

# One-pot Synthesis of Novel (2-Oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine Derivatives from Methyl 2-(*N*-Triphenylphosphoranylidene)aminonicotinate, Aryl Isocyanates and Primary Amines: Sequential Aza-Wittig / Cycloaddition / Ring-Transformation Reactions

Tomohiro Okawa,<sup>a</sup> Naoto Osakada,<sup>a</sup> Shoji Eguchi,<sup>a,\*</sup> and Akikazu Kakehi<sup>b</sup>

<sup>a</sup> Department of Molecular Design and Engineering, Graduate School of Engineering,  
Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-01, Japan

E-mail: eguchi@apchem.nagoya-u.ac.jp

<sup>b</sup> Department of Chemistry and Material Engineering, Faculty of Engineering,  
Shinshu University, Wakasato, Nagano 380, Japan

**Abstract** : (2-Oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** were obtained unexpectedly, instead of pyrido[2,3-*d*]pyrimidine derivatives, by the intermolecular aza-Wittig reaction of methyl 2-(*N*-triphenylphosphoranylidene)aminonicotinate **3** with aryl isocyanates followed by attempted heterocyclization by use of *prim*-amines. A novel sequential aza-Wittig / cycloaddition / ring-transformation mechanism for the formation of **10** has been reported based on the isolation and characterization of the key intermediates, pyrido[1,2-*a*][1,3,5]triazines **15** formed *via* [4+2] cycloaddition of the initially produced carbodiimide with aryl isocyanates.

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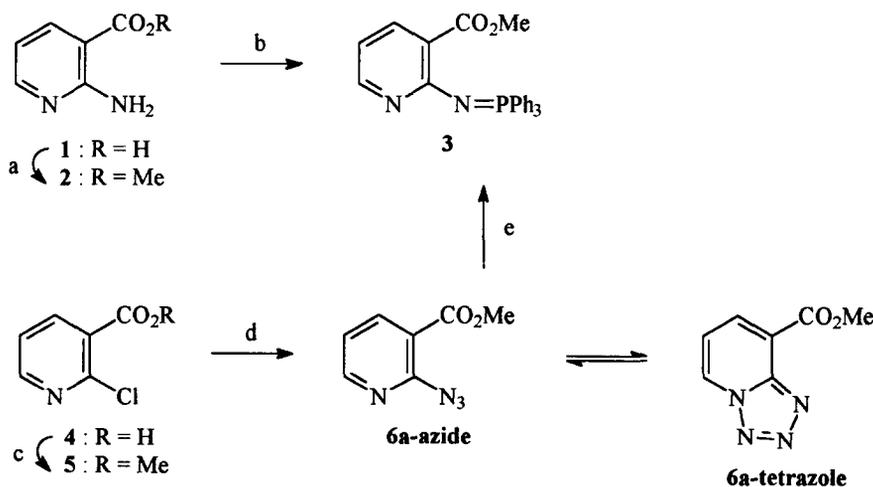
## INTRODUCTION

Over the past decade, the aza-Wittig reaction has been one of the most useful methodologies<sup>1-4</sup> drawing increased attention for its utility in the formation of C=N bonds (imine, amidine and guanidine, *etc.*) and heterocumulene bonds (carbodiimide, *etc.*), and in synthesis of nitrogen heterocyclic compounds. We and other workers have recently demonstrated that the intramolecular aza-Wittig reaction is a powerful tool for synthesis of 5-8 membered heterocycles<sup>2,5,6</sup> including natural products such as DC-81,<sup>7,8</sup> *l*-vasicinone,<sup>9</sup> (-)-benzomalvin A<sup>10</sup> and (+)-fumiquinazoline G<sup>11</sup> *etc.* On the other hand, the intermolecular aza-Wittig reaction followed by electrocyclization, cycloaddition or heterocyclization, *i.e.*, the tandem aza-Wittig methodology has been utilized for synthesis of many important heterocyclic compounds by Molina,<sup>3</sup> Wamhoff,<sup>4</sup> Quintela,<sup>12</sup> Saito<sup>13</sup> and Noguchi<sup>14,15</sup> *et al.* Besides, (-)-pancracine and (-)-coccinice were synthesized by use of the intermolecular aza-Wittig reaction.<sup>16</sup> Furthermore, *N*-vinyliminophosphorane have been studied by Nitta<sup>17</sup> and Palacios<sup>18</sup> *et al.* We have been interested in the preparation and the reactivity of *N*-heteroaryliminophosphoranes and the corresponding carbodiimides because these species seem to have been less studied, notwithstanding their promising role as building blocks for synthesis of heterocyclic compounds. For example, we have reported facile

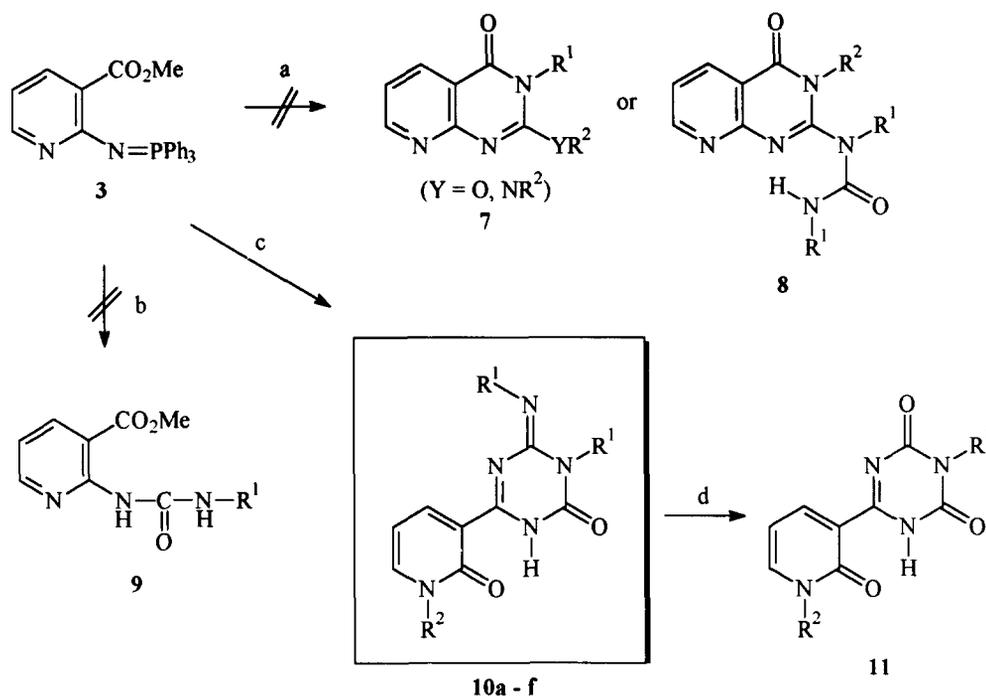
synthesis of 4(3*H*)-pteridinones *via* the intermolecular aza-Wittig reaction and heterocyclization,<sup>19-21</sup> and pyrazino[2,3-*e*][1,4]diazepin-5-ones *via* the intramolecular aza-Wittig reaction.<sup>22</sup> According to our methods for synthesis of 4(3*H*)-pteridine derivatives, we investigated the synthesis of pyrido[2,3-*d*]pyrimidies or 5-deaza analogues of pteridine derivatives. Pyrido[2,3-*d*]pyrimidine derivatives are known to the fundamental skeleton of 5,10-dideaza-5,6,7,8-tetrahydrofolic acid (DDATHF)<sup>23</sup> and this analogs which are deaza derivatives of methotrexate (MTX). MTX and DDATHF have been shown to possess the antineoplastic and immunosuppressive activities, and the establishment of the facile and regioselective construction of these fundamental heterocyclic skeletons is very important. However, we unexpectedly obtained (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** in stead of pyrido[2,3-*d*]pyrimidine derivatives **7** or **8** by our methodology. As a part of our continued research programs on the intermolecular aza-Wittig reaction and the reactivity of carbodiimides, we wish to report here a novel sequential reaction of methyl 2-(*N*-triphenylphosphoranylidene)aminonicotinate **3** with aryl isocyanate and then *pri*-amine to yield (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10**, and a reasonable mechanism of their formation.

## RESULTS AND DISCUSSION

At first, we investigated the preparation for the iminophosphorane derivatives. Methyl 2-(*N*-triphenylphosphoranylidene)aminonicotinate **3** could be derived from the corresponding azide derivative **6a** *via* the Staudinger reaction but this route was inefficient due to longer reaction steps (Scheme 1, **4** → **5** → **6a** → **3**, the overall yield was 36 %). Thus, we adopted the Appel's method<sup>24</sup> for the direct conversion of amine derivative **2** to iminophosphorane **3**. Methyl 2-aminonicotinate **2** was conveniently prepared from 2-aminonicotinic acid **1** by



**Scheme 1** Reagents and conditions : (a) DMC, Et<sub>3</sub>N, MeOH, 0 °C, 1 h → rt, 1 h, 84 %; (b) PPh<sub>3</sub>, C<sub>2</sub>Cl<sub>6</sub>, Et<sub>3</sub>N, benzene, reflux, 3 h, 99 %; (c) SOCl<sub>2</sub>, reflux, 2 h, then MeOH, Et<sub>3</sub>N, 81 %; (d) NaN<sub>3</sub>, DMSO, 80 °C, 2 h, 45 %; (e) PPh<sub>3</sub>, benzene, reflux, 2 h, 99 %.  
DMC = 2-chloro-1,3-dimethylimidazolinium chloride.



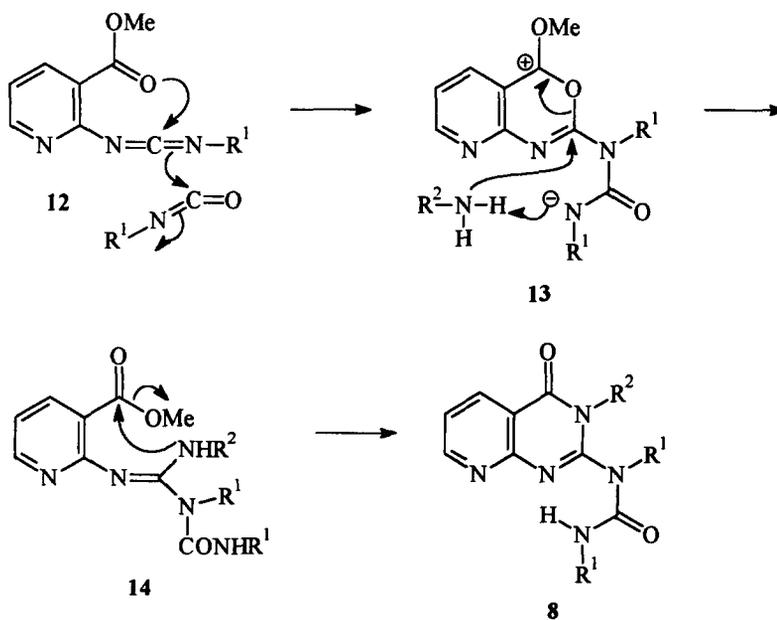
**Scheme 2** Reagents and conditions : (a)  $R^1NCO$ , benzene, reflux, 2 h then  $R^2OH$  or  $R^2NH$ , reflux, 2 h; (b)  $R^1NCO$ , benzene, reflux, 2 h then  $H_2O$ , rt, 2 h; (c)  $R^1NCO$ , benzene, reflux, 2 h then  $R^2NH_2$ , reflux, 2 h; (d) catalyzed HCl in methanol, 50 °C, 48 h ( $R^1 = Ph$ ,  $R^2 = i-Pr$ ).

esterification with DMC (2-chloro-1,3-dimethylimidazolium chloride).<sup>25</sup> The ester derivative **2** could not be efficiently obtained by standard acid-catalyzed method or using condensation reagents such as DCC and DEPC (diethylphosphoryl cyanide).<sup>26</sup> The ester derivative **2** was converted to the iminophosphorane derivative **3** with a  $PPh_3-C_2Cl_6-Et_3N$  reagent system by the Appel's method (Scheme 1, the overall yield was 83 %).

In the next step, we investigated the intermolecular aza-Wittig reaction and the reactivity of the corresponding carbodiimide intermediate. The intermolecular aza-Wittig reaction of iminophosphorane **3** with phenyl isocyanate (3.5 equiv.) in dry benzene at room temperature for 12 h, followed by the reaction with allylamine (an excess to consume the surplus isocyanate) at 80 °C for 3 h afforded a novel heterocyclic product, (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivative **10a** in 75 % yield. The structure of this compound could not be completely elucidated by IR,  $^1H$  NMR,  $^{13}C$  NMR and mass spectroscopic analyses and was established by X-ray crystallographic analysis (*vide infra*). However, the expected pyrido[2,3-*d*]pyrimidine derivative **7** or the related derivative **8** having two phenyl isocyanate moieties were not produced at all (Scheme 2, Table 1). In the above reaction, phenyl isothiocyanate in stead of phenyl isocyanate did not show any reactivity for the iminophosphorane derivative with pyridine ring even at reflux in xylene. The reaction with other aryl isocyanates and *pri*-amines gave the same skeletal compounds **10b-f** in the same way. Before addition of *pri*-

**Table 1** The synthesis of 6-[1-alkyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-aryl-4-arylimino-3,4-dihydro-1,3,5-triazin-2(1*H*)-ones **10**.

Entry	R <sup>1</sup>	Equiv. <sup>a</sup>	R <sup>2</sup>	Product	Yield (%) <sup>b</sup>
1	C <sub>6</sub> H <sub>5</sub>	3.5	allyl	<b>10a</b>	75
2	C <sub>6</sub> H <sub>5</sub>	1.0 <sup>c</sup>	allyl	<b>10a</b>	28
3	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	3.5	allyl	<b>10b</b>	74
4	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	1.0 <sup>c</sup>	allyl	<b>10b</b>	21
5	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	3.5	allyl	<b>10c</b>	80
6	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	1.0 <sup>c</sup>	allyl	<b>10c</b>	34
7	C <sub>6</sub> H <sub>5</sub>	3.5	isopropyl	<b>10d</b>	58
8	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	3.5	isopropyl	<b>10e</b>	64
9	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	3.5	isopropyl	<b>10f</b>	69

<sup>a</sup> Equivalent of R<sup>1</sup>NCO.<sup>b</sup> Isolated yield.<sup>c</sup> A little less than 1.0 equiv.**Scheme 3**

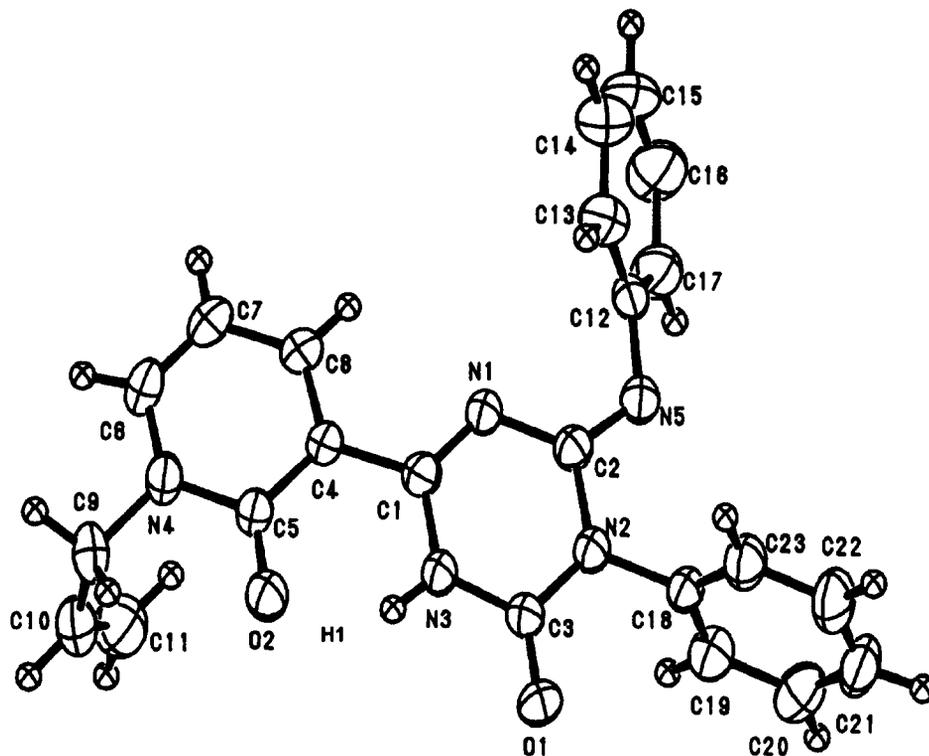
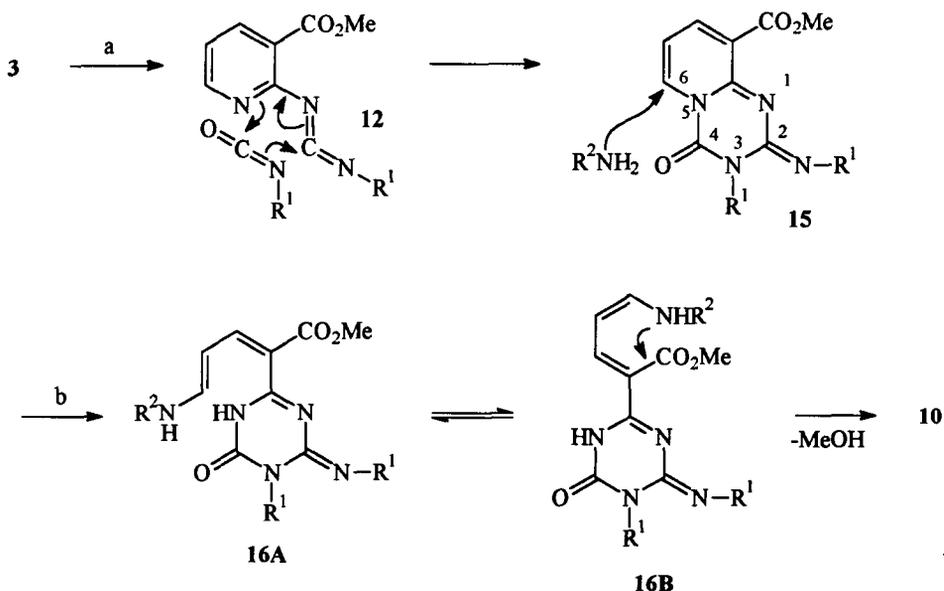


Fig. 1 ORTEP drawing of 6-[1-allyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-phenyl-4-phenylimino-3,4-dihydro-1,3,5-triazin-2(1*H*)-one **10a**

amine, the corresponding carbodiimide intermediate **12** was neither detectable by IR nor isolable even in the reaction with use of less than 1.0 equiv. of isocyanate. Also, formation of urea derivative **9** could not be confirmed by the addition of water to the carbodiimide intermediate, affording only complex mixture (Scheme 2). The addition of alcohols or *sec*-amines instead of *pri*-amines to the reactant of iminophosphorane **3** and phenyl isocyanate was examined in order to obtain new heterocyclic compounds, pyrido[2,3-*d*]pyrimidine derivatives **7**. However, the expected cyclic products were not obtained at all by the addition of alcohols or *sec*-amines affording intractable complex mixtures, and the compounds **10** were obtained only by the addition of *pri*-amines. The spectroscopic data, especially mass spectroscopic analysis, indicated the obtained compounds were produced from the iminophosphorane derivative **3**, isocyanates (two molecules) and *pri*-amine. According to the previous synthesis of 4(3*H*)-pteridinones,<sup>19,20</sup> pyrido[2,3-*d*]pyrimidine derivatives **7** were assumed to be the expected products (Scheme 2). Moreover, according to Wamhoff's<sup>27</sup> and Molina's reports,<sup>28</sup> pyrido[2,3-*d*]pyrimidine derivative **8** having two phenyl isocyanate moieties was expected to be produced *via* the mechanism shown in Scheme 3. However, various spectroscopic data (IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and mass spectroscopic analyses) did not fully compatible with the assumed structure. Especially, the distinction between pyrido[2,3-*d*]pyrimidine **8** and (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine **10** was difficult. Additionally, the obtained heterocyclic

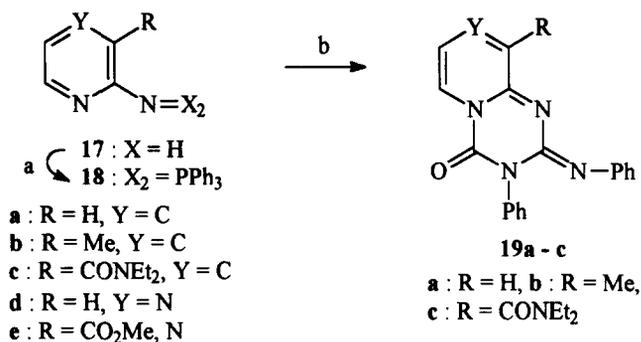
compound ( $R^1 = \text{Ph}$ ,  $R^2 = i\text{-Pr}$ ) was hydrolyzed by HCl in methanol into a new heterocyclic compound whose molecular weight was 324. If **8** was obtained, this molecular weight was suggestive that the inconceivable carbamic acid derivative must be formed (not shown). Thus, after the structure of **10** was determined, **11** was reasonably assigned as the hydrolysis product (yield 57 %, Scheme 2). Finally, X-ray crystallographic analysis of crystallized sample established the structure as **10a** 1,3,5-triazine derivative having a 2(1*H*)-pyridone ring (Fig. 1). Tables 4 and 5 summarize the main geometrical characteristics (bond lengths and torsion angles, respectively) of the molecule **10a** according to the numbering scheme shown in Fig. 1. The bond lengths indicated partial double (imine) bond character at the N1–C1 (1.294 Å) and N5–C2 (1.268 Å) bonds. Furthermore, N2–C2 (1.421 Å), N2–C18 (1.459 Å) and N5–C12 (1.418 Å) bonds were indicated as C–N single bonds. The O2...H1 distance (1.88 Å) is indicative of intramolecular hydrogen bonding. The configuration of C2–N5 imine bond was characterized as anti form by the torsion angle around C2–N5 due to the steric repulsion between two phenyl ring. The conformation of [1,3,5]triazine ring and 2(1*H*)-pyridone ring was decided by the torsion angle, so these rings were quite planar due to at least the O2...H1 intramolecular hydrogen bonding as one of the factors. As for purification of **10**, though the spots of (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** and inevitable by-product triphenylphosphine *P*-oxide on TLC (Merck) were entirely same, the use of Chromatorex® was effective for separation of these compounds (see, experimental section).

We then undertook to elucidate the mechanism of formation of (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** as follows. Even when a slightly less than 1.0 equiv. of aryl isocyanate was used in the intermolecular aza-Wittig reaction, **10** were obtained exclusively but in lower yields (21 ~ 34 %), however, pyrido[2,3-*d*]pyrimidine derivatives **7** and **8** were not obtained at all (Table 1, Entries 2, 4, 6). These facts

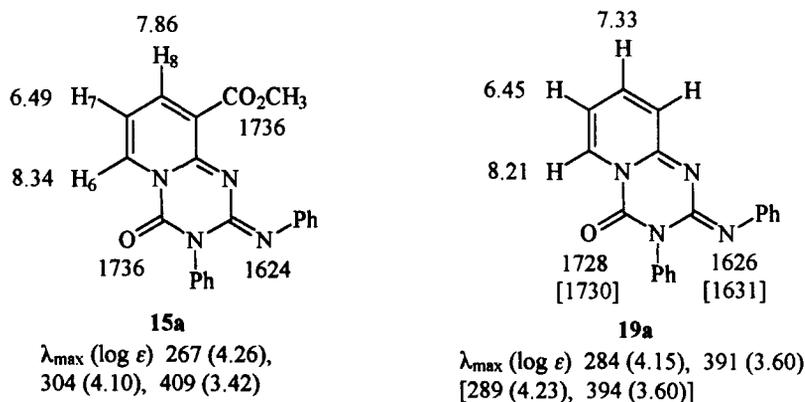


**Scheme 4** Reagents and conditions : (a)  $\text{R}^1\text{NCO}$ ; (b)  $\text{R}^2\text{NH}_2$ .

suggested that guanidine-type intermediates derivable from the corresponding carbodiimides and *pri*-amines were not produced. We propose the mechanism to produce (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazines **10** as explained in Scheme 4. First, iminophosphorane **3** was converted into the corresponding carbodiimides **12** by the intermolecular aza-Wittig reaction with aryl isocyanate and thus, produced **12** spontaneously reacted with the residual aryl isocyanates *via* the [4+2] heterocycloaddition between the N=C-N=C moiety of the carbodiimide intermediates **12** as 4 $\pi$  component and the C=N moiety of the isocyanates as 2 $\pi$  component to pyrido[1,2-*a*][1,3,5]triazine derivatives **15**. Additionally, because pyrido[2,3-*d*]pyrimidine derivatives **7** were not obtained by use of alcohols or *sec*-amines, the corresponding carbodiimide intermediates **12** should be highly reactive for the



**Scheme 5** Reagents and conditions: (a) PPh<sub>3</sub>, C<sub>2</sub>Cl<sub>6</sub>, Et<sub>3</sub>N, benzene, reflux, 3 h; (b) PhNCO, benzene, rt, 24 h.



**Fig. 2** Comparison of <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz,  $\delta$ ), <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz,  $\delta$ ), IR (KBr, cm<sup>-1</sup>) and UV (CH<sub>2</sub>Cl<sub>2</sub>, nm), data between **15a** and **19a**. Values in brackets are reported ones in ref. 29. In **15a**, C6: 139.76, C7: 110.96, C8: 129.01, C9: 124.47 and in **19a**, C6: 143.04, C7: 109.56, C8: 132.19, C9: 126.76. For other data, see Experimental section.

**Table 2** The synthesis of the iminophosphorane derivatives **18**.

Entry	R	Y	Product	Yield (%) <sup>a</sup>
1	H	C	<b>18a</b>	88
2	Me	C	<b>18b</b>	84
3	CONEt <sub>2</sub>	C	<b>18c</b>	83
4	H	N	<b>18d</b>	64
5	CO <sub>2</sub> Me	N	<b>18e</b>	99

<sup>a</sup> Isolated yield.**Table 3** The synthesis of 3-phenyl-2-phenyliminopyrido[1,2-*a*][1,3,5]triazin-4-ones **15a** and **19a - c**.

Entry	R	Product	Yield (%) <sup>a</sup>
1	CO <sub>2</sub> Me	<b>15a</b>	31
2	H	<b>19a</b>	41
3	Me	<b>19b</b>	33 <sup>b</sup>
4	CONEt <sub>2</sub>	<b>19c</b>	37

<sup>a</sup> Recrystallization yield.<sup>b</sup> This yield was determined by <sup>1</sup>H NMR because **19b** could not be separated from Ph<sub>3</sub>P=O.

cycloaddition. Subsequent nucleophilic addition of *pri*-amines to pyrido[1,2-*a*][1,3,5]triazine derivatives **15** at the 6-position resulted in the cleavage of the pyridine ring to **16A**, followed by the geometrical isomerization (*E, E* → *Z, Z*) to **16B** via a proton shift due to vinylogous amine. Finally, **16B** cyclized by the nucleophilic attack of the amino group to the ester group, affording (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** (Scheme 4). Heretofore, examples of [4+2] cycloaddition of *N*-heteroarylcarbodiimides have been quite rare. As the only case, Bödecker *et al.* reported [4+2] cycloaddition of *N*-phenyl-*N'*-2-pyridyl carbodiimide generated from *N*-(2-pyridyl)iminophosphorane and phenyl isocyanate, with phenyl isocyanate to give 3-phenyl-2-phenylimino-4(3*H*)-pyrido[1,2-*a*][1,3,5]triazinone.<sup>29</sup> In the paper, however, the spectroscopic data were not satisfactorily mentioned and the novel [4+2] cycloadducts, pyrido[1,2-*a*][1,3,5]triazine derivatives **15** and **19** were necessary to be elucidated in detail. In the present case, the corresponding [4+2] cycloadducts **15** as the key intermediates were difficult to isolate by chromatographic technique because of facile decomposition, however, these compounds could be isolable by repeated recrystallizations. Spectroscopic (IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and UV) comparison of pyrido[1,2-*a*][1,3,5]triazine derivative **15a** and the independently prepared pyrido[1,2-*a*][1,3,5]triazine derivative **19a** supported that these products have the same pyrido[1,2-*a*][1,3,5]triazine ring skeletons (Fig. 2).

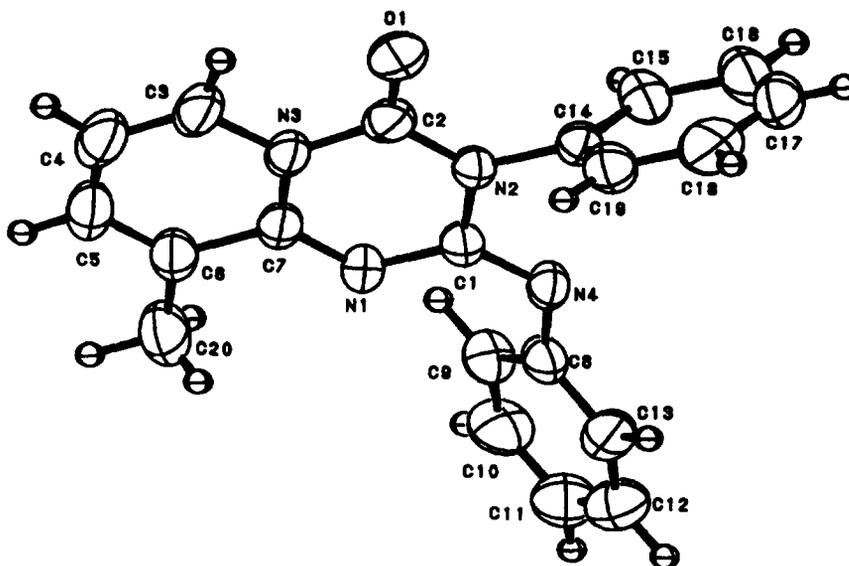
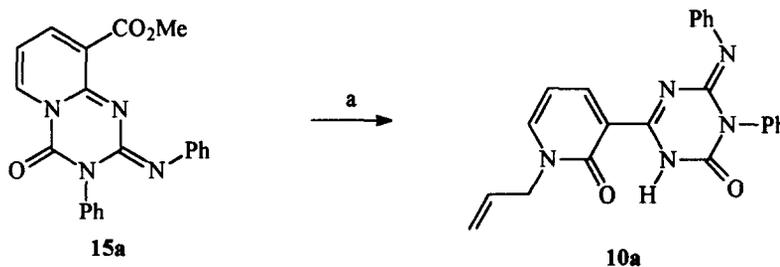
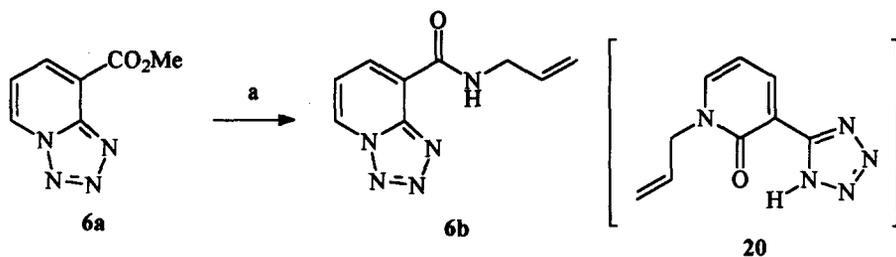


Fig. 3 ORTEP drawing of 9-Methyl-3-phenyl-2-phenylimino-2,3-dihydro-pyrido[1,2-*a*][1,3,5]triazin-4-one **19b**

We investigated to synthesize other [4+2] cycloadducts as an examination for the generalization. Amine derivatives **17** having pyridine or pyrazine ring were converted into the corresponding iminophosphoranes **18** by Appel's method (Scheme 5 and Table 2). These iminophosphorane derivatives **18a** - **18c** having other functional group (R = Me, CONEt<sub>2</sub>) underwent the [4+2] cycloaddition with phenyl isocyanate at room temperature (Scheme 5, Table 3). All of these pyrido[1,2-*a*][1,3,5]triazine derivatives **19** could be purified by only recrystallization but not by silica gel column chromatography. **19b** was established by X-ray crystallographic analysis (Fig. 3). This crystal consisted of pyrido[1,2-*a*][1,3,5]triazine derivative **19b** and triphenylphosphine *P*-oxide, whose ratio was 1:1. Tables 6 and 7 summarize the main geometrical characteristics (bond lengths, bond angles and torsion angles, respectively) of the molecule **19b** according to the numbering scheme shown in Fig. 3. The bond lengths indicated partial double (imine) bond character at the N1-C7 (1.305 Å) and N4-C1 (1.280 Å)



Scheme 6 Reagents and conditions : (a) allylamine, benzene, reflux, 3 h, 94 %.



**Scheme 7** Reagents and conditions : (a) allylamine, benzene, reflux, 3 h, the corresponding amide derivative **6b** was produced in 83 %.

bonds. Furthermore, N2–C1 (1.416 Å), N2–C14 (1.454 Å) and N4–C8 (1.418 Å) bonds were indicated as C–N single bonds. The configuration of C1–N4 imine bond was characterized as *trans* form by the torsion angle around C1–N4 due to the steric repulsion between two phenyl ring. The length of N1–C1 (1.365 Å) showed that presence of guanidine function and flexibility of isomerization for C=N double bond. Torsion angle of **19b** indicated that pyrido[1,2-*a*][1,3,5]triazine skeleton was approximately plane and one phenyl function and pyrido[1,2-*a*][1,3,5]triazine ring were almost perpendicular (C1–N2–C14–C15: 81.0°). Also, the other phenyl ring and pyrido[1,2-*a*][1,3,5]triazine ring were at an angle of about 45° (C1–N4–C8–C9: 47.2°). The corresponding [4+2] cycloadducts, pyrazino[1,2-*a*][1,3,5]triazine derivatives were not obtained from the iminophosphorane derivatives having pyrazine ring **18d**, **18e** in the same conditions. The nucleophilicity of nitrogen of pyridine is higher than that of nitrogen of pyrazine to make the difference of the reactivity between pyridine and pyrazine derivatives.<sup>30,31</sup> Furthermore, the isolated pyrido[1,2-*a*][1,3,5]triazine derivative **15a** could be converted into the corresponding (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivative **10a** by addition of allylamine (Scheme 6, yield 94 %) to confirm the proposed mechanism described in Scheme 4. In the above similar reaction, pyrido[1,2-*a*][1,3,5]triazine derivative **19a** was not reactive with allylamine. Additionally, in the substrate having unaromatized and fused pyridine skeleton, the subsequent pyridine ring cleavage and recyclization reaction such as pyrido[1,2-*a*][1,3,5]triazine derivatives **15** → (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** was scarcely known. However, fused tetrazole derivative **6a** was not converted into tetrazole derivative **20** but instead, the corresponding amide derivative **6b** was obtained (Scheme 7). In the present system, the initial [4+2] cycloadducts undergo a facile ring transformation with *pri*-amine, providing an unprecedented behavior and a novel route to (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives.

In summary, we found that iminophosphorane derivatives **3** was converted, in a one-pot process, to (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** *via* the [4+2] cycloaddition with aryl isocyanates, followed by ring cleavage of the pyridine moiety and recyclization to (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives **10** with *pri*-amines. The unusual chemical reactivity of *N*-heteroarylcarbodiimides and the intriguing ring-transformation rendered it an interesting heterocyclic system deserving of further works. Further studies on the reactivity of *N*-heteroaryl carbodiimides, their [4+2] cycloaddition and the novel ring transformation are in progress in our laboratories.

## EXPERIMENTAL SECTION

**General.** Thin layer chromatography (TLC) was performed on E. Merck Kieselgel 60F<sub>254</sub> 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. <sup>1</sup>H and <sup>13</sup>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<sub>3</sub> or DMSO-*d*<sub>6</sub> solution with Me<sub>4</sub>Si as internal standard. Chemical shifts were reported in parts per million (δ). Infrared spectra (IR) were recorded on a JASCO FT / IR 5300 spectrophotometer. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a JEOL JMS-AX 505 HA (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) eluted with mixed solvents [hexane (H), ethyl acetate (A)].

**Reagents and solvents.** Benzene was stored over Na. Alcohols or amines were stored over 3 Å molecular sieves. Isocyanates were dried over CaH<sub>2</sub>, distilled, and stored over 3 Å molecular sieves. All reactions were carried out under nitrogen. 2-Aminonicotinic acid **1**, 2-chloronicotinic acid **4**, 2-aminopyridine **17a** and methyl 3-aminopyrazine-2-carboxylate **17e** were purchased from Tokyo Kasei Co., Ltd. 2-Amino-3-picoline **17b** and aminopyrazine **17d** were purchased from Aldrich®. These reagents were used without further purification.

**Synthesis of methyl 2-aminonicotinate **2**** (see, step a of Scheme 1).

To a mixture of 2-aminonicotinic acid **1** (540 mg, 3.91 mmol) and DMC (963 mg, 5.70 mmol, 1.46 equiv.) in MeOH (10.0 mL) was added dropwise triethylamine (1154 mg, 11.4 mmol, 2.91 equiv.). The resultant mixture was stirred at room temperature for 1 h under nitrogen. The mixture was then evaporated under reduced pressure to afford a residue. The residue was purified on a silica-gel column chromatography using H-A (3:1, v/v) as an eluent to give the titled ester derivative **2** as a white solid (501 mg, 3.29 mmol, 84 %). *R*<sub>f</sub> = 0.49 (A:H 1:1); white solid; mp 76-79 °C; IR (KBr) 3439, 3277, 3150, 2955, 1698, 1632, 1570, 1453, 1298, 1250, 1111, 777, 509 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.22 (1H, dd, *J* = 4.8, 2.0 Hz, H-6), 8.12 (1H, dd, *J* = 7.7, 1.9 Hz, H-4), 6.62 (1H, dd, *J* = 7.8, 4.8 Hz, H-5), 6.8-6.2 (2H, br, NH<sub>2</sub>), 3.88 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 167.89 (CO<sub>2</sub>), 159.93 (C-2), 154.06 (C-6), 140.48 (C-4), 112.91 (C-5), 106.43 (C-3), 52.04 (OCH<sub>3</sub>); MS (EI) *m/z* (rel. intensity) (152.15) 153 (6 %, M+1), 152 (100, M), 121 (41), 120 (36), 94 (34), 93 (58), 92 (21), 66 (17), 65 (6); MS (CI) 153 (MH); Anal. Calcd for C<sub>7</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.35; H, 5.50; N, 18.11.

**Synthesis of methyl 2-(triphenylphosphoranylidene)aminonicotinate **3**** (see, step b of Scheme 1).

To a mixture of ester derivative **2** (77 mg, 0.51 mmol), triphenylphosphine (198 mg, 0.75 mmol, 1.5 equiv.) and hexachloroethane (179 mg, 0.76 mmol, 1.5 equiv.) in dry benzene (5.0 mL) was added dropwise triethylamine (153 mg, 1.51 mmol, 3.0 equiv.). The resultant mixture was heated at reflux for 3.5 h under nitrogen and the cooled mixture was filtered to remove the precipitates and evaporated under reduced pressure to afford a solid residue. The residue was purified on a silica-gel column chromatography using H-A (1:1, v/v) as an eluent to give the titled iminophosphorane derivative **3** as a pale yellow solid (205 mg, 0.50 mmol, 98 %). *R*<sub>f</sub> = 0.59 (A); pale yellow solid; mp 173-176 °C; IR (KBr) 3050, 1715, 1582, 1551, 1483, 1431, 1348, 1252, 1111, 1020, 768, 720, 694, 521 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.01-7.85 (2H + 6H, m, H-4 + H-6 + C<sub>6</sub>H<sub>5</sub>), 7.53-7.36 (9H, m, C<sub>6</sub>H<sub>5</sub>), 6.44 (1H, dd, *J* = 7.6, 4.8 Hz, H-5), 3.95 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 168.89 (CO<sub>2</sub>), 162.87 (d, *J* = 6.6 Hz, C-2), 151.14 (C-6), 140.23 (d, *J* = 3.2 Hz, C-4), 133.79 (d, *J* = 9.8 Hz, C-3), 131.88 (d, *J*

= 2.8 Hz, C-4'), 130.49 (d,  $J = 100.0$  Hz, C-1'), 128.60 (d,  $J = 10.3$  Hz, C-2'), 117.39 (d,  $J = 21.4$  Hz, C-3), 111.83 (C-5), 51.86 (OCH<sub>3</sub>); MS (EI)  $m/z$  (rel. intensity) (412.43) 412 (13 %, M), 399 (4), 398 (31), 397 (100), 381 (4), 379 (7), 353 (6), 260 (6), 206 (5), 201 (16), 183 (16); MS (CI) 413 (MH); Anal. Calcd for C<sub>25</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub>P: C, 72.81; H, 5.13; N, 6.79. Found: C, 72.86; H, 5.12; N, 6.75.

**Synthesis of methyl 2-chloronicotinate 5** (see, step c of Scheme 1).

A suspension of 2-chloronicotinic acid 4 (450 mg, 2.86 mmol) in thionyl chloride (SOCl<sub>2</sub>, 2.0 mL) was heated at reflux for 2.5 h under nitrogen. After SOCl<sub>2</sub> was evaporated under reduced pressure, the residue was dilute with dry methanol (2.0 mL) and was added dropwise triethylamine (318 mg, 3.14 mmol, 1.1 equiv.) at 0 °C. The mixture was stirred at room temperature for overnight. The solvent was evaporated under reduced pressure to afford an oily residue. The residue was purified on a silica-gel column chromatography using H-A (3:1, v/v) as an eluent to give the titled ester derivative 5 as a colorless oil (398 mg, 2.32 mmol, 81 %).  $R_f = 0.35$  (A:H 1:1); colorless oil; IR (neat) 2992, 2955, 1738, 1580, 1451, 1404, 1279, 1192, 1140, 1065, 833, 768, 743 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz)  $\delta$  8.53 (1H, dd,  $J = 4.8, 2.0$  Hz, H-6), 8.18 (1H, dd,  $J = 7.8, 2.0$  Hz, H-4), 7.34 (1H, dd,  $J = 7.7, 4.7$  Hz, H-5), 3.97 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz)  $\delta$  165.44 (CO<sub>2</sub>), 152.38 (C-6), 150.53 (C-2), 140.73 (C-4), 127.17 (C-3), 122.44 (C-5), 53.04 (OCH<sub>3</sub>); MS (EI)  $m/z$  (rel. intensity) (171.58) 171 (20 %, M), 142 (18), 140 (100), 112 (21); MS (CI) 172 (MH); Anal. Calcd for C<sub>7</sub>H<sub>6</sub>ClNO<sub>2</sub>: C, 49.00; H, 3.52; N, 8.16. Found: C, 48.97; H, 3.56; N, 8.15.

**Synthesis of methyl tetrazolo[1,5-*a*]pyridine-8-carboxylate 6a** (see, step d of Scheme 1).

A solution of ester derivative 5 (295 mg, 1.72 mmol) and sodium azide (335 mg, 5.16 mmol, 3.0 equiv.) in dimethyl sulfoxide (6.0 mL) was heated at 90 °C for 24 h in a sealed tube. The mixture was diluted with water (50 mL) and extracted with chloroform (60 mL  $\times$  3). The combined extracts were washed by brine (50 mL) and dried (MgSO<sub>4</sub>) and evaporated under reduced pressure and the crude product was purified on a silica-gel column using H-A (3:1, v/v) as an eluent to give the titled tetrazole derivative 6 (138 mg, 0.77 mmol, 45 %).  $R_f = 0.56$  (A:H 1:1); yellow needle crystals; mp 160-163 °C; IR (KBr) 3014, 1721, 1562, 1493, 1441, 1426, 1345, 1130, 1215, 1101, 997, 775 cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 200 MHz)  $\delta$  9.57 (1H, dd,  $J = 7.0, 1.0$  Hz, H-5), 8.46 (1H, dd,  $J = 7.0, 1.0$  Hz, H-7), 7.56 (1H, t,  $J = 7.0$  Hz, H-6), 3.98 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 50 MHz)  $\delta$  163.18 (CO<sub>2</sub>), 146.93 (C-8a), 137.36 (C-5), 131.21 (C-7), 118.43 (C-8), 117.10 (C-6), 53.14 (OCH<sub>3</sub>); MS (EI)  $m/z$  (rel. intensity) (178.15) 178 (9 %, M), 151 (7), 150 (100), 147 (10), 105 (8), 91 (22), 64 (17), 59 (21); MS (CI) 179 (MH); HRMS Calcd for C<sub>7</sub>H<sub>6</sub>N<sub>4</sub>O<sub>2</sub> 178.0491, Found 178.0507; Anal. Calcd for C<sub>7</sub>H<sub>6</sub>N<sub>4</sub>O<sub>2</sub>: C, 47.19; H, 3.39; N, 31.45. Found: C, 46.89; H, 3.45; N, 31.69.

**Alternative synthesis of iminophosphorane 3 from azide or tetrazole derivative 6a** (see, step e of Scheme 1).

A solution of azide or tetrazole derivative 6a (35 mg, 0.20 mmol) and triphenylphosphine (57 mg, 0.22 mmol, 1.1 equiv.) in dry benzene (2.5 mL) was heated at reflux for 2 h under nitrogen. Then the mixture was evaporated under reduced pressure to afford a solid residue. The residue was purified on a silica-gel column chromatography using H-A (1:1, v/v) as an eluent to give the corresponding iminophosphorane derivative 3 (80 mg, 0.19 mmol, 99 %).

**Synthesis of (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives 10a - 10f** (see, Scheme 2). **General procedure:**

To a solution of iminophosphorane derivative 3 (166 mg, 0.40 mmol) in dry benzene (10 mL) was added phenyl isocyanate (168 mg, 1.41 mmol, 3.5 equiv.). The mixture was stirred at room temperature for overnight under

nitrogen. To the mixture was added allyl amine (1.0 mL) and was heated at reflux for 3 h. Then the mixture was evaporated under reduced pressure to afford a solid residue. The residue was purified on a silica-gel column chromatography using H-A (1:1, v/v) as an eluent and Chromatorex® NH-DM-1020) column chromatography using H-A (3:1, v/v) as an eluent for remove triphenylphosphine *P*-oxide to give 6-[1-allyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-phenyl-4-phenylimino-3,4-dihydro-1,3,5-triazin-2(1*H*)-one **10a** (120 mg, 0.30 mmol, 75 %). The other (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivatives were synthesized by the similar methodology.

**6-[1-Allyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-phenyl-4-phenylimino-3,4-dihydro-1,3,5-triazin-2(1*H*)-one (10a):**

yield 75 %; *R<sub>f</sub>* = 0.12 (A:H 1:1); orange solid; mp 215-217 °C; IR (KBr) 1709, 1630, 1580, 1550, 1483, 1469, 1395, 1310, 1221, 1011, 764, 692 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 12.41 (1H, br s, NH), 8.48 (1H, dd, *J* = 7.4, 2.2 Hz, H-6'), 7.59 (1H, dd, *J* = 6.4, 2.2 Hz, H-4'), 7.50-7.35 (6H, m, C<sub>6</sub>H<sub>5</sub>), 7.29-7.21 (1H, m, C<sub>6</sub>H<sub>5</sub>), 7.02-6.94 (3H, m, C<sub>6</sub>H<sub>5</sub>), 6.42 (1H, t, *J* = 6.8 Hz, H-5'), 5.96 (1H, ddt, *J* = 17.0, 10.2, 6.0 Hz, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.36 (1H, dq, *J* = 10.2, 0.8 Hz, CH=CH<sub>2</sub>), 5.24 (1H, dq, *J* = 17.0, 0.9 Hz, CH=CH<sub>2</sub>), 4.66 (2H, dt, *J* = 5.8, 1.4 Hz, NCH<sub>2</sub>CH=CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 162.25 (C), 154.78 (C), 149.92 (C), 148.92 (C), 148.58 (C), 145.11 (C-6'), 143.00 (C-4'), 136.47 (C), 131.49 (CH<sub>2</sub>CH=CH<sub>2</sub>), 129.66 (2CH), 129.05 (2CH), 128.64 (CH), 128.44 (2CH), 123.41 (2CH), 122.79 (CH), 120.16 (CH=CH<sub>2</sub>), 117.68 (C-3'), 107.68 (C-5'), 52.11 (NCH<sub>2</sub>CH=CH<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (397.44) 398 (8 %, M+1), 397 (41, M), 396 (100), 195 (5), 194 (35), 163 (3), 161 (4), 121 (3), 91 (3), 77(4); MS (CI) 398 (MH); HRMS Calcd for C<sub>23</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub> 397.1539, Found 397.1547; Anal. Calcd for C<sub>23</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>: C, 69.51; H, 4.82; N, 17.62. Found: C, 69.66; H, 4.95; N, 17.35.

**6-[1-Allyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-(4-chlorophenyl)-4-(4-chlorophenyl)imino-3,4-dihydro-1,3,5-triazin-2(1*H*)-one (10b):**

yield 74 %; *R<sub>f</sub>* = 0.27 (A:H 1:1); orange solid; mp 257-260 °C; IR (KBr) 1736, 1688, 1647, 1553, 1489, 1437, 1393, 1194, 1119, 777, 721 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 12.55 (1H, br s, NH), 8.47 (1H, dd, *J* = 7.6, 2.2 Hz, H-6'), 7.63 (1H, dd, *J* = 6.6, 2.2 Hz, H-4'), 7.49-7.42 (2H, m, C<sub>6</sub>H<sub>4</sub>), 7.34-7.16 (4H, m, C<sub>6</sub>H<sub>4</sub>), 6.92-6.84 (2H, m, C<sub>6</sub>H<sub>4</sub>), 6.47 (1H, dd, *J* = 7.4, 6.6 Hz, H-5'), 5.96 (1H, ddt, *J* = 17.0, 10.4, 5.8 Hz, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.36 (1H, dq, *J* = 10.4, 0.9 Hz, CH=CH<sub>2</sub>), 5.24 (1H, dq, *J* = 17.2, 0.9 Hz, CH=CH<sub>2</sub>), 4.66 (2H, dt, *J* = 5.8, 1.3 Hz, NCH<sub>2</sub>CH=CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 162.28 (C), 155.13 (C), 149.56 (C), 149.12 (C), 147.38 (C), 145.22 (C-6'), 143.27 (C-4'), 134.76 (C), 134.55 (C), 131.36 (CH<sub>2</sub>CH=CH<sub>2</sub>), 130.45 (2CH), 129.95 (2CH), 128.47 (2CH), 127.99 (C), 124.81 (2CH), 120.38 (CH=CH<sub>2</sub>), 117.40 (C-3'), 107.81 (C-5'), 52.20 (NCH<sub>2</sub>CH=CH<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (466.33) 469 (5 %, M+4), 468 (15, M+3), 467 (32, M+2), 466 (62, M+1), 465 (49, M), 464 (100), 266 (6), 265 (6), 264 (42), 263 (10), 262 (71), 161 (11), 152 (6), 125 (7); MS (CI) 468 (MH+2), 466 (MH); Anal. Calcd for C<sub>23</sub>H<sub>17</sub>Cl<sub>2</sub>N<sub>5</sub>O<sub>2</sub>: C, 59.24; H, 3.67; N, 15.02. Found: C, 59.37; H, 3.78; N, 14.78.

**6-[1-Allyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-(4-methoxyphenyl)-4-(4-methoxyphenyl)imino-3,4-dihydro-1,3,5-triazin-2(1*H*)-one (10c):**

yield 80 %; *R<sub>f</sub>* = 0.39 (A); orange oil; IR (neat) 1720, 1593, 1550, 1502, 1460, 1395, 1308, 1244, 1169, 1034, 837, 762 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 12.34 (1H, br s, NH), 8.51 (1H, dd, *J* = 7.4, 2.1 Hz, H-6'), 7.60 (1H, dd, *J* = 6.5, 2.1 Hz, H-4'), 7.33-7.25 (2H, m, C<sub>6</sub>H<sub>4</sub>), 7.04-6.92 (4H, m, C<sub>6</sub>H<sub>4</sub>), 6.83-6.78 (2H, m, C<sub>6</sub>H<sub>4</sub>), 6.45 (1H, t, *J* = 7.1 Hz, H-5'), 5.97 (1H, ddt, *J* = 17.0, 10.4, 5.8 Hz, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.36 (1H, dq, *J* = 10.2, 0.8 Hz,

CH=CH<sub>2</sub>), 5.24 (1H, dq,  $J = 17.0, 0.9$  Hz, CH=CH<sub>2</sub>), 4.66 (2H, dt,  $J = 5.8, 1.4$  Hz, NCH<sub>2</sub>CH=CH<sub>2</sub>), 3.83 (3H, s, OCH<sub>3</sub>), 3.79 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz)  $\delta$  162.25 (C), 159.52 (C), 155.71 (C), 154.36 (C), 150.21 (C), 148.94 (C), 144.96 (C-6'), 142.90 (C-4'), 142.13 (C), 131.52 (CH<sub>2</sub>CH=CH<sub>2</sub>), 129.96 (2CH), 124.48 (2CH), 123.15 (C), 120.12 (CH=CH<sub>2</sub>), 117.80 (C-3'), 114.93 (2CH), 113.64 (2CH), 107.65 (C-5'), 55.55 (2OCH<sub>3</sub>), 52.09 (NCH<sub>2</sub>CH=CH<sub>2</sub>); MS (EI)  $m/z$  (rel. intensity) (457.49) 458 (19%, M+1), 457 (69, M), 456 (84), 416 (5), 255 (14), 254 (100), 239 (40), 161 (8), 149 (6), 148 (47), 133 (16); MS (CI) 458 (MH); HRMS Calcd for C<sub>25</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub> 457.1750, Found 457.1762; Anal. Calcd for C<sub>25</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub>: C, 65.64; H, 5.07; N, 15.31. Found: C, 65.88; H, 5.23; N, 14.91.

**6-[1-Isopropyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-phenyl-4-phenylimino-3,4-dihydro-1,3,5-triazin-2(1H)-one (10d):**

yield 58 %;  $R_f = 0.53$  (A); orange solid; mp 296-297 °C; IR (KBr) 1719, 1630, 1580, 1549, 1487, 1390, 1242, 1144, 1084, 1007, 762, 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz)  $\delta$  12.58 (1H, br s, NH), 8.44 (1H, dd,  $J = 7.4, 2.2$  Hz, H-6'), 7.66 (1H, dd,  $J = 6.6, 2.0$  Hz, H-4'), 7.54-7.45 (2H, m, C<sub>6</sub>H<sub>5</sub>), 7.41-7.34 (3H, m, C<sub>6</sub>H<sub>5</sub>), 7.28-7.21 (2H, m, C<sub>6</sub>H<sub>5</sub>), 7.02-6.94 (3H, m, C<sub>6</sub>H<sub>5</sub>), 6.45 (1H, t,  $J = 7.0$  Hz, H-5'), 5.31 (1H, septet,  $J = 6.8$  Hz, NCH(CH<sub>3</sub>)<sub>2</sub>), 1.41 (6H, d,  $J = 6.8$  Hz, CH(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz)  $\delta$  162.24, (C), 155.06, (C), 150.01, (C), 149.01, (C), 148.91, (C), 144.22, (C-6'), 138.98, (C-4'), 136.52, (C), 129.64, (2CH), 129.06, (2CH), 128.61, (CH), 128.41, (2CH), 123.48, (2CH), 122.73, (CH), 117.28, (C-3'), 107.83, (C-5'), 48.20 (NCH(CH<sub>3</sub>)<sub>2</sub>), 21.98 (CH(CH<sub>3</sub>)<sub>2</sub>); MS (EI)  $m/z$  (rel. intensity) (399.45) 400 (8 %, M+1), 399 (41, M), 398 (100), 357 (4), 356 (16), 313 (5), 195 (6), 194 (58), 179 (4), 121 (8), 77 (4); MS (CI) 400 (MH); HRMS Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>5</sub>O<sub>2</sub> 399.1695, Found 399.1696; Anal. Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>5</sub>O<sub>2</sub>: C, 69.16; H, 5.30; N, 17.53. Found: C, 69.36; H, 5.38; N, 17.25.

**6-[1-Isopropyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-(4-chlorophenyl)-4-(4-chlorophenyl)imino-3,4-dihydro-1,3,5-triazin-2(1H)-one (10e):**

yield 64 %;  $R_f = 0.17$  (A:H 1:1); orange solid; mp 211-213 °C; IR (KBr) 1725, 1630, 1578, 1549, 1485, 1389, 1242, 1088, 1007, 762, 739 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz)  $\delta$  12.70 (1H, br s, NH), 8.44 (1H, dd,  $J = 7.4, 2.2$  Hz, H-6'), 7.71 (1H, dd,  $J = 6.8, 2.2$  Hz, H-4'), 7.50-7.43 (2H, m, C<sub>6</sub>H<sub>4</sub>), 7.35-7.28 (2H, m, C<sub>6</sub>H<sub>4</sub>), 7.24-7.17 (2H, m, C<sub>6</sub>H<sub>4</sub>), 6.93-6.85 (2H, m, C<sub>6</sub>H<sub>4</sub>), 6.52 (1H, dd,  $J = 7.4, 6.8$  Hz, H-5'), 5.33 (1H, septet,  $J = 6.8$  Hz, NCH(CH<sub>3</sub>)<sub>2</sub>), 1.43 (6H, d,  $J = 7.0$  Hz, CH(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz)  $\delta$  162.26 (C), 155.43 (C), 149.67 (C), 149.21 (C), 147.47 (C), 144.32 (C-6'), 139.28 (C-4'), 134.80 (C), 134.57 (C), 130.47 (2CH), 129.98 (2CH), 128.47 (2CH), 127.98 (C), 124.86 (2CH), 117.04 (C-3'), 107.94 (C-5'), 48.35 (NCH(CH<sub>3</sub>)<sub>2</sub>), 22.01 (CH(CH<sub>3</sub>)<sub>2</sub>); MS (EI)  $m/z$  (rel. intensity) (468.34) 471 (7 %, M+4), 470 (17, M+3), 469 (42, M+2), 468 (74, M+1), 467 (64, M), 466 (100), 424 (11), 264 (47), 263 (12), 262 (78), 121 (31); MS (CI) 468 (MH), 470 (MH+2), 472 (MH+4); Anal. Calcd for C<sub>23</sub>H<sub>19</sub>Cl<sub>2</sub>N<sub>5</sub>O<sub>2</sub>: C, 58.99; H, 4.09; N, 14.95. Found: C, 59.24; H, 4.01; N, 14.78.

**6-[1-Isopropyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-(4-methoxyphenyl)-4-(4-methoxyphenyl)imino-3,4-dihydro-1,3,5-triazin-2(1H)-one (10f):**

yield 69 %;  $R_f = 0.46$  (A); orange solid; mp 141-143 °C; IR (KBr) 1719, 1649, 1630, 1593, 1551, 1501, 1468, 1391, 1298, 1244, 1179, 1103, 1034, 835, 762, 648 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz)  $\delta$  12.50 (1H, br s, NH), 8.47 (1H, dd,  $J = 7.6, 2.4$  Hz, H-6'), 7.66 (1H, dd,  $J = 6.7, 2.1$  Hz, H-4'), 7.33-7.26 (2H, m, C<sub>6</sub>H<sub>4</sub>), 7.03-6.87 (4H, m, C<sub>6</sub>H<sub>4</sub>), 6.85-6.78 (2H, m, C<sub>6</sub>H<sub>4</sub>), 6.47 (1H, t,  $J = 7.0$  Hz, H-5'), 5.32 (1H, septet,  $J = 6.8$  Hz, NCH(CH<sub>3</sub>)<sub>2</sub>), 3.83 (3H, s, OCH<sub>3</sub>), 3.78 (3H, s, OCH<sub>3</sub>), 1.41 (6H, d,  $J = 6.8$  Hz, CH(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz)  $\delta$

**Table 4** Selected bond lengths (Å) of **10a**.<sup>a</sup>

O1-C3	1.213(3)	N4-C5	1.405(3)
O2-C5	1.237(3)	N4-C6	1.351(4)
N1-C1	1.294(3)	N4-C9	1.472(4)
N1-C2	1.386(3)	N5-C2	1.268(3)
N2-C2	1.421(3)	N5-C12	1.418(3)
N2-C3	1.371(3)	C1-C4	1.472(4)
N2-C18	1.459(3)	C4-C5	1.443(4)
N3-C1	1.359(3)	C4-C8	1.374(4)
N3-C3	1.376(3)	C6-C7	1.346(5)
N3-H1	0.87(3)	O2...H1	1.88(3)

<sup>a</sup> Estimated standard deviations in the least significant figure are given in parentheses.

**Table 5** Selected torsion angles (°) of **10a**.<sup>a</sup>

(1)-(2)-(3)-(4)		(1)-(2)-(3)-(4)	
O1-C3-N2-C2	176.3(3)	N3-C1-C4-C5	3.5(4)
O1-C3-N2-C18	0.0(4)	N3-C1-C4-C8	-172.0(3)
O1-C3-N3-C1	-178.1(3)	N3-C3-N2-C2	-3.8(4)
O2-C5-N4-C6	177.4(3)	N3-C3-N2-C18	179.5(3)
O2-C5-N4-C9	-8.9(4)	N4-C5-C4-C1	-172.6(2)
O2-C5-C4-C1	7.3(4)	N4-C5-C4-C8	2.8(4)
O2-C5-C4-C8	-177.2(3)	N4-C6-C7-C8	2.3(5)
N1-C1-N3-C3	-2.1(5)	N5-C2-N1-C1	173.8(3)
N1-C1-C4-C5	-179.5(3)	N5-C2-N2-C3	-173.3(3)
N1-C1-C4-C8	5.0(4)	N5-C2-N2-C18	3.4(4)
N1-C2-N2-C3	4.6(4)	C1-C4-C8-C7	174.9(3)
N1-C2-N2-C18	-178.7(2)	C2-N1-C1-C4	-174.0(2)
N1-C2-N5-C12	6.0(4)	C2-N2-C18-C19	-100.8(3)
N2-C2-N1-C1	-3.9(4)	C2-N5-C12-C13	59.6(4)
N2-C2-N5-C12	-176.3(2)	C3-N2-C18-C19	76.0(4)
N2-C3-N3-C1	2.4(4)	C3-N3-C1-C4	174.8(3)
N3-C1-N1-C2	2.8(4)	C4-C5-N4-C9	171.0(3)
		C5-N4-C9-C10	-81.7(4)

<sup>a</sup> 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) and estimated standard deviations in the least significant figure are given in parentheses.

162.17 (C), 159.58 (C), 155.71 (C), 154.69 (C), 150.30 (C), 149.01 (C), 144.05 (C-6'), 142.16 (C), 138.80 (C-4'), 129.98 (2CH), 124.52 (2CH), 123.19 (C), 117.41 (C-3'), 114.98 (2CH), 113.65 (2CH), 107.73 (C-5'), 55.53 (2OCH<sub>3</sub>), 48.13 (NCH(CH<sub>3</sub>)<sub>2</sub>), 21.98 (CH(CH<sub>3</sub>)<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (459.50) 460 (18 %, M+1), 459 (73, M), 458 (78), 416 (7), 255 (13), 254 (100), 239 (29), 209 (12), 149 (6), 148 (30), 133 (8), 121 (13); MS (CI) 460 (MH); HRMS Calcd for C<sub>25</sub>H<sub>15</sub>N<sub>5</sub>O<sub>4</sub> 459.1907, Found 459.1903; Anal. Calcd for C<sub>25</sub>H<sub>15</sub>N<sub>5</sub>O<sub>4</sub>: C, 65.35; H, 5.48; N, 15.24. Found: C, 65.46; H, 5.71; N, 14.90.

**Hydrolysis of 10d into 6-[1-isopropyl-(2-oxo-1,2-dihydropyridin-3-yl)]-3-phenyl-1,3,5-triazin-2,4(1H,3H)-dione (11)** (see, step d of Scheme 2).

A solution of 10d (34.1 mg, 0.085 mmol) in 1 drop of concentrated hydrochloric acid in methanol (7.0 mL) was stirred for 48 h at 50 °C in a sealed glass tube. After neutralization by saturated NaHCO<sub>3</sub>, the mixture was diluted with water (30 mL) and extracted with chloroform (50 mL × 3). The combined extracts were dried (MgSO<sub>4</sub>) and evaporated under reduced pressure and the crude product was purified on a silica-gel column using H-A (1:1, v/v) as an eluent to give the titled (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivative 11 (15.8 mg, 0.049 mmol, 57 %). *R<sub>f</sub>* = 0.31 (A); white solid; mp 296-297 °C; IR (KBr) 1719, 1649, 1630, 1580, 1547, 1489, 1391, 1242, 1071, 762, 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 13.40 (1H, br s, NH), 9.00 (1H, dd, *J* = 7.4, 2.2 Hz, H-6'), 7.81 (1H, dd, *J* = 6.7, 2.2 Hz, H-4'), 7.56-7.40 (3H, m, C<sub>6</sub>H<sub>5</sub>), 7.35-7.30 (2H, m, C<sub>6</sub>H<sub>5</sub>), 6.63 (1H, dd, *J* = 7.4, 6.8 Hz, H-5'), 5.36 (1H, septet, *J* = 6.7 Hz, NCH(CH<sub>3</sub>)<sub>2</sub>), 1.46 (6H, d, *J* = 6.8 Hz, CH(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 162.36 (C), 160.66 (C), 156.44 (C), 150.16 (C), 145.25 (C-6'), 140.23 (C-4'), 134.65 (C), 129.81 (2CH), 129.28 (CH), 128.43 (2CH), 116.11 (C-3'), 108.06 (C-5'), 48.62 (NCH(CH<sub>3</sub>)<sub>2</sub>), 22.01 (CH(CH<sub>3</sub>)<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (324.34) 325 (15 %, M+1), 324 (71, M), 232 (52), 206 (8), 205 (59), 190 (8), 177 (21), 164 (10), 163 (100), 161 (11), 160 (9), 121 (52), 119 (12); MS (CI) 325 (MH); HRMS Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub> 324.1222, Found 324.1225; Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 62.95; H, 4.97; N, 17.27. Found: C, 63.16; H, 5.05; N, 16.98.

**Synthesis of diethyl 2-aminonicotinamide 17c.**

The synthetic route was same as the method of synthesis of methyl 2-aminonicotinate 2. yield 77 %; *R<sub>f</sub>* = 0.14 (A:H 2:1); white solid; mp 117-118 °C; IR (KBr) 3403, 3181, 1649, 1613, 1572, 1462, 1445, 1292, 1088, 770 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.10 (1H, dd, *J* = 5.1, 1.9 Hz, H-6), 7.37 (1H, dd, *J* = 7.4, 1.8 Hz, H-4), 6.66 (1H, dd, *J* = 7.4, 5.0 Hz, H-5), 5.05 (2H, br s, NH<sub>2</sub>), 3.43 (4H, q, *J* = 7.1 Hz, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 1.20 (6H, t, *J* = 7.1 Hz, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 169.75 (CONEt<sub>2</sub>), 156.88 (C-2), 149.63 (C-6), 135.50 (C-4), 115.78 (C-3), 113.36 (C-5), 41.56 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 13.61 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (193.25) 194 (3 %, M+1), 193 (26, M), 192 (4), 122 (6), 121 (100), 94 (7), 93 (27), 73 (2), 72 (79), 66 (9); MS (CI) 194 (MH); Anal. Calcd for C<sub>10</sub>H<sub>15</sub>N<sub>3</sub>O: C, 62.15; H, 7.82; N, 21.74. Found: C, 62.05; H, 8.01; N, 21.65.

**Synthesis of iminophosphorane derivative 18** (see, step a of Scheme 5). **General procedure:**

The synthetic route was same as the method of synthesis of methyl 2-(triphenylphosphoranylidene)aminonicotinate 3. The data of 18e had been already shown by the previous report.<sup>20</sup>

**2-(Triphenylphosphoranylidene)aminopyridine (18a):**

yield 88 %; *R<sub>f</sub>* = 0.29 (A:H 1:1); white solid; mp 124-128 °C; IR (KBr) 1588, 1543, 1462, 1427, 1337, 1109, 1046, 1017, 999, 779, 752, 718, 694, 619 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 7.88-7.77 (1H + 6H, m, H-6 + C<sub>6</sub>H<sub>5</sub>), 7.55-7.28 (1H + 9H, m, H-4 + C<sub>6</sub>H<sub>5</sub>), 6.92 (1H, dt, *J* = 8.2, 0.9 Hz, H-5), 6.44 (1H, ddd, *J* = 12.1, 5.0, 1.0

Hz, H-3);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz)  $\delta$  164.18 (d,  $J = 6.3$  Hz, C-2), 147.48 (C-6), 136.97 (d,  $J = 4.7$  Hz, C-4), 133.55 (d,  $J = 9.6$  Hz, C-3'), 131.81 (d,  $J = 2.6$  Hz, C-4'), 130.80 (d,  $J = 98.6$  Hz, C-1'), 128.64 (d,  $J = 11.9$  Hz, C-2'), 117.58 (d,  $J = 24.2$  Hz, C-3), 112.54 (C-5); MS (EI)  $m/z$  (rel. intensity) (354.39) 355 (14 %, M+1), 354 (65, M), 353 (100), 278 (4), 277 (22), 260 (7), 199 (5), 185 (5), 184 (4), 183 (33); MS (CI) 355 (MH); Anal. Calcd for  $\text{C}_{23}\text{H}_{19}\text{N}_2\text{P}$ : C, 77.95; H, 5.40; N, 7.90. Found: C, 77.94; H, 5.41; N, 7.89.

**2-(Triphenylphosphoranylidene)amino-3-picoline (18b):**

yield 84 %;  $R_f = 0.73$  (A:H 1:1); white solid; mp 45–46 °C; IR (KBr) 3056, 1589, 1555, 1483, 1460, 1422, 1341, 1325, 1182, 1111, 1067, 1022, 999, 847, 775, 747, 716, 694, 617  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  7.92–7.81 (6H, m,  $\text{C}_6\text{H}_5$ ), 7.68 (1H, ddt,  $J = 5.0, 2.0, 0.6$  Hz, H-6), 7.54–7.35 (1H + 9H, m, H-4 +  $\text{C}_6\text{H}_5$ ), 6.39 (1H, dd,  $J = 7.1, 5.1$  Hz, H-5), 2.42 (3H, s,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz)  $\delta$  163.09 (d,  $J = 6.4$  Hz, C-2), 144.93 (C-6), 136.42 (d,  $J = 3.4$  Hz, C-4), 133.63 (d,  $J = 9.8$  Hz, C-3'), 131.65 (d,  $J = 2.9$  Hz, C-4'), 131.39 (d,  $J = 101.6$  Hz, C-1'), 128.52 (d,  $J = 12.2$  Hz, C-2'), 125.77 (d,  $J = 22.3$  Hz, C-3), 112.65 (C-5), 19.08 ( $\text{CH}_3$ ); MS (EI)  $m/z$  (rel. intensity) (368.42) 369 (23 %, M+1), 368 (100, M), 367 (69), 353 (10), 291 (34), 213 (11), 185 (8), 184 (15), 183 (94), 108 (10); MS (CI) 369 (MH); HRMS Calcd for  $\text{C}_{24}\text{H}_{21}\text{N}_2\text{P}$  368.1442, Found 368.1439; Anal. Calcd for  $\text{C}_{24}\text{H}_{21}\text{N}_2\text{P}$ : C, 78.24; H, 5.75; N, 7.60. Found: C, 77.84; H, 5.96; N, 7.79.

**Diethyl 2-(triphenylphosphoranylidene)aminonicotinamide (18c):**

yield 83 %;  $R_f = 0.44$  (A:H 2:1); white solid; mp 169–170 °C; IR (KBr) 2975, 1624, 1586, 1549, 1476, 1458, 1427, 1337, 1289, 1111, 1020, 720, 694, 621  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  7.89–7.77 (1H + 6H, m, H-6 +  $\text{C}_6\text{H}_5$ ), 7.54–7.30 (1H + 9H, m, H-4 +  $\text{C}_6\text{H}_5$ ), 6.46 (1H, dd,  $J = 7.2, 5.2$  Hz, H-5), 4.04–3.94 (1H, m,  $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 3.49–3.16 (3H, m,  $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 1.36 (3H, t,  $J = 7.1$  Hz,  $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 1.01 (3H, t,  $J = 7.2$  Hz,  $\text{N}(\text{CH}_2\text{CH}_3)_2$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz)  $\delta$  171.51 ( $\text{CONEt}_2$ ), 159.63 (d,  $J = 6.0$  Hz, C-2), 148.14 (C-6), 134.98 (d,  $J = 3.9$  Hz, C-4), 133.58 (d,  $J = 9.6$  Hz, C-3'), 131.82 (d,  $J = 2.8$  Hz, C-4'), 130.78 (d,  $J = 101.6$  Hz, C-1'), 128.52 (d,  $J = 12.2$  Hz, C-2'), 126.37 (d,  $J = 24.5$  Hz, C-3), 112.16 (C-5), 42.59 ( $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 38.80 ( $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 14.32 ( $\text{N}(\text{CH}_2\text{CH}_3)_2$ ), 13.19 ( $\text{N}(\text{CH}_2\text{CH}_3)_2$ ); MS (EI)  $m/z$  (rel. intensity) (453.52) 454 (4 %, M+1), 453 (16, M), 452 (24), 383 (18), 382 (66), 381 (18), 354 (24), 353 (100), 262 (11), 183 (23); MS (CI) 454 (MH); HRMS Calcd for  $\text{C}_{28}\text{H}_{28}\text{N}_3\text{OP}$  453.1970, Found 453.1977; Anal. Calcd for  $\text{C}_{28}\text{H}_{28}\text{N}_3\text{OP}$ : C, 74.15; H, 6.22; N, 9.27. Found: C, 74.06; H, 6.37; N, 9.21.

**2-(Triphenylphosphoranylidene)aminopyrazine (18d):**

yield 64 %;  $R_f = 0.27$  (A:H 1:1); white solid; mp 180.5–182 °C; IR (KBr) 3061, 1574, 1493, 1472, 1414, 1345, 1111, 1015, 999, 721, 694  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  8.03 (1H, dd,  $J = 1.4, 0.8$  Hz, pyrazine), 7.87–7.75 (6H, m,  $\text{C}_6\text{H}_5$ ), 7.70–7.65 (2H, m, pyrazine), 7.59–7.39 (9H, m,  $\text{C}_6\text{H}_5$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz)  $\delta$  160.67 (d,  $J = 6.3$  Hz, C-2), 142.30 (d,  $J = 25.7$  Hz, C-3), 141.45 (C-5 + C-6), 133.45 (d,  $J = 9.7$  Hz, C-3'), 132.25 (d,  $J = 2.4$  Hz, C-4'), 129.71 (d,  $J = 98.0$  Hz, C-1'), 128.85 (d,  $J = 12.4$  Hz, C-2'); MS (EI)  $m/z$  (rel. intensity) (355.38) 356 (16 %, M+1), 355 (81, M), 354 (100), 301 (11), 278 (7), 260 (7), 185 (10), 183 (29), 108 (5); MS (CI) 356 (MH); Anal. Calcd for  $\text{C}_{22}\text{H}_{18}\text{N}_3\text{P}$ : C, 74.36; H, 5.11; N, 11.82. Found: C, 74.35; H, 5.10; N, 11.84.

**Synthesis of pyrido[1,2-*a*][1,3,5]triazine derivatives 15 and 19 (see, Scheme 5). General procedure:**

To a solution of iminophosphorane derivative **18a** (103 mg, 0.29 mmol) in dry benzene (3.0 mL) was added phenyl isocyanate (121 mg, 1.02 mmol, 3.5 equiv.). The mixture was stirred at room temperature for overnight under nitrogen. Then the mixture was evaporated under reduced pressure to afford a solid residue. The residue was purified by repeated recrystallization to give pyrido[1,2-*a*][1,3,5]triazine derivative **19a** (0.12 mmol, 37.6

mg, 41 %). The other pyrido[1,2-*a*][1,3,5]triazine derivatives were synthesized by the similar methodology.

**Methyl (4-oxo-3-phenyl-2-phenylimino-2,3-dihydro-pyrido[1,2-*a*][1,3,5]triazine)-9-carboxylate (15a):**

yield 31 %; *R<sub>f</sub>* = 0.24 (A:H 1:1); red solid; mp 159-160 °C; IR (KBr) 1736, 1719, 1624, 1561, 1489, 1370, 1263, 1121, 1074, 756, 669 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.34 (1H, dd, *J* = 7.3, 1.7 Hz, H-6), 7.86 (1H, dd, *J* = 6.9, 1.7 Hz, H-8), 7.59-7.44 (3H, m, C<sub>6</sub>H<sub>5</sub>), 7.42-7.35 (2H, m, C<sub>6</sub>H<sub>5</sub>), 7.27-7.17 (2H, m, C<sub>6</sub>H<sub>5</sub>), 7.12-7.06 (2H, m, C<sub>6</sub>H<sub>5</sub>), 7.01-6.93 (1H, m, C<sub>6</sub>H<sub>5</sub>), 6.49 (1H, t, *J* = 7.0 Hz, H-7), 3.74 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 165.30 (CO<sub>2</sub>), 148.25 (C), 148.07 (C), 147.92 (C), 145.98 (C), 143.04 (C-6), 136.48 (C), 132.19 (C-8), 129.95 (2CH), 129.16 (CH), 128.49 (2CH), 128.25 (2CH), 126.76 (C-9), 124.00 (2CH), 123.35 (CH), 109.56 (C-7), 52.94 (OCH<sub>3</sub>); UV (λ max/log ε) 266/4.26; 304/4.10; 409/4.09; MS (EI) *m/z* (rel. intensity) (372.38) 373 (11 %, M+1), 372 (54, M), 371 (100), 313 (9), 236 (10), 222 (8), 194 (6), 170 (8), 119 (8), 77 (5); MS (CI) 373 (MH); HRMS Calcd for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub> 372.1222, Found 372.1221; Anal. Calcd for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 67.73; H, 4.33; N, 15.05. Found: C, 67.96; H, 4.38; N, 14.77.

**3-Phenyl-2-phenylimino-2,3-dihydro-pyrido[1,2-*a*][1,3,5]triazin-4-one (19a):**

yield 41 %; *R<sub>f</sub>* = 0.25 (A:H 1:1); orange solid; mp 194-195 °C; IR (KBr) 1728, 1649, 1626, 1593, 1562, 1545, 1491, 1372, 1273, 1138, 1105, 758, 720, 693 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.21 (1H, ddd, *J* = 7.4, 1.6, 0.8 Hz, H-6), 7.58-7.18 (7H, m, C<sub>6</sub>H<sub>5</sub>), 7.33 (1H, ddd, *J* = 9.2, 6.3, 1.7 Hz, H-8), 7.05-6.92 (3H, m, C<sub>6</sub>H<sub>5</sub>), 6.83 (1H, ddd, *J* = 9.3, 1.3, 0.8 Hz, H-9), 6.45 (1H, ddd, *J* = 7.4, 6.5, 1.3 Hz, H-7); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 151.67 (C), 148.58 (C), 148.43 (C), 147.17 (C), 139.76 (C-6), 136.80 (C), 129.90 (2CH), 129.01 (C-8), 128.91 (CH), 128.65 (2CH), 128.56 (2CH), 124.47 (C-9), 123.27 (2CH), 122.95 (CH), 110.96 (C-7); UV (λ max/log ε) 284/4.15; 391/3.60; MS (EI) *m/z* (rel. intensity) (314.35) 315 (6 %, M+1), 314 (36, M), 196 (10), 195 (100), 194 (42), 169 (9), 119 (26), 91 (14), 78 (98); MS (CI) 315 (MH); Anal. Calcd for C<sub>19</sub>H<sub>14</sub>N<sub>4</sub>O: C, 72.60; H, 4.49; N, 17.82. Found: C, 72.69; H, 4.50; N, 17.72.

**9-Methyl-3-phenyl-2-phenylimino-2,3-dihydro-pyrido[1,2-*a*][1,3,5]triazin-4-one (19b):**

yield 33 %; *R<sub>f</sub>* = 0.41 (A:H 1:1); orange solid; mp 156-158 °C; IR (KBr) 3056, 1736, 1647, 1607, 1574, 1555, 1483, 1437, 1385, 1084, 756, 694 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.13 (1H, ddd, *J* = 7.2, 1.6, 0.8 Hz, H-6), 7.74-6.91 (1H + 10H, m, H-8 + C<sub>6</sub>H<sub>5</sub>), 6.40 (1H, t, *J* = 7.0 Hz, H-7), 2.14 (3H, s, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 151.21 (C), 148.81 (C), 148.52 (C), 147.06 (C), 137.50 (C-6), 136.90 (C), 132.98 (C-9), 129.82 (2CH), 128.88 (CH), 128.59 (2CH), 128.32 (2CH), 126.70 (C-8), 123.80 (2CH), 122.85 (CH), 110.61 (C-7), 17.40 (CH<sub>3</sub>); MS (EI) *m/z* (rel. intensity) (328.37) 329 (9 %, M+1), 328 (45), 327 (100), 209 (23), 208 (26), 164 (4), 132 (4), 119 (5), 92 (9), 65 (6); MS (CI) 329 (MH); Anal. Calcd for C<sub>20</sub>H<sub>16</sub>N<sub>4</sub>O + C<sub>18</sub>H<sub>15</sub>OP = C<sub>38</sub>H<sub>31</sub>N<sub>4</sub>O<sub>2</sub>P: C, 75.23; H, 5.15; N, 9.24. Found: C, 75.22; H, 5.15; N, 9.25.

**Diethyl (4-oxo-3-phenyl-2-phenylimino-2,3-dihydro-pyrido[1,2-*a*][1,3,5]triazine)-9-carboxamide (19c):**

yield 37 %; *R<sub>f</sub>* = 0.39 (A); red solid; mp 174-175 °C; IR (KBr) 2978, 2934, 1736, 1624, 1561, 1485, 1370, 1263, 1115, 1069, 752, 693 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 8.22 (1H, dd, *J* = 7.3, 1.7 Hz, H-6), 7.57-7.35 (5H, m, C<sub>6</sub>H<sub>5</sub>), 7.34 (1H, dd, *J* = 6.6, 1.6 Hz, H-8), 7.18-7.09 (2H, m, C<sub>6</sub>H<sub>5</sub>), 6.93-6.85 (3H, m, C<sub>6</sub>H<sub>5</sub>), 6.49 (1H, dd, *J* = 7.3, 6.7 Hz, H-7), 3.63-3.45 (1H, m, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 3.26-2.92 (3H, m, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 0.98 (3H, t, *J* = 7.1 Hz, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 0.88 (3H, t, *J* = 7.1 Hz, N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 165.10 (CONET<sub>2</sub>), 148.50 (C), 148.37 (C), 148.14 (C), 146.40 (C), 137.44 (C-6), 136.60 (C), 133.00 (C-9), 129.90 (2CH), 129.31 (C-8), 129.08 (CH), 128.50 (2CH), 128.40 (2CH), 123.24 (2CH), 122.86 (CH), 110.33 (C-7), 42.95 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 39.44 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 14.13 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 12.35 (N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (413.48) 414 (18

**Table 6** Selected bond lengths (Å) of **19b**<sup>a</sup>

O1-C2	1.200(4)	N3-C7	1.376(4)
N1-C1	1.365(4)	N4-C1	1.280(4)
N1-C7	1.305(4)	N4-C8	1.418(4)
N2-C1	1.416(4)	C3-C4	1.335(5)
N2-C2	1.370(4)	C4-C5	1.398(6)
N2-C14	1.454(4)	C5-C6	1.357(5)
N3-C2	1.431(4)	C6-C7	1.446(4)
N3-C3	1.398(4)	C6-C20	1.485(6)

<sup>a</sup> Estimated standard derivations in the least significant figure are given in parentheses.

**Table 7** Selected torsion angles (°) of **19b**<sup>a</sup>

(1)-(2)-(3)-(4)		(1)-(2)-(3)-(4)	
O1-C2-N2-C1	178.3(3)	N3-C3-C4-C5	-0.2(6)
O1-C2-N2-C14	6.7(5)	N3-C7-N1-C1	2.3(4)
O1-C2-N3-C3	-3.0(4)	N3-C7-C6-C5	-1.0(4)
O1-C2-N3-C7	178.8(3)	N3-C7-C6-C20	179.8(4)
N1-C1-N2-C2	5.5(4)	N4-C1-N1-C7	174.5(3)
N1-C1-N2-C14	177.0(3)	N4-C1-N2-C2	-174.0(3)
N1-C1-N4-C8	5.3(5)	N4-C1-N2-C14	-2.5(4)
N1-C7-N3-C2	0.3(4)	C1-N1-C7-C6	-177.3(3)
N1-C7-N3-C3	-177.8(3)	C1-N2-C14-C15	81.0(4)
N1-C7-C6-C5	178.5(3)	C1-N4-C8-C9	47.2(4)
N1-C7-C6-C20	-0.6(5)	C2-N2-C14-C15	-106.9(3)
N2-C1-N1-C7	-4.9(4)	C2-N3-C3-C4	-179.3(3)
N2-C1-N4-C8	-175.2(3)	C2-N3-C7-C6	179.8(3)
N2-C2-N3-C3	178.2(3)	C3-N3-C7-C6	1.8(4)
N2-C2-N3-C7	0.1(4)	C3-C4-C5-C6	0.9(6)
N3-C2-N2-C1	-3.0(4)	C4-C3-N3-C7	-1.2(5)
N3-C2-N2-C14	-174.6(3)	C4-C5-C6-C7	-0.3(5)
		C4-C5-C6-C20	178.8(5)

<sup>a</sup> 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) and estimated standard derivations in the least significant figure are given in parentheses.

**Table 8** Crystal analysis parameters of **10a** and **19b**.

	<b>10a</b>	<b>19b</b>
Experimental formula	C <sub>23</sub> H <sub>19</sub> N <sub>5</sub> O <sub>2</sub>	C <sub>38</sub> H <sub>31</sub> N <sub>4</sub> O <sub>2</sub> P
Formula weight	397.44	606.66
Crystal color, habit	yellow prism	yellow prism
Crystal dimensions (mm)	0.240 × 0.540 × 0.620	0.180 × 0.420 × 0.680
Crystal system	triclinic	triclinic
Lattice parameters <i>a</i> (Å)	10.222 (3)	13.105 (6)
<i>b</i> (Å)	11.492 (4)	14.229 (5)
<i>c</i> (Å)	9.669 (4)	9.398 (4)
α (°)	99.16 (3)	102.31 (3)
β (°)	103.35 (3)	109.54 (3)
γ (°)	66.07 (2)	90.76 (4)
V (Å <sup>3</sup> )	1007.4 (6)	1607 (1)
Space group	P $\bar{1}$ (#2)	P $\bar{1}$ (#2)
Z value	2	2
Dcalc. (g/cm <sup>3</sup> )	1.310	1.254
F000	416	636
μ (MoKα) (cm <sup>-1</sup> )	0.81	1.20
Temperature (K)	293	296
R: R <sub>w</sub>	0.050: 0.055	0.040: 0.043

%, M+1), 413 (75, M), 412 (78), 314 (32), 223 (100), 222 (83), 195 (36), 194 (42), 119 (46), 72 (55); MS (CI) 414 (MH); HRMS Calcd. for C<sub>24</sub>H<sub>23</sub>N<sub>5</sub>O<sub>2</sub> 413.1852, Found 413.1848; Anal. Calcd for C<sub>24</sub>H<sub>23</sub>N<sub>5</sub>O<sub>2</sub>: C, 69.72; H, 5.61; N, 16.94. Found: C, 69.67; H, 5.76; N, 16.74.

**Synthesis of (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivative 10a from pyrido[1,2-*a*][1,3,5]triazine derivative 15a** (see, Scheme 6).

To a solution of pyrido[1,2-*a*][1,3,5]triazine derivative **15a** (18.0 mg, 0.048 mmol) in dry benzene (3.0 mL) was added allylamine (0.3 mL). The mixture was heated at reflux for 3 h under nitrogen. Then the mixture was evaporated under reduced pressure to afford a solid residue. The residue was purified on a silica gel column chromatography using H-A (1:1, v/v) as an eluent to give (2-oxo-1,2-dihydropyridin-3-yl)-1,3,5-triazine derivative **10a** (18.0 mg, 0.045 mmol, 94 %).

**Synthesis of allyl tetrazolo[1,5-*a*]pyridine-8-carboxamide 6b** (see, Scheme 7).

To a solution of tetrazole derivative **6a** (41.0 mg, 0.23 mmol) in dry benzene (3.0 mL) was added allylamine (1.0 mL). The mixture was heated at reflux for 3 h under nitrogen. Then the mixture was evaporated under reduced pressure to afford a solid residue. The residue was purified on a silica gel column chromatography using H-A (1:1,

v/v) as an eluent to give allyl tetrazolo[1,5-*a*]pyridine-8-carboxamide **6b** (38.6 mg, 0.19 mmol, 83%). *R*<sub>f</sub> = 0.23 (A:H 1:1); mp 96-97 °C; IR (KBr) 3366, 3054, 1657, 1644, 1566, 1545, 1487, 1427, 1294, 1152, 1105, 995, 918, 774 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 9.13 (1H, br s, CONH), 8.99 (1H, dd, *J* = 6.8, 1.0 Hz, H-5), 8.63 (1H, dd, *J* = 7.1, 1.1 Hz, H-7), 7.45 (1H, t, *J* = 6.9 Hz, H-6), 6.02 (1H, ddt, *J* = 17.3, 10.3, 5.5 Hz, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.37 (1H, dq, *J* = 17.2, 1.5 Hz, CH=CH<sub>2</sub>), 5.25 (1H, dq, *J* = 10.2, 1.4 Hz, CH=CH<sub>2</sub>), 4.24 (2H, tt, *J* = 5.7, 1.6 Hz, NHCH<sub>2</sub>CH=CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) δ 160.74 (CONH), 147.10 (C-8a), 135.27 (CH<sub>2</sub>CH=CH<sub>2</sub>), 133.61 (C-5), 128.00 (C-7), 121.63 (C-8), 117.23 (C-6), 117.17 (CH=CH<sub>2</sub>), 42.07 (NHCH<sub>2</sub>CH=CH<sub>2</sub>); MS (EI) *m/z* (rel. intensity) (203.20) 203 (36 %, M), 175 (100), 158 (16), 148 (59), 147 (16), 134 (33), 132 (22), 121 (75), 119 (29), 104 (25), 93 (51), 92 (28), 91 (74), 78 (30), 65 (15), 64 (26); MS (CI) 204 (MH); Anal. Calcd for C<sub>9</sub>H<sub>9</sub>N<sub>5</sub>O: C, 53.20; H, 4.46; N, 34.46. Found: C, 53.35; H, 4.54; N, 34.23.

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- 30 For example, p*K*<sub>a</sub> of pyrazine is 0.6 at 20 °C and p*K*<sub>a</sub> of pyridine is 5.42 at 25 °C by Kagaku Binran.
- 31 The electron density [(s<sup>2</sup> + px<sup>2</sup> + py<sup>2</sup> + pz<sup>2</sup>)<sup>1/2</sup>] on the nitrogen of pyrazine having 3-ester and 2-carbodiimide functions was 0.253 and that on the nitrogen of pyridine having same substituents was 0.485 by PM3 calculation.

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