Pyrido[2,3-*d*]pyrimidine Derivatives: Synthesis via the Intermolecular Aza-Wittig Reaction/Heterocyclization and the Crystal Structure

Tomohiro Okawa,[a] Mieko Toda,[a] Shoji Eguchi*[a] Akikazu Kakehi[b]

[a] Department of Molecular Design and Engineering, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-01, Japan
Fax +81(52)7893199; E-mail: eguchi@apchem.nagoya-u.ac.jp
[b] Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato 500, Nagano 380, Japan

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Abstract: Pyrido[2,3-*d*]pyrimidine derivatives **5** were synthesized by the intermolecular aza-Wittig reaction of 2-(triphenylphosphoranylidene)aminonicotinamides **3** derived from 2-aminonicotinic acid **(1)**, with carboxylic acid chloride followed by heterocyclization via imidoyl chloride intermediate **4**. The structure of 3-allyl-2-(4-nitrophenyl)-4(3*H*)-pyrido[2,3-*d*]pyrimidinone **(5b)** was established by X-ray crystallographic analysis. This methodology has been applied also to a novel synthesis of 4(3*H*)-quinazolinone **14**.

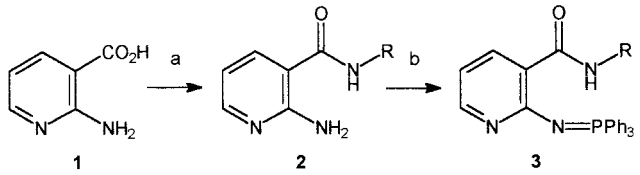
Key words: iminophosphoranes, intermolecular aza-Wittig reaction, heterocyclization, 4(3*H*)-pyrido[2,3-*d*]pyrimidinone, X-ray crystallographic analysis

Pyrido[2,3-*d*]pyrimidine, 5-deaza analogues of pteridine derivatives are known to be the fundamental skeleton of 5,10-dideaza-5,6,7,8-tetrahydrofolic acid (DDATHF)[1] and also the deaza derivatives of methotrexate (MTX). MTX and DDATHF have been shown to possess antineoplastic and immunosuppressive activities, and the establishment of a facile and regioselective construction of these fundamental heterocyclic skeletons is important.

The aza-Wittig reaction has been one of the most useful methodologies for the formation of C=N bonds and azaheterocumulenes, which are useful intermediates for synthesis of nitrogen heterocycles.[2–5] We have been interested in the preparation and the reactivity of *N*-heteroaryliminophosphoranes because these species seem to have been less studied, in spite of their promising potential as building blocks for the synthesis of heterocycles. For example, we have reported the facile synthesis of 4(3*H*)-pteridinones via the intermolecular aza-Wittig reaction and heterocyclization,[6,7] and pyrazino[2,3-*e*][1,4]diazepin-5-ones via the intramolecular aza-Wittig reaction.[8]

In addition, the reaction of the iminophosphoranes with carboxylic acid chlorides to give heterocyclic compounds has been reported by Zbiral,[9] Wamhoff[10] and Molina *et al*.[11,12] They have shown that upon warming or in the presence of *tert*-amines, imidoyl chlorides are formed, which react with internal nucleophiles to afford various heterocycles such as oxazoles,[9] 3,1-oxazin-4-ones,[10] 1,2,4-triazolo[5,1-*c*]-1,2,4-triazines[11] and 6-substituted quinazolino[4,3-*b*]quinazolin-8-ones,[12] *etc*. As part of our continued research programs on the aza-Wittig reaction, we unexpectedly obtained (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives instead of pyrido[2,3-*d*]pyrimidine derivatives from methyl 2-(*N*-triphenylphosphoranylidene)aminonicotinate, aryl isocyanates and primary amines via the intermolecular aza-Wittig reaction, [4+2] heterocycloaddition and heterocyclization.[13] Thus, we investigated another route for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives by utilizing iminophosphoranes having *sec*-amide functions and carboxylic acid chlorides. We wish to report here a facile and efficient synthetic route to pyrido[2,3-*d*]pyrimidine derivatives **5** by the intermolecular aza-Wittig reaction of iminophosphorane derivatives having *sec*-amide functions **3** with various carboxylic acid chlorides followed by heterocyclization.

At first, we investigated the preparation for the iminophosphorane derivatives as follows. The required *sec*-amide derivatives **2a–e** were prepared from 2-aminonicotinic acid **(1)**, primary amines and DEPC[14] (diethylphosphoryl cyanide) as condensation reagent in moderate yields (Scheme 1 and Tables 1–3). In this reaction, the desired compounds could not be obtained by using 1,3-cyclohexylcarbodiimide. Subsequently, *sec*-amides **2a–e** were converted into the corresponding iminophosphorane derivatives **3a–e** in good yield by triphenylphosphine/hexachloroethane/triethylamine reagent system (the Appel method, i.e. the modified Kirsanov reaction)[15] (Scheme 1 and Tables 4–6).



Reagents and conditions: (a) RNH_2/DEPC/Et_3N/DME, 0 °C; then 1 h at r.t. (32–59%); (b) Ph_3P/hexachloroethane/Et_3N/benzene, reflux, 2 h (81–95%)

Scheme 1

Finally, the synthesis of pyrido[2,3-*d*]pyrimidine derivatives **5a–j** was examined by the intermolecular aza-Wittig reaction and heterocyclization by refluxing the iminophosphoranes **3** with acid chlorides in the presence of triethylamine in anhydrous toluene (Scheme 2 and Tables 7–9). In the formation of pyrido[2,3-*d*]pyrimidines, imidoyl chlorides **4** are assumed to be the key intermediates in the consecutive reaction even though **4** could not be detected due to its high reactivity.

Furthermore, X-ray crystallographic analysis was performed to confirm the structure of pyrido[2,3-*d*]pyrimidine **5b** (Figure). As summarized in the Figure and Table 10, the presence of the pyrido[2,3-*d*]pyrimidine skeleton

Table 1. Secondary Amides **2a–e** Prepared

Product	R	Yield (%)[a]	mp (°C)	R_f[b]	IR (KBr or neat), ν (cm^{-1})
2a	CH_2=$CHCH_2$	46	116–119	0.42	3439, 3297, 3148, 1630, 1578, 1534, 1453, 1254, 997, 766
2b	*i*-Pr	54	159–161	0.41	3439, 3306, 3156, 2975, 1624, 1576, 1535, 1453, 1256, 764
2c	Bn	59	123–127	0.61	3448, 3424, 3326, 1642, 1601, 1576, 1524, 1451, 1258, 777, 754, 702
2d	*t*-Bu	32	135–137	0.58	3371, 3332, 3156, 2977, 1636, 1575, 1539, 1456, 1317, 1257, 1221, 775
2e	DMPM[c]	54	155–157	0.58	3428, 3314, 3130, 1626, 1578, 1523, 1458, 1259, 1208, 1158, 1135, 1045, 834, 761

[a] Isolated yield.
[b] Eluent = EtOAc.
[c] DMPM = 2,4-dimethoxyphenylmethyl.

Table 2. ^1H and ^{13}C NMR Spectral Data of Compounds **2a–e**

Product	^1H NMR ($CDCl_3$/TMS, 200 MHz); δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS, 50 MHz), δ
2a	4.05 (2 H, tt, *J* = 5.7, 1.5, NHC*H*$_2$CH=CH$_2$), 5.20 [1 H, dq, *J* = 10.2, 1.5, CH=C*H*$_2$ (*cis*)], 5.26 [1 H, dq, *J* = 17.2, 1.5, CH=C*H*$_2$ (*trans*)], 5.93 (1 H, ddt, *J* = 17.2, 10.2, 5.7, CH_2C*H*=CH_2), 6.22 (1 H, br, CONH), 6.38 (2 H, br, NH_2), 6.60 (1 H, dd, *J* = 7.7, H-5), 7.64 (1 H, dd, *J* = 7.7, 1.8, H-4), 8.16 (1 H, dd, *J* = 4.9, 1.8, H-6)	42.33 (NH*C*H$_2$CH=CH$_2$), 110.73 (C-3), 112.68 (C-5), 117.24 (CH=*C*H$_2$), 134.31 (CH_2*C*H=CH_2), 135.84 (C-4), 152.22 (C-6), 159.13 (C-2), 168.14 (CONH)
2b	1.26 [6 H, d, *J* = 6.6, CH(C*H*$_3$)$_2$], 4.24 [1 H, d-septet, *J* = 7.8, 6.6, NHC*H*(CH$_3$)$_2$], 5.87 (1 H, br, CONH), 6.31 (2 H, br, NH_2), 6.59 (1 H, dd, *J* = 7.6, 4.9, H-5), 7.57 (1 H, dd, *J* = 7.6, 1.8, H-4), 8.15 (1 H, dd, *J* = 4.9, 1.8, H-6)	22.87 [CH(*C*H$_3$)$_2$], 41.91 [NH*C*H(CH$_3$)$_2$], 111.27 (C-3), 112.67 (C-5), 135.65 (C-4), 152.02 (C-6), 159.14 (C-2), 167.57 (CONH)
2c	4.57 (2 H, d, *J* = 5.6, NHC*H*$_2$C$_6$H$_5$), 6.37 (2 H, br, NH_2), 6.54 (1 H, dd, *J* = 7.8, 4.9, H-5), 6.51–6.58 (1 H, br, CONH), 7.24–7.41 (5 H, m), 7.61 (1 H, dd, *J* = 7.8, 1.8, H-4), 8.12 (1 H, dd, *J* = 4.9, 1.8, H-6)	43.96 (NH*C*H$_2$C$_6$H$_5$), 110.60 (C-3), 112.65 (C-5), 128.05 (C'-4), 128.17 (C'-2), 129.19 (C'-3), 135.88 (C-4), 138.30 (C'-1), 152.27 (C-6), 159.19 (C-2), 168.20 (CONH)
2d	1.45 [9 H, s, C(C*H*$_3$)$_3$], 5.86 (1 H, br, CONH), 6.27 (2 H, br, NH_2), 6.57 (1 H, dd, *J* = 7.7, 5.0, H-5), 7.53 (1 H, dd, *J* = 7.7, 1.8, H-4), 8.12 (1 H, dd, *J* = 5.0, 1.8, H-6)	28.92 [C(*C*H$_3$)$_3$], 51.93 [NH*C*(CH$_3$)$_3$], 112.41 (C-3), 112.63 (C-5), 135.70 (C-4), 151.65 (C-6), 159.04 (C-2), 168.05 (CONH)
2e	3.81 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 4.51 (2 H, d, *J* = 5.6 Hz, NHC*H*$_2$A), 6.33 (2 H, br, NH_2), 6.57 (1 H, dd, *J* = 7.8, 4.9, H-5), 6.43–7.27 (3 H + 1 H, m, C_6H_3 + CONH), 7.55 (1 H, dd, *J* = 7.8, 1.8, H-4), 8.13 (1 H, dd, *J* = 4.9, 1.8, H-6)	39.56 (NH*C*H$_2$Ar), 55.61 (2 OCH_3), 99.04 (C'-3), 104.35 (C'-5), 111.21 (C-3), 112.64 (C-5), 118.73 (C'-1), 131.08 (C'-6), 135.80 (C-4), 151.99 (C-6), 159.13 (C-2 and/or C'-2 or C'-4), 161.17 (C'-2 and/or C'-4), 167.87 (CONH)

Table 3. MS and HRMS Data of Compounds **2a–e**

Product	MS (70 eV), *m*/*z* (%)	HRMS (70 eV), *m*/*z*, found (formula, calc.)
2a	178 (8, M^+ + 1), 177 (48, M^+), 122 (19), 121 (100), 95 (4), 94 (25), 93 (56), 92 (3), 67 (3), 66 (16)	177.0904 ($C_9H_{11}N_3O$, 177.0902)
2b	180 (7, M^+ + 1), 179 (55, M^+), 178 (4), 164 (5), 137 (3), 122 (8), 121 (100), 120 (8), 94 (11), 93 (38), 92 (3), 66 (9)	179.1062 ($C_9H_{13}N_3O$, 179.1059)
2c	228 (13, M^+ + 1), 227 (76, M^+), 122 (5), 121 (45), 107 (17), 106 (100), 94 (21), 93 (35), 91 (39), 79 (7), 66 (10), 65 (8)	227.1059 ($C_{13}H_{13}N_3O$, 227.1059)
2d	194 (6, M^+ + 1), 193 (43, M^+), 178 (10), 137 (29), 122 (6), 121 (100), 120 (22), 94 (17), 93 (30), 92 (3), 66 (12)	193.1213 ($C_{10}H_{15}N_3O$, 193.1215)
2e	288 (4, M^+ + 1), 287 (21, M^+), 167 (8), 166 (100), 152 (3), 151 (22), 121 (15), 93 (4)	287.1271 ($C_{15}H_{17}N_3O_3$, 287.1270)

was confirmed. The structure of 4(3*H*)-pyrido[2,3-*d*]pyrimidinones by X-ray crystallographic analysis has not been reported previously to the best of our knowledge.[16] The torsion angles of **5b** indicated that the pyrido[2,3-*d*]pyrimidine skeleton was approximately planar, and the allyl function and the pyrido[2,3-*d*]pyrimidine ring were almost perpendicular (C2–N2–C14–C15: 100.5° and C3–N2–C14–C15: 83.0°, Figure and Table 10). Also, the phenyl ring and the pyrido[2,3-*d*]pyrimidine ring were at an angle of about 65° (N1–C2–C8–C9: 113.7° and N2–C2–C8–C9: 64.2°, Figure and Table 10). All pyrido[2,3-*d*]pyrimidines **5** were purified by both silica gel (BW-300 and

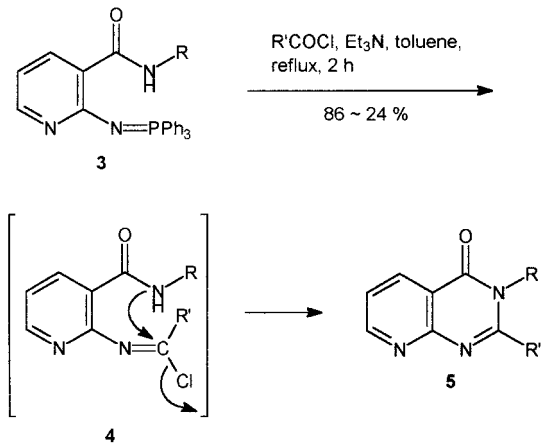
Table 4. Iminophosphoranes **3a–e** Prepared

Product	R	Yield (%)[a]	mp (°C)	R_f[b]	IR (KBr or neat), ν (cm^{-1})
3a	CH_2=$CHCH_2$	95	178–179	0.79	3030, 1647, 1537, 1420, 1321, 1109, 995, 721
3b	*i*-Pr	91	214–215	0.82	3136, 1640, 1574, 1535, 1420, 1329, 1250, 1111, 1011, 997, 720
3c	Bn	88	57–60	0.56	3158, 1647, 1578, 1543, 1422, 1329, 1248, 1111, 1011, 997, 720
3d	*t*-Bu	81	168–170	0.86	3202, 1648, 1543, 1419, 1327, 1277, 1255, 1111, 995, 720
3e	DMPM[c]	88	60–62	0.71	3426, 1644, 1577, 1542, 1508, 1420, 1329, 1262, 1111, 996, 719

[a] Isolated yield.
[b] Eluents for **3a, b, d, e** = EtOAc, for **3e** = EtOAc/hexane (1:1).
[c] DMPM = 2,4-dimethoxyphenylmethyl.

Table 5. ^1H and ^{13}C NMR Data of Compounds **3a–e**

Product	^1H NMR ($CDCl_3$/TMS, 200 MHz); δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS, 50 MHz); δ, *J* (Hz)
3a	4.17 (2 H, tt, *J* = 5.8, 1.6, NHCH_2CH=CH_2), 5.13 [1 H, dq, *J* = 10.1, 1.6, CH=CH_2 (*cis*)], 5.29 [1 H, dq, *J* = 17.2, 1.6, CH=CH_2 (*trans*)], 6.01 (1 H, ddt, *J* = 17.2, 10.1, 5.8, CH_2C*H*=CH_2), 6.60 (1 H, dd, *J* = 7.6, 4.9, H-5), 7.38–7.59 (9 H, m, C_6H_5), 7.71–7.82 (6 H, m, C_6H_5), 7.84 (1 H, ddd, *J* = 4.9, 2.1, 0.5, H-4), 8.43 (1 H, ddd, *J* = 7.6, 2.6, 2.1, H-6), 11.44 (1 H, br s, CONH),	42.36 (NH*C*H_2CH=CH_2), 113.54 (C-5), 116.24 (CH=*C*H_2), 118.68 (d, *J* = 18.4, C-3), 128.84 (d, *J* = 12.1, C'-3), 129.72 (d, *J* = 100.0, C'-1), 132.26 (d, *J* = 2.7, C'-4), 133.49 (d, *J* = 9.8, C'-2), 135.82 (CH_2*C*H=CH_2), 139.62 (d, *J* = 2.9, C-4), 149.46 (C-6), 161.47 (d, *J* = 7.3, C-2), 167.23 (CONH)
3b	1.22 [6 H, d, *J* = 6.7, CH(CH_3)$_2$], 4.34 [1 H, septet, *J* = 6.7, NHC*H*(CH_3)$_2$], 6.60 (1 H, dd, *J* = 7.7, 4.8, H-5), 7.40–7.60 (9 H, m, C_6H_5), 7.73–7.85 (1 H + 6 H, m, H-4 + C_6H_5), 8.43 (1 H, ddd, *J* = 7.7, 2.7, 2.2, H-6), 11.08 (1 H, d, *J* = 6.8, CON*H*CH)	23.27 [CH(*C*H_3)$_2$], 41.08 [NH*C*H(CH_3)$_2$], 113.59 (C-5), 118.98 (d, *J* = 18.8, C-3), 128.83 (d, *J* = 12.4, C'-3), 129.86 (d, *J* = 101.0, C'-1), 132.27 (d, *J* = 2.7, C'-4), 133.55 (d, *J* = 9.8, C'-2), 139.58 (d, *J* = 2.9, C-4), 149.21 (C-6), 161.42 (d, *J* = 7.3, C-2), 166.40 (CONH)
3c	4.74 (2 H, d, *J* = 5.8, NHC$H_2$$C_6H_5$), 6.60 (1 H, dd, *J* = 7.6, 4.8, H-5), 7.24–7.53 (9 H + 5 H, m, C_6H_5 + C_6H_5), 7.60–7.72 (6 H, m, C_6H_5), 7.84 (1 H, ddd, *J* = 4.8, 2.2, 0.5, H-4), 8.47 (1 H, ddd, *J* = 7.6, 2.8, 2.2, H-6), 11.74 (1 H, br, CONH)	43.69 (NH*C*$H_2$$C_6H_5$), 113.56 (C-5), 118.57 (d, *J* = 18.4, C-3), 127.31 (C"-4), 128.34 (C"-2), 128.78 (d, *J* = 12.2, C'-3), 128.85 (C"-3), 129.59 (d, *J* = 100.9, C'-1), 132.16 (d, *J* = 2.7, C'-4), 133.39 (d, *J* = 9.8, C'-2), 139.72 (d, *J* = 2.8, C-4), 140.03 (C"-1), 149.50 (C-6), 161.53 (d, *J* = 7.2, C-2), 167.52 (CONH)
3d	1.41 [9 H, s, C(CH_3)$_3$], 6.58 (1 H, dd, *J* = 7.6, 4.8, H-5), 7.38–7.59 (9 H, m, C_6H_5), 7.71–7.83 (1 H + 6 H, m, H-4 + C_6H_5), 8.41 (1 H, ddd, *J* = 7.6, 2.6, 2.0, H-6), 10.86 (1 H, br, CONH)	29.30 [C(*C*H_3)$_3$], 50.66 [NH*C*(CH_3)$_3$], 113.58 (C-5), 119.83 (d, *J* = 19.0, C-3), 128.77 (d, *J* = 12.0, C'-3), 129.90 (d, *J* = 100.9, C'-1), 132.19 (d, *J* = 2.7, C'-4), 133.61 (d, *J* = 9.6, C'-2), 139.32 (d, *J* = 2.9, C-4), 148.93 (C-6), 161.48 (d, *J* = 7.5, C-2), 166.45 (d, *J* = 1.7, CONH)
3e	3.55 (3 H, s, OCH_3), 3.79 (3 H, s, OCH_3), 4.65 (2 H, d, *J* = 5.8, (NHCH_2Ar), 6.36–6.43 (2 H, m, C_6H_3), 6.58 (1 H, dd, *J* = 7.6, 4.8, H-5), 7.32–7.55 (1 H + 9 H, m, C_6H_3 + C_6H_5), 7.66–7.78 (6 H, m, C_6H_5), 7.81 (1 H, ddd, *J* = 4.8, 2.1, 0.5, H-4), 8.44 (1 H, ddd, *J* = 7.6, 2.9, 2.1, H-6), 11.48 (1 H, br, CONH)	38.69 (NH*C*H_2Ar), 55.24 (OCH_3), 55.53 (OCH_3), 98.85 (C"-3), 104.12 (C"-5), 113.44 (C-5), 118.94 (d, *J* = 18.8, C-3), 120.40 (C"-1), 128.78 (d, *J* = 12.5, C'-3), 129.82 (d, *J* = 100.8, C'-1), 130.76 (C"-6), 132.09 (d, *J* = 2.8, C'-4), 133.43 (d, *J* = 9.7, C'-2), 139.64 (d, *J* = 2.8, C-4), 149.23 (C-6), 158.95 (C"-2 or C"-4), 160.41 (C"-2 or C"-4), 161.53 (d, *J* = 7.4, C-2), 167.30 (CONH)



Scheme 2

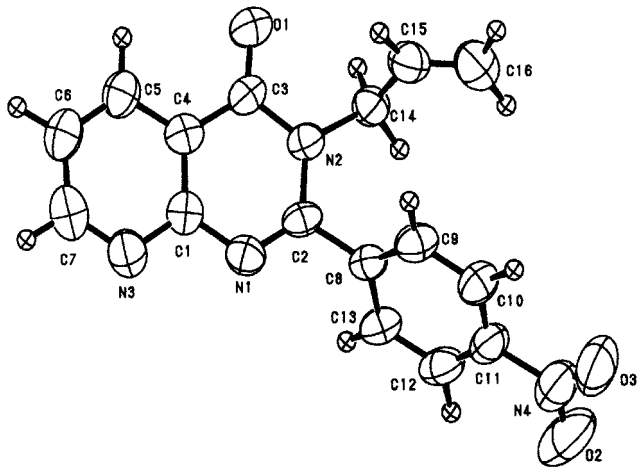


Figure. ORTEP Diagram of 3-Allyl-2-(4-nitrophenyl)-4(3*H*)-pyrido[2,3-*d*]pyrimidinone (**5b**)

Table 6. MS and HRMS Data of Compounds **3a–e**

Product	MS (70 eV), *m*/*z* (%)	HRMS (70 eV), *m*/*z*, found (formula, calc.)
3a	438 (24, $M^+ + 1$), 437 (83, M^+), 397 (11), 396 (40), 382 (24), 381 (41), 354 (22), 353 (100), 262 (14), 201 (20), 183 (36)	437.1660 ($C_{27}H_{24}N_3OP$, 437.1657)
3b	440 (10, $M^+ + 1$), 439 (33, M^+), 424 (13), 397 (18), 396 (63), 383 (23),382 (100), 381 (86), 354 (23), 353 (91), 262 (15), 201 (26), 183 (34)	439.1811 ($C_{27}H_{26}N_3OP$, 439.1813)
3c	488 (23, $M^+ + 1$), 487 (70, M^+), 396 (22), 383 (8), 382 (34), 354 (24), 353 (100), 201 (12), 183 (18)	487.1818 ($C_{31}H_{26}N_3OP$, 487.1813)
3d	453 (16, M^+), 439 (9), 438 (29), 397 (16), 396 (54), 382 (23), 381 (100), 353 (8), 262 (10), 201 (16), 124 (24), 108 (5)	453.1968 ($C_{28}H_{28}N_3OP$, 453.1970)
3e	548 (25, $M^+ + 1$), 547 (81, M^+), 532 (7), 383 (10), 382 (48), 381 (43), 354 (24), 353 (100), 262 (8), 201 (9), 183 (15)	547.2024 ($C_{33}H_{30}N_3O_3P$, 547.2025)

Table 7. Pyrido[2,3-*d*]pyrimidines **5a–k** Prepared

Product	R	R'	Yield (%)[a]	mp (°C)	R_f[b]	IR (KBr or neat), ν (cm^{-1})
5a	$CH_2CH{=}CH_2$	Ph	86	154–157	0.11	2948, 1686, 1566, 1433, 1375, 1346, 1250, 1221, 1130, 968, 912, 799, 704
5b	$CH_2CH{=}CH_2$	4-$NO_2C_6H_4$	72	140–144	0.45	3148, 1680, 1578, 1520, 1431, 1377, 1352, 1221, 1096, 860, 799, 704
5c	*i*-Pr	Ph	73	201–203	0.52	3428, 3057, 1678, 1589, 1437, 1397, 1348, 1298, 1221, 1073, 802, 702
5d	*i*-Pr	4-$NO_2C_6H_4$	79	272–274	0.64	3426, 3056, 1680, 1582, 1522, 1437, 1395, 1348, 1289, 1219, 1175, 1071, 856, 710
5e	Bn	Ph	69	154–156	0.58	3067, 1674, 1572, 1497, 1431, 1364, 1304, 1254, 1223, 1179, 806, 777, 704
5f	Bn	4-$NO_2C_6H_4$	74	201–203	0.59	3423, 1682, 1578, 1517, 1434, 1384, 1346, 1220, 1104, 859, 799, 698
5g	*t*-Bu	Ph	24	143–146	0.44	2971, 1674, 1588, 1558, 1429, 1340, 1211, 1181, 795, 702
5h	*t*-Bu	4-$NO_2C_6H_4$	37	296–300	0.31	3445, 1678, 1588, 1559, 1522, 1431, 1352, 1290, 1177, 858, 797
5j	DMPM[c]	4-$NO_2C_6H_4$	71	197–200	0.14	3435, 1685, 1575, 1523, 1437, 1350, 1302, 1209, 1103, 1034, 859, 795
5k	$CH_2CH{=}CH_2$	*i*-Pr	83	134–136	0.21	2962, 1675, 1582, 1437, 1392, 1308, 1226, 1100, 936, 802

[a] Isolated yield.
[b] Eluents for **5b–f** = EtOAc, for **5a, g–k** = EtOAc/hexane (1:1).
[c] DMPM = 2,4-dimethoxyphenylmethyl.

Chromatorex→ NH-DM-1020) column chromatography and recrystallization from ethyl acetate and hexane because R_f values of these compounds on TLC (silica gel) were the same as that of triphenylphosphine oxide, which was the inevitable byproduct in the aza-Wittig reaction (see Experimental section). Besides, reaction with isobutyryl chloride (R' = alkyl) produced the desired pyrido[2,3-*d*]pyrimidine derivative **5j** in the same way (83% yield).

Moreover, the synthesis of 3*H*-pyrido[2,3-*d*]pyrimidine derivatives using primary amides was studied (Scheme 3). At first, the primary amide derivative **6** was prepared from the amine **1**, DEPC and a ten-fold excess of ammonium chloride (46% yield).[17] Subsequently, the corresponding iminophosphorane **7** was prepared by the Appel method (24% yield); however, the nitrile derivatives **8** and **9** were produced as byproducts (22 and 10% yield, respectively). The yield of **7** was determined by ^1H NMR because of the difficulty in separation of the product **7** from triphenylphosphine oxide, the inevitable byproduct in the preparation of iminophosphoranes. In this reaction, the triphenylphosphine/hexachloroethane/triethylamine reagent system worked also as a dehydrating reagent, affording the nitriles **8** and **9**.

Table 8. ^{1}H and ^{13}C NMR Data of Compounds **5a–j**

Product	^{1}H NMR ($CDCl_3$/TMS, 200 MHz); δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS, 50 MHz), δ
5a	4.65 (2 H, dt, *J* = 5.2, 1.4, NC*H*$_2$CH=CH$_2$), 4.98 [1 H, dq, *J* = 17.2, 1.4, CH=C*H*$_2$(*trans*)], 5.22 [1 H, dq, *J* = 10.4, 1.4, CH=C*H*$_2$(*cis*)], 5.90 (1 H, ddt, *J* = 17.2, 10.4, 5.2, CH$_2$C*H*=CH$_2$), 7.47 (1 H, dd, *J* = 8.0, 4.6, H-6); 7.49–7.55 (3 H, m, C_6H_5), 7.60–7.65 (2 H, m, C_6H_5), 8.67 (1 H, dd, *J* = 8.0, 2.1, H-5), 9.02 (1 H, dd, *J* = 4.6, 2.1, H-7)	48.72 (N*C*H$_2$CH=CH$_2$), 116.20 (C-4a), 118.19 (CH=*C*H$_2$), 122.86 (C-6), 128.52 (C'-2 or C'-3), 128.78 (C'-2 or C'-3), 130.72 (C'-4), 132.20 (CH$_2$*C*H=CH$_2$), 135.04 (C'-1), 136.85 (C-5), 156.86 (C-7), 157.73 (C-2 or C-8a), 160.14 (C-2 or C-8a), 162.93 (C-4)
5b	4.62 (2 H, dt, *J* = 5.2, 1.6, NC*H*$_2$CH=CH$_2$), 4.98 [1 H, dtd, *J* = 17.4, 1.6, 0.7, CH=C*H*$_2$ (*trans*)], 5.29 [1 H, dtd, *J* = 10.5, 1.6, 0.7, CH=C*H*$_2$(*cis*)], 5.91 (1 H, ddt, *J* = 17.4, 10.5, 5.1, CH$_2$C*H*=CH$_2$), 7.53 (1 H, dd, *J* = 8.0, 4.5, H-6), 7.81–7.88 (2 H, m, C_6H_4), 8.35–8.41 (2 H, m, C_6H_4), 8.69 (1 H, dd, *J* = 8.0, 2.0, H-5), 9.05 (1 H, dd, *J* = 4.5, 2.0, H-7)	48.59 (N*C*H$_2$CH=CH$_2$), 116.46 (C-4a), 118.51 (CH=*C*H$_2$), 123.52 (C-6), 124.07 (C'-3), 129.88 (C'-2), 131.85 (CH$_2$*C*H=CH$_2$), 137.01 (C-5), 140.70 (C'-1), 149.26 (C'-4), 157.09 (C-7), 157.36 (C-2 or C-8a), 157.89 (C-2 or C-8a), 162.44 (C-4)
5c	1.60 [6 H, d, *J* = 6.8, CH(C*H*$_3$)$_2$], 4.47 [1 H, septet, *J* = 6.8, NC*H*(CH$_3$)$_2$], 7.44 (1 H, dd, *J* = 8.0, 4.4, H-6), 7.49–7.61 (5 H, m, C_6H_5), 8.62 (1 H, dd, *J* = 8.0, 1.8, H-5), 8.98 (1 H, dd, *J* = 4.4, 1.8, H-7)	19.66 [CH(*C*H$_3$)$_2$], 54.64 [N*C*H(CH$_3$)$_2$], 117.38 (C-4a), 122.66 (C-6), 127.85 (C'-2), 129.07 (C'-3), 130.38 (C'-4), 136.24 (C'-1), 136.47 (C-5), 156.56 (C-7), 157.36 (C-2 or C-8a), 160.48 (C-2 or C-8a), 163.15 (C-4)
5d	1.63 [6 H, d, *J* = 6.8, CH(C*H*$_3$)$_2$], 4.29 [1 H, septet, *J* = 6.8, NC*H*(CH$_3$)$_2$], 7.50 (1 H, dd, *J* = 8.0, 4.4, H-6), 7.76–7.83 (2 H, m, C_6H_4), 8.34–8.44 (2 H, m, C_6H_4), 8.64 (1 H, dd, *J* = 8.0, 1.8, H-5), 9.01 (1 H, dd, *J* = 4.4, 1.8, H-7)	19.44 [CH(*C*H$_3$)$_2$], 54.75 [N*C*H(CH$_3$)$_2$], 117.38 (C-4a), 123.04 (C-6), 124.17 (C'-3), 128.91 (C'-2), 136.38 (C-5), 141.73 (C'-1), 148.79 (C'-4), 156.52 (C-7), 156.72 (C-2 or C-8a), 157.88 (C-2 or C-8a), 162.76 (C-4)
5e	5.32 (2 H, s, NC*H*$_2$C$_6$H$_5$), 6.99–6.92 (2 H, m, C_6H_5), 7.19–7.27 (3 H, m, C_6H_5), 7.37–7.50 (5 H, m, C_6H_5), 7.48 (1 H, dd, *J* = 8.0, 4.6, H-6), 8.68 (1 H, dd, *J* = 8.0, 2.0, H-5), 9.02 (1 H, dd, *J* = 4.6, 2.0, H-7)	49.37 (N*C*H$_2$C$_6$H$_5$), 116.30 (C-4a), 122.93 (C-6), 127.28 (C_6H_5), 128.03 (C_6H_5), 128.60 (C_6H_5), 128.79 (C_6H_5), 129.01 (C'-4 or C"-4), 130.65 (C'-4 or C"-4), 135.11 (C'-1 or C"-1), 136.48 (C'-1 or C"-1), 137.06 (C-5), 156.94 (C-7), 157.76 (C-2 or C-8a), 160.25 (C-2 or C-8a), 163.39 (C-4)
5f	5.28 (2 H, s, NC*H*$_2$C$_6$H$_5$), 6.92–6.88 (2 H, m, C_6H_5), 7.22–7.29 (3 H, m, C_6H_5), 7.55 (1 H, dd, *J* = 8.0, 4.6, H-6), 7.54–7.61 (2 H, m, C_6H_4), 8.22–8.29 (2 H, m, C_6H_4), 8.73 (1 H, dd, *J* = 8.0, 2.0, H-5), 9.06 (1 H, dd, *J* = 4.6, 2.0, H-7)	49.17 (N*C*H$_2$C$_6$H$_5$), 116.53 (C-4a), 123.61 (C-6), 123.96 (C'-3 or C"-2), 126.95 (C'-3 or C"-2), 128.43 C"-4), 129.33 (C'-2 or C"-3), 129.81 (C'-2 or C"-3), 135.86 (C"-1), 137.25 (C-5), 140.76 (C'-1), 149.08 (C'-4), 157.17 (C-7), 157.40 (C-2 or C-8a), 158.06 (C-2 or C-8a), 162.97 (C-4)
5g	1.52 [9H, s, C (C*H*$_3$)$_3$], 7.38 (1 H, dd, *J* = 7.9, 4.6, H-6), 7.44–7.52 (3 H, m, C_6H_5), 7.64–7.70 (2 H, m, C_6H_5), 8.54 (1 H, dd, *J* = 7.9, 1.9, H-5), 8.92 (1 H, dd, *J* = 4.6, 1.9, H-7)	31.13 [C(*C*H$_3$)$_3$], 64.72 [N*C*(CH$_3$)$_3$], 117.50 (C-4a), 122.25 (C-6), 128.57 (C-2' or C-3'), 128.70 (C-2' or C-3'), 130.52 (C'-4), 136.45 (C-5), 140.57 (C'-1), 156.13 (C-7), 156.53 (C-2 or C-8a), 160.71 (C-2 or C-8a), 166.74 (C-4)
5h	1.54 [9 H, s, C(C*H*$_3$)$_3$], 7.46 (1 H, dd, *J* = 7.9, 4.6, H-6), 7.83–7.90 (2 H, m, C_6H_4), 8.33–8.40 (2 H, m, C_6H_4), 8.57 (1 H, dd, *J* = 7.9, 2.0, H-5), 8.97 (1 H, br, H-7)	31.22 [C(*C*H$_3$)$_3$], 64.91 [NC(*C*H$_3$)$_3$], 117.71 (C-4a), 123.06 (C-6), 124.09 (C'-3), 129.52 (C'-2), 136.68 (C-5), 146.28 (C'-1), 148.93 (C'-4), 156.07 (C-2 or C-8a), 156.38 (C-7), 158.37 (C-2 or C-8a), 166.14 (C-4)
5i	3.53 (OCH$_3$), 3.76 (OCH$_3$), 5.19 (NC*H*$_2$Ar), 6.30 (1 H, d, *J* = 2.4, H'-3), 6.37 (1 H, dd, *J* = 8.2, 2.4, H'-5), 6.88 (1 H, d, *J* = 8.2, H'-6), 7.51 (1 H, dd, *J* = 8.0, 4.6, H-6), 7.63–7.69 (2 H, m, C_6H_4), 8.23–8.29 (2 H, m, C_6H_4), 8.68 (1 H, dd, *J* = 8.0, 2.0, H-5), 9.03 (1 H, dd, *J* = 4.6, 2.0, H-7)	44.98 (N*C*H$_2$Ar), 55.16 (OCH$_3$), 55.51 (OCH$_3$), 98.53 (C"-3), 104.56 (C"-5), 116.10 (C"-1), 116.50 (C-4a), 123.33 (C-6), 123.70 (C'-3), 129.47 (C"-6), 129.74 (C'-2), 137.11 (C-5), 141.19 (C'-1), 148.96 (C'-4), 156.89 (C-7), 157.40 (C-2 or C-8a), 157.95 (C-2" or C-4"), 158.44 (C-2 or C-8a), 161.17 (C-2" or C-4"), 163.11 (C-4)
5j	1.43 [6 H, d, *J* = 6.6, CH(C*H*$_3$)$_2$], 3.18 [1 H, septet, *J* = 6.6, CC*H*(CH$_3$)$_2$], 4.85 (2 H, dt, *J* = 4.8, 1.8, NC*H*$_2$CH=CH$_2$), 5.07 [1 H, dtd, *J* = 17.2, 1.8, 0.7, CH=C*H*$_2$(*trans*)], 5.27 [1 H, dtd, *J* = 10.6, 1.8, 0.7, CH=C*H*$_2$(*cis*)], 6.00 (1 H, ddt, *J* = 17.2, 10.6, 4.8, CH$_2$C*H*=CH$_2$), 7.41 (1 H, dd, *J* = 7.9, 4.6, H-6), 8.60 (1 H, dd, *J* = 7.9, 2.0, H-5), 8.97 (1 H, br s, H-7)	21.45 [CH(*C*H$_3$)$_2$], 32.30 [C*C*H(CH$_3$)$_2$], 45.21 (N*C*H$_2$CH=CH$_2$), 115.66 (C-4a), 117.29 (CH=*C*H$_2$), 122.30 (C-6), 132.36 (CH$_2$*C*H=CH$_2$), 136.98 (C-5), 156.55 (C-7), 157.91 (C-2 or C-8a), 162.96 (C-2 or C-8a), 166.27 (C-4)

Subsequently, reaction of the obtained iminophosphorane **7** with acid chloride to form 4*H*-pyrido[2,3-*d*]pyrimidines **10** was examined. However, the desired 4*H*-pyrido[2,3-*d*]pyrimidines **10** could not be obtained at all, only the iminophosphorane with nitrile function **8** was formed exclusively (Scheme 4). The tautomer **7'** of **7** as detectable by ^{1}H NMR reacted with carboxylic acid chloride to give **8** via **11**. As an alternative route to **10**, attempted deprotection of the 2,4-dimethoxyphenylmethyl (DMPM) function of pyrido[2,3-*d*]pyrimidine **5i** with TFA,[18] CAN[19] or DDQ[20] resulted in failure, affording no trace of the desired compound. Thus, the synthesis of 3*H*-pyrido[2,3-*d*]-

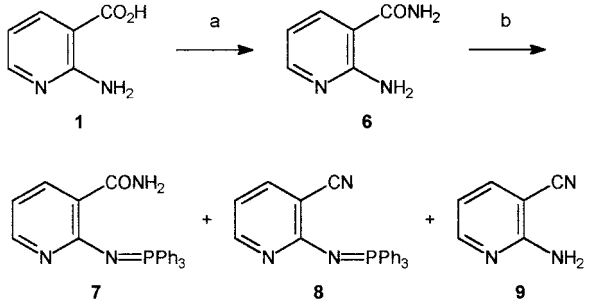
Table 9. MS and HRMS Data of Compounds **5a–j**

Product	MS (70 eV), *m/z* (%)	HRMS (70 eV), *m/z*, found (formula, calc.)
5a	264 (11, $M^+ + 1$), 263 (64, M^+), 262 (100), 248 (38), 234 (9), 180 (7), 131 (6), 104 (7), 78 (7), 77 (7)	263.1057 ($C_{16}H_{13}N_3O$, 263.1059)
5b	309 (13, $M^+ + 1$), 308 (74, M^+), 307 (100), 294 (10), 293 (64), 291 (12), 261 (26), 186 (8), 131 (7), 78 (8)	308.0901 ($C_{16}H_{12}N_4O_3$, 308.0909)
5c	266 (16, $M^+ + 1$), 265 (92, M^+), 264 (79), 224 (13), 223 (65), 222 (15), 209 (11), 120 (100), 104 (10), 103 (9)	265.1208 ($C_{16}H_{15}N_3O$, 265.1215)
5d	311 (13, $M^+ + 1$), 310 (67, M^+), 309 (60), 293 (17), 269 (15), 268 (90), 263 (12), 254 (13), 222 (51), 120 (100), 78 (11)	310.1064 ($C_{16}H_{14}N_4O_3$, 310.1066)
5e	314 (17, $M^+ + 1$), 313 (85, M^+), 312 (100), 209 (6), 207 (5), 181 (9), 91 (29)	313.1205 ($C_{20}H_{15}N_3O$, 313.1215)
5f	359 (17, $M^+ + 1$), 358 (90, M^+), 357 (100), 341 (6), 312 (7), 311 (18), 254 (6), 252 (8), 181 (10), 91 (70), 78 (6), 65 (6)	358.1068 ($C_{20}H_{14}N_4O_3$, 358.1066)
5g	279 (8, M^+), 224 (28), 223 (99), 222 (6), 195 (4), 179 (4), 121 (6), 120 (100), 103 (5), 93 (6), 92 (5), 77 (5)	279.1372 ($C_{17}H_{17}N_3O$, 279.1372)
5h	324 (6, M^+), 270 (6), 269 (44), 268 (100), 238 (8), 223 (7), 222 (26), 194 (6), 121 (5), 120 (62)	324.1220 ($C_{17}H_{16}N_4O_3$, 324.1222)
5i	418 (15, M^+), 281 (3), 280 (19), 209 (3), 152 (7), 151 (100), 121 (14), 91 (3)	418.1274 ($C_{22}H_{18}N_4O_5$, 418.1277)
5j	229 (21, M^+), 228 (18), 215 (12), 214 (100), 200 (8), 199 (7), 188 (13), 187 (14), 186 (70), 174 (16), 78 (8)	229.1218 ($C_{13}H_{15}N_3O$, 229.1215)

Table 10. Selected Bond Angles, Bond Lengths and Torsion Angles of **5b**

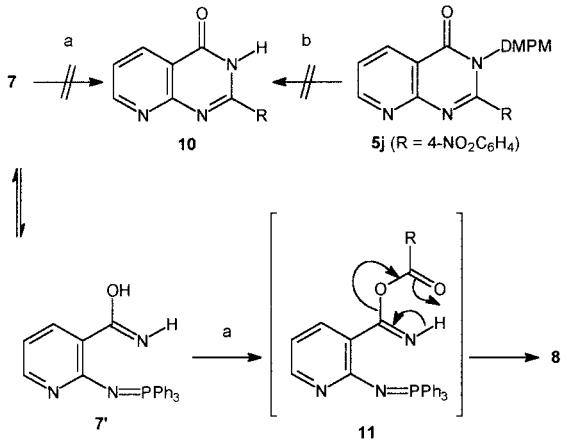
Bond Angles (°)[a]				Bond Lengths (Å)[a]				Torsion Angles (°)[b]			
C1-N1-C2	117.0(3)	O1-C3-N2	120.4(3)	O1-C3	1.225(4)	N4-C11	1.487(5)	(1)-(2)-(3)-(4)		(1)-(2)-(3)-(4)	
C2-N2-C3	120.8(3)	N2-C3-C4	114.5(3)	O2-N4	1.201(5)	C1-C4	1.395(4)	O1-C3-N2-C2	–179.9 (3)	N2-C2-N1-C1	–3.9(5)
C2-N2-C14	122.4(3)	C1-C4-C3	120.2(3)	O3-N4	1.223(5)	C2-C8	1.485(4)	O1-C3-N2-C14	–3.4(4)	N1-C1-C8-C9	–113.7(4)
C1-N3-C7	115.4(3)	C3-C4-C5	120.8(3)	N1-C1	1.383(4)	C3-C4	1.445(4)	O1-C3-C4-C1	176.0(3)	N2-C2-C8-C9	64.2(4)
N1-C1-N3	114.5(3)	C4-C5-C6	117.8(4)	N1-C2	1.293(4)	C4-C5	1.398(5)	O1-C3-C4-C5	–3.0(5)	N2-C14-C15-C16	136.9(4)
N1-C2-N2	125.2(3)	C5-C6-C7	119.4(4)	N2-C2	1.395(4)	C5-C6	1.366(5)	C1-N1-C2-N8	173.8(6)	C2-N2-C14-C15	–100.5(4)
N1-C2-C8	117.6(3)	N3-C7-C6	125.2(4)	N2-C3	1.397(4)	C6-C7	1.378(6)	C4-C5-C6-C7	–1.3(6)	C3-N2-C14-C15	83.0(4)
				N2-C14	1.489(4)	C8-C9	1.393(4)	C4-C1-N3-C7	–1.1(5)	C8-C2-N2-C14	11.0(4)
				N3-C1	1.357(4)	C14-C15	1.500(5)				
				N3-C7	1.335(5)	C15-C16	1.314(5)				

[a] The estimated standard deviations in the least significant figure are given in parentheses.
[b] The sign is positive if when looking from atom (2) to atom (3) a clockwise motion of atom (1) would superimpose it on atom (4). The estimated standard deviations in the least significant figure are given in parentheses.



Reagents and conditions: (a) NH_4Cl/DEPC/Et_3N/DME, 0 °C; then 1 h at r.t. (46%); (b) Ph_3P/hexachloroethane/Et_3N/benzene, reflux, 2 h (**7**, 24%; **8**, 22%; **9**, 10%)

Scheme 3

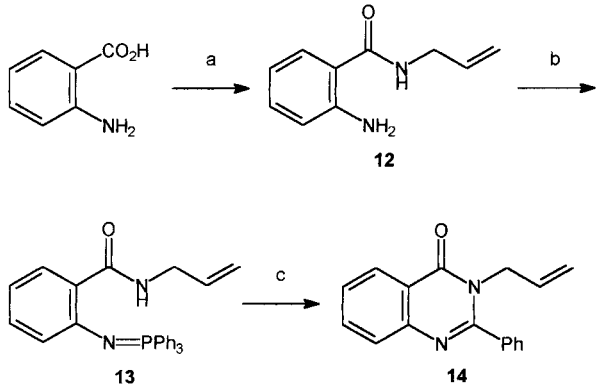


Reagents and conditions: (a) CH_2=$CHCH_2NH_2$/DEPC/Et_3N/DME, 0 °C; then 1 h at r.t. (91%); (b) Ph_3P/hexachloroethane/Et_3N/benzene, reflux, 2 h (77%); (c) PhCOCl/Et_3N/toluene, reflux, 2 h (54%)

Scheme 4

pyrimidines **10** was difficult to carry out by the present method.

Finally, we investigated the synthesis of 4(3*H*)-quinazolinone derivatives by the same methodology as follows. The iminophosphorane having a secondary amide function **13** prepared from anthranilic acid in two steps was treated with benzoyl chloride similarly to afford 4(3*H*)-quinazolinone **14** in 54% yield (Scheme 5). This compound was easily purified by silica gel column chromatography. This method provides a complement to syntheses of 4(3*H*)-quinazolinones by the intramolecular aza-Wittig version[21] and the intermolecular aza-Wittig reaction with isocyanates.[22]



Reagents and conditions: (a) CH_2=$CHCH_2NH_2$/DEPC/Et_3N/DME, 0 °C, then 1 h at r.t. (91%); (b) Ph_3P/hexachloroethane/Et_3N/benzene, reflux, 2 h (77%); (c) PhCOCl/Et_3N/toluene, reflux, 2 h (54%)

Scheme 5

In conclusion, this methodology by the intermolecular aza-Wittig reaction with acid chloride followed by heterocyclization provided a facile and efficient synthesis of 4(3*H*)-pyrido[2,3-*d*]pyrimidinones and 4(3*H*)-quinazolinones via imidoyl chloride intermediates derived from *N*-pyridyliminophosphorane and *N*-phenyliminophosphorane derivatives, respectively.

TLC was performed on E. Merck Kieselgel 60F_{254} pre-coated silica gel plates (0.25 mm layer thickness). Melting points were determined with a Yanagimoto micro-melting-point hot stage apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 or 500 spectrometer at 200 or 500 and 50 or 125 MHz, respectively, for samples in $CDCl_3$ or DMSO-d_6 solution with TMS as internal standard. Chemical shifts were reported in parts per million (δ). IR were recorded on a JASCO FT/IR 5300 spectrophotometer. MS and HRMS were recorded on a JEOL JMS-AX 505 HA spectrometer (EI and CI, 70eV). Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. Flash chromatography was performed with a silica gel column (Fuji Davison BW-300 or Fuji Silysia Chemical Ltd. Chromatorex® NH-DM-1020) eluting with mixed solvents [EtOAc (A), hexane (H)].
Benzene and toluene were stored over Na. All reactions were carried out under N_2. 2-Aminonicotinic acid **(1)** was purchased from Tokyo Kasei Co., Ltd. This reagent was used without further purification.

Allyl 2-Aminonicotinamide (2a); **Typical Procedure:**
To a suspension of **1** (138 mg, 1.00 mmol) in anhyd 1,2-dimethoxyethane (DME) (10.0 mL) was added dropwise DEPC (93%, 0.165 mL, 1.00 mmol) and Et_3N (0.140 mL, 1.00 mmol), respectively at 0 °C. The resultant solution was stirred at 0 °C for 1 h and at 40 °C for 1 h under N_2. The mixture was diluted with EtOAc (100 mL) and washed successively with H_2O (10 mL), satd aq $NaHCO_3$ solution (10 mL), H_2O (10 mL) and brine (10 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to afford the crude product, which was purified by silica gel column chromatography using EtOAc and hexane (1:1 → 2:1, v/v) as eluent and subsequently recrystallized from a mixture of EtOAc and hexane to give the secondary amide derivative **2a**; white needles (80.8 mg, 0.46 mmol, 46%).

The other secondary amides **2b–e** and the primary amide derivative **6** were also obtained by a similar method (see, Table 1 and Scheme 3). Also, the secondary amide derivative **12** was prepared by the above method (Scheme 5). The spectral data of **2a–e** are given in Tables 1–3.

2-Aminonicotinamide **(6)**: yield 46 %; R_f 0.22 (EtOAc); white solid; mp 199–202 °C.
IR (KBr): ν = 3463, 3351, 3275, 3167, 1672, 1622, 1578, 1562, 1453, 1410, 1252, 770, 754, 642 cm^{-1}.
^{1}H NMR (DMSO-d_6, 200 MHz): δ = 6.56 (1H, dd, J = 7.7, 4.7 Hz, H-5), 7.17 (2H, br s, NH_2), 7.31 (1H, br, $CONH_2$), 7.93 (1H + 1H, dd + br, J = 7.7, 1.7 Hz, H-4 + $CONH_2$), 8.07 (1H, dd, J = 4.8, 1.8 Hz, H-6).
^{13}C NMR (DMSO-d_6, 50 MHz): δ = 109.02 (C-3), 111.54 (C-5), 137.45 (C-4), 151.95 (C-6), 159.63 (C-2), 170.38 ($CONH_2$).
MS (EI): *m/z* (%) = 138 (6, M^++1), 137 (100, M^+), 121 (11), 120 (20), 94 (17), 93 (30), 92 (11), 84 (12), 67 (3), 66 (25), 65 (4).
HRMS: *m/z* calcd for $C_6H_7N_3O$ 137.0589, found 137.0587.

Allyl Anthranilic Carboxamide **(12)**: yield 91%; R_f 0.35 (EtOAc/hexane, 1:2); white solid; mp 83–84 °C.
IR (KBr): ν = 3422, 3297, 1620, 1588, 1530, 1302, 1262, 1157, 993, 930, 750 cm^{-1}.
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.04 (2H, tt, J = 5.7, 1.6 Hz, NCH_2CH=CH_2), 5.18 [1H, dq, J = 10.2, 1.4 Hz, CH=CH_2 (*cis*)], 5.26 [1H, dq, J = 17.2, 1.6 Hz, CH=CH_2 (*trans*)], 5.52 (2H, br s, NH_2), 5.94 (1H, ddt, J = 17.2, 10.2, 5.6 Hz, CH_2CH=CH_2), 6.16–6.17 (1H, br, CONH), 6.61–6.71 (2H, m, C_6H_4), 7.21 (1H, ddd, J = 8.2, 7.2, 1.6 Hz, C_6H_4), 7.34 (1H, dd, J = 7.8, 1.6 Hz, C_6H_4).
^{13}C NMR ($CDCl_3$, 50 MHz): δ = 42.14, 116.25, 116.84, 116.93, 117.68, 127.44, 132.73, 134.67, 149.21, 169.65.
MS (EI): *m/z* (%) = 177 (8, M^++1), 176 (72, M^+), 130 (3), 121 (11), 120 (100), 119 (33), 94 (3), 65 (28), 64 (3).
HRMS: *m/z* calcd for $C_{10}H_{12}N_2O$ 176.0950, found 176.0946.

Allyl 2-(Triphenylphosphoranylideneamino)nicotinamide (3a); Typical Procedure:
To a stirred mixture of **2a** (102 mg, 0.57 mmol), hexachloroethane (134 mg, 0.57 mmol, 1.0 equiv) and Ph_3P (150 mg, 0.57 mmol, 1.0 equiv) in anhyd benzene (5.0 mL) was added dropwise Et_3N (0.16 mL, 1.15 mmol, 2.0 equiv). The resultant solution was heated at reflux for 2 h. After cooling, the mixture was filtered under reduced pressure in order to remove the precipitates and the filtrate was evaporated under reduced pressure to give a solid residue, which was purified on a silica gel column using EtOAc and hexane (1:2 → 1:1, v/v) as eluent to afford **3a** (238 mg, 0.54 mmol, 95%).
The other iminophosphorane derivatives **3b–e** were also obtained by a similar method (Table 2). The synthesis of **7** and the preparation of nitrile derivatives **8** and **9** were carried out by a similar method (Scheme 3). Also, the iminophosphorane derivative **13** was synthesized by the above method (Scheme 5). The spectral data of **3a–e** are assembled in Tables 4–6.

2-(Triphenylphosphoranylidene)aminonicotinamide **(7)**: yield 32%; R_f 0.12 (hexane/EtOAc, 1:1); white solid; mp 258–261 °C.
IR (KBr): ν = 3218, 1657, 1578, 1455, 1421, 1308, 1244, 1112, 997, 718, 692 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.90 (1H, d, J = 5.0 Hz, $CONH_2$), 6.60 (1H, dd, J = 7.6, 4.8 Hz, H-5), 7.40–7.82 (15H, m, C_6H_5), 7.87 (1H, dd, J = 4.3, 2.1 Hz, H-4), 8.40 (1H, ddd, J = 7.6, 2.8, 2.2 Hz, H-6), 11.02 (1H, d, J = 2.6 Hz, $CONH_2$).
^{13}C NMR ($CDCl_3$, 50 MHz): δ = 113.47 (C-5), 118.18 (d, J = 19.0 Hz, C-3), 128.89 (d, J = 12.4 Hz, C'-3), 129.71 (d, J = 101.0 Hz, C'-1), 132.73 (C'-4 coupling constant could not be detected because the other peak was concealed by Ph_3P=O), 133.43 (d, J = 9.6 Hz, C'-2), 139.96 (d, J = 2.8 Hz, C-4), 150.12 (C-6), 162.02 (d, J = 7.3 Hz, C-2), 169.68 ($CONH_2$).
MS (EI): m/z (%) = 398 (19, M^++1), 397 (100, M^+), 396 (17), 379 (18), 378 (7), 353 (18), 320 (15), 260 (9), 183 (37).
MS (CI): m/z = 397 (MH^+).
HRMS: m/z calcd for $C_{24}H_{20}N_3OP$ 397.1344, found 397.1335.

2-(Triphenylphosphoranylidene)aminonicotinonitrile **(8)**: yield 22%; R_f 0.74 (hexane/EtOAc, 1:1); pale yellow solid; mp 229–231°C.
IR (KBr): ν = 3435, 2214, 1580, 1549, 1431, 1342, 1256, 1113, 1014, 719, 692 cm^{-1}.
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.44 (1H, dd, J = 7.5, 4.9 Hz, H-5), 7.40–7.59 (9H, m, C_6H_5), 7.63 (1H, ddd, J = 7.5, 2.6, 1.9 Hz, H-4), 7.81–7.95 (1H + 6H, m, H-6 + C_6H_5).
^{13}C NMR ($CDCl_3$, 50 MHz): δ = 101.03 (d, J = 25.3 Hz, CN), 111.62 (C-5), 119.86 (C-3), 128.81 (d, J = 12.5 Hz, C'-3), 129.49 (d, J = 100.6 Hz, C'-1), 132.29 (d, J = 2.9 Hz, C'-4), 133.60 (d, J = 9.9 Hz, C'-2), 141.88 (d, J = 3.7 Hz, C-4), 151.73 (C-6), 165.23 (d, J = 5.1 Hz, C-2).
MS (EI): m/z (%) = 380 (18, M^++1), 379 (79, M^+), 378 (100), 353 (9), 302 (9), 300 (3), 261 (4), 260 (18), 259 (4), 224 (3), 190 (6), 185 (4), 184 (3), 183 (29).
HRMS: m/z calcd for $C_{24}H_{18}N_3P$ 379.1238, found 379.1242.

2-Aminonicotinonitrile **(9)**: yield 10%; R_f 0.37 (hexane/EtOAc, 1:1); white solid; mp 103–106°C.
IR (KBr): ν = 3423, 3329, 3206, 2216, 1664, 1639, 1593, 1563, 1492, 1249, 762 cm^{-1}.
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.28 (2H, br, NH_2), 6.72 (1H, dd, J = 7.6, 5.0 Hz, H-5), 7.71 (1H, dd, J = 7.6, 1.8 Hz, H-4), 8.26 (1H, dd, J = 5.0, 1.8 Hz, H-6).
^{13}C NMR ($CDCl_3$, 50 MHz): δ = 91.64 (CN), 113.80 (C-5), 116.84 (C-3), 141.84 (C-4), 153.34 (C-6), 159.75 (C-2).
MS (EI): m/z (%) = 120 (6 %, M^++1), 119 (100, M^+), 118 (3), 93 (3), 92 (59), 91 (3), 84 (4), 66 (5), 65 (4), 64 (4).
HRMS: m/z calcd for $C_6H_5N_3$ 119.0483, found 119.0486.

Allyl 2-(Triphenylphosphoranylidene)aminobenzoic Carboxamide (13): yield 77%; R_f 0.12 (EtOAc/hexane, 1:2); pale yellow solid; mp 213–215°C.
IR (KBr): ν = 3019, 1631, 1590, 1533, 1468, 1437, 1335, 1269, 1110, 1013, 997, 758, 722, 693 cm^{-1}.
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.08 (2H, tt, J = 5.7, 1.6 Hz, $NCH_2CH{=}CH_2$), 4.98 [1H, dq, J = 10.0, 1.6 Hz, $CH{=}CH_2$ (*cis*)], 5.14 [1H, dq, J = 17.2, 1.8 Hz, $CH{=}CH_2$ (*trans*)], 5.86 (1H, ddt, J = 17.0, 10.2, 5.6 Hz, $CH_2CH{=}CH_2$), 6.45 (1H, dt, J = 8.0, 1.2 Hz, C_6H_4), 6.75 (1H, td, J = 7.5, 1.2 Hz, C_6H_4), 6.90 (1H, ddd, J = 8.0, 7.2, 2.0 Hz, C_6H_4), 7.43–7.59 (9H, m, C_6H_5), 7.61–7.75 (6H, m, C_6H_5), 8.30 (1H, dd, J = 7.8, 2.2 Hz, C_6H_4), 11.40 (1H, br t, J = 5.6 Hz, $CONHCH_2$).
^{13}C NMR ($CDCl_3$, 50 MHz): δ = 42.18, 115.55, 117.99, 122.92 (d, J = 12.0 Hz), 125.35 (d, J = 20.4 Hz), 129.36 (d, J = 12.2 Hz), 129.90 (d, J = 100.0 Hz), 131.13, 131.95 (d, J = 2.5 Hz), 132.68 (d, J = 2.8 Hz), 132.89 (d, J = 9.7 Hz), 136.00, 150.32 (d, J = 3.2 Hz), 168.34 (d, J = 1.8 Hz).
MS (EI): m/z (%) = 437 (27, M^++1), 436 (91, M^+), 435 (13), 382 (7), 380 (82), 378 (7), 353 (19), 352 (100), 262 (13), 201 (19), 197 (7), 191 (7), 183 (33).
HRMS: m/z calcd for $C_{28}H_{25}N_2OP$ 436.1705, found 436.1709.

3-Allyl-2-phenyl-4(3*H*)-pyrido[2,3-*d*]pyrimidinone (5a); Typical Procedure:
To a stirred solution of **3a** (263 mg, 0.60 mmol) in anhyd toluene (5.0 mL) was added dropwise benzoyl chloride (0.14 mL, 1.20 mmol, 2.0 equiv) and Et_3N (0.17 mL, 1.20 mmol, 2.0 equiv) and the mixture was refluxed for 2 h. After completion of the reaction (monitored by TLC), the mixture was diluted with H_2O (20 mL) and extracted with $CHCl_3$ (2 × 50 mL). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel using EtOAc and hexane (1:2, v/v) as eluent, Chromatorex® column chromatography using EtOAc and hexane (1:10, v/v) as eluent and, subsequently, recrystallization from EtOAc and hexane to give **5a** (136 mg, 0.52 mmol, 86 %). The other pyrido[2,3-*d*]pyrimidine derivatives **5b–j** were synthesized following the same procedure as above (Tables 7–9). Furthermore, the preparation of nitrile derivative **8** and the synthesis of 4(3*H*)-quinazolinone derivative **14** were carried out by the same method (Scheme 4 and Scheme 5, respectively). The spectral data of **5a–j** are given in Tables 7–9.

X-ray Crystal Structure Analysis of 5b:
A pale prism crystal of $C_{16}H_{12}N_4O_3$ having approximate dimensions of 0.180 × 0.980 × 1.000 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC5S diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71069 Å) and a 2 KW stationary anode generator. Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 24 carefully centered reflections in range 37.38° < 2θ < 39.95° corresponded to an orthorhombic cell with dimensions: a = 27.380 (4) Å, b = 13.579 (3) Å, c = 7.871 (4) Å, V = 2927 (3) $Å^3$, α = 90°, β = 90°, γ = 90°. For Z = 8 and F. W. = 308.30, the calculated density is 1.399 g/cm^3. Based on the systematic absences of (0kl: k ≠ 2n, h0l: l ≠ 2n, hk0: h ≠ 2n), and the successful solution and refinement of the structure, the space group was determined to be Pbca (#61). The data were collected at a temperature of 23 ± 1°C using the ω-2θ scan technique to a maximum 2θ value of 55.0°. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.20° with a take-off angle of 6.0°. Scans of (0.97 + 0.30 tan θ)° were made at a speed of 16.0°/min. (in omega). The weak reflections (I < 10.0σ(I)) were rescanned (maximum of 2 rescans) and the counts were accumulated to assure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 40 cm. A total of 3834 was collected. The intensities of three representative reflections which were measured after every 150 reflections remained constant throughout data collection indicating crystal and electronic stability (no decay correction was applied). The linear absorption coefficient for Mo Kα is 0.9 cm^{-1}. Azimuthal scans of several reflections indicated no need for an absorption correction. The data were corrected for Lorentz and polarization effects. A correction for secondary extinction was applied (coefficient = 0.19934 × 10^{-5}). The structure was solved by direct method.[23] The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1543 observed reflections (I > 2.00σ(I)) and 257 variable parameters and converged (largest parameter shift was 0.01 times its esd) with unweighed and weighed agreement factors of: R = 0.057 and R_w = 0.057. The standard deviation of an observation of unit weight was 1.69. The weighing scheme was based on counting statistics and included a factor (p = 0.03, p: p-factor) to downweight the intense reflections. Plots of $\Sigma w(|Fo|-|Fc|)^2$ versus |Fo|, reflection order in data collection, sinθ/γ, and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.24 and 0.27 $e^-/Å^3$, respectively. Natural atom scattering factors were taken from Cromer and Waber.[24] Anomalous dispersion effects were

included in Fcalc;[25] the value for Δf' and Δf'' were those of Cromer.[26] All calculations were performed using the TEXSAN[27] crystallographic software package of Molecular Structure Corporation. Atomic coordinate bond lengths and angle, torsion angle and thermal parameters of **5b** have been deposited with the Cambridge Crystallographic Data Centre.

3-Allyl-2-phenyl-4(3H)-quinazolinone **(14)**: yield 54 %; R_f 0.44 (A:H 1:2); white solid; mp 78–79 °C.

IR (KBr): ν = 3065, 1680, 1605, 1588, 1566, 1472, 1427, 1375, 1333, 1252, 772, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.64 (2H, dt, J = 5.2, 1.7 Hz, $NCH_2CH=CH_2$), 4.94 [1H, dq, J = 17.2, 1.5 Hz, $CH=CH_2$ (*trans*)], 5.17 [1H, dq, J = 10.4, 1.3 Hz, $CH=CH_2$ (*cis*)], 5.88 (1H, ddt, J = 17.2, 10.2, 5.2 Hz, $CH_2CH=CH_2$), 7.44–7.59 (1H + 5H, m, C_6H_4 + C_6H_5), 7.75–7.79 (2H, m, C_6H_4), 8.35 (1H, ddd, J = 8.0, 1.3, 1.0 Hz, C_6H_4).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 48.38, 117.68, 120.98, 127.04, 127.26, 127.71, 128.12, 128.79, 130.16, 132.37, 134.64, 135.42, 147.43, 156.45, 162.16.

MS (EI): *m/z* (%) = 263 (10 M^++1), 262 (61, M^+), 261 (100), 248 (6), 247 (43), 245 (4), 233 (4), 208 (3), 205 (3), 185 (4), 179 (4), 77 (4).

HRMS: *m/z* calcd for $C_{17}H_{14}N_2O$ 262.1106, found 262.1103.

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