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Amination, III[1,2]. Trimethylsilanol as Leaving Group, V[3]

Silylation–Amination of Hydroxy N-Heterocycles

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Hydroxy N-heterocycles such as **18**, **21**, **26**, and others are efficiently aminated in a one-step/one-pot procedure by silylation-amination to give **20**, **23** – **25** etc. Silylation converts aromatic hydroxy N-heterocycles into activated and lipophilic intermediates of type **3**, **8** which react *in situ* with ammonia, primary or secondary amines to form the corresponding mono-, bis- or tris-aminated products (**5**, **10**). This addition-elimination of amines to *O*-silylated heterocycles in Lewis acid-catalyzed and proceeds usually in high yields if the leaving group trimethylsilanol is converted *in situ* by excess silylated agent into hexamethyldisiloxane. Scope and limitations of this simple procedure are discussed.

Aminierung, III[1,2]. Trimethylsilanol als austretende Gruppe, V[3]

Silylierung-Aminierung von Hydroxy-N-heterocyclen

Durch Silylierung-Aminierung lassen sich Hydroxy-N-heterocyclen (z. B. **18**, **21**, **26** u. a.) bequem in einer Einstufen-Eintopfreaktion aminieren (→ **20**, **23** – **25** etc.). Aromatische Hydroxy-N-heterocyclen werden durch Silylierung in aktivierte und lipophile Zwischenprodukte vom Typ **3**, **8** umgewandelt, die sich *in situ* mit Ammoniak, primären oder sekundären Aminen zu den entsprechenden mono-, bis- und tris-aminierten Produkten (**5**, **10**) umsetzen. Die Additions-Eliminierungsreaktion von Aminen an *O*-silylierte Heterocyclen ist Lewissäure-katalysiert und verläuft gewöhnlich in hohen Ausbeuten, falls die austretende Gruppe Trimethylsilanol *in situ* durch überschüssiges Silylierungsmittel in Hexamethyldisiloxan umgewandelt wird. Anwendungsbreite und Grenzen dieser einfachen Methode werden diskutiert.

Since many drugs and plant protection products are amino-nitrogen heterocycles, the preparation of such products is of scientific and technical interest.

Aromatic nitrogen heterocycles with a hydroxy group α or γ to a nitrogen, which are often readily available, have hitherto been transformed into the corresponding amino compound by a two-step procedure as reviewed by *Shepherd* and *Fedrick*[4]:

a) Conversion by $POCl_3$ into the α- or γ-chloro compound[4], transformation of the chlorides into the even more reactive trimethylammonium salts[5] or conversion of the hydroxy group by sulfonyl chlorides into the *O*-sulfonates[6] followed b) by nucleophilic addition-elimination reaction with ammonia, primary, or secondary amines.

The one-step amination of hydroxy N-heterocycles by heating with excess hexamethylphosphoric triamide (HMPT)[7] or tributylphosphoric triamide[8] and a mixture of secondary amines and phosphorus pentaoxide[9] or phosphoryl chloride[10] to

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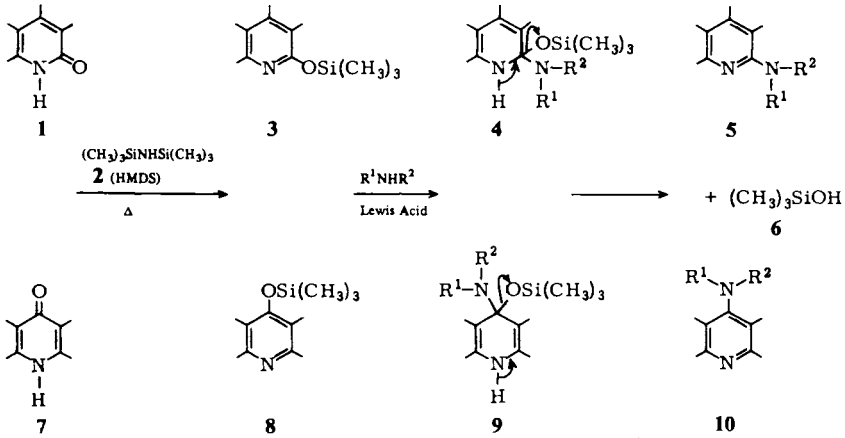
200–250°C gives generally only a 15–65% yield of the corresponding aminated heterocycles.

As described in a preliminary communication[1,11], aminations of hydroxy N-heterocycles are achieved by a simple one-step/one-pot procedure by silylation-amination.

Silylation[12], e. g. by hexamethyldisilazane (HMDS) (**2**), transforms heterocycles like **1** or **7** into the fully aromatic silylated heterocyclic systems **3** or **8** with evolution of ammonia. **3** or **8** can be subsequently or better concomitantly aminated by heating with ammonia, primary, or secondary amines into the desired aminated end products **5** or **10** with formation of trimethylsilanol (**6**) as leaving group.



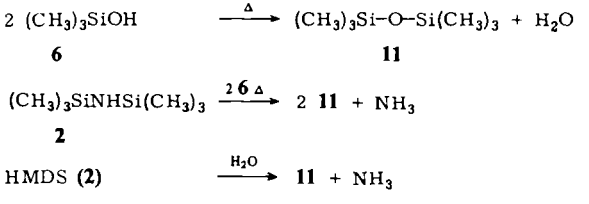
As we observed previously during the silylation-amination of purines or purine nucleosides[2] the amination of these fully aromatic silylated systems like **3** or **8** proceeds usually *only* in the presence of Lewis acids[13] via the addition products **4** or **9** which then eliminate trimethylsilanol (**6**) to afford **5** or **10**.

Only cyclic trimethylsilyl imino ether systems which are conjugated with a carbonyl group as in persilylated uridine[14] or very reactive systems like 3-methoxy-1,2,4-triazine[15] can undergo addition-elimination reactions readily without Lewis acid catalysts.

1. Silylation versus Alkylation

Although the trimethylsilyloxy group resembles an alkoxy group, there are some distinct differences between trimethylsilanol (**6**), methanol, or *tert*-butyl alcohol as leaving groups:

a) Trimethylsilanol (**6**) dimerizes on heating, especially in the presence of acids or bases[16], to form hexamethyldisiloxane (**11**) and water.



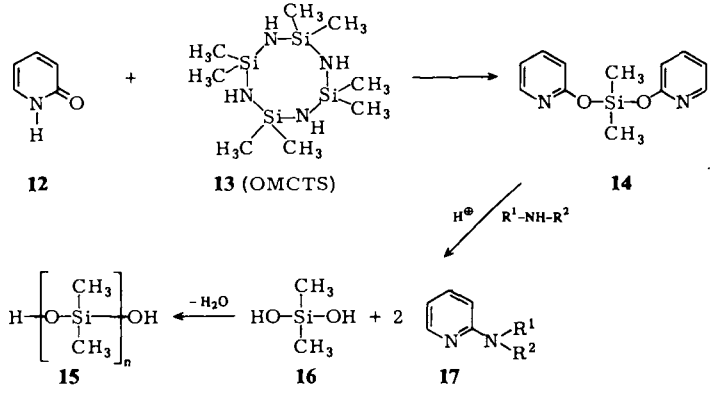
To remove the water which is formed on dimerization of **6** to **11**, at least one additional equivalent of a silylating agent like HMDS (**2**) (b.p. 126°C) has to be employed which can then react with **6** or water to give **11** and will also convert any free bases **1** or **7** into the silylated compounds **3** or **8**.

When trimethylsilanol (**6**) (b. p. 98–99°C) or hexamethyldisiloxane (b. p. 99°C) (**11**) are distilled from the reaction mixture as soon as they are formed, an azeotropic mixture of **6** and **11** (b.p. 70–90°C)[16] is frequently observed, the amount of which indicates the progress of the silylation-amination.

At normal pressure the ammonia formed on silylation with HMDS (**2**) is evolved so rapidly that it does *not* react with **3** or **8**.

Since HMDS boils at 126°C and the least reactive hydroxy N-heterocycle 2(1*H*)-pyridinone (**12**) (cf. discussion under 1c) has to be heated much higher to undergo silylation-amination, we have reacted **12** with the stable crystalline octamethylcyclotetrasilazane (OMCTS) **13**, m. p. 97°C, b. p. 225°C[17], to afford an activated silylated intermediate which is probably **14** [cf. also the preparation of 2,4-bis[4-(2-hydroxyethyl)piperazino]-quinazoline (**24**), 3,6-bis(benzylamino)pyridazine (**51**) as well as of 4-(benzylamino)-pyridine (**54**)].

Heating of the dimer **14** with amines R^1NHR^2 in the presence of Lewis acids to ca. 180–220°C gives eventually rise to the desired aminated pyridine **17** and the unstable dimethylsilanol (**16**) which polymerizes with elimination of water to form silicon oil **15** or cyclic oligomers like hexamethylcyclotrisiloxane or octamethylcyclotetrasiloxane.



b) Alkylation of aromatic hydroxy N-heterocycles with diazomethane, diazoethane, or isopropyl iodide gives usually a mixture of *O*- and *N*-methylated products[18] which rearrange in the absence of catalysts only at high temperatures[19]. In contrast to *O*- or *N*-alkyl groups, *O*- or *N*-silyl groups are very mobile[20], and silylation gives therefore always rise to the thermodynamically controlled products – in our case the *O*-persilylated aromatic hydroxy heterocycles – like **3** and **8** – in practically quantitative yields.

Due to the high affinity of silicon to oxygen and the gain in aromatic energy it can be safely assumed that the silyl groups in these aromatic hydroxy N-heterocycles are practically *always* attached to oxygen[2,14,21].

c) Silylation rapidly transforms the often rather insoluble high melting hydroxy N-heterocycles into highly soluble, often volatile and activated aromatic heterocycles[22].

d) Very importantly, any additional phenolic or aliphatic hydroxyl groups in the heterocyclic or amine moiety are also rapidly silylated on treatment with HMDS (**2**) (cf. the silylation-amination of nucleosides[2,14]) or OMCTS (**13**) and thus are protected and solubilized during the silylation-amination.

To follow these silylation-amination reactions analytically (e. g. by tlc) these protecting *O*-silyl groups can be rapidly removed with Bu_4NF[23]. After the reaction is complete the silyl groups are split off preparatively in practically quantitative yield by transsilylation with excess boiling methanol for 0.5 – 3 h to afford the free aminated heterocycle and methyl trimethylsilyl ether (b. p. 59 °C)[16] which can be readily distilled from the transsilylation mixture using a small Vigreux column. On working with OMCTS (**13**), the non volatile silicon oil **15** or the cyclic trimer or tetramer, which are formed on workup, are removed by extraction with pentane.

2. Silylation-Amination

Since silylation and amination do not interfere with each other, both processes can be performed simultaneously in a one-pot reaction. The added amine component, which is applied in a 1 – 3 molar excess, helps to solubilize the hydroxy N-heterocycles for rapid silylation and subsequently amination. The silylation is furthermore accelerated by the added Lewis acid.

Which factors do influence the rate and ease of this silylation-amination?

a) The nature of the leaving group trimethylsilanol (**6**). Trimethylsilanol (**6**) can roughly be compared to methanol or ethanol which have a reactivity towards aminolysis of only ca. 10^{-5} to 10^{-6} compared to chlorine[24]. The *O*-trimethylsilyl group is, however, sterically much less demanding than a *tert*-butoxy group which is due to the increased O – Si bond length in **6**[25] and therefore interferes relatively little with the addition-elimination reactions[26].

b) The nature of the amine $R^1 - NH - R^2$. The more basic and sterically less hindered amines undergo a much more rapid amination of the silylated heterocycles. On extended heating the amines are gradually transsilylated by HMDS with evolution of ammonia to furnish silylated primary or secondary amines which are also silylating agents and therefore react readily with trimethylsilanol (**6**), water or starting hydroxy N-heterocycles **1** or **7**.

Since we usually employed a two to threefold excess of primary or secondary amine we could be assured that enough *free* amine was always available for the addition-elimination to the aminated end product. After the reaction the excess of amines like benzylamine or 2-phenylethylamine can often be readily removed by distillation at 100 – 120 °C/0.1 Torr during workup.

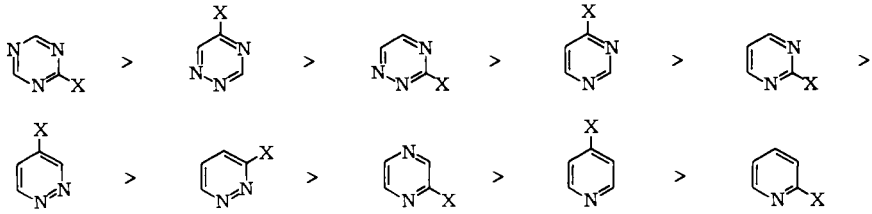
Furthermore, the excess of amines served as a solvent for the silylation-amination as these reactions were usually done without any solvent. Only in few cases [cf. Ref.[2]] as well as the preparation of 4-pyrrolidinopyridine (**53**)] pyridine could be employed as solvent, when the basicity of the persilylated hydroxy N-heterocycle was high enough compared to pyridine to ascertain that the silylated hydroxy N-heterocycle was also protonated in the equilibrium.

As already mentioned, the ammonia formed during silylation or transsilylation is so rapidly evolved that it usually reacts only with the silylated hydroxy N-heterocycle to form the corresponding amino heterocycles under pressure in an autoclave as described in our previous papers[2,14]. With weakly basic amines like aniline only the more reactive heterocyclic systems are aminated[2]. That means, e.g., that the least reactive 2(1*H*)-pyridinone (**12**) cannot be aminated with anilines via silylation-amination.

c) The nature of the aromatic heterocyclic system.

As summarized by *Shepherd* and *Fedrick*[4] the aromaticity (and basicity) of heterocyclic systems increases with a decreasing number of nitrogen atoms. Consequently, the reactivity of the leaving groups X in α- or β-positions to the nitrogen decreases in the same order as illustrated by the following sequence[4]. Due to the annelated benzene ring, quinoline or phthalazine have enhanced reactivities which correspond roughly with the diazines or triazines.

Reactivities



X = Cl, OCH_3, OEt, $OSi(CH_3)_3$

Due to this increase in aromaticity and basicity and consequent decrease in reactivity, the formation of the non-aromatic addition intermediates of type **4** or **9** becomes less and less favored and is most difficult in the case of silylated 2-pyridone.

d) The nature of the Lewis acid catalysts. With a few exceptions like the aforementioned 2-methoxy-1,2,4-triazines[15] most of the aromatic triazines, diazines, quinazolines, quinolines, and pyridines can *only* be aminated in the presence of such catalysts.

The acid (or Lewis acid)-catalyzed addition-elimination of ammonia and amines to α or γ-halogen-substituted N-heterocycles was first investigated by *Banks*[13] and subsequently by many other authors[13].

Furthermore, *Johnson*[27a] as well as *Kappe*[27b] observed the direct acid-catalyzed amination of the rather reactive 4(1*H*)-quinolinone – with water as the leaving group.

As we found in our previous work on the amination of purine-nucleosides[2] the most practical catalysts for the silylation-amination are $(NH_4)_2SO_4$, *p*-toluenesulfonic acid hydrate, trifluoromethanesulfonic acid, and perfluorobutanesulfonic acid which are probably transformed *in situ* into the corresponding bis(trimethylsilyl) sulfate[28], trimethylsilyl *p*-toluenesulfonate[29], trimethylsilyl triflate, and trimethylsilyl perfluorobutanesulfonate[30]. However, these acids may also be present as amine salts.

In the case of trifluoromethanesulfonic acid, previously we actually employed trimethylsilyl trifluoromethanesulfonate as catalyst[2]. On reacting amine hydrochlorides, e.g. dopamine hydrochloride, NH_4Cl is formed during silylation which sublimes partly into the condensor. But enough NH_4Cl or amine hydrochloride is usually present in the reaction mixture to ensure a smooth silylation-amination (cf. Ref.[2]). $ZnCl_2$ and $SnCl_4$ work sometimes as well but were not considered

as practical, whereas mercuric chloride which was used in our initial work[1,2], oxidizes the primary and secondary amines employed as well as the end products and gives often rise to mercury-containing side products which are difficult to remove quantitatively[2].

Although the employed primary and secondary amines are usually much more basic than the silylated hydroxy N-heterocycles, it can be assumed that there will always be some proton or Lewis acid transfer to the silylated hydroxy N-heterocycles in the equilibrium to effect the amination.

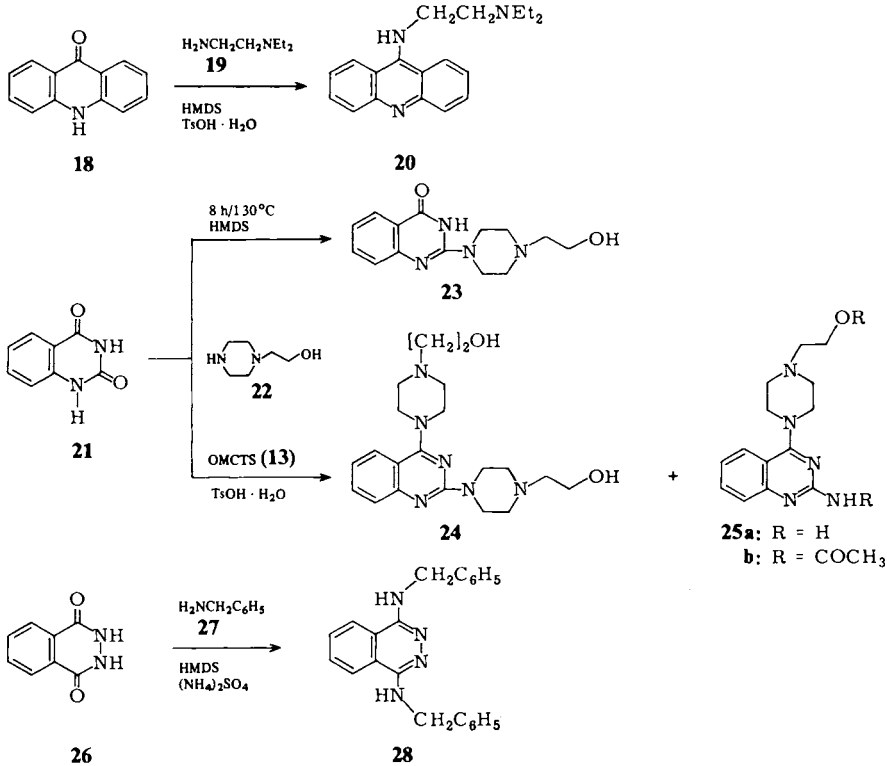
3. Practical Examples

As the reactivity of persilylated hydroxy N-heterocycles increases with increasing number of nitrogen atoms and likewise with increasing number of annelated rings (compare discussion under 2c) we first describe the silylation-aminations of the most reactive heterocyclic systems. We then proceed to less reactive systems and finally to the silylation-amination of the least reactive 2(1*H*)-pyridinone (**12**).

The examples have been arbitrarily selected to cover most of the commonly known heterocyclic systems used as drugs and plant-protection products and are only partially optimized.

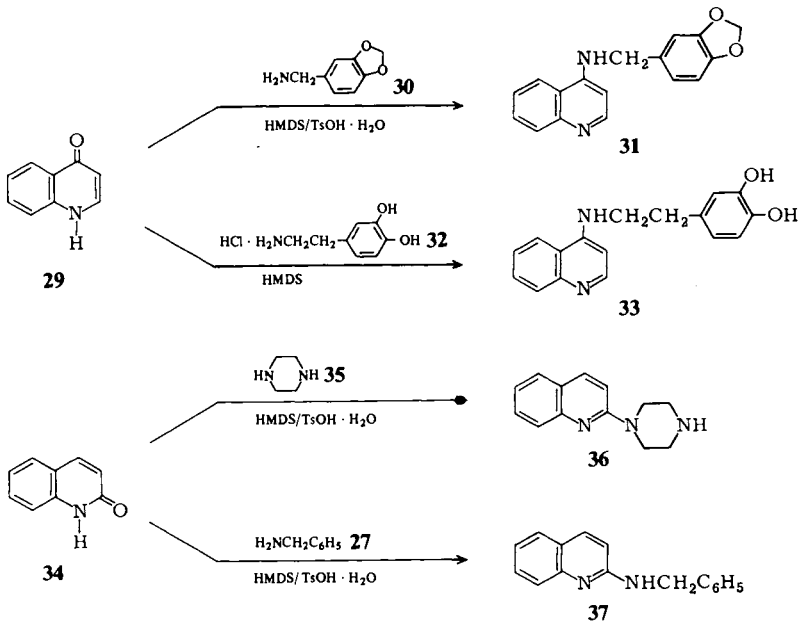
a) Aminations of Acridine, Quinazoline, Phthalazine, and Quinoline Systems

9(10*H*)-Acridinone (**18**) was reacted with 2-(diethylamino)ethylamine (**19**) in the presence of excess HMDS (**2**) and *p*-toluenesulfonic acid hydrate (TsOH · H_2O) as a catalyst to afford crystalline 9-[2-(diethylamino)ethylamino]acridine (**20**)[31] in 82% yield.



2,4(1*H*,3*H*)-Quinazolinedione (**21**) gave with two equivalents of 1-(2-hydroxyethyl)-piperazine (**22**), HMDS (**2**), and TsOH · H_2O as catalyst at 130°C a 68% yield of the crystalline 2-monosubstituted quinazoline **23**[32]. Reaction of **21** with 5 equivalents of **22**, octamethylcyclotetrasilazane (OMCTS) (**13**), and TsOH · H_2O for 24 h at 180°C afforded 56% of the desired 2,4-bisaminated quinazoline **24**. We furthermore isolated ca. 24% of 2-amino-4-[4-(2-hydroxyethyl)piperazino]quinazoline (**25a**), which was acetylated to the crystalline diacetate **25b**. Since the ^1H NMR spectrum of **25b** did not show any pronounced down field shift of the aromatic region containing the 5-(*peri*) hydrogen atom compared to **25a**, the amide group is in the 2-position. The question remains to be answered whether **25a** is formed by decomposition of **24** or by transamination of **24** with OMCTS (**13**).

2,3-Dihydro-1,4-phthalazinedione (**26**) gave with benzylamine (**27**) the dibenzyl derivative **28** in 87% yield. 4(1*H*)-Quinolinone (**29**) was reacted with 1,3-benzodioxole-5-methanamine (**30**) and HMDS in the presence of catalytic amounts of *p*-toluenesulfonic acid hydrate to afford the corresponding substituted 4-aminoquinoline (**31**) in 82% yield. The analogous reaction of **29** with dopamine hydrochloride (**32**) as amine moiety and catalyst furnished the 4-amino derivative **33** as monohydrate in 75% yield.



Reaction of 2(1*H*)-quinolinone (**34**) with piperazine (**35**) afforded the experimental drug quipazine (**36**)[33] in 74% yield, whereas benzylamine (**27**) gave 91% of 2-(benzylamino)quinoline (**37**)[34].

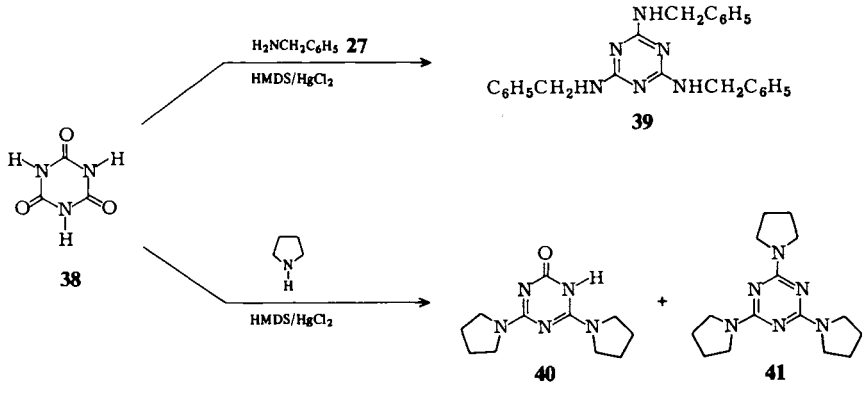
b) Amination of Triazine, Pyrimidine, and Pyridazine Systems

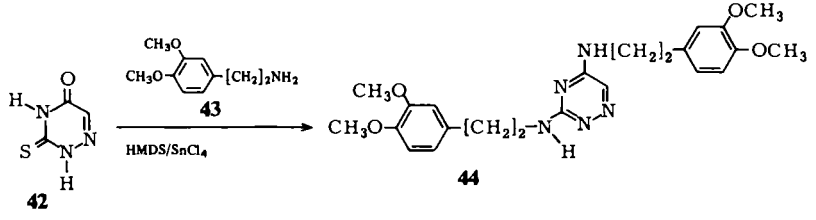
Cyanuric acid (**38**) was silylated and then treated with benzylamine (**27**) and mercuric chloride to afford 2,4,6-tris(benzylamino)-1,3,5-triazine (**39**) in 73% yield. Silylated **38**

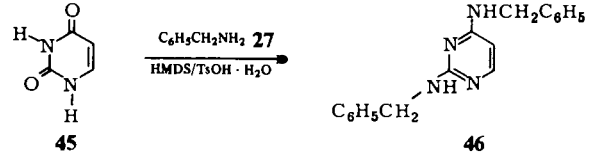
was reacted with pyrrolidine at 120°C to give a mixture of 52% of the dipyrrolidinotriazine **40** and 10% of the tri product **41**[35]. Using the more efficient method as described later for the preparation of 4-pyrrolidinopyridine (**53**), a much higher yield of **41** would certainly be obtained.

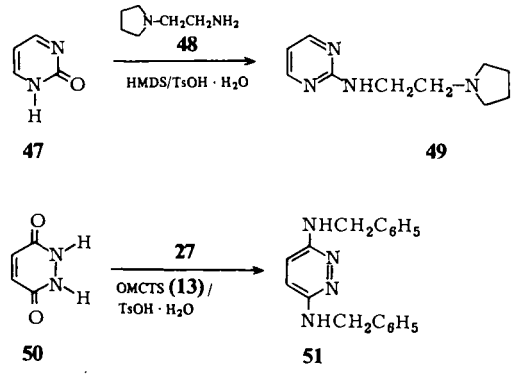
It is obvious that these two last examples are of no practical interest, since it would be much more convenient to aminate cyanuric chloride as described in the experimental part for the preparation of **41**.

Analogously, amination of 5-hydroxy-3-mercapto-1,2,4-triazine (**42**) with homoveratrylamine (**43**) in the presence of $SnCl_4$ using the older and inefficient two-step procedure afforded the corresponding 3,5-bis(homoveratrylamino)-1,2,4-triazine **44** in 63% yield as well as probably some evil-smelling hexamethyldisilthiane, $(CH_3)_3Si-S-Si(CH_3)_3$, which was not identified.









Silylation-amination of uracil (**45**) with excess benzylamine (**27**) in the presence of *p*-toluenesulfonic acid hydrate furnished 2,4-bis(benzylamino)pyrimidine (**46**) in 84% yield.

Some preliminary experiments demonstrated that uracil (**45**) can be transformed by heating with HMDS, NH_3, and *p*-toluenesulfonic acid hydrate in an autoclave in ca. 40 – 50% yield into 2,4-diaminopyrimidine (compare the amination of guanosine to 2-aminoadenosine)[2], however, this reaction was not further investigated. 2(1*H*)-Pyrimidinone (**47**) and 2-pyrrolidinoethylamine (**48**) analogously gave the corresponding 2-aminated product **49**[36] in 83% yield which was characterized as its dihydrochloride. 1,2-Dihydro-3,6-pyridazinedione (**50**), benzylamine (**27**), and OMCTS (**13**) furnished 3,6-bis(benzylamino)pyridazine (**51**)[37] in 62% yield.

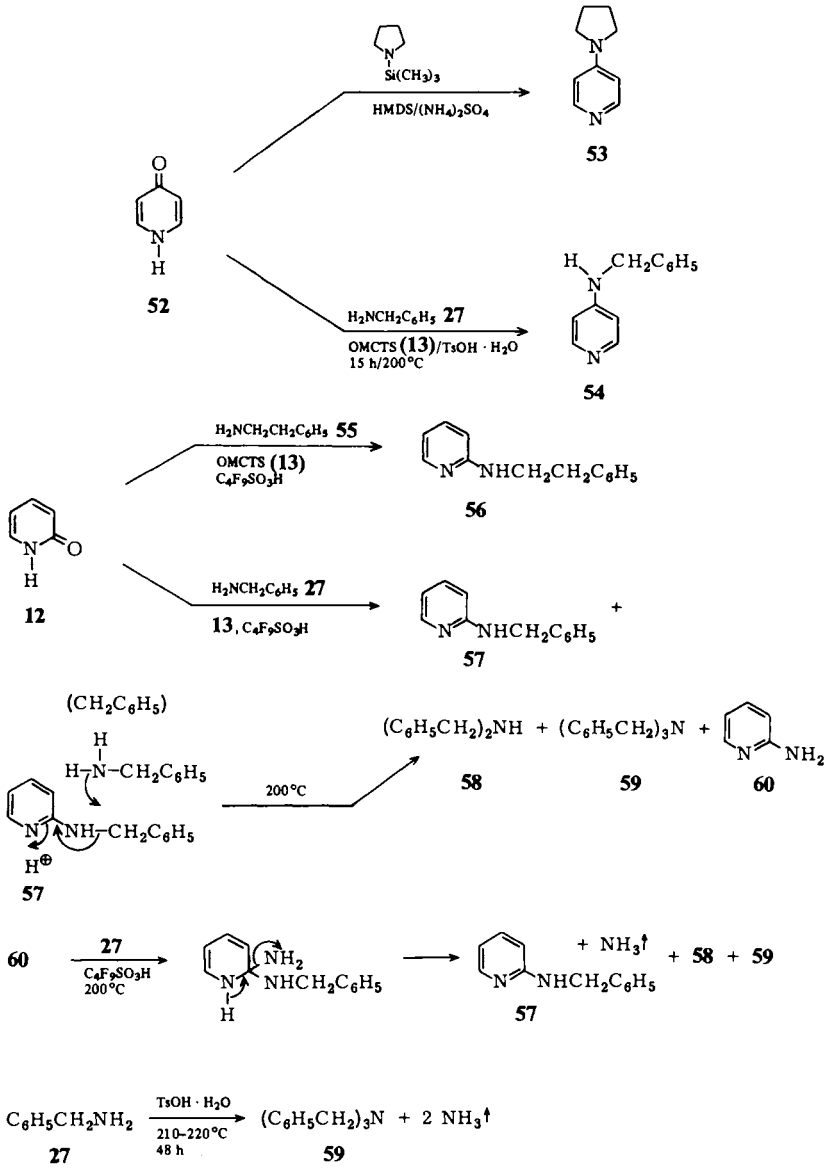
c) Amination of Pyridine Systems

The silylation-amination of 4(1*H*)-pyridinone (**52**) with pyrrolidine or more effectively with silylated pyrrolidine, which boils at 138 – 140 °C, proceeded in 81% yield on heating to 160 °C at normal pressure and in 92% yield on heating to 150 °C in pyridine in an autoclave to give the acylation catalyst 4-pyrrolidinopyridine (PPY) (**53**)[1]. Analogously, silylation-amination of **52** with benzylamine (**27**) and OMCTS (**13**) for 15 h/200 °C afforded 4-(benzylamino)pyridine (**54**) in 76% yield.

In contrast to the rather smooth silylation-amination of 4(1*H*)-pyridinone (**52**), the silylation-amination of 2(1*H*)-pyridinone (**12**), the least reactive hydroxy N-heterocycle (compare the discussion under 1a and 2c), was only possible at about 200 °C. Thus heating of **12** with 2-phenylethylamine (**55**) and OMCTS (**13**) for 24 h at 200 °C furnished 2-(2-phenylethylamino)pyridine (**56**)[38] in 71% yield.

On heating of **12** with benzylamine (**27**), OMCTS (**13**) or HMDS, and perfluorobutanesulfonic acid for 48 h to 180 – 190 °C a complicated reaction ensued. We isolated 40 – 47% of the desired 2-(benzylamino)pyridine (**57**)[39] as well as dibenzylamine (**58**), tribenzylamine (**59**), and some 2-aminopyridine (**60**) which were produced via benzyl transfer from **57** or benzylamine (**27**).

Heating of 2-aminopyridine (**60**) with **27** and perfluorobutanesulfonic acid for 40 h at 200 °C afforded 54% 2-(benzylamino)pyridine (**57**) as well as dibenzylamine (**58**) and tribenzylamine (**59**).



$$C_6H_5CH_2NH_2 \xrightarrow[210\text{–}220\,^\circ C,\ 48\ h]{TsOH \cdot H_2O} (C_6H_5CH_2)_3N + 2\ NH_3\uparrow$$

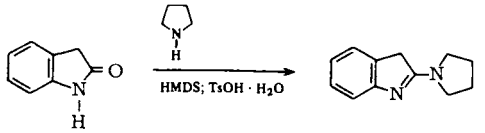
27 **59**

To demonstrate the benzyl transfer, we have heated benzylamine (**27**) with catalytic amounts of perfluorobutanesulfonic acid or *p*-toluenesulfonic acid hydrate and obtained a high yield of tribenzylamine (**59**) with concomitant evolution of ammonia.

Such an acid-catalyzed benzyl transfer was previously observed by *Gittos* and *Wilson*[40], who refluxed benzylamine and benzylammonium chloride for 16 h to afford mainly dibenzylammonium chloride and ammonia, and recently by *Stadlbauer* and *Kappe*[27b].

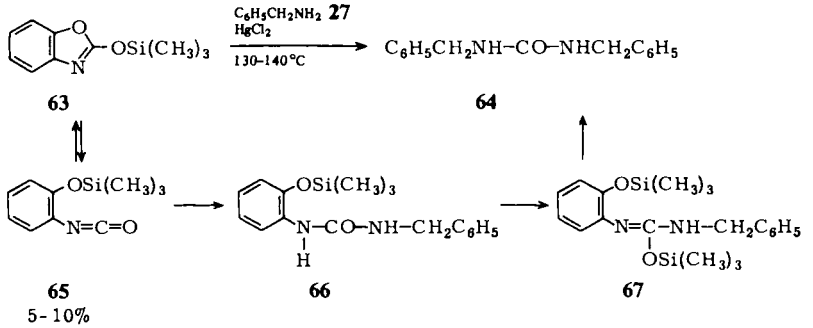
d) Amination of 5-Membered Hydroxy N-Heterocycles

Heating 2-hydroxyindole (**61**), pyrrolidine, HMDS, and *p*-toluenesulfonic acid hydrate for 1 h at 130°C afforded 76% of air-sensitive crystalline 2-pyrrolidino-3*H*-indole (**62**)[1,41].



61 **62**

However, neither **61** nor **62** are aromatic hydroxy 5-ring heterocycles. Thus we reacted 2-(trimethylsilyloxy)benzoxazole (**63**) with benzylamine (**27**), $HgCl_2$, and some excess HMDS. However, we isolated only the known *N,N'*-dibenzylurea (**64**)[42] in about 60% yield and not the expected 2-(benzylamino)benzoxazole[43]. The formation for this urea (**64**) is due to the presence of 5 – 10% of 2-(trimethylsilyloxy)phenyl isocyanate (**65**) in the equilibrium at 130°C[44], which reacts readily with excess benzylamine to give **66**. This intermediate is subsequently silylated to the silyl imino ether **67** which adds another benzylamine to afford finally the urea **64**.



63 **64**

65 5-10% **66** **67**

After this abortive experiment and the obvious possibility that other 5-ring heterocycles might react similarly, we have discontinued trying to apply the silylation-amination to further 5-membered hydroxy N-heterocycles.

We thank *J. Ziesche* for performing some silylation-aminations, Dr. *D. Rosenberg* and Dr. *G. A. Hoyer* for the physical data and Dr. *R. Schliebs*, Bayer Leverkusen, for a generous gift of perfluorobutanesulfonic acid.

Experimental Part

Melting points: Kofler melting point microscope, uncorrected. – UV spectra: Cary 14 spectrometer. – NMR spectra: Varian A 60 and HR-100. – Thin layer chromatography (tlc): E. Merck silica plates F_{254} and alumina plates.

Materials: The amine moieties were distilled under vacuum, when possible: Trimethylchlorosilane (TCS) and hexamethyldisilazane (HMDS) were commercial products and redistilled prior

to use. 2,2,4,4,6,6,8,8-Octamethylcyclotetrasilazane (OMCTS) (**13**) was obtained from Dow Corning Inc. as a crude mixture containing also hexamethylcyclotrisilazane and other products. Vacuum distillation according to Ref.[17] followed by recrystallization from hexane gave pure **13**, m. p. 97°C. On standing for several months, the concentrated mother liquors crystallized to afford further amounts of **13**. **13** is now commercially available from Petrarch Systems, Inc. Perfluorobutanesulfonic acid was a gift from Bayer Aktien-Gesellschaft, Leverkusen.

The crystalline hydroxy N-heterocycles were used as such. Only the crude commercial 4(1*H*)-pyridinone (**52**), containing water and NaCl, was purified by extraction with boiling chloroform to give on evaporation pure **52**. This compound could also be purified by silylation with HMDS and distillation of 4-(trimethylsilyloxy)pyridine which was used for the preparation of 4-pyrrolidinopyridine (**53**).

N-[2-(Diethylamino)ethyl]-9-acridinamine (**20**): 1.95 g (10 mmol) of 9(10*H*)-acridinone (**18**), 3.49 g (30 mmol) of 2-(diethylamino)ethylamine (**19**), 3.6 ml (15 mmol) of HMDS as well as 0.19 g (1.0 mmol) of *p*-toluenesulfonic acid hydrate were refluxed for 12 h at 140°C oil bath temperature. After cooling and addition of 100 ml of methanol, the reaction mixture was refluxed for 1 h and evaporated. The residue was dissolved in 100 ml of methylene chloride and extracted with ice-cold 2 N NaOH. After reextracting the aqueous phase, the combined methylene chloride phase was dried (Na_2SO_4), filtered and evaporated to give 3.1 g of crude residue. Extraction with 100 ml of boiling diethyl ether afforded 2.9 g of soluble material, which was chromatographed on a column of 120 g of alumina (A II, neutral) prepared with diethyl ether. Elution with 250 ml of ether gave 0.09 g of impurities. The next fractions (1 l) afforded 2.6 g of a yellow homogenous oil, which was crystallized from 100 ml of hexane to give in two crops 2.4 g (82%) of pure **20**, m. p. 58°C. – UV (methanol): λ_{max} = 267 (4.77); 337 (3.03); 411 (4.03); 432 nm (3.91). – ^{1}H NMR ($CDCl_3$): δ = 1.1 (t, *J* = 7 Hz, CH_3); 2.6 (m, CH_2NCH_2); 3.85 (m, NH – CH_2); 7.2 – 8.2 (m).

$C_{19}H_{23}N_3$ (293.4) Calcd. C 77.77 H 7.9 N 14.32 Found C 77.85 H 8.18 N 14.66

2-[4-(2-Hydroxyethyl)-1-piperazinyl]-4(3H)-quinazolinone (**23**): 3.24 g (20 mmol) of 2,4(1*H*,3*H*)-quinazolinedione (**21**), 5.28 g (40 mmol) of *N*-(2-hydroxyethyl)piperazine (**22**), 0.38 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate, and 11.53 ml (55 mmol) of HMDS were heated for 8 h at 130°C with simultaneous distillation of hexamethyldisiloxane (**11**). After adding 10 ml of pyridine, the reaction mixture was heated for further 10 h at 130°C bath temperature and the residue evaporated *in vacuo*. On recrystallization of the brownish residue from ethyl acetate/methanol (9:1), 3.73 g (68%) of pure crystalline **23**, m. p. 204.5°C, was obtained in three crops. The mother liquor still contained **23**. – UV (methanol): λ_{max} (log ε) = 236 (4.5), 271 (4.08), 307 (3.2), 316 (3.2), 336 nm (287). – ^{1}H NMR (D_2O): δ = 2.65 (m, NCH_2), 3.8 (m, NCH_2 + CH_2OH), 7 – 7.6 (m; 6,7,8-H), 7.85 (d, *J* = 7 Hz, 5-H).

$C_{14}H_{18}N_4O_2$ (274.3) Calcd. C 61.29 H 6.61 N 20.43 Found C 61.09 H 6.46 N 20.32

2,4-Bis[4-(2-hydroxyethyl)-1-piperazinyl]quinazoline (**24**) *and 4-[4-(2-Hydroxyethyl)-1-piperazinyl]-2-quinazolinamine* (**25a**): 3.24 g (20 mmol) of 2,4(1*H*,3*H*)-quinazolinedione (**21**), 13.02 g (100 mmol) of *N*-(2-hydroxyethyl)piperazine (**22**), 0.38 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate, and 11.71 g (40 mmol) of OMCTS (**13**) were heated for 48 h at 190 – 200°C oil bath temperature (inside the reaction mixture 175 – 180°C), whereupon NH_3 was evolved. The dark mixture was cooled, dissolved in 250 ml of methanol and the solution refluxed for 4 h. After evaporation, the residue was heated at 130°C/11 min, whereupon excess **22** (7.6 g) distilled. The darkbrown residue was dissolved in 300 ml of hot water and charcoal was added. Filtration and evaporation gave 8.0 g of crude product, which was chromatographed in methylene chloride on a column of alumina (240 g, A II neutral). Elution with methylene chloride (1 l) was followed by elution with ethyl acetate saturated with water. The first 1000 ml of ethyl acetate gave only

impurities whereas the next 1250 ml afforded 1.3 g (24%) of **25a**. The subsequent 2500 ml of eluate yielded 4.3 g (56%) of **24**. – ^{1}H NMR ($CDCl_3$): δ = 2.6 (m, NCH_2), 3.6 (m, $ArNCH_2$), 3.9 (m, CH_2OH), 6.9–7.8 (m). – MS: *m/e* = 387 (M^+ + H); 371; 369 (M + H – H_2O); 357; 343 (M + H – C_2H_4O); 286; *274* (M + H – $C_6H_{11}NO$); 231; 199; 173; 161; 56; 35.

$C_{20}H_{30}N_6O_2$ (386.5) Calcd. C 62.15 H 7.82 N 21.75 Found C 61.42 H 7.49 N 21.48

As yet **25a** has refused to crystallize. – ^{1}H NMR ($CDCl_3$): δ = 2.6 (m, NCH_2); 3.65 (m, CH_2OH); 3.9 (m, $ArNCH_2$), 6.95–7.7 (m).

Thus **25a** was dissolved in 25 ml of pyridine and 10 ml of acetic anhydride, the solution kept 18 h at 24°C and heated 1 h at 70°C. After evaporation and repeated codistillation with toluene at 0.1 Torr, the residue was chromatographed on a column of neutral Al_2O_3 (70 g, A II) prepared with toluene/ethyl acetate (1:1) and eluted with the same mixture to give crystals which were recrystallized from cyclohexane to give pure diacetate **25b**, m.p. 107.5°C. – UV (methanol): λ_{max} = 247 (4.48), 368 nm (3.58). – ^{1}H NMR ($CDCl_3$): δ = 2.1 (S, $OCOCH_3$); 2.65 (S, $NCOCH_3$); 2.6 (m, NCH_2); 4.9 (m, $ArNCH_2$); 4.22 (m, CH_2OCOCH_3); 7.1–7.7 (m).

$C_{18}H_{23}N_5O_3$ (357.4) Calcd. C 60.49 H 6.49 N 19.6 Found C 58.65 H 6.49 N 18.76

N,N'-Dibenzyl-1,4-phthalazinediamine (**28**): 4.68 g (30 mmol) of 2,3-dihydro-1,4-phthalazinedione (**26**), 16.07 ml (150 mmol) of benzylamine (**27**), 22 ml (105 mmol) of HMDS, and 0.79 g (6.0 mmol) of $(NH_4)_2SO_4$ were heated with stirring to 155°C (oil bath temperature) whereupon NH_3 was evolved and **26** rapidly dissolved within 10 min. During the first 13 h at 155–165°C 11 ml of a mixture of trimethylsilanol (**6**) and hexamethyldisiloxane (**11**), b.p. 75°C, distilled over. Further heating for 11 h gave another 4 ml distillate. After cooling and brief treatment with ca. 25 ml of methanol, evaporation gave 19.7 g of a crude residue which was extracted with 150 ml of ether, filtered, and evaporated to yield 11.1 g of yelloish oil which crystallized from ethyl acetate to afford in two crops 8.85 g (87%) of pure **28**, m.p. 122°C. – UV (methanol): λ_{max} = 343 nm (3.81). – ^{1}H NMR ([D_6]DMSO): δ = 4.65 (s, CH_2), 7.3 (m, C_6H_5), 7.8 (m, 6-, 7-H), 8.3 (5-, 8-H). – MS: *m/e* = 340, 234 (M – $C_6H_5CH_2NH$); 219, 205, 129, 106 ($C_6H_5CH_2NH$), 91, 79.

$C_{22}H_{20}N_4$ (340.4) Calcd. C 77.62 H 5.92 N 16.46 Found C 76.04 H 5.94 N 15.94

N-(1,3-Benzodioxol-5-ylmethyl)-4-quinolinamine (**31**): 2.9 g (20 mmol) of anhydrous 4(1*H*)-quinolinone (**29**) and 6.05 g (40 mmol) of 1,3-benzodioxole-5-methanamine (**30**) were heated for 4 h at 160–165°C oil bath temperature with 6.3 ml (30 mmol) of HMDS and 0.38 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate, whereupon 3 ml of hexamethyldisiloxane (**11**), b.p. 98–99°C, had distilled over. After cooling to room temperature, the crude product was treated with 60 ml of methanol and the orange solution evaporated to give 8.95 g of an orange colored viscous oil which was chromatographed in ethyl acetate on a column of 100 g of silicagel. Elution with 1.8 l of ethyl acetate afforded 4.6 g (82%) of colorless crystals which were recrystallized from ca. 25 ml of ethyl acetate to afford in two crops 3.95 g (71%) of analytically pure material, m.p. 126–128°C. – UV (methanol): λ_{max} (log ε) = 214 (4.61), 234 (4.33), 327 nm (4.15). – ^{1}H NMR ($CDCl_3$): δ = 4.4 (d, *J* = 5 Hz, CH_2N), 5.9 (s, OCH_2O), 6.4 (d; 5 Hz; 3-H), 6.8 (m), 7.2–8.0 (m), 8.55 (d, *J* = 5 Hz; 2-H).

$C_{17}H_{14}N_2O_2$ (278.3) Calcd. C 73.36 H 5.07 N 10.07 Found C 73.07 H 5.57 N 10.10

4-[2-(4-Quinolinylamino)ethyl]-1,2-benzenediol Monohydrate (**33** · H_2O): 2.90 g (20 mmol) of anhydrous 4(1*H*)-quinolinone (**29**) and 7.59 g (40 mmol) of dopamine hydrochloride (**32**) were heated for 21 h at 145°C oil bath temperature with 4.67 ml (70 mmol) of HMDS. After cooling and treatment with hot methanol, the precipitated product was recrystallized from water and washed with a small amount of methanol to give 4.5 g (75%) of pure crystalline **33** · H_2O, m.p.

193 – 196 °C. – UV (methanol): λ_{max} (log ε) = 216 (4.53), 232 (4.27), 289 (3.67), 329 nm (2.51). – ^{1}H NMR ([D$_6$]DMSO): δ = 2.8 (t, *J* = 6 Hz, ArCH$_2$), 3.5 (t, *J* = 6 Hz, NCH$_2$), 6.5 (d, *J* = 5 Hz; 3'-H), 6.55 – 6.8 (m), 7.3 – 8.2 (m), 8.45 (d, *J* = 5 Hz, 2'-H).

$C_{17}H_{16}N_2O_2 \cdot H_2O$ (298.3) Calcd. C 68.44 H 6.08 N 9.39 Found C 68.23 H 6.03 N 8.90

2-(1-Piperazinyl)quinoline (**36**): 2.93 g (20 mmol) of 2(1*H*)-quinolinone (**34**), 6.98 g (80 mmol) of piperazine (**35**), 0.38 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate, and 6.27 ml (30 mmol) of HMDS were heated for 15 h at 160 °C oil bath temperature with simultaneous distillation of hexamethyldisiloxane (**11**). The crude brown reaction product was dissolved in methanol, some high melting (300 °C) yellow crystals were filtered off, and the filtrate was evaporated. Recrystallization from ethanol/water (1 : 2) afforded in two crops 3.44 g (74%) of pure **36** · H_2O, m. p. 81.3 °C (lit.[33] 82 – 83 °C). – UV (methanol): λ_{max} (log ε) = 248 (4.53), 345 nm (3.73). – ^{1}H NMR (CDCl$_3$): δ = 3.0 (t, *J* = 5 Hz, NH*CH*$_2$), 3.7 (H, *J* = 5 Hz; NCH$_2$), 6.9 (d, *J* = 8 Hz; 3-H), 7.1 – 7.7 (m), 7.9 (d, *J* = 8 Hz, 4-H).

$C_{13}H_{15}N_3 \cdot H_2O$ (231.3) Calcd. C 67.50 H 7.41 N 18.17 Found C 68.39 H 6.90 N 17.74

2-(Benzylamino)quinoline = *N-Benzyl-2-quinolinamine* (**37**): 2.902 g (20 mmol) of **34**, 6.43 g (60 mmol) of benzylamine, 0.39 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate, and 6.3 ml (30 mmol) of HMDS were heated for 2 h at 140 °C and for 6 h at 160 °C with distillation of hexamethyldisiloxane (**11**). The crude residue was dissolved in 50 ml of methylene chloride and 5 ml of 2 N NaOH and the aqueous phase extracted with methylene chloride. The combined extracts were dried (Na$_2$SO$_4$) and evaporated to give 4.75 g of crude crystalline residue which was extracted with 5 × 100 ml of hexane and these extracts were evaporated to afford colorless crystals. Recrystallization from benzene furnished in two crops 4.25 g (91%) of pure **37**, m. p. 98 – 99 °C (lit.[34] 99 – 100 °C).

$C_{16}H_{14}N_2$ (234.3) Calcd. C 82.02 H 6.02 N 11.96 Found C 81.64 H 6.72 N 12.00

N,N',N''-Tribenzyl-1,3,5-triazinetriamine (**39**): 6.45 g (50 mmol) of cyanuric acid (**38**) was heated with 250 ml of HMDS and 1 ml of TCS until **38** had dissolved. After evaporating the large excess of HMDS, 32.7 ml (300 mmol) of benzylamine (**27**) and 1.353 g (5.0 mmol) of mercuric chloride were added and the suspension heated for 96 h at 185 °C, whereupon the reaction was complete. After treatment with methanol and filtration, the methanol was evaporated and the residue heated to 80 °C/0.1 Torr to remove the excess benzylamine. The residual light yellow viscous oil (19.2 g) crystallized from 350 and 150 ml ethanol to afford in two crops 14.51 g (73%) of **39**, m. p. 103 – 105 °C. – UV (methanol): λ_{max} (log ε) = 261 (3.01), 268 nm (2.8). – ^{1}H NMR (CDCl$_3$): δ = 4.5 (d, CH$_2$), 5.65 (H, NH), 7.2 (m, aromat. H).

$C_{24}H_{24}N_6$ (396.5) Calcd. C 72.70 H 6.10 N 21.20 Found C 72.87 H 6.10 N 21.13

4,6-Dipyrrolidino-1,3,5-triazin-2(1H)-one (**40**) *and 2,4,6-Tripyrrolidino-1,3,5-triazine* (**41**): 12.9 g (0.10 mol) of cyanuric acid (**38**) was heated in 150 ml of HMDS and 30 ml TCS until (**38**) had dissolved. Then most of the excess of HMDS and TCS was distilled off. After adding 125 ml (1.2 mol) of pyrrolidine and 24.4 g (0.09 mol) of mercuric chloride, the reaction mixture was refluxed for 7 d at 120 °C oil bath temperature and evaporated. The residue was extracted with ethyl acetate and the extract evaporated. The residue crystallized from ethanol to afford 3.0 g (10%) of pure crystalline **41**, m. p. 184 – 186 °C (lit.[35] 185 – 188 °C), identical with an authentic sample prepared by reacting cyanuric chloride at 10 °C with an excess of pyrrolidine, whereupon the temperature rises to 60 °C, and subsequent addition of water and recrystallization of the precipitate from ethanol.

The mother liquor of **41** and the ethyl acetate insoluble part were combined and recrystallized from ethanol to afford 12.3 g (52%) of pure **40**, m. p. 230 °C. – IR (KBr): 1655 cm^{-1}. – UV

(methanol): λ_{max} (log ε) = 230 nm (4.77). – ^{1}H NMR ($CDCl_3$): δ = 1.9 (s, CH_2), 3.6 (s, NCH_2). – MS: *m/e* = 235 (M^+), 207 (M – CO), 206, 179 (M – C_4H_8), 166 (M – C_4H_7N), 138 (207 – C_4H_7N), 136 (179 – HCNO), 123, 97, 95, 70.

$C_{11}H_{17}N_5O$ (235.3) Calcd. C 55.15 H 7.28 N 29.77 Found C 55.77 H 7.30 N 29.84

N,N'-Bis[2-(3,4-dimethoxyphenyl)ethyl]-1,2,4-triazine-3,5-diamine (**44**): 2.583 g (20 mmol) 5-hydroxy-3-mercapto-1,2,4-triazine (**42**) were silylated by heating with 75 ml of HMDS and 0.5 ml of TCS until **42** had dissolved. After evaporating most of the excess HMDS, 10 ml (60 mmol) of homoveratrylamine (**43**) was added, the mixture cooled to +2°C and 0.26 ml (2.0 mmol) of $SnCl_4$ added. After heating for 48 h at 145°C oil bath temperature, the cooled residue was taken up in 200 ml of methanol, filtered and the dark filtrate evaporated to give 20.4 g of a dark brown viscous residue which was chromatographed in ethyl acetate on a column of 350 g of neutral alumina (A III). Elution with 2 l of ethyl acetate gave yelloish amines, whereas elution with ethyl acetate/methanol (99:1 and 98:2) (5 l) afforded ca. 5.55 g (63%) of homogenous product which crystallized from toluene to give analytically pure **44**, m.p. 136–137°C. – ^{1}H NMR ($CDCl_3$): δ = 2.85 + 3.65 (t, CH_2CH_2), 3.8 + 3.82 (s, OCH_3), 6.75 (m, aromat. H), 7.85 (s, triazine-H).

$C_{23}H_{29}N_5O_4$ (439.5) Calcd. C 62.85 H 6.65 N 14.65 Found C 62.87 H 6.75 N 15.72

N,N'-Dibenzyl-2,4-pyrimidinediamine (**46**): 3.36 g (30 mmol) of uracil (**45**), 9.82 ml (90 mmol) of benzylamine, 15.72 ml (75 mmol) of HMDS, and 0.571 g (3.0 mmol) of *p*-toluenesulfonic acid hydrate were heated for 24 h at 145°C oil bath temperature with distillation of hexamethyldisiloxane (**11**). After keeping over night with 100 ml of methanol and evaporation, the brown oily residue (13.2 g) was dissolved in 100 ml of methylene chloride/ether (1:1) and filtered over a column of 250 g of neutral alumina (A II). After eluting some benzylamine, the next fractions gave on treatment with cyclohexane in several crops 6.10 g of pure **46**, m.p. 68–70°C. Rechromatography of the combined mother liquors in methanol on silicagel (40 g) afforded another crop of 1.18 g of crystalline **46**. Combined yield 7.28 g (84%), m.p. 68–70°C. – UV (methanol): λ_{max} (log ε) = 217 (4.5), 289 nm (3.93). – ^{1}H NMR ($CDCl_3$): δ = 4.5 (dd, *J* = 7 Hz, CH_2N), 5.7 (d, *J* = 6 Hz, 5-H), 7.25 (m, C_6H_5), 7.8 (d, *J* = 6 Hz; 6-H).

$C_{18}H_{18}N_4$ (302.4) Calcd. C 74.45 H 6.25 N 19.30 Found C 74.40 H 6.53 N 19.39

N-(2-Pyrrolidinoethyl)-2-pyrimidinamine Dihydrochloride (**49** · 2 HCl): 2.65 g (20 mmol) of 2(1*H*)-pyrimidinone hydrochloride (**47** · HCl), 8.4 ml (40 mmol) of HMDS, 4.57 g (40 mmol) of 2-pyrrolidinoethylamine (**48**) and 0.38 g (2.0 mmol) of *p*-toluenesulfonic acid hydrate were heated for 8 h at 160°C oil bath temperature, whereupon colorless crystals sublimed into the upper part of the round bottom flask. After cooling, the dark brown reaction mixture was taken up in methanol which was evaporated. Finally, extraction with 3 × 150 ml of boiling toluene afforded 3.2 g (83%) of crude yellow-brownish oil (**49**) which was obtained pure on distillation at 130–150°C/0.2 Torr in a Kugelrohr apparatus. Treatment of distilled **49** with excess HCl gas in absol. ether afforded the crystalline dihydrochloride of **49** which was recrystallized from isopropyl alcohol, m.p. 159–162°C. – ^{1}H NMR (D_2O): δ = 2.1 (m, CH_2CH_2), 3.3–3.7 (m, NCH_2; $NHCH_2$), 6.8 (t, *J* = 4 Hz, 5-H), 8.3 (d, *J* = 4 Hz, 4-, 8-H).

$C_{10}H_{18}Cl_2N_4$ (265.2) Calcd. C 45.29 H 6.84 Cl 26.74 N 21.13
Found C 45.36 H 6.94 Cl 26.72 N 21.05

3,6-Bis(benzylamino)pyridazine = *N,N'-Dibenzyl-3,6-pyridazinediamine* (**51**): 2.24 g (20 mmol) of 3,6-dihydroxypyridazine (**50**), 6.44 g (22 mmol) of OMCTS (**13**), 4.8 ml (44 mmol) of benzylamine (**27**), and 0.80 g (4.0 mmol) of *p*-toluenesulfonic acid hydrate were heated up during 45 min to 200°C oil bath temperature and kept for 5 h at 200°C. After cooling, the mixture was stirred for 30 min in 100 ml of methanol, evaporated and the silicon oil removed by extraction with

3 × 20 ml of pentane. The residue was dissolved in methylene chloride, the solution washed with 10 ml of ice-cold 2 N NaOH, dried (Na_2SO_4), and evaporated. The residue was extracted repeatedly with boiling methylene chloride/cyclohexane, the extracts were evaporated and the residue recrystallized from cyclohexane/ethyl acetate to afford in several crops 3.6 g (62%) of pure **51**, m. p. 118–120°C (lit.[37] 114°C). – ^{1}H NMR ($CDCl_3$): δ = 4.5 (s; CH_2), 6.5 (s, CH), 7.25 (m, C_6H_5).

$C_{18}H_{18}N_4$ (290.4) Calcd. C 74.45 H 6.25 N 19.30 Found C 74.62 H 6.26 N 19.45

4-Pyrrolidinopyridine (**53**)

a) 20.7 ml (250 mmol) of pyrrolidine, 31.5 ml (150 mmol) of HMDS, 1.32 g (10 mmol) of $(NH_4)_2SO_4$, and 10 ml of absol. pyridine were refluxed for 6 h at 150–160°C oil bath temperature with exclusion of humidity, whereupon the formation of 1-(trimethylsilyl)pyrrolidine, b. p. 138–140°C, with evolution of NH_3 was practically complete. 9.51 g (100 mmol) of redistilled 4(1*H*)-pyridinone (**52**) and 10 ml of absol. pyridine were added and the reaction mixture heated for 6 h to 150–160°C with simultaneous distillation over a 20 cm Vigreux column giving ca. 50 ml of distillate, b. p. 70–100°C. The remaining reaction mixture was refluxed for further 12 h and then a mixture of 8.27 ml (100 mmol) of pyrrolidine and 10.05 ml (50 mmol) of HMDS was added which had previously been refluxed separately for 6 h as described above. After heating for further 40 h, the reaction mixture was cooled, ether added and extracted with ice-cold 2 N NaOH. Reextraction with ether, drying (Na_2SO_4), and evaporation gave 13.5 g of crude **53** which was distilled in a Kugelrohr apparatus at 130°C/2 Torr to afford 12 g (81%) of 4-pyrrolidinopyridine, which was crystallized from pentane, m. p. 56–58°C, identical with an authentic sample.

b) Heating of 16.7 g (100 mmol) of 4-(trimethylsilyloxy)pyridine with 21.5 g (150 ml) of 1-(trimethylsilyl)pyrrolidine, 4.2 ml (50 mmol) of pyrrolidine, 1.32 g (10 mmol) of $(NH_4)_2SO_4$, and 10 ml of absol. pyridine for 15 h at 150°C in a 150 ml autoclave and workup as described gave 13.5 g (92%) crude crystalline **53**. – ^{1}H NMR ($CDCl_3$): δ = 2 (m, CH_2CH_2), 3.25 (m; NCH_2), 6.33 (d, *J* = 6.5 Hz, 3-, 5-H), 8.17 (d, *J* = 6.5 Hz, 2-, 6-H).

$C_9H_{12}N_2$ (148.2) Calcd. C 72.94 H 8.16 N 18.90 Found C 72.70 H 8.24 N 18.68

Preparation of 1-(Trimethylsilyl)pyrrolidine: 41.35 ml (0.50 mol) of pyrrolidine, 52.4 ml (0.25 mol) of HMDS, and 0.5 ml of TCS were heated for 6 h at 150°C oil bath temperature with evolution of ammonia. Distillation gave a main fraction of 44.6 g (62.2%) of pure product, b. p. 139–140°C, which was slightly turbid due to traces of NH_4Cl.

4-(Benzylamino)pyridine = N-Benzyl-4-pyridinamine (**54**): 1.9 g (20 mmol) of **52**, 8.75 ml (80 mmol) of benzylamine **27**, 4.39 g (15 mmol) of OMCTS (**13**), and 0.38 g (2 mmol) of *p*-toluenesulfonic acid hydrate were heated for 15 h with stirring at 200°C oil bath temperature. After cooling to 24°C and addition of 120 ml of methanol, the dark solution was refluxed for 4 h, evaporated and the residue taken up in 100 ml of CH_2Cl_2. Extraction with 3 × 40 ml portions of 2 N H_2SO_4 followed by basification with ice-cold NaOH to pH = 9–10 gave an oily emulsion, which was extracted with 4 × 75 ml of ether. After drying (Na_2SO_4), the ether phase afforded on char-coal treatment and evaporation 3.9 g of crude, yellow oil, which started to crystallize on heating with 200 ml of hexane. After filtration and concentration of the mother liquors we obtained 3 crops of combined 2.81 g (76.4%) of pure **54**, m. p. 108–110°C (lit.[45] 108 to 109.5°C).

$C_{12}H_{12}N_2$ (184.2) Calcd. C 78.23 H 6.57 N 15.21 Found C 78.43 H 6.86 N 15.20

2-(2-Phenylethylamino)pyridine = N-(2-Phenylethyl)-2-pyridinamine (**56**): 1.9 g (20 mmol) of 2(1*H*)-pyridinone (**12**), 4.39 g (15 mmol) of OMCTS (**13**), 10.05 ml (80 mmol) of 2-phenylethylamine (**56**), and 0.5 ml (3 mmol) of perfluorobutanesulfonic acid were heated for 25 h to 200°C

oil bath temperature. After cooling to room temperature, 150 ml of methylene chloride was added and the solution washed subsequently with 50 ml of 2 N NaOH and 100 ml of sat. NaCl solution. After drying (Na_2SO_4) and evaporation 14.1 g of brown oil was obtained which was filtered in toluene over a column of 300 g of silicagel to give 2.8 g (71%) of pure **56** which was homogenous on tlc. – UV (methanol): λ_{max} (log ε) = 239 (4.05), 261 (2.84), 312 nm (3.69). – ^1H NMR ($CDCl_3$): δ = 2.95 (t, *J* = 7 Hz, $PhCH_2$), 3.55 (t, *J* = 7 Hz, NCH_2), 6.35 (d, *J* = 8 Hz, 3-H), 6.55 (m, 5-H), 7.2–7.5 (m, 4-H in Ph), 8.1 (d, *J* = 5 Hz, 6-H).

$C_{13}H_{14}N_2$ (198.3) Calcd. C 78.75 H 7.12 N 14.13 Found C 79.03 H 6.94 N 14.08

2-(Benzylamino)pyridine = N-Benzyl-2-pyridinamine (**57**)

a) 1.9 g (20 mmol) of **12**, 6.3 ml (30 mmol) of HMDS, 8.75 ml (80 mmol) of benzylamine (**27**), and 0.5 ml (3 mmol) of perfluorobutanesulfonic acid were heated for 46 h at 200 °C oil bath temperature (reaction temperature 186 °C). The reaction mixture was taken up in 100 ml of CH_2Cl_2, washed with 25 ml of ice-cold 2 N NaOH, and dried (Na_2SO_4) to give 9.7 g partially crystalline yellow residue which was chromatographed on 150 g of SiO_2 in toluene. The first fractions (600 ml) eluted 2.1 g of tribenzylamine (**59**), m. p. 90–92 °C. Elution with toluene (450 ml), toluene/ethyl acetate (95:5 and 90:10) (1.2 l) furnished a mixture of **57** and dibenzylamine (**58**) from which 1.46 g (40%) of pure **57**, m. p. 94–95 °C (lit.[39] 94 °C) were obtained in two crops by crystallization from hexane at –25 °C and identified with an authentic sample. The combined mother liquors were rechromatographed to give 2.6 g of **58**, identified by comparison with an authentic sample.

b) 1.9 g (20 mmol) of **12**, 4.39 g (15 mmol) of OMCTS (**13**), 8.75 ml (80 mmol) of benzylamine, and 0.5 ml (3 mmol) of perfluorobutanesulfonic acid were heated 48 h at 200 °C oil bath temperature (reaction temperature 184–186 °C), worked up and chromatographed as described under a) to give 2.48 g of pure **59**, m. p. 92–94 °C, and 1.73 g (47%) of pure **57**, m. p. 94–95 °C.

The polar eluates of experiments a) and b) contained varying amounts of 2-pyridinamine (**60**), identified by tlc comparison (silica plates, acetone, R_F = 0.45) with an authentic sample.

c) 2.82 g (30 mmol) of **60**, 6.56 ml (60 mmol) of benzylamine, and 0.5 ml (3 mmol) of perfluorobutanesulfonic acid were stirred for 42 h at 200 °C and worked up with ice-cold CH_2Cl_2/5 N NaOH to give 8.04 g crude crystalline product. Chromatography in toluene/ethyl acetate on silica gel as described above gave 0.79 g of **59**, m. p. 90–92 °C, and 2.89 g (54%) of **57**, m. p. 94–95 °C, as well as 0.93 g of **58**.

Tribenzylamine (**59**) *from Benzylamine* (**27**)

a) 3.28 ml (30 mmol) of benzylamine, 2.923 g (10 mmol) of OMCTS (**13**), and 0.5 ml (3 mmol) of perfluorobutanesulfonic acid were heated for 42 h at 100 °C oil bath temperature. After cooling, the residue was refluxed for 30 min with 50 ml of methanol and after evaporation was shaken with 150 ml of CH_2Cl_2 and 20 ml of ice-cold 2 N NaOH. The crystalline precipitate was filtered and worked up with water and CH_2Cl_2. The combined CH_2Cl_2 phase was dried (Na_2SO_4) and evaporated to give 4.4 g of brown, partially crystalline residue, which was chromatographed in toluene on 90 g of SiO_2 to afford 1.25 g (43.5%) of **59**, m. p. 90–92 °C, and 0.69 g (23%) of **58**.

b) Heating of 3.28 ml (30 mmol) of benzylamine with 0.5 ml (3 mmol) of $C_4F_9SO_3H$ (without OMCTS (**13**)) for 42 h/200 °C gave analogously 1.51 g (52.5%) of **59** and 0.90 g (31%) of **58**.

c) Heating of 3.28 ml (30 mmol) of benzylamine with 0.571 g (3 mmol) of *p*-toluenesulfonic acid hydrate for 48 h at 210–220 °C afforded on workup a residue, which crystallized on standing at 24 °C, thus consisting nearly completely of **59**.

2-Pyrrolidino-3H-indole (**62**): 6.66 g (50 mmol) of 2-indolinone (**61**), 12.52 ml (150 mmol) of pyrrolidine, and 15.5 ml (75 mmol) of HMDS were refluxed for 3 h with 0.475 g (2.5 mmol) of *p*-toluenesulfonic acid hydrate under argon (oil bath temperature 125–130°C). After 1 h heating, **62** started to crystallize. After cooling to 24°C, the crystals were filtered and washed with 40–50 ml of acetone to give 7.07 g (76%) of pure sand-colored crystals, m. p. 140–142°C (lit.[41] 142°C), which can be readily recrystallized from boiling acetone under argon (tlc system: toluene/ethyl acetate 1:1, alumina plates, R_F = 0.4). – ^{1}H NMR ($CDCl_3$): δ = 1.8–2.2 (m, CH_2CH_2), 3.3–3.7 (m, NCH_2; 3H), 6.8–7.3 (m).

$C_{12}H_{14}N_2$ (186.3) Calcd. C 77.38 H 7.58 N 15.04 Found C 77.51 H 7.77 N 14.75

N,N'-Dibenzylurea (**64**) *from Benzoxazolone:* 6.75 g (50 mmol) of benzoxazolone, 100 ml of HMDS, and 0.5 ml of TCS were refluxed for 1 h at 130–140°C oil bath temperature. After evaporating the excess HMDS, 10.9 ml (100 mmol) of benzylamine and 1.35 g (5.0 mmol) of $HgCl_2$ were added and the mixture heated for 24 h at 145°C oil bath temperature. The mixture was cooled, treated with methanol for 3 h and the metallic mercury filtered. The filtrate crystallized on concentration to give in two crops 7.2 g (60%) of *N,N'*-dibenzylurea, m. p. 170°C (lit.[42] 169°C), which was identified by NMR and analysis.

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