005, 748.
5c	72.07 (71.79)	5.62 (5.42)	12.01 (12.43)	3380 (N-H), 3112 (Ph-H), 2936, 2834 (C-H), 1678 (C=O), 1584, 1448, 1143.
5d	63.63 (63.54)	5.56 (5.49)	12.37 (12.78)	3362 (N-H), 3024 (Ph-H), 2935, 2866 (C-H), 1669 (C=O), 1588, 1385, 1159.
5e	63.63 (63.42)	5.56 (5.45)	12.37 (12.58)	3424 (N-H), 3151 (Ph-H), 2930 (C-H), 1685 (C=O), 1578, 1400, 1209, 1089.
5f	63.63 (63.76)	5.56 (5.25)	12.37 (12.56)	3147 (Ph-H), 2964, 2944 (C-H), 1686 (C=O), 1559, 1511, 1091, 870.
5g	62.95 (62.67)	4.44 (4.65)	11.75 (12.01)	3366 (N-H), 3014 (Ph-H), 2937 (C-H), 1668 (C=O), 1581, 1511, 1281, 1072.
5h	64.57 (64.34)	5.42 (5.61)	12.05 (12.44)	3135 (Ph-H), 2940, 2832 (C-H), 1689 (C=O), 1582, 1490, 1187, 1092, 889.
5i	64.29 (64.59)	5.83 (5.81)	12.00 (12.33)	3429 (N-H), 3049 (Ph-H), 2958 (C-H), 1678 (C=O), 1580, 1511, 1200, 1087.
5j	66.60 (66.31)	6.53 (6.29)	11.00 (11.20)	3136 (Ph-H), 2958, 2931, 2871 (C-H), 1687 (C=O), 1558, 1402, 1092, 807.
5k	64.92 (64.74)	6.08 (6.24)	11.65 (11.96)	3151 (Ph-H), 2974, 2868 (C-H), 1686 (C=O), 1545, 1511, 1243, 1089, 802.
5l	61.73 (61.50)	4.96 (4.76)	12.00 (11.93)	3135 (Ph-H), 2931, 2856 (C-H), 1688 (C=O), 1559, 1513, 1248, 1117, 896.
5m	61.67 (61.75)	4.05 (4.19)	15.63 (15.55)	3135 (Ph-H), 2946, 2857 (C-H), 1700 (C=O), 1560, 1492, 1262, 1095, 1002.
5n	67.12 (77.74)	5.03 (5.22)	11.18 (11.30)	3422 (N-H), 3180 (Ph-H), 2934 (C-H), 1674 (C=O), 1561, 1509, 1091, 1050.
5o	69.40 (69.81)	5.12 (5.11)	11.56 (11.35)	3423 (N-H), 3182 (Ph-H), 2930 (C-H), 1685 (C=O), 1585, 1508, 1222, 1146.
5p	63.98 (63.74)	5.15 (5.49)	12.44 (12.42)	3110 (Ph-H), 2961, 2932 (C-H), 1690 (C=O), 1556, 1505, 1249, 1117, 1051.
5q	65.38 (64.97)	5.49 (5.63)	13.26 (13.64)	3389 (N-H), 3143 (Ph-H), 2939 (C-H), 1700 (C=O), 1585, 1511, 1156, 1088.
5r	66.03 (65.75)	5.77 (5.98)	12.83 (13.11)	3444 (N-H), 3239 (Ph-H), 1678 (C=O), 1557, 1517, 1450, 1155, 805.

All products of type **5** were purified by recrystallization from CH_2Cl_2 and petroleum ether. The results are listed in Table 1. All target compounds are white crystals and their melting points are high. The structures were confirmed by their spectroscopic data (Tables 2–4). For example, the IR spectra of **5a** revealed absorption bands at 1710 cm^{-1} (C=O), 3178 cm^{-1} (Ph-H), and 2985, 2924 cm^{-1} (C-H). The ^1H NMR spectra of **5a** showed the singlet of Me at the pyridine ring

Table 3. ^1H NMR spectral data of compounds **5**

Compound	^1H NMR (ppm, $CDCl_3$, TMS, 400 MHz)
5a	1.89–1.97 (m, 4H, $2CH_2$), 2.81–3.27 (m, 4H, $2CH_2$), 2.98 (s, 3H, CH_3), 3.30–3.41 (m, 4H, $2CH_2$), 3.68–3.74 (m, 4H, $2CH_2$), 6.94–7.26 (m, 5H, Ar-H).
5b	1.92–1.99 (m, 4H, $2CH_2$), 2.93–3.26 (m, 4H, $2CH_2$), 3.07 (s, 3H, CH_3), 6.87 (s, 1H, C=CH), 6.92 (s, 1H, C=CH), 7.26–7.57 (m, 5H, Ar-H), 7.83 (s, 1H, C=CH).
5c	1.91–1.98 (m, 4H, $2CH_2$), 2.89–3.37 (m, 4H, $2CH_2$), 2.97 (s, 3H, CH_3), 4.37 (s, 1H, NH), 2.90–2.94 (m, 2H, CH_2), 3.67–3.86 (m, 2H, CH_2), 7.04–7.55 (m, 5H, Ar-H).
5d	0.87–0.91 (m, 6H, $2CH_3$), 1.89–1.96 (m, 4H, $2CH_2$), 2.88–3.29 (m, 4H, $2CH_2$), 2.95 (s, 3H, CH_3), 1.97–2.04 (m, 1H, CH), 1.56–1.63 (m, 2H, CH_2), 4.43 (s, 1H, NH), 7.26–7.62 (m, 4H, Ar-H).
5e	1.43 (s, 9H, $3CH_3$), 1.90–1.97 (m, 4H, $2CH_2$), 2.89–3.28 (m, 4H, $2CH_2$), 2.95 (s, 3H, CH_3), 4.19 (s, 1H, NH), 7.27–7.62 (m, 4H, Ar-H).
5f	0.93 (t, 6H, $J = 7.2$ Hz, $2CH_3$), 1.91–1.96 (m, 4H, $2CH_2$), 2.89–3.27 (m, 4H, $2CH_2$), 2.97 (s, 3H, CH_3), 3.25 (q, 4H, $J = 7.2$ Hz, $2CH_2$), 7.27–7.53 (m, 4H, Ar-H).
5g	1.80 (s, 1H, NH), 1.86–1.93 (m, 4H, $2CH_2$), 2.89–3.29 (m, 4H, $2CH_2$), 2.99 (s, 3H, CH_3), 4.70–4.77 (m, 2H, CH_2), 6.21 (s, 1H, C=CH), 6.32(s, 1H, C=CH), 6.62 (s, 1H, C=CH), 7.28–7.58 (m, 4H, Ar-H).
5h	1.38 (s, 4H, $2CH_2$ of pyridyl), 1.51 (s, 2H, CH_2 of pyridyl), 1.90–1.96 (m, 4H, $2CH_2$), 2.88–3.27 (m, 4H, $2CH_2$), 2.97 (s, 3H, CH_3), 3.18–3.29 (m, 4H, $2CH_2N$), 7.27–7.50 (m, 4H, Ar-H).
5i	0.76 (t, 3H, $J = 7.2$ Hz, CH_3), 1.38 (s, 6H, $2CH_3$), 1.81 (q, 2H, $J = 7.2$ Hz, CH_2), 1.90–1.98 (m, 4H, $2CH_2$), 2.89–3.26 (m, 4H, $2CH_2$), 2.96 (s, 3H, CH_3), 4.11 (s, 1H, NH), 7.27–7.62 (m, 4H, Ar-H).
5j	0.86 (t, 6H, $J = 7.2$ Hz, $2CH_3$), 1.12–1.20 (m, 4H, $2CH_2$), 1.25–1.28 (m, 4H, $2CH_2$), 1.90–1.96 (m, 4H, $2CH_2$), 2.89–3.28 (m, 4H, $2CH_2$), 2.97 (s, 3H, CH_3), 3.10–3.22 (m, 4H, $2CH_2N$), 7.27–7.50 (m, 4H, Ar-H).
5k	0.78 (d, 6H, $J = 7.2$ Hz, $2CH_3$), 1.34–1.46 (m, 4H, $2CH_2$), 1.90–1.97 (m, 4H, $2CH_2$), 2.88–3.27 (m, 4H, $2CH_2$), 2.96 (s, 3H, CH_3), 3.02–3.17 (m, 4H, $2CH_2N$), 7.27–7.50 (m, 4H, Ar-H).
5l	1.90–1.98 (m, 4H, $2CH_2$), 2.89–3.27 (m, 4H, $2CH_2$), 2.99 (s, 3H, CH_3), 3.23–3.36 (m, 4H, $2CH_2$), 3.51–3.59 (m, 4H, $2CH_2$), 7.26–7.52 (m, 4H, Ar-H).
5m	1.91–1.97 (m, 4H, $2CH_2$), 2.92–3.23 (m, 4H, $2CH_2$), 3.06 (s, 3H, CH_3), 6.89 (s, 1H, C=CH), 6.98 (s, 1H, C=CH), 7.24–7.53 (m, 4H, Ar-H), 7.86 (s, 1H, C=CH).
5n	1.88–1.96 (m, 4H, $2CH_2$), 2.88–3.35 (m, 4H, $2CH_2$), 2.96 (s, 3H, CH_3), 4.29 (s, 1H, NH), 2.91–2.93 (m, 2H, CH_2), 3.72–3.78 (m, 2H, CH_2), 7.04–7.49 (m, 4H, Ar-H).
5o	1.90–1.97 (m, 4H, $2CH_2$), 2.89–3.36 (m, 4H, $2CH_2$), 2.95 (s, 3H, CH_3), 4.31 (s, 1H, NH), 2.90–2.93 (m, 2H, CH_2), 3.71–3.79 (m, 2H, CH_2), 7.05–7.30 (m, 4H, Ar-H).
5p	1.89–1.95 (m, 4H, $2CH_2$), 2.89–3.24 (m, 4H, $2CH_2$), 2.98 (s, 3H, CH_3), 3.23–3.28 (m, 4H, $2CH_2N$), 3.54∼3.59 (m, 4H,$2CH_2O$), 7.21–7.41 (m, 4H, Ar-H).
5q	0.90 (t, $J = 7.6$ Hz, 3H, CH_3), 1.62 (q, $J = 7.6$ Hz, 2H, CH_2), 1.88–1.96 (m, 4H, $2CH_2$), 2.87–3.29 (m, 4H, $2CH_2$), 2.94 (s, 3H, CH_3 of pyridyl), 3.41–3.49 (m, 2H, NCH_2), 3.75 (s, 1H, NH), 7.26–7.32 (m, 4H, Ar-H).
5r	0.93 (t, $J = 7.2$ Hz, 3H, CH_3), 1.32 (q, $J = 7.2$ Hz, 2H, CH_2), 1.54–1.61 (m, 2H, CH_2), 1.90–1.94 (m, 4H, $2CH_2$), 2.87–3.30 (m, 4H, $2CH_2$), 2.95 (s, 3H, CH_3 of pyridyl), 3.46–3.50 (m, 2H, NCH_2), 4.35 (s, 1H, NH), 7.26–7.33 (m, 4H, Ar-H).

Table 4. EI–mass spectra of compounds **5**

Compound	MS (EI, m/z, %)
5a	434 (36), 432 (M^+, 100), 406 (59), 393 (18), 387 (56), 346 (29).
5b	413 (M^+, 100), 399 (32), 386 (39), 346 (6), 76 (23.70).
5c	468 (12), 467 ($M^+ + 1$, 42), 466 (M^+, 90), 375 (25), 362 (100), 361 (39), 347 (26), 334 (19), 90 (18).
5d	455 (49), 452 (M^+, 100), 437 (13), 398 (18), 396 (21), 395 (31), 56 (38), 43 (37).
5e	454 (34), 453 ($M^+ + 1$, 11), 452 (M^+, 100), 398 (48), 396 (75), 395 (99), 391 (48), 367 (29), 56 (25).
5f	454 (20), 453 (M^+, 78), 426 (34), 424 (100), 380 (16), 314 (15), 313 (34).
5g	479 (23), 477(M^+, 25), 476 (100), 447 (21), 419 (14), 395 (19), 80 (40), 52 (18).
5h	466 (35), 465 ($M^+ + 1$, 28), 464 (M^+, 100), 438 (11), 436 (31), 380 (12), 326 (12), 216 (12), 194 (34).
5i	468 (14), 467 (15), 466 (M^+, 46), 399 (25), 398 (28), 396 (100), 381 (15), 367 (17).
5j	511 (34), 510 ($M^+ + 1$, 30), 509 (M^+, 100), 480 (33), 466 (13), 452 (83), 409 (50), 341 (38), 299 (43).
5k	482 ($M^+ + 1$, 28), 481 (M^+, 100), 440 (31), 437 (97), 409 (30), 380 (27), 329 (15), 327 (37), 298 (15).
5l	469 (31), 468 ($M^+ + 1$, 26), 467 (M^+, 100), 435 (8), 421 (16), 410 (19).
5m	450 (30), 448 (M^+, 100), 433 (17), 420 (10), 419 (13).
5n	503 (13), 502 ($M^+ + 1$, 14), 501 (M^+, 56), 485 (30), 396 (100), 380 (63), 368 (17), 365 (13), 102 (11).
5o	486 ($M^+ + 1$, 20), 485 (M^+, 74), 393 (17), 381 (100), 377 (23), 366 (29), 352 (22), 351 (11).
5p	451 (M^+, 100), 422 (9), 419 (9), 406 (25), 394 (25), 364 (9).
5q	423 ((M^+, 100), 408 (15), 394 (8), 380 (43), 365 (16), 352 (10), 95 (13).
5r	437 (M^+, 100), 394 (10), 381 (11), 379 (11), 365 (11), 95 (19), 57 (13).

at 2.98 ppm and signals of the cyclohexenyl CH_2 at 1.89–1.97 and 2.81–3.27 ppm. The signals of the morpholin CH_2 were at 3.30–3.41 and 3.68–3.74 ppm. The other signals appeared at 6.94–7.26 (*m*, 5H, Ar-H). The MS spectrum of **5a** shows the molecule ion peak at m/z 432 with 100% abundance. All the fragmentation ions were consistent with their structures and can be clearly assigned. The structure of **5a** was also established on the basis of elemental analysis data (Table 2), and the errors between found values and calculated values are no more than 0.5%.

The preliminary fungicidal activities of compounds **5** were measured in a concentration of 50 mg/L using a reported procedure.[8] Six fungi, *Fusarium oxysporium, Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria*, and *Bipolaris maydis*, were tested, and the data of inhibition rates are listed in Table 5. It was found that some of the target compounds induce a good inhibition effect against *Rhizoctonia solani* and *Botrytis cinereaper.* For example, the inhibition rates of compound **5l** against *Rhizoctonia solani* was 98.05% and against *Botrytis cinereapers* was 100%. It is worth noting that the chloro-containing compound **5l** displayed much better fungicidal activity than nonsubstituted phenyl compound **5a**. The biological evaluation showed that some 2-substituted tetrahydrobenzo[4′,5′]thieno-[3′,2′:5,6]pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones have fungicidal activities and could be further developed as lead compounds.

In conclusion, we have developed a facile and efficient regioselective method for the preparation of pyrido[4,3-*d*]pyrimidine derivatives. The thienopyridine

Table 5. Fungicidal activity of some compounds **5** (50 ppm)

Compound	Inhibition rate (%)					
	Fusarium oxysporium	*Rhizoctonia solani*	*Botrytis cinereapers*	*Gibberella zeae*	*Dothiorella gregaria*	*Bipolaris maydis*
5a	49.35	63.46	70.91	44.23	56.08	51.20
5c	39.63	56.06	67.91	34.50	38.29	42.22
5d	58.06	84.54	88.10	62.16	60.00	77.27
5h	48.39	80.41	73.81	45.95	52.00	63.64
5i	51.61	85.57	95.24	62.16	68.00	68.18
5l	83.55	98.05	100.00	71.89	67.43	80.76
5n	61.29	82.47	93.33	56.76	60.00	72.73
5o	50.75	73.79	82.36	54.85	55.94	64.38
5p	66.66	86.05	91.23	68.43	62.79	74.57

derivative **2** reacts with Ph_3P and Br_2 to give iminophosphorane **3** in excellent yield. Iminophosphorane **3** is an important intermediate in organic synthesis. The results of preliminary bioassay indicated that some compounds posses inhibition activities against *Rhizoctonia solani* and *Botrytis cinereapers* at a dosage of 50 mg/L.

EXPERIMENTAL

Melting points were measured on a WRS-1B digital apparatus and are uncorrected. MS were measured on a Finnigan Trace MS spectrometer. IR spectra were recorded on a PE-983 IR spectrometer as KBr pellets, in cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian Mercury 400 spectrometer and resonances are given in parts per million (ppm) relative to tetramethyl silane (TMS). Elemental analyses were taken on a Vario EL III instrument. All of the solvents and materials were reagent grade and purified as required.

Preparation of Thienopyridine Derivatives 2[9]

The thienopyridine derivative **2** was prepared according to literature[9] procedures.

Preparation of Iminophosphorane 3[10]

A solution of triphenylphosphine (2.6 g, 10 mmol) in dichloromethane (50 mL) at 0 °C was treated with bromine (1.60 g, 10 mmol). The resulting reaction mixture was stirred at 0 °C for 30 min and then treated with triethylamine (2.1 g, 20 mmol), followed immediately by the addition of the thienopyridine derivative **2** (2.77 g, 10 mmol). After **2** was added, the cooling bath was removed and the reaction mixture was allowed to stir at 25 °C for 20 h.The reaction mixture was washed with water and then dried. After removal of the solvent, residue was recrystallized from EtOH to give **3** in 93% yield.

Preparation of Carbodiimides 4 and Compounds 5a–5n[10]

The aryl isocyanate (1.1 mmol) to a solution of **3** (0.525 g, 1 mmol) in dry CH_2Cl_2 (20 ml) was added under N_2 at room temperature. After the reaction mixture was stirred for 1.5 h, alkylamine (1.1 mmol) was added to the reaction solution and stirred for an addition 30 min. Then the solvent was removed under reduced pressure, and 20 ml of anhydrous EtOH with several drops of EtONa in EtOH were added. The mixture was stirred for 5–10 h at room temperature. The mixture was filtered, furnishing a white solid, which was either recrystallized from CH_2Cl_2/petroleum ether or purified on silica gel to give 2-alkylamino-3-aryl-5-methyl-8,9,10,11-tetrahydrobenzo [4′,5′]thieno[3′,2′:5,6]pyrido[4,3-*d*]pyrimidin-4(3*H*)-ones **5a–5n**.

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