PYRIMIDO[4,5-*d*]PYRIMIDINES, PYRIMIDO[4',5':4,5]PYRIMIDO[6,1-*a*]-AZEPINES, AND AN IMIDAZO[5,1-*f*][1,2,4]TRIAZINE BY THREE COMPONENT REACTION

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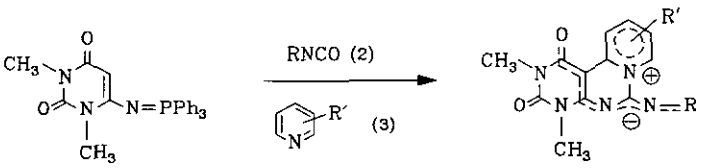
Dedicated to Edward C. Taylor on the occasion of his 70th birthday

Abstract - Recent examples of the three component reaction: iminophosphoranes / isocyanates / heteroarenes (imines) are described. The uracil (**1**) affords with *O*-methyl-ε-caprolactim ether and isocyanates the pyrimido-[4',5':4,5]pyrimido[6,1-*a*]azepines (**6a-c**) and with benzylideneaniline (**8**) the pyrimido[4,5-*d*]pyrimidines (**9a-d**), while azodicarboxylate gives the isofervenuline, pyrimido[4,5-*e*][1,2,4]triazine (**11**). Furthermore, pyrimido[4,5-*d*]-pyrimidine (**15**) is obtained *via* **14** from **1**, *N*-phenylbenzimidoyl chloride (**13**), and phenylisocyanate, while the tautomeric mixture **17A** ⇌ **17B** results from treatment of 6-aminouracil (**16**) with **13**; interception with dimethyl acetylenedicarboxylate gives the pyrido[2,3-*d*]pyrimidine (**19**).

Iminophosphoranes are of great importance in modern organic chemistry, as they are versatile key compounds in manifold heterocyclic syntheses.[1] From these, the Aza-Wittig reaction represents a valuable method for the construction of heterocyclic systems.[2] Continuing our investigations on the synthetic potential of

the iminophosphoranes of heterocyclic ß-enamino esters[3] and uracils,[4] we have recently reported on a novel three component reaction (iminophosphoranes / isocyanates / heteroarenes) which allows an elegant access to a broad range of novel heterocyclic ring systems.

As an example, 1,3-dimethyl-6-triphenylphosphoranylideneaminouracil (**1**) reacted in an one-step reaction with isocyanates (**2**) and pyridines (**3**) to give the intensively colored zwitterionic tricycles (**4**):[5]



1 4

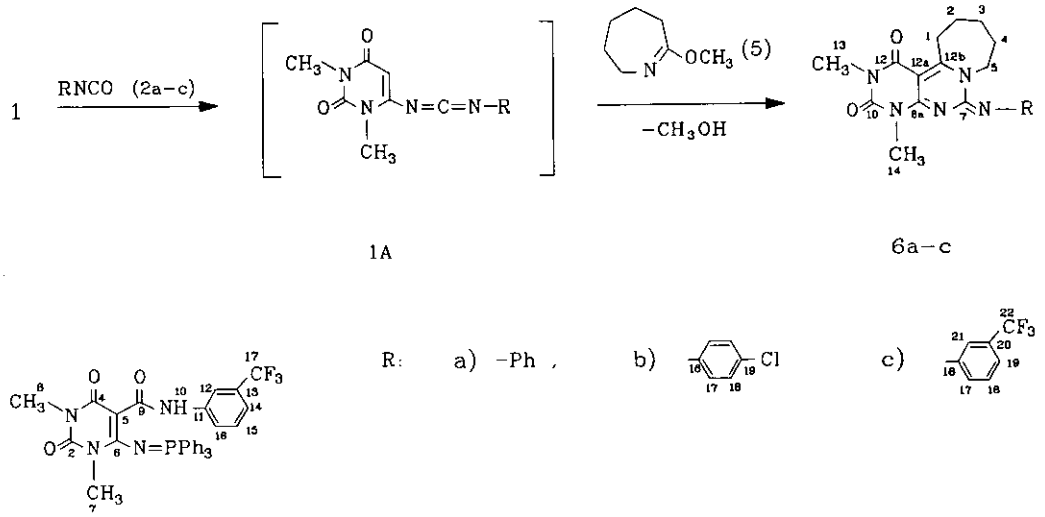
R: -Ph , , , , etc.

R': 4-CH_3 , 4-CO_2CH_3 , 3-$CO_2C_2H_5$, etc.

Scheme 1

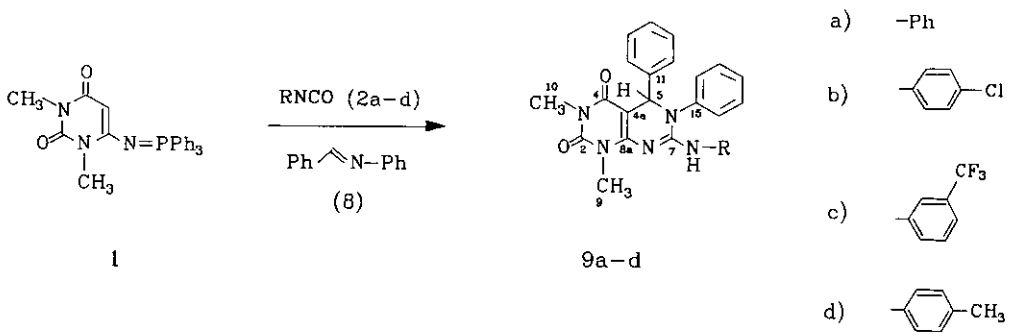
This novel heteroannulation procedure has proved to be rather versatile, as the isocyanates and the heteroarenes could be varied over a large range. The heteroarene component covers the range of manifold substituted pyridines (including also naturally occurring pyridine alkaloids) up to isoquinolines and phthalazines.[6]

Now, we want to report our first successful attempts to prepare pyrimido[4,5-*d*]pyrimidines, 6:6:7-fused azepines, and isofervenulines. In this course, **1** reacted with the isocyanates (**2a-c**) and *O*-methyl-ε-caprolactim ether (**5**) in dry acetonitrile in satisfactory to very good yields and gave the intensively yellow colored pyrimido[4',5':4,5]pyrimido[6,1-*a*]azepines (**6a-c**), to our knowledge the first members of a novel ring system. On the synthesis of an 6:6:7-system isomeric to **6** we had reported previously.[7] Employing 3-trifluoromethylphenylisocyanate (**2c**), the iminophosphorane (**7**) was formed as a side product.



Scheme 2

In an analogous way, **1** gave with the isocyanates (**2a-d**) and benzylideneaniline (**8**) the partially saturated pyrimido[4,5-*d*]pyrimidines (**9a-d**):[8]

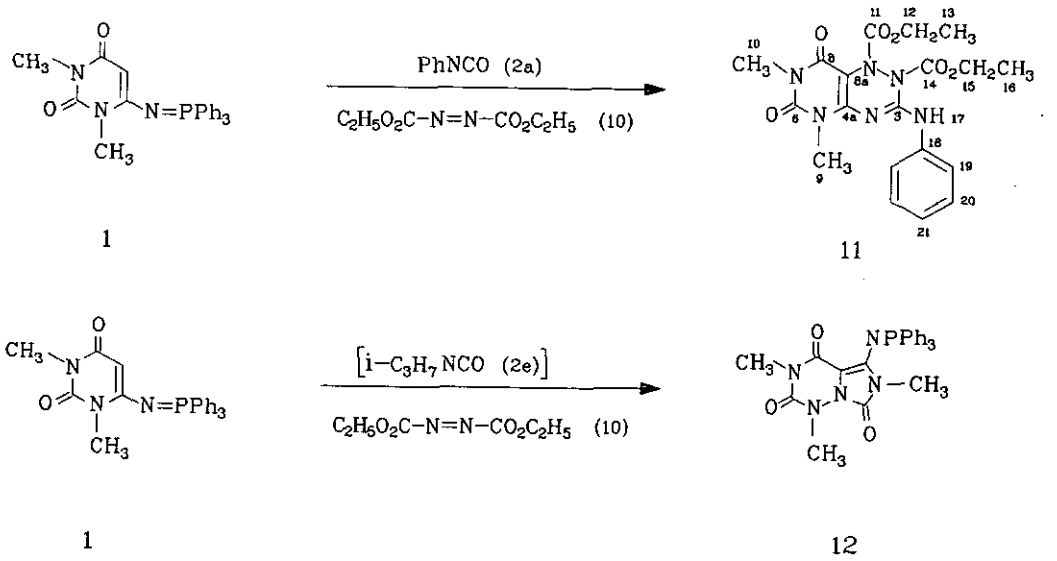


Scheme 3

Both reactions most obviously proceeded *via* an *in situ* generated uracil-6-carbodiimide (**1A**) formed by an initiating Aza-Wittig reaction, which in turn is intercepted in a [4+2] cycloaddition by the C=N-increment of the imine or lactimether moiety. The primary cycloadduct with the ε-caprolactim ether (**5**) expelled spontaneously methanol, the latter reacting with excess isocyanate to give urethane.

The proposed mechanism is supported by the following facts: (1) Calculations carried out by Nitta on vinyl

heterocumulenes[9] and by us on selected uracil model compounds[4d] pointed to a principal readiness of our (non-isolable) carbodiimide (**1A**) towards [4+2] cycloadditions. (2) Employing diethyl azodicarboxylate (**10**) as "dienophile", a significant dependency of the reaction course has been found on the activity of the isocyanate used. This reveals that an *initial* Aza-Wittig reaction is essential: thus, in the case of phenylisocyanate (**2a**) the pyrimido[4,5-*e*][1,2,4]triazine (**11**), a derivative of the alkaloid isofervenuline was formed, while isopropylisocyanate (**2e**) turned out to be too less reactive for this Aza-Wittig/cycloaddition sequence. Instead, without any participation of the isocyanate a competing heterocyclic transformation reaction occured to give the imidazo[5,1-*f*][1,2,4]triazine (**12**), as observed by us already in 1986.[4b-d]

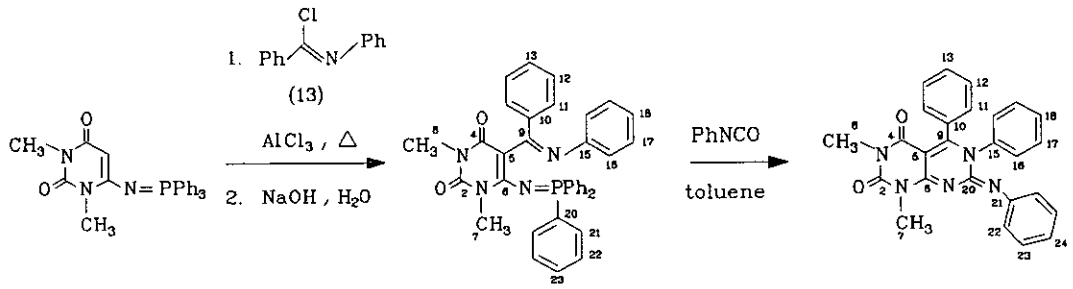


1 11

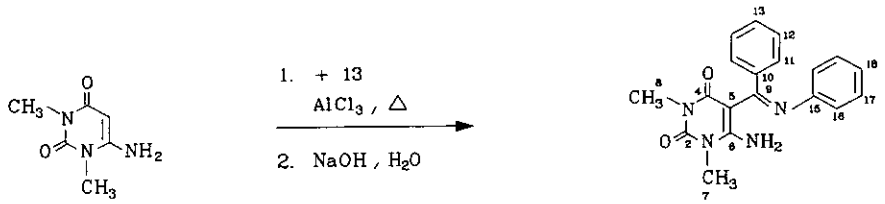
1 12

Scheme 4

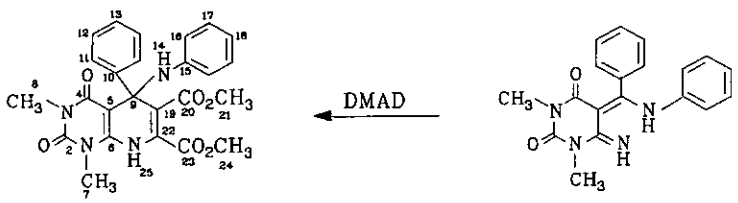
(3) As it is well known, C-5 of the uracil is considerably nucleophilic[4a,10] due to nearly intact dicarboximide and enamine substructures (^{13}C nmr: δ 100.9 ppm), and there are numerous Michael type additions known to occur at C-5.[11] However, the addition of an imino group requires enforced reaction conditions: refluxing of the uracil-6-iminophosphorane (**1**) with *N*-phenylbenzimidoyl chloride (**13**) and equimolar amounts of $AlCl_3$ in *o*-dichlorobenzene gave after hydrolysis with aq. NaOH the 5-iminouracil (**14**); the latter one was easily 6π-electron cyclized to **15** with isocyanates[8] (yield 58%). The 6-aminouracil (**16**), however, being unprotected by phosphorylation, under these conditions gave the Michael adduct (**17**) (yield 64%), which existed in two tautomeric forms. According to some published ^1H nmr values of



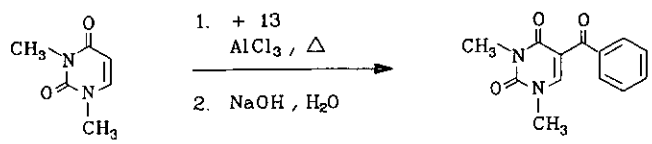
1 14 15



16 17A



19 17B



20 21

Scheme 5

amidines and guanidines influenced by tautomerism,[12] the *ortho* and *para*-H of the *N*-phenyl group in iminoform (**17A**) have been found at high field (16-H: δ 6.58 ppm; 18-H: δ 6.89 ppm), while the *meta*-H of the aminoform (**17B**) was highly deshielded (17-H: δ 7.44 ppm). From the integration followed a ratio **A/B** = 9:1 in $CDCl_3$, and 1:6 in DMSO. Accordingly, the ^{13}C nmr of **17** revealed a double set of signals (except the two methyl signals). Furthermore, the tautomeric 1,3-diene in **17B** could be easily intercepted by [4+2] cycloaddition with dimethyl acetylenedicarboxylate (**18**, DMAD) to give **19** in 72% yield.

1,3-Dimethyluracil (**20**) lacks this stabilization by tautomerism, and treatment with the imidoyl chloride (**13**) afforded in low yield directly 5-benzoyl-1,3-dimethyluracil (**21**), which is accessible independently.[13]

ACKNOWLEDGMENT

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EXPERIMENTAL

Melting points are uncorrected.- ir spectra: Perkin-Elmer 157-G.- ^1H nmr spectra: Bruker WP-90, AC-200, AM-400, TMS as internal standard.- ^{13}C nmr spectra: Bruker WP-90, AC-200, AM-400, $CDCl_3$, 77.10 ppm internal standard.- ms spectra: MS-30 and MS-50, A. E. I. Kratos, Manchester, DE 180-210°C, 70 eV, 300 μA.- Elemental analyses: Analytische Abteilung des Instituts.

Preparation of the 9,11-Dimethyl-7-aryliminopyrimido[4',5':4,5]pyrimido[6,1-*a*]azepine-10,12-(9*H*,11*H*)-diones (**6a-c**) and the 6-Triphenylphosphoranylideneamino-5-(3-trifluormethylphenyl)amidopyrimidine-2,4-(1*H*,3*H*)-dione (**7**)

4.15 g (10 mmol) of 1,3-dimethyl-5-triphenylphosphoranylideneaminouracil (**1**), 2.54 g (20 mmol) of *O*-methyl-ε-caprolactim ether and the isocyanate [phenyl- **2a**: 2.62 g (22 mmol); 4-chlorophenyl- **2b**: 3.68 g (24 mmol); 3-trifluorophenyl- **2c**: 7.48 g (40 mmol)] and 50 ml of abs. acetonitrile were heated in an Ar-atmosphere. -**6a,b** [3h reflux]: After cooling, the yellow precipitate of **6a,b** was collected by filtration. **6c**,**7**

[10 h reflux]: After the solvent had been distilled off, the yellow residue was treated with aqueous ethanol (95%) and heated under reflux for 10 min. **7** crystallized spontaneously as colourless prisms; cooling of the filtrate gave **6c** as yellow crystals. Recrystallization of **6a,b,c,7** from ethanol/ethyl acetate.

6a: yield 3.33 g (95%); mp 191-192°C. Anal. Calcd for $C_{29}H_{21}N_5O_2$: C, 64.9; H, 6.0; N, 19.9; Found C, 65.2; H, 6.2; N, 20.0. Ir (KBr): 1700, 1600 cm^{-1}. Ms, m/z (%): 351 (81, M^+), 350 (M^+-1, 100). ^1H Nmr ($CDCl_3$) δ 1.75-1.95 (m, 6*H*; 2-H, 3-H, 4-H), 3.31 (s, 3*H*; 13-H), 3.32 (s, 3*H*; 14-H), 2.95-3.73 (m, 2*H*; 1-H), 4.60-4.80 (m, 2*H*; 5-H), 6.91-7.44 (m, 5*H*; $H_{ar.}$). ^{13}C Nmr ($CDCl_3$) δ 23.88 (C-3), 25.82 (C-2), 28.10 (C-13), 28.26 (C-4), 29.05 (C-1), 29.14 (C-14), 46.15 (C-5), 92.62 (C-12a), 122.27 (C-19), 122.96 (C-17), 128.21 (C-18), 147.62 (C-16), 148.32 (C-7), 151.03 (C-8a), 154.34 (C-10), 160.27 (C-12), 171.35 (C-12b).

6b: yield 3.42 g (89%); mp 208-209°C. Anal. Calcd for $C_{19}H_{20}N_5O_2Cl$: C, 59.1; H, 5.2; N, 18.2; Found: C, 59.4; H, 5.4; N, 18.2. Ir (KBr): 1700, 1640 cm^{-1}. Ms, m/z (%): 385 (M^+, 100). ^1H Nmr ($CDCl_3$) δ 1.75-1.96 (m, 6*H*; 2-H, 3-H, 4-H), 3.31 (s, 3*H*; 13-H), 3.33 (s, 3*H*; 14-H), 3.75-3.88 (m, 2*H*; 1-H), 4.60-4.70 (m, 2*H*; 5-H), 7.01-7.27 (m, 4*H*; $H_{ar.}$). ^{13}C Nmr ($CDCl_3$) δ 23.95 (C-3), 25.87 (C-2), 28.22 (C-13), 28.35 (C-4), 29.10 (C-1), 29.28 (C-14), 46.30 (C-5), 93.01 (C-12a), 124.45 (C-17), 127.09 (C-19), 128.22 (C-18), 147.11 (C-16), 148.10 (C-7), 151.03 (C-8a), 154.55 (C-10), 160.27 (C-12), 171.46 (C-12b).

6c: yield 1.67 g (40%); mp 169°C. Anal. Calcd for $C_{20}H_{20}N_5O_2F_3$: C, 57.3; H, 4.8; N, 16.7; Found: C, 57.3; N, 4.9; N, 16.7. Ir (KBr): 1700, 1650 cm^{-1}. Ms, m/z (%): 419 (M^+, 100). ^1H Nmr ($CDCl_3$) δ 1.75-1.96 (m, 6*H*; 2-H, 3-H, 4-H), 3.29 (s, 3*H*; 13-H), 3.32 (s, 3*H*; 14-H), 3.78-3.88 (m, 2*H*; 1-H), 4.60-4.72 (m, 2*H*; 5-H), 7.19-7.42 (m, 3*H*; 17-H, 18-H, 19-H), 7.49 (s, 1*H*; 21-H). ^{13}C Nmr ($CDCl_3$) δ 23.85 (C-3), 25.73 (C-2), 28.10 (C-13), 28.21 (C-4), 28.94 (C-1), 29.09 (C-14), 46.22 (C-5), 93.15 (C-12a), 118.58 (Q, $^3J_{CF}$= 3.9 Hz; C-21), 120.04 (Q, $^3J_{CF}$= 3.8 Hz; C-19), 124.44 (Q, $^1J_{CF}$= -272.3 Hz; CF_3), 126.83 (C-17), 128.53 (C-18), 130.23 (Q, $^2J_{CF}$= 31.5 Hz; C-20), 148.48 (C-16), 148.93 (C-7), 150.84 (C-8a), 154.61 (C-10), 160.08 (C-12), 171.46 (C-12b).

7: yield 1.20 g (20%); mp 231°C. Anal. Calcd for $C_{32}H_{26}N_4O_3F_3$: C, 63.8; H, 4.3; N, 9.3; Found: C, 62.8; H, 4.4; N, 9.6. Ir (KBr): 1690, 1430 cm^{-1}. Ms, m/z (%): 602 (M^+; 5), 442 (100). ^1H Nmr ($CDCl_3$) δ 3.48 (s, 3*H*; 8-H), 3.60 (s, 3*H*; 7-H), 7.05-7.70 (m, 19*H*; $H_{ar.}$), 11.60 (br s, 1*H*; NH). ^{13}C Nmr ($CDCl_3$) δ 28.05 (S; C-8), 31.65 (S; C-7), 89.53 (D, $^3J_{PC}$= 2.0 Hz; C-5), 116.59 (Q, $^3J_{CF}$= 4.0 Hz; C-12), 118.65 (Q, $^3J_{CF}$= 4.1 Hz; C-14), 122.59 (S; C-16), 124.14 (Q, $^1J_{CF}$= -272.5 Hz; C-17), 128.39

(D, $^{3}J_{PC}$= 12.9 Hz; C-20), 128.52 (S; C-15), 130.34 (Q, $^{2}J_{CF}$= 31.8 Hz; C-13), 131.00 (D; C-18), 131.48 (D, $^{4}J_{PC}$= 12.9 Hz; C-21), 132.04 (D, $^{2}J_{PC}$= 10.1 Hz; C-19), 139.61 (S; C-11), 151.50 (D, $^{4}J_{PC}$= 3.1 Hz; C-2), 158.74 (D, $^{4}J_{PC}$= 10.5 Hz; C-4), 164.87 (S; C-9), 164.46 (S; C-6).

Preparation of the 7-Arylamino-5,6-dihydro-1,3-dimethyl-5,6-diphenylpyrimido[4,5-*d*]pyrimidine-1,3-(2*H*,4*H*)-diones (**9a,b,c,d**)

4.15 g (10 mmol) of uracil (**1**), 1.81 g (10 mmol) of benzylideneaniline (**8**) and the isocyanate [**2a**: 2.14 g (18 mmol); **2b**: 2.76 g (18 mmol); **2c**: 3.74 g (20 mmol); **2d**: 2.93 g (22 mmol)] were heated in 50 ml of abs. acetonitril under reflux and Ar-atmosphere for 2-4 h. The solutions were concentrated and the colourless precipitates of **9a,b,c** were filtered off and recrystallized from ethanol/ethyl acetate. **9d** was obtained as an oil which crystallized on heating with 10 ml of ethanol/ethyl acetate (1:1) and cooling overnight as pale greenish-yellow prisms.

9a: yield 3.06 g (70%); mp 244°C. Anal. Calcd for $C_{26}H_{23}N_5O_2$: C, 71.3; H, 5.3; N, 16.0; Found: C, 71.1; H, 5.3; N, 16.0. Ir (KBr): 3278, 1670, 1640 cm^{-1}. Ms, m/z (%): 437 (20; M^+), 360 (100). ^{1}H Nmr ($CDCl_3$) δ 3.26 (s, 3*H*; 10-H), 3.51 (s, 3*H*; 9-H), 5.67 (s, 1*H*; 5-H), 6.23 (br s, 1*H*; NH), 7.02-7.45 (m, 15*H*; $H_{ar.}$). ^{13}C Nmr ($CDCl_3$) δ 27.60 (C-10), 29.55 (C-9), 61.59 (C-5), 89.65 (C-4a), 121.77 (CH), 124.46 (CH), 126.42 (CH), 126.78 (CH), 128.09 (CH), 128.40 (CH), 128.70 (CH), 128.74 (CH), 130.07 (CH), 137.60 (C-11), 140.24 (C-15), 142.85 (C-19), 151.26 (C-7), 152.28 (C-8a), 152.62 (C-2), 160.33 (C-4).

9b: yield 2.12 g (45%); mp 226-228°C. Anal. Calcd for $C_{26}H_{22}N_5O_2Cl$: C, 66.2; H, 4.7; N, 14.8; Found: C, 65.1; H, 4.8; N, 15.0. Ir (KBr): 3280 (NH), 1670, 1640 (s) cm^{-1}. Ms, m/z (%): 471 (M^+, 10), 394 (100). ^{1}H Nmr ($CDCl_3$) δ 3.26 (s, 3*H*), 3.51 (s, 3*H*), 5.66 (s, 1*H*), 6.20 (br s, 1*H*; NH), 7.00-7.44 (m, 14*H*). ^{13}C Nmr ($CDCl_3$) δ 27.17 (C-10), 29.08 (C-9), 60.35 (C-5), 89.57 (C-4a), 123.17 (CH), 124.55 (CH), 125.52 (CH), 126.41 (CH), 127.44 (CH), 127.86 (CH), 128.06 (CH), 129.09 (CH), 137.09 (C-11), 141.88 (C-15), 142.67 (C-19), 150.65 (C-7), 151.54 (C-8a), 152.51 (C-2), 159.87 (C-4).

9c: yield 3.08 g (61%); mp 301°C. Anal. Calcd for $C_{27}H_{22}N_5O_2F_3$: C, 64.1; H, 4.4; N, 13.9; Found: C, 63.4; H, 4.7; N, 14.2. Ir (KBr): 3250, 1670, 1640 cm^{-1}. Ms: m/z (%): 505 (M^+,7), 428 (100). no Nmr spectra because of insufficient solubility.

9d: yield 0.81 g (18%); mp 222-225°C. Anal. Calcd for $C_{27}H_{25}N_5O_2$: C, 71.8; H, 5.5; N, 15.5; Found: C, 71.9; H, 5.6; N, 15.2. Ir (KBr): 3250, 1670, 1640 cm^{-1}. Ms, m/z (%): 451 (M^+,12), 374 (100). ^{1}H Nmr ($CDCl_3$) δ 2.26 (s, 3*H*; Ar-CH_3), 3.15 (s, 3*H*; 10-H), 3.48 (s, 3*H*; 9-H), 5.64 (s, 1*H*; 5-H), 6.39 (br

s, 1*H*; NH), 6.97-7.46 (m, 14*H*; $H_{ar.}$). no ^{13}C Nmr spectra because of insolubility.

Preparation of the Diethyl 1,2,5,6,7,8-Hexahydro-5,7-dimethyl-6,8-dioxo-3-phenylaminopyrimido[4,5-*e*]-[1,2,4]triazine-1,2-dicarboxylate (11)

4.15 g (10 mmol) of **1**, 1.74 g (10 mmol) of diethyl azodicarboxylate (**10**) and 1.19 g (10 mmol) of phenylisocyanate in 70 ml of dry acetonitril were heated under Ar until no traces of the uracil were detectable by tlc. The solvent was distilled off and the colourless residue was recrystallized from ethanol.

11: yield: 1.80 g (42%); mp 324°C. Anal. Calcd for $C_{19}H_{22}N_6O_6$: C, 53.01, H, 5.15, N, 19.52; Found: C, 52.67, H, 5.17, N, 19.50. Ir (KBr): 3260, 1770, 1735 cm^{-1}. Ms, m/z (%): 430 (M^+, 100). ^1H Nmr ($CDCl_3$) δ 1.11-1.42 (m, 6*H*; 13-H, 16-H), 3.35 (s, 3*H*; 9-H), 3.42 (s, 3*H*; 10-H), 3.86-4.53 (m, 4*H*; 12-H, 15-H), 7.17-7.68 (m, 5*H*), 9.46 (br s; NH) . ^{13}C Nmr ($CDCl_3$) δ 14.10 (C-13)*, 14-17 (C-16)*, 28.18 (C-9), 29.97 (C-10), 64.26 (C-12)*, 64.77 (C-15)*, 100.45 (C-8a), 121.46 (C-19), 125.71 (C-21), 129.06 (C-20), 136.06 (C-18), 148.35 (C-4a), 148,08 (C-6), 151.56 (C-3), 1563.07 (C-1), 156.14 (C-11)*, 157.14 (C-14)* [*: interchangeable].

Preparation of the 1,3-Dimethyl-5-(*N*-phenylbenzimidoyl)pyrimidine-2,4(1*H*,3*H*)-diones (14, 17) and 1,3-Dimethyl-5-benzoylpyrimidine-2,4(1*H*,3*H*)-dione (21)

A suspension of the uracil [**1**: 4.15 g (5 mmol); **16**: 1.55 g (10 mmol); **20**: 1.35 g (10 mmol)] and 2.16 g (10 mmol) benzimidoyl chloride (**13**) in 100 ml of *o*-dichlorobenzene was treated with 1.33 g (10 mmol) of aluminium(III) chloride in small portions and heated for 5 h. After cooling, the solution was treated with 50 ml of H_2O, then with 20% aqueous NaOH. a) Filtration of the precipitate gave **17**, which was washed with ether and recrystallized twice from acetonitrile. b) Stirring of the suspension for an additional hour, separating, drying (Na_2SO_4) and concentrating the organic layer *in vacuo* gave the iminophosphorane (**14**) and the benzoylated product (**21**) after cooling overnight. The crude products (**14**, **21**) were chromatographed on silica gel (ethyl acetate).

14: yield 1.8 g (39%); mp 188°C. HRms: Calcd for $C_{37}H_{31}N_4O_2P$: 594.2184 mmu, Found: 594.2179 mmu. Ir: 1675, 1630, 1430 cm^{-1}. Ms, m/z (%): 596 (M^+, 5), 517 (100). ^1H Nmr ($CDCl_3$) δ 2.73 (s, 3*H*; 8-H), 3.46 (s, 3*H*; 7-H), 6.72 (dt, J= 8 Hz and 1.9 Hz, 2*H*; 16-H), 7.02 (t, J= 8 Hz, 1*H*; 18-H), 6.84-7.73 (m, 22*H*). ^{13}C Nmr ($CDCl_3$) δ 27.93 (C-8), 31.91 (C-7), 98.38 (D, $^3J_{PC}$= 8.1 Hz; C-5), 119,89 (C-16), 125.78 (D, $^1J_{PC}$= 111.3 Hz; C-20), 127.33 (C-18), 128.30 (D, $^3J_{PC}$= 14.6 Hz; C-22), 128.96 (C-17), 129.21 (C-12), 129.89 (C-13), 132.09 (C-11), 132.15 (D, $^2J_{PC}$= 10.2 Hz; C-21), 132.55 (D, $^4J_{PC}$= 3.0 Hz; C-23), 138.99 (C-10), 151.41 (C-2), 151.61 (C-15), 152.32 (C-6), 162.13 (C-9), 163.55 (C-4).

17: yield 2.2 g (64%); mp 239°C. Anal. Calcd for $C_{19}H_{18}N_4O_2$: C, 68.3; H, 5.4; N, 16.8; Found: C, 67.9; H, 5.4; N, 16.3. Ir (KBr): 3430, 1740, 1700 cm^{-1}. Ms, m/z (%): 334 (M^+, 26), 333 (100). ^1H Nmr (DMSO-d_6, predominantly tautomeric form B) δ 3.03 (s, 3*H*; 8-H), 3.14 (s, 3*H*; 7-H), 6.62 (broad, 2*H*; 14-H, 19-H), 6.83 (dd, J= 7.0 Hz and 1.1 Hz, 2*H*; 16-H), 6.96 (tt, 1*H*; J= 7.0 Hz and 1.1 Hz; 18-H), 7.23 (t, J= 8.4 Hz, 2*H*; 12-H), 7.44 (m, 2*H*; 17-H), 7.46 (m, 1*H*; 13-H), 7.88 (dd, J= 8.4 Hz and 2.8 Hz, 2*H*; 11-H). ^1H Nmr ($CDCl_3$, predominantly tautomeric form A) δ 3.20 (s, 3*H*; 8-H), 3.48 (s, 3*H*; 7-H), 6.58 (dd, J= 8.1 Hz and 1.5 Hz, 2*H*; 16-H), 6.89 (tt, J= 8.4 Hz and 1.5 Hz, 1*H*; 18-H), 6.96-7.20 (m, 7*H*), 8.73 (broad, 2*H*, D_2O-exch.; NH_2). ^{13}C Nmr ($CDCl_3$) δ 27.32 (C-8), 29.72 (C-7), 84.20/87.18 (C-5), 121.84/118.17 (C-16), 122.36/123.27 (C-18), 126.83/128.12 (C-17), 127.02/130.48 (C-11), 127.67/128.25 (C-12), 127.80/128.96 (C-13), 138.71/138.48 (C-10), 149.20/150.26 (C-15), 151.85/152.08 (C-2), 156.06/152.01 (C-6), 160.33/161.94 (C-4), 168.87/159.94 (C-9).

21: yield: 0.49 g (20%); mp 159-161°C. Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.9; H, 4.9; N, 11.5; Found: C, 63.9; H, 4.8; N, 11.7. All data are in full agreement to those reported earlier.[13]

1,3-Dimethyl-7-(*N*-phenylimino)pyrimido[4,5-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (15)

0.26 g (0.5 mmol) of **14** , 0.2 g (1.7 mmol) of phenylisocyanate (**2a**) in 60 ml of acetonitrile were heated under reflux for 4 h. The solvent was distilled off *in vacuo* and the yellow residue was chromatographed on silica gel (ethyl acetate).

yield: 0.13 g (58%); mp 301-302°C. HRms: Calcd for $C_{26}H_{21}N_5O_2$: 435.1682; Found: 435.1695. Ir (KBr): 1720, 1670 cm^{-1}. Ms, m/z (%): 435 (M^+, 12), 105 (100). ^1H Nmr ($CDCl_3$) δ 3.14 (s, 3*H*; 8-H), 3.37 (s, 3*H*; 7-H), 6.84-7.37 (m, 15*H*). ^{13}C Nmr ($CDCl_3$) δ 28.07 (C-8), 29.37 (C-7), 94.06 (C-5), 122.49 (C-22), 122.89 (C-16), 127.42 (C-24), 127.90 (C-18), 128.00 (C-23), 128.09 (C-17), 128.13 (C-12), 129.00 (C-13), 129.12 (C-11), 132.55 (C-10), 138.27 (C-15), 148.06 (C-21), 148.96 (C-20), 151.32 (C-2), 155.17 (C-9), 158.68 (C-4), 165.66 (C-6).

Dimethyl 5-Anilino-1,3-dimethyl-2,4-dioxo-5-phenyl-1,2,3,4,5,8-hexahydropyrido[2,3-*d*]pyrimidine-6,7-dicarboxylate (19)

0.5 g (6 mmol) of **17** and 2.0 g (14 mmol) of dimethyl acetylenedicarboxylate (DMAD, **18**) in 70 ml of abs. toluene were heated under reflux for 9 h. After the solvent had been distilled off *in vacuo*, the residue was chromatographed on silica gel (ethyl acetate).

yield: 2.0 g (72%); mp 156-157°C. HRms: Calcd for $C_{25}H_{24}N_4O_6$: 476.1690; Found: 476.1695. Ir (KBr): 3440, 1735, 1710, 1665 cm^{-1}. Ms, m/z (%): 476 (M^+; <1), 417 (100). ^1H Nmr ($CDCl_3$) δ 2.97 (NH),

3.02 (NH), 3.13 (s, 3*H*; 21-H), 3.40 (s, 3*H*; 8-H), 3.51 (s, 3*H*; 7-H), 3.81 (s, 3*H*; 24-H), 6.84-7.46 (m, 10*H*). ^{13}C Nmr ($CDCl_3$) δ 27.70 (C-8), 29.16 (C-7), 43.69 (C-9), 51.78 (C-21), 53.37 (C-24), 81.63 (C-19), 93.57 (C-5), 127.75 (C-16), 127.95 (C-11), 128.27 (C-13), 128.69 (C-17), 128.82 (C-12), 129.24 (C-18), 133.32 (C-10), 138.37 (C-15), 152.38 (C-2), 152.97 (C-6), 160.28 (C-4), 163.68 (C-22), 169.28 (C-20), 170.51 (C-23).

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