Suzuki-aza-Wittig, Suzuki-condensation and aza-Wittig-electrocyclic ring-closure tandem reactions for synthesis of fused nitrogen-containing ring systems

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Abstract
We describe tandem combinations of Suzuki-aza-Wittig, Suzuki-condensation and aza-Wittig-electrocyclic ring closure reactions for the synthesis of new pyridazino[4,5-*c*]isoquinolinone, pyridazino[4,5-*c*]quinolinone and pyrimido[5,4-*c*]quinoline derivatives.

Keywords: Halopyridazin-3(2*H*)-one, Suzuki reaction, aza-Wittig reaction, tandem reaction, iminophosphoranes

Introduction

In our previous studies we reported the synthesis of several new polycyclic pyridazines *via* inter- and intramolecular nucleophilic substitutions[1] as well as by using Pd-catalyzed reactions.[2] In this paper the application of Suzuki-aza-Wittig tandem, Suzuki-condensation (ring closure) tandem, as well as aza-Wittig-electrocyclization tandem reactions are described. The aza-Wittig reaction[3] is a widely used preparative method for the synthesis of several types of organic compounds.

Synthesis of the pyridazino[4,5-*c*]isoquinoline ring system from an isoquinoline precursor is well known in the literature.[4] In our recent studies we showed another route,[5] in which pyridazino[4,5-*c*]isoquinoline derivatives **4** and **7** were synthesized by Suzuki cross-coupling reactions from 4-chloro-5-methoxy pyridazin-3(2*H*)-ones,[6] and 5-chloro-4-methoxypyridazin-3(2*H*)-ones,[7] respectively (Scheme 1). Now, on the basis of our previous experiences we were interested in new synthetic routes consisting of halogen→nitrogen displacements on the pyridazinone ring system with subsequent ring closure reactions. Incorporation of the nitrogen atom into the target ring was carried out *via* transformation of dihalopyridazinones into haloiminophosphoranes, or haloamine intermediates.

On the other hand, we elaborated a synthetic method towards 4,5-annelated diazinones *via* carbodiimides. The synthesis of fused pyridazinones started from the appropriate azides[8]. The basis of this procedure is the conversion of aryliminophosphoranes to carbodiimides by using phenylisocyanate. Iminophosphorane derivatives of pyridazinones[9] and uracil[10] are known in the literature, as well as the methodology for preparation of carbodiimides.[11] Appropriate diarylcarbodiimide can be subjected to ring closure reaction by refluxing in dry solvent, usually toluene.[12] In our present work this commonly used reaction sequence was applied for the conversion of diazines.

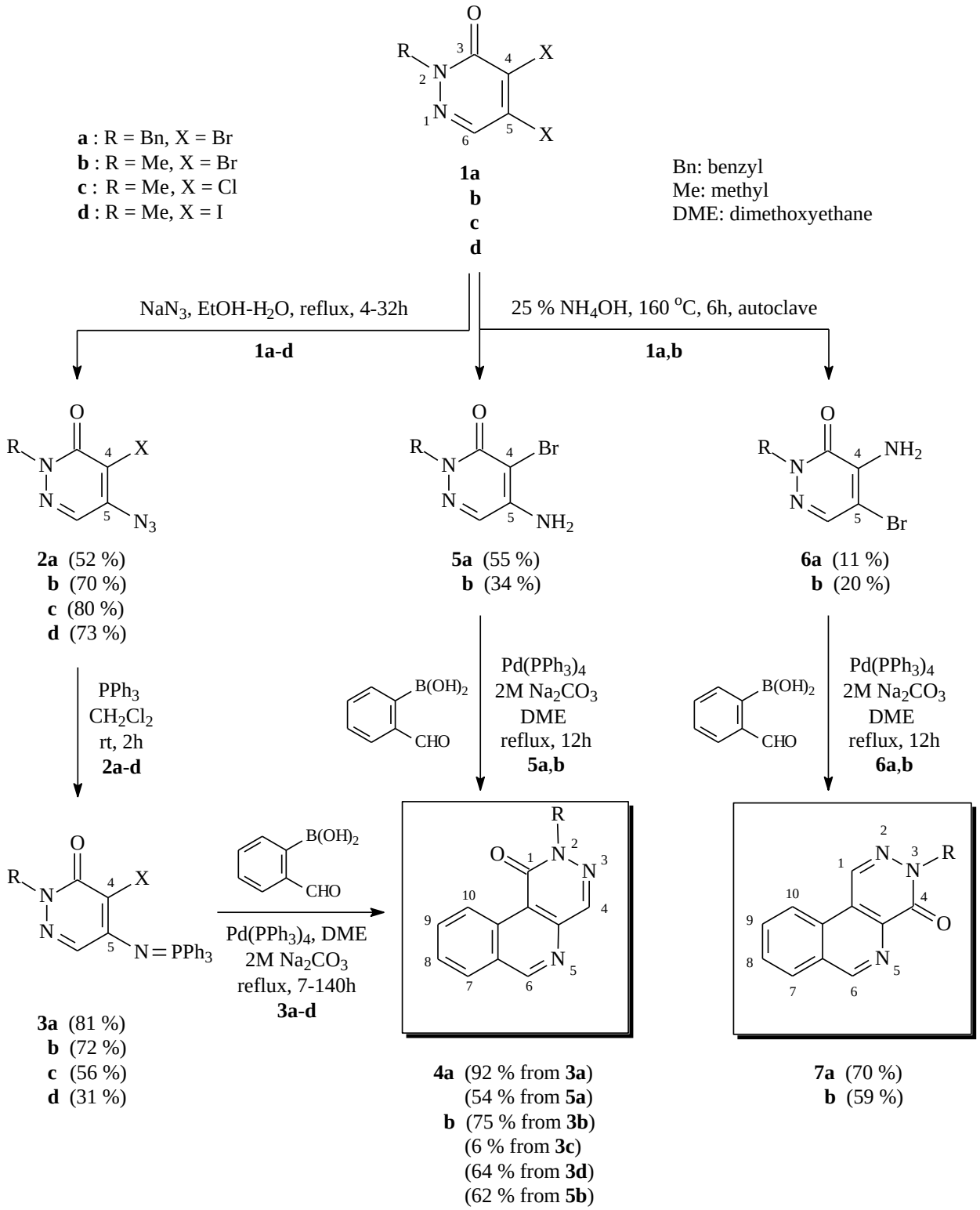
The pyridazino[4,5-*c*]quinoline ring system has been earlier described in the literature,[13] where the pyridazine part was built up on a quinoline moety. However, in our synthetic strategy the target ring system was obtained starting from a pyridazine nucleus.
Electrocyclization reaction of an uracil carbodiimide was carried out for the synthesis of pyrimido[5,4-*c*]quinoline derivatives.

Results and Discussion

We have published two general methods for the incorporation of a nitrogen atom into a polycyclic system. The first method involved the formation of an azide intermediate,[8,14] while the second one was realized *via* a halogen atom displacement of dihalopyridazine by an amino group[15,16] (Scheme 1).

The starting 2-alkyl-4,5-dibromopyridazin-3(2*H*)-ones **1a-c**, were synthesized according the literature *via* alkylation of dichloro-,[17] dibromo-,[18] or diiodopyridazin-3(2*H*)-one.[19] Compound **1d** was obtained similarly, while the literature described its synthesis by the reaction of the 2-methyldichloro compound **1c** with concentrated HI.[20]

Regioselective amination of 4,5-dibromo-2-methylpyridazin-3(2*H*)-one **1b**,[21] and 2-benzyl-4,5-dibromopyridazin-3(2*H*)-one **1a**[22] could not be achieved by reaction with aqueous ammonia to the appropriate 5-amino-4-bromo derivatives **5a**[23] and **5b**[21] as the isomeric 4-amino-5-bromo compounds **6a** and **6b**[21] were also formed in minor amounts. The same problem was encountered in the case of the published[15,16] reactions of 4,5-dichloro-2-methylpyridazin-3(2*H*)-one **1c**[17] with different amines. On the contrary, **2a**, **2b**,[24] **2c**[24] and **2d** i.e. the azido derivatives of **1a-d** were obtained selectively from the appropriate dihalopyridazinones by reaction with sodium azide. Reduction of the azides to amines could be problematic; however, the formation of iminophosphorane from the azides could serve as another possibility.



Scheme 1. Suzuki-aza-Wittig and Suzuki-condensation tandem reactions of pyridazinones.

Suzuki-aza-Wittig tandem reaction

Iminophosphorane derivatives of pyridazine[9] and uracil[10] are well known in the literature. The 4-halo-5-iminophosphoranes **3a-d** were prepared from the reaction of the related azides with triphenylphosphine followed by the reaction with 2-formylphenylboronic acid to obtain pyridazino[4,5-*c*]isoquinolin-1(2*H*)-ones **4a,b** (Scheme 1).

Iminophosphoranes **3a-d**, which contain different halogen atoms at position 4, were produced in various yields: iodo derivative **3d** was obtained with the lowest yield (31%), probably as a consequence of steric hindrance. Suzuki cross coupling – condensation tandem reaction has taken place with lowest yield (6%) when starting with chloroiminophosphorane **3c**, as the increasing reactivity order of halogens in Suzuki reaction is Cl→Br→I. According to the above listed parameters methyl- and benzyl-dibromopyridazinones proved to be the optimal precursors.

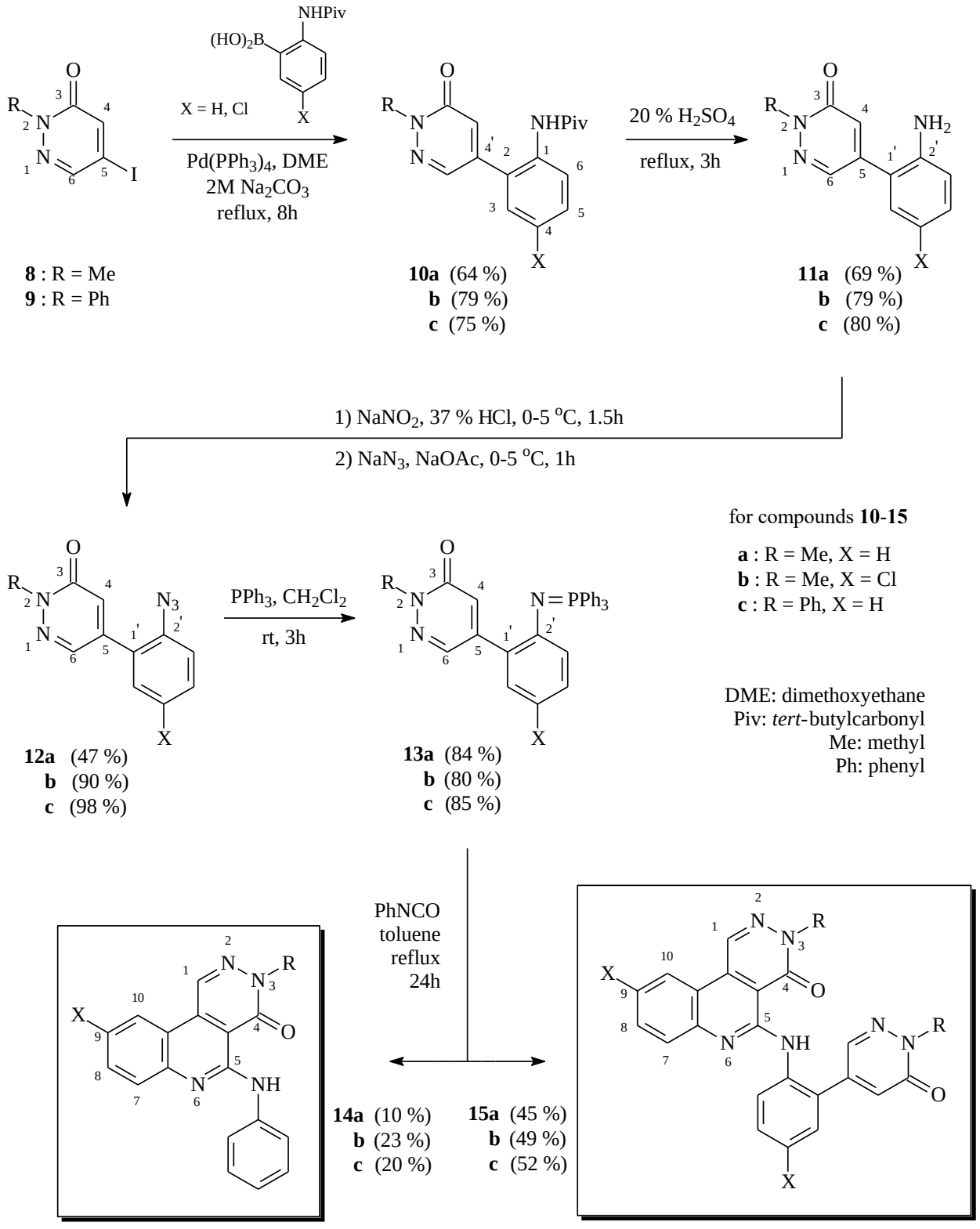
Suzuki-condensation tandem reaction

In the case when the amino compound can be produced from the azide by reduction, the Suzuki-condensation tandem reaction can be chosen. Azide→amine→Suzuki reaction steps may be more efficient, than the azide→iminophosphorane→Suzuki sequence. A similar problem of selectivity was observed during preparation of **5a**[23] and **5b**[21] as mentioned above.

4-Azido-5-bromo-2-methylpyridazin-3(2*H*)-one could not be prepared selectively under apolar conditions (sodium azide, anhydrous toluene, 15-crown-5, heating) from 4,5-dibromo-2-methylpyridazin-3(2*H*)-one **1b**. Ring closure of 4-nitrogen analogues **6a** and **6b** prepared as described above gave compounds **7a** and **7b**. Haloamines **5** and **6** were transformed to pyridazino[4,5-*c*]isoquinolines **4** and **7** *via* Suzuki – condensation tandem reaction using 2-formylphenylboronic acid. Halogen displacements by ammonia, as well as *Suzuki* – condensation tandem have proceeded in the case of 2-benzyl derivatives with higher yields than in the case of 2-methyl derivatives. Generally, if the amino compound can be prepared from a halogen precursor directly and selectively, then the synthesis route azide→iminophosphorane→Suzuki reaction can be neglected. In this case the target compound can be obtained from the dihalogen derivative through a haloamine and Suzuki – condensation tandem reaction with 2-formylphenylboronic acid. Otherwise, Suzuki cross-coupling reaction has to be carried out with haloiminophosphoranes.

Aza-Wittig – electrocyclic ring closure tandem reaction

The above Suzuki−aza-Wittig tandem reactions started from 4,5-dibromopyridazinones. As an extension of this tandem methodology, we elaborated the synthesis of pyridazino[4,5-*c*]-quinolines from iminophosphoranes (Scheme 2).



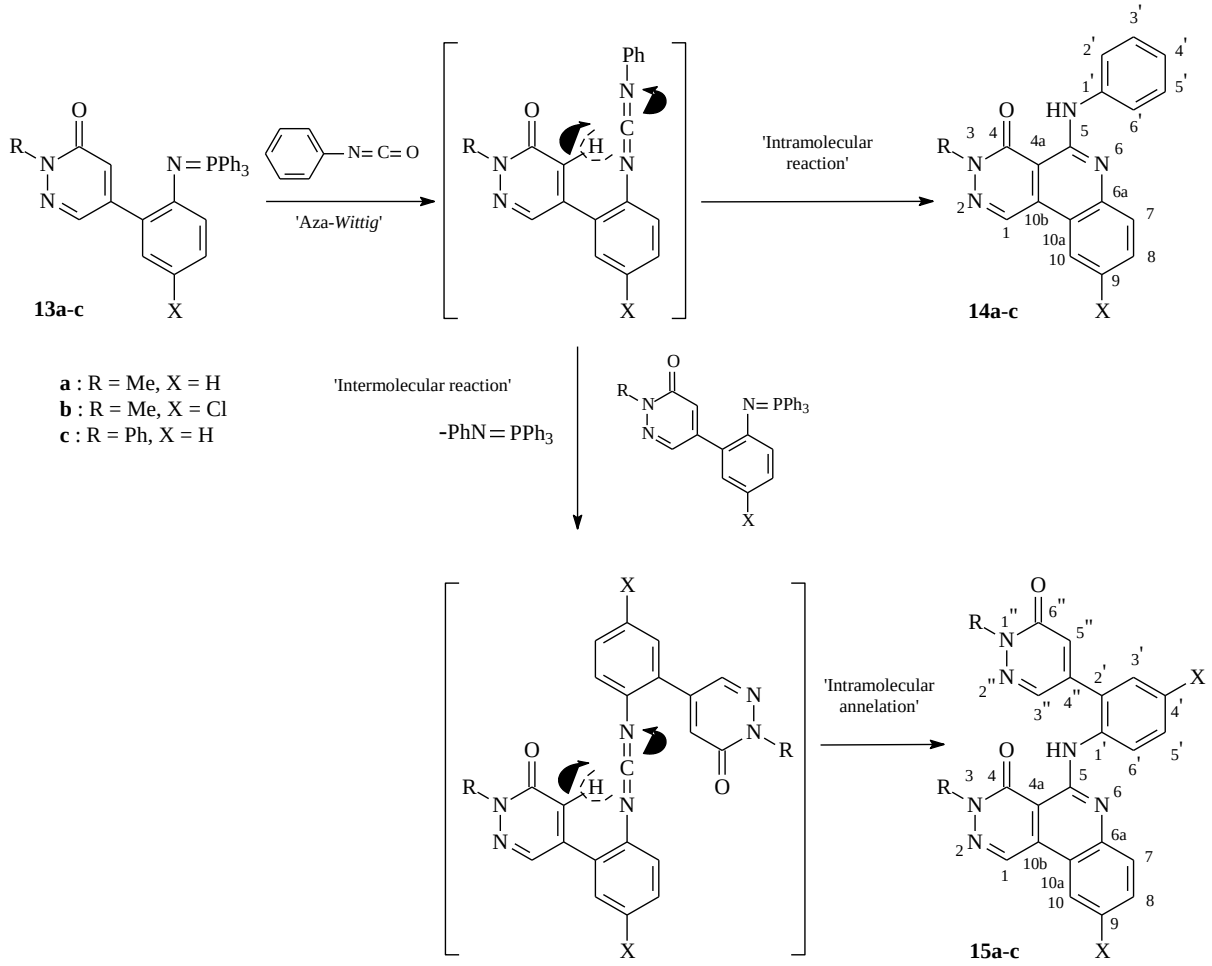
Scheme 2. Aza-Wittig – electrocyclization tandem reactions of pyridazinoiminophosphoranes.

In an earlier paper[8] we described Suzuki cross coupling reactions of 5-iodo-2-methylpyridazin-3(2*H*)-one **8**[25] with arylboronic acids. This series has recently been completed using 5-iodo-2-phenylpyridazin-3(2*H*)-one **9**.[19] Accordingly, **8** and **9** were reacted with 2-pivaloylamino phenylboronic acid and its 5-chloro derivative to obtain the protected aniline derivatives **10a-c**. Deprotection of the protected anilines **10a-c** gave the free amines **11a-c**. The latter compounds were diazotized followed by treating the diazonium salts formed with NaN_3 to give the corresponding azides **12a-c** (Scheme 2). These azides were reacted with triphenylphosphine in dichloromethane to give iminophosphoranes **13a-c**.

In the light of the reported procedure of the tandem-type reaction,[26] the iminophosphoranes **13a-c** were reacted with phenylisocyanate in toluene to give the corresponding carbodiimide intermediates, followed by *in situ* thermal cyclization at 140°C for 24 h in a one-pot reaction. The reaction product was found to be a mixture of two compounds which were easily separated by column chromatography and identified as the pyridazino[4,5-*c*]quinolines; **14a-c** (minor products) and **15a-c** (major products).

These results can be explained (see Scheme 3) on the basis of intramolecular reactions being usually favored (running faster) while the attack of another iminophosphorane at the *sp* carbon atom of the carbodiimide led to bis-carbodiimides which underwent a ring closure reaction. Thus, the 5-phenylamino derivatives obtained *via* a direct intramolecular route were formed in lower yields compared to the 5-pyridazinylphenylamino compounds.

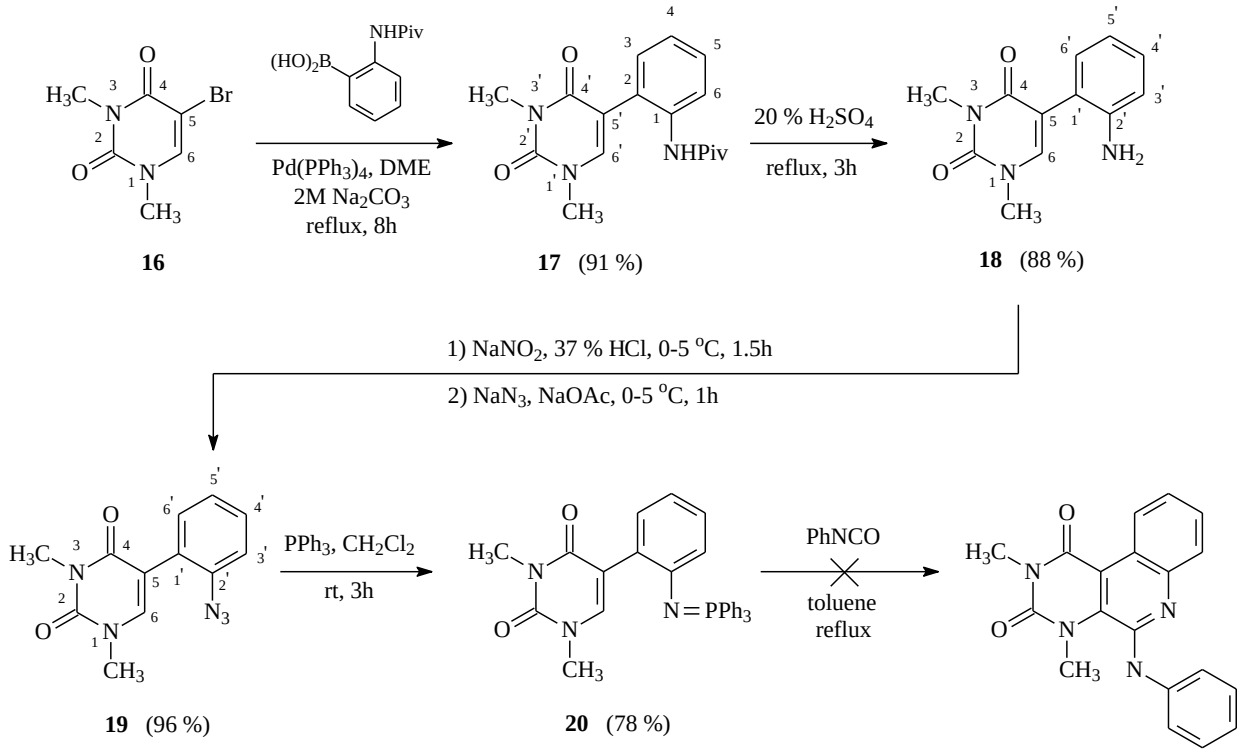
A plausible mechanism for the thermal cyclization of the carbodiimide intermediates is presented (Scheme 3). These carbodiimides, formed by aza-Wittig reaction between iminophosphoranes **13a-c** and phenylisocyanate, could undergo thermal cyclization in two ways. In the case of the major product, a *N,N'*-bis(pyridazinylphenyl)carbodiimide is formed by intermolecular reaction of the carbodiimide with another molecule of the iminophosphorane, along with elimination of phenyliminotriphenylphosphorane. In this first step the nitrogen atom of the iminophosphorane attacks at the *sp* carbon atom of the carbodiimide as a nucleophile. Then the *N,N'*-bis(pyridazinylphenyl)carbodiimide intermediate reacts in a subsequent intramolecular ring closure reaction giving the main product. In the case of the minor product, the carbon atom at position 4 on the pyridazinone ring initiates the nucleophile attack at the carbon of the carbodiimide and phenylamino-pyridazine is formed by a direct intramolecular step. These concurrent reaction pathways could be explained with the stronger nucleophilicity of the iminophosphorane nitrogen atom compared to the pyridazine ring carbon at position 4.



Scheme 3. Proposed mechanism of aza-Wittig – electrocyclization reactions.

Electrocyclic ring closure *via* a carbodiimide intermediate

i) As the aza-Wittig type reaction was successful on pyridazinones, we wanted to apply this tandem cyclization on other diazines, first on uracil derivatives. Aminophenyl uracil derivative **18** - synthesized from 5-bromo-1,3-dimethyl-uracil **16** by Suzuki cross coupling reaction *via* the protected amino compound **17** according to the method described previously[14] - was the first model compound for testing the aza-Wittig type reactions (Scheme 4).



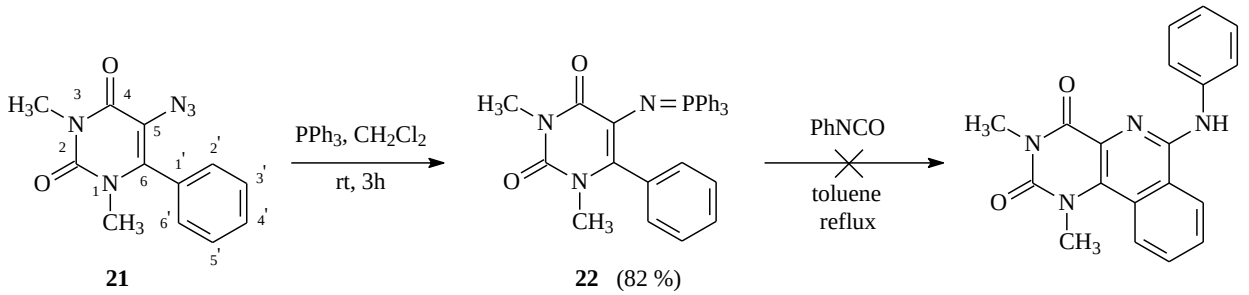
16 **17** (91 %) **18** (88 %)

19 (96 %) **20** (78 %)

Scheme 4. Synthesis and reaction of a 5-phenyluracil derivative.

The amine **18** was first transformed to its azido-derivative **19**, then in a subsequent step by reaction with triphenylphosphine to the iminiphosphorane derivative **20** and the latter was treated with phenylisocyanate. Our idea was to prepare a carbodiimide *in situ* and to carry out a subsequent cyclization. Unfortunately, the desired pyrimidoisoquinoline could not be isolated from the complex reaction mixture. This failure is probably due to the very low electron density of the uracil carbon at position 6.

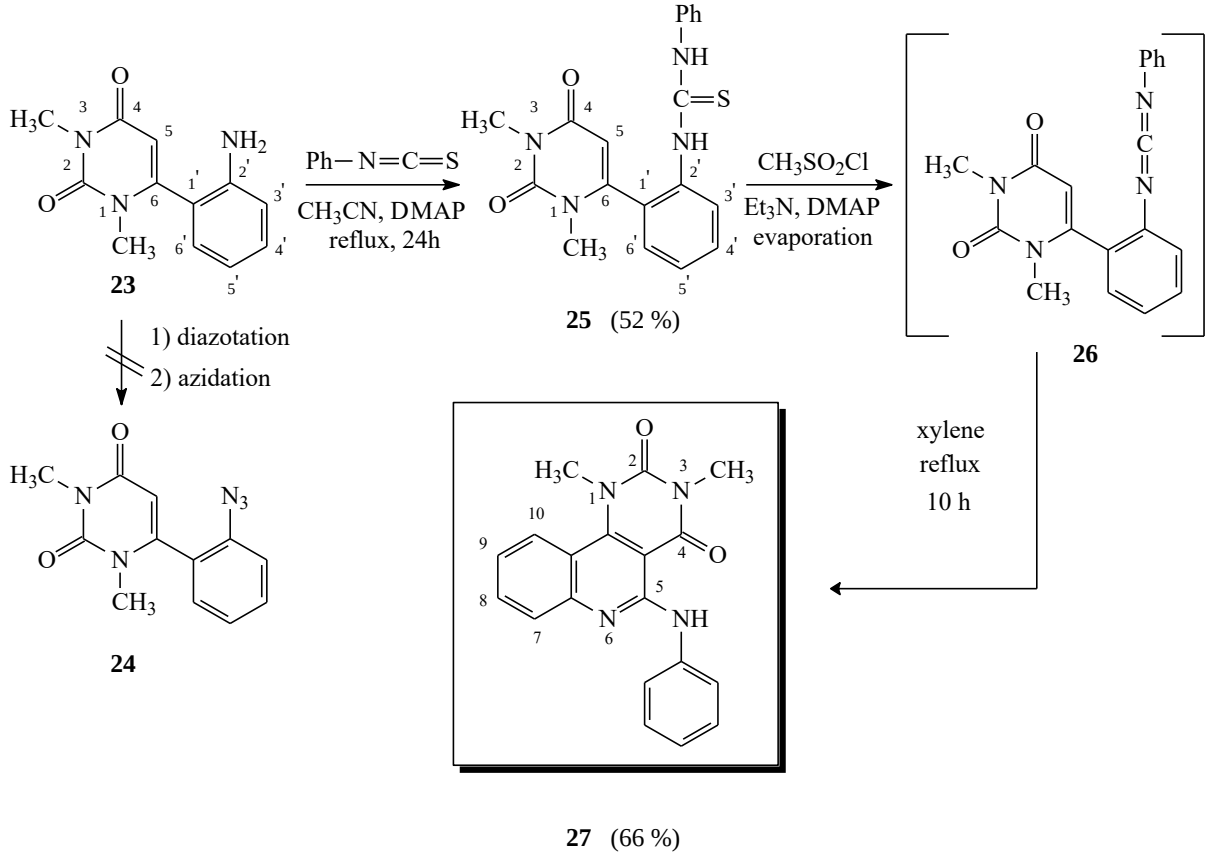
A similar situation was observed in another experiment; iminophosphorane **22** produced from azido-uracil derivative **21**[2] gave with phenylisocyanate a complex mixture (Scheme 5) from which the desired pyrimidoquinoline could not be isolated. This could also be a consequence of the lower electron density of the substituted phenyl ring: the adjacent C-6 atom of the uracil core is rather electron deficient and can withdraw electrons at *ortho*-position of the phenyl ring.



21 **22** (82 %)

Scheme 5. Reaction of a 6-phenyluracil derivative.

ii) Since carbodiimide was the proposed key intermediate for the tandem reactions of pyridazinones, it seemed promising to synthesize a carbodiimide directly in the case of other uracils. Suitable precursors could be found again among our own published uracils[14] (Scheme 6).

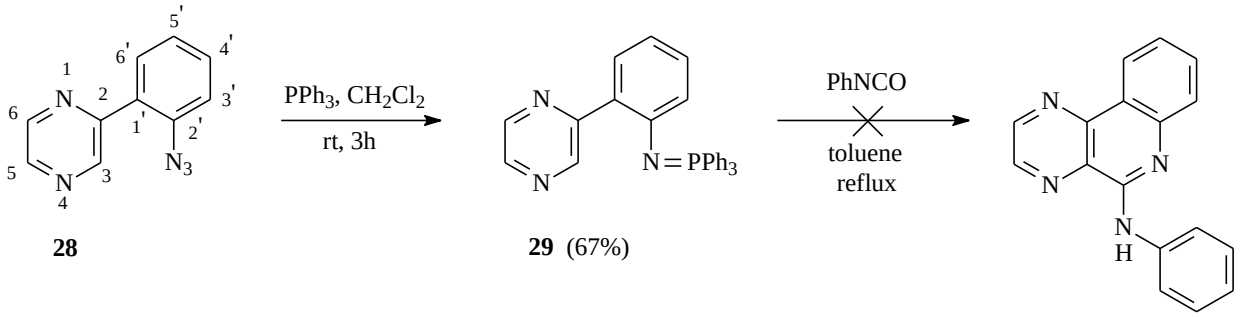


Scheme 6. Ring closure reaction of a 6-phenyluracil derivative.

Azido derivative **24** of the chosen aminophenyl uracil derivative **23**[14] could not be isolated earlier; for this reason first the thiourea derivative **25** derived from **23** was prepared with phenylisothiocyanate according to a published method.[27] In the next step, carbodiimide **26** was generated *in situ* with methanesulfonylchloride in dry toluene, then **26** was transformed by refluxing in xylene to the cyclized product **27**. This route is not a tandem sequence, but similar to it. We observed only direct intramolecular reaction on the uracil nucleus, contrary to the analogues applied in the procedures with pyridazinones. This can be explained with the stronger nucleophilicity of the carbon atom at position 5 of the uracil core, compared to the carbodiimide nitrogen. Therefore intramolecular electrocyclization took place without formation of a dimeric carbodiimide intermediate and thus the pyrimido[5,4-*c*]quinoline ring system[28] was directly produced instead. This finding could be explained in the following way: the nitrogen atom of the carbodiimide is a relatively weaker nucleophilic center than the carbon at position 5 of the uracil

ring. Therefore, the direct intramolecular route is more favorable compared to the formation of a disubstituted carbodiimide, which occurred in the case of pyridazinones.

The pyrazinyl azidophenyl compound **28** (Scheme 7) prepared by us earlier[14] was the next model studied in the above methodology applied for pyridazines. Similarly to the previous procedure, in the first step iminophosphorane derivative **29** derived from the pyrazine **28** was formed. Next, phenylisocyanate was reacted with this precursor but here again a complex mixture was formed from which the desired pyrazinoquinoline could not be isolated.

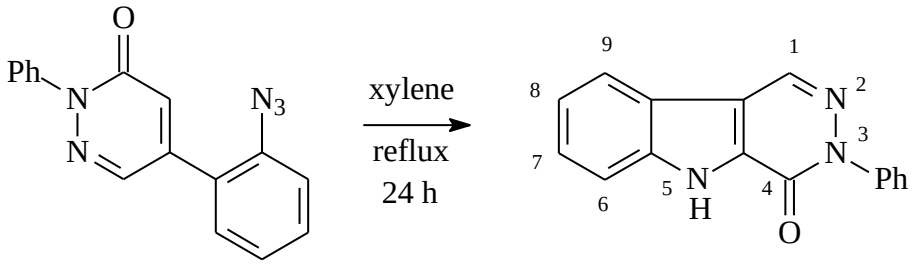


28 **29** (67%)

Scheme 7. Reaction of a 2-phenylpiridazine derivative.

Ring closure *via* nitrene intermediate

According to our previous method cited above,[8] a protected aniline derivative of an *N*-phenyl substituted pyridazinone (**10c** in Scheme 2) was also a convenient starting compound for internal ring closure following our cyclization protocol established. Thus, after deprotection of the aniline derivative to the amine this compound was diazotized to a diazonium salt which, *in situ*, was subjected to an aza-transfer azidation reaction to an aryl azide. Heat treatment of azide **12c** generated a nitrene, attached selectively to only one of the adjacent positions of the pyridazine ring. Heating **12c** in refluxing xylene gave 5*H*-pyrazino[4,5-*b*]indole **30** (Scheme 8). (The same ring closure reactions of compounds **12a** as well as **12b** were described in literature 8.)



12c **30** (59 %)

Scheme 8. Ring closure reaction of azidophenyl pyridazinone.

Conclusions

Two new methods for the synthesis of the pyridazino[4,5-*c*]isoquinoline ring system are reported. 2-Substituted pyridazino[4,5-*c*]isoquinolines **4a** and **4b** were produced in Suzuki-aza-Wittig tandem reactions. Dibromo derivatives proved to be optimal halogen precursors. The pyridazinoisoquinolines **4a** and **4b**, as well as **7a** and **7b** were synthesized by Suzuki-condensation tandem reaction. Both the halogen displacement reactions with ammonia and Suzuki-condensation tandem reactions proceeded with higher yields when starting with one of the *N*-2 benzyl derivatives.

Application of the Suzuki-aza-Wittig tandem reaction on pyridazinones is recommended mainly in the following cases:

- if the precursor haloamine cannot be prepared regioselectively from the dihalogen compound,
- if the haloamine can be obtained only by reduction from haloazido derivative, or
- if the derivative substituted at the required position can be formed selectively in one step from the appropriate dihalogen compound.

Our present method is synthetically convenient and contains fewer steps, than the previously published route.[5] Moreover, in the present method both haloamine regioisomers were produced in one step.

On the other hand, another method was developed for the synthesis of the pyridazino[4,5-*c*]-quinoline and the pyrimido[5,4-*c*]quinoline ring systems. The desired compounds were produced *via* carbodiimide intermediates by electrocyclic ring closure.

Elaboration of these methods could open efficient accesses to fused nitrogen-containing ring systems.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 200 (^{1}H NMR 200 MHz; ^{13}C NMR 50 MHz), a Bruker Avance-500 (^{1}H NMR 500 MHz; ^{13}C NMR 125 MHz), a Bruker DRX-400 (^{1}H NMR 400 MHz; ^{13}C NMR 100 MHz) or a Varian MERCURY plus (^{1}H NMR 400 MHz; ^{13}C NMR 100 MHz) spectrometer in the solvent indicated at room temperature, using the ^{2}H signal of the solvent as the lock. The ^{1}H and ^{13}C chemical shifts were referred to TMS (δ_{TMS}=0 ppm). Chemical shifts (δ) are given in ppm and coupling constant (*J*) values in Hz. The structures of compounds were elucidated using COSY, HSQC, HMBC (NMR) methods. Melting points were determined in a Büchi Melting Point B-540 apparatus and the values are uncorrected. IR spectra were recorded in potassium bromide pellets with a Perkin-Elmer 1600 FT-IR spectrophotometer. Mass spectra were taken on a Finnigan MAT 8430 spectrometer [resolution: 1250, ion accelerating voltage: 3 kV, ion source temperature: 250 ºC/Electron Ionization Mass Spectra (EIMS) and Chemical Ionization Mass Spectra (CIMS), 25 ºC/Fast

Atom Bombardment Mass Spectra (FABMS)] and a quadrupole-time-of-flight mass spectrometer (Q-Tof-II, Micromass, Manchester, UK; cone voltage approx. 35V and capillary voltage approx. 3.3 kV). Elemental analyses were performed on a Carlo Erba Elemental Analyzer Model 1012 apparatus.

Commercially available solvents were purified by standard procedures prior to use, whereas reagents (Reanal, Budapest, or Sigma-Aldrich Kft., Budapest) were used as received. Standard flash chromatography on silica (Kieselgel 60, Aldrich, 0.040-0.063 mm) and/or recrystallization as indicated, was applied for purification of crude products. Thin layer chromatography was done on commercially available silica plates (Silica gel 60 F_{254}, Merck).

Compounds **1a**,[22] **1b**,[21] **1c**,[17] **5b**,[21] **6b**,[21] **8**,[25] **9**,[19] **10a**,[8] **10b**,[8] **11a**,[8] **11b**,[8] **12a**,[8] **12b**,[8] **21**,[2,14] **23**[14] and **28**[14] were synthesized according to the literature. Compound **5a** was also synthesized according to the literature[23] and **6a** was also isolated from the same reaction mixture. Spectroscopic data of **1d**,[20] **2b**,[24] **2c**,[24] **4a**,[5] **4b**,[5] **7a**[5] and **7b**[5] are corresponding to those reported in the literature for identical compounds produced *via* routes different from the ones described herein.

Method A. General procedure for the reaction of 1a-d dihalopyridazinones with sodium azide

To a suspension of the 4,5-dihalopyridazinone derivative **1a-d** (8.3 mmol) in ethanol (58 mL) and water (29 mL), sodium azide (16.6 mmol) was added, and the mixture was refluxed until the starting material was consumed as judged by TLC analysis. The hot reaction mixture was filtered and the filtrate was evaporated to dryness *in vacuo*. The solid residue was taken up in water (20 mL) and extracted with chloroform (3x20 mL). The combined organic layers were dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo*, and the crude product **2a-d** was purified by column chromatography or by recrystallization as given below.

5-Azido-2-benzyl-4-bromopyridazin-3(2*H*)-one (2a). Reaction time: 4 h; eluent used for flash column chromatography: toluene. Yellow crystals, yield 1.33 g, 52%, mp 66-67 ºC; R_f (toluene-methanol 4:1): 0.69. IR (ν_{max}, cm^{-1}): 3288, 3104, 2960, 2132, 1638, 1594, 1420, 1354, 1314, 1218, 1112, 1074, 742, 700 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ_H 7.62 (1H, s, H-6), 7.46-7.26 (m, 5H, phenyl protons), 5.32 (s, 2H, C*H*$_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ_C 157.3 (C-3), 141.7 (C-5), 135.3 (C-1'), 129.0 (C-2',6'), 128.8 (C-6), 128.6 (C-3',5'), 128.3 (C-4'), 113.6 (C-4), 56.4 (CH_2); C' are benzyl aromatic carbons. Anal. Calcd for $C_{11}H_8BrN_5O$ (306.12): C, 43.16; H, 2.63; N, 22.88%. Found: C, 43.13; H, 2.46; N, 22.63%.

5-Azido-4-bromo-2-methylpyridazin-3(2*H*)-one (2b). Reaction time: 9 h. Yellow crystals, yield 53%, 1.01 g, mp 104-106 ºC (from dry ethanol, lit.[24] mp 103-104 ºC).

5-Azido-4-chloro-2-methylpyridazin-3(2*H*)-one (2c). Reaction time: 32 h; eluent used for flash column chromatography: toluene. Yellow crystals, yield 31%, 0.47 g, mp 86-86.5 ºC (lit.[24] mp 90-91ºC).

5-Azido-4-iodo-2-methylpyridazin-3(2*H*)-one (2d). Reaction time: 12 h. Yellow crystals, yield 73%, 1.68 g, mp 116-118 ºC (from dichloromethane); R_f (toluene-methanol 4:1): 0.49. IR (ν_{max}, cm^{-1}): 3032, 2940, 2126, 1624, 1580, 1546, 1382, 1318, 1292, 688. ^{1}H NMR (200 MHz, CD_3OD): δ_H 7.81 (s, 1H, H-6), 3.80 (s, 3H, C*H*$_3$). ^{13}C NMR (50 MHz, CD_3OD): δ_C 158.2 (C-3), 149.4 (C-5), 130.2 (C-6), 91.6 (C-4), 41.6 (CH_3). Anal. Calcd for $C_5H_4IN_5O$ (277.03): C, 21.68; H, 1.46; N, 25.28%. Found: *C*, 21.58; H, 1.33; N, 24.81%.

Method B. General procedure for the reaction of azides with triphenylphosphine

A round-bottom flask was purged with argon and charged with the appropriate azido compound derivative (13.10 mmol) and dry dichloromethane (100 mL). Under stirring, the mixture was flushed with argon for approximately 5 min. Subsequently triphenylphosphine (13.50 mmol) was added and the reaction mixture was stirred at room temperature for three hours. The solvent was evaporated *in vacuo*, and the crude solid product **3a-d** was recrystallized from dichloromethane or purified by column chromatography.

2-Benzyl-4-bromo-5-(triphenylphosphoranylideneamino)pyridazin-3(2*H*)-one (3a). Colourless crystals, yield 81%, 5.70 g, mp 197-198 ºC; R_f (chloroform-ethyl acetate 9:1): 0.76. IR (ν_{max}, cm^{-1}): 3050, 2924, 1624, 1568, 1476, 1412, 1354, 1326, 1198, 1108, 720, 692, 528. ^{1}H NMR (200 MHz, $CDCl_3$): δ_H 7.83-7.18 (m, 20H, phenyl protons), 6.96 (s, 1H, H-6), 5.23 (s, 2H, C*H*$_2$). ^{13}C NMR (50 MHz, $CDCl_3$): δ_C 159.9 (C-3), 151.2 (C-5), 137.0 (C-1'), 133.8 (C-6), 132.7 (C-4"), 132.4 (C-2",6"), 129.2 (C-1"), 129.1 (C-3",5"), 128.8 (C-2',6'), 128.4 (C-3',5'), 127.5 (C-4'), 109.9 (C-4), 54.9 (*C*H$_2$); C' are benzyl aromatic carbons, C" are phenyl carbons; P-C coupling constants: $^1J_{(P,\ C\text{-}1")}$ 101, $^2J_{(P,\ C\text{-}2",\ -6")}$ 10, $^3J_{(P,\ C\text{-}3",\ -5")}$ 12, $^4J_{(P,\ C\text{-}4")}$ 2.2, $^3J_{(P,\ C\text{-}4)}$ 24, and $^3J_{(P,\ C\text{-}6)}$ 11 Hz. Anal. Calcd for $C_{29}H_{23}BrN_3OP$ (540.381): C, 64.46; H, 4.29; N, 7.78%. Found: C, 64.54; H, 4.19; N, 7.71%.

4-Bromo-2-methyl-5-(triphenylphosphoranylideneamino)pyridazin-3(2*H*)-one (3b). Colourless crystals, yield 72%, 4.39 g, mp 223-223.8 ºC; R_f (toluene-methanol 7:3): 0.33. IR (ν_{max}, cm^{-1}): 3052, 2940, 1638, 1568, 1478, 1436, 1396, 1332, 1226, 1108, 942, 720, 692, 530, 504. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 7.82-7.63 (m, 15H, phenyl protons), 6.88 (s, 1H, H-6), 3.50 (s, 3H, C*H*$_3$). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 158.3 (C-3), 150.9 (C-5), 132.9 (C-4'), 132.3 (C-6), 132.1 (C-2',6'), 129.4 (C-3',5'), 128.4 (C-1'), 110.0 (C-4), 39.4 (*C*H$_3$); C' are phenyl carbons; P-C coupling constants: $^1J_{(P,\ C\text{-}1')}$ 101, $^2J_{(P,\ C\text{-}2',\ -6')}$ 11, $^3J_{(P,\ C\text{-}3',\ -5')}$ 12, $^4J_{(P,\ C\text{-}4')}$ 2.3, $^3J_{(P,\ C\text{-}4)}$ 24, and $^3J_{(P,\ C\text{-}6)}$ 12 Hz. Anal. Calcd for $C_{23}H_{19}BrN_3OP$ (464.30): C, 59.50; H, 4.12; N, 9.05%. Found: C, 59.95; H, 4.07; N, 9.06%.

4-Chloro-2-methyl-5-(triphenylphosphoranylideneamino)pyridazin-3(2*H*)-one (3c). Colourless crystals, yield 56%, 3.09 g, mp 218-219 ºC; R_f (toluene-methanol 4:1): 0.45. IR (ν_{max}, cm^{-1}): 3446, 3048, 2928, 2856, 1630, 1570, 1478, 1394, 1326, 1106, 720, 688, 528. ^{1}H NMR (200 MHz, DMSO-d_6): δ_H 7.85-7.58 (m, 15H, phenyl protons), 6.99 (s, 1H, H-6), 3.50 (s, 3H, C*H*$_3$). ^{13}C NMR (50 MHz, DMSO-d_6): δ_C 158.0 (C-3), 149.0 (C-5), 133.2 (C-6), 132.9 (C-4'), 132.1 (C-2',6'), 129.4 (C-3',5'), 128.7 (C-4), 128.6 (C-1'), 39.2 (*C*H$_3$). C' are phenyl carbons; P-C coupling constants: ^1J(P, C-1') 101, ^2J(P, C-2',6') 10, ^3J(P, C-3',5') 12, ^4J(P, C-4') 2.2, ^3J(P,

C-4) 24, and ^{3}J(P, C-6) 13 Hz. Anal. Calcd for $C_{23}H_{19}ClN_3OP$ (419.85): C, 65.80; H, 4.56; N, 10.01%. Found: C, 65.69; H, 4.46; N, 9.89%.

4-Iodo-2-methyl-5-(triphenylphosphoranylideneamino)pyridazin-3(2*H*)-one (3d). Yellow crystals, yield 31%, 2.07 g, mp 234-235 °C; R_f (toluene-methanol 4:1): 0.41. IR (ν_{max}, cm^{-1}): 3050, 2936, 1626, 1566, 1478, 1430, 1398, 1334, 1308, 1106, 950, 720, 690, 528, 508. ^{1}H NMR (200 MHz, $CDCl_3$): δ_H 7.85-7.40 (m, 15H, phenyl protons), 6.77 (s, 1H, H-6), 3.68 (s, 3H, C*H*$_3$). ^{13}C NMR (50 MHz, $CDCl_3$): δ_C 155.5 (C-3), 149.5 (C-5), 132.6 (C-4'), 132.4 (C-2',6'), 131.6 (C-6), 129.0 (C-3',5'), 128.9 (C-1'), 92.9 (C-4), 40.1 (*C*H$_3$); C' are phenyl carbons; P-C coupling constants: $^{1}J_{(P, C-1')}$ 101, $^{2}J_{(P, C-2', -6')}$ 10, $^{3}J_{(P, C-3', -5')}$ 12, $^{4}J_{(P, C-4')}$ 2.6, $^{3}J_{(P, C-4)}$ 23, and $^{3}J_{(P, C-6)}$ 11 Hz. Anal. Calcd for $C_{23}H_{19}IN_3OP$ (511.29): C, 54.03; H, 3.75; N, 8.22%. Found: C, 54.01; H, 3.62; N, 8.11%.

Method C. General procedure for the synthesis of (4a,b) *via Suzuki*-reaction from the appropriate haloiminophosphoranes

A round-bottom flask was purged with argon and charged with the iminophosphorane derivative **3a-d** (2.0 mmol) and dry 1,2-dimethoxyethane (30 mL). While stirring, the mixture was flushed with argon for approximately 10 min. Subsequently tetrakis(triphenylphosphine)-palladium(0) (0.12 mmol), 2-formylphenylboronic acid (2.8 mmol) and sodium carbonate solution (2M, 10 mL) were added and the reaction mixture was heated at the temperature given below. The solvent was evaporated *in vacuo*, the crude black oil obtained was taken up in water (80 mL) and extracted with chloroform (3x80 mL). The combined organic layers were dried over anhydrous magnesium sulfate. The solvent was evaporated *in vacuo*, and the brown residue was purified by flash column chromatography as given below.

2-Benzyl-pyridazino[4,5-*c*]isoquinolin-1(2*H*)-one (4a). Starting from 2-benzyl-4-bromo-5-(triphenyliminophosphoranyl)pyridazin-3(2*H*)-one **3a**, reaction conditions: 7 h at 120 °C; eluent used for flash column chromatography: toluene-methanol 95:5. Colourless crystals, yield 92%, 0.39 g, mp 173-174 °C (lit.[5] mp 173 °C).

2-Methyl-pyridazino[4,5-*c*]isoquinolin-1(2*H*)-one (4b). (a) Starting from 4-bromo-2-methyl-5-(triphenyliminophosphoranyl)pyridazin-3(2*H*)-one **3b**, reaction conditions: 7 h at 120°C; eluent used for flash column chromatography: toluene-methanol 4:1. Colourless crystals, yield 75%, 0.31 g, mp 155.5-156 °C (lit.[5] mp 149-151 °C). (b) Starting from 4-chloro-2-methyl-5-(triphenyliminophosphoranyl)pyridazin-3(2*H*)-one **3c**, reaction conditions: 140 h at 150°C; eluent used for flash column chromatography: toluene-methanol 99:1. yield 6%, 0.03 g, mp 154 °C. (c) Starting from 4-iodo-2-methyl-5-(triphenyliminophosphoranyl)pyridazin-3(2*H*)-one **3d**, reaction conditions: 18 h at 120 °C; eluent used for flash column chromatography: toluene-methanol 9:1. yield 64%, 0.27 g, mp 155 °C.

Method D. General procedure for the synthesis of (4a,b), *via Suzuki*-reaction from the appropriate haloamines

A round-bottom flask was purged with argon and charged with the amino derivative **5a** or **5b** (2.0 mmol) and dry 1,2-dimethoxyethane (30 mL). While stirring, the mixture was flushed with argon for approximately 10 min. Subsequently tetrakis(triphenylphosphine)-palladium(0) (0.12 mmol), 2-formylphenylboronic acid (4.0 mmol) and sodium carbonate solution (2M, 2.0 mL) were added, and the reaction mixture was heated at 110 °C for 12 hours. The reaction mixture was poured onto ice-water (60 mL), was extracted with dichloromethane (3x45 mL) and the combined organic layers were dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* and the residue was purified by flash column chromatography as given below.

2-Benzyl-pyridazino[4,5-*c*]isoquinolin-1(2*H*)-one (4a). Starting from 5-amino-2-benzyl-4-bromopyridazin-3(2*H*)-one **5a**, eluent used for flash column chromatography: toluene-methanol 4:1. Yield 54%, 0.31 g, mp 171-172 °C (lit.: 173 °C)[5].

2-Methyl-pyridazino[4,5-*c*]isoquinolin-1(2*H*)-one (4b). Starting from **5b**, eluent used for flash column chromatography: toluene-methanol 7:3. Yield , 62%, 0.39 g, mp 154-155 °C (lit.: 149-151 °C)[5].

Method E. Synthesis and characterization of haloamines (5a) and (6a)

5-Amino-2-benzyl-4-bromopyridazin-3(2*H*)-one (5a). Reaction of 2-benzyl-4,5-dibromopyridazin-3(2*H*)-one **1a** (7.12 mmol) with ammonia (50 mL, 25%) was run in an autoclave (160°C, 6 h) under stirring. After cooling, the resulting precipitate was collected by filtration, washed with water, and recrystallized to give **5a** as Colourless crystals, yield 55%, 1.10 g, mp 230.5-231 °C (from ethanol, lit.[24] mp 217-219 °C); R_f (toluene-methanol 20:1): 0.10. IR (ν_{max}, cm^{-1}): 3444, 3288, 3240, 3164, 3026, 2960, 1636, 1600, 1454, 1418, 1206, 738, 700. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 7.55 (s, 1H, H-6), 7.31-7.24 (m, 5H, phenyl protons), 6.76 (s, 2H, NH_2), 5.16 (s, 2H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 157.1 (C-3), 147.4 (C-5), 137.3 (C-1'), 129.6 (C-6), 128.4 (C-3',5'), 127.6 (C-2',6'), 127.3 (C-4'), 95.4 (C-4), 54.0 (*C*H_2); C' are phenyl carbons. Anal. Calcd for $C_{11}H_{10}BrN_3O$ (280.12): C, 47.17; H, 3.60; N, 15.00; Br, 28.52%. Found: C, 47.08; H, 3.37; N, 14.96; Br, 28.70%.

4-Amino-2-benzyl-5-bromopyridazin-3(2*H*)-one (6a). Obtained by flash chromatography purification of the mother liquor of **5a** (prepared from **1a**). Pale yellow crystals, yield 11%, 0.22 g, mp 109.7-110.2 °C; R_f (toluene-methanol 20:1): 0.37. IR (ν_{max}, cm^{-1}): 3470, 3384, 3300, 2962, 2928, 1604, 1542, 1510, 1454, 1336, 1224, 878, 836. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 7.79 (s, 1H, H-6), 7.32-7.26 (m, 5H, phenyl protons), 6.72 (s, 2H, NH_2), 5.20 (s, 2H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 154.2 (C-3), 143.1 (C-4), 139.4 (C-6), 136.7 (C-1'), 128.4 (C-3',5'), 127.8 (C-2',6'), 127.4 (C-4'), 95.5 (C-5), 54.1 (*C*H_2); C' are phenyl carbons; MS (ESI): *m/z* (%) 92, 201, 203, 280, 282; HRMS (ESI) calcd. for $C_{11}H_{10}BrN_3O$ $[M+H]^+$: 280.0085, found: 280.0078.

Compounds **7a,b** were prepared according to Method D above.

3-Benzyl-piridazino[4,5-*c*]isoquinolin-4(3*H*)-one (7a). Starting from 4-amino-2-benzyl-5-bromopyridazin-3(2*H*)-one **6a**, eluent used for flash column chromatography: toluene-methanol 4:1. Yield 70%, 0.08 g, mp 239-240 ºC (lit.: 240 ºC)[5].

3-Methylpiridazino[4,5-*c*]isoquinolin-4(3*H*)-one (7b). Starting from 4-amino-5-bromo-2-methylpyridazin-3(2*H*)-one **6b**, eluent used for flash column chromatography: toluene-methanol 7:3. Yield 59%, 0.12 g, mp 287-290 ºC (lit.: 287-295 ºC)[5].

***N*-[2-(6-Oxo-1-phenyl-1,6-dihydropyridazin-4-yl)phenyl]pivalamide (10c).** 5-Iodo-2-phenyl-3(2*H*)-pyridazinone **9** (2.98 g, 10.00 mmol) and tetrakis(triphenylphosphine)-palladium(0) (0.58 g, 0.50 mmol) as a catalyst were dissolved in dimethoxyethane (60 mL, distilled over $SnCl_2$) and were stirred under argon at room temperature for 30 min. Pivaloylamino-phenylboronic acid (2.76 g, 12.50 mmol) and sodium carbonate solution (2M, 10 mL) were then added and the mixture was refluxed for 8 hours. The reaction mixture was poured onto ice-water (80 mL) and was extracted with chloroform (3x100 mL). Evaporation of the organic layer gave a crude product which was recrystallized. Yellow crystals, yield 75%, 2.61 g, mp 191.1-192.0 °C (from acetonitrile); R_f (toluene-metanol 4:1): 0.25. IR (ν_{max}, cm^{-1}): 3308, 2956, 1660, 1512, 1450, 1298, 758, 694. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.94 (d, $J_{3',5'}$ 2.1 Hz, 1H, H-3'), 7.77 (d, $J_{5,6}$ 8.1 Hz, 1H, H-6), 7.60 (d, $J_{2",3"}=J_{5",6"}$ 7.7 Hz, 2H, H-2",6"), 7.58 (s, 1H, NH), 7.48 (m, 1H, H-5), 7.45 (t, 2H, H-3",5"), 7.38 (t, $J_{3",4"}=J_{4",5"}$ 8.0 Hz, 1H, H-4"), 7.33 (m, 1H, H-3), 7.32 (m, 1H, H-4), 6.96 (d, 1H, H-5'), 1.26 (s, 9H, $CO(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.9 ($OCC(CH_3)_3$), 159.6 (C-6'), 143.1 (C-4'), 141.0 (C-1"), 137.9 (C-3'), 134.7 (C-1), 130.7 (C-5), 129.2 (C-3), 128.7 (C-3",5"), 128.5 (C-5'), 128.4 (C-2), 128.3 (C-4"), 126.2 (C-4), 125.8 (C-6), 125.1 (C-2",6"), 39.5 ($C(CH_3)_3$), 27.4 ($C(CH_3)_3$); H" and C" are phenyl protons and carbons, resp. MS (ESI): *m/z* (%) 310, 327, 344, 365. HRMS (ESI) calcd. for $C_{21}H_{21}N_3O_2$ $[M+H]^+$: 348.1712, found: 348.1705.

5-(2-Aminophenyl)-2-phenylpyridazin-3(2*H*)-one (11c). *N*-[2-(6-Oxo-1-phenyl-1,6-dihydro-pyridazin-4-yl)phenyl]pivalamide **10c** (2.29 g, 6.59 mmol) was added to sulfuric acid (20%, 115 mL) and the mixture was refluxed for 3 hours. After cooling, the pH of the mixture was adjusted to pH 8 by addition of aqueous ammonia (25%). The mixture was then extracted with chloroform (3x100 mL) and the crude product obtained after evaporation of the organic layer was recrystallized. Pale brown crystals, yield 80%, 1.38 g, mp 144.5-145.8 °C (from acetonitrile); R_f (chloroform-methanol 40:1): 0.38. IR (ν_{max}, cm^{-1}): 3390, 3354, 2960, 1654, 1582, 1490, 752, 692. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.10 (d, $J_{4,6}$ 1.9 Hz, 1H, H-6), 7.67 (d, $J_{2",3"}=J_{5",6"}$ 7.9 Hz, 2H, H-2",6"), 7.50 (t, 2H, H-3",5"), 7.41 (t, $J_{3",4"}=J_{4",5"}$ 7.5 Hz, 1H, H-4"), 7.26 (t, $J_{3',4'}=J_{4',5'}$ 7.2 Hz, 1H, H-4'), 7.19 (d, $J_{5',6'}$ 7.5 Hz, 1H, H-6'), 7.15 (d, 1H, H-4), 6.89 (t, 1H, H-5'), 6.80 (d, 1H, H-3'), 3.90 (s, 2H, NH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 160.0 (C-3), 143.2 (C-2'), 141.3 (C-1"), 138.1 (C-6), 134.8 (C-5), 131.0 (C-4'), 129.6 (C-6'), 128.8 (C-3",5"), 128.2 (C-3",5"), 128.2 (C-4,4"), 125.2 (C-2",6"), 119.9 (C-1'), 119.7 (C-5'), 117.1 (C-3'). H" and C" are phenyl protons and carbons, resp. MS (ESI): *m/z* (%) 256, 261; HRMS (ESI) calcd. for $C_{16}H_{13}N_3O$ $[M+H]^+$: 264.1137, found: 264.1128.

5-(2-Azidophenyl)-2-phenylpyridazin-3(2*H*)-one (12c). 5-(2-Aminophenyl)-2-phenylpyridazin -3(2*H*)-one (**11c**) (2.00 g, 7.6 mmol) was dissolved in 37% hydrochloric acid (60 mL) and was cooled at 0°C with stirring. A solution of sodium nitrite (1.11 g, 16.14 mmol) in water (41 mL) was added dropwise at such a rate that the temperature of the reaction mixture did not exceed 5 °C. The mixture was stirred at this temperature for 1.5 hours. A solution of sodium azide (1.01 g, 16.14 mmol) and anhydrous sodium acetate (8.73 g, 106.4 mmol) in water (37 mL) was then added at 0-5 °C and the mixture was stirred at this temperature for an additional 1 hour. Then the mixture was neutralized with a saturated sodium carbonate solution and extracted with dichloromethane (3x70 mL). The organic layer was evaporated without heating and the residue was suspended with diethyl ether to yield brown crystals which were filtered off. The product decomposed on air and was therefore stored under argon atmosphere in a refrigerator. Brown crystals, yield 98%, 2.15 g; R_f (chloroform-methanol 40:1): 0.68. IR (ν_{max}, cm^{-1}): 3057, 2124, 1670, 1488, 1292, 756, 720, 686. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.10 (d, $J_{4,6}$ 2.2 Hz, 1H, H-6), 7.68 (m, 2H, H-2",6"), 7.54 (t, $J_{3',4'}$=$J_{4',5'}$ 8.0 Hz, 1H, H-4'), 7.51 (m, 2H, H-3",5"), 7.42 (d, $J_{5',6'}$ 7.0 Hz, 1H, H-6'), 7.42 (m, 1H, H-4"), 7.38 (d, 1H, H-3'), 7.29 (t, 1H, H-5'), 7.12 (d, 1H, H-4). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 159.9 (C-3), 141.8 (C-5), 141.3 (C-1"), 138.2 (C-6), 137.9 (C-2'), 131.4 (C-4'), 130.4 (C-6'), 129.2 (C-4), 128.3 (C-3",5"), 128.3 (C-4"), 126.0 (C-1'), 125.5 (C-5'), 125.3 (C-2",6"), 119.1 (C-3'). H" and C" are phenyl protons and carbons, resp.

Compounds **13a-c** were prepared according to Method B above.

5-(2-Triphenylphosphoranylideneaminophenyl)-2-methylpyridazin-3(2*H*)-one (13a). Yellow crystals, yield 84%, 0.17 g, mp 81-82 °C; R_f (ethyl acetate-chloroform 4:1): 0.51. IR (ν_{max}, cm^{-1}): 3854, 3422, 1654, 1586, 1472, 1436, 1338, 1106, 750, 718, 694. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.42 (d, $J_{4,6}$ 1.5 Hz, 1H, H-6), 7.67 (m, 6H, H-2",6"), 7.54 (m, 6H, H-3",5"), 7.46 (m, 3H, H-4"), 7.20 (d, $J_{5',6'}$ 7.0 Hz, 1H, H-6'), 7.08 (d, 1H, H-4), 6.94 (t, $J_{3',4'}$= $J_{4',5'}$ 7.0 Hz, 1H, H-4'), 6.70 (t, 1H, H-5'), 6.54 (d, 1H, H-3'), 3.83 (s, 3H, NCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 161.5 (C-3), 149.2 (C-2'), 147.0 (C-5), 140.1 (C-6), 132.5-128.5 (C-4',6',1",2",3",4",5",6"), 126.2 (C-4), 122.2 (C-3'), 117.6 (C-5'), 39.4 (NCH_3); H' and C' are phenyl protons and carbons, resp. of the phenylamino group; H" and C" are phenyl protons and carbons, resp. of the triphenylphosphoranylidene group. Anal. Calcd for $C_{29}H_{24}N_3OP$ x $1/2H_2O$ (470.51): C, 74.03; H, 5.36; N, 8.93%. Found: C, 74.41; H, 5.22; N, 8.70%.

5-(5-Chloro-2-triphenylphosphoranylideneaminophenyl)-2-methylpyridazin-3(2*H*)-one (13b). Yellow crystals, yield 80%, 0.31 g, mp 181.2-181.8 °C; R_f (chloroform-methanol 50:1): 0.20. IR (ν_{max}, cm^{-1}): 3052, 1654, 1582, 1468, 1436, 1326, 1108, 806, 720, 694. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 8.29 (d, $J_{4,6}$ 2.0 Hz, 1H, H-6), 7.68 (m, 6H, H-2",6"), 7.63 (m, 6H, H-3",5"), 7.54 (m, 3H, H-4"), 7.28 (dd, $J_{4',6'}$ 3.0 Hz, $J_{3',6'}$ 2.0 Hz, 1H, H-6'), 7.08 (d, 1H, H-4), 6.94 (dd, $J_{3',4'}$ 8.7 Hz, 1H, H-4'), 6.36 (dd, 1H, H-3'), 3.71 (s, 3H, NCH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 159.9 (C-3), 148.1 (C-2'), 144.7 (C-1'), 138.6 (C-6), 132.2 (C-4"), 132.0 (C-2",6"), 129.6 (C-5), 129.5 (C-4'), 129.2 (C-1"), 129.0 (C-3",5"), 128.9 (C-6'), 125.9 (C-4'), 122.5 (C-3'), 120.7 (C-5'), 39.0 (NCH_3). P-C coupling constants: ^1J(P, C-1") 100 Hz, ^2J(P, C-2",6") 10 Hz, ^3J(P, C-3",5") 12 Hz, ^4J(P, C-4") 2.3 Hz, ^3J(P, C-3') 11 Hz, ^4J(P, C-6') 1 Hz; H'

and C' are phenyl protons and carbons, resp. of the phenylamino group; H" and C" are phenyl protons and carbons, resp. of the triphenylphosphoranylidene group. Anal. Calcd for $C_{29}H_{23}ClN_3OP$ (495.95): C, 70.23; H, 4.67; N, 8.47%. Found: C, 70.27; H, 4.70; N, 8.35%.

2-Phenyl-5-(2-triphenylphosphoranylideneaminophenyl)pyridazin-3(2*H*)-one (13c). Yellow oil, yield 85%, 0.89 g; R_f (chloroform-methanol 40:1): 0.44. IR (ν_{max}, cm^{-1}): 3052, 2924, 1660, 1586, 1472, 1434, 1336, 1106, 718, 692. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.56 (d, $J_{4,6}$ 8.0 Hz, 1H, H-6), 7.73 (m, 2H, H-2",6"), 7.54 (m, 3H, H-4"'), 7.51 (m, 2H, H-3",5"), 7.46 (m, 6H, H-3"',5"'), 7.39 (m, 1H, H-4"), 7.30 (m, 6H, H-2"',6"'), 7.29 (m, 1H, H-6'), 7.15 (d, 1H, H-4), 6.99 (m, 1H, H-4'), 6.76 (m, 1H, H-5'), 6.58 (m, 1H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): extremely broadened δ_C signals. H" and C" are phenyl protons and carbons, resp. of the *N*-phenyl group; H"' and C"' are phenyl protons and carbons, resp. of the triphenylphosphoranylidene group. MS (ESI): *m/z* (%) 520, 525; HRMS (ESI) calcd. for $C_{34}H_{26}N_3OP$ $[M+H]^+$: 524.1892, found: 524.1897.

Method F. General procedure for the ring closure reaction of (13a-c) with phenylisocyanate

The appropriate iminophosphorane (1.00 mmol) **13a-c** was dissolved in dry toluene (20 mL), purged with argon and was cooled to 0 °C. Under stirring, a solution of phenylisocyanate (0.15 mL, 1.34 mmol) in toluene (10 mL) was added dropwise to the iminophosphorane at such a rate that the temperature of the reaction mixture did not exceed 5°C. The mixture was stirred at this temperature for 1 h. Then the mixture was refluxed at 140°C for 24 hours followed by evaporation *in vacuo*. After separation by column chromatography two products **14** and **15** were obtained.

3-Methyl-5-phenylamino-pyridazino[4,5-*c*]quinolin-4(3*H*)-one (14a). Yellow crystals, yield 10%, 0.04 g, 0.13 mmol, mp 178-181 °C; R_f (ethyl acetate-chloroform 9:1): 0.85. IR (ν_{max}, cm^{-1}): 3568, 3422, 3062, 2852, 1654, 1640, 1598, 1542, 744. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 11.86 (s, 1H, N*H*), 9.31 (s, 1H, H-1), 8.59 (d, $J_{9,10}$ 8.3 Hz, 1H, H-10), 8.03 (d, $J_{2',3'}$=$J_{5',6'}$ 7.9 Hz, 2H, H-2',6'), 7.80 (m, 2H, H-7,8), 7.50 (m, 1H, H-9), 7.41 (t, $J_{3',4'}$ 7.4 Hz, 2H, H-3',5'), 7.08 (t, $J_{4',5'}$ 7.4 Hz, 1H, H-4'), 3.87 (s, 3H, N-CH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 159.8 (C-4), 151.1 (C-5), 148.3 (C-6a), 139.7 (C-1'), 134.9 (C-4a), 134.0 (C-1), 132.6 (C-8), 128.9 (C-3',5'), 128.3 and 116.4 (C-10a and C-10b), 126.8 (C-7), 124.3 (C-10), 124.0 (C-9), 122.5 (C-4'), 119.5 (C-2',6'), 39.5 (N-*C*H_3). H', C': are phenyl protons and carbons, resp. MS (ESI): *m/z* (%) 303, 274; HRMS (ESI) calcd. for $C_{18}H_{15}N_4O$ $[M+H]^+$: 303.1246, found: 303.1252.

9-Chloro-3-methyl-5-phenylamino-pyridazino[4,5-*c*]quinolin-4(3*H*)-one (14b). Yellow crystals, yield 23%, 0.07 g, 0.19 mmol, mp 259.5-260 °C; R_f (chloroform-methanol 40:1): 0.92. IR (ν_{max}, cm^{-1}): 3428, 2924, 1654, 1614, 1598, 1540, 1108, 820, 752. ^{1}H NMR (500 MHz, CF_3COOD): δ_H 9.14 (s, 1H, H-1), 8.44 (s, 1H, H-10), 7.86 (d, $J_{7,8}$ 8.9 Hz, 1H, H-8), 7.66 (m, 2H, H-3',5'), 7.61 (m, 2H, H-7,4'), 7.49 (d, $J_{2',3'}$=$J_{5',6'}$ 7.3 Hz, 2H, H-2',6'), 4.13 (s, 3H, N-CH_3). ^{13}C NMR (125 MHz, CF_3COOD): δ_C 162.0 (C-4), 153.5 (C-5), 140.2 (C-4a), 139.0 (C-8), 137.1 (C-6a,9), 135.4 (C-1), 133.6 (C-3',5'), 133.4 (C-1'), 133.3 (C-4'), 128.0 (C-2',6'), 126.4 (C-10), 122.0 (C-7), 118.8 (C-10a), 112.8 (C-10b), 42.8 (N-*C*H_3). H'and C' are phenyl protons and

carbons, resp. MS (ESI): *m/z* (%) 337, 308; HRMS (ESI) calcd. for $C_{18}H_{14}ClN_4O$ $[M+H]^+$: 337.0856, found: 337.0844.

3-Phenyl-5-phenylamino-pyridazino[4,5-*c*]quinolin-4(3*H*)-one (14c). Yellow crystals, yield 20%, 0.08 g, 0.21 mmol, mp 189-190 °C; R_f (chloroform-ethylacetate 10:1): 0.88. IR (ν_{max}, cm^{-1}): 3426, 2924, 1724, 1658, 1602, 1578, 1552, 1448, 1314, 756, 688. ^1H NMR (500 MHz, DMSO-d_6): δ_H 11.70 (s, 1H, NH), 9.46 (s, 1H, H-1), 8.64 (d, $J_{9,10}$ 8.2 Hz, 1H, H-10), 8.02 (d, $J_{2',3'}=J_{5',6'}$ 7.8 Hz, 2H, H-2',6'), 7.83 (m, 2H, H-7, -8), 7.67 (d, $J_{5",6"}$ 7.7 Hz, 1H, H-6"), 7.59 (t, $J_{4",5"}$ 7.5 Hz, 1H, H-5"), 7.52 (m (overlapping), 2H, H-9,4"), 7.40 (t, 2H, H-3',5'), 7.08 (t, $J_{3',4'}=J_{4',5'}$ 7.4 Hz, 1H, H-4'). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 159.8 (C-4), 151.3 (C-5), 148.6 (C-6a), 141.3 (C-1'), 139.6 (C-1"), 134.9 (C-10b), 134.8 (C-1), 132.9 (C-8), 128.9 (C-3",5"), 128.8 (C-3',5'), 128.4 (C-9), 126.9 (C-7), 126.3 (C-2',6'), 124.4 (C-10), 124.2 (C-4'), 122.6 (C-4"), 119.6 (C-2",6"), 116.4 (C-10a), 110.0 (C-4a). H', C': N^3- phenyl protons; H" and C": *N*-5-phenyl protons and carbons, resp. of the phenylamino group. MS (ESI): *m/z* (%) 272, 365; HRMS (ESI) calcd. for $C_{23}H_{16}N_4O$ $[M+H]^+$: 365.1402, found: 365.1397.

5-[2-(1,6-Dihydro-1-methyl-6-oxopyridazin-4-yl)-phenylamino]-3-methylpyridazino[4,5-*c*]-quinolin-4(3*H*)-one (15a). Yellow crystals, yield 45%, 0.12 g, 0.29 mmol, mp 274-275 °C; R_f (ethyl acetate-chloroform 9:1): 0.36. IR (ν_{max}, cm^{-1}): 3445, 1651, 1583, 1542, 1401, 1189, 1117, 758. ^1H NMR (400 MHz, CF_3COOD): δ_H 9.22 (s, 1H, H-1), 8.62 (s, 1H, H-3"), 8.50 (d, $J_{9,10}$ 8.3 Hz, 1H, H-10), 7.97 (t, $J_{7,8}=J_{8,9}$ 8.1 Hz, 1H, H-8), 7.88-7.75 (m, 6H, H-9,3',4',5',6',5"), 7.65 (d, 1H, H-7), 4.08 (s, 3H) and 4.05 (s, 3H): (N^3-CH_3 and N^1-"CH_3). ^{13}C NMR (100 MHz, CF_3COOD): δ_C 166.4 (C-4), 164.2 (C-6"), 156.1 (C-5), 149.1 (C-4"), 146.2 (C-3"), 143.2 (C-10b), 140.9 (C-8), 140.6 (C-6a), 137.9 (C-5'), 137.7 (C-1), 135.9 (C-3',4'), 135.5 (C-1'), 134.1 (C-2'), 132.5 (C-9), 131.7 (C-6'), 130.6 (C-5"), 129.0 (C-10), 122.8 (C-7), 120.2 (C-10a), 114.3 (C-4a), 45.0 and 44.6: (N^1-"*C*H$_3$ and N^3-*C*H$_3$). H' and C' are phenyl protons and carbons, resp.; H" and C" are pyridazinyl protons and carbons and carbons, resp. MS (ESI): *m/z* (%) 199, 212, 411. Anal. Calcd for $C_{23}H_{18}N_6O_2$ (410.43): C, 67.31; H, 4.42; N, 20.48%. Found: C, 67.00; H, 4.38; N, 20.39%.

5-[2-(1,6-Dihydro-1-methyl-6-oxopyridazin-4-yl)-4-chlorophenyl-amino]-9-chloro-3-methyl -pyridazino[4,5-*c*]quinolin-4(3*H*)-one (15b). Yellow crystals, yield 49%, 0.10 g, 0.20 mmol, mp 316.8-317.2 °C; R_f (chloroform-methanol 40:1): 0.62. IR (ν_{max}, cm^{-1}): 3422, 3070, 1654, 1582, 1562, 1534, 1406, 1330, 826, 708. ^1H NMR (500 MHz, CF_3COOD): δ_H 9.15 (s, 1H, H-1), 8.52 (s, 1H, H-3"), 8.48 (s, 1H, H-10), 7.91 (d, $J_{7,8}$ 9.0 Hz, 1H, H-8), 7.80 (d, $J_{5',6'}$ 9.0 Hz, 1H, H-5'), 7.79 (s, 1H, H-5"), 7.73 (s, 1H, H-3'), 7.72 (d, 1H, H-6'), 7.64 (dd, $J_{7,10}$ 1.6 Hz, 1H, H-7), 4.07 (s, 3H) and 4.02 (s, 3H): (N^3-CH_3 and $N^{1"}$-CH_3). ^{13}C NMR (125 MHz, CF_3COOD): δ_C 167.2 and 164.2 (C-4 and C-6"), 156.4 (C-5), 147.5 (C-4"), 145.3 (C-3"), 143.0 (C-4'), 142.4 (C-10b), 141.3 (C-8), 139.8 (C-6a), 139.3 (C-9), 137.8 (C-5'), 137.6 (C-1'), 137.5 (C-1), 136.0 (C-3'), 133.4 (C-6'), 132.6 (C-2'), 131.8 (C-5"), 128.7 (C-10), 124.2 (C-7), 121.6 (C-10a), 115.0 (C-4a), 45.0 (N^3-*C*H$_3$, $N^{1"}$-*C*H$_3$); H' and C' are phenyl protons and carbons, resp.; H" and C": are pyridazinyl protons and carbons, resp. Anal. Calcd for $C_{23}H_{16}Cl_2N_6O_2$ (479.33): C, 57.63; H, 3.36; N, 17.53; Cl, 14.79%. Found: C, 57.87; H, 3.43; N, 17.20, Cl, 14.77%.

5-[2-(1,6-Dihydro-6-oxo-1-phenylpyridazin-4-yl)-phenylamino]-3-phenylpyridazino[4,5-*c*]-quinolin-4(3*H*)-one (15c). Yellow crystals, yield 52%, 0.15 g, 0.27 mmol, mp 310-311 ºC; R_f (chloroform-ethyl acetate 10:1): 0.19. IR (ν_{max}, cm^{-1}): 3424, 3058, 2924, 1662, 1648, 1588, 1568, 1536, 1450, 756, 684. ^{1}H NMR (500 MHz, CF_3COOD): δ_H 9.3 (s, 1H, H-1), 8.53 ($J_{3",5"}$ 1.9 Hz, 1H, H-3"), 8.50 (d, $J_{9,10}$ 8.3 Hz, 1H, H-10), 7.95 (t, $J_{7,8}$=$J_{8,9}$ 7.9 Hz, 1H, H-8), 7.78 (s, 1H, H-5"), 7.77 (s, 1H, H-9), 7.73-7.80 (overlapping, 4H, H-3',4',5',6'), 7.67 (d, $J_{7,9}$ 7.9 Hz, 1H, H-7), 7.30-7.60 (overlapping, 10H, Ph-H). ^{13}C NMR (125 MHz, CF_3COOD): δ_C 165.3 and 164.5 (C-4 and C-6"), 156.5 (C-5), 148.6 (C-4"), 145.4 (C-3"), 143.8 (C-10b), 143.1 and 143.0 (Ph-C-1"' and Ph-C-1""), 141.4 (C-8), 141.2 (C-6a), 138.6 (C-1), 137.9 (C-5'), 136.0 (C-3',4'), 135.5 (C-1'), 135.2; 135.1; 134.1; 134.0 (Ph-C-2"',6"',3"',5"',4"',2"",6"",3"",5"",4""), 134.3 (C-2'), 133.4 (C-6'), 132.9 (C-9), 131.4 (C-5"), 129.3 (C-10), 122.9 (C-7), 120.5 (C-10a), 115.1 (C-4a). H"": N^3-phenyl protons; H"': $N^{1''}$-phenyl protons. MS (ESI): *m/z* (%) 536, 541; HRMS (ESI) calcd. for $C_{33}H_{22}N_6O_2$ $[M+H]^+$: 535.1882, found: 535.1884.

***N*-[2-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-yl)phenyl]pivalamide (17).** 5-Bromo-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione **16** (0.44 g, 2.00 mmol) and tetrakis(triphenylphosphine)-palladium(0) (0.12 g, 0.10 mmol) as a catalyst were dissolved in dimethoxyethane (12 mL, distilled over $SnCl_2$) and were stirred at room temperature under argon for 30 min. Pivaloylamino-phenylboronic acid (0.71 g, 3.20 mmol) and sodium carbonate solution (2M, 1.0 mL) were then added and the mixture was refluxed for 8 hours. The reaction mixture was poured onto ice-water (30 mL) and was extracted with chloroform (3x30 mL). Evaporation of the organic layer gave a crude product which was recrystallized. Colourless crystals, yield 91%, 0.57 g, mp 165-166 °C (from ethyl acetate); R_f (chloroform−ethyl acetate 1:1): 0.63. IR (ν_{max}, cm^{-1}): 3286, 2954, 1704, 1676, 1638, 1576, 1510, 1440, 1356, 1296, 1164, 924, 786, 750, 688. ^{1}H NMR (200 MHz, $CDCl_3$): δ_H 8.63 (s, 1H, NH), 7.72 (d, $J_{3,4}$ 8.0 Hz, 1H, H-3), 7.47-7.03 (m, 4H, H-6',4,5,6), 3.47 (s, 3H) and 3.46 (s, 3H): (N^1-CH_3 and N^3-CH_3), 1.21 (s, 9H, $CO(CH_3)_3$). ^{13}C NMR (50 MHz, $CDCl_3$): δ_C 177.3 ($OCC(CH_3)_3$), 163.3 (C-4'), 151.1 (C-2'), 143.8 (C-6'), 136.7 (C-1), 130.0 (C-3), 129.1 (C-4), 127.0 (C-2), 126.3 (C-5), 125.5 (C-6), 113.2 (C-5'), 39.3 ($C(CH_3)_3$), 37.3 (N^1-CH_3), 28.5 (N^3-CH_3), 27.5 ($C(CH_3)_3$). Anal. Calcd for $C_{17}H_{21}N_3O_3$ (315.37): C, 64.74; H, 6.71; N, 13.32%. Found: C, 64.82; H, 6.69; N, 13.34%.

5-(2-Aminophenyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (18). *N*-[2-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-yl)phenyl]pivalamide **17** (0.27 g, 0.87 mmol) was added to sulfuric acid (20%, 20 mL) and the mixture was refluxed for 3 hours. After cooling, the pH of the mixture was adjusted to pH 8 by addition of aqueous sodium hydroxide (40%). The mixture was then extracted with chloroform (3x30 mL) and the crude product obtained after evaporation of the organic layer was recrystallized. Pale brown crystals, yield 88%, 0.18 g, mp 190.0-191.0 °C (from chloroform-petroleum ether 1:1); R_f (chloroform−ethyl acetate 1:1): 0.34. IR (ν_{max}, cm^{-1}): 3396, 3328, 1696, 1646, 1620, 1494, 1448, 1352, 1298, 780, 754, 690. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.25 (s, 1H, H-6), 7.17 (td, $J_{4',3'}$=$J_{4',5'}$ 8.0 Hz, $J_{4',6'}$ 1.3 Hz, 1H, H-4'), (dd, $J_{6',5'}$ 8.8 Hz, 1H, H-6'), 6.78-6.74 (m, 2H, H-5', H-3'), 3.99 (s, 2H, NH_2), 3.42 (s, 3H) and 3.41 (s, 3H): (N^1-CH_3 and N^3-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 163.0 (C-4), 152.1 (C-2), 146.6 (C-2'),

143.4 (C-6), 131.5 (C-6'), 130.2 (C-4'), 120.7 (C-1'), 119.7 (C-5'), 117.9 (C-3'), 114.2 (C-5), 37.7 (N^1-CH_3), 29.0 (N^3-CH_3). Anal. Calcd for $C_{12}H_{13}N_3O_2$ (231.25): C, 62.33; H, 5.67; N, 18.17%. Found: C, 61.73; H, 5.58; N, 18.05%.

5-(2-Azidophenyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (19). Prepared from **18** according to the procedure given for **12c**. Yellow crystals, yield 96%, 0.34 g; R_f (chloroform-ethyl acetate 10:1): 0.27. IR (ν_{max}, cm^{-1}): 3068, 2928, 2116, 1704, 1654, 1632, 1574, 1496, 1444, 1348, 930, 784, 750. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.40 (m, 1H, H-4'), 7.29 (dd, $J_{5',6'}$ 8.0 Hz, $J_{4',6'}$ 1.6 Hz, 1H, H-6'), 7.23 (s, 1H, H-6), 7.22 (dd, $J_{3',4'}$ 8.0 Hz, $J_{3',5'}$ 0.8 Hz, 1H, H-3'), 7.17 (td, $J_{4',5'}$ 8.0 Hz, 1H, H-5'), 3.46 (s, 3H, N^1-CH_3), 3.41 (s, 3H, N^3-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 162.7 (C-4), 152.2 (C-2), 142.9 (C-6), 139.3 (C-2'), 132.7 (C-6'), 130.3 (C-4'), 125.4 (C-5'), 125.1 (C-1'), 119.2 (C-3'), 111.5 (C-5), 37.8 (N^1-CH_3), 28.9 (N^3-CH_3).

Compounds **20** and **22** were prepared according to method B above.

1,3-Dimethyl-5-(2-triphenylphosphoranylideneaminophenyl)pyrimidine-2,4(1*H*,3*H*)-dione (20). Yellow oil, yield 78%, 0.46 g; R_f (toluene-methanol 4:1): 0.40. IR (ν_{max}, cm^{-1}): 3052, 3006, 2926, 1700, 1656, 1586, 1482, 1436, 1338, 1274, 750, 694. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.65 (m, 6H, H-2",6"), 7.49 (m, 3H, H-4"), 7.41 (m, 6H, H-3",5"), 7.32 (s, 1H, H-6), 7.27 (m, 1H, H-6'), 6.85 (td, $J_{4',5'}$=$J_{5',6'}$ 7.4 Hz, $J_{3',5'}$ 1.8 Hz, 1H, H-5'), 6.69 (t, $J_{3',4'}$ 7.0 Hz, 1H, H-4'), 6.52 (dt, $J_{3',6'}$ 1.0 Hz, 1H, H-3'), 3.36 (s, 3H) and 3.35 (s, 3H): (N^1-CH_3 and N^3-CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 163.3 (C-4), 152.7 (C-2), other signals are extremely broadened. H" are phenyl protons of the triphenylphosphoranylidene group. MS (ESI): *m/z* (%) 239, 279, 344, 388; HRMS (ESI) calcd. for $C_{30}H_{26}N_3O_2P$ $[M+H]^+$: 492.1841, found: 492.1801.

1,3-Dimethyl-6-phenyl-5-(triphenylphosphoranylideneamino)pyrimidine-2,4(1*H*,3*H*)-dione (22). Yellow crystals, yield 82%, 0,62 g, mp 217-218 °C (from dry ethanol); R_f (ethyl acetate-chloroform 4:1): 0.50. IR (ν_{max}, cm^{-1}): 3052, 1686, 1634, 1588, 1570, 1480, 1434, 1348, 1106, 746, 714, 694, 524. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 7.55 (t, $J_{2',3'}$=$J_{3',4'}$=$J_{4',5'}$=$J_{5',6'}$ 6.6 Hz, 2H, H-3',5'), 7.52 (t, $J_{4',5'}$ 7.9 Hz, 1H, H-4'), 7.46 (m, 3H, H-4"), 7.45 (m, 6H, H-2",6"), 7.42(d, 2H, H-2',6'), 7.36 (m, 6H, H-3",5"), 3.08 (s, 3H, N^3-CH_3), 3.00(s, 3H, N^1-CH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 162.3 (C-4), 149.8 (C-2), 137.4 (C-6), 134.7 (C-1',1"), 131.9 (C-2",6"), 129.9 (C-2',6'), 128.7 (C-5), 128.4 (C-3',5',3",5"), 127.9 (C-4',4"), 34.4 (N^1-CH_3), 28.2 (N^3-CH_3). P-C coupling constants: ^1J(P, C-1") 102 Hz, ^2J(P, C-2",6") 9.5 Hz, ^3J(P, C-3",5") 11.7 Hz, ^4J(P, C-4") 2.5 Hz; H' and C' are phenyl protons and carbons, resp. of the phenyl group; H" and C" are phenyl protons and carbons, resp. of the triphenylphosphoranylidene group. Anal. Calcd for $C_{30}H_{26}N_3O_2P$ x $1/2C_2H_5OH$ (514.56): C, 72.36; H, 5.68; N, 8.17%. Found: C, 72.32; H, 5.22; N, 8.09%.

***N*-[2-(1,3-Dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)phenyl]-*N'*-phenylthiourea (25).** Compound **21** (0.23 g, 1.00 mmol) was dissolved in dry acetonitrile (10 mL), then phenylisothiocyanate (0.14 g, 0.12 ml, 1.00 mmol) and 4-dimethylaminopyridine (0.02 g, 0.17 mmol) were added. The mixture was refluxed at 85°C under argon for 24 hours. The precipitated crystals were separated by filtration. Colourless crystals, yield 52%, 0.19 g, mp 212-212.5 °C; R_f (chloroform-methanol 40:1): 0.20. IR (ν_{max}, cm^{-1}): 3280, 3130, 2964, 1694, 1652, 1534, 1508,

1444, 1272, 762, 700. ^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ_H 9.86 (s, 1H, NH-C-1"), 9.38 (s, 1H, NH-C-2'), 7.62 (dd, $J_{5',6'}$ 7.9 Hz, $J_{4',6'}$ 0.9 Hz, 1H, H-6'), 7.53 (td, $J_{4',5'}$ 7.6 Hz, $J_{3',5'}$ 1.8 Hz, 1H, H-5'), 7.44 (dd, $J_{3',4'}$ 7.6 Hz, 1H, H-3'), 7.39 (d, $J_{2",3"}$=$J_{5",6"}$ 6.6 Hz, 2H, H-2",6"), 7.38 (m (overlapping), 1H, H-4'), 7.31 (t, $J_{4",5"}$ 7.5 Hz, 2H, H-3",5"), 7.13 (t, $J_{3",4"}$ 7.3 Hz, 1H, H-4"), 5.69 (s, 1H, H-5), 3.24 (s, 3H, N^3-CH$_3$), 3.07 (s, 3H, N^1-CH$_3$). ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ_C 180.4 (C=S), 161.5 (C^4=O), 152.0 (C^2=O), 151.7 (C-6), 139.0 (C-1"), 136.8 (C-2'), 130.1 (C-5'), 129.6 (C-1'), 129.3 (C-4'), 128.9 (C-6'), 128.5 (C-3",5"), 126.2 (C-3'), 124.7 (C-4"), 123.5 (C-2",6"), 101.9 (C-5), 33.8 (N^1-CH$_3$), 27.5 (N^3-CH$_3$). H" and C": phenyl protons and carbons, resp. of the phenyl group at S=C-NH-*Ph*. MS (ESI): *m/z* (%) 283, 327, 344, 388; HRMS (ESI) calcd. for $C_{19}H_{18}N_4O_2S$ $[M+H]^+$: 367.1229, found: 367.1240.

1,3-Dimethyl-5-phenylaminopyrimido[5,4-*c*]quinoline-2,4(1*H*, 3*H*)-dione (27). Compound **25** (0.30 g, 0.82 mmol) was dissolved in dichloromethane (200 mL), then triethylamine (0.32 g, 0.44 mL, 3.14 mmol) and 4-dimethylaminopyridine (0.03 g, 0.23 mmol) were added. Methanesulfonylchloride (0.61 g, 0.41 mL, 5.30 mmol) was dropped into the solution and the mixture was stirred at ambient temperature for 3 hours. Then the mixture was evaporated *in vacuo* and the obtained crude carbodiimide intermediate **26** was immediately dissolved in hot dry xylene (10 mL of xylene/1 g of substrate). After 10 hours of reflux xylene was distilled off *in vacuo* and the crude product was purified by column chromatography and subsequent recrystallization. Yellowish brown crystals, yield 66%, 0.18 g, mp 208-208.5 °C (from methanol); R_f (chloroform-methanol 40:1): 0.77. IR (ν_{max}, cm^{-1}): 4400-1800 (broad), 1700, 1660, 1596, 1548, 1352, 1042, 800, 754, 690. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 11.26 (s, 1H, NH), 8.01 (d, $J_{9,10}$ 7.5 Hz, 1H, H-10), 7.94 (d, $J_{2',3'}$=$J_{5',6'}$ 10.0 Hz, 2H, H-2',6'), 7.75 (d, $J_{7,8}$ 7.5 Hz, 1H, H-7), 7.62 (t, $J_{8,9}$ 7.5 Hz, 1H, H-8), 7.36 (t, $J_{3',4'}$=$J_{5',6'}$ 8.0 Hz, 2H, H-3',5'), 7.22 (t, 1H, H-9), 7.07 (t, 1H, H-4'), 3.91 (s, 3H, N^1-CH$_3$), 3.50 (s, 3H, N^3-CH$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 163.9 (C^4=O), 152.9 (C^2=O), 152.5, 152.0 and 150.9 (C-6a, C-10b and C-5), 140.6 (C-1'), 133.1 (C-8), 129.4 (C-3',5'), 128.8 (C-7), 126.1 (C-10), 123.4 (C-4'), 122.5 (C-9), 121.3 (C-2',6'), 114.0 (C-10a), 98.3 (C-4a), 41.5 (N^1-CH$_3$), 29.2 (N^3-CH$_3$). MS (ESI): *m/z* (%) 300, 327, 344, 388; HRMS (ESI) calcd. for $C_{19}H_{16}N_4O_2$ $[M+H]^+$: 333.1352, found: 333.1353.

2-(2-Triphenylphosphoranylideneaminophenyl)pyrazine (29). Prepared according to Method B above. Yellow crystals, yield 67%, 0.28 g, mp 142.5-143.5 °C; R_f (toluene-methanol 4:1): 0.45. IR (ν_{max}, cm^{-1}): 3052, 1656, 1590, 1484, 1464, 1436, 1350, 1298, 716, 694. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 9.63 (m, 1H, H-3), 8.59 (m, 1H, H-5), 8.38 (d, 1H, H-6), 7.68 (m, 7H, H-6',2",6"), 7.53 (m, 3H, H-4"), 7.45 (m, 6H, H-3",5"), 6.97 (m, 1H, H-4'), 6.83 (m, 1H, H-5'), 6.63 (m, 1H, H-3'). ^{13}C NMR (125 MHz, $CDCl_3$): extremely broadened δ_C signals. H" and C" are phenyl protons and carbons, resp. of the triphenylphosphoranylidene group. Anal. Calcd for $C_{28}H_{22}N_3P$ (431.8): C, 77.94; H, 5.14; N, 9.74%. Found: C, 77.76; H, 5.09; N, 9.60%. MS (ESI): *m/z* (%) 388, 409, 476; HRMS (ESI) calcd. for $C_{28}H_{22}N_3P$ $[M+H]^+$: 432.1630, found: 432.1637.

3-Phenylpyridazino[4,5-*b*]indole-4(3*H*)-one (30). A solution of 5-(2-azidophenyl)-2-phenylpyridazin-3(2*H*)-one **12c** (0.73 g, 2.52 mmol) in dry xylene (5 mL) was refluxed for 24 hours, the solvent was then removed under reduced pressure and the residue was recrystallized.

Pale brown crystals, yield 59%, 0.39 g, mp 323-324 ^{o}C (from isopropyl alcohol); R_f (toluene-methanol 4:1): 0.56. IR (ν_{max}, cm^{-1}): 3150, 3086, 3010, 1656, 1600, 1532, 1454, 1308, 760, 738. ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 12.91 (s, 1H, N^5-H), 8.92 (s, 1H, H-1), 8.21 (d, $J_{8,9}$ 8,0 Hz, 1H, H-9), 7.65 (d (overlapping), $J_{6,7}$ 7.5 Hz, 1H, H-6; m, 2H, H-2',6'), 7.54 (m (overlapping), 1H, H-7), 7.53 (m, 2H, H-3', 5'), 7.43 (t, $J_{7,8}$ 7.3 Hz, 1H, H-8), 7.36 (t, $J_{3',4'}$=$J_{4',5'}$ 7.5 Hz, 1H, H-4'). ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 154.4 (C-4), 142.0 (C-1'), 139.4 (C-5a), 133.7 (C-1), 131.7 (C-4a), 128.4 (C-3',5'), 127.5 (C-8), 127.1 (C-7), 126.2 (C-2',6'), 121.6 (C-4'), 121.5 (C-9), 120.7 (C-9a), 116.9 (C-9b), 113.1 (C-6). H'and C' are phenyl protons and carbons, resp. Anal. Calcd for $C_{16}H_{11}N_3O$ x 1/2 H_2O (270.29): C, 71.10; H, 4.47; N, 15.55%. Found: C, 71.37; H, 4.15; N, 15.36%. MS (ESI): *m/z* (%) 171, 219, 235, 262, 263; HRMS (ESI) calcd. for $C_{16}H_{11}N_3O$ $[M+H]^+$: 262.0980, found: 262.0992.

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