Reactivity of Some 3-Substituted Derivatives of 2,6-Dihalogenopyridines Towards Potassium Amide in Liquid Ammonia [a]

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Reactions of 2,6-dichloro-3-phenyl-, 2,6-dibromo-3-phenyl-, 2,6-dichloro-3-dimethylamino- and 2,6-dibromo-3-dimethylaminopyridine with potassium amide in liquid ammonia were investigated. Whereas 2,6-dichloro-3-phenylpyridine yields 4-amino-2-benzylpyrimidine, from 2,6-dibromo-3-phenylpyridine as a product of a novel ring fission 2-amino-1-cyano-1-phenyl-but-1-en-3-yne was isolated, together with 4-amino-6-bromo-3-phenylpyridine and 2,6-diamino-3-phenylpyridine. It was shown that neither 2-amino-6-bromo-3-phenyl- nor 6-amino-2-bromo-3-phenylpyridine are intermediates in the formation of the 2,6-diamino derivative, as these bromo compounds are transformed in the basic medium into 1,3-dicyano-1-phenylpropene. From both 2,6-dichloro-3-dimethylamino- and 2,6-dibromo-3-dimethylaminopyridine mixtures are obtained from which only 2-amino-1-cyano-1-dimethylamino-but-1-en-3-yne and 4-amino-6-halogeno-3-dimethylaminopyridine were isolated.

Mechanisms for the reactions studied are proposed, *i.e.* a S_N(ANRORC) mechanism for the aminodebromination of 2,6-dibromo-3-phenylpyridine into the corresponding 2,6-diamino compound.

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An interesting and remarkable feature of the chemical reactivity of 2,6-dichloro(bromo)pyridines is their transformation into 4-amino-2-methylpyrimidine when subjected to treatment with potassium amide in liquid ammonia [2, 3]. This ring transformation reaction has been proposed to start by the attack of the strong nucleophilic amide ion on the C-4 position, leading to 4-amino-2,6-dihalogenodihydropyridinide, a subsequent opening of the dihydropyridinide ring by fission of the C_3-C_4 bond and recyclisation of the azahexatriene system obtained.

In this paper we want to present the results of a study directed to investigate the influence of some substituents at C-3 in 2,6-dihalogenopyridines on the occurrence of the ring transformation and especially their influence on the formation of σ-adducts and open-chain compounds. For that purpose we choose the 3-phenyl- and 3-dimethylamino substituents having divergent electronic character and different steric size [4].

Results and Discussion.

A. Reaction of 2,6-Dihalogeno-3-phenylpyridines **1**, **2** with Potassium Amide in Liquid Ammonia.

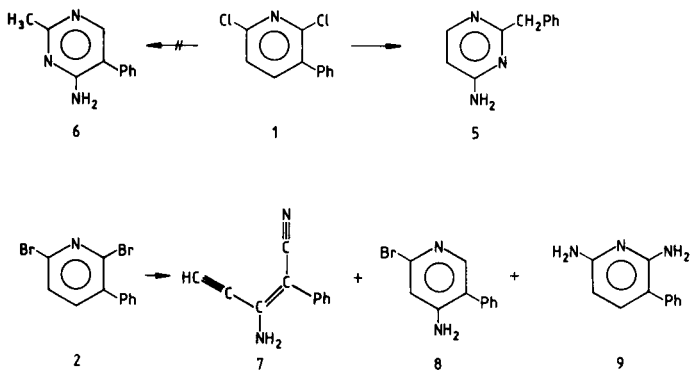
Reaction of 1 equivalent of 2,6-dichloro-3-phenylpyridine (**1**) with 8 equivalents of potassium amide in liquid ammonia at −33° gave besides tar, 4-amino-2-benzylpyrimidine (**5**, 15%) and some benzylcyanide (5%). Analysis (glc) of the reaction mixture obtained did not show a trace of the isomeric product 4-amino-2-methyl-5-phenylpyrimidine (**6**) (see Table 1).

Table 1

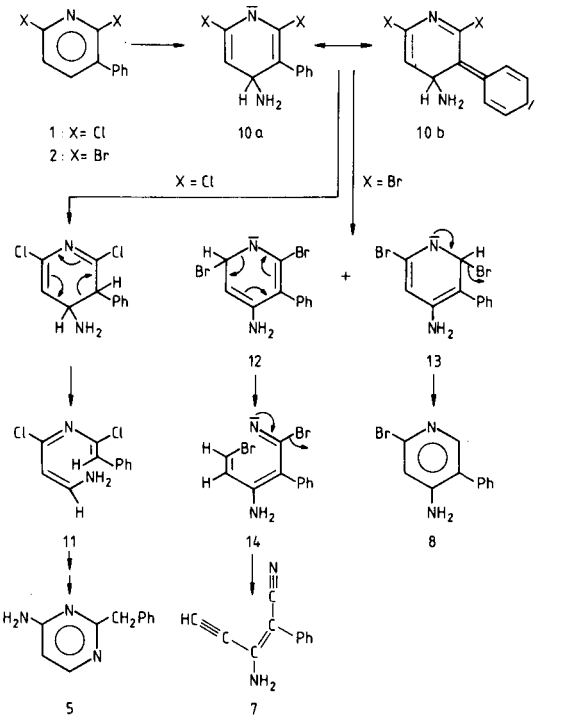
Aminations of the Substrates Carried Out at −33°

Substrate	mmole	Dosed as	ml NH_3	eq KNH_2	Reaction time (minutes)	Isolated Compounds (yield %)
1	2.5	as such	50	20.0	150	**5** (15) $PHCH_2CN$ (5)
2	2.5	as such	50	20.0	2	**7** (10) **8** (5-10) **9** (5-10) $PhCH_2CN$ (5)
3	25	in ether, 15 ml	350	160	180	**21** (5-10) **22** (2)
4	25	in ether, 15 ml	350	160	2	**21** (5) **23** (2)
9	2.5	as such	50	20	120	**9** (>90)
15	2.5	in DME, 5 ml	50	6.9	5	**17** (~70)
16	1.4	in DME, 5 ml	50	3.8	5	**17** (~65)
24	2.5	in DME, 5 ml	50	10.8	30	**26** (>90)

Scheme 1



Scheme 2



A quite different product pattern was found when 2,6-dibromo-3-phenylpyridine (**2**) was reacted with potassium amide in liquid ammonia. As the main product was isolated 2-amino-1-cyano-1-phenylbut-1-en-3-yne (**7**, 10%) and in addition the *tele*-substitution product 4-amino-2-bromo-5-phenylpyridine (**8**, 5-10%), and the *ipso*-substitution product 2,6-diamino-3-phenylpyridine (**9**, 5-10%) together with some benzylcyanide (5%) and tar.

It is assumed that the formation of **5**, **7** and **8** involved as the common intermediate adduct **10**. This σ-adduct is resonance-stabilized by the presence of the phenyl group at C-3. By ^{1}H nmr spectroscopy, however neither the intermediacy of these adducts nor of the C-4 adducts supposed to be formed in the amination of the 2,6-dihalogenopyridines could be established indicating that the rate of ring opening of these adducts is faster than their formation.

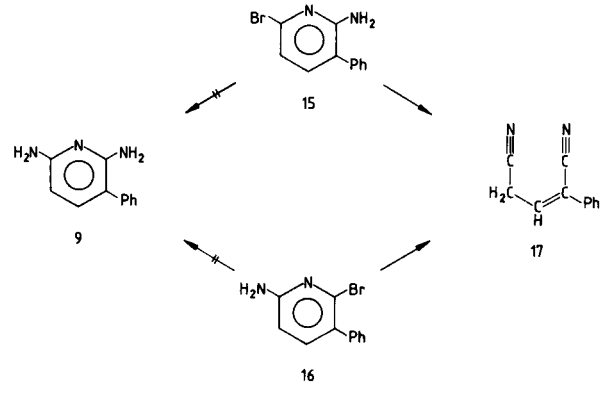
In the amination of **1** *via* **10** (X = Cl), the protonation step required before ring opening occurs on the benzylic anionic C-3 atom. Ring opening between C-3 and C-4 gives the aminodichloroazatriene (**11**), in which one of chloro atom is replaced by the amino group. Recyclisation gives **5**. It has been proposed previously [2] that the aminodechlorination in related systems should occur before recyclisation of **11**. There is however strong evidence, that open-chain compounds like **11** do not undergo ring closure in the presence of potassium amide; only after neutralization of the amide ion by an ammonium salt, the usual reagent added to the reaction mixture before working-up, cyclisation takes place [5].

Benzylcyanide may be formed as a cleavage product from an intermediate occurring in a side-reaction.

The formation of both **7** and **8** from **2** can be rationalized by assuming that in **10** (X = Br) a 1,3-hydrogen shift takes place (which probably occurs in two steps, since an antarafacial concerted 1,3-hydrogen shift leading to the dihydropyridinides **12** and **13** can be excluded). A subsequent electrocyclic opening of the ring in **12** leads to intermediate **14** which by elimination of hydrogen bromide and bromide expulsion gives **7**. Bromide expulsion from **13**, as indicated, gives product **8**. It is remarkable that, in contrast to **1**, compound **2** is not transformed into the pyrimidine derivative **5**. Apparently adduct **10** (X = Br) prefers to follow the routes *via* **13** and **14**. From these intermediates the bromide ion adjacent to the phenyl group probably departs much easier than chloride from the chloro analogues of **13** and **14**.

It was established that **9** cannot be formed from 2-amino-6-bromo- (**15**) and/or its isomer 6-amino-2-bromo-3-phenylpyridine (**16**), since treatment of both compounds with potassium amide in liquid ammonia yields as nearly sole product 1,3-dicyano-1-phenylprop-1-ene (**17**).

Scheme 3



The formation of **17** is not surprising, as it has already been found that treatment of 2-amino-6-bromopyridine with potassium amide in liquid ammonia gives a similar reaction product, *i.e.* 1,3-dicyanopropene [3]. Based on the

Table 2

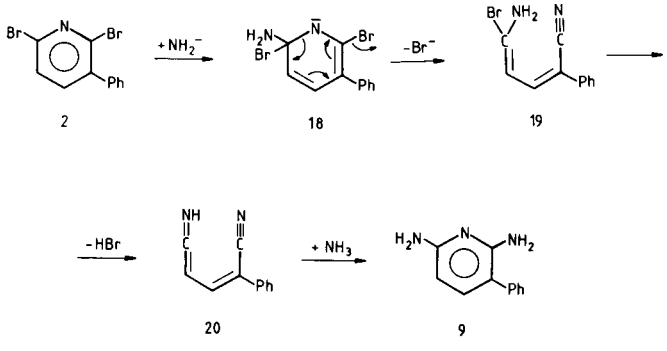
GLC Relative Retention Times of Reaction Products and Reference Compounds [1]

Amination of	Column	Compound [2]	R_T
1, 2, 15, 16	K 250[F]	benzyl cyanide	0.05
		7	0.17
		1	0.48
		6	0.48
		5	0.85
		9	1.00
		2	1.07
		15	1.12
		16	1.59
		8	2.24
1, 2, 15,	K 269[B]	**1**	0.19
		6	0.36
		2	0.44
		15	0.82
		9	1.00
3, 4	K 250[F]	**21**	0.22
		3	0.48
		31	0.78
		22	0.98
		4	1.00
		23	1.50

[1] Carrier gas: nitrogen. Column K 250[F]: glass, 200 cm × 6 min o.d., chromosorb WHP 100/120 + 3% SP-2250. Column 269[B]: glass, 200 cm × 2 mm o.d., chromosorb WHP 100/120 + 8.9% Carbowax High Polymers. [2] Compound **17** decomposed on both columns.

results mentioned above we suggest that the formation of **9** takes place by a sequence of reactions involving addition ring-opening and ring-closure [S_N(ANRORC) mechanism]. Several pathways can be assumed corresponding with the data available. Tentatively we propose the route given below. The first step is the addition of the amide ion to C-6 yielding adduct **18** which is stabilized by the phenyl group. Expulsion of bromide from C-2 and fission of the N(1)-C(6) bond leads to **19**. This intermediate is converted into the ketenimine **20** which after addition of ammonia, gives cyclisation into **9**. Recent ^{15}N labelling studies on the formation of 2-amino-3,5-dinitropyridine from 2-chloro-3,5-dinitropyridine by potassium amide/ammonia (liquid) [6] show that also in these conversions a S_N(ANRORC) process takes place.

Scheme 4

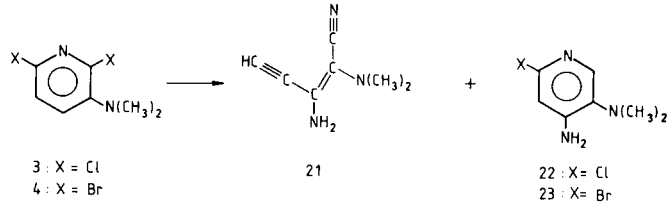


B. Reaction of 2,6-Dichloro-3-dimethylaminopyridine (**3**) and 2,6-Dibromo-3-dimethylaminopyridine (**4**) with Potassium Amide in Liquid Ammonia.

After we had found that the reactivity of the 3-phenyl derivatives of the 2,6-halogenopyridines and that of the parent substances towards potassium amide in liquid ammonia differ considerably, we were interested how the course of the aminations would be changed, when an electron-donating substituent such as the dimethylamino group instead of electron-accepting phenyl group is present at C-3.

The following results were obtained. Products analogous to the open-chain compound **7** and the *tele*-product **8** *i.e.* 2-amino-1-cyano-1-dimethylaminobut-1-en-3-yne (**21**) and respectively 4-amino-6-chloro-3-dimethylaminopyridine (**22**) and 4-amino-6-bromo-3-dimethylaminopyridine (**23**) were formed, not only from the bromo derivative **4**, but also from chloro compound **3**. The yields of all products were low (<10%). Neither **3** nor **4** yielded a pyrimidine derivative (see Table 1). In none of the reaction mixtures the presence of 2,6-diamino-3-dimethylaminopyridine was detected.

Scheme 5



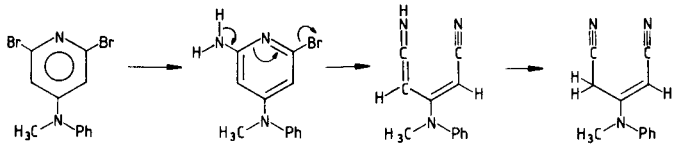
The formation of **21, 22** and **23** can occur similarly as that of the products **7** an **8** obtained in the amination of **2**, suggesting the initial formation of a C-4 adduct. More than the phenyl group the dimethylamino group favours the expulsion of halide from the analogues of **13** and **14** (dimethylamino group instead of phenyl group). This may explain why **3** instead of being transformed into a pyrimidine derivative, reacts like **4**. In the light of the mechanism presented from the formation of **9** it can be expected that the formation of 2,6-diamino-3-dimethylaminopyridine does not take place, since the required initial addition of the amide ion to C-6 in **3** and **4**, is now prevented by the strong electron-releasing character of the dimethylamino group.

C. Reaction of 2,6-Dibromo-4-(*N*-methylanilino)pyridine (**24**) with Potassium Amide in Liquid Ammonia.

As explained in Sections A and B the formation of the ring transformation product **5**, the open-chain products **7** and **21**, the *tele*-amination products **8, 22** and **23** and the 2,6-diamino compound **9** from compounds **1-4**, involves a nearly exclusive fast kinetically controlled addition of the

amide ion at C-4. To substantiate the importance of the C-4 addition in the reactions of 2,6-dihalogeno compounds **1-4** we investigated the reactivity of 2,6-dibromo-4-(*N*-methylanilino)pyridine (**24**) in which the addition at C-4 is hampered by the presence of the substituent at the C-4 position and no substituents are present at position 3 influencing the reactivity at C-2 and C-6. When **24** was treated for 30 minutes with potassium amide in liquid ammonia nearly exclusively 1,3-dicyano-2-(*N*-methylanilino)prop-1-ene (**26**) was formed in a yield of about 90%. A similar ring opening has occurred as observed in the amination of **15** and **16**. The first step is amino-debromination at C-2 yielding 2-amino-6-bromo-4-(*N*-methylanilino)pyridine (**25**), which is converted into **26** by a mechanism analogous to the one, described for the transformation of 2-amino-6-bromopyridine into 1,3-dicyanopropene [3].

Scheme 6



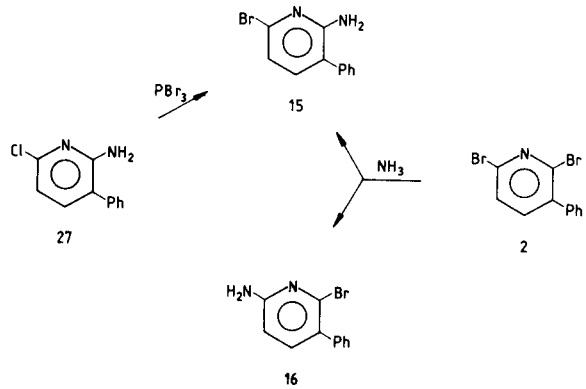
24 25 26

Synthesis of Starting Materials and Reference Compounds.

In general, the synthesis of known starting materials and reference compounds was carried out by literature procedures, and the structure of the compounds obtained was confirmed by physical means, mainly ^{1}H nmr and ir spectroscopy.

The preparation of some compounds deserve some comments. 2-Amino-6-bromo-3-phenylpyridine (**15**) was prepared by a chloro-bromo exchange in 2-amino-6-chloro-3-phenylpyridine (**27**), using phosphorus tribromide, or by an amino-debromination reaction in 2,6-dibromo-3-phenylpyridine (**2**) with aqueous ammonia. In the last-mentioned reaction the isomeric 6-amino-2-bromo-3-phenylpyridine (**16**) was also obtained.

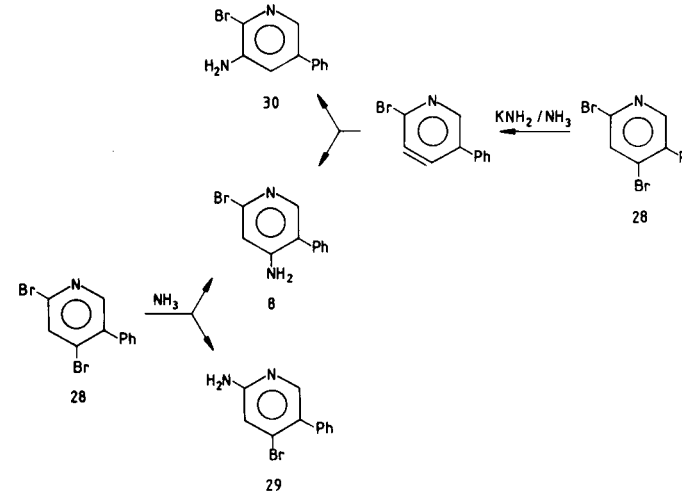
Scheme 7



27 15 2 16

4-Amino-2-bromo-5-phenylpyridine (**8**) was prepared by reacting 2,4-dibromo-5-phenylpyridine (**28**) with aqueous ammonia. However in this reaction the isomeric 2-amino-4-bromo-5-phenylpyridine (**29**) was also formed. In order to distinguish **8** from **29** we prepared **8** also in a different way, namely by reacting **28** with potassium amide in liquid ammonia. From results of related work on 2,4-dibromopyridine [7] it could be expected that **28** would react *via* a 3,4-didehydropyridine intermediate into a mixture of **8** and 3-amino-2-bromo-5-phenylpyridine (**30**). This has been found indeed. The amino compound, which has been found in both reactions must be assigned 4-amino-2-bromo-5-phenylpyridine (**8**).

Scheme 8



30 28 8 28 29

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H nmr spectra were recorded on a Varian EM 390 spectrometer or a Hitachi Perkin Elmer R-24B spectrometer. The ir spectra were recorded on a Hitachi EPI-G3 or on a Perkin-Elmer 237. Mass spectra were recorded on an AEI MS 902 instrument or on a VG micromass 7070F spectrometer, connected with a GLC OV-17 column. Glc data are found in Table 2. Column chromatography was performed with Kieselgel 60 (Merck).

Aminations.

The procedure applied for the amination has been described previously [2,3]. Due to the solubility problems it appeared necessary to dissolve some compounds in ether or DME before adding to the potassium amide/liquid ammonia solutions (see for more detailed information, Table 1). The structures of the compounds obtained were established by nmr spectrometry and when possible confirmed by comparison with independently prepared reference compounds.

Preparation of Starting Material.

2,6-Dichloro-3-phenylpyridine (**1**).

This compound was prepared according to a prescription published in the literature [8], mp 91-92° (ethanol); nmr (deuteriochloroform): δ 7.62 (d, J = 7.8 Hz, 1H, H-4), 7.43 (s, 5H, Ph), 7.29 (d, J = 7.8 Hz, 1H, H-5).

2,6-Dibromo-3-phenylpyridine (**2**).

A mixture of **1** (16.4 g, 73.2 mmoles) and phosphorus oxybromide (200

g, 697 mmoles) was shaken in sealed tubes during 24 hours at 190°. The content of the tubes was poured onto ice. After basification with potassium carbonate a solid was obtained which was dissolved in ethanol (200 ml) and boiled with norit. Filtration and evaporation of the solvent gave crude **2** (20.9 g). This product was again heated with phosphorus oxybromide (200 g) during 24 hours at 190°. After working up and recrystallization from methanol **2** (14.2 g, 66%) was obtained, mp 74-75°; nmr (deuteriochloroform): δ 7.47 (s, 2H, H-4 + H-5), 7.40 (s, 5H, Ph); (acetone-d_6): δ 7.67 (s, 2H, H-4 + H-5), 7.44 (s, 5H, Ph); ms: m/e 311/313 (Br = 79).

Anal. Calcd. for $C_{11}H_7Br_2N$: C, 42.21; H, 2.25. Found: C, 42.07; H, 2.24.

2,6-Dibromo-3-dimethylaminopyridine (**4**).

This compound was prepared by a general reductive alkylation procedure [9] with some minor variations. A mixture of 2,4-dibromo-3-aminopyridine [10] (9.4 g = 37.3 mmoles), formaldehyde (20 g of a 35% solution in water) and formic acid (32 g) was heated first on a steam bath for 2 hours and then for 14 hours at 100° in an oil bath. After dilution with water and neutralization with 6*N* sodium hydroxide and by extraction with ether 10.2 g of an oil was obtained, bp 114-116°/0.5 mm; (lit [11] 112-114°/0.3 mm); n_D^{22} = 1.6250; nmr (deuteriochloroform): δ 7.33 and 7.17 (2d, AB, J = 7.8 Hz, 2H, H-4 + H-5), 2.82 (s, 6H, Me); ms: m/e 278 (Br = 79).

Anal. Calcd. for $C_7H_8Br_2N_2$: C, 30.03; H, 2.88. Found: C, 29.97; H, 2.88.

2,6-Dichloro-3-dimethylaminopyridine (**3**).

This compound was prepared from 3-amino-2,6-dichloropyridine [10] by a similar method as described for the preparation of **4**, oil, bp 96-97°/0.2 mm, n_D^{20} = 1.5780, yield 85%; nmr (deuteriochloroform): δ 7.27 and 7.17 (2d, AB, J = 8.1 Hz, 2H, H-4 + H-5), 2.83 (s, 6H, Me); ms: m/e 190 (Cl = 35).

Anal. Calcd. for $C_7H_8Cl_2N_2$: C, 44.01; H, 4.22. Found: C, 43.91; H, 4.33.

2,6-Dibromo-4-(*N*-methylanilino)pyridine (**24**).

A solution of *N*-methylaniline (19 g, 178 mmoles) in anhydrous ether (15 ml) was added to a stirred solution of potassium amide, prepared by dissolving potassium (0.73 g, 18.7 mg-atom) in liquid ammonia (200 ml). After 10 minutes a solution of 2,4,6-tribromopyridine [12] (5.7 g, 18 mmoles) in anhydrous ether (100 ml) was added. The reaction mixture was stirred for 4 hours, then the reaction was stopped by addition of ammonium chloride and the excess of *N*-methylaniline was removed by steam distillation. Crude **24** (6.25 g) was obtained by extracting the residue with chloroform, whereupon it was recrystallized from ethanol (3.88 g, 63%); mp 133-134°; nmr (deuteriochloroform): δ 7.28 (m, 5H, Ph), 6.58 (s, 2H, H-3 + H-5), 3.28 (s, 3H, Me); ms: m/e 340 (Br = 79).

Anal. Calcd. for $C_{12}H_{10}Br_2N_2$: C, 42.13; H, 2.95. Found: C, 42.16; H, 2.98.

Preparation of Reference Compounds.

4-Amino-2-benzylpyrimidine (**5**, mp 140-142°, [13]) and 2,6-diamino-3-phenylpyridine (**9**), mp 112-113.5° [7]; nmr (deuteriochloroform): δ 7.37 (s, 5H, Ph), 7.17 (d, J = 7.8 Hz, 1H, H-4), 5.95 (d, J = 7.8 Hz, 1H, H-5), 4.43 and 4.28 (two br s, 4H, NH_2)] were prepared according to literature procedures.

4-Amino-2-methyl-5-phenylpyrimidine (**6**).

This compound was synthesized according to a general procedure of Takamizawa *et al.* [14]. From acetamidine hydrochloride (9.5 g, 100 mmoles) and isobutoxymethylenephenylacetonitrile [15] (20.2 g, 100 mmoles), crude **6** (7.2 g, 39%) was obtained which was recrystallized from ethanol-water (1:1), giving pure **6** (3.9 g, 21%), mp 138-139°; nmr (deuteriochloroform): δ 7.98 (s, 1H, H-6), 7.38 (s, 5H, Ph), 5.80 (br s, 2H, NH_2), 2.50 (s, 3H, Me); ms: m/e 185.

Anal. Calcd. for $C_{11}H_{11}N_3$: C, 71.32; H, 5.99. Found: C, 71.17; H, 5.96.

2-Amino-6-bromo-3-phenylpyridine (**15**).

A mixture of 2-amino-6-chloro-3-phenylpyridine (**27**, 1.24 g, 54.8 mmoles [8]) and phosphorus tribromide (55 ml) was shaken in tubes during 6 hours at 180°. The mixture was then poured out onto ice and basified with potassium carbonate. Crude **15** (7.43 g, 47%) was filtered off. Recrystallization from ethanol gave pure **15** (4.74 g, 34%), mp 160.5-161.5°; ir (chloroform): 3500, 3400 cm^{-1} (NH_2); nmr (deuteriochloroform): δ 7.40 (s, 5H, Ph), 7.17 (d, J = 7.5 Hz, 1H, H-4), 6.87 (d, J = 7.5 Hz, 1H, H-5), 4.80 (br s, 2H, NH_2); ms: m/e 248 (Br = 79).

Anal. Calcd. for $C_{11}H_9BrN_2$: C, 53.03; H, 3.64. Found: C, 53.26; H, 3.84.

2-Amino-6-bromo-3-phenylpyridine (**15**) and 6-Amino-2-bromo-3-phenylpyridine (**16**).

A mixture of **2** (4.0 g, 12.8 mmoles) and aqueous ammonia (21 ml, d 0.91) was shaken in a tube during 30 hours at 160°. Extraction of the reaction mixture with dichloromethane gave, after evaporation of the solvent a solid material which was subjected to column chromatography (silicagel, petroleum ether 60/80-ethyl acetate 7:3), 0.53 g of **15** (16%, R_f 0.44) and 1.63 g of **16** (51%, R_f 0.22) were isolated. Recrystallization of **15** from ethanol afforded pure **15** (0.44 g, 13%) mp 162.0-163.0°; mixed mp with an independently prepared specimen of **15** (see above) did not show a depression. Recrystallization of **16** from ethanol gave 1.09 g of **16** (34%), mp 140.5-141.5°; ir (chloroform): 3500, 3400 cm^{-1} (NH_2); nmr (deuteriochloroform): δ 7.37 (d + s, 6H, H-4 + Ph), 6.47 (d, J = 8.4 Hz, 1H, H-5), 4.67 (br s, 2H, NH_2); ms: m/e 248 (Br = 79).

Anal. Calcd. for $C_{11}H_9N_2$: C, 53.03; H, 3.64. Found: C, 53.17; H, 3.50.

2-Amino-4-bromo-5-phenylpyridine (**29**) and 4-Amino-2-bromo-5-phenylpyridine (**8**).

The preparation of this mixture needs as starting material 2,4-di bromo-5-phenylpyridine (**28**). Since this compound is unknown we first describe its preparation from 2,4-dihydroxy-5-phenylpyridine.

2,4-Dihydroxy-5-phenylpyridine.

A mixture of ethyl α-formylphenyl acetate [16] (5 g), THF (75 ml) and aqueous ammonia (5 ml, d 0.91) was stirred for 30 minutes at 70°. After removing the THF, the residue was extracted with ether (100 ml) from which an oil (5 g) was isolated, containing ethyl aminoethylenephenyl acetate together with another unidentified compound (tlc: silicagel, benzene, R_f 0.25 and 0.08; no starting material was left). According to the procedure described by Wibaut and Kooyman [17] this crude mixture (20 g) was reacted with diethyl malonate (16.5 g) yielding 2,4-dihydroxy-3-ethoxycarbonyl-5-phenylpyridine, (9 g, melting range of the crude product 193-196°). Twenty-one g of this crude product was converted into 2,4-dihydroxy-5-phenylpyridine by heating it with concentrated hydrochloric acid *cf.* Errera [18], melting range 171-177°.

2,4-Dibromo-5-phenylpyridine (**28**).

A mixture of 2,4-dihydroxy-5-phenylpyridine (10 g, 53.5 mmoles) and phosphorus oxybromide (70 g) was heated at 140° for 4 hours. After working up and recrystallization from ethanol 2,4-dibromo-5-phenylpyridine (**28**, 12.9 g, 77%) was obtained, mp 99-100°; nmr (deuteriochloroform): δ 8.23 (s, 1H, H-6), 7.80 (s, 1H, H-3), 7.40 (s, 5H, Ph); ms: m/e 311 (Br = 79).

Anal. Calcd. for $C_{11}H_7BrN$: C, 42.21; H, 2.81. Found: C, 42.05; H, 2.75.

2-Amino-4-bromo-5-phenylpyridine (**29**) and 4-Amino-2-bromo-5-phenylpyridine (**8**).

A mixture of **28** (9.27 g, 29.6 mmoles) and aqueous ammonia (135 ml, d 0.9) was shaken in tubes during 24 hours at 160°. Extraction with dichloromethane gave a mixture from which **29** (3.09 g, R_f 0.38) and **8** (3.04 g, R_f 0.71) could be isolated by column chromatography (silicagel/petroleum ether 60/80-ethyl acetate 1:1), yield of **29**, after recrystallization from heptane is 2.22 g (30%), mp 150.5-151.5°; ir (chloroform): 3510,

3400 cm^{-1} (NH_2); ^{1}H nmr (deuteriochloroform): δ 7.97 (s, 1H, H-6), 7.37 (s, 5H, Ph), 6.80 (s, 1H, H-3), 4.60 (br s, 2H, NH_2); ms: m/e 248 (Br = 79).

Anal. Calcd. for $C_{11}H_9BrN_2$: C, 53.03; H, 3.64. Found: C, 53.30; H, 3.49.

The yield of **8** after recrystallization from heptane/ethyl acetate was 2.11 g (29%), mp 127.5-128.5°; ir (chloroform): 3500, 3400 cm^{-1} (NH_2); ^{1}H nmr (deuteriochloroform): δ 7.87 (s, 1H, H-6), 7.40 (s, 5H, Ph), 6.77 (s, 1H, H-3), 4.40 (br s, 2H, NH_2); ms: m/e 248 (Br = 79).

Anal. Calcd. for $C_{11}H_9Br_2N$: C, 53.03; H, 3.64. Found: C, 53.17; H, 3.58.

3-Amino-2-bromo-5-phenylpyridine (**30**) and 4-Amino-2-bromo-5-phenylpyridine (**8**).

A solution of **28** (1.27 g, 4.05 mmoles) in absolute ether (10 ml) was added to a solution of potassium amide, prepared from potassium (0.81 g, 20.8 mg-atom) and liquid ammonia (150 ml) by the general procedure [2]. After 8 minutes the reaction mixture was quenched with ammonium chloride and ammonia was evaporated off. The residue was extracted with dichloromethane to give a solid mass (0.96 g). Applying preparative tlc (aluminium oxide, tetrachloromethane-ethyl acetate-methanol 36:2:1) afforded **30** (0.24 g, R_f 0.79) and a mixture (0.53 g) of **30** and **8** (R_f 0.66). The recrystallization of this mixture from ethanol gave an additional amount of **30** (0.08 g). The mother liquor was evaporized to dryness and the residue was recrystallized several times from heptane, affording pure **8** (mp 127-128°, mixed mp wth **8**, prepared from the reaction of **27** with aqueous ammonia, 127.5-128.5°). Recrystallization from heptane gave pure **30** (0.07 g, 7%), mp 173.5-174.5°; ir (chloroform): 3480, 3390 cm^{-1} (NH_2); ^{1}H nmr (deuteriochloroform): δ 7.98 (s, $J_{2,4}$ = 2.1 Hz, 1H, H-6), 7.45 (s, 5H, Ph), 7.15 (s, $J_{2,4}$ = 2.1 Hz, 1H, H-4), 4.18 (br s, NH_2); ms: m/e 248 (Br = 79).

Anal. Calcd. for $C_{11}H_9BrN_2$: C, 53.03; H, 3.64. Found: C, 52.91; H, 3.64.

Identification of Isolated Reaction Products.

The reaction conditions applied for the amination and the yield of products obtained are mentioned in Table 1. All reaction mixtures were analysed by glc. The retention times of the products are collected in Table 2. The compounds were usually isolated by preparative tlc or by preparative glc.

1. Amination of **1**.

Analysis of the reaction mixture by tlc (silicagel/chloroform) gave benzyl cyanide (R_f 0.70) and **5** (R_f 0.00), (silicagel/chloroform-ethyl acetate 3:2) (R_f 0.66).

2. Amination of **2**.

Analysis of the reaction by tlc (silicagel, chloroform) gave **7** (R_f 0.41), **8** (R_f 0.27) and , (R_f 0.06).

2-Amino-1-cyano-1-phenylbut-1-en-3-yne (**7**).

This compound was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 7.36 (s, 5H, Ph), 4.7 (br s, 2H, NH_2), 3.41 (s, 1H, C≡CH); ir (chloroform): 3500, 3395 cm^{-1} (NH_2), 3295, 2100 cm^{-1} (C≡CH), 2250 cm^{-1} (CN); ms: accurate mass Calcd. for $C_{11}H_8N_2$ 168.069; Found: 168.0641.

3. Amination of **3**.

Anslysis of the reaction mixture by tlc (silcagel, chloroform-ethyl acetate 3:1) gave **20** (R_f 0.68) and **21** (R_f 0.49).

2-Amino-1-cyano-1-dimethylaminobut-1-en-3-yne (**21**).

This compound was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 4.80 (br s, 2H, NH_2), 3.35 (s, 1H, C≡CH), 2.42 (s, 6H, Me); ir (chloroform): 3500, 3380 cm^{-1} (NH_2), 3300, 2110 cm^{-1} (C≡CH), 2790 cm^{-1} (NMe), 2190 cm^{-1} (CN); ms: accurate mass Calcd. for $C_7H_9N_3$ 135.080; Found: 135.0781.

4-Amino-2-chloro-5-dimethylaminopyridine (**22**).

This compound was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 7.82 (s, 1H, H-6), 6.57 (s, 1H, H-3), 4.70 (br s, 2H, NH_2), 2.70 (s, 6H, Me); ir (chloroform): 3490, 3380 cm^{-1} (NH_2), 2780, cm^{-1} (NMe); ms: accurate mass Calcd. for $C_7H_{10}ClN_3$ (Cl = 35) 171.056; Found: 171.0550.

4. Amination of **4**.

4-Amino-2-bromo-5-dimethylaminopyridine (**23**).

This compound had mp 88-90°; ^{1}H nmr (deuteriochloroform): δ 7.76 (s, 1H, H-6), 6.70 (s, 1H, H-3), 4.75 (br s, 2H, NH_2), 2.68 (s, 6H, Me); ir (chloroform): 3520, 3400 cm^{-1} (NH_2); ms: accurate mass Calcd. for $C_7H_{10}BrN_3$ (Br = 79) 215.006; Found: 215.0052.

2-(or 6-)Amino-6(or 2-)-bromo-3-dimethylaminopyridine (**31**).

This compound, formed by aminating **4** (mole ratio **4** to potassium amide = 1:2.2, reaction time 2 minutes), was isolated in 10-15% yield by using preparative tlc (silicagel/petroleum ether 60/80-ethyl acetate 4:1, R_f = 0.46); mp 108-110° (hexane); ^{1}H nmr (deuteriochloroform): δ 6.99 (d, J = 7.8 Hz, 1H, H-4), 6.73 (d, J = 7.8 Hz, 1H, H-5), 4.90 (br s, 2H, NH_2), 2.60 (s, 6H, Me); ir (chloroform): 3490, 3380 cm^{-1} (NH_2); ms: accurate mass Calcd. for $C_7H_{10}BrN_3$ (Br = 79) 215.0059; Found: 215.0068.

Anal. Calcd. for $C_7H_{10}BrN_3$: C, 38.91; H, 4.66. Found: C, 38.97; H, 4.61.

5. Amination of **15** and of **16**.

On reacting **15** or **16** with an excess of potassium amide nearly exclusively 1,3-dicyano-1-phenylprop-1-ene (**17**) was obtained (see Table 1).

1,3-Dicyano-1-phenylpropene (**17**).

This compound was isolated in 65-80% yield when applying preparative tlc (silica gel, chloroform-ethyl acetate 76:5, R_f 0.49) as an oil which decomposed on standing; ^{1}H nmr (deuteriochloroform): δ 7.45 (s, 5H, Ph), 6.68 (t, 1H, CH), 3.61 (d, 2H, CH_2); ir (chloroform): 2275, 2200 cm^{-1} (CN); ms: accurate mass Calcd. for $C_{11}H_8N_2$ 168.0687; Found 168.0692.

6. Amination of **24**.

On the amination of **24** with an 4-fold of excess of potassium amide for 30 minutes and work-up of the reaction mixture by preparative tlc (silica gel/chloroform-acetate 19:1, R_f 0.65) gave 1,3-dicyano-2-(*N*-methylanilino)propene (**26**) in about 90% yield, as an oil which solidified in the refrigerator, mp 75.0-75.5° (ether, −30°); ^{1}H nmr (deuteriochloroform): δ 7.38 (m, 5H, Ph), 4.25 (s, 1H, CH), 3.47 (s, 2H, CH_2), 3.26 (s, 3H, Me); ms: accurate mass Calcd. for $C_{12}H_{11}N_3$: 197.0953; Found: 197.0954.

Anal. Calcd. for $C_{12}H_{11}N_3$: C, 73.07; H, 5.62. Found: C, 72.92; H, 5.31.

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