

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

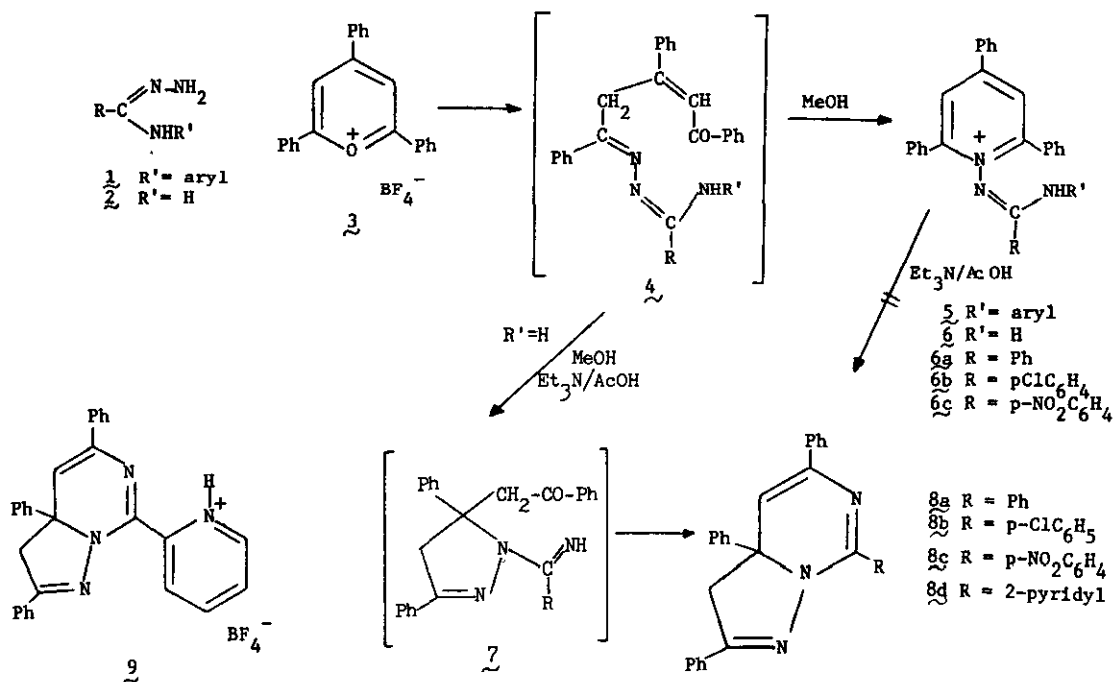
By Alan R. Katritzky* and Alberto Tárraga Tomás

Department of Chemistry, University of Florida, Gainesville, Florida 32611, U.S.A.

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 $RC(NH_2)_2:NNH_2$ (2)		Preparation of 1-(N-Arylamidino)-2,4,6-triphenylpyridinium tetrafluoroborates (6)											
Entry	R	Mp (°C)	Yield	Mp (°C)	Crystal Form	Recryst. Solvent	Found C	Found H	Found N	Molecular Formula	Required C	Required H	Required N
a	C_6H_5	77-79	47	134-135	Prisms	Ethanol	69.93	4.75	8.13	$C_{30}H_{24}F_4N_3$	70.17	4.67	8.18
b	p-Cl- C_6H_4	87-89	59	256-258	Needles	Ethanol	65.43	4.49	7.59	$C_{30}H_{23}ClF_4N_3$	65.75	4.20	7.67
c	$pNO_2C_6H_4$	140-141	32	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	2-pyridyl	95-96		95-96 ^e									

^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)

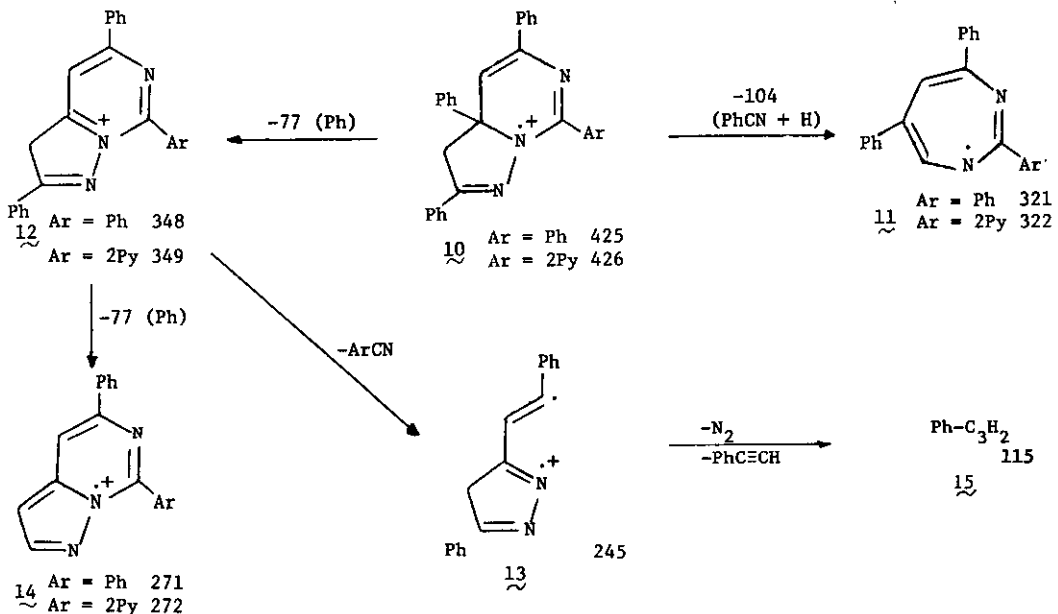
Entry	R	Yield	Mp (°C)	Crystal Form	Recryst. Solvent	Found C	Found H	Found N	Molecular Formula	Required C	Required H	Required N
8a	C_6H_5	32	198-199	Needles	Ethanol	84.45	5.67	9.82	$C_{30}H_{23}N_3$	84.70	5.41	9.88
8b	pCl- C_6H_4	45	280-283	Needles	Chloroform	78.16	4.59	8.90	$C_{30}H_{22}ClN_3$	78.34	4.78	9.14
8c	$pNO_2C_6H_4$	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	Benzene	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 ($\underline{2}$, R=2-Py), the salt $\underline{9}$ is formed; in methanol, it gives the derivative $\underline{8}$ with base (Table 2). The pyridinium salt $\underline{6}$ does not give the bicyclic derivative $\underline{8}$ when treated with base.

Structures $\underline{8}$ are based on spectral evidence. In particular each compound displayed in the ^1H nmr spectra a double doublet near 3.6 ppm ($J=18$ Hz) indicating a CH_2 group and a singlet at $\delta=6.2$ 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 $\underline{10}$. The base peaks occur at M-77 for the loss of C_6H_5 , presumably to give ions of type $\underline{12}$. Peaks are also shown for the loss of $(\text{PhCN} + \text{H})$ for the molecular ion, perhaps to give $\underline{11}$. Structure $\underline{12}$ appears to fragment both by loss of ArCN to give $\underline{13}$ and $\underline{15}$ and by loss of Ph, perhaps to give $\underline{14}$.



Scheme 2: Mass Spectral Fragmentation

We believe that the formation of $\underline{8}$ involves an alternative ring-closure of the intermediate $\underline{7}$. 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 derivatives⁶: (a) thermolysis of 1,2,3,5-oxathiadiazole 2-oxides⁷ and (b) pyrolysis of 2,4,6-triphenylpyridine imidoyl-N-imides ($\underline{3}$).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)

Ar	Ar'	Entry	ArCCl : NAr' (2)			Pyridine Imides (3)		
			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 ₃ C ₆ H ₄	b	98	50-52	c	74	124-128	122-125
Ph	p-ClC ₆ H ₄	c	99	60-61	62 ^d	72	114-118	116-119
Ph	o-ClC ₆ H ₄	d	86	40-41	41 ^e	89	201-204	204-206
Ph	p-BrC ₆ H ₄	e	99	68-70	70 ^f	75	168-170 ^g	
p-CH ₃ C ₆ H ₄	p-ClC ₆ H ₄	f	97	73-75 ^h		73	115-120 ⁱ	
m-ClC ₆ H ₄	p-CH ₃ C ₆ H ₄	g	60	i		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; C₁₄H₁₂ClN 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-H₂O (1:1:1); Found: C, 74.12; H, 4.50; N, 6.96; Br, 13.68; C₃₆H₂₆BrN₃

requires C, 74.48; H, 4.48; N, 7.24; Br, 13.79%; ν_{\max} (CHBr₃): 1620, 1520, 1485, 1360, 1255, 1070, 930, 880, 830, 760 cm⁻¹. ¹H nmr (CDCl₃);

δ (ppm): 6.1-7.9 (26 H, m). ^h Found: C, 63.79; H, 4.09; N, 5.31; Cl, 26.57; C₁₄H₁₁NCl₂ requires C, 63.87; H, 4.18; N, 5.32; Cl, 26.61%;

ν_{\max} (CHBr₃): 1650, 1610, 1480, 1250, 1170, 1160, 1090, 900, 820, 780, 710 cm⁻¹; ¹H nmr (CDCl₃), δ (ppm): 6.8-8.2 (8 H, m), 2.4 (3 H, s).

ⁱ Prisms from acetone-EtOH-H₂O (1:1:1); Found: C, 80.60; H, 5.13; N, 7.60; Cl, 6.50; C₃₇H₂₈ClN₃ requires C, 80.80; H, 5.09; N, 7.64;

Cl, 6.46%; ν_{\max} (CHBr₃): 1620, 1600, 1520, 1450, 1360, 1330, 875, 830, 750 cm⁻¹; ¹H nmr (CDCl₃), δ (ppm): 6.1-7.9 (25 H, m), 2.03 (3 H,

s). ^j Yellow oil used as a crude product; ν_{\max} (CHBr₃): 1650, 1570, 1500, 1470, 1410, 1180, 1160, 960, 840, 820, 790, 760 cm⁻¹; ¹H nmr

(CDCl₃), δ (ppm): 6.7-8.2 (8 H, m), 2.3 (3 H, s). ^k Prisms from acetone-EtOH-H₂O (1:1:1); Found: C, 78.60; H, 5.31; N, 7.45; Cl,

6.27; C₃₇H₂₈ClN₃·H₂O requires: C, 78.23; H, 5.28; N, 7.40; Cl, 6.25; ν_{\max} (CDCl₃): 3600, 1620, 1600, 1520, 1510, 1450, 1410, 1360, 1330,

880, 830, 750; ¹H nmr (CDCl₃), δ (ppm): 6.3-7.85 (25 H, m), 2.15 (3 H, s).

Table 4. Preparation of Pyridinium Tetrafluoroborates (20)

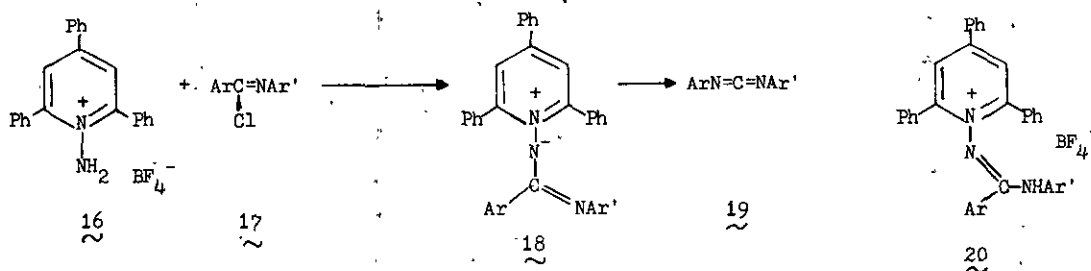
Entry	Yield (%)	Mp (°C)	Crystal form	Required			Molecular Formula	Found		
				C	H	N		C	H	N
a ^a	84	246-250	Needles	73.34	4.75	7.13	C ₃₆ H ₂₈ BF ₄ N ₃	73.11	4.81	7.07
b ^b	68	214-217	Plates	73.63	4.97	6.96	C ₃₇ H ₃₀ BF ₄ N ₃	73.43	5.02	6.92
c ^c	77	190-192	Plates	67.34	4.52	6.54	C ₃₆ H ₂₇ BClF ₄ N ₃ ·H ₂ O ^d	67.56	4.80	6.40
d ^e	60	270-272	Prisms	69.28	4.33	6.73	C ₃₆ H ₂₇ BClF ₄ N 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 ₄ N ₃ ·H ₂ O ^h	62.86	4.30	6.09
f ⁱ	65	265-269	Plates	69.64	4.54	6.58	C ₃₇ H ₂₉ BClF ₄ N 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 ₄ N ₃ ^l	69.91	4.61	6.70

^a ν_{\max} (CHBr₃): 3295, 1620, 1600, 1570, 1500, 1390, 1235, 1060, 755, 735 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)₂SO]: 9.9 (1 H, s), 8.4 (2 H, s), 6.0-8.2 (25 H, m). ^b ν_{\max} (CHBr₃): 3290, 1620, 1600, 1560, 1510, 1410, 1390, 1240, 1060, 760, 750, 730 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)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) [(CD₃)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} (CHBr₃): 3285, 1620, 1560, 1500, 1450, 1420, 1400, 1230, 1060, 760, 730 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)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} (CHBr₃): 3600, 3290, 1620, 1600, 1560, 1485, 1410, 1380, 1240, 1060, 760, 735 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)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} (CHBr₃): 3290, 1620, 1600, 1560, 1490, 1410, 1390, 1350, 1230, 1060, 890, 830, 770, 760, 750 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)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} (CHBr₃): 3290, 1620, 1600, 1560, 1515, 1415, 1240, 1060, 890, 760 cm⁻¹; ¹H nmr δ (ppm) [(CD₃)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 tetrafluoroborates 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.



(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 , $(\text{CD}_3)_2\text{SO}$ 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 $253\text{-}255^\circ\text{C}$); 1-amino-2,4,6-triphenylpyridinium tetrafluoroborate (16), mp $168\text{-}169^\circ\text{C}$ (lit.¹⁰ mp 168°C).

General procedure for the formation of 1-(N-arylamidino)-2,4,6-triphenylpyridinium tetrafluoroborates (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} (CHBr₃) 3400, 3360, 3260, 1660, 1620, 1600, 1580, 1510, 1350, 1060, 770; δ (CF₃-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. C₂₉H₂₃BF₄N₄ requires C, 67.70; H, 4.47, N, 10.89%). ν_{\max} (CHBr₃) 3280, 1650, 1620, 1510, 1495, 1450, 1060, 770, 755; δ [(CD₃)₂SO]: 7.2-8.8 (19 H, m), 6.6 (1 H, s), 4.1 (2 H, s). ¹³C nmr δ (CF₃-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 Et₃N (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)-H₂O (1 ml), and K₂CO₃ (0.138 g, 1 mmol) were stirred at 20 °C for 1 h. H₂O (10 ml) was added and the solution extracted with CH₂Cl₂ (30 ml). The dried (MgSO₄) CH₂Cl₂ 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 Et₃N (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.	¹ H nmr			¹³ C nmr					
	3-CH ₂ (dd)		5-CH (s)	Aromatic multiplet	3-CH ₂ (t) ²	3a-C (s)	4-C (d)	Aromatic multiplet	
	δ_1	J(Hz)	δ_2	δ	δ	δ	δ	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 (CHBr₃) 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'-benzamido)-2,4,6-triphenylpyridinium tetrafluoroborates 20(a-g).- 1-Amino-2,4,6-triphenylpyridinium tetrafluoroborate (1 g, 2.43 mmol), acetone (10 ml), H₂O (2 ml) and K₂CO₃ (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 HBF₄ and water (15 ml). The solution was extracted with CH₂Cl₂ (40 ml) and the CH₂Cl₂ layer dried (MgSO₄) 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), H₂O (2 ml) and K₂CO₃ (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. H₂O (20 ml) was added and the solution extracted with CH₂Cl₂ (50 ml). The CH₂Cl₂ layer was dried (MgSO₄) and evaporated under reduced pressure (30 °C/20 mmHg) (see Table 1).

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