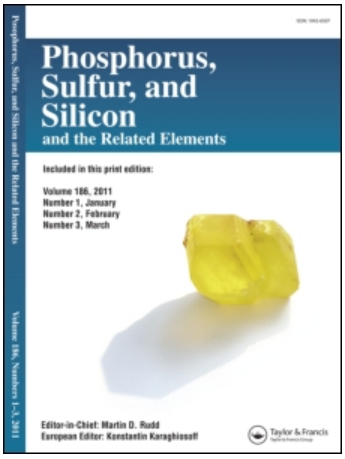

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One-Pot Synthesis and Fungicidal Activities of Derivatives of Imidazo [2,1-b]-1,3,4-thiadiazol-5(6*H*)-one

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*The isothiocyanates **2**, obtained from aza-Wittig reactions of vinyliminophosphoranes **1** with CS_2, reacted with hydrazine to give 3-amino-2-thioxo-4-imidazolidinones **4**. One-pot reactions of **4**, aromatic isocyanates, Ph_3P, C_2Cl_6, and Et_3N generated imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones **7**. Compound **7** exhibited good fungicidal activities, especially against Sclerotinia sclerotiorum de Bary and Botrytis Cinerea Pers.*

Keywords Imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one; aza-Wittig reaction; fungicidal activities; synthesis

INTRODUCTION

Many 4*H*-imidazol-4-ones have shown biological and pharmaceutical activities,[1–3] and some 2-alkylthioimidazolones exhibit significant fungicidal activities.[4–6] The introduction of a thiadiazole ring to the imidazolone system is expected to influence significantly biological activities. However, there are few reports on the synthesis and biological activities of imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones.[7,8]

The aza-Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of nitrogen

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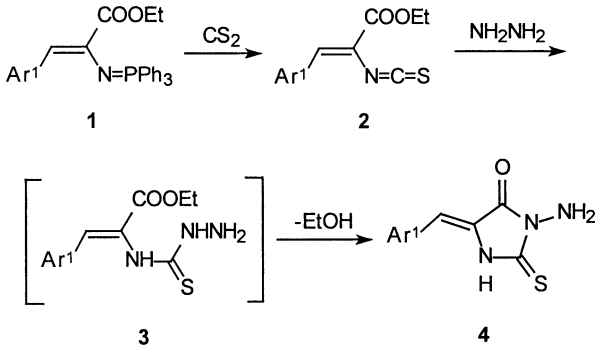
heterocyclic compounds.[9–11] Recently, we have been interested in the synthesis of imidazolones via an aza-Wittig reaction with the aim of evaluating their fungicidal activities.[8,12–14] Here we wish to report further a one-pot synthesis and fungicidal activities of imidazo [2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones.

RESULTS AND DISCUSSION

Iminophosphorane **1** reacted with CS_2 to give isothiocyanates **2**, which were allowed to react with hydrazine to give 3-amino-2-thioxo-4-imidazolidinones **4** in 77–94% yields (Scheme 1). The formation of **4**

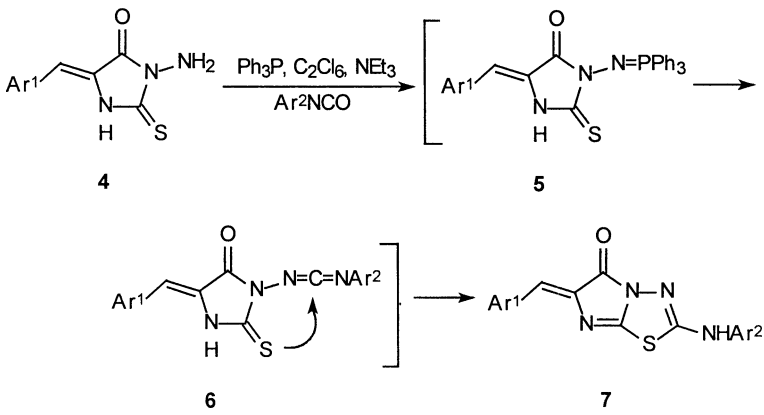


SCHEME 1

can be rationalized in terms of an initial nucleophilic addition of hydrazine to give the thiourea intermediate **3** which cyclizes to give **4**.

In our previous report,[8] 3-amino-2-thioxo-4-imidazolidinones **4** were transformed into a corresponding iminophosphorane and were further converted to imidazo[2,1-b]-1,3,4-thiadiazol- 5(6*H*)-ones. Here, we try to convert **4** directly to imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones in a one-pot fashion so as to simplify the operation. When triethylamine was added to a mixture of 3-amino-2-thioxo-4-imidazolidinones **4**, aromatic isocyanates, triphenyphosphine, and hexachloroethane in CH_2Cl_2, the color of the reaction mixture turned red, and 2-arylamino-imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones **7** were successfully isolated as crystalline solids in better overall yields (47–68%, Scheme 2, Table I). In these cases, iminophosphoranes **5**, generated in situ from **4**, reacted immediately with aromatic isocyanates to give **7** in moderate yields via the cyclization of carbodiimides **6** across the mercapto group.

Structures of **7** have been compared with our previous results or characterized spectroscopically. For example, the ^{1}H NMR spectral data in 7**j** show signals for -CH_3 and -NHAr at δ2.28 and δ10.87 as singlets.



SCHEME 2

Signals of alkenyl hydrogen were overlapped with signals of Ar (δ7.99 – 6.75). The ^{13}C NMR spectrum data of **7j** showed the signals of C=O, C_8, and C_2 at 163.8, 159.4, and 153.0 ppm, respectively. The signals of fufuryl C-2, C-5, and methyl C appeared at 150.0, 146.9, and 21.2 ppm, respectively. In the IR spectral data of **7j**, the stretching resonance peak of N—H appears at 3291 cm^{-1}. The strong stretching resonance peak of imidazolone C=O appears at 1693 cm^{-1}. The stretching of C=C shows a relatively strong absorbtion at about 1634 cm^{-1} due to a resonance

TABLE I One-Pot Preparation of Imidazo[2,1-b]-1,3,4-Thiadiazol-5(6*H*)-Ones 7

	Ar^1	Ar^2	Yield (%)*
7a	Ph	4-Me-C_6H_4	68
7b	Ph	3-Me-C_6H_4	51
7c	Ph	Ph	58
7d	Ph	4-Cl-C_6H_4	52
7e	Ph	4-Br-C_6H_4	47
7f	4-Cl-C_6H_4	3-Me-C_6H_4	66
7g	4-Cl-C_6H_4	Ph	56
7h	4-MeO-C_6H_4	4-Me-C_6H_4	66
7i	4-MeO-C_6H_4	Ph	59
7j	2-Furfuryl	4-Me-C_6H_4	62
7k	2-Furfuryl	3-Me-C_6H_4	57
7l	2-Furfuryl	Ph	48
7m	2-Furfuryl	4-Cl-C_6H_4	53
7n	2-Furfuryl	4-Br-C_6H_4	55

*Isolated yields of **7** based on imidazolidinones **4**.

TABLE II Fungicidal Activities of Imidazo[2,1-b]-1,3,4-Thiadiazol-5(6*H*)-Ones 7 (50 mg/L, Relative Inhibition of Growth %)

Compound	*Fusarium oxysporum*	*Pyricularia oryzae*	*Botrytis Cinerea Pers.*	*Gibberella zeae*	*Sclerotinia sclerotiorum de Bary*
7a	38	59	100	38	100
7b	25	49	49	32	91
7c	38	46	94	32	98
7d	38	62	97	46	98
7e	79	87	100	73	100
7f	88	100	100	95	100
7g	33	56	100	86	98
7h	88	79	100	86	100
7i	54	51	94	86	100
7j	38	46	86	68	98
7k	54	74	100	73	100
7l	50	67	100	59	96
7m	46	64	97	89	100
7n	38	54	91	54	78

effect. The MS spectrum of **7j** shows a molecule ion peak at *m*/*z* 324 with 37% abundance.

Biological activities of **7** were investigated, and the results showed that they exhibited good fungicidal activities, especially against *Sclerotinia sclerotiorum de Bary* and *Botrytis Cinerea Pers*. For example, **7f** showed 100% inhibition of *Sclerotinia sclerotiorum de Bary*, *Pyricularia oryzae*, and *Botrytis Cinerea Pers* in 50 mg/L (see Table II).

EXPERIMENTAL

Melting points were uncorrected. MS were measured on a Finnigan Trace MS spectrometer. IR were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. NMR were recorded in DMSO-d_6 on a Varian Mercury 400 spectrometer, and resonances are given in ppm (δ) relative to TMS. Elementary analyses were taken on a Vario EL III elementary analysis instrument.

One-Pot Preparation of Imidazo[2,1-b]-1,3,4-Thiadiazol-5(6*H*)-Ones 7

To a mixture of imidazolidinone **4**[8] (3 mmol), Ar^2NCO (3 mmol), PPh_3 (1.05 g, 4 mmol), and C_2Cl_6 (0.95 g, 4 mmol) in dry CH_2Cl_2 (15 mL) was

added dropwise NEt_3 (0.81 g, 8 mmol) at r.t. The color of the reaction mixture turned red. After the solution was stirred for 2–4 hr. The solvent was removed under reduced pressure, and the residue was recrystallized from EtOH to give 2-arylamino-imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-ones **7**.

2-(4-Methylphenylamino)-5-phenylmethylene-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7a)
Yellow crystals, m.p. 280–282°C, lit.[8] 279–280°C.

2-(3-Methylphenylamino)-5-phenylmethylene-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-One (7b)
Yellow crystals, m.p. 272–273°C, lit.[8] 270–271°C.

2-Phenylamino-5-phenylmethylene-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7c)
Yellow crystals, m.p. 276–277°C, lit.[8] 277–278°C.

2-(4-Chlorophenylamino)-5-phenylmethylene-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7d)
Yellow crystals, m.p. 254–255°C, lit.[8] 254–256°C.

2-(4-Bromophenylamino)-5-phenylmethylene-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7e)
Yellow crystals, m.p. 249–251°C, lit.[8] 251–252°C.

2-(3-Methylphenylamino)-5-(4-chlorophenylmethylene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7f)
Yellow crystals, m.p. 233–235°C, lit.[8] 232–234°C.

2-Phenylamino-5-(4-chlorophenylmethylene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7g)
Yellow crystals, m.p. 240–242°C, lit.[8] 242–244°C.

2-(4-Methylphenylamino)-5-(4-methoxyphenylmethylene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7h)
Yellow crystals, m.p. 268–269°C, lit.[8] 267–268°C.

2-Phenylamino-5-(4-methoxyphenylmethylene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7i)
Yellow crystals, m.p. 209–210°C, lit.[8] 211–212°C.

2-(4-Methylphenylamino)-5-(2-furfurylidene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7j)

Yellow crystals, m.p. 260°C, decomposed. ^{1}H NMR (DMSO-d_6, 400 MHz) δ10.87 (s, 1H, NH), 7.99–6.75 (m, 8H, Ar-H and =CH), 2.28 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ163.8 (C=O), 159.4 (C_8), 153.0 (C_2), 150.0, 146.9, 139.4, 138.8, 129.1, 124.1, 118.7, 118.5, 113.9, 113.2 (ArC), 21.2 (CH_3); IR (cm^{-1}), 3291 (NH), 1693 (C=O), 1634, 1588, 1250; MS (*m/z*, %), 324 (M^+, 37), 296 (38), 132 (100), 106 (26). Elemental anal. calcd. for $C_{16}H_{12}N_4O_2S$: C, 59.25; H, 3.73; N, 17.27. Found: C, 59.38; H, 3.77; N, 17.05.

2-(3-Methylphenylamino)-5-(2-furfurylidene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7k)

Yellow crystals, m.p. 260°C, decomposed. ^{1}H NMR (DMSO-d_6, 400 MHz) δ10.57 (s, 1H, NH), 7.99–6.75 (m, 8H, Ar-H and =CH), 2.33 (s, 3H, CH_3);^{13}C NMR (DMSO-d_6, 400 MHz) δ163.6 (C=O), 159.3 (C_8), 152.6 (C_2), 150.2, 146.7, 139.0, 138.6, 129.0, 128.5, 122.4, 119.2, 118.5, 117.3, 113.5, 113.1 (ArC), 20.8 (CH_3); IR (cm^{-1}), 3285 (NH), 1696 (C=O), 1634, 1586, 1267; MS (*m/z*, %), 324 (M^+, 27), 296 (30), 132 (100). Elemental anal. calcd. for $C_{16}H_{12}N_4O_2S$: C, 59.25; H, 3.73; N, 17.27. Found: C, 59.35; H, 3.53; N, 17.24.

2-Phenylamino-5-(2-furfurylidene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7l)

Yellow crystals, m.p. 263°C, decomposed. ^{1}H NMR (DMSO-d_6, 400 MHz) δ10.71 (s, 1H, NH), 7.97–6.74 (m, 9H, Ar-H and =CH); ^{13}C NMR (DMSO-d_6, 400 MHz) δ163.9 (C=O), 159.4 (C_8), 152.8 (C_2), 150.0, 146.8, 139.2, 138.6, 129.2, 123.0, 118.6, 118.1, 113.7, 113.0 (ArC); IR (cm^{-1}), 3290 (NH), 1692 (C=O), 1637, 1593, 1251; MS (*m/z*, %), 310 (M^+, 78), 282 (78), 118 (100). Elemental anal. calcd. for $C_{15}H_{10}N_4O_2S$: C, 58.06; H, 3.25; N, 18.05. Found: C, 58.14; H, 3.07; N, 18.06.

2-(4-Chlorophenylamino)-5-(2-furfurylidene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6H)-one (7m)

Yellow crystals, m.p. 260°C, decomposed. ^{1}H NMR (DMSO-d_6, 400 MHz) δ10.53 (s, 1H, NH), 8.54–6.50 (m, 8H, Ar-H and =CH); ^{13}C NMR (DMSO-d_6, 400 MHz) δ164.0 (C=O), 159.6 (C_8), 153.0 (C_2), 150.1, 146.9, 139.3, 138.9, 129.3, 123.5, 118.5, 118.3, 114.1, 113.8 (ArC); IR (cm^{-1}), 3280 (NH), 1689 (C=O), 1635, 1591, 1248; MS (*m/z*, %), 344 (M^+, 30), 316 (39), 152 (100). Elemental anal. calcd. for $C_{15}H_9ClN_4O_2S$: C, 52.26; H, 2.63; N, 16.25. Found: C, 52.21; H, 2.84; N, 16.37.

*2-(4-Bromophenylamino)-5-(2-furfurylidene)-imidazo[2,1-b]-1,3,4-thiadiazol-5(6*H*)-one (7n)*

Yellow crystals, m.p. 270°C, decomposed. ^{1}H NMR (DMSO-d_6, 400 MHz) δ11.54 (s, 1H, NH), 7.97–6.74 (m, 8H, Ar-H and =CH);^{13}C NMR (DMSO-d_6, 400 MHz) δ163.6 (C=O), 159.5 (C_8), 153.1 (C_2), 150.0, 146.7, 139.3, 138.9, 129.5, 123.8, 118.3, 118.1, 113.9, 113.3 (ArC); IR (cm^{-1}), 3270 (NH), 1689 (C=O), 1631, 1594, 1248; MS (*m/z*, %), 388 (M^+, 73), 360 (77), 196 (100). Elemental anal. calcd. for $C_{15}H_9BrN_4O_2S$: C, 46.29; H, 2.33; N, 14.39. Found: C, 46.15; H, 2.57; N, 14.23.

REFERENCES

[1] A. I. Khodair and J. P. Gesson, *Phosphorus, Sulfur, and Silicon*, **142,** 167 (1998).
[2] A. I. Khodair, H. I. El-Subbagh, and A. M. Al-Obaid, *Phosphorus, Sulfur, and Silicon*, **140,** 159 (1998).
[3] H. M. Elokdah, T. S. Sulkowski, and D. P. Strike, WO 9719931 (1997); *Chem. Abstr.*, **127,** 95279a (1997).
[4] B. L. Pilkington, S. E. Russell, A. J. Whittle, W. R. Mound, M. D. Turnbull, A. M. Kozakiewicz, and W. G. Whittingham, GB 2329180 (1999); *Chem. Abstr.*, **131,** 44817z (1999).
[5] G. Emeric, J. Hutt, and J. Perez, WO 9602538 (1996); *Chem. Abstr.*, **125,** 10818m (1996).
[6] J. P. Bascou, A. Gadras, J. Perez, G. Emeric, G. Lacroix, and C. Veyrat, EP 668270 (1995); *Chem. Abstr.*, **123,** 340128t (1995).
[7] C. S. Andotra, T. C. Langer, and A. Kotha, *J. Indian Chem. Soc.*, **74,** 125 (1997).
[8] M. W. Ding, B. Q. Fu, and L. Cheng, *Synthesis*, 1067 (2004).
[9] W. Kurosawa, T. Kan, and T. Fukuyama, *J. Amer. Chem. Soc.*, **125,** 8112 (2003).
[10] A. Csampai, G. Turos, V. Kudar, K. Simon, H. Oeynhausen, H. Wamhoff, and P. Sohar, *Eur. J. Org. Chem.*, 717 (2004).
[11] J. A. R. Rodrigues, R. A. Abramovitch, J. D. F. De Sousa, and G. C. Leiva, *J. Org. Chem.*, **69,** 2920 (2004).
[12] Y. Sun and M. W. Ding, *Phosphorus, Sulfur, and Silicon*, **178,** 2137 (2003).
[13] M. W. Ding, Y. Sun, S. J. Yang, X. P. Liu, and Z. J. Liu, *Synth. Commun.*, **33,** 1651 (2003).
[14] M. W. Ding, G. P. Zeng, and Z. J. Liu, *Phosphorus, Sulfur, and Silicon*, **177,** 1315 (2002).