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Unexpected Synthesis of 2,4,5-Trisubstituted Oxazoles via a Tandem Aza-Wittig/Michael/Isomerization Reaction of Vinyliminophosphorane

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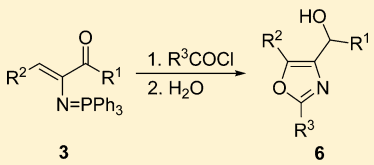
Supporting Information

ABSTRACT: 2,4,5-Trisubstituted oxazoles **6** were unexpectedly prepared from a tandem reaction of vinyliminophosphorane **3** with various acyl chlorides in a one-pot fashion.



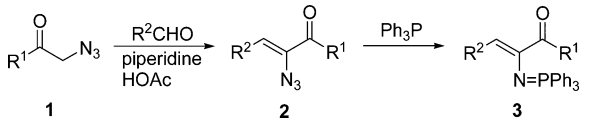
3 **6**

Oxazoles represent an important class of heterocycles since they occur in a multitude of natural products and possess a broad spectrum of biological properties in medicinal chemistry. For example, some oxazoles were found to display good TRPV1 antagonistical activity,[1] antifungal activity,[2] analgesic activity,[3] anti-inflammatory activity,[4] and antiproliferative activity.[5] In addition, oxazole rings were also found as the building block in many natural marine products such as neopeltolide and ariakemicins A and B.[6] The structural diversity and complexity of the oxazoles has generated much interest in the development of mild methods for their synthesis.[7] Recently, some 2,4-disubstituted oxazoles were prepared by the oxidation of the oxazolidine formed from the direct condensation of serine with aldehydes.[8] 2,4,5-Trisubstituted oxazoles have also been obtained via a one-pot Friedel–Crafts/Robinson–Gabriel reaction using a general oxazolone template.[9] The substituted oxazoles can be produced efficiently from the propargylic alcohols and amides with use of p-toluenesulfonic acid monohydrate (PTSA) as a bifunctional catalyst.[10] Another method is based on a copper or iodine-catalyzed tandem oxidative cyclization,[11] gold-catalyzed intermolecular alkyne oxidation,[12] copper(I)-catalyzed cycloaddition of acyl azides and 1-alkynes,[13] and silver-catalyzed reaction of primary amide with activated β-bromoketone.[14]

The aza-Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of nitrogen-containing heterocyclic compounds.[15] The utility of vinyliminophosphoranes for the synthesis of heterocycles has also been demonstrated convincingly. Owing to its good stability, vinyliminophosphorane may be considered to be an equivalent of the unstable enamine and was utilized in synthesis of various heterocycles, such as isoquinolines, pyridines, and pyrroles.[16] Some oxazoles were also prepared by intramolecular aza-Wittig reaction of vinyliminophosphoranes,[17] or by a one-pot aza-Wittig/nucleophilic substitution reaction starting from the α-azidoketones.[18] Recently, we have been interested in the synthesis of various heterocycles via aza-Wittig reaction.[19] Herein we report a fundamentally new approach to the synthesis of 2,4,5-trisubstituted oxazoles via a tandem aza-Wittig/Michael/isomerization reaction of vinyliminophosphorane in one-pot fashion.

Vinyl azides **2**, obtained easily from condensation of azides **1** with aromatic aldehydes in the presence of piperidinium acetate,[20] reacted with triphenylphosphine to give vinyliminophosphoranes **3** in good yields (Scheme 1).

Scheme 1. Preparation of Vinyliminophosphorane 3



1 **2** **3**

The vinyliminophosphorane **3** (1 equiv) was allowed to react with various acyl chlorides (1.2 equiv) in toluene at refluxing temperature for 3 h, and then the reaction mixture was hydrolyzed and refluxed for further 3–4 h. The reaction mixture was neutralized by NaOH solution. The final product was verified surprisingly to be oxazole **6** (Scheme 2), and the expected dihydrooxazoles **7** were not obtained. As indicated in Table 1, good yields of oxazoles **6** were reached no matter aromatic or alkyl acyl chlorides were used. The structure of oxazoles **6** was confirmed by their spectrum data. For example, the IR spectra of **6a** revealed O–H absorption bands at 3368 cm^{-1} but no C=O absorption bands. The ^1H NMR spectrum of **6a** shows two doublets at 6.05 and 3.53 ppm due to the CH and OH respectively. The signals attributable to the Ar-Hs are found at 8.10–7.25 ppm as a multiplet. The ^{13}C NMR spectrum data in **6a** showed the signals of CHOH at 68.5 ppm but no signals of C=O carbon. The MS spectrum of **6a** shows

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Scheme 2. Preparation of Oxazoles 6

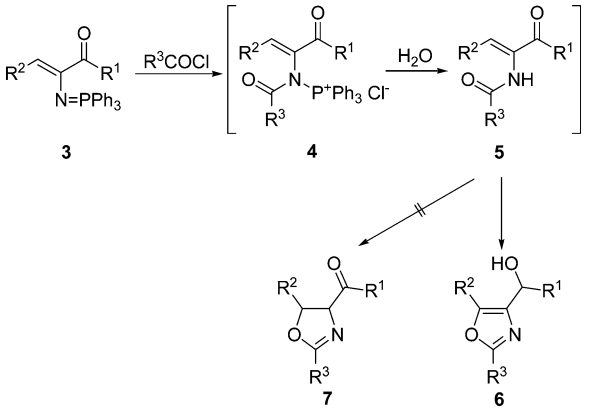


Table 1. Preparation of 2,4,5-Trisubstituted Oxazoles 6

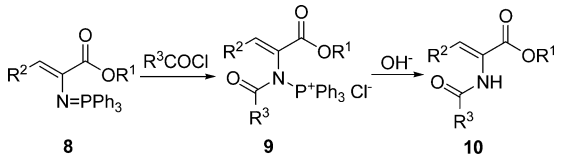
compd	R^1	R^2	R^3	yield[a] (%)
6a	Ph	Ph	Ph	80
6b	Ph	Ph	4-ClC_6H_4	79
6c	Ph	Ph	4-FC_6H_4	75
6d	Ph	Ph	4-$CH_3C_6H_4$	77
6e	Ph	Ph	2-ClC_6H_4	80
6f	Ph	Ph	3-ClC_6H_4	88
6g	Ph	4-ClC_6H_4	Ph	79
6h	Ph	4-$CH_3C_6H_4$	Ph	74
6i	Ph	4-$CF_3C_6H_4$	Ph	80
6j	Ph	4-$CH_3C_6H_4$	4-$NO_2C_6H_4$	71
6k	4-ClC_6H_4	Ph	Ph	82
6l	4-ClC_6H_4	4-FC_6H_4	Ph	78
6m	4-ClC_6H_4	4-$CH_3C_6H_4$	Ph	81
6n	Ph	Ph	CH_3	86
6o	Ph	Ph	*n*-Pr	88

[a]Isolated yields.

a molecular ion peak at m/z 327 with 59% abundance. Furthermore, a single crystal of **6n** was obtained from the CH_2Cl_2 solution, and X-ray structure analysis verified the proposed structure (Figure 1 in the Supporting Information).

The aza-Wittig reaction between iminophosphorane and acyl chloride generally takes place to form amide after hydrolysis. For example, the reaction of analogous α-alkoxycarbonyl iminophosphorane **8** with acyl chloride gave hygroscopic N-acylated aminophosphonium salt **9**, which hydrolyzed by 2 N NaOH to afford only amide **10** in good yield in benzene at room temperature with no oxazole formation (Scheme 3).[21]

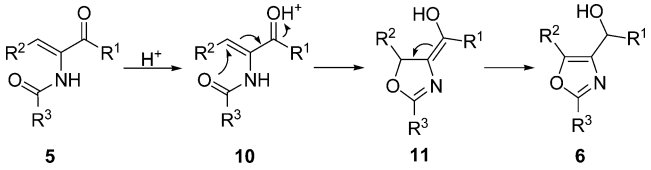
Scheme 3. Literature Synthesis of Amide 9 through Aza-Wittig Reaction



The initial purpose of this research was to prepare the amide **5** by aza-Wittig reaction of vinyliminophosphorane **3** with acyl chloride. But in our cases, 2,4,5-trisubstituted oxazoles **6** were obtained instead. This is probably duo to the starting material we used being the α-carbonyl iminophosphorane **3**.

A possible mechanism for formation of oxazoles **6** is proposed (Scheme 4). It presumably involves an initial reaction

Scheme 4. Possible Mechanism for Oxazole Formation



of iminophosphorane **3** with acyl chloride to give the N-acylated aminophosphonium salt **4**, which hydrolyzed to give the amide intermediate **5**. Then an intramolecular Michael addition of **5** takes place under the acidic condition to produce **11**, which undertakes further isomerization to give oxazole **6** directly through 1,3-H shift. It is deduced that conversion of the enol **11** to dihydrooxazole ketone **7** does not take place under the reaction condition. The reaction of vinyliminophosphorane **3** with acyl chloride at room temperature gave a mixture of amide **5**, a small amount of oxazole **6**, and unreacted iminophosphorane **3**, from which the key intermediate amide **5** could be isolated. Cyclization of the amide **5** under acidic heating conditions took place to provide oxazole **6**; however, no product **6** can be detected as the amide **5** was treated with NaOH or NaH. The above experiments imply that the formation of oxazole **6** occurs only under acidic conditions.

In conclusion, we have demonstrated an efficient method for the synthesis of a wide range of 2,4,5-trisubstituted oxazoles under mild conditions. In light of its quite simple operation, easily available starting materials, good yields and ability to proceed without a catalyst, this protocol provides an efficient alternative to the biologically important 2,4,5-trisubstituted oxazoles, which are highly valuable building blocks for medicinal chemistry and natural product synthesis.

EXPERIMENTAL SECTION

Preparation of Vinyliminophosphorane 3. A solution of triphenylphosphine (4 mmol, 1.05 g) in dry CH_2Cl_2 (10 mL) was added dropwise to a well-stirred solution of vinyl azides **2**[20] (4 mmol) in CH_2Cl_2 (10 mL) at room temperature. After the stirring was continued for 2−4 h, the solvent was evaporated under reduced pressure and the residue was recrystallized from CH_2Cl_2−petroleum ether to give vinyliminophosphorane **3**.

*1,3-Diphenyl-2-((triphenylphosphoranylidene)amino)prop-2-en-1-one (**3a**).* Yellow crystals (1.78 g, 92%). Mp: 164−166 °C (lit.[22] mp 163−163.5 °C). IR (KBr): 1638, 1411, 1233, 1110 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.19 (d, J = 7.8 Hz, 2H), 7.80−7.16 (m, 23H), 6.21 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 196.8, 144.8, 139.2, 138.1, 133.7, 133.0, 132.4, 132.3, 132.2, 130.9, 130.7, 130.6, 129.5, 129.4, 129.0, 128.9, 128.2, 128.1, 128.0, 127.9, 127.8, 127.5, 124.1. MS: m/z = 483 (38, M^+), 378 (33), 262 (100), 183 (68), 108 (26). Anal. Calcd for $C_{33}H_{26}NOP$: C, 81.97; H, 5.42; N, 2.90. Found: C, 82.09; H, 5.38; N, 2.81.

*3-(4-Chlorophenyl)-1-phenyl-2-((triphenylphosphoranylidene)-amino)prop-2-en-1-one (**3b**).* Yellow crystals (1.96 g, 95%). Mp: 180−182 °C. IR (KBr): 1640, 1421, 1230, 1109 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.13 (d, J = 8.4 Hz, 2H), 7.77−7.23 (m, 22H), 6.14 (d, J = 6.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 196.5, 145.2, 138.9, 136.6, 133.3, 132.6, 132.2, 132.1, 131.1, 130.9, 130.8, 130.7, 130.6, 130.5, 130.4, 128.9, 128.8, 128.2, 128.1, 128.0, 127.9, 127.8, 127.5, 122.0. MS: m/z = 517 (20, M^+), 412 (20), 262 (100), 183 (69), 108 (26). Anal. Calcd for $C_{33}H_{25}ClNOP$: C, 76.52; H, 4.86; N, 2.70. Found: C, 76.79; H, 4.98; N, 2.81.

*1-Phenyl-3-(p-tolyl)-2-((triphenylphosphoranylidene)amino)-prop-2-en-1-one (**3c**).* Yellow crystals (1.72 g, 87%). Mp: 177−179

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°C. IR (KBr): 1635, 1419, 1236, 1111 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.12 (d, J = 7.2 Hz, 2H), 7.80−7.10 (m, 22H), 6.24 (d, J = 7.2 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 196.5, 144.0, 139.3, 136.1, 135.2, 133.8, 133.1, 132.2, 132.1, 130.7, 130.5, 130.3, 129.5, 129.3, 128.9, 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 124.6, 21.2. MS: m/z = 497 (39, M^+), 392 (30), 262 (100), 183 (51), 108 (18). Anal. Calcd for $C_{34}H_{28}NOP$: C, 82.07; H, 5.67; N, 2.82. Found: C, 82.21; H, 5.88; N, 2.66.

1-Phenyl-3-(4-(trifluoromethyl)phenyl)-2-((triphenylphosphoranylidene)amino)prop-2-en-1-one (**3d**). Yellow crystals (2.07 g, 94%). Mp: 124−125 °C. IR (KBr): 1664, 1321, 1261, 1119 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.27 (d, J = 8.4 Hz, 2H), 7.77−7.30 (m, 22H), 6.13 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 196.6, 146.8, 141.7, 138.5, 132.9, 132.3, 132.2, 131.2, 131.1, 131.0, 130.9, 129.1, 129.0, 128.8, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 124.7, 124.6, 120.3. MS: m/z = 551 (5, M^+), 378(17), 262 (97), 183 (100), 105 (58). Anal. Calcd for $C_{34}H_{25}F_3NOP$: C, 74.04; H, 4.57; N, 2.54. Found: C, 73.81; H, 4.78; N, 2.61.

1-(4-Chlorophenyl)-3-phenyl-2-((triphenylphosphoranylidene)-amino)prop-2-en-1-one (**3e**). Yellow crystals (1.84 g, 89%). Mp: 184−185 °C. IR (KBr): 1637, 1417, 1237, 1108 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.18 (d, J = 7.8 Hz, 2H), 7.78−7.16 (m, 22H), 6.14 (d, J = 6.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 195.5, 144.6, 137.8, 137.3, 136.8, 133.3, 132.6, 130.9, 130.8, 130.7, 130.4, 130.3, 129.4, 129.2, 128.2, 128.1, 128.1, 127.9, 127.7, 126.2, 125.7, 123.6, 123.4. MS: m/z = 517 (29, M^+), 378 (41), 262 (100), 183 (64), 108 (27). Anal. Calcd for $C_{33}H_{25}ClNOP$: C, 76.52; H, 4.86; N, 2.70. Found: C, 76.39; H, 5.03; N, 2.56.

1-(4-Chlorophenyl)-3-(4-fluorophenyl)-2-((triphenylphosphoranylidene)amino)prop-2-en-1-one (**3f**). Yellow crystals (1.84 g, 86%). Mp: 134−136 °C. IR (KBr): 1643, 1416, 1228, 1107 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.17 (d, J = 6.0 Hz, 2H), 7.76−6.97 (m, 21H), 6.11 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 195.5, 162.0, 160.4, 144.3, 137.4, 136.9, 134.1, 133.3, 132.6, 132.2, 132.1, 131.0, 130.8, 130.4, 130.3, 128.3, 128.2, 128.1, 128.0, 127.8, 122.6, 114.6, 114.7. MS: m/z = 535 (30, M^+), 396 (23), 262 (100), 183 (54), 108 (23). Anal. Calcd for $C_{33}H_{24}ClFNOP$: C, 73.95; H, 4.51; N, 2.61. Found: C, 74.15; H, 4.31; N, 2.49.

1-(4-Chlorophenyl)-3-(p-tolyl)-2-((triphenylphosphoranylidene)-amino)prop-2-en-1-one (**3g**). Yellow crystals (1.91 g, 90%). Mp: 129−131 °C. IR (KBr): 1635, 1430, 1247, 1109 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.09 (d, J = 7.8 Hz, 2H), 7.78−7.11 (m, 21H), 6.16 (d, J = 7.2 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 195.5, 144.0, 137.7, 136.7, 136.3, 135.0, 133.6, 132.9, 132.4, 132.3, 132.2, 130.9, 130.7, 130.5, 130.3, 129.5, 129.4, 128.7, 128.6, 128.2, 128.1, 128.0, 127.9, 127.8, 124.5, 21.4. MS: m/z = 531 (29, M^+), 392 (21), 262 (100), 183 (61), 108 (29). Anal. Calcd for $C_{34}H_{27}ClNOP$: C, 76.76; H, 5.12; N, 2.63. Found: C, 76.87; H, 4.88; N, 2.86.

Preparation of 2,4,5-Trisubstituted Oxazoles 6. To a solution of iminophosphorane **3** (1 mmol) in 20 mL of toluene were added various acyl chlorides (1.2 mmol) at room temperature, and the mixture was refluxed for 3 h. Then water (0.02 g) was added, and the mixture was refluxed for further 3−4 h. The reaction mixture was added to the NaOH (5 mL, 2 N) solution, stirred at room temperature for 15 min, extracted with EtOAc, washed with brine, and dried over Na_2SO_4. The solution was filtered and concentrated under reduced pressure, and the residue was purified by short column chromatography on silica gel (ethyl acetate/petroleum ether = 3/8) to give the 2,4,5-trisubstituted oxazoles **6**.

(2,5-Diphenyloxazol-4-yl)(phenyl)methanol (**6a**). White crystals (0.26 g, 80%). Mp: 155−157 °C. IR (KBr): 3368, 1486, 1223, 1050 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.10−7.25 (m, 15H), 6.05 (d, J = 7.8 Hz, 1H), 3.53 (d, J = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 160.1, 146.1, 141.8, 138.0, 130.4, 128.8, 128.6, 128.5, 127.9, 127.7, 126.9, 126.4, 126.1, 68.5. MS: m/z = 327 (59, M^+), 250 (15), 222 (21), 105 (100). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.45; H, 5.40; N, 4.35.

[2-(4-Chlorophenyl)-5-phenyloxazol-4-yl](phenyl)methanol (**6b**). White crystals (0.29 g, 79%). Mp: 159−161 °C. IR (KBr): 3375, 1481, 1092, 691 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.03−7.25 (m, 14H), 6.04 (d, J = 7.8 Hz, 1H), 3.39 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 157.9, 146.5, 142.6, 139.9, 135.3, 129.2, 128.9, 128.7, 128.6, 128.3, 128.0, 127.7, 127.6, 127.0, 126.5, 125.5, 67.3. MS: m/z = 361 (56, M^+), 256 (15), 284 (13), 206 (22), 139 (100). Anal. Calcd for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 73.13; H, 4.22; N, 4.02.

[2-(4-Fluorophenyl)-5-phenyloxazol-4-yl](phenyl)methanol (**6c**). White crystals (0.26 g, 75%). Mp: 187−189 °C. IR (KBr): 3373, 1496, 1229, 1047 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.11−7.14 (m, 14H), 6.04 (d, J = 7.8 Hz, 1H), 3.42 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 164.3, 162.6, 158.1, 146.3, 142.7, 139.7, 128.9, 128.7, 128.5, 128.0, 127.7, 127.0, 126.6, 123.4, 116.4, 116.3, 67.3. MS: m/z = 345 (59, M^+), 240 (25), 223 (18), 123 (100), 105 (52). Anal. Calcd for $C_{22}H_{16}FNO_2$: C, 76.51; H, 4.67; N, 4.06. Found: C, 76.42; H, 4.47; N, 4.25.

[2-(4-Methylphenyl)-5-phenyloxazol-4-yl](phenyl)methanol (**6d**). White crystals (0.26 g, 77%). Mp: 164−165 °C. IR (KBr): 3377, 1497, 1052, 692 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.98 (d, J = 7.8 Hz, 2H), 7.61−7.25 (m, 12H), 6.03 (d, J = 7.8 Hz, 1H), 3.49 (d, J = 7.8 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 159.1, 145.8, 142.8, 142.7, 140.6, 139.6, 129.7, 129.0, 128.6, 128.0, 127.9, 127.0, 126.6, 126.5, 126.0, 124.0, 67.4, 67.3, 21.1. MS: m/z = 341 (48, M^+), 264 (20), 236 (25), 119 (100), 105 (52). Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10. Found: C, 81.05; H, 5.73; N, 3.89.

[2-(2-Chlorophenyl)-5-phenyloxazol-4-yl](phenyl)methanol (**6e**). White crystals (0.29 g, 80%). Mp: 108−109 °C. IR (KBr): 3369, 1493, 1457, 1048, 692 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.09 (d, J = 7.2 Hz, 1H), 7.65−7.25 (m, 13H), 6.07 (d, J = 7.8 Hz, 1H), 3.52 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 156.9,146.7, 142.7, 139.5, 131.8, 131.2, 130.9, 128.9, 128.8, 128.0, 127.6, 127.0, 126.6, 126.5, 125.4, 67.5, 67.4. MS: m/z = 361 (39, M^+), 284 (19), 256 (24), 139 (100), 105 (83). Anal. Calcd for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 73.28; H, 4.29; N, 3.64.

[2-(3-Chlorophenyl)-5-phenyloxazol-4-yl](phenyl)methanol (**6f**). White crystals (0.32 g, 88%). Mp: 167−169 °C. IR (KBr): 3389, 1542, 1472, 1051, 696 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.08 (s, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.62−7.25 (m, 12H), 6.04 (d, J = 7.8 Hz, 1H), 3.38 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 157.5, 146.8, 142.6, 142.5, 139.9, 134.0, 131.3, 130.5, 129.0, 128.9, 128.5, 128.1, 127.6, 127.1, 126.7, 126.6, 125.5, 124.7, 67.2. MS: m/z = 361 (44, M^+), 284 (21), 256 (31), 139 (74), 105 (94). Anal. Calcd for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 72.81; H, 4.63; N, 3.96.

[5-(4-Chlorophenyl)-2-phenyloxazol-4-yl](phenyl)methanol (**6g**). White crystals (0.28 g, 79%). Mp: 158−160 °C. IR (KBr): 3372, 1487, 1089, 770, 688 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.09−7.25 (m, 14H), 6.01 (d, J = 6.0 Hz, 1H), 3.48 (d, J = 7.2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 159.0, 146.4, 141.7, 139.3, 131.6, 130.8,129.2, 129.0, 128.8, 128.5, 128.0, 127.7, 126.6, 126.5, 126.1, 66.7. MS: m/z = 361 (19, M^+), 250 (8), 222 (14), 105 (100). Anal. Calcd for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 73.26; H, 4.29; N, 3.97.

[5-(4-Methylphenyl)-2-phenyloxazol-4-yl](phenyl)methanol (**6h**). White crystals (0.25 g, 74%). Mp: 175−176 °C. IR (KBr): 3361, 1550, 1489, 1063, 790, 688 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.10−7.15 (m, 14H), 6.01 (s, 1H), 3.46 (br, 1H), 2.32 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 158.8, 146.0, 139.9, 139.8, 139.7, 136.0, 130.7, 129.2, 128.9, 128.6, 127.8, 126.7, 126.5, 126.0, 67.2, 20.7. MS: m/z = 341 (30, M^+), 250 (10), 222 (23), 105 (100). Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10. Found: C, 80.72; H, 5.73; N, 3.92.

[2-Phenyl-5-(4-trifluoromethylphenyl)oxazol-4-yl](phenyl)-methanol (**6i**). White crystals (0.32 g, 80%). Mp: 155−156 °C. IR (KBr): 3364, 1489, 1325, 1121, 1066 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.08−7.25 (m, 14H), 6.10 (d, J = 7.8 Hz, 1H), 3.56 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 159.0, 147.4,

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146.7, 138.9, 138.8, 130.8, 129.2, 129.0, 128.9, 127.7, 127.6, 127.5, 127.3, 126.6, 126.1, 125.3, 124.9, 123.5, 66.8, 66.7. MS: m/z = 395 (30, M^+), 291 (12), 250 (17), 222 (17), 105 (100). Anal. Calcd for $C_{23}H_{16}F_3NO_2$: C, 69.87; H, 4.08; N, 3.54. Found: C, 69.62; H, 4.21; N, 3.43.

*[5-(4-Methylphenyl)-2-(4-nitrophenyl)oxazol-4-yl](phenyl)-methanol (**6j**).* Yellow crystals (0.28 g, 71%). Mp: 196−198 °C. IR (KBr): 3377, 1520, 1337, 1107, 1071 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.33−8.26 (m, 4H), 7.65−7.18 (m, 9H), 6.04 (d, J = 7.2 Hz, 1H), 3.13 (d, J = 7.2 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 157.0, 148.2, 147.5, 140.8, 139.5, 136.1, 132.0, 129.0, 128.6, 127.3, 127.1, 126.7, 126.5, 124.5, 67.2, 20.7. MS: m/z = 386 (100, M^+), 369 (22), 267 (72), 220 (26), 105 (57). Anal. Calcd for $C_{23}H_{18}N_2O_4$: C, 71.49; H, 4.70; N, 7.25. Found: C, 71.62; H, 4.87; N, 7.09.

*(4-Chlorophenyl)(2,5-diphenyloxazol-4-yl)methanol (**6k**).* White crystals (0.30 g, 82%). Mp: 163−165 °C. IR (KBr): 3346, 1489, 1092, 702 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.09−7.25 (m, 14H), 6.00 (d, J = 4.2 Hz, 1H), 3.61 (d, J = 6.0 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 159.0, 145.1, 142.5, 140.4, 133.2, 130.7, 129.1, 128.9, 128.2, 128.0, 127.0, 126.6, 126.5, 126.1, 67.6. MS: m/z = 361 (100, M^+), 284 (10), 256 (20), 139 (29), 105 (100). Anal. Calcd for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 73.19; H, 4.60; N, 3.63.

*(4-Chlorophenyl)[5-(4-fluorophenyl)-2-phenyloxazol-4-yl]-methanol (**6l**).* White crystals (0.30 g, 78%). Mp: 157−159 °C. IR (KBr): 3380, 1489, 1236, 1093 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.09−7.02 (m, 14H), 5.98 (d, J = 7.2 Hz, 1H), 3.53 (d, J = 7.2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 162.1, 160.5, 159.0, 145.2, 140.1, 138.6, 133.2, 130.8, 129.1, 128.9, 128.5, 128.4, 128.2, 126.6, 126.5, 126.1, 114.6, 66.8. MS: m/z = 379 (23, M^+), 275 (5), 256 (12), 139 (26), 105 (100). Anal. Calcd for $C_{22}H_{15}ClFNO_2$: C, 69.57; H, 3.98; N, 3.69. Found: C, 69.38; H, 4.16; N, 3.81.

*(4-Chlorophenyl)[5-(4-methylphenyl)-2-phenyloxazol-4-yl]-methanol (**6m**).* White crystals (0.30 g, 81%). Mp: 153−155 °C. IR (KBr): 3380, 1490, 1230, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.11−7.17 (m, 13H), 5.97 (d, J = 7.8 Hz, 1H), 3.31 (d, J = 7.8 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 158.9, 145.0, 140.6, 139.4, 136.1, 133.1, 130.8, 129.1, 128.9, 128.6, 128.2, 126.7, 126.5, 126.4, 126.1, 67.4, 20.7. MS: m/z = 375 (25, M^+), 256 (19), 139 (37), 111 (18), 105 (100). Anal. Calcd for $C_{23}H_{18}ClNO_2$: C, 73.50; H, 4.83; N, 3.73. Found: C, 73.36; H, 4.98; N, 3.48.

*(2-Methyl-5-phenyloxazol-4-yl)(phenyl)methanol (**6n**).* White crystals (0.23 g, 86%). Mp: 126−127 °C. IR (KBr): 3222, 1494, 1426, 1049, 696 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.54−7.25 (m, 10H), 5.96 (d, J = 7.8 Hz, 1H), 3.56 (d, J = 7.8 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 160.5, 146.0, 142.0, 136.5, 128.7, 128.4, 128.2, 128.0, 127.5, 126.7, 126.0, 68.3, 13.8. MS: m/z = 265 (75, M^+), 223 (20), 39 (34), 160 (60), 117 (32), 105 (79). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.18; H, 5.63; N, 5.31.

*(Phenyl)(5-phenyl-2-propyloxazol-4-yl)methanol (**6o**).* White crystals (0.26 g, 88%). Mp: 90−91 °C. IR (KBr): 3217, 1492, 1208, 1049 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 7.56−7.28 (m, 10H), 5.97 (d, J = 7.8 Hz, 1H), 3.18 (d, J = 8.4 Hz, 1H), 2.79 (t, J = 7.2 Hz, 2H), 1.86−1.82 (m, 2H), 1.03 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 163.8, 145.8, 142.1, 136.2, 133.0, 129.2, 128.7, 128.5, 128.2, 127.7, 126.7, 126.0, 68.5, 30.1, 20.5, 13.8. MS: m/z = 293 (56, M^+), 223 (71), 188 (48), 117 (33), 105 (85). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.91; H, 6.39; N, 4.86.

Isolation of the Intermediate 5a. To a solution of iminophosphorane **3a** (0.97 g, 2 mmol) in 20 mL of toluene was added benzoyl chloride (0.34 g, 2.4 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was then hydrolyzed by the NaOH (5 mL, 2 N) solution, extracted with EtOAc, washed with brine, and dried over Na_2SO_4. The solution was filtered and concentrated under reduced pressure, and the residue was purified by short column chromatography on silica gel to give the amide **5a** (0.21 g, 32%). When amide **5a** was heated in toluene with HCl gas passed for 3 h, oxazole **6a** was finally obtained. However, no product **6a** was detected as the amide **5a** was heated in toluene in the presence of NaOH or NaH.

*N-(1-Oxo-1,3-diphenylprop-2-en-2-yl)benzamide (**5a**).* Mp: 156−157 °C. ^1H NMR ($CDCl_3$, 600 MHz): δ = 8.41 (s, 1H), 7.90−7.34 (m, 15H), 6.79 (s, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 194.1, 165.5, 136.5, 133.6, 133.2, 132.6, 132.5, 132.0, 130.8, 129.9, 129.3, 129.2, 128.8, 128.5, 128.1, 127.5. MS: m/z = 327 (11, M^+), 206 (7), 105 (100), 77 (46). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.55; H, 5.01; N, 4.35.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H NMR and ^{13}C NMR spectra for compounds **3**, **5a**, and **6**; crystal data for **6n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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