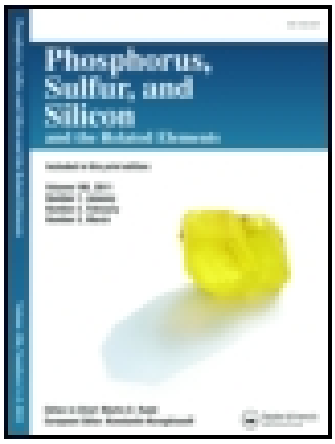

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Synthesis and Fungicidal Activities of 4H-Imidazolin-4-ones Containing Sulfur Substituent

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SYNTHESIS AND FUNGICIDAL ACTIVITIES OF 4H-IMIDAZOLIN-4-ONES CONTAINING SULFUR SUBSTITUENT

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*4H-Imidazolin-4-ones **3** and **4** were synthesized respectively by base catalytic reactions of 4-methylthiophenol or phenthiol with carbodiimides **2**, which were obtained via aza-Wittig reaction of iminophosphorane **1** with aromatic isocyanates. **3** and **4** exhibited good fungicidal activity against* Pellicularia sasakii.

Keywords: Aza-Wittig reaction; fungicidal activities; 4H-Imidazolin-4-ones; synthesis

INTRODUCTION

4H-Imidazolin-4-ones are important heterocycles having fungicidal activities, especial some 2-alkylthioimidazolinones.[1–3] Since a new mitochondrial respiratory inhibitor **1** (RPA407213) was found to show high fungicidal activities, many other 2-methylthioimidazolinones were synthesized to evaluated their fungicidal activities.[4–7] Recently, we are interested in the synthesis of biologically active imidazolinones via tandem aza-Wittig reaction.[8–10] Here we wish to report further the synthesis and fungicidal activity of some new 4H-imidazolin-4-one derivatives containing sulfur substituent.

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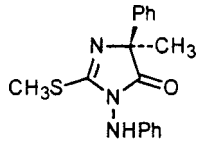
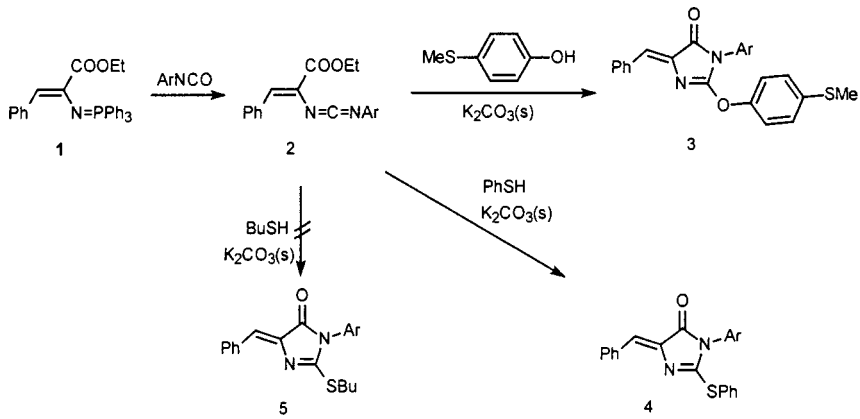


RPA 407213

RESULTS AND DISCUSSION

The easily accessible vinyliminophosphorane **1** reacted with aromatic isocyanates to give carbodiimides **2**, which were allowed to react with 4-methylthiophenol in presence of catalytic solid potassium carbonate to give the imidazolinones **3** at room temperature. Imidazolinones **4** was also obtained in good yields when phenthiol was used. Since the direct reaction of carbodiimide **2** with 4-methylthiophenol or phenthiol will take place at high temperature which will result in complex mixture,[11] the presence of solid potassium carbonate is necessary for the reaction to occur at room temperature. However, when butylthiol was utilized in presence or absence of K_2CO_3(s) or NaOH(s), no 2-butylthioimidazolinone **5** was obtained (see Table I.)



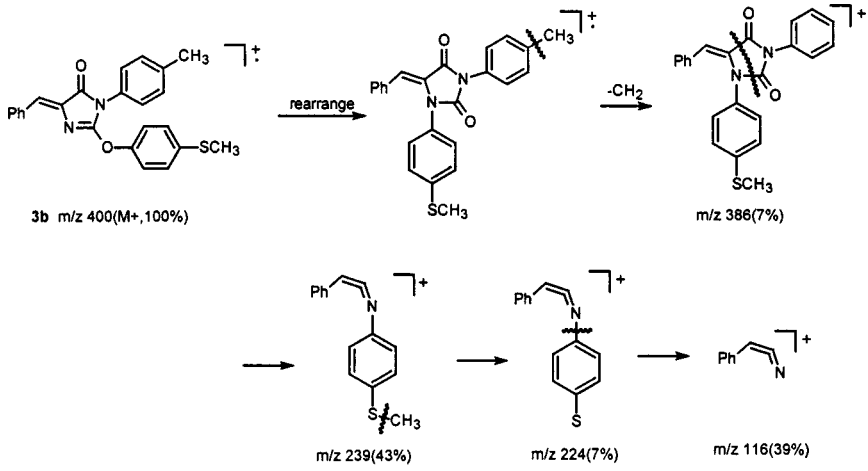
The structure of **3** and **4** has been characterized spectroscopically. For example, the ^{1}H NMR spectral data in **3b** show the signals of $-SCH_3$ and $-CH_3$ at 2.48 ppm and 2.39 ppm as single absorption respectively. The chemical shift of alkenyl hydrogen is 7.05 with single absorption. In the IR spectral data of **3b**, the strong stretching resonance peak of imidazolinone C=O appears at 1720 cm^{-1}. The stretching resonance of C=C shows relatively strong absorbtion at about 1648 cm^{-1} due to resonance effect. The stretching resonance of C=N shows strong absorbtion

TABLE I Preparation of 4H-Imidazolin-4-ones **3** and **4**

Compound	Ar	Reaction time (hr)	Yield (%)[a]
3a	Ph	7	77
3b	4-Me—Ph	8	82
3c	4-Cl—Ph	6	87
3d	3-Cl—Ph	6	89
4a	Ph	12	78
4b	4-Me—Ph	12	76
4c	4-Cl—Ph	10	75
4d	3-Cl—Ph	10	74
5a	Ph	6	0

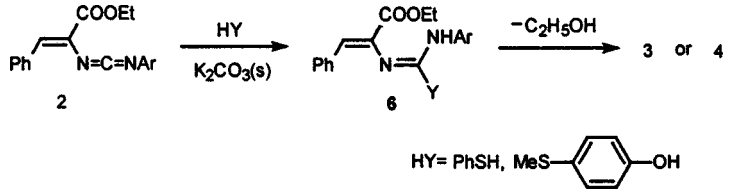
[a]Isolated yields based on iminophosphosphorane used.

at about 1560 cm^{-1}. The strong absorbtion at about 1290 cm^{-1} is probably due to the stretching resonance of C—O—C. The MS spectrum of **3b** shows strong molecule ion peak at m/z 400 with 100% abundance. Rearrangement occurs in the MS condition and the split of **3b** can be described as follows.



The use of catalytic amount of solid K_2CO_3 gave good yields of **3** or **4**. The best reaction time was approximately 6–12 h (Table I). Although the reactivity of the carbodiimides **2** was different with respect to substituent on the benzene ring, the reaction was carried out smoothly at room temperature. The formation of **3** or **4** can be rationalized in terms of an initial nucleophilic addition of 4-methylthiophenol or phenthiol under potassium carbonate to give the intermediates **6** which directly cyclize to give **3** or **4**. When methylene dichloride was used as solvent

in some cases, the intermediates **6** were isolated and characterized by ^{1}H NMR and MS.



The biological activity of **3** and **4** was investigated and the results showed that they exhibited fungicidal activities, especially against *Pellicularia sasakii*. For example, **3c** showed 95% inhibition of *Pellicularia sasakii* in 50 mg/L (see Table II).

EXPERIMENTAL

Melting points were uncorrected. MS were measured on a HP5988A spectrometer. IR were recorded on a Shimadzu IR-408 infrared spectrometer. NMR were taken on a Varian XL-200 spectrometer. Elementary analysis were taken on a CHN 2400 elementary analysis instrument.

Preparation of Vinyliminophosphorane 1

Vinyliminophosphorane **1** was prepared by the Staudinger reaction of vinyl azide and triphenyl phosphine according to the literature report.[12] m.p. 148–150°C (Lit.[12] m.p. 149°C).

Preparation of 4H-Imidazolin-4-ones 3

To a solution of vinyliminophosphorane **1** (2.25 g, 5 mmol) in dry methylene dichloride (15 mL) was added aromatic isocyanate (5 mmol) under nitrogen at room temperature. After the reaction mixture was stand

TABLE II The Fungicidal Activities of 4H-Imidazolin-4-ones **3** and **4** (50 mg/L, relative inhibition %)

Compound	**3a**	**3b**	**3c**	**3d**	**4a**	**4b**	**4c**	**4d**
Pellicularia sasaki	92	74	87	86	87	4	95	91
Rhizoctonia solani	26	26	7	0	0	0	0	0
Botryosphaeria berengeriana	26	0	0	26	33	26	0	0

for 3–6 h, the solvent was removed off under reduced pressure and ether/petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. Filtered, the solvent was removed to give carbodiimide **2**, which was used directly without further purification.

To a solution of **2** prepared above in CH_3CN (30 mL) was added 4-methylthiophenol (0.70 g, 5 mmol) and catalytic solid K_2CO_3 (0.05 g). The reaction mixture was stirred for 6–8 h and filtered; the filtrate was condensed and the residual was recrystallized from methylene dichloride/petroleum ether to give 4H-imidazolin-4-ones **3**.

2-(4-Methylthiophenoxy)-3-pheny-5-phenylmethylene-4H-imidazolin-4-one (3a)

Light yellow crystals, m.p. 138–140°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.96–7.20 (m, 14H, Ar—H), 7.06 (s, 1H,=CH), 2.48 (s, 3H, SCH_3); IR (cm^{-1}), 1721, 1650, 1562, 1280; MS (m/z), 386 (M^+, 100%), 239 (51%), 224 (9%), 116 (44%). Elemental Anal. Calcd. for $C_{23}H_{18}N_2O_2S$: C, 71.48; H, 4.69; N, 7.25. Found: C, 71.34; H, 4.84; N, 7.37.

2-(4-Methylthiophenoxy)-3-(4-methylpheny)-5-phenylmethylene-4H-imidazolin-4-one (3b)

Light yellow crystals, m.p. 146–148°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.98–7.18 (m, 13H, Ar—H), 7.05 (s, 1H, =CH), 2.48 (s, 3H, SCH_3), 2.39 (s, 3H, CH_3); IR (cm^{-1}), 1720, 1650, 1560, 1290; MS (m/z), 400 (M^+, 100%), 386 (7%), 239 (43%), 224 (7%), 116 (39%). Elemental Anal. Calcd. for $C_{24}H_{20}N_2O_2S$: C, 71.98; H, 5.03; N, 6.99. Found: C, 71.73; H, 5.26; N, 6.74.

2-(4-Methylthiophenoxy)-3-(4-chloropheny)-5-phenylmethylene-4H-imidazolin-4-one (3c)

Light yellow crystals, m.p. 154–156°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.98–7.20 (m, 13H, Ar—H), 7.06 (s, 1H, =CH), 2.50 (s, 3H, SCH_3); IR (cm^{-1}), 1728, 1650, 1568, 1292; MS (m/z), 420 (M^+, 100%), 239 (48%), 224 (8%), 116 (44%). Elemental Anal. Calcd. for $C_{23}H_{17}CLN_2O_2S$: C, 65.63; H, 4.07; N, 6.66. Found: C, 65.37; H, 3.93; N, 6.83.

2-(4-Methylthiophenoxy)-3-(3-chloropheny)-5-phenylmethylene-4H-imidazolin-4-one (3d)

Light yellow crystals, m.p. 88–90°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.98–7.18 (m, 13H, Ar—H), 7.07 (s, 1H, =CH), 2.50 (s, 3H, SCH_3); IR (cm^{-1}), 1726, 1650, 1565, 1290; MS (m/z), 420 (M^+, 100%), 239 (57%), 224 (10%), 116 (52%). Elemental Anal. Calcd. for $C_{23}H_{17}ClN_2O_2S$: C, 65.63; H, 4.07; N, 6.66. Found: C, 65.51; H, 4.25; N, 6.47.

Preparation of 4H-Imidazolin-4-ones 4

To a solution of **2** prepared above in CH_3CN (30 mL) was added phenthiol (0.55 g, 5 mmol) and catalytic solid K_2CO_3 (0.05 g). The reaction mixture was stirred for 10–12 h and filtered; the filtrate was condensed and the residual was recrystallized from methylene dichloride/petroleum ether to give 4H-imidazolin-4-ones **4**.

2-Phenylthio-3-pheny-5-phenylmethylene-4H-imidazolin-4-one (4a)

Yellow crystals, m.p. 152–154 °C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.94–7.20 (m, 15H, Ar—H), 6.96 (s, 1H, =CH); IR (cm^{-1}), 1712, 1628, 1490, 1210; MS (m/z), 356 (M^+, 100%), 247 (32%), 212 (40%), 109 (63%). Elemental Anal. Calcd. for $C_{22}H_{16}N_2OS$: C, 74.13; H, 4.52; N, 7.86. Found: C, 74.27; H, 4.36; N, 7.93.

2-Phenylthio-3-(4-methylpheny)-5-phenylmethylene-4H-imidazolin-4-one (4b)

Yellow crystals, m.p. 108–110°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.92–7.18 (m, 14H, Ar—H), 6.93 (s, 1H, =CH), 2.40 (s, 3H, CH_3); IR (cm^{-1}), 1710, 1630, 1485, 1210; MS (m/z), 370 (M^+, 100%), 261 (57%), 226 (34%), 116 (40%). Elemental Anal. Calcd. for $C_{23}H_{18}N_2OS$: C, 74.57; H, 4.90; N, 7.56. Found: C, 74.43; H, 4.81; N, 7.59.

2-Phenylthio-3-(4-chloropheny)-5-phenylmethylene-4H-imidazolin-4-one (4c)

Yellow crystals, m.p. 194–196°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.92–7.18 (m, 14H, Ar—H), 6.94 (s, 1H, =CH); IR (cm^{-1}), 1720, 1630, 1490, 1205; MS (m/z), 390 (M^+, 100%), 281 (38%), 246 (30%), 109 (49%). Elemental Anal. Calcd. for $C_{22}H_{15}ClN_2OS$: C, 67.60; H, 3.87; N, 7.17. Found: C, 67.84; H, 3.81; N, 7.23.

2-Phenylthio-3-(3-chloropheny)-5-phenylmethylene-4H-imidazolin-4-one (4d)

Yellow crystals, m.p. 154–156°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.94–7.18 (m, 14H, Ar—H), 6.94 (s, 1H, =CH); IR (cm^{-1}), 1720, 1628, 1492, 1208; MS (m/z), 390 (M^+, 100%), 281 (21%), 246 (31%), 109 (55%). Elemental Anal. Calcd. for $C_{22}H_{15}ClN_2OS$: C, 67.60; H, 3.87; N, 7.17. Found: C, 67.33; H, 3.93; N, 7.05.

REFERENCES

[1] B. L. Pilkington, S. E. Russell, A. J. Whittle, W. R. Mound, M. D. Turnbull, A. M. Kozakiewicz, and W. G. Whittingham, Brit. UK Pat. Appl. (GB) 2329180 (1999).
[2] G. Emeric, J. Hutt, and J. Perez, PCT Int. Appl. (WO) 9602538 (1996).
[3] J. P. Bascou, A. Gadras, J. Perez, G. Emeric, G. Lacroix, and C. Veyrat, Eur. Pat. Appl. (EP) 668270 (1995).
[4] B. L. Pilkington, S. E. Russell, A. J. Whittle, W. R. Mound, M. D. Turnbull, A. M. Kozakiewicz, D. J. Hughes, and W. G. Whittingham, Brit. UK Pat. Appl. (GB) 2327676 (1999).
[5] J. A. Bruhn, M. C. Crompton, and S. R. Foor, PCT Int. Appl. (WO) 9833382 (1998).
[6] J. P. Bascou, G. Lacroix, A. Gadras, and J. Perez, Eur. Pat. Appl. (EP) 629616 (1994).
[7] G. Lacroix, R. Peignier, and R. Pepin, Eur. Pat. Appl. (EP) 551048 (1993).
[8] M. W. Ding, Z. F. Xu, and T. J. Wu, *Synth. Commun.*, **29,** 1171 (1999).
[9] M. W. Ding, H. Y. Tu, and Z. J. Liu, *Synth. Commun.*, **27,** 3657 (1997).
[10] M. W. Ding, H. Y. Tu, Z. J. Liu, and N. B. Zhuang, *Chem. J. Chinese Universities*, **18,** 572 (1998).
[11] M. Mikolajczyk and P. Pielbasinski, *Tetrahedron*, **37,** 233 (1981).
[12] P. Molina, A. Pastor, and M. J. Vilaplana, *Tetrahedron*, **49,** 7769 (1993).