Methyl 3-(triphenylphosphoranylideneamino)pyrazine-2-carboxylate: synthesis, crystal structure and use in pteridin-4(3*H*)-ones synthesis[1]

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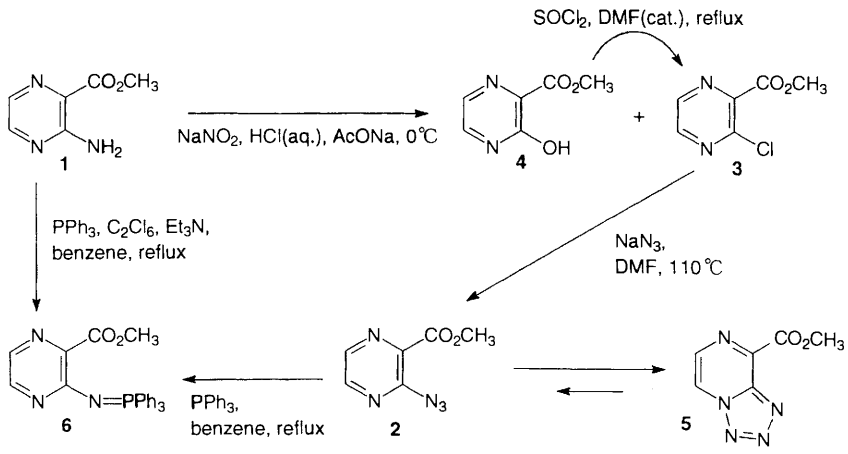
The title iminophosphorane 6 has been prepared from methyl 3-aminopyrazine-2-carboxylate 1 by a modified Kirsanov method using a triphenylphosphine–hexachloroethane–triethylamine system. The crystal structure of 6 illustrated an iminophosphorane function (N=P bond). 2,3-Disubstituted pteridin-4(3*H*)-ones were obtained in a one-pot reaction of 6 with isocyanates, followed by heterocyclization on addition of alcohols or amines.

Over the past decade, the aza-Wittig reactions of aza-ylides have received increased attention in view of their utility in the synthesis of C=N (imine) bond-containing compounds, in particular nitrogen heterocyclic compounds.[2,3] The key intermediate iminophosphorane can be conveniently generated by a Staudinger reaction from azide derivatives and phosphorus(III) reagents such as triphenylphosphine or by a Kirsanov reaction from primary amines and phosphorus(V) reagents such as dichlorotriphenylphosphorane.[4] Iminophosphoranes react with carbonyl compounds to form imines, and with isocyanates, isothiocyanates, carbon dioxide and carbon disulfide, to afford the corresponding heterocumulenes.[5] In addition, the reactivity of iminophosphoranes is widely variable depending on the N and P substituents as well as the carbonyl function. We have demonstrated recently that the intramolecular aza-Wittig reaction is a powerful tool for the synthesis of 5–7 membered nitrogen heterocycles such as oxazoles,[6] imidazolinones,[7] iminolactams,[8] quinazolin-4(3*H*)-ones,[7,9-12] and 1,4-benzodiazepin-5-ones.[13] On the other hand, an intermolecular aza-Wittig reaction followed by electrocyclization, intramolecular cycloaddition or heterocyclization, *i.e.* the tandem aza-Wittig and cyclization sequence, has been utilized for the synthesis of pyridines, pyrimidines and many other important nitrogen heterocycles by Molina,[2b] Wamhoff,[14] and Motoki *et al.*[15] Also, *N*-vinyliminophosphoranes have been utilized for the synthesis of heterocycles by Nitta *et al.*[16] We became interested in the preparation of *N*-heteroaryliminophosphoranes because these species have been little studied,[4] and are promising building blocks for the synthesis of nitrogen heterocycles. Fused heterocycles have been prepared *via* such iminophosphorane intermediates recently[2,14] and we have reported the synthesis of pteridin-4(3*H*)-ones by such a route in a preliminary communication.[17] This paper reports detailed results on the synthesis of methyl 3-(triphenylphosphoranylideneamino)pyrazine-2-carboxylate **6**, together with a crystal structure of this compound and its use in the synthesis of 2,3-disubstituted pteridin-4(3*H*)-ones. Pteridine derivatives are of importance since their tetrahydro derivatives (*e.g.* tetrahydrofolic acid) are coenzymes for neurotransmitters (catecholamines and indoleamines),[18] pyrimidine nucleotides,[19] and methionine;[20] further, methotrexate and its analogues have been shown to possess potent, broad spectrum antitumour activity.[21] Although there are several syntheses of the pteridine skeleton by condensation of guanidines, the synthesis of 2,3-disubstituted pteridin-4(3*H*)-ones by such routes is problematic.[22] We report here a convenient synthesis of such compounds by utilizing an aza-Wittig reaction/heterocyclization sequence.

Results and discussion

Direct azidation of 3-aminopyrazine-2-carboxylic acid by the standard method using sodium nitrite and sodium azide in aqueous acid failed to afford the corresponding azide, presumably because either the diazo intermediate decomposes and/or the products are difficult to extract. Attempted azidation of the methyl ester derivative, **1** under the similar conditions afforded only the side products **3** and **4** in moderate yields (49 and 40%, respectively). These results indicated that the corresponding diazonium intermediate was too reactive and reacted with chloride ion and hydroxide ion in the solution before reacting with azide anion to produce azide **2**. As a second approach, the 3-chloro derivative **3**, readily obtained from the 3-hydroxy derivative **4**, was treated with sodium azide in DMF to give, by nucleophilic azidation,[23] the tetrazolo[1,5-*a*]pyrazine derivative **5** (68%) (Scheme 1).

Recent deoxidative azidation of pyrazine *N*-oxide with trimethylsilyl azide is known to be ineffective for derivatives containing an electron-withdrawing substituent, *e.g.* a CO_2Me group.[23] Since azide–tetrazole equilibration is well documented,[24] compounds **5** were treated with triphenylphosphine (1.1 equiv.) in benzene at reflux for 2 h to afford quantitatively the corresponding iminophosphorane **6**, *via* the Staudinger reaction (Scheme 1).[4] The iminophosphorane **6** was also obtained, and more conveniently in 96% yield, as pale yellow crystals by a modified Kirsanov reaction[4] of methyl 3-aminopyrazine-2-carboxylate **1** with *in situ* generated dichlorotriphenylphosphorane using a hexachloroethane–triphenylphosphine–triethylamine reagent system (Scheme 1).[25] The same reaction using carbon tetrachloride instead of hexachloroethane gave **6** only in modest yield (42%) presumably as a result of a side reaction. The molecular structure was supported by the spectral data (IR, ^1H NHR, ^{13}C NMR and mass spectrum) and an X-ray crystallographic analysis. As summarized in Fig. 1 and Table 1, the imino(triphenyl)phosphorane structure was supported by the similarity of the P–N bond length and N–P–C bond angle to those reported for *p*-bromophenylimino(triphenyl)phosphorane (P–N bond length: 1.567 Å, P–N–C bond angle: 124.2°)[26] and *N*-[2-(triphenylphosphoranylideneamino)benzoyl]-L-valine ethyl ester (1.601 Å, 124.0°).[27]



Scheme 1

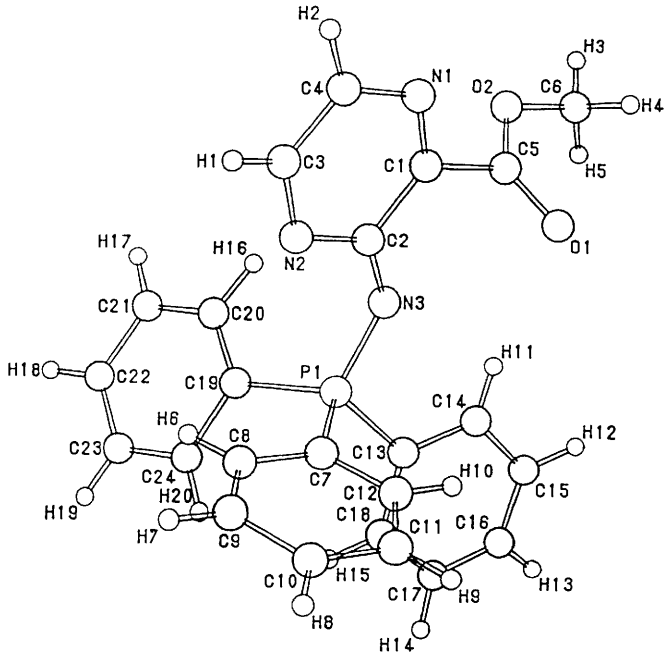


Fig. 1 X-Ray structure of the pyrazin-2-yliminophosphorane **6** showing the atom labelling

Table 1 Bond lengths and bond angles of **6**

Bond length (Å)		Bond angle (°)	
P(1)–N(3)	1.60	N(3)–P(1)–C(7)	116.0
P(1)–C(7)	1.83	N(3)–P(1)–C(13)	104.1
P(1)–C(13)	1.81	N(3)–P(1)–C(19)	112.0
P(1)–C(19)	1.80	P(1)–N(3)–C(2)	125.0
C(2)–N(3)	1.32		

Table 2 R = Ph

Entry	R'Y	Compd.	Yield (%)[a]
1	MeO	**10a**	70
2	EtO	**10b**	45
3	PrO	**10c**	44
4	Pr^iO	**10d**	36
5	Et_2N	**10e**	92

[a] Isolated yields.

In confirming the iminophosphorane structure of **6**, we examined its reaction with phenyl isocyanate. A mixture of **6** and phenyl isocyanate (3.5 equiv.) in dry benzene was stirred at room temperature. After disappearance of **6** (TLC monitored), the products were purified on a silica gel column chromatography to give the urea derivative **8** (34%) and the unwanted pteridinone **9a** (31%) the identity of which was established on the basis of spectral results. Isolation of these products indicates, most reasonably, that the reaction involves formation of the corresponding carbodiimide **7**, followed by addition of aniline which might be generated *via* decomposition of phenyl isocyanate by moisture (Scheme 2). Encouraged by the above findings, we treated **7** with the appropriate alcohols or secondary amines in order to prepare other pteridin-4(3*H*)-ones (Scheme 2). Generally, the carbodiimide **7** was formed from **6** with isocyanate (3.5 equiv.) in benzene at room temperature (TLC monitored) after which an alcohol or an amine (excess) was added and the mixture heated for 3 h. Purification of the reaction mixture by silica gel column chromatography gave 2,3-disubstituted pteridin-4(3*H*)-one derivatives **10** in 29–92% overall yields (see Tables 2–4). In these stepwise reactions, completion of cyclization was difficult to determine because moisture-induced decomposition of the intermediate **B** to **1** and carbamates or ureas occurred during TLC (Scheme 2). Therefore, low-yield entries might well be improved by longer periods of heating. Additionally, the intermolecular aza-Wittig reaction of **6** with alkyl isocyanates (R = Pr, Pr^i, $PhCH_2$ and 1-adamantyl, *etc.*) was very slow at room temperature although proceeding smoothly at 40–140 °C. In the case of 1-adamantyl isocyanates, however, severe steric hindrance prevented reaction even after 7 days at 140 °C. Also, with isopropyl isocyanate at 140 °C, large amounts of unwanted side-product were produced.

Table 3 R = Alkyl, R'Y = MeO

Entry	R	Compd.	Yield (%)[a]
1	Pr	**10f**	85
2	Pr^i	**10g**	Trace[b]
3	Bn	**10h**	44

[a] Isolated yields. [b] Compound **9b** was obtained instead of **10g**. **9b** was 3-isopropyl-2-isopropylaminopteridin-4(3*H*)-one.

Table 4 R = Aryl, R'Y = MeO

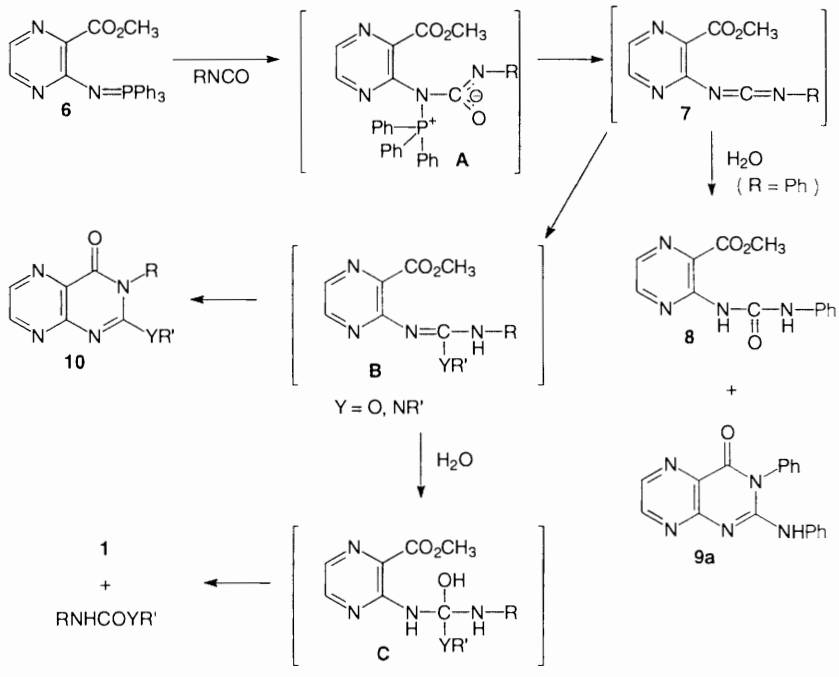
Entry	R	Compd.	Yield (%)[a]
1	$4\text{-}CH_3C_6H_4$	**10i**	55
2	$3\text{-}CH_3C_6H_4$	**10j**	55
3	$2\text{-}CH_3C_6H_4$	**10k**	29
4	$4\text{-}CH_3OC_6H_4$	**10l**	55
5	$3\text{-}CH_3OC_6H_4$	**10m**	81
6	$2\text{-}CH_3OC_6H_4$	**10n**	53
7	$3\text{-}CF_3C_6H_4$	**10o**	48
8	$4\text{-}ClC_6H_4$	**10p**	77
9	1-Naphthyl	**10q**	30

[a] Isolated yields.

Table 5

Entry	R	R′	Compd.	**12** Yield (%)[a]	**13** Yield (%)
1	Ph	Pr^i	**a**	82	ND[b]
2	Ph	Allyl	**b**	45	39
3	Ph	Prop-2-ynyl	**c**	32	ND
4	4-ClC_6H_4	Allyl	**d**	55	16
5	4-ClC_6H_4	Prop-2-ynyl	**e**	18	ND
6	4-$CH_3OC_6H_4$	Allyl	**f**	28	20

[a] Isolated yields. [b] ND Not detected.



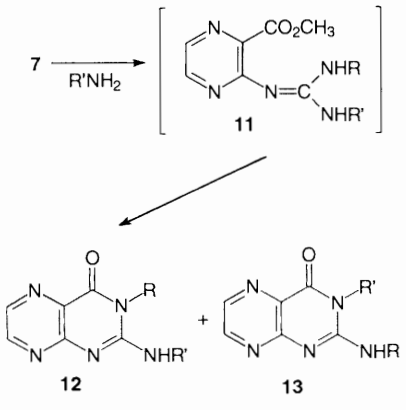
Scheme 2

Table 6

Entry	R	Compd.	Yield (%)[a]
1	Ph	**15a**	99
2	4-ClC_6H_4	**15b**	100
3	4-$CH_3OC_6H_4$	**15c**	87

[a] Isolated yields.

Results for the cyclization of **7** with primary amines are summarized in Table 5. Two isomeric pteridin-4(3*H*)-ones **12** and **13** may be produced in the reaction of **7** with primary amines *via* a guanidine-type intermediate **11** (Scheme 3). In fact,

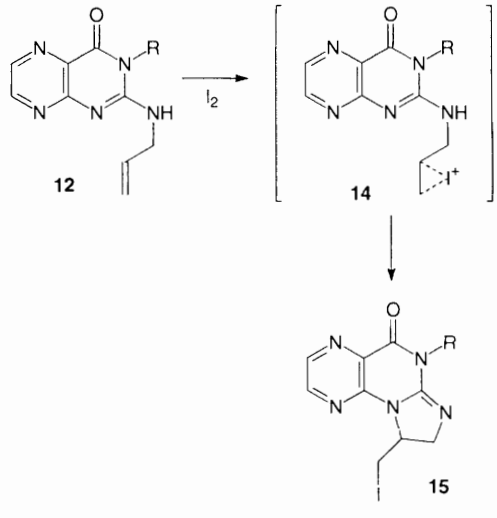


Scheme 3

the reaction with allylamine gave **12** and **13** but the reaction with isopropylamine afforded only **12**, compound **13** not being formed for steric reasons.

2-Allylaminopteridin-4(3*H*)-one derivatives **12** were further converted into imidazolo[1,2-*a*]pteridines **15** by treatment with iodine in high yield (Scheme 4, Table 6). Pteridines, biologically important polyazaheterocycles, may usefully be synthesized by the route described above.[28]

In summary, we have demonstrated that the *N*-heteroaryliminophosphorane, methyl 3-(triphenylphosphoranylideneamino)pyrazine-2-carboxylate **6**, can be obtained in high yield as a relatively stable crystalline compound by a modified Kirsanov reaction. The iminophosphorane structure was evidenced by an X-ray crystallographic analysis. The iminophosphorane **6** was a useful intermediate for the synthesis of



Scheme 4

2,3-disubstituted pteridin-4(3*H*)-ones by an intermolecular aza-Wittig reaction with isocyanates followed by heterocyclization with alcohols or amines. The further application of aza-Wittig reaction methodology to the synthesis of various fused-pyrimidine derivatives is in progress in our laboratories.

Experimental

General

Thin layer chromatography (TLC) was performed on E. Merck Kieselgel 60 F_{254} pre-coated silica plates (0.15 mm layer thickness). Melting points were determined with a Yanagimoto micro-melting-point hot-stage apparatus and are uncorrected. ^1H 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 [$^2H_6$]-DMSO solution with Me_4Si as internal standard. Chemical shifts are reported in ppm (δ). Coupling constants, J_H and J_C values, are given in Hz. IR spectra 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/or CI, 70 eV). Microanalyses were performed with a Perkin-Elmer 2400S elemental analyser. Flash chromatography was performed with a silica gel column (Fuji Davison BW-300) 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_2, distilled, and stored over 3 Å molecular sieves. All reactions were carried out under nitrogen. Methyl 3-aminopyrazine-2-carboxylate **1** was purchased from Tokyo Kasei Co., Ltd. This reagent was used without further purification.

Preparation of azide derivatives from amine derivatives

To an ice-cooled solution of anthranilic acid (5.001 g, 36.47 mmol) in concentrated hydrochloric acid (18 mol dm^{-3}; 36 cm^3) and water (36 cm^3) was added dropwise a solution of sodium nitrite (2.776 g, 40.23 mmol, 1.1 equiv.) in water (30 cm^3) at a rate such that the temperature of the reaction mixture remained < 5 °C. After completion of the nitrite addition, the diazonium solution was filtered and added dropwise to a stirred solution of sodium azide (2.608 g, 40.12 mmol, 1.1 equiv.) and sodium acetate (36.00 g) in water (60 cm^3). The solution was stirred for 15 min after which it was acidified with concentrated hydrochloric acid to give *o*-azidobenzoic acid as white needles (4.100 g, 25.13 mmol, 69%). However, similar azidation of methyl 3-aminopyrazine-2-carboxylate **1** (505 mg, 3.30 mmol) as a starting material failed to afford an azide derivative but, instead, the esters **3** and **4** together with recovered ester **1** (23.3 mg, 0.15 mmol, 5%) were obtained after silica gel column chromatography (H:A 3:1, v/v).

Methyl 3-chloropyrazine-2-carboxylate 3. White solid (277 mg, 1.61 mmol, 49%), mp 39–40 °C (Found: C, 42.0; H, 2.8; N, 16.1. $C_6H_5ClN_2O_2$ requires C, 41.76; H, 2.92; N, 16.23%); R_F 0.51 (H:A 1:1); ν_{max}(neat)/cm^{-1} 2957, 1744, 1551, 1528, 1447, 1383, 1298, 1152, 1071, 849 and 756; δ_H($CDCl_3$, 200 MHz) 8.61 (1 H, d, *J* 2.4), 8.56 (1 H, d, *J* 2.4) and 4.05 (3 H, s); δ_C($CDCl_3$, 50 MHz) 164.1, 148.2, 146.1, 144.5, 142.2 and 53.6; *m/z* 172 (M^+, 19%), 149 (16), 144 (20), 143 (12), 142 (61), 141 (31), 116 (28), 115(18), 114 (100), 113 (51) and 86 (12).

Methyl 3-hydroxypyrazine-2-carboxylate 4. Pale yellow solid (205 mg, 1.33 mmol, 40%), mp 155–156 °C (Found: C, 46.9; H, 3.8; N, 18.2. $C_6H_6N_2O_3$ requires C, 46.76; H, 3.92; N, 18.18%); R_F 0.11 (H:A 1:1); ν_{max}(KBr)/cm^{-1} 2951, 1717, 1682, 1665, 1597, 1458, 1321, 1200, 1155, 837 and 806; δ_H([$^2H_6$]-DMSO, 200 MHz) 12.86 (1 H, br), 7.72 (1 H, d, *J* 3.6), 7.47 (1 H, d, *J* 3.6) and 3.81 (3 H, s); δ_C([$^2H_6$]-DMSO, 50 MHz) 164.7, 154.4, 145.5, 133.1, 124.0 and 52.4; *m/z* 154 (M^+, 62%), 124 (51), 123 (11), 96 (100), 95 (31), 94 (27), 68 (53) and 67 (11).

Synthesis of methyl 3-chloropyrazine-2-carboxylate 3 from methyl 3-hydroxypyrazine-2-carboxylate 4

To a solution of the ester **4** (41.0 mg, 0.266 mmol) in dry toluene (4 cm^3) was added thionyl chloride (0.02 cm^3, 0.276 mmol, 1.0 equiv.) and a catalytic amount of DMF (one drop) by syringe. After the mixture had been stirred at 80 °C under nitrogen for 3 h, it was evaporated under reduced pressure, and the residue was purified by column chromatography (silica gel, H:A 2:1, v/v as eluent) to afford the title ester **3** (36.8 mg, 0.213 mmol, 80%).

Synthesis of methyl tetrazolo[1,5-*a*]pyrazine-4-carboxylate 5

A solution of the ester **3** (116 mg, 0.67 mmol) and sodium azide (88 mg, 1.35 mmol, 2.0 equiv.) in DMF (4 cm^3) was stirred at 120 °C under nitrogen for 1 h. After completion of the reaction (TLC), the mixture was diluted with water (10 cm^3) and extracted with chloroform (50 cm^3 × 3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to afford the crude product which was purified on a silica gel column using H:A (1:1, v/v) as an eluent to give the title ester as a yellow solid **5** (82 mg, 0.46 mmol, 68%), mp 136–137 °C (Found: M^+, 179.0447. $C_6H_5N_5O_2$ requires *M*, 179.0443); R_F 0.30 (H:A, 1:2); ν_{max}(KBr)/cm^{-1} 3094, 1736, 1474, 1439, 1354, 1327, 1254, 1146, 1103, 1076, 1001 and 804; δ_H([$^2H_6$]-DMSO, 200 MHz) 9.69 (1 H, d, *J* 4.6), 8.69 (1 H, d, *J* 4.6) and 4.05 (3 H, s); δ_C([$^2H_6$]-DMSO, 50 MHz) 161.8, 143.9, 141.5, 133.0, 123.2 and 53.5; *m/z* 179 (M^+, 7%), 151 (57), 148 (56), 121 (22), 106 (24), 95 (13), 94 (11), 93 (91), 92 (11), 80 (100), 79 (74), 69 (11), 67 (24), 66 (14) and 65 (17).

Synthesis of *N*-heteroaryl iminophosphoranes; methyl 2-(triphenylphosphoranylidene)aminopyrazine-3-carboxylate 6

To a mixture of the ester **1** (271 mg, 1.77 mmol), hexachloroethane (627 mg, 2.65 mmol, 1.5 equiv.) and triphenylphosphine (696 mg, 2.66 mmol, 1.5 equiv.) in dry benzene (20 cm^3) was added dropwise triethylamine (436 mg, 4.30 mmol, 2.4 equiv.). The resultant mixture was heated at reflux for 5 h under nitrogen, after which it was cooled, filtered to remove the precipitate and evaporated under reduced pressure to afford a solid residue which was purified on a silica gel column using AcOEt–hexane (1:1, v/v) as an eluent to give the corresponding iminophosphorane **6** (702 mg, 1.70 mmol, 96%).

Alternative synthesis of *N*-heteroaryl iminophosphoranes; the ester 6 from the tetrazole 5

A mixture of the ester **5** (78 mg, 0.44 mmol) and triphenylphosphine (126 mg, 0.48 mmol, 1.1 equiv.) in dry benzene (10 cm^3) was heated at reflux for 2 h under nitrogen. The mixture was then evaporated under reduced pressure to afford a residue which was purified on a silica gel column using H:A (1:1, v/v) as an eluent to give the corresponding iminophosphorane **6** (180 mg, 0.44 mmol, 100%) as a pale yellow solid mp 148–149 °C (Found: C, 69.8; H, 4.8; N, 10.2. $C_{24}H_{20}N_3O_2P$ requires: C, 69.73; H, 4.88; N, 10.16%); R_F 0.47 (H:A 1:1); ν_{max}(KBr)/cm^{-1} 3061, 2948, 1740, 1555, 1505, 1458, 1433, 1277, 1132, 1115, 721 and 694; δ_H($CDCl_3$, 200 MHz) 7.81–7.93 (7 H, m), 7.75 (1 H, d, *J* 2.4), 7.40–7.59 (9 H, m) and 4.03 (3 H, s); δ_C($CDCl_3$, 50 MHz) 167.1, 158.9 (d, *J* 6.5), 144.7, 137.8 (d, *J* 22.9), 133.6 (d, *J* 10.0), 132.3 (d, *J* 1.3), 131.5, 129.4, (d, *J* 100.5), 128.8 (d, *J* 12.5) and 52.4; *m/z* 413 (M^+, 23%), 399 (25), 398 (100), 354 (20), 352 (8), 277 (6), 262 (12), 261 (6), 201 (7), 183 (25) and 108 (10).

Synthesis of the pteridin-4(3*H*)-ones 10a–q: general procedure

To a solution of the iminophosphorane **6** (103 mg, 0.25 mmol) in dry benzene (10 cm^3) was added dropwise an appropriate isocyanate (*ca.* 3.5 equiv.) with exclusion of moisture. After the mixture had been stirred at room temperature overnight, the iminophosphorane **6** had disappeared (TLC) and it was

therefore treated with an appropriate alcohol or amine (*ca.* 10 equiv.). The resultant solution was stirred at 85 °C (benzene reflux) for 3 h after which it was evaporated under reduced pressure and the solid residue was purified on a silica gel column using H:A (1:1→1:2→only A, v/v) as eluents to give the pteridin-4(3*H*)-one derivatives **10** (*e.g.* **10a**; 44.6 mg, 0.175 mol, 70%). In the absence of an alcohol or amine under these conditions (*vide supra*), none of the desired pteridin-4(3*H*)-one derivatives were obtained but instead, the urea derivatives **8** and the unwanted pteridin-4(3*H*)-one derivative **9a** were produced.

Methyl 2-(phenylcarbamoylamino)pyrazine-3-carboxylate 8. Pale yellow solid (18.4 mg, 68%), mp 162–163 °C (Found: M^+, 272.0916. $C_{13}H_{12}N_4O_3$ requires *M*, 272.0909); R_F 0.13 (H:A 1:1); ν_{max}(KBr)/cm^{-1} 2924, 1698, 1613, 1561, 1476, 1447, 1310, 1262, 1115, 1024 and 814; δ_H($CDCl_3$, 200 MHz) 11.17 (1 H, br), 10.30 (1 H, br), 8.45 (1 H, d, *J* 2.3), 8.37 (1 H, d, *J* 2.3), 7.56–7.62 (2 H, m), 7.32–7.41 (2 H, m), 7.08–7.17 (1 H, m) and 4.08 (3 H, s); δ_C($CDCl_3$, 50 MHz) 166.3, 151.5, 150.7, 144.6, 138.2, 136.6, 129.4, 127.9, 124.4, 120.8 and 53.8; *m*/*z* 272 (M^+, 52%), 153 (76), 148 (11), 123 (12), 120 (22), 119 (27), 95 (59), 94 (16), 93 (100), 91 (10) and 77 (11).

2-Anilino-3-phenylpteridin-4(3*H*)-one 9a. Pale yellow solid (9.8 mg, 31%), mp 245–246 °C (Found: M^+, 315.1108. $C_{18}H_{13}N_5O$ requires: *M*, 315.1120); R_F 0.16 (H:A 1:2); ν_{max}(KBr)/cm^{-1} 2996, 1703, 1605, 1589, 1561, 1474, 1451, 1408, 1269, 1026, 750 and 694; δ_H($CDCl_3$, 200 MHz) 8.79 (1 H, d, *J* 2.1), 8.59 (1 H, d, *J* 2.1), 7.66–7.78 (3 H, m), 7.45–7.56 (4 H, m), 7.30–7.39 (2 H, m), 7.12–7.20 (1 H, m) and 6.26 (1 H, s); δ_H([$^2H_6$]-DMSO, 200 MHz) 8.75 (1 H, d, *J* 2.1), 8.50 (1 H, d, *J* 2.1), 8.01 (1 H, s), 7.53–7.69 (5 H, m), 7.43–7.49 (2 H, m), 7.29–7.34 (2 H, m) and 7.12–7.20 (1 H, m); δ_C([$^2H_6$]-DMSO, 50 MHz) 161.4, 155.7, 151.4, 150.4, 140.6, 138.3, 134.7, 130.5, 130.1, 129.6, 128.5 and 125.2 (two quaternary carbons were not detected); *m*/*z* 315 (M^+, 37%), 314 (100), 286 (2), 238 (2), 223 (4), 195 (7), 169 (2), 168 (2), 92 (2) and 77 (14).

2-Methoxy-3-phenylpteridin-4(3*H*)-one 10a. Pale yellow solid (44.6 mg, 70%), mp 193–195 °C (Found: M^+, 254.0804. $C_{13}H_{10}N_4O_2$ requires *M*, 254.0804); R_F 0.21 (A); ν_{max}(KBr)/cm^{-1} 3061, 1707, 1605, 1595, 1561, 1537, 1447, 1410, 1354, 1290, 1090, 961 and 694; δ_H($CDCl_3$, 200 MHz) 8.87 (1 H, d, *J* 2.0), 8.73 (1 H, d, *J* 2.0), 7.26–7.31 (3 H, m), 7.15–7.17 (2 H, m) and 4.11 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.5, 156.1, 154.6, 150.4, 143.1 134.1 131.9, 130.0, 129.9, 128.3 and 57.1; *m*/*z* 254 (M^+, 100%), 253 (10), 239 (18), 237 (26), 233 (7), 196 (5), 195 (15), 134 (5) and 119 (21).

2-Ethoxy-3-phenylpteridin-4(3*H*)-one 10b. Pale yellow solid (15.6 mg, 45%), mp 205–208 °C (Found: M^+, 268.0961. $C_{14}H_{12}N_4O_2$ requires *M*, 268.0960); R_F 0.25 (A); ν_{max}(KBr)/cm^{-1} 2922, 1715, 1589, 1561, 1535, 1426, 1393, 1329, 1296, 1090, 1011, 901 and 698; δ_H($CDCl_3$, 200 MHz) 8.86 (1 H, d, *J* 2.0), 8.71 (1 H, d, *J* 2.0), 7.52–7.56 (3 H, m), 7.25–7.30 (2 H, m), 4.62 (2 H, q, *J* 7.1) and 1.30 (3 H, t, *J* 7.1); δ_C($CDCl_3$, 50 MHz) 161.6, 155.5, 154.7, 150.4, 143.0, 134.6 131.8, 129.9, 129.7, 128.3, 66.4 and 14.1; *m*/*z* 268 (M^+, 39%), 240 (100), 239 (15), 212 (13), 195 (12), 121 (15), 120 (26), 119 (14), 105 (14), 104 (34), 93 (16) and 77 (17).

3-Phenyl-2-propoxypteridin-4(3*H*)-one 10c. Pale yellow solid (10.3 mg, 44%), mp 185–187 °C (Found: M^+, 282.1121. $C_{15}H_{14}N_4O_2$ requires *M*, 282.1117); R_F 0.25 (A); ν_{max}(KBr)/cm^{-1} 2924, 1713, 1593, 1561, 1539, 1476, 1426, 1391, 1331, 1294, 1092, 937, 824 and 694; δ_H($CDCl_3$, 200 MHz) 8.85 (1 H, d, *J* 2.1), 8.71 (1 H, d, *J* 2.1), 7.49–7.56 (3 H, m), 7.26–7.31 (2 H, m), 4.51 (2 H, t, *J* 6.5), 1.67 (2 H, tq, *J* 6.5, 7.4) and 0.82 (3 H, t, *J* 7.4); δ_C($CDCl_3$, 50 MHz) 161.6, 155.8, 154.7, 150.3, 142.9 134.6 131.8, 129.9, 129.7, 128.2, 71.9, 21.8 and 10.1; *m*/*z* 282 (M^+, 31%), 241 (49), 240 (100), 239 (30), 212 (38), 195 (18), 148 (18), 121 (33), 120 (35), 119 (26), 93 (30) and 77 (20).

2-Isopropoxy-3-phenylpteridin-4(3*H*)-one 10d. Pale yellow solid (11.3 mg, 36%), mp 148–149 °C (Found: M^+, 282.1121. $C_{15}H_{14}N_4O_2$ requires *M*, 282.1117); R_F 0.30 (A); ν_{max}(KBr)/cm^{-1} 2924, 1719, 1588, 1561, 1541, 1420, 1375, 1294, 1090, 916, 824 and 694; δ_H($CDCl_3$, 200 MHz) 8.85 (1 H, d, *J* 2.1), 8.70 (1 H, d, *J* 2.1), 7.49–7.60 (3 H, m), 7.23–7.29 (2 H, m), 5.62 (1 H, sep, *J* 6.2) and 1.30 (6 H, d, *J* 6.2); δ_C($CDCl_3$, 50 MHz) 161.7, 155.2, 150.3, 142.8, 134.7, 131.8, 129.8, 129.7, 129.6, 128.2, 74.6 and 21.6; *m*/*z* 282 (M^+, 29%), 241 (16), 240 (100), 239 (12), 212 (12), 195 (12), 148 (12), 121 (16), 120 (16), 119 (13) and 93 (13).

2-Diethylamino-3-phenylpteridin-4(3*H*)-one 10e. Pale yellow solid (67.8 mg, 92%), mp 154–155 °C (Found: M^+, 295.1442. $C_{16}H_{17}N_5O$ requires *M*, 295.1433); R_F 0.23 (A); ν_{max}(KBr)/cm^{-1} 2990, 1701, 1555, 1528, 1478, 1415, 1385, 1279, 1213, 1078, 822 and 750; δ_H($CDCl_3$, 200 MHz) 8.75 (1 H, d, *J* 2.1), 8.54 (1 H, d, *J* 2.1), 7.58–7.34 (5 H, m), 3.28 (4 H, q, *J* 7.1) and 0.91 (6 H, t, *J* 7.1); δ_C($CDCl_3$, 50 MHz) 162.8, 156.7, 155.3, 150.5, 141.5, 138.2, 130.8, 129.8, 129.0, 128.9, 45.3 and 12.4; *m*/*z* 295 (M^+, 34%), 267 (17), 266 (100), 223 (10), 195 (14), 191 (9), 190 (23), 176 (18), 149 (14) and 119 (10).

2-Methoxy-3-propylpteridin-4(3*H*)-one 10f. Pale yellow solid (26.7 mg, 86%), mp 123–124 °C (Found: M^+, 220.0968. $C_{10}H_{12}N_4O_2$ requires *M*, 220.0960); R_F 0.22 (A); ν_{max}(KBr)/cm^{-1} 2967, 1703, 1597, 1559, 1541, 1453, 1420, 1265, 1229, 1192, 988 and 739; δ_H($CDCl_3$, 200 MHz) 8.83 (1 H, d, *J* 2.2), 8.69 (1 H, d, *J* 2.2), 4.24 (3 H, s), 4.13 (2 H, t, *J* 7.6), 1.76 (2 H, sext, *J* 7.6, 1.8) and 1.00 (3 H, t, *J* 7.4); δ_C($CDCl_3$, 50 MHz) 161.5, 156.4, 154.2, 150.1, 142.9, 131.2, 56.8, 44.2, 21.4 and 11.2; *m*/*z* 220 (M^+, 100%), 205 (8), 192 (9), 179 (26), 178 (34), 177 (19), 163 (13), 148 (13), 148 (62), 121 (9), 120 (48), 93 (12) and 79 (10).

In the case of 1-isopropyl isocyanate the major compound was **9b** not **10g**.

2-Isopropylamino-3-(1-methylethyl)pteridin-4(3*H*)-one 9b. Pale yellow solid (8.9 mg, 35%), mp 191–192 °C (Found: M^+, 247.1436. $C_{12}H_{17}N_5O$ requires *M*, 247.1433); R_F 0.21 (A); ν_{max}(KBr)/cm^{-1} 3007, 1711, 1568, 1535, 1478, 1420, 1364, 1269, 1225, 1182, 1128, 777 and 737; δ_H($CDCl_3$, 200 MHz) 8.67 (1 H, d, *J* 2.0), 8.46 (1 H, d, *J* 2.0), 5.53 (1 H, quint, *J* 7.2), 4.80 (1 H, d, *J* 6.8), 4.62 (1 H, sep, *J* 6.5), 1.60 (6 H, d, *J* 7.2) and 1.36 (6 H, d, *J* 6.5); δ_C($CDCl_3$, 50 MHz) 162.3, 155.6, 151.5, 150.3, 140.6, 129.7, 45.1, 44.4, 22.9 and 20.1; *m*/*z* 247 (M^+, 100%), 205 (25), 204 (71), 190 (17), 164 (43), 163 (16), 162 (52), 149 (18), 147 (7), 136 (7), 120 (10), 119 (18) and 94 (9).

3-Benzyl-2-methoxypteridin-4(3*H*)-one 10h. White solid (17.1 mg, 44%), mp 161–162 °C (Found: M^+, 268.0962. $C_{14}H_{12}N_4O_2$ requires *M*, 268.0960); R_F 0.26 (A); ν_{max}(KBr)/cm^{-1} 3046, 2957, 1705, 1597, 1561, 1451, 1408, 1262, 1219, 1113, 988, 737, 710 and 694; δ_H($CDCl_3$, 200 MHz) 8.82 (1 H, d, *J* 2.0), 8.70 (1 H, d, *J* 2.0), 7.41–7.47 (2 H, m), 7.29–7.38 (3 H, m), 5.34 (2 H, s) and 4.22 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.7, 156.2, 154.2, 150.3, 143.0, 135.9, 131.4, 129.047, 129.015, 128.5, 57.0 and 45.7; *m*/*z* 268 (M^+, 100%), 253 (11), 236 (8), 225 (11), 208 (7), 163 (11), 148 (9), 120 (9), 104 (7) and 91 (34).

2-Methoxy-3-*p*-tolylpteridin-4(3*H*)-one 10i. White solid (15.3 mg, 55%), mp 205–209 °C (Found: M^+, 268.0971. $C_{14}H_{12}N_4O_2$ requires *M*, 268.0960); R_F 0.28 (A); ν_{max}(KBr)/cm^{-1} 2957, 1711, 1603, 1449, 1408, 1356, 1294, 1092, 1040, 968, 822 and 737; δ_H($CDCl_3$, 200 MHz) 8.86 (1 H, d, *J* 2.0), 8.72 (1 H, d, *J* 2.0), 7.32–7.38 (2 H, m), 7.13–7.19 (2 H, m), 4.11 (3 H, s) and 2.45 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.6, 156.2, 154.5, 150.3, 143.1, 140.0, 131.8, 130.7, 128.2, 127.9, 57.1 and 21.4; *m*/*z* 268 (M^+, 100%), 267 (28), 253 (55), 251 (41), 237 (21), 209 (26), 133 (50), 132 (22), 105 (35), 104 (21) and 91 (25).

2-Methoxy-3-*m*-tolylpteridin-4(3*H*)-one 10j. Pale yellow solid (26.4 mg, 55%), mp 191–192 °C (Found: M^+, 268.0959. $C_{14}H_{12}N_4O_2$ requires: *M*, 268.0960); R_F 0.29 (A); ν_{max}(KBr)/cm^{-1} 2922, 1717, 1603, 1561, 1539, 1443, 1408, 1350, 1294, 1194, 1094, 737 and 694; δ_H($CDCl_3$, 200 MHz) 8.86 (1 H, d, *J* 2.1), 8.72 (1 H, d, *J* 2.1), 7.40–7.48 (1 H, m), 7.29–7.34 (1 H, m), 7.05–7.10 (2 H, m), 4.11 (3 H, s) and 2.44 (3 H, s); δ_C($CDCl_3$, 50 MHz)

161.5, 156.1, 154.5, 150.3, 143.1, 140.2, 134.3, 131.8, 130.7, 129.8, 128.7, 125.1, 57.1 and 21.4; *m/z* 268 (M^+, 100%), 267 (12), 253 (22), 251 (21), 209 (11), 133 (18), 105 (9), 104 (8) and 91 (11).

2-Methoxy-3-*o*-tolylpteridin-4(3*H*)-one 10k. Pale yellow solid (8.3 mg, 29%), mp 144–146 °C (Found: M^+, 268.0961. $C_{14}H_{12}N_4O_2$ requires *M*, 268.0960); R_F 0.27 (A); ν_{max}(K-Br)/cm^{-1} 2957, 1713, 1601, 1562, 1541, 1447, 1412, 1354, 1300, 785 and 762; δ_H($CDCl_3$, 200 MHz) 8.88 (1 H, d, *J* 2.0), 8.74 (1 H, d, *J* 2.0), 7.33–7.44 (3 H, m), 7.15–7.20 (1 H, m), 4.11 (3 H, s) and 2.14 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.0, 156.1, 154.8, 150.4, 143.2, 135.8, 133.7, 131.8, 131.7, 130.2, 128.3, 127.7, 57.2 and 17.5; *m/z* 268 (M^+, 100%), 253 (10), 252 (16), 251 (98), 238 (10), 237 (67), 208 (16), 133 (14), 105 (10) and 104 (13).

2-Methoxy-3-(4-methoxyphenyl)pteridin-4(3*H*)-one 10l. White solid (17.6 mg, 55%), mp 170–173 °C (Found: M^+, 284.0898. $C_{14}H_{12}N_4O_3$ requires *M*, 284.0909); R_F 0.25 (A); ν_{max}(KBr)/cm^{-1} 2959, 1711, 1599, 1561, 1512, 1445, 1410, 1354, 1298, 1250, 1092 and 1026; δ_H($CDCl_3$, 500 MHz) 8.86 (1 H, d, *J* 2.0), 8.72 (1 H, d, *J* 2.5), 7.17–7.20 (2 H, m), 7.04–7.07 (2 H, m), 4.11 (3 H, s) and 3.88 (3 H, s); δ_C($CDCl_3$, 125 MHz) 161.6, 160.3, 156.2, 154.3, 150.1, 142.9, 131.7, 129.1, 126.7, 115.1, 57.2, 55.8; *m/z* 284 (M^+, 100%), 283 (6), 269 (16), 253 (6), 241 (10), 226 (7), 225 (7), 149 (31), 134 (17), 121 (8) and 106 (8).

2-Methoxy-3-(3-methoxyphenyl)pteridin-4(3*H*)-one 10m. White solid (46.5 mg, 81%), mp 172–173 °C (Found: M^+, 284.0918. $C_{14}H_{12}N_4O_3$ requires *M*, 284.0909); R_F 0.26 (A); ν_{max}(KBr)/cm^{-1} 3000, 1719, 1597, 1561, 1539, 1447, 1412, 1354, 1290, 1032 and 743; δ_H($CDCl_3$, 200 MHz) 8.86 (1 H, d, *J* 2.2), 8.72 (1 H, d, *J* 2.2), 7.46 (1 H, t, *J* 8.1), 7.05 (1 H, ddd, *J* 8.4, 2.6, 0.9), 6.87 (1 H, ddd, *J* 7.7, 1.9, 0.9), 6.82 (1 H, t, *J* 2.0), 4.11 (3 H, s) and 3.84 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.4, 160.9, 156.0, 154.5, 150.3, 143.1, 135.4, 131.8, 130.7, 120.3, 115.4, 114.1, 57.1 and 56.6; *m/z* 284 (M^+, 100%), 283 (16), 269 (15), 267 (13), 253 (7), 226 (6), 225 (11), 149 (18) and 120 (6).

2-Methoxy-3-(2-methoxyphenyl)pteridin-4(3*H*)-one 10n. Pale yellow solid (30.3 mg, 53%), mp 166–168 °C (Found: M^+, 284.0895. $C_{14}H_{12}N_4O_3$ requires *M*, 284.0909); R_F 0.25 (A); ν_{max}(KBr)/cm^{-1} 2928, 1717, 1605, 1561, 1539, 1503, 1445, 1410, 1354, 1271, 1119, 1024 and 754; δ_H($CDCl_3$, 200 MHz) 8.85 (1 H, d, *J* 2.1), 8.71 (1 H, d, *J* 2.1), 7.45–7.53 (1 H, m), 7.06–7.27 (1 H, m), 4.10 (3 H, s) and 3.79, (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.1, 156.4, 154.9, 150.6, 150.2, 144.9, 142.8, 131.4, 129.6, 127.1, 121.4, 112.5, 57.0 and 56.0; *m/z* 284 (M^+, 83%), 283 (17), 269 (8), 255 (9), 254 (18), 253 (100), 225 (8), 149 (18), 134 (10), 120 (14) and 106 (11).

2-Methoxy-3-(3-trifluoromethylphenyl)pteridin-4(3*H*)-one 10o. Pale yellow solid (32.2 mg, 48%), mp 82–83 °C (Found: M^+, 322.0675. $C_{14}H_9F_3N_4O_2$ requires *M*, 322.0678); R_F 0.07 (H:A 1:1); ν_{max}(KBr)/cm^{-1} 1723, 1607, 1562, 1541, 1447, 1412, 1352, 1333, 1292, 1177, 1138 and 1098; δ_H($CDCl_3$, 200 MHz) 8.89 (1 H, d, *J* 2.0), 8.74 (1 H, d, *J* 2.0), 7.66–7.81 (2 H, m), 7.49–7.59 (2 H, m) and 4.13 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.3, 155.5, 154.5, 150.6, 143.4, 134.9, 132.6 (q, *J* 33.2), 132.0, 131.6, 130.7, 126.8 (q, *J* 3.5), 125.6 (q, *J* 3.9), 123.7 (q, *J* 271.7) and 57.3; *m/z* 322 (M^+, 100%), 307 (14), 305 (29), 277 (9), 264 (8), 263 (15), 187 (27), 159 (16), 149 (8), 145 (8) and 120 (8).

3-(4-Chlorophenyl)-2-methoxypteridin-4(3*H*)-one 10p. Pale yellow solid (46.7 mg, 77%), mp 153–154 °C (Found: M^+, 288.0415. $C_{13}H_9ClN_4O_2$ requires *M*, 288.0414); R_F 0.13 (H:A 1:2); ν_{max}(KBr)/cm^{-1} 1715, 1605, 1562, 1541, 1493, 1476, 1446, 1412, 1354, 1296 and 1090; δ_H($CDCl_3$, 200 MHz) 8.88 (1 H, br), 8.73 (1 H, br), 7.53 (2 H, d, *J* 8.8), 7.24 (2 H, d, *J* 8.8) and 4.12 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.4, 155.9, 154.4, 150.5, 143.2, 135.9, 132.8, 131.6, 130.3, 129.7 and 57.2; *m/z* 290 (M + 2, 32%), 289 (M + 1, 17), 288 (M^+, 100), 273 (18), 271 (15), 257 (7), 229 (9), 155 (8), 153 (25), 148 (7) and 125 (19).

2-Methoxy-3-(1-naphthyl)pteridin-4(3*H*)-one 10q. White solid (9.3 mg, 30%), mp 154–155 °C (Found: M^+, 304.0968. $C_{17}H_{12}N_4O_2$ requires *M*, 322.0960); R_F 0.26 (A); ν_{max}(K-Br)/cm^{-1} 1719, 1655, 1603, 1561, 1541, 1410, 1348, 1117 and 775; δ_H($CDCl_3$, 200 MHz) 8.92 (1 H, d, *J* 2.1), 8.77 (1 H, d, *J* 2.1), 7.96–8.06 (2 H, m), 7.44–7.68 (5 H, m) and 4.03 (3 H, s); δ_C($CDCl_3$, 50 MHz) 156.6, 150.5, 143.3, 134.9, 131.9, 131.2, 130.6, 129.8, 129.2, 128.0, 127.1, 126.6, 126.0, 121.7 and 57.2 (two quaternary carbons were not detected); *m/z* 304 (M^+, 100%), 289 (3), 287 (10), 273 (5), 245 (8), 169 (22), 141 (8), 140 (8), 127 (3) and 114 (3).

2-Isopropylamino-3-phenylpteridin-4(3*H*)-one 12a. Pale yellow solid (58.9 mg, 82%), mp 222–224 °C (Found: M^+, 281.1278. $C_{15}H_{15}N_5O$ requires *M*, 281.1277); R_F 0.20 (A); ν_{max}(KBr)/cm^{-1} 2975, 2928, 1703, 1578, 1561, 1530, 1474, 1414, 1281, 1210, 1127, 733 and 696; δ_H($CDCl_3$, 200 MHz) 8.73 (1 H, d, *J* 2.2), 8.50 (1 H, d, *J* 2.0), 7.60–7.72 (3 H, m), 7.32–7.37 (2 H, m), 4.47 (1 H, sepd, *J* 6.6 and 1.2), 4.23 (1 H, dd, *J* 6.6 and 1.2) and 1.45 (6 H, d, *J* 6.6); δ_C($CDCl_3$, 50MHz) 161.6, 156.4, 151.5, 150.4, 140.6, 134.0, 131.4, 130.9, 129.4, 128.9, 44.3 and 22.6; *m/z* 281 (M^+, 47%), 280 (4), 266 (5), 239 (20), 238 (100), 195 (7), 169 (4), 119 (13), 118 (21) and 77 (15).

2-Allylamino-3-phenylpteridin-4(3*H*)-one 12b. Pale yellow solid (24.9 mg, 45%), mp 217–218 °C (Found: M^+, 279.1125. $C_{15}H_{13}N_5O$ requires *M*, 279.1120); R_F 0.10 (A); ν_{max}(KBr)/cm^{-1} 2922, 1701, 1582, 1562, 1532, 1472, 1414, 1287, 1209, 1101, 731 and 698; δ_H($CDCl_3$, 200 MHz) 8.74 (1 H, d, *J* 2.0), 8.52 (1 H, d, *J* 2.0), 7.59–7.71 (3 H, m), 7.35–7.40 (2 H, m), 5.88 (1 H, ddt, *J* 16.9, 10.5 and 5.4), 5.13 (1 H, dq, *J* 10.8 and 1.3), 5.10 (1 H, dq, *J* 16.9 and 1.5), 4.58 (1 H, t, *J* 5.4) and 4.20 (2 H, tt, *J* 5.6 and 1.6); δ_C($CDCl_3$, 50 MHz) 161.5, 156.3, 152.1, 150.4, 141.0, 133.9, 133.7, 131.5, 131.0, 130.4, 129.0, 117.1 and 44.4; *m/z* 279 (M^+, 100%), 278 (40), 265 (10), 264 (60), 238 (8), 195 (6), 169 (6), 119 (7), 118 (6) and 77 (17).

3-Allyl-2-anilinopteridin-4(3*H*)-one 13b. Pale yellow solid (21.6 mg, 39%), mp 112–113 °C (Found: M^+, 279.1120. $C_{15}H_{13}N_5O$ requires *M*, 279.1120); R_F 0.20 (A); ν_{max}(KBr)/cm^{-1} 2926, 1686, 1561, 1528, 1451, 1412, 1223, 1074 and 691; δ_H($CDCl_3$, 200 MHz) 8.77 (1 H, d, *J* 2.0), 8.58 (1 H, d, *J* 2.0), 7.58–7.63 (2 H, m), 7.37–7.46 (2 H, m), 7.16–7.24 (1 H, m), 7.00 (1 H, br), 6.01 (1 H, ddt, *J* 17.4, 10.0 and 5.4), 5.58 (1 H, dq, *J* 10.0 and 0.8), 5.56 (1 H, dq, *J* 17.4 and 0.8) and 4.01 (2 H, dt, *J* 5.6 and 1.7); δ_C($CDCl_3$, 50 MHz) 161.6, 156.9, 155.3, 150.7, 150.5, 141.9, 137.3, 132.2, 129.7, 125.7, 122.4, 120.0 and 45.1; *m/z* 279 (M^+, 100%), 278 (89), 265 (9), 264 (55), 251 (10), 250 (40), 238 (16), 236 (11), 224 (30), 195 (9), 188 (14), 117 (12) and 77 (32).

3-Phenyl-2-prop-2-ynylaminopteridin-4(3*H*)-one 12c. Yellow solid (18.1 mg, 32%), mp 212–215 °C (Found: M^+, 277.0964. $C_{15}H_{11}N_4O_2$ requires *M*, 277.0964); R_F 0.17 (A); ν_{max}(K-Br)/cm^{-1} 3057, 2924, 1701, 1615, 1584, 1562, 1534, 1472, 1289, 1256, 1211, 750 and 669; δ_H($CDCl_3$, 200 MHz) 8.77 (1 H, d, *J* 2.2), 8.56 (1 H, d, *J* 2.2), 7.61–7.72 (3 H, m), 7.35–7.40 (2 H, m), 4.68 (1 H, t, *J* 5.2), 4.37 (2 H, dd, *J* 5.2 and 2.6) and 2.23 (1 H, t, *J* 2.6); δ_C($CDCl_3$, 50 MHz) 161.3, 155.9, 151.6, 150.5, 141.4, 133.6, 131.5, 131.1, 130.5, 129.0, 79.0, 72.7 and 32.1; *m/z* 277 (M^+, 24%), 276 (18), 250 (10), 249 (66), 248 (100), 208 (10), 131 (11), 118 (9), 104 (7), 91 (6) and 77(17).

2-Allylamino-3-(4-chlorophenyl)pteridin-4(3*H*)-one 12d. Yellow solid (70.4 mg, 55%), mp 233–235 °C (Found: M^+, 313.0715. $C_{15}H_{12}ClN_5O$ requires *M*, 313.0730); R_F 0.17 (H:A 1:2); ν_{max}(KBr)/cm^{-1} 3021, 1705, 1588, 1562, 1537, 1491, 1472, 1412, 1208, 1094 and 928; δ_H($CDCl_3$, 200 MHz) 8.74 (1 H, d, *J* 2.1), 8.52 (1 H, d, *J* 2.1), 7.59–7.66 (2 H, m), 7.29–7.36 (2 H, m), 5.89 (1 H, ddt, *J* 16.8, 10.6 and 5.6), 5.15 (1 H, dq, *J* 10.8 and 1.3), 5.13 (1 H, dq, *J* 16.8 and 1.3), 4.56 (1 H, t, *J* 5.6) and 4.20 (2 H, tt, *J* 5.6 and 1.5); δ_C($CDCl_3$, 50 MHz) 161.4, 156.2, 151.8, 150.6, 141.1, 137.3, 133.5, 132.3, 131.7, 130.4, 130.2, 117.4 and 44.5; *m/z* 315 (M + 2, 32%), 314 (M + 1, 31), 313 (M^+, 100), 312 (42), 300 (24), 299 (13), 298 (76), 229 (6), 203 (6), 188 (6), 152 (8), 151 (6), 119 (7), 111 (10) and 75 (6).

3-Allyl-2-(4-chlorophenylamino)pteridin-4(3*H*)-one 13d. Pale yellow solid (20.5 mg, 16%), mp 87–88 °C (Found: M^+, 313.0732. $C_{15}H_{12}ClN_5O$ requires *M*, 313.0730); R_F 0.24 (H:A

1:2); ν_{max}(KBr)/cm^{-1} 2924, 1686, 1603, 1561, 1528, 1493, 1460, 1422 and 824; δ_H($CDCl_3$, 200 MHz) 8.78 (1 H, d, *J* 2.0), 8.60 (1 H, d, *J* 2.0), 7.50–7.60 (2 H, m), 7.33–7.41 (2 H, m), 6.98 (1 H, br), 6.10 (1 H, ddt, *J* 17.1, 10.7 and 5.4), 5.58 (1 H, dq, *J* 10.8 and 0.7), 5.56 (1 H, dq, *J* 17.1 and 1.0) and 5.00 (2 H, dt, *J* 5.4 and 1.7); δ_C($CDCl_3$, 50 MHz) 161.5, 155.1, 150.7, 150.4, 142.1, 135.9, 132.2, 131.0, 130.3, 129.7, 123.7, 120.0 and 45.1; *m/z* 315 (M + 2, 32%), 314 (M + 1, 34), 313 (M^+, 100), 312 (62), 300 (19), 298 (64), 284 (32), 276 (27), 274 (94), 258 (23), 188 (24), 153 (18), 121 (19), 111 (16), 93 (35) and 66 (16).

3-(4-Chlorophenyl)-2-prop-2-ynylaminopteridin-4(3*H*)-one 12e. Yellow solid (16.0 mg, 18%), mp 131–132 °C (Found: M^+, 311.0562. $C_{15}H_{10}ClN_5O$ requires *M*, 311.0574); R_F 0.17 (A); ν_{max}(KBr)/cm^{-1} 2926, 1701, 1588, 1561, 1530, 1474, 1412, 1263, 1090 and 1017; δ_H($CDCl_3$, 200 MHz) 8.76 (1 H, d, *J* 2.1), 8.55 (1 H, d, *J* 2.1), 7.59–7.64 (2 H, m), 7.29–7.36 (2 H, m), 4.75 (1 H, t, *J* 5.2), 4.37 (2 H, dd, *J* 5.2 and 2.5) and 2.25 (1 H, t, *J* 2.5); δ_C($CDCl_3$, 50 MHz) 161.3, 155.9, 151.3, 150.6, 141.5, 137.4, 132.0, 131.7, 130.4, 130.3, 78.9, 72.8 and 32.1; *m/z* 313 (M + 2, 8%), 312 (M + 1, 13), 311 (M^+, 25), 310 (26), 285 (18), 284 (38), 283 (55), 282 (100), 248 (8), 242 (11), 152 (12), 131 (15) and 111 (9).

2-Allylamino-3-(4-methoxyphenyl)pteridin-4(3*H*)-one 12f. Yellow solid (28.8 mg, 28%), mp 153–154 °C (Found: M^+, 309.1224. $C_{16}H_{15}N_5O_2$ requires *M*, 309.1226); R_F 0.09 (A); ν_{max}(KBr)/cm^{-1} 2926, 1701, 1584, 1562, 1530, 1510, 1470, 1414, 1252, 1107, 1028 and 824; δ_H($CDCl_3$, 200 MHz) 8.72 (1 H, d, *J* 2.0), 8.50 (1 H, d, *J* 2.0), 7.24–7.31 (2 H, m), 7.08–7.15 (2 H, m), 5.89 (1 H, ddt, *J* 16.7, 10.9 and 5.5), 5.13 (1 H, dq, *J* 10.9 and 1.3), 5.12 (1 H, dq, *J* 16.7 and 1.5), 4.71 (2 H, t, *J* 5.5), 4.20 (2 H, tt, *J* 5.6 and 1.6) and 3.88 (3 H, s); δ_C($CDCl_3$, 50 MHz) 161.8, 161.3, 156.2, 152.2, 150.3, 140.7, 133.7, 130.3, 130.0, 125.9, 117.0, 116.5, 55.7 and 44.3; *m/z* 309 (M^+, 100%), 308 (38), 295 (13), 294 (81), 253 (6), 202 (6), 148 (11), 147 (13), 146 (6), 133 (13), 108 (13) and 92 (6).

3-Allyl-2-(4-methoxyphenylamino)pteridin-4(3*H*)-one 13f. Yellow solid (20.0 mg, 20%), mp 86–88 °C (Found: M^+, 309.1231. $C_{16}H_{15}N_5O$ requires *M*, 309.1226); R_F 0.16 (A); ν_{max}(KBr)/cm^{-1} 2926, 1690, 1613, 1562, 1528, 1510, 1460, 1424, 1244, 1107, 1024 and 826; δ_H($CDCl_3$, 200 MHz) 8.72 (1 H, d, *J* 2.0), 8.53 (1 H, d, *J* 2.0), 7.42–7.47 (2 H, m), 6.98–6.94 (2 H, m), 6.94 (1 H, s), 6.02 (1 H, ddt, *J* 17.6, 10.0 and 5.4), 5.508 (1 H, d, *J* 17.2), 5.504 (1 H, d, *J* 10.8), 4.98 (2 H, dt, *J* 5.4 and 1.6) and 3.81 (3 H, s); δ_C($CDCl_3$, 50 MHz) 157.9, 155.5, 152.1, 151.0, 150.6, 141.5, 132.0, 130.0, 127.1, 124.8, 120.0, 114.8, 55.7 and 44.9; *m/z* 309 (M^+, 100%), 308 (29), 295 (12), 294 (65), 293 (9), 281 (27), 280 (20), 266 (17), 254 (21), 148 (11), 147 (20), 146 (10) and 108 (9).

Synthesis of imidazo[1,2-*a*]pteridine derivatives 15 by iodoimidazolination of 2-allylaminopteridin-4(3*H*)-one derivatives 12: general procedure

To a solution of the 2-allylaminopteridin-4(3*H*)-one **12a** (10.6 mg, 0.038 mmol) in THF (5 cm^3) was added iodine (20 mg, 0.079 mmol, 2.1 equiv.) and sodium hydrogen carbonate (7.4 mg, 0.088 mmol, 2.3 equiv.). The mixture was stirred at room temperature under nitrogen until starting material had disappeared (TLC). The reaction mixture was treated with saturated aqueous sodium sulfite to reduce the excess of iodine after which it was diluted with water and extracted with AcOEt (20 cm^3 × 3). The combined layer extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue was purified on a silica gel column (H:A 1:2, v/v, as eluent) to afford the imidazo[1,2-*a*]pteridine derivative **15a** (15.2 mg, 0.038 mmol, 99%).

1-Iodomethyl-4-phenyl-1,2-dihydroimidazo[1,2-*a*]pteridin-5(4*H*)-one 15a. Yellow solid (15.2 mg, 99%), mp 122–123 °C; R_F 0.15 (A); ν_{max}($CHCl_3$)/cm^{-1} 1717, 1649, 1545, 1493, 1422, 1074, 930 and 791; δ_H($CDCl_3$, 200 MHz) 8.42 (2 H, s), 7.47–7.60 (3 H, m), 7.35–7.39 (2 H, m), 4.70–4.82 (1 H, m), 4.17 (1 H, dd, *J* 14.8 and 9.7), 3.93 (1 H, dd, *J* 10.2 and 6.4), 3.74 (1 H, dd, *J* 14.8 and 5.0) and 3.61 (1 H, dd, *J* 10.2 and 2.4); δ_C($CDCl_3$, 50 MHz) 159.5, 150.9, 148.2, 147.8, 139.2, 135.4, 130.2, 129.8, 128.7, 128.5, 59.0, 58.2 and 9.1; *m/z* 405 (M^+, 100%), 404 (45), 279 (13), 278 (77), 277 (25), 276 (22), 265 (5), 264 (36), 132 (5), 131 (15) and 77 (22). In the HRMS, the M^+ peak of **15a** (405.0087) was hidden by one of the perfluorocarbon peaks ($C_{10}F_{15}$, 404.9760) used as a standard.

4-(4-Chlorophenyl)-1-iodomethyl-1,2-dihydroimidazo[1,2-*a*]pteridin-5(4*H*)-one 15b. Yellow solid (36.4 mg, 100%), mp 79–82 °C (Found: M^+, 438.9697. $C_{15}H_{11}ClIN_5O$ requires *M*, 438.9695); R_F 0.36 (A); ν_{max}(KBr)/cm^{-1} 1711, 1647, 1574, 1541, 1493, 1454, 1420, 1196, 1090, 858 and 754; δ_H($CDCl_3$, 200 MHz) 8.43 (2 H, s), 7.48–7.55 (2 H, m), 7.28–7.35 (2 H, m), 4.49–4.81 (1 H, m), 4.16 (1 H, dd, *J* 14.7 and 9.7), 3.95 (1 H, dd, *J* 10.3 and 6.1), 3.73 (1 H, dd, *J* 14.7 and 5.1) and 3.59 (1 H, dd, *J* 10.3 and 2.3); δ_C($CDCl_3$, 50 MHz) 159.4, 150.6, 148.1, 147.9, 139.2, 135.8, 133.8, 130.4, 129.9, 128.5, 58.9, 58.1 and 9.2; *m/z* 441 (M + 2, 32%), 440 (M + 1, 24), 439 (M^+, 100), 438 (22), 314 (26), 313 (30), 312 (89), 311 (48), 310 (28), 300 (12), 298 (39), 165 (13) and 111 (11).

1-Iodomethyl-4-(4-methoxyphenyl)-1,2-dihydroimidazo[1,2-*a*]pteridin-5(4*H*)-one 15c. Yellow solid (28.6 mg, 87%), mp 83–85 °C (Found: M^+, 435.0183. $C_{16}H_{14}IN_5O_2$ requires *M*, 435.0192); R_F 0.13 (A); ν_{max}(KBr)/cm^{-1} 2928, 1711, 1645, 1543, 1512, 1493, 1454, 1420, 1300, 1250, 1196, 1030 and 750; δ_H($CDCl_3$, 50 MHz) 8.42 (2 H, s), 7.24–7.32 (2 H, m), 7.00–7.08 (2 H, m), 4.69–4.81 (1 H, m), 4.16 (1 H, dd, *J* 14.8 and 9.8), 3.92 (1 H, dd, *J* 10.2 and 6.4), 3.81 (3 H, s), 3.73 (1 H, dd, *J* 14.8 and 5.1) and 3.61 (1 H, dd, *J* 10.2 and 2.4); δ_C($CDCl_3$, 50 MHz) 160.4, 159.7, 151.4, 151.1, 148.1, 147.7, 139.1, 129.4, 127.9, 115.4, 59.0, 58.2, 55.6 and 9.1; *m/z* 435 (M^+, 87%), 434 (19), 309 (16), 308 (75), 307 (100), 306 (73), 294 (23), 292 (8), 279 (9), 278 (13), 264 (13), 161 (8) and 77 (8).

X-Ray crystal structure analysis of 6[29]

$C_{24}H_{20}N_3O_2P$, $M = 413.41$, Orthorhombic, space group $P2_12_12_1$, $a = 14.76(3)$, $b = 32.69(2)$, $c = 9.06(1)$ Å, $V = 4373(11)$ Å^3, $Z = 8.0$, $D_c = 1.256$ g cm^{-3}. A white, hygroscopic prism (0.22 × 0.48 × 0.66 mm) was mounted on a Rigaku AFC5S diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.710\,69$ Å). Data collection using the ω scan technique to a maximum 2θ value of 54.9° gave 5581 reflections. The structure was solved by direct method and refined by full-matrix least squares technique (TEXSAN[30] system as the computer program, and MITHRIL[31] as the structure solution method). The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included by calculation and were not refined. Final cycle of the refinement was calculated by 1384 observed reflections [$I > 3.00\sigma(I)$] and 541 variable parameters and *R* and R_w values are 0.063 and 0.065. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.[29]

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