A DIRECT SYNTHESIS OF 2-ALKOXY-4H-IMIDAZOL-4-ONES

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Abstract: 2-Alkoxy-4H-imidazol-4-ones **4** were synthesized by aza-Wittig reaction of iminophosphorane **1** with phenyl isocynate to give carbodiimide **2** and subsequent reaction of **2** with ROH in the presence of catalytic RO^-Na^+.

Introduction

4H-Imidazol-4-ones are important heterocycles having good biological and pharmaceutical activities(1,2). Some 2-alkoxyimidazolones were recently found to show significant fungicidal actitities(3,4). They were generally prepared from reaction of 2-methylthio-4H-imidazol-4-ones with RO^-Na^+(3). Recently we are interested in synthesis of new imidazolone derivatives, some of them having been shown potential fungicidal activities(5-8). In the present work we describe a direct access to 2-alkoxyimidazolone via reaction of functionalized carbodiimide with ROH in the presence of catalytic RO^-Na^+.

Results and Discussion

The easily accessible vinyliminophosphoranes **1** reacted with aromatic isocyanates to give carbodiimides **2**. The direct reaction of **2** with ROH took place very slowly even at refluxing ROH, however, when the reaction was carried out under catalytic RO^-Na^+, the reaction carried out smoothly and the final product obtained was verified to be 2-alkoxy-4H-imidazol-4-ones **4**.

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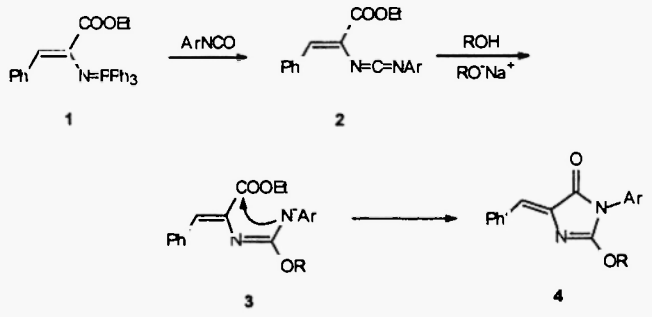

Scheme 1

The structure of **4** has been characterized spectroscopically. For example, the ^{1}H NMR spectrum data in **4a** showed the signals of alkenyl hydrogen and OCH_3 at 7.03ppm and 4.19ppm as single absorption respectively. In the IR spectrum data of **4a**, the strong stretching resonance peak of imidazolone C=O appears at 1731cm^{-1}. The stretching resonance of C=C shows relatively strong absorption at about 1656cm^{-1} due to resonance effect. The MS spectrum of **4a** shows molecule ion peak at m/z 278 with 33% abundance.

The use of catalytic RO^-Na^+ gave moderate yields of **4**. The reaction condition was related to Ar substituent. When Ar is phenyl or 3-methylphenyl, the reaction was carried out at refluxing temperature; when Ar is 4-chlorophenyl or 3-chlorophenyl, the reaction could be carried out at room temperature (Table 1). The formation of **4** can be rationalized in terms of an initial nucleophilic addition of RO^-Na^+ to give the intermediate **3** which directly cyclized to give **4** (Scheme 1).

Experimental

Melting points were uncorrected. MS were measured on a HP5988A spectrometer. IR were recorded on a PE-983 infrared spectrometer. NMR were taken on a Varian XL-200 spectrometer. Elementary analyses were taken on a CHN 2400 elementary analysis instrument. Iminophosphorane **1** was prepared by the literature report (9).

Table 1. Preparation of 2-Alkoxy-4H-imidazol-4-ones **4**

Compound	Ar	R	Condition	Yield (%)*
4a	Ph	Me	66°C/2 hr	50
4b	Ph	Et	78°C/3 hr	40
4c	3-Me-Ph	Me	66°C/4 hr	35
4d	3-Me-Ph	Et	78°C/4 hr	42
4e	4-Cl-Ph	Me	r.t./1 hr	55
4f	4-Cl-Ph	Et	r.t./1 hr	51
4g	4-Cl-Ph	*n*-Pr	r.t./2 hr	58
4h	3-Cl-Ph	Me	r.t./1 hr	57
4i	3-Cl-Ph	Et	r.t./2 hr	50
4j	3-Cl-Ph	*n*-Pr	r.t./1 hr	45

*isolated yields based on iminophosphorane **1**

General Preparation of 2-Alkoxy-4H-imidazol-4-ones 4-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 stood for 3~6 hours, 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 ROH (30 mL) was added several drops of RO^-Na^+ in ROH. The reaction mixture was stirred for 1~4 hours at refluxing or room temperature and was condensed. The residual was recrystallized from methylene dichloride/petroleum ether to give 2-alkoxy-4H-imidazol-4-ones **4**.

4a: light yellow crystals, m. p. 127~128°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.10~7.22 (m, 10H, Ar-H), 7.03 (s, 1H, =CH), 4.19 (s, 3H, OCH_3); IR (cm^{-1}), 1731, 1656, 1588, 1300, 1161; MS (m/z, %), 278 (M^+, 33), 144 (3), 134 (90), 119 (100), 116 (22); Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.38; H, 5.04; N, 10.07. Found: C, 73.39; H, 4.92; N, 9.95.

4b: yellow crystals, m. p. 98~100°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.09~7.22 (m, 10H, Ar-H), 7.00 (s, 1H, =CH), 4.66 (q, 2H, J=7.3 Hz, OCH_2), 1.46 (t, 3H, J=7.3 Hz, CH_3); IR (cm^{-1}), 1725, 1656, 1581, 1306, 1161; MS (m/z, %), 292 (M^+, 18), 263 (23), 144 (9), 119 (19), 116 (100); Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.97; H, 5.48; N, 9.59. Found: C, 73.70; H, 5.39; N, 9.61.

4c: light yellow crystals, m. p. 162~163°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.19~7.13 (m, 9H, Ar-H), 6.95 (s, 1H, =CH), 4.17 (s, 3H, OCH_3), 2.36 (s, 3H, Ph-CH_3); IR (cm^{-1}), 1728, 1654, 1577, 1296, 1158; MS (m/z, %), 292 (M^+, 7), 277 (8), 144 (21), 119 (100); Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.97; H, 5.48; N, 9.59. Found: C, 73.70; H, 5.25; N, 9.66.

4d: yellow crystals, m. p. 151~152°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.16~7.12 (m, 9H, Ar-H), 6.92 (s, 1H, =CH), 4.62 (q, 2H, J=7.2Hz, OCH_2), 2.39 (s, 3H, Ph-CH_3), 1.43 (t, 3H, J=7.2Hz, CH_3); IR (cm^{-1}), 1721, 1654, 1580, 1298, 1168; MS (m/z, %), 306 (M^+, 12), 276 (6), 144 (16), 116 (100); Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.51; H, 5.88; N, 9.15. Found: C, 74.22; H, 6.15; N, 9.41.

4e: yellow crystals, m. p. 155~156°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.09~7.21 (m, 9H, Ar-H), 7.02 (s, 1H, =CH), 4.18 (s, 3H, OCH_3); IR (cm^{-1}), 1727, 1657, 1590, 1309, 1163; MS (m/z, %), 312 (M^+, 55), 168 (55), 153 (100), 125 (22); Anal. Calcd. for $C_{17}H_{13}ClN_2O_2$: C, 65.28; H, 4.16; N, 8.96. Found: C, 65.17; H, 4.34; N, 9.17.

4f: yellow crystals, m. p. 158~159°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.08~7.21 (m, 9H, Ar-H), 7.00 (s, 1H, =CH), 4.65 (q, 2H, J=6.8Hz, OCH_2), 1.46 (t, 3H, J=6.8Hz, CH_3); IR (cm^{-1}), 1728, 1653, 1590, 1308, 1178; MS (m/z, %), 326 (M^+, 33), 298 (25), 153 (9), 116 (100); Anal. Calcd. for $C_{18}H_{15}ClN_2O_2$: C, 66.16; H, 4.59; N, 8.58. Found: C, 65.94; H, 4.74; N, 8.31.

4g: yellow crystals, m. p. 152~153°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.08~7.21 (m, 9H, Ar-H), 7.00 (s, 1H, =CH), 4.54 (t, 2H, J=6.3Hz, OCH_2), 1.89~0.97 (m, 5H, CH_2CH_3); IR (cm^{-1}), 1724, 1654, 1587, 1300, 1162; MS (m/z, %), 340 (M^+, 4), 298 (11), 172 (2), 117 (100); Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 4.99; N, 8.22. Found: C, 67.20; H, 5.20; N, 7.98.

4h: light yellow crystals, m. p. 133~135°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.09~7.21 (m, 9H, Ar-H), 7.03 (s, 1H, =CH), 4.20 (s, 3H, OCH_3); IR (cm^{-1}), 1728, 1659, 1592, 1317, 1165; MS (m/z, %), 312 (M^+, 71), 201 (5), 168 (84), 153 (100), 116 (34); Anal. Calcd. for $C_{17}H_{13}ClN_2O_2$: C, 65.28; H, 4.16; N, 8.96. Found: C, 65.09; H, 4.30; N, 9.21.

4i: yellow crystals, m. p. 135~137°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.08~7.22 (m, 9H, Ar-H), 7.01 (s, 1H, =CH), 4.62 (q, 2H, J=6.8Hz, OCH_2), 1.48 (t, 3H, J=6.8Hz, CH_3); IR (cm^{-1}), 1726, 1656, 1589, 1315, 1162; MS (m/z, %), 326 (M^+, 28), 297 (36), 201 (5), 154 (9), 117 (100); Anal. Calcd. for $C_{18}H_{15}ClN_2O_2$: C, 66.16; H, 4.59; N, 8.58. Found: C, 66.00; H, 4.71; N, 8.33.

4j: yellow crystals, m. p. 98~100°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.09~7.21 (m, 9H, Ar-H), 7.00 (s, 1H, =CH), 4.55 (t, 2H, J=6.8 Hz, OCH_2), 1.90~0.97 (m, 5H, CH_2CH_3); IR (cm^{-1}), 1728, 1658, 1590, 1305, 1162; MS (m/z, %), 341 (M^++1, 11), 297 (34), 172 (6), 144 (20), 117 (100); Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 4.99; N, 8.22. Found: C, 67.22; H, 5.26; N, 8.01.

Acknowledgements

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