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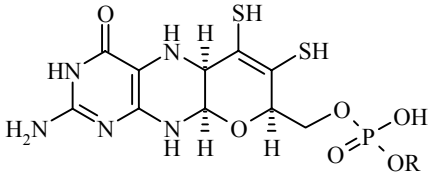
REACTION OF SOME HETEROCYCLIC FORMAMIDINES WITH TRIMETHYL-SILYLETHYNYLLITHIUM*

W. Ajana, M. Helliwell, D. Collison, C. D. Garner, J. A. Joule

The reaction of a 2-[(dimethylamino)methyleneamino]pteridine, two 2-[(dimethylamino)-methyleneamino]pyrimidines, and a 2-[(dimethylamino)methyleneamino]pyrido[2,3-d]pyrimidine with trimethylsilylethynylithium in the presence of benzyl chloroformate leads to the corresponding 2-[bis(trimethylsilylethynyl)methylamino]-substituted heterocycles. A series of such substrates was prepared and some of the factors which permit this transformation were delineated. An X-ray crystal structure was determined of one of the products – 2-[bis(trimethylsilylethynyl)methylamino]-5,6,7,8-tetrahydro-3-(2,2-dimethylpropanoyloxymethyl)quinazolin-4-one.

Keywords: [bis(trimethylsilylethynyl)methylamino]heterocycles, [(dimethylamino)methyleneamino]-protected heterocyclic amines; trimethylsilylethynyllithium.

We have been engaged for some time on efforts [1-5] to synthesize the organic component of the cofactors of the oxomolybdoenzymes, now known to have structure **1** [6, 7], and generally referred to as molybdopterin (MPT). The metal in the cofactors is linked *via* the corresponding dianion of the ene-1,2-dithiol (dithiolene). In some cofactors R = H and in others R = nucleoside. We have recently reported [8] a total synthesis of **2** which is **1** in protected/masked form.



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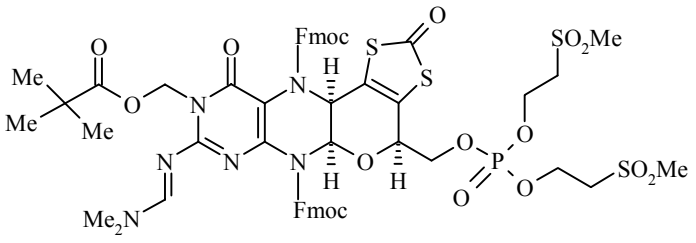

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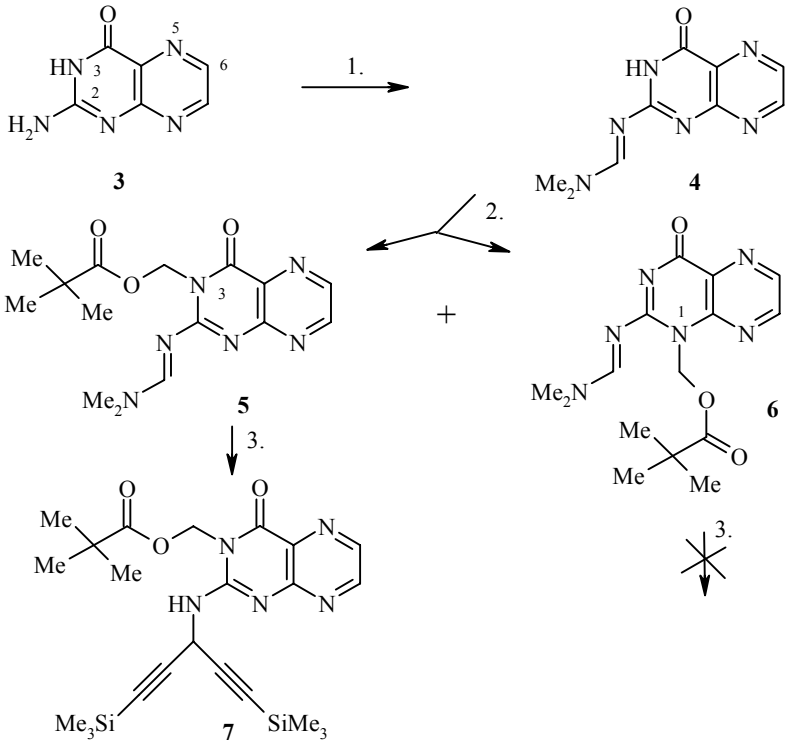
* Dedicated to Professor Edmunds Lukevics on his 65th birthday.

Chemistry Department, The University of Manchester, Manchester M13 9PL, U. K.; e-mail: joule@man.ac.uk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1506-1518, November, 2001. Original article submitted August 13, 2001.

The synthesis of MPT required the intermediacy of a pteridine carrying a side chain at C(6). Based on reported examples of the nucleophilic addition of organometallic reagents to N^+-acyl azinium salts [9-13], α to the nitrogen, it occurred to us that we might be able to construct a suitable intermediate rapidly by introduction of a side chain into a simple pteridine. We chose pterin,* **3**, itself, since this is readily synthesized [14, 15] and would also give us the required substitution pattern in the pyrimidine ring, though for reaction with an organometallic reagent, masking of the 2-amino group and N(3)-hydrogen atom would be required. Once the active hydrogens had been removed, we envisaged acylation at the more nucleophilic pyrazine ring nitrogen, N(5), then addition of a suitable carbon nucleophile at C(6), which would also incidentally generate the required oxidation level in the pyrazine ring.

Scheme 1



Reagents: 1. *t*-BuO(Me$_2$N)$_2$CH, DMF, rt (82%); 2. ClCH$_2$OCOCMe$_3$, NaI, K$_2$CO$_3$, DMF, rt (**5**, 15%, **6** 26%); 3. ClCO$_2$Bn, THF, 0°C then Me$_3$SiC≡CLi, THF, -78°C→rt (21%)

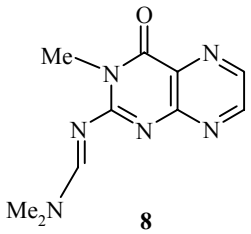
Pterin **3** was converted into doubly protected derivatives by successive reactions with Bredereck's reagent (*t*-BuO(Me$_2$N)$_2$CH) giving **4** and then this was reacted with chloromethyl pivaloate and base, giving a separable mixture of N(3)-protected **5** and N(1)-protected **6** derivatives (pivaloyloxymethyl (POM) derivatives), with the latter predominating. The evidence which distinguishes these two isomers is discussed later.

Since methods exist for the conversion of alkynes into 1,3-dithiol-2-ones [16, 17] and into 1,3-dithiole-2-thiones [18, 19], and since our synthetic work [1-5] has used both of these as protected/masked forms of the dithiolene unit required for MPT, we now examined the reaction of both **5** and **6** with trimethylsilylethynyllithium in the presence of benzyl chloroformate. No reaction took place with **6** but **5** gave a

* Pterin is the usual trivial designation for 2-aminopteridin-4-one.

product $C_{23}H_{33}N_5O_3Si_2$, clearly not of the desired type. ^{1}H NMR analysis showed the continued presence of the two pyrazine ring protons, the absence of a dimethylamino group, and the presence of *two* trimethylsilyl groups, implying the addition of two trimethylsilylacetylene units. The key to the structure lies in an N–H signal as a doublet coupled to a C–H at δ 6.08. We assign structure **7** to this product (Scheme 1) on the basis of these data and by analogy with an X-ray crystal structure determination on an analogue (see below). The absence of a residue corresponding to the chloroformate called into question the role of this component of the reaction mixture – is it required at all? Treatment of **5** with trimethylsilylethynyllithium alone resulted only in the isolation of the hydrolysis product of **5**, hence we believe that the chloroformate plays a key role (see later for suggested mechanism).

It seemed surprising that the 3-protected formamidine **5** took part in the process, whereas its 1-protected isomer **6** did not. We surmised that the size and/or location of the protecting group might be factors; so we prepared the N(3)- **8** and N(1)- **9** methylated derivatives as a separable mixture, by reaction of **4** with iodomethane in the presence of potassium carbonate. Neither of these N-methyl derivatives reacted in any way with trimethylsilylethynyllithium in the presence of benzyl chloroformate.



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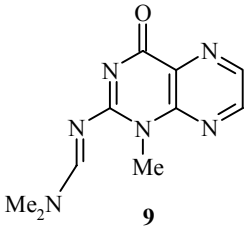

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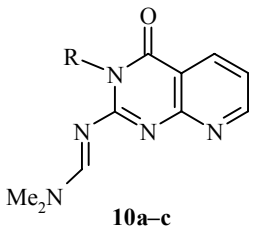
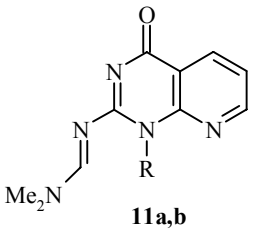
A search of the literature revealed no other examples of such transformations of formamidines though bis(alkynyl)methylamines have been described, deriving from reaction of alkynyl Grignard reagents with dimethylformamide dimethylacetal [20] and from alkynyllithium addition to alkynyl imines [21, 22]. Since the considerable further synthetic potential of such bis(alkynyl)methylamines has been demonstrated in simpler systems [20, 21, 23] we thought it worth continuing our investigation, in spite of the disappointing result in the context of MPT synthesis.

Synthesis of Substrates

To examine the generality in terms of systems other than pteridines, we made comparable substrates in five other series. We prepared N-methyl (**10b** and **11a)** and N-POM (**10c** and **11b**) derivatives by N-alkylations of 2-[(dimethylamino)methyleneamino]pyrido[2,3-*d*]pyrimidin-4-one (**10a**), in turn prepared by reaction of 2-aminopyrido[2,3-*d*]pyrimidin-4-one [24] with Bredereck's reagent. The N-methyl derivatives **10b** and **11a** could not be distinguished; the evidence which distinguishes the two POM-isomers, **10c** and **11b**, is discussed later.



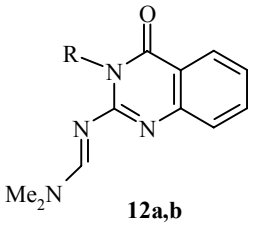
10a–c



11a,b

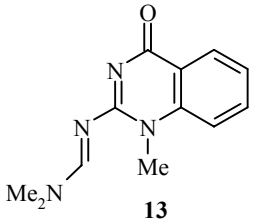
10 a R = H, **b** R = Me, **c** R = $Me_3CCO_2CH_2$; **11 a** R = Me, **b** R = $Me_3CCO_2CH_2$

Base-catalyzed N-methylation of 2-[(dimethylamino)methyleneamino]quinazolin-4-one (**12a**), prepared in the usual way from 2-aminoquinazolin-4-one [25], produced only one methylated product. In order to determine which isomer this was, N-methylisatoic anhydride [26] was reacted with cyanamide; this yielded unambiguously 2-amino-1-methylquinazolin-4-one which, by reaction with Bredereck's reagent, gave a product **13**. This last product proved to be different from that obtained from the N-methylation of **12a**, which must therefore be assigned structure **12b**.



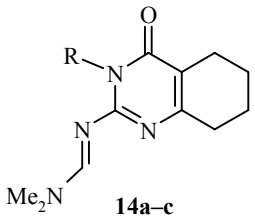
12a,b

12 a R = H, **b** R = Me

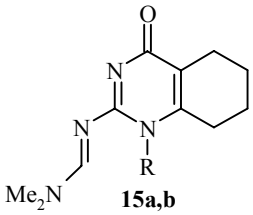


13

N-Methyl and N-POM derivatives of 2-[(dimethylamino)methyleneamino]-5,6,7,8-tetrahydroquinazolin-4-one (**14a**), synthesised in the usual way from 2-amino-5,6,7,8-tetrahydroquinazolin-4-one [27], were formed as separable mixtures of 1- and 3-alkylation products, thus giving us access to the pairs of isomers **14b**, **15a** and **14c**, **15b**. The N-methylated pair **14b** and **15a** could not be distinguished spectroscopically; the evidence which distinguishes the two POM-isomers, **14c** and **15b**, is discussed later.



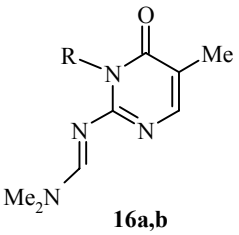
14a–c



15a,b

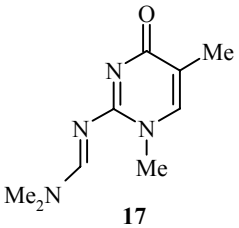
14 a R = H, **b** R = Me, **c** R = $Me_3CCO_2CH_2$; **15 a** R = Me, **b** = $Me_3CCO_2CH_2$

Conversion of 2-amino-5-methylpyrimidin-4-one [28] into a formamidine derivative, **16a**, then methylation gave a separable mixture of derivatives **16b** and **17**, which were not distinguished structurally.



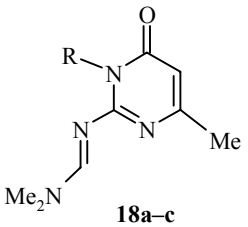
16a,b

16 a R = H, **b** R = Me

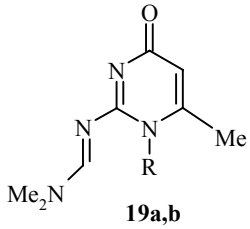


17

Methylation, or reaction with chloromethyl pivaloate, of 2-[(dimethylamino)methyleneamino]-6-methylpyrimidin-4-one (**18a**), prepared from 2-ami-no-6-methylpyrimidin-4-one [29], produced separable mixtures of the pairs of isomers **18b**, **19a**, and **18c**, **19b**, respectively. The evidence which distinguishes the N-methylated isomers, **18b** and **19a**, is discussed below.



18a–c

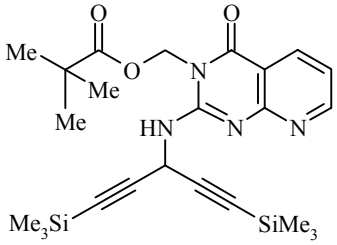


19a,b

18 a R = H, **b** R = Me, **c** R = $Me_3CCO_2CH_2$; **19 a** R = Me, **b** R = $Me_3CCO_2CH_2$

Reactions with Trimethylsilylethynyllithium

Just as with the two N-methylated pteridines **8** and **9**, the N-methylated formamidines, **10b**, **11a**, **12b**, **13**, **14b**, **15a**, **16b**, **17**, failed to react with the combination of trimethylsilylethynyllithium and benzyl chloroformate. For the pairs of isomeric POM derivatives, **10c**, **11b** and **14c**, **15b**, in each case only one of the isomers reacted, just as with the pair of N-POM pteridines, **5b** and **6**. Where reaction occurred, products of the type described above for the pteridine were obtained, and thus the structures **20** and **21** can be assigned.



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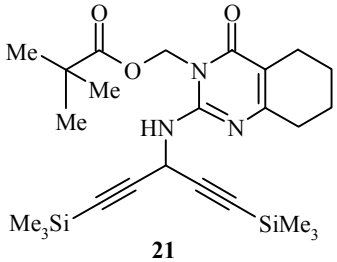


21

We were able to determine the structure of **21** by X-ray crystallography; a *Chem3D* representation using the atomic coordinates for this molecule is shown in Fig. 1.

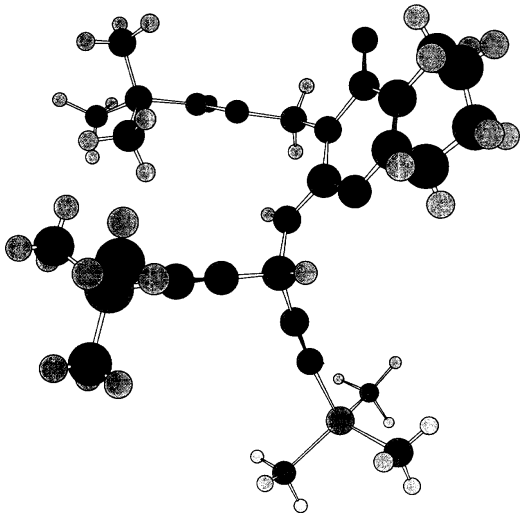
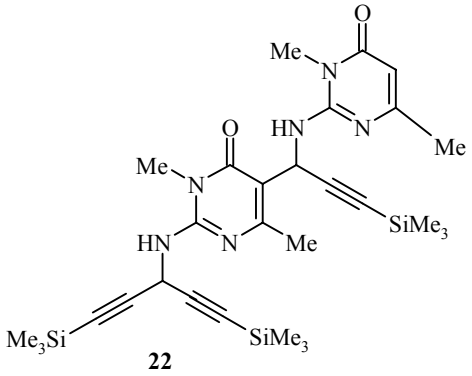


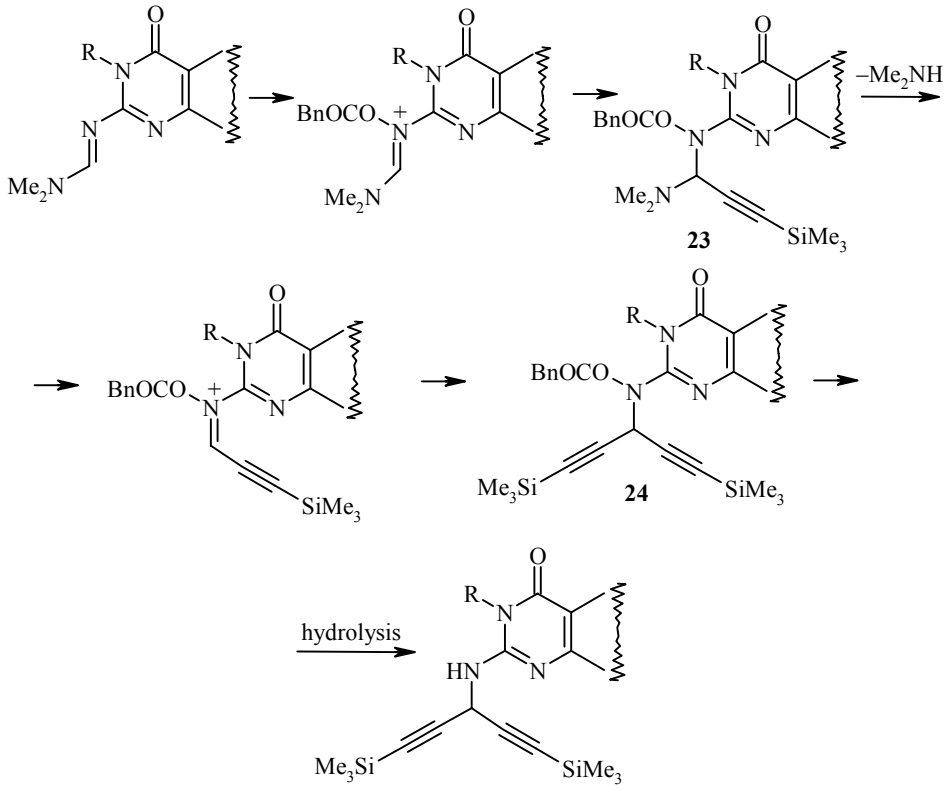
Fig. 1. *Chem3D* drawing of **21** using the atomic coordinates determined by X-ray crystallography.



22

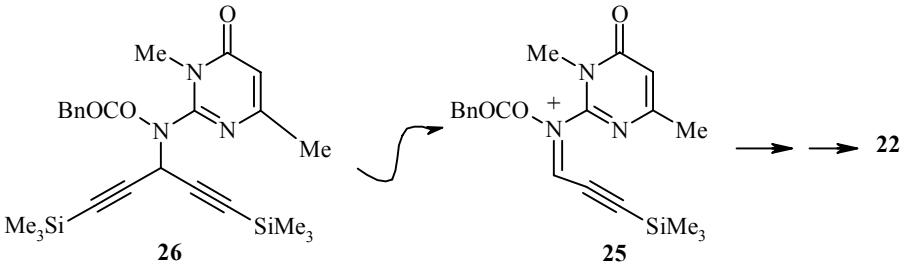
The pyrimidinone **18b** was the only N-methyl derivative which produced a product on exposure to the chloroformate and the alkynyl lithium; however, this product clearly contained two heterocyclic moieties and three trimethylsilyl substituents. We propose the structure **22** for this product. In order to rationalize the formation of this product, it is first necessary to consider the mechanism which can be proposed for the formation of the simpler bis(trimethylsilylethynyl)methylamino compounds. We suggest that the process is initiated by interaction of the chloroformate with the formamidine unit, followed by addition of the alkynyllithium giving **23**. Loss of dimethylamine (possibly under the influence of the chloroformate) and then a second nucleophilic addition would generate a species **24**, the hydrolysis of which during work-up would provide the observed products (Scheme 2).

Scheme 2



In the case of the pyrimidinone **18b**, we speculate that intermediate **25,** acting as an electrophile, attacks a pyrimidinone **26** (which would represent the final stage in the other examples) to lead to the proposed structure for the final product, **22** (Scheme 3).

Scheme 3



N-Methyl and N-POM 1-/3-Isomers

In most instances it has not been possible to assign structures unam-biguously to the N-1/N-3 isomers produced by the alkylations described in this paper. For only one pair, **14c**/**15b**, can we be absolutely sure of the assignment, based on the X-ray crystal structure determination (Fig. 1) of product **21** which must have derived from **14c**. However, where the chloroformate/alkynyllithium reaction was successful, *only one of the two isomers* of the POM-blocked pairs **5**/**6** and **10c**/**11b** and the N-methyl blocked pyrimidinones **18b**/**19a** reacted. We suggest therefore that, for reasons which are not yet clear, the conditions necessary for successful reaction are only met when N(3) is blocked and not N(1). On this assumption, we have assigned the structures shown above to the isomeric pairs **5**/**6**, **10c**/**11b**, and **18b**/**19a**.

Conclusions

We have described here a potentially useful method for the synthesis of heterocyclic bis(alkynyl)methylamino-heterocycles and delineated its generality. In the future we shall be examining the potential of bis(trimethylsilylethynyl)methylamino-heterocycles for the elaboration of poly-heterocyclic systems. In particular, we shall be looking for possible cyclisation reactions involving existing ring heteroatoms and the alkyne substituents, thereby generating new heterocyclic rings.

EXPERIMENTAL

General. ^{1}H NMR spectra were recorded on an Inova-300 Athos (300 MHz) spectrometer. ^{13}C NMR spectra were recorded on an Inova-300 Athos spectrometer running at 75 MHz. All chemical shifts (δ, ppm) are quoted downfield from TMS; J values are given in Hz. Mass spectra were recorded on a Fisons VG Trio 2000 (EI/CI{NH_3}) instrument (abundance relative to the base peak given in parentheses as a percentage; only fragment ions of intensity ≥10% of the base peak are cited), and a Concept IS (MM/FAB) spectrometer for accurate mass determinations. Melting points were recorded on a Reichart heated stage microscope and are uncorrected.

Flash column chromatography was carried out using Merck 9385 silica gel 60 (230-400 mesh). All ethers were dried over sodium wire and distilled under an atmosphere of dry argon using benzophenone as an indicator of degree of hydration. Dimethylformamide was dried over 4 Å molecular sieves. All other chemicals were purified using the appropriate standard procedure as described in "*Purification of Laboratory Chemicals*" by D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, Pergamon Press. Organic solutions were dried over anhydrous $MgSO_4$. Solid products were dried under reduced pressure using P_4O_{10} as a desiccant.

General Method for the Formation of Formamidine Derivatives, as Illustrated by the Synthesis of 2-[(Dimethylamino)methyleneamino]pteridin-4-one (4). To a suspension of pterin **3** (5 g, 30.7 mmol) in anhydrous DMF (20 ml) under N_2 was added Bredereck's reagent (*t*-butoxybis(dimethylamino)methane) (7.6 ml, 36.8 mmol) and the mixture stirred at room temperature overnight. Methanol (10 ml) and ether (60 ml) were added and the precipitated yellow solid filtered off and washed with ether. After drying at 100°C under vacuum, the formamidine **4** had mp >230°C. ^{1}H NMR (DMSO-d_6), δ: 12.00 (1H, s, NH); 8.82 (1H, s, Me_2NCH=N); 8.75 (1H, d, *J* = 2.1 Hz, H-7); 8.50 (1H, d, *J* = 2.1 Hz, H-6); 3.24 (3H, s, NCH_3); 3.11 (3H, s, NCH_3). ^{13}C NMR (DMSO-d_6), δ:162.2, 159.6, 159.5, 158.6, 140.6, 131.5, 35.2. *m/z* (EI): 218 (M^+, 100 %), 203 (30), 148 (40), 120 (15). Found, %: C 48.9; H 4.8; N 37.8. HRMS: M^+ 218.0913. $C_9H_{10}N_6O$. Calculated, %: C 49.5; H 4.6; N 38.5. M 218.0916.

General Method for the Synthesis of N(1)- and N(3)-POM Derivatives, as Illustrated by the Synthesis of 2-[(Dimethylamino)methyleneamino]-3-(2,2-dimethylpropanoyloxymethyl)pteridin-4-one (5) and 2-[(Dimethylamino)methyleneamino]-1-(2,2-dimethylpropanoyloxymethyl)pteridin-4-one (6). Formamidine **4** (5 g, 23.0 mmol), K_2CO_3 (3.2 g, 23.0 mmol), NaI (0.15 g, 4.6 mmol), and chloromethyl pivaloate (5 ml, 34.5 mmol) were suspended/dissolved in dry DMF (20 ml) and the mixture stirred at room temperature overnight. After concentration under high vacuum, the residue was dissolved in CH_2Cl_2, the solution washed with brine and then water, dried and evaporated to leave a green solid. Dissolution in hot EtOAc led, on cooling, to the crystallization of 1-POM-product **6** (2.0 g, 26 %), mp 208°C. ^{1}H NMR ($CDCl_3$), δ: 9.00 (1H, s, Me_2NCH=N); 8.70 (1H, d, *J* = 2.2 Hz, H-7); 8.60 (1H, d, *J* = 2.2 Hz, H-6); 6.60 (2H, s, CH_2O); 3.23 (3H, s, NCH_3); 3.20 (3H, s, NCH_3); 1.12 (9H, s, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 178.0, 168.3, 160.8, 160.1, 146.7, 142.9, 142.7, 131.7, 66.5, 42.4, 39.4, 36.3, 27.5. *m/z* (EI): 332 (M^+, 40 %), 231 (35), 219 (60), 149 (10), 85 (40), 57 (100). Found, %: C 54.1; H 6.3; N 24.3. $C_{15}H_{20}N_6O_3$. Calculated, %: C 54.2; H 6.1; N 25.3. After concentration of the mother liquors, the 3-POM-product **5** (1.1 g, 15%) crystallized out; mp 211-213°C. ^{1}H NMR ($CDCl_3$), δ: 8.94 (1H, s, Me_2NCH=N); 8.78 (1H, d, *J* = 2.0 Hz, H-7); 8.55 (1H, d, *J* = 2.0 Hz); 6.38 (2H, s, CH_2O); 3.24 (3H, s, NCH_3); 3.15 (3H, s, NCH_3); 1.16 (9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 177.9, 162.3, 159.7, 157.8, 155.6, 150.5, 141.6, 131.3, 66.4, 42.1, 36.1, 27.5. *m/z* (EI): 332 (M^+, 20%), 231 (35), 219 (40), 85 (40), 57 (100). Found, %: C 54.8; H 6.3; N 24.5. HRMS: M^+ 332.1597. $C_{15}H_{20}N_6O_3$. Calculated, %: C 54.2; H 6.1; N 25.3. M 332.1597.

General Method for the Synthesis of N(1)- and N(3)-Methylated Derivatives Using DBU, as Illustrated by the Synthesis of 2-[(Dimethylamino)methyleneamino]-3-methylpteridin-4-one (8) and 2-[(Dimethylamino)methyleneamino]-1-methylpteridin-4-one (9). Formamidine **4** (0.3 g, 1.4 mmol) was suspended in dry CH_2Cl_2 (5 ml), then diazabicycloundecane (DBU) (0.6 ml, 4.2 mmol) was added dropwise, under N_2. After stirring for 0.25 h, the temperature was lowered to -40°C, then Me_2SO_4 (0.4 ml, 4.2 mmol) was added during 7 min, then the temperature raised to room temperature during 2 h. The mixture was washed with water, dried, and the solvent evaporated. The resulting oil was purified by chromatography. Eluting with CH_2Cl_2/MeOH (98:2) gave the first isomer (0.15 g, 46%); mp >230°C. ^{1}H NMR ($CDCl_3$), δ: 9.00 (1H, s, Me_2NCH=N); 8.76 (1H, d, *J* = 2.0 Hz, H-7); 8.57 (1H, d, *J* = 2.0 Hz, H-6); 3.76 (3H, s, NCH_3); 3.28 (3H, s, NCH_3); 3.25 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ: 163.0, 159.6, 158.7, 155.1, 150.1, 141.3, 131.1, 42.0, 35.9, 30.8. *m/z* (EI): 232 (M^+, 20%), 217 (10), 189 (25), 84 (60), 49 (100). Found, %: C 51.7; H 5.3; N 35.8. $C_{10}H_{12}N_6O$. Calculated, %: C 51.7; H 5.2; N 36.2. Further elution (95:5) gave the second isomer mixed with DBU. This mixture was dissolved in CH_2Cl_2, DBU removed by washing with weak acid, then the organic solution dried and evaporated to leave the second isomer (0.10 g, 30%), mp >230°C. ^{1}H NMR ($CDCl_3$), δ: 9.06

(1H, s, $Me_2NCH=N$); 8.68 (1H, d, *J* = 2.0 Hz, H-7); 8.62 (1H, d, *J* = 2.0 Hz, H-6); 3.92 (3H, s, NCH_3); 3.28 (3H, s, NCH_3); 3.26 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ:168.0, 160.2, 160.0, 148.8, 146.0, 141.0, 131.3, 41.6, 35.5, 30.3. Found, %: C 51.6; H 5.2; N 35.8. $C_{10}H_{12}N_6O$. Calculated, %: C 51.7; H 5.2; N 36.2.

General Method for Reaction of Formamidines with Trimethylsilylethynyllithium and Benzyl Chloroformate, as Illustrated by the Synthesis of 2-[Bis(trimethylsilylethynyl)methylamino]-3-(2,2-dimethylpropanoyloxymethyl)pteridin-4-one (7). POM-Derivative **5** (300 mg, 0.9 mmol) was dissolved in dry THF (3 ml), then benzyl chloroformate (308 mg, 1.8 mmol) was added dropwise at 0°C under N_2. After stirring for 1 h at 0°C the temperature was lowered to -78°C and trimethylsilylethynyllithium (2 equiv) added rapidly. After 0.5 h at -78°C and overnight at room temperature, aq. NH_4Cl (5%) was added and the THF evaporated. The organic products were extracted into CH_2Cl_2, the solution dried and evaporated, and the product isolated by chromatography, elution with CH_2Cl_2/MeOH (99:1) giving compound **7** (92 mg, 21%). ^1H NMR ($CDCl_3$), δ: 8.56 (1H, d, *J* = 2.2 Hz, H-7); 8.43 (1H, d, *J* = 2.2. Hz, H-6); 7.28 (1H, d, *J* = 7.4 Hz, NH); 6.14 (2H, s, CH_2O); 6.08 (1H, d, *J* = 7.4 Hz, HNCH); 1.08 (9H, s, $C(CH_3)_3$); 0.00 (18H, s, $2Si(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 180.1, 166.7, 152.2, 148.0, 146.3, 143.2, 131.3, 99.7, 88.9, 65.4, 39.5, 36.6, 27.4, 0.1. *m/z* (CI): 485 (MH^+, 15%), 368 (15), 86 (40), 58 (100). HRMS: M^+ 483.2135. $C_{23}H_{33}N_5O_3Si_2$. Calculated: M 483.2122.

2-[(Dimethylamino)methyleneamino]pyrido[2,3-*d*]pyrimidin-4-one (10a). Prepared from 2-aminopyrido[2,3-*d*]pyrimidin-4-one using Bredereck's reagent, the formamidine **10a**, amorphous glass (85%) had ^1H NMR ($CDCl_3$), δ: 9.03 (1H, s, $Me_2NCH=N$); 8.80 (1H, dd, *J* = 2.0, 4.6 Hz, H-7); 8.46 (1H, dd, *J* = 2.0, 7.8 Hz, H-5); 7.18 (1H, dd, *J* = 4.6, 7.8 Hz, H-6); 3.21 (3H, s, NCH_3); 3.14 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ: 172.0, 162.1, 161.1, 160.9, 156.6, 135.9, 120.8, 115.7, 48.4, 36.1. *m/z* (EI): 218 (25 %), 217 (M^+, 100), 202 (50), 147 (60), 119 (65). HRMS: M^+ 217.0965. $C_{10}H_{11}N_5O$. Calculated: M 217.09635.

2-[(Dimethylamino)methyleneamino]-3-methylpyrido[2,3-*d*]pyrimidin-4-one (10b) and 2-[(Dimethylamino)methyleneamino]-1-methylpyrido[2,3-*d*]pyrimidin-4-one (11a). Using DBU as base, a mixture was obtained chromatography of which gave the first isomer (11%) with mp >230°C. ^1H NMR ($CDCl_3$), δ: 8.94 (1H, s, $Me_2NCH=N$); 8.76 (1H, dd, *J* = 2.0, 4.6 Hz, H-7); 8.46 (1H, dd, *J* = 2.0, 7.8 Hz, H-5); 7.13 (1H, dd, *J* = 4.6, 7.8 Hz, H-6); 3.65 (3H, s, NCH_3); 3.20 (3H, s, NCH_3); 3.16 (3H, NCH_3). ^{13}C NMR ($CDCl_3$), δ: 163.8, 158.7, 158.3, 158.0, 155.5, 136.2, 118.7, 113.3, 41.2, 31.1, 29.6. *m/z* (EI): 232 (25 %), 231 (M^+, 20), 216 (40), 172 (35), 146 (100). Found, %: C 57.9; H 6.1; N 30.5. HRMS: M^+ 231.1125. $C_{11}H_{13}N_5O$. Calculated, %: C 57.1; H 5.7; N 30.3. M 231.1120. The second isomer (29%) had mp >230°C. ^1H NMR ($CDCl_3$), δ: 9.01 (1H, s, $Me_2NCH=N$); 8.68 (1H, dd, *J* = 1.9, 4.7 Hz, H-7); 8.60 (1H, dd, *J* = 1.9, 8.6 Hz, H-5); 7.30 (1H, dd, *J* = 4.7, 8.6 Hz, H-6); 3.96 (3H, s, NCH_3); 3.26 (3H, s, NCH_3); 3.25 (3H, s, NCH_3). Found, %: C 56.6; H 5.9; N 29.6. HRMS: M^+-H 230.1169. $C_{11}H_{13}N_5O$. Calculated, %: C 57.1; H 5.7; N 30.3. M-H 230.1168.

General Method for the Synthesis of N(1)- and N(3)-POM Derivatives Using Sodium Hydride, as Illustrated by the Synthesis of 2-[(Dimethylamino)methyleneamino]-3-(2,2-dimethylpropanoyl-oxymethyl)pyrido[2,3-*d*]pyrimidin-4-one (10c) and 2-[(Dimethylamino)methyleneamino]-1-(2,2-dimethylpropanoyloxymethyl)pyrido[2,3-*d*]pyrimidin-4-one (11b). To a suspension of formamidine **10a** (2 g, 9.1 mmol) in dry DMF, at 0°C and under N_2, NaH (0.44 g, 10.9 mmol) was added. The cooling bath was removed and after stirring for 1 h at room temperature, chloromethyl pivaloate (1.6 ml, 10.9 mmol) was added and the mixture stirred overnight at room temperature. The DMF was evaporated under vacuum, then the resulting oil purified by chromatography, CH_2Cl_2 eluting the first isomer **11b** (1.2 g, 41%). ^1H NMR ($CDCl_3$), δ: 9.00 (1H, s, $Me_2NCH=N$); 8.80 (1H, dd, *J* = 2.0, 4.5 Hz, H-7); 8.50 (1H, dd, *J* = 2.0, 7.8 Hz, H-5); 7.20 (1H, dd, *J* = 4.5, 7.8 Hz, H-6); 6.40 (2H, s, CH_2O); 3.30 (3H, s, NCH_3); 3.20 (3H, s, NCH_3); 1.20 (9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 177.8, 163.7, 159.4, 159.2, 157.6, 156.6, 137.2, 119.7, 114.1, 66.1, 41.9, 39.3, 35.8, 27.5. *m/z* (EI): 332 (40%), 331(M^+, 60), 230 (40), 218 (90), 57 (100). HRMS: M^+ 331.1647. $C_{16}H_{21}N_5O_3$. Calculated: M 331.1644. The second isomer **10c** (0.8 g, 27%), eluted with CH_2Cl_2/MeOH (98:2), had mp 117-118°C. ^1H NMR ($CDCl_3$), δ:9.00 (1H, s, $Me_2NCH=N$); 8.64 (1H, dd, *J* = 1.9, 4.6 Hz, H-7); 8.55 (1H, dd, *J* = 1.9, 7.8 Hz, H-5); 7.31 (1H, dd, *J* = 4.6, 7.8 Hz, H-6), 6.67 (2H, s, CH_2O), 3.34 (3H, s, NCH_3), 3.18 (3H, s, NCH_3), 1.16

(9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$),δ: 178.2, 170.0, 160.8, 160.4, 153.1, 151.8, 137.7, 121.1, 114.9, 66.7, 42.1, 39.3, 36.1, 27.5. *m/z* (EI): 331 (M^+, 20%), 230 (10), 218 (40), 133 (70), 57 (100). HRMS: M^+ 331.1637. $C_{16}H_{21}N_5O_3$. Calculated: M 331.1644.

2-[(Dimethylamino)methyleneamino]quinazolin-4-one (12a). A solution of 2-aminoquinazolin-4-one (1 g, 6.2 mmol) was heated at 60°C in a mixture of DMF (10 ml) and DMF·DMA (4 ml, 31.0 mmol) under N_2 for 0.5 h. The solvents were removed under vacuum, then CH_2Cl_2, Et_2O, and *n*-hexane added and the resulting white precipitate filtered off, washed with Et_2O, and dried to give the formamidine **12a,** mp 154-156°C (0.9 g, 67%). ^1H NMR (DMSO-d_6), δ: 7.42 (1H, s, Me_2NCH=N); 7.23 (1H, dd, *J* = 1.6, 7.6 Hz, H-5); 7.08 (ddd, *J* = 1.6, 7.6, 7.8 Hz, H-7); 6.81 (1H, ddd, *J* = 1.8, 7.6, 7.6 Hz, H-6); 6.68 (1H, dd, *J* = 1.6, 7.8 Hz, H-8); 2.91 (6H, s, 2 NCH_3). ^{13}C NMR (DMSO-d_6), δ: 162.6, 153.4, 149.9, 135.2, 128.4, 128.2, 122.9, 121.9, 120.8, 39.8. *m/z* (EI): 216 (M^+, 50 %), 200 (30), 145 (50), 119 (60), 90 (60), and 44 (100). HRMS: M^+ 216.1011. $C_{11}H_{12}N_4O$. Calculated: M 216.1011.

2-[(Dimethylamino)methyleneamino]-3-methylquinazolin-4-one (12b). Alkylation of compound **12a** using NaH gave the 3-methyl derivative **12b** (50%) isolated by chromatography using CH_2Cl_2/MeOH (98:2); mp 138-140°C. ^1H NMR ($CDCl_3$), δ: 8.55 (1H, s, Me_2NCH=N); 8.15 (1H, dd, *J* = 1.6, 8.0 Hz, H-5); 7.55 (1H, ddd, *J* = 1.6, 7.6, 8.0 Hz, H-7); 7.40 (1H, dd, *J* = 1.1, 8.0 Hz, H-8); 7.20 (1H, ddd, *J* = 1.1, 7.6, 8.0 Hz, H-6); 3.62 (3H, s, NCH_3); 3.12 (3H, s, NCH_3); 3.06 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ:163.6, 157.0, 155.4, 148.3, 133.5, 126.6, 125.1, 123.1, 118.6, 40.9, 34.8, 29.5. *m/z* (EI): 231 (M^+, 70 %), 230 (100), 186 (70), 160 (30), 119 (20). Found, %: C 62.3; H 6.2; N 24.0. HRMS: M^+ 230.1168. $C_{12}H_{14}N_4O$. Calculated, %: C 62.6; H 6.1; N 24.3. M 230.1167.

2-Amino-1-methylquinazolin-4-one. A solution of N-methyl isatoic anhydride (2.5 g, 14.1 mmol) and cyanamide (0.65 g, 15.5 mmol) in dry DMF was stirred at room temperature overnight. The DMF was evaporated under vacuum and water added. After standing overnight at 4°C a white solid had precipitated which was filtered off and dried to give 2-amino-1-methylquinazolin-4-one, mp 190-193°C (2.1 g, 85%). ^1H NMR ($CDCl_3$), δ: 7.97 (1H, dd, *J* = 1.6, 7.4 Hz, H-5); 7.65 (1H, ddd, *J* = 1.6, 8.0, 8.0 Hz, H-7); 7.48 (1H, dd, *J* = 1.0, 8.0 Hz, H-8); 7.34 (2H, bs, NH_2); 7.27 (1H, ddd, *J* = 1.0, 7.4, 8.0 Hz, H-6); 3.53 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ: 167.9, 156.9, 141.7, 132.9, 127.2, 123.0, 119.1, 114.6, 32.7. *m/z* (EI): 176 (75 %), 175 (M^+, 100), 133 (25), 105 (75), 77 (30). HRMS: M^+ 175.0743. $C_9H_9N_3O$. Calculated: M 175.0764.

2-[(Dimethylamino)methyleneamino]-1-methylquinazolin-4-one (13). Prepared from 2-amino-1-methylquinazolin-4-one using Bredereck's reagent, the formamidine **13**, amorphous glass (83%) had ^1H NMR ($CDCl_3$), δ: 9.01 (1H, s, Me_2NCH=N); 8.37 (1H, dd, *J* = 1.6, 7.8 Hz, H-5); 7.66 (1H, ddd, *J* = 1.6, 7.6, 7.8 Hz, H-7); 7.40-7.33 (2H, m, H-6 and H-8); 3.87 (3H, s, NCH_3); 3.24 (3H, s, NCH_3); 3.21 (3H, s, NCH_3). ^{13}C NMR ($CDCl_3$), δ:169.6, 159.3, 141.7, 132.7, 127.9, 123.4, 119.6, 114.1, 41.1, 35.1, 33.8. *m/z* (EI): 230 (M^+, 30 %), 186 (35), 175 (80), 105 (50), 44 (100). HRMS: M^+ 230.1170. $C_{12}H_{14}N_4O$. Calculated: M 230.1168.

2-[(Dimethylamino)methyleneamino]-5,6,7,8-tetrahydroquinazolin-4-one (14a). Prepared from 2-amino-5,6,7,8-tetrahydroquinazolin-4-one using Bredereck's reagent, the formamidine **14a** (84%) had mp 202-204°C. ^1H NMR ($CDCl_3$), δ: 8.60 (1H, s, Me_2NCH=N); 3.17 (3H, s, NCH_3); 3.10 (3H, s, NCH_3); 2.56-2.49 (4H, m, $2CH_2$); 1.82-1.74 (4H, m, $2CH_2$). ^{13}C NMR ($CDCl_3$), δ: 164.6, 161.8, 157.6, 155.9, 41.1, 34.9, 31.9, 22.5, 22.1, 21.7. *m/z* (EI): 220 (M^+, 100%), 205 (30), 122 (20), 98 (30). Found, %: C 60.2; H 7.6; N 25.5. $C_{11}H_{16}N_4O$. Calculated, %: C 60.0; H 7.3; N 25.4.

2-[(Dimethylamino)methyleneamino]-5,6,7,8-tetrahydro-3-methylquinazolin-4-one (14b) and 2-[(Dimethylamino)methyleneamino]-5,6,7,8-tetrahydro-1-methylquinazolin-4-one (15a). Alkylation using MeI with KOH in EtOH gave a mixture which was separated by chromatography giving the first isomer (62%). ^1H NMR ($CDCl_3$), δ: 8.45 (1H, s, Me_2NCH=N; 3.54 (3H, s, NCH_3); 3.15 (3H, s, NCH_3); 3.10 (3H, s, NCH_3); 2.52-2.47 (4H, m, $2CH_2$); 1.75-1.71 (4H, m, $2CH_2$). ^{13}C NMR ($CDCl_3$), δ: 164.5, 159.0, 157.3, 156.7, 114.1, 41.5, 35.4, 32.0, 29.8, 23.0, 22.9, 22.7. *m/z* (EI): 234 (M^+, 100%), 219 (25), 190 (60), 162 (15), 112 (30). HRMS: M^+ 234.1475. $C_{12}H_{18}N_4O$. Calculated M 234.1481. Then the second isomer (18%), ^1H NMR ($CDCl_3$), δ: 8.70 (1H, s, Me_2NCH=N); 3.50 (3H, s, NCH_3); 3.10 (3H, s, NCH_3); 3.03 (3H, s, NCH_3); 2.60-2.30 (4H, m,

$2CH_2$); 1.80-1.50 (4H, m, $2CH_2$). *m/z* (EI): 235 (40%), 234 (M^+, 100), 219 (25), 190 (60), 162 (20), 112 (30). HRMS: M^+ 234.1479. $C_{12}H_{18}N_4O$. Calculated: M 234.1481.

2-[(Dimethylamino)methyleneamino]-5,6,7,8-tetrahydro-3-(2,2-dimethylpropanoyloxymethyl)-quinazolin-4-one (14c) and 2-[(Dimethylamino)methyleneamino]-5,6,7,8-tetrahydro-1-(2,2-dimethyl-propanoyloxymethyl)quinazolin-4-one (15b). A mixture of these derivatives was prepared using chloromethyl pivaloate and NaH and separated by chromatography when CH_2Cl_2/MeOH (99:1) gave first the 1-POM-isomer **15b** (22%); mp 117-118°C. ^{1}H NMR ($CDCl_3$), δ: 8.50 (1H, s, Me_2NCH=N); 6.25 (2H, s, CH_2O); 3.14 (3H, s, NCH_3); 3.04 (3H, s, NCH_3); 2.40-2.60 (4H, m, $2CH_2$); 1.65-1.85 (4H, m, $2CH_2$); 1.16 (9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 177.5, 163.1, 159.9, 156.9, 155.5, 113.9, 65.5, 41.0, 38.7, 34.9, 31.8, 27.0, 22.4, 22.3, 22.0. *m/z* (EI): 335 (80%), 334 (M^+, 100), 233 (40), 221 (60). HRMS: M^+ 334.2002. $C_{17}H_{26}N_4O_3$. Calculated: M 334.2005. Second to be eluted was the 3-POM-isomer **14c**; mp 118-123°C. ^{1}H NMR ($CDCl_3$), δ: 8.55 (1H, s, Me_2NCH=N); 6.05 (2H, s, CH_2O); 3.04 (3H, s, NCH_3); 3.03 (3H, s, NCH_3); 2.63 (2H, t, J = 6.0 Hz, CH_2); 2.41 (2H, t, J = 6.0 Hz, CH_2); 1.71-1.64 (4H, m, $2CH_2$); 1.70 (9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 177.6, 166.0, 163.6, 158.7, 110.1, 82.0, 42.3, 39.2, 35.3, 32.4, 27.3, 22.8, 22.6, 21.7. *m/z* (EI): 335 (30%), 334 (M^+, 50), 221 (30), 219 (70), 57 (100). HRMS: M^+ 334.2008. $C_{17}H_{26}N_4O_3$. Calculated: M 334.2005.

2-[(Dimethylamino)methyleneamino]-5-methylpyrimidin-4-one (16a). Prepared from 5-amino-5-methylpyrimidin-4-one using Bredereck's reagent, formamidine **16a** (80%) had mp 163°C. ^{1}H NMR (CD_3OD/$CDCl_3$), δ: 8.50 (1H, s, Me_2NCH=N); 7.53 (1H, s, H-6;, 3.11 (3H, s, NCH_3); 3.04 (3H, s, NCH_3); 1.94 (3H, s, CCH_3). ^{13}C NMR (CD_3OD/ $CDCl_3$), δ: 164.9, 158.8, 158.2, 150.6, 115.3, 40.8, 34.7, 12.8. *m/z* (EI): 180 (M^+, 25%), 165 (10), 84 (30), 49 (100). Found, %: C 53.3; H 6.9; N 31.1. HRMS: M^+ 180.1016. $C_8H_{12}N_4O$. Calculated, %: C 53.3; H 6.7; N 31.1. M 180.1011.

2-[(Dimethylamino)methyleneamino]-3,5-dimethylpyrimidin-4-one (16b) and 2-[(Dimethylamino)-methyleneamino]-1,5-dimethylpyrimidin-4-one (17). Using MeI with KOH in EtOH, a mixture of N-methylated derivatives was formed from **16a** and separated by chromatography, CH_2Cl_2/MeOH (9.5:0.5) eluted the first isomer (46 %) with mp 122-124°C. ^{1}H NMR ($CDCl_3$), δ: 8.50 (1H, s, Me_2NCH=N); 7.54 (1H, s, H-6); 3.60 (3H, s, NCH_3); 3.15 (3H, s, NCH_3); 3.11 (3H, s, NCH_3); 2.00 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$), δ: 176.3, 158.5, 157.5, 150.0, 116.0, 41.5, 35.4, 29.9, 13.8. *m/z* (EI): 195 (30%), 194 (M^+, 70), 150 (60), 49 (100). HRMS: M^+ 194.1172. $C_9H_{14}N_4O$. Calculated: M 194.1168. The second isomer (23%), eluted with CH_2Cl_2/MeOH (9:1), had mp 121-122°C. ^{1}H NMR ($CDCl_3$) δ: 8.83 (1H, s, Me_2NCH=N); 7.01 (1H, s, H-6); 3.51 (3H, s, NCH_3); 3.15 (3H, s, NCH_3); 1.98 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$), δ: 173.4, 159.0, 158.9, 140.2, 118.1, 41.6, 38.7, 35.5, 14.3. *m/z* (EI): 195 (100 %), 194 (M^+, 50), 179 (10), 98 (35). Found, %: C 56.9; H 7.4; N 29.7. HRMS: M^+ 194.1164. $C_9H_{14}N_4O$. Calculated, %: C 55.7; H 7.5; N 28.8. M 194.1168.

2-[(Dimethylamino)methyleneamino]-6-methylpyrimidin-4-one (18a). Prepared from 2-amino-6-methylpyrimidin-4-one using Bredereck's reagent, the formamidine **18a** (86%) had mp 180-181°C. ^{1}H NMR (D_2O), δ: 8.25 (1H, s, Me_2NCH=N); 5.68 (1H, s, H-5); 3.01 (3H, s, NCH_3); 2.88 (3H, s, NCH_3); 2.00 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$), δ: 174.0, 162.8, 162.6, 161.8, 107.2, 44.1, 37.7, 22.7. *m/z* (EI): 180 (M^+, 60%), 165 (25), 110 (28), 98 (25), 84 (30), 49 (100). HRMS: M^+ 180.1013. $C_8H_{12}N_4O$. Calculated: M 180.1011.

2-[(Dimethylamino)methyleneamino]-3,6-dimethylpyrimidin-4-one (18b) and 2-[(Dimethylamino)-methyleneamino]-1,6-dimethylpyrimidin-4-one (19a). Methylation of **18a** was carried out using MeI with KOH in EtOH to give a mixture (83 %) which was separated by chromatography to give the first isomer eluting with CH_2Cl_2/MeOH (99:1), mp 157°C. ^{1}H NMR ($CDCl_3$), δ:8.52 (1H, s, Me_2NCH=N); 5.96 (1H, s, H-5); 3.54 (3H, s, NCH_3); 3.18 (3H, s, NCH_3); 3.12 (3H, s, NCH_3); 2.16 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$),δ: 164.2, 162.5, 158.5, 157.4, 104.7, 41.0, 34.8, 28.8, 23.5. *m/z* (EI): 195 (100%), 194 (55), 150 (50). Found, %: C 55.2; H 7.2; N 28.6. HRMS: M^+ 194.1167. $C_9H_{14}N_4O$. Calculated, %: C 55.7; H 7.3; N 28.8. M 194.1168. The second isomer was eluted with CH_2Cl_2/MeOH (98:2) and had mp 157-158°C. ^{1}H NMR ($CDCl_3$), δ: 8.63 (1H, s, Me_2NCH=N); 5.71 (1H, s, H-5); 3.44 (3H, s, NCH_3); 3.02 (3H, s, NCH_3); 2.98 (3H, s, NCH_3); 2.10 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$), δ: 171.5, 159.5, 158.7, 150.6, 108.2, 40.9, 34.8, 32.5, 19.7. *m/z* (EI): 194 (M^+, 10%), 125 (100), 97 (30), 84 (60), 49 (40). HRMS: M^+ 194.1161. $C_9H_{14}N_4O$. Calculated: 194.1168.

2-[(Dimethylamino)methyleneamino]-3-(2,2-dimethylpropanoyloxymethyl)-6-methylpyrimidin-4-one (18c) and 2-[(Dimethylamino)methyleneamino]-3-(2,2-dimethylpropanoyloxymethyl)-6-methylpyrimidin-4-one (19b). Sodium hydride was used to promote the formation of POM derivatives from **18a** as a mixture which was separated by chromatography, elution with CH_2Cl_2/MeOH (99:1) giving the first isomer, amorphous gum. ^{1}H NMR ($CDCl_3$), δ: 8.60 (1H, s, Me_2NCH=N); 6.27 (2H, CH_2O); 5.98 (1H, s, H-5); 3.20 (3H, s, NCH_3); 3.10 (3H, s, NCH_3); 2.20 (3H, s, CCH_3); 1.2 (9H, s, $C(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 178.0, 164.5, 163.8, 158.6, 158.3, 105.7, 65.6, 41.7, 39.2, 35.6, 27.5, 24.5. *m/z* (EI): 294 (M^+, 25%), 193 (45), 181 (70), 98 (45), 57 (100). HRMS: M^+ 294.1692. $C_{14}H_{22}N_4O_3$. Calculated: M 294.1692. Further elution with the same solvent mixture gave the second isomer, amorphous glass which had ^{1}H NMR ($CDCl_3$), δ: 8.72 (1H, s, Me_2NCH=N); 6.24 (1H, s, H-5); 6.14 (2H, s, CH_2O); 3.20 (6H, s, $N(CH_3)_2$); 2.40 (3H, s, NCH_3); 1.20 (9H, s, $C(CH_3)_3$). *m/z* (EI): 295 (50%), 294 (M^+, 55), 209 (40), 193 (50), 181 (100), 165 (75), 57 (80). HRMS: M^+ 294.1690. $C_{14}H_{22}N_4O_3$. Calculated: M 294.1692.

2-[Bis(trimethylsilylethynyl)methylamino]-3-(2,2-dimethylpropanoyloxymethyl)pyrido[2,3-*d*]-pyrimidin-4-one (20). The trimethylsilylethynyllithium/benzyl chloroformate product **20,** amorphous semi-solid (23%) showed ^{1}H NMR ($CDCl_3$), δ: 8.45 (1H, dd, *J* = 1.8, 4.7 Hz, H-7); 8.36 (1H, dd, *J* = 1.8, 7.7 Hz, H-5); 7.16 (1H, dd, *J* = 4.7, 7.7 Hz, H-6); 7.14 (1H, d, *J* = 7.6 Hz, NH); 6.20 (2H, s, CH_2O); 6.11 (1H, d, *J* = 7.6 Hz, CH); 1.40 (9H, s, $C(CH_3)_3$); 0.00 (18H, s, $2Si(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 180.1, 168.4, 153.2, 152.7, 151.1, 138.0, 128.7, 121.5, 100.1, 88.6, 65.6, 39.5, 36.4, 27.4, 0.20. *m/z* (EI): 482 (M^+, 10%), 367 (25), 159 (10), 84 (30), 49 (100). HRMS: M^+ 482.2174. $C_{24}H_{34}N_4O_3Si_2$. Calculated: M 482.2169.

2-[Bis(trimethylsilylethynyl)methylamino]-5,6,7,8-tetrahydro-3-(2,2-dimethylpropanoyloxymethyl)-quinazolin-4-one (21). The trimethylsilylethynyllithium/benzyl chloroformate product **21**; mp 186-187°C, displayed ^{1}H NMR ($CDCl_3$), δ: 6.26 (1H, d, *J* = 7.3 Hz, NH); 5.81 (2H, s, CH_2O); 5.77 (1H, d, *J* = 7.3 Hz, CH); 2.28-2.24 (4H, m, $2CH_2$); 1.54-1.50 (4H, m, $2CH_2$); 1.06 (9H, s, $C(CH_3)_3$); 0.00 (18H, s, $2Si(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 179.2, 162.2, 160.9, 148.3, 110.0, 100.4, 87.2, 64.2, 38.8, 35.4, 31.9, 26.9, 22.2, 22.0, -0.4. *m/z* (EI): 486 (100%), 485 (M^+, 15), 386 (10), 102 (30), 90 (60). HRMS: M^+ 485.2532. $C_{25}H_{39}N_3O_3Si_2$. Calculated: M 485.2530. Crystal data monoclinic, *V* = 2932.0(14) Å^3; *a* = 12.558(3) Å, *b* = 10.472(3) Å, *c* = 22.518(6) Å; β= 98.07(2)°. Space group $P2_1/a$; *Z* = 4; d_{calc} = 1.100 mg·m^{-3}; *h* -15 to 14, *k* -11 to 13, *l* -28 to 28.

5-[1-(3,6-Dimethyl-4-oxopyrimidin-2-ylamino)-3-trimethylsilylprop-2-yn-1-yl]-2-[bis(trimethylsilyl-ethynyl)methylamino]-3,6-dimethylpyrimidin-4-one (22). Formed from amidine **18b** with benzyl chloroformate/trimethylsilylethynyllithium in 35% yield compound **22**, amorphous gum. ^{1}H NMR ($CDCl_3$), δ: 7.02 (1H, d, *J* = 8.9 Hz, NH); 6.14 (1H, d, *J* = 8.9 Hz, CH); 6.00 (1H, d, *J* = 8.2 Hz, NH); 5.93 (1H, d, *J* = 8.2 Hz, CH); 3.29 (3H, s, NCH_3); 2.29 (3H, s, NCH_3); 2.29 (3H, s, CCH_3); 1.98 (3H, s, CCH_3); 0.03 (9H, s, $Si(CH_3)_3$); 0.01 (9H, s, $Si(CH_3)_3$); 0.00 (9H, s, $Si(CH_3)_3$). ^{13}C NMR ($CDCl_3$), δ: 163.6, 163.0, 161.7, 160.2, 152.1, 149.8, 110.4, 103.1, 101.2, 100.3, 87.7, 87.6, 86.0, 42.1, 35.6, 27.0. 26.6, 23.9, 21.6, -0.09, -0.40, -0.45. *m/z* (EI): 592 (M^+, 30%, 477 (25), 454 (25), 385 (10), 179 (25), 139 (100). HRMS: M^+ 592.2830. $C_{29}H_{44}N_6O_2Si_3$. Calculated: M 592.2834.

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