PYRAZOLO(1,5-c)PYRIMIDINES FROM PYRYLIUM SALTS AND AMIDRAZONES AND PYRIDINE IMIDOYL-N-IMIDES FROM IMIDOYL CHLORIDES

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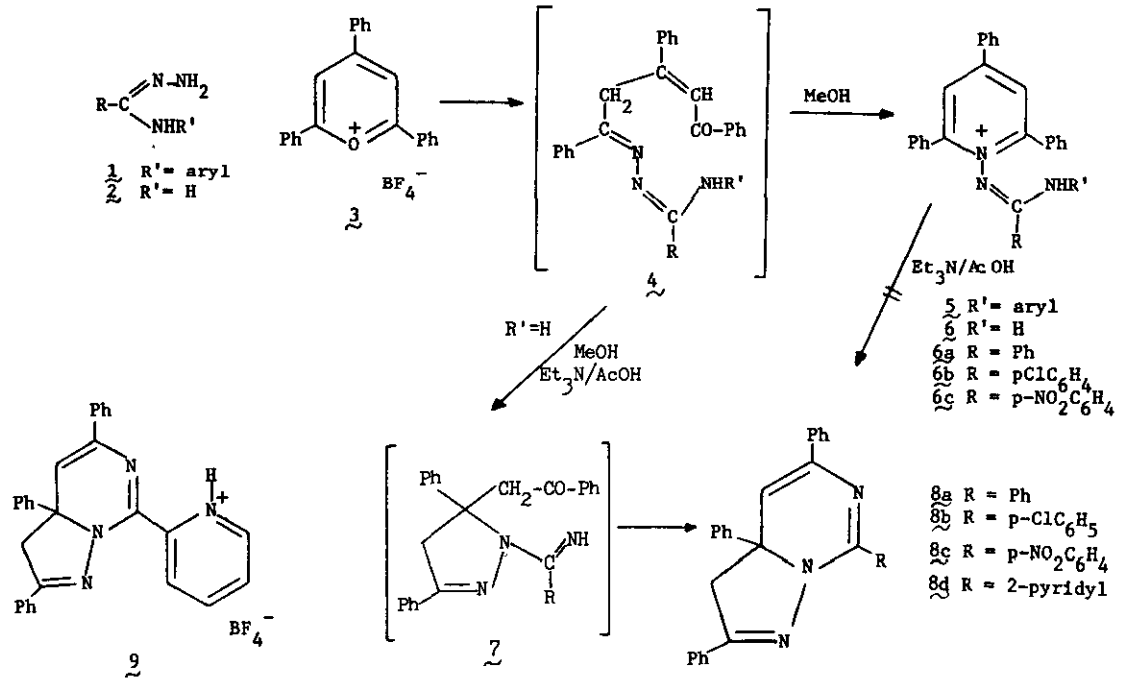
2,4,6-Triphenylpyrylium salts react with unsubstituted amidrazones to give dihydropyrazolo(1,5-c)pyrimidines or salts of pyridine imidoyl-N-imides. Pyridine imidoyl-N-imides are conveniently prepared from N-aminopyridinium and imidoyl chlorides.

We have previously shown that substituted amidrazones 1 react with triphenylpyrylium to give pyridinium salts 5 which can be converted to carbodiimides.[1] We have now studied the corresponding unsubstituted amidrazones 2. When treated in methanol with the pyrylium they do indeed give the analogous salts 6, for the case of R=phenyl, p-chlorophenyl and p-nitrophenyl (Table 1). In the presence of NEt_3/HOAc, the reaction takes a different course and bicyclic products 8 are formed.



Scheme 1

Table 1

Preparation of $RC(NH_2):NNH_2$ (2)

Entry	R	Mp (°C)	Lit. Mp (°C)	Yield
a	C_6H_5	77-79	78-79[a]	47
b	p-ClC_6H_4	87-89	87-89[b]	59
c	p-$NO_2C_6H_4$	140-141	144[d]	32
d	2-pyridyl	95-96	95-96[e]	

Preparation of 1-(N-Arylamidino)-2,4,6-triphenylpyridinium tetrafluoroborates (6)

Entry	Mp (°C)	Crystal Form	Recryst. Solvent	Found C	Found H	Found N	Molecular Formula	Required C	Required H	Required N
a	134-135	Prisms	Ethanol	69.93	4.75	8.13	$C_{30}H_{24}BF_4N_3$	70.17	4.67	8.18
b	256-258	Needles	Ethanol	65.43	4.49	7.59	$C_{30}H_{23}BClF_4N_3$[c]	65.75	4.20	7.67
c	296-298	Prisms	Methanol	64.89	4.40	9.60	$C_{30}H_{23}BF_4N_2O_2$	64.51	4.12	10.03
d										

[a] W.J. van der Burg, Rec. Trav. Chim., 1955, 74, 262. [b] E.C. Taylor and S.F. Martin, J. Org. Chem., 1972, 37, 3959. [c] Cl: found 6.80; required 7.67. [d] J. Bertrand, C. Dobritz, and H. Beerens, Bull. Soc. Pharm. Lille, 1956, 39-48. [e] F.H. Case, J. Org. Chem., 1965, 30, 931.

Table 2. Preparation of 7-Aryl-2,3a,5-triphenyl-3a,8-dihydro-3H-pyrazolo[1,5-c]pyrimidine (8)

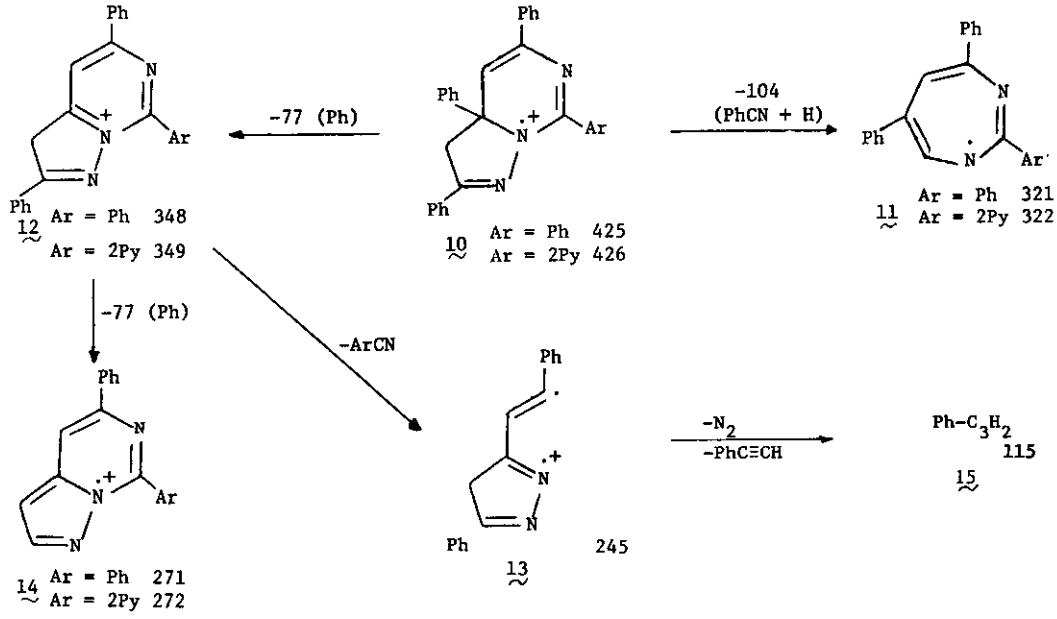
Entry	R	Yield	Mp (°C)	Crystal Form	Recryst. Solvent	Found C	Found H	Found N	Molecular Formula	Required C	Required H	Required N
8a	C_6H_5	32	198-199	Needles	Ethanol	84.45	5.67	9.82	$C_{30}H_{23}N_3$	84.70	5.41	9.88
8b	p-ClC_6H_4	45	280-283	Needles	Chloroform	78.16	4.59	8.90	$C_{30}H_{22}ClN_3$[a]	78.34	4.78	9.14
8c	p-$NO_2C_6H_4$	78	225-228	Plates	Ethanol	76.70	4.79	11.82	$C_{30}H_{22}N_4O_2$	76.59	4.68	11.91
8d	2-pyridyl	89	239-240	Needles	Bencene	81.35	5.42	13.20	$C_{29}H_{22}N_4$	81.69	5.16	13.14

[a] Cl: found: 7.56, required: 7.72.

In the case of the 2-pyridyl derivative (2, R=2-Py), the salt 9 is formed; in methanol, it gives the derivative 8 with base (Table 2). The pyridinium salt 6 does not give the bicyclic derivative 8 when treated with base.

Structures 8 are based on spectral evidence. In particular each compound displayed in the ^{1}H nmr spectra a double doublet near 3.6 ppm (J=18 Hz) indicating a CH_2 group and a singlet at δ=6.2 indicating a CH group. In the ^{13}C spectrum, this CH_2 was confirmed by a triplet at δ 51: the aliphatic region also showed a singlet at δ 65 for C-3a, and a doublet at δ 108 was assigned to the β-enamine type carbon at C-4.

Mass spectra (Scheme 2) showed the expected molecular ion peaks for 10. The base peaks occur at M-77 for the loss of C_6H_5, presumably to give ions of type 12. Peaks are also shown for the loss of (PhCN + H) for the molecular ion, perhaps to give 11. Structure 12 appears to fragment both by loss of ArCN to give 13 and 15 and by loss of Ph, perhaps to give 14.



Scheme 2: Mass Spectral Fragmentation

We believe that the formation of 8 involves an alternative ring-closure of the intermediate 7. Some examples of pyrazolo[1,5-c]pyrimidines are known,[2,3,4,5] but compounds with an angular phenyl group were previously not reported.

Two methods exist for the conversion of carboxylic acid derivatives into unsymmetrical diaryl carbodiimides derivatives[6]: (a) thermolysis of 1,2,3,5-oxathiadiazole 2-oxides[7] and (b) pyrolysis of 2,4,6-triphenylpyridine imidoyl-N-imides (3).[1] The former requires five stages from a carboxylic acid.[7] Method (b) employed the reaction of amidrazones with pyryliums, and subsequent

Table 3. Preparation of Imidoyl Chlorides (17) and Pyridine Amides (18)

			ArCCl : NAr' (2)			Pyridine Imides (3)		
Ar	Ar'	Entry	Yield(%)	Mp (°C)	Lit. Mp (°C)	Yield (%)	Mp (°C)	Lit.[a] Mp (°C)
Ph	Ph	a	99	39-40	40[b]	72	119-124	120-123
Ph	p-$CH_3C_6H_4$	b	98	50-52	[c]	74	124-128	122-125
Ph	p-ClC_6H_4	c	99	60-61	62[d]	72	114-118	116-119
Ph	o-ClC_6H_4	d	86	40-41	41[e]	89	201-204	204-206
Ph	p-BrC_6H_4	e	99	68-70	70[f]	75	168-170[g]	
p-$CH_3C_6H_4$	p-ClC_6H_4	f	97	73-75[h]		73	115-120[i]	
m-ClC_6H_4	p-$CH_3C_6H_4$	g	60	[j]		60	114-116[k]	

[a] See Ref. 3. [b] See Ref. 4. [c] Found: C, 73.20; H, 5.22; N, 6.10; Cl, 15.46; $C_{14}H_{12}ClN$ requires C, 73.15; H, 5.28; N, 6.06; Cl, 15.41. [d] R. Ta-Shma and Z. Rappoport, J. Amer. Chem. Soc. 1977, 99, 1854. [e] G. Bock, Chem. Ber. 1967, 100, 2876. [f] R.M. Acheson and M.J.T. Robinson, J. Chem. Soc. 1953, 237. [g] Needles from acetone-EtOH-H_2O (1:1:1); Found: C, 74.12; H, 4.50; N, 6.96; Br, 13.68; $C_{36}H_{26}BrN_3$ requires C, 74.48; H, 4.48; N, 7.24; Br, 13.79%; ν_{max} ($CHBr_3$):1620,1520, 1485, 1360,1255, 1070,930, 880, 830,760 cm^{-1}. ^1H nmr ($CDCl_3$); δ (ppm): 6.1-7.9 (26 H, m). [h] Found: C, 63.79; H, 4.09; N, 5.31; Cl, 26.57; $C_{14}H_{11}NCl_2$ requires C, 63.87; H, 4.18; N, 5.32; Cl, 26.61%; ν_{max} ($CHBr_3$): 1650, 1610, 1480, 1250, 1170, 1160, 1090, 900, 820, 780, 710 cm^{-1}; ^1H nmr ($CDCl_3$), δ (ppm): 6.8-8.2 (8 H, m), 2.4 (3 H, s). [i] Prisms from acetone-EtOH-H_2O (1:1:1); Found: C, 80.60; H, 5.13; N, 7.60; Cl, 6.50; $C_{37}H_{28}ClN_3$ requires C, 80.80; H, 5.09; N, 7.64; Cl, 6.46%; ν_{max} ($CHBr_3$): 1620, 1600, 1520, 1450, 1360, 1330, 875, 830, 750 cm^{-1}; ^1H nmr ($CDCl_3$), δ (ppm): 6.1-7.9 (25 H, m), 2.03 (3 H, s). [j] Yellow oil used as a crude product; ν_{max} ($CHBr_3$): 1650, 1570, 1500, 1470, 1410, 1180, 1160, 960, 840, 820, 790, 760 cm^{-1}; ^1H nmr ($CDCl_3$), δ (ppm): 6.7-8.2 (8 H, m), 2.3 (3 H, s). [k] Prisms from acetone-EtOH- H_2O (1:1:1); Found: C, 78.60; H, 5.31; N, 7.45; Cl, 6.27; $C_{37}H_{28}ClN_3.H_2O$ requires: C, 78.23; H, 5.28; N, 7.40; Cl, 6.25; ν_{max} ($CDCl_3$): 3600, 1620, 1600, 1520, 1510, 1450, 1410, 1360, 1330, 880, 830, 750; ^1H nmr ($CDCl_3$), δ (ppm): 6.3-7.85 (25 H, m), 2.15 (3 H, s).

Table 4. Preparation of Pyridinium Tetrafluoroborates (20)

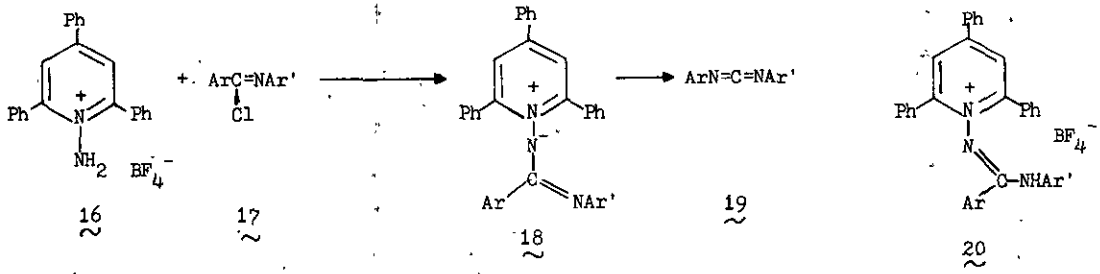
Entry	Yield (%)	Mp (°C)	Crystal form	Required C	Required H	Required N	Molecular Formula	Found C	Found H	Found N
a[a]	84	246-250	Needles	73.34	4.75	7.13	$C_{36}H_{28}BF_4N_3$	73.11	4.81	7.07
b[b]	68	214-217	Plates	73.63	4.97	6.96	$C_{37}H_{30}BF_4N_3$	73.43	5.02	6.92
c[c]	77	190-192	Plates	67.34	4.52	6.54	$C_{36}H_{27}BClF_4N_3 \cdot H_2O$[d]	67.56	4.80	6.40
d[e]	60	270-272	Prisms	69.28	4.33	6.73	$C_{36}H_{27}BClF_4N_3$[f]	69.12	4.38	6.70
e[g]	78	178-182	Plates	62.97	4.22	6.12	$C_{36}H_{27}BBrF_4N_3 \cdot H_2O$[h]	62.86	4.30	6.09
f[i]	65	265-269	Plates	69.64	4.54	6.58	$C_{37}H_{29}BClF_4N_3$[j]	69.73	4.59	6.54
g[k]	64	200-206	Plates	69.64	4.54	6.58	$C_{37}H_{29}BClF_4N_3$[l]	69.91	4.61	6.70

[a] ν_{max} ($CHBr_3$): 3295, 1620, 1600, 1570, 1500, 1390, 1235, 1060, 755, 735 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 9.9 (1 H, s), 8.4 (2 H, s), 6.0-8.2 (25 H, m). [b] ν_{max} ($CHBr_3$): 3290, 1620, 1600, 1560, 1510, 1410, 1390, 1240, 1060, 760, 750, 730 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 9.75 (1 H, s), 8.4 (2 H, s), 5.9-8.2 (24 H, m), 1.95 (3 H, s). [c] ν_{max} 3600, 3290, 1620, 1600, 1560, 1490, 1460, 1410, 1380, 1240, 1060, 760, 735 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 10.05 (1 H, s), 8.55 (2 H, s), 6.1-8.2 (24 H, m). [d] Cl: found: 5.54%; required 5.53%. [e] ν_{max} ($CHBr_3$): 3285, 1620, 1560, 1500, 1450, 1420, 1400, 1230, 1060, 760, 730 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 9.9 (1 H, s), 8.55 (2 H, s), 6.6-8.2 (24 H, m). [f] Cl: found: 5.73%. required: 5.69%. [g] ν_{max} ($CHBr_3$): 3600, 3290, 1620, 1600, 1560, 1485, 1410, 1380, 1240, 1060, 760, 735 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$] 9.9 (1 H, s), 8.4 (2 H, s), 5.9-8.1 (24 H, m). [h] Br: found 11.72%, required 11.66%. [i] ν_{max} ($CHBr_3$): 3290, 1620, 1600, 1560, 1490, 1410, 1390, 1350, 1230, 1060, 890, 830, 770, 760, 750 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 9.8 (1 H, s), 8.35 (2 H, s), 5.9-8.0 (23 H, m). [j] Cl: found 5.50%, required 5.56%. [k] ν_{max} ($CHBr_3$): 3290, 1620, 1600, 1560, 1515, 1415, 1240, 1060, 890, 760 cm^{-1}; ^1H nmr δ (ppm) [$(CD_3)_2SO$]: 8.7 (1 H, s), 5.9-7.9 (25 H), 2.1 (3 H, s). [l] Cl: found 5.60%, required 5.56%.

deprotonation of the pyridinium salt: amidrazones are prepared by a three step method from acids involving amide and thioamide.[1]

We have now found that the 2,4,6-triphenylpyridine imidoyl-N-imides 18(a-g) (Table 3) can advantageously be prepared directly from the N-aminopyridinium 16 and imidoyl chlorides 17 (Table 4). The diarylimidoyl chlorides were prepared by the procedure reported for N-phenylbenzimidoyl chloride.[8]

Reaction of 16 and 17(a-g) gives the desired product which could be isolated as the tetra-*fluoroborates* 20(a-g) (Table 5) or more advantageously directly as the free bases 18(a-g). The pyrolysis of 18(a-d) has already been described: however, pyrolysis of 18(e-g) gave only poor yields of isolated carbodiimides. Apparently the high temperatures required caused side reactions to occur.



16 17 18 19 20

(for designation of a-g, see Table 4)

Scheme 3

EXPERIMENTAL

Ir spectra were measured for samples in $CHBr_3$ solution and nmr spectra for solutions in $CDCl_3$, $(CD_3)_2SO$ or CF_3COOH ($SiMe_4$ as internal reference). The following were prepared by the literature methods indicated: *2,4,6-triphenylpyrylium tetrafluoroborate* (3), mp 253 °C (lit.[9] mp 253-255 °C); 1-amino-2,4,6-triphenylpyridinium tetrafluoroborate (16), mp 168-169 °C (lit.[10] mp 168 °C).

General procedure for the formation of 1-(N-arylamidino)-2,4,6-triphenylpyridinium tetra-fluoroborates (6a-6c).- 2,4,6-Triphenylpyrylium tetrafluoroborate (3) (1 g, 2.5 mmol), the amidrazone (2.5 mmol), and methanol (10 ml) were refluxed for 12 h. The pyridinium crystallised on cooling (see Table 1). Spectral data follow: 1-(N-Benzamidino)- (6a): ν_{max} ($CHBr_3$) 3430, 3360, 3270, 1655, 1620, 1600, 1550, 1490, 1440, 1405, 1230, 1060, 885, 760, 740; δ ($CDCl_3$) 7.8-6.9 (22 H, m), 6.2 (2 H, s). 1-(N-p-chloro benzamidino)- (6b): ν_{max} ($CHBr_3$) 3420, 3360, 3260, 3240, 1650, 1620, 1600, 1550, 1500, 1410, 1240, 1060, 835, 760; δ (CF_3COOH) 7.0-8.6 (23 H, m). 1-(N-p-nitro-

benzamidino)- (6c): ν_{max} ($CHBr_3$) 3400, 3360, 3260, 1660, 1620, 1600, 1580, 1510, 1350, 1060, 770; δ (CF_3-COOH): 6.8-7.8 (23 H, m).

Preparation of the pyridinium salt (9).- 2,4,6-Triphenylpyridinium tetrafluoroborate (3) (1 g, 2.5 mmol), 2-picolinamidrazone (0.36 g, 2.5 mmol) and methanol (16 ml) were refluxed for 12 h. The pyridinium crystallised on cooling (0.70 g, 55%) as needles, mp 264-265 °C, from ethanol (Found: C, 67.78; H, 4.52; N, 10.84. $C_{29}H_{23}BF_4N_4$ requires C, 67.70; H, 4.47, N, 10.89%). ν_{max} ($CHBr_3$) 3280, 1650, 1620, 1510, 1495, 1450, 1060, 770, 755; δ [$(CD_3)_2SO$]: 7.2-8.8 (19 H, m), 6.6 (1 H, s), 4.1 (2 H, s). ^{13}C nmr δ(CF_3-COOH): 50 (t, C-3), 71 (s, C-3a), 106 (d, C-4), 123-146 (aromatics).

General procedure for the formation of 7-aryl-2,3a,5-triphenyl-3a,8-dihydro-3H-pyrazolo [1,5-c]pyrimidine (8a-8c).- 2,4,6-Triphenylpyrylium tetrafluoroborate (1 g, 2.5 mmol) suspended in methanol (8 ml) and Et_3N (0.2525 g, 2.5 mmol) was refluxed for 30 min with an equimolecular amount of the amidrazone. AcOH (1 ml) was added and the mixture refluxed for 10 h. The compounds crystallised on cooling (see Table 2).

7-(2-pyridyl)-2,3a,5-triphenyl-3a,8-dihydro-3H-pyrazolo[1,5-c]pyrimidine (8d).- Procedure A. Pyridinium salt (9) (0.514 g, 1 mmol) dissolved in acetone (5 ml)-H_2O (1 ml), and K_2CO_3 (0.138 g, 1 mmol) were stirred at 20 °C for 1 h. H_2O (10 ml) was added and the solution extracted with CH_2Cl_2 (30 ml). The dried ($MgSO_4$) CH_2Cl_2 layer was evaporated at 20 °C/20 mmHg (0.38 g, 89%). Procedure B. 2,4,6-Triphenylpyrylium tetrafluoroborate (1 g, 2.5 mmol) dissolved in methanol (10 ml) and Et_3N (0.38 g, 3.7 mmol) were refluxed for 9 h. The compound crystallised on cooling (0.75 g, 70% yield).

Table 5. Spectral[a] Data for Compound 8

Compound No.	^1H nmr: 3-CH_2 (dd) δ_1	J(Hz)	δ_2	5-CH (s) δ	Aromatic multiplet δ	^{13}C nmr: 3-CH_2 (t) δ	3a-C (s) δ	4-C (d) δ	Aromatic multiplet δ
8a	3.40	18	3.70	6.18	7.2-8.3[b]	50.8	65.2	107.8	123-151
8b	3.48	18	3.80	6.20	7.1-8.4[c]	53.7	65.1	106.6	116-130
8c	3.60	18	3.91	6.30	7.3-8.6[c]	50.7	65.3	107.0	123-151
8d	3.68	18	4.00	6.28	7.1-8.3[c]	50.6	65.2	107.6	128-157

[a] Ir band ($CHBr_3$) at: 8a: 1600, 1520, 1490, 1445, 1420, 1340, 1070, 1015, 755 cm^{-1}; 8b: 1600, 1575, 1520, 1490, 1450, 1430, 1340, 1090, 1010, 835, 760, 750 cm^{-1}; 8c: 1600, 1530, 1490, 1445, 1430, 1340, 1010, 855, 755; 8d: 1600, 1590, 1535, 1475, 1445, 1420, 1340, 1285, 1230, 1060, 1035, 1015, 990, 800, 755, 740, 715 cm^{-1}. [b] 20 H. [c] 19 H.

General Procedure for the formation of diarylimidoyl chlorides 17(b-g).- Benzanilides were refluxed for 4 h with 10% molar excess of thionyl chloride. The excess of thionyl chloride was distilled off (50 °C/20 mmHg) and the resulting imidoyl chlorides crystallised from dry petroleum ether (see Table 4).

General procedure for the formation of 1-(N-aryl-N'-benzamidino)-2,4,6-triphenylpyridinium tetrafluoroborates 20(a-g).- 1-Amino-2,4,6-triphenylpyridinium tetrafluoroborate (1 g, 2.43 mmol), acetone (10 ml), H_2O (2 ml) and K_2CO_3 (0.672 g, 4.86 mmol) were stirred at 20 °C for 30 min. Diarylimidoyl chloride (2.43 mmol) was added and the solution stirred at 20 °C for 2 h, followed by addition of HBF_4 and water (15 ml). The solution was extracted with CH_2Cl_2 (40 ml) and the CH_2Cl_2 layer dried ($MgSO_4$) and evaporated under reduced pressure (30 °C/20 mmHg) (see Table 5).

General procedure for the formation of 2,4,6-triphenylpyridine 1-(N-arylbenzimidoyl)-imides 18(a-g).- 1-Amino-2,4,6-triphenylpyridinium tetrafluoroborate (1 g, 2.43 mmol) in acetone (10 ml), H_2O (2 ml) and K_2CO_3 (0.672 g, 4.86 mmol) were stirred at 20 °C for 30 min. Diarylimidoyl chloride (2.43 mmol) was added and the solution stirred at 20 °C for 2 h. H_2O (20 ml) was added and the solution extracted with CH_2Cl_2 (50 ml). The CH_2Cl_2 layer was dried ($MgSO_4$) and evaporated under reduced pressure (30 °C/20 mmHg) (see Table 1).

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