Pergamon

Tetrahedron Vol. 50, No. 27, pp. 8127-8142, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $7.00+0.00

0040-4020(94)00425-0

Selectivities in the Formation of Pyridines and Pyrimidines by Ammonia-induced Cyclocondensations of Vinamidiniums

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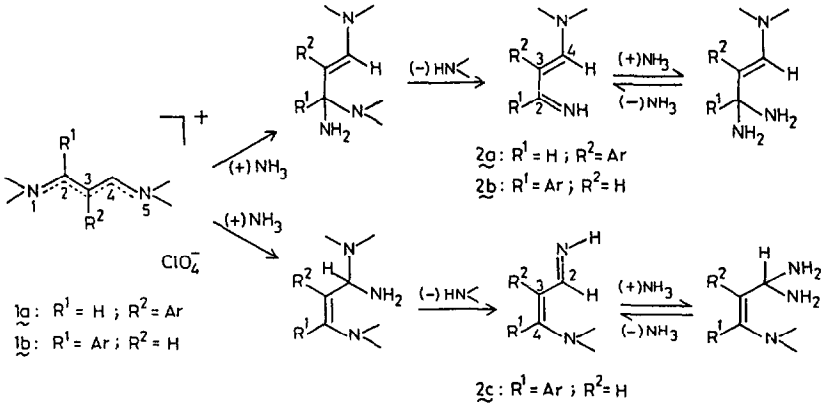
Abstract: Arylvinamidines (2-, 3- or 4-aryl-4-(N,N-dimethyl)amino-1-azabuta-1,3-dienes), generated from 1,1,5,5-tetramethyl-2- or -3-phenyl-1,5-diazapentadienium salts, cyclocondense orientation-specifically under two regioselections forming 1-4' + 4-3' and 1-2' + 4-1' bonds on exposure to ammonia. The initial cyclates aromatise eliminatively to give mixtures of diarylpyridines and arylpyrimidines. The 2-arylvinamidines do not participate as 2-centre reactants and their 4-aryl isomers not as 4-centre reactants in the cyclocondensations which appear to be stepwise and not concerted. Reasons for the selective participation appear to be that the required eliminations from the initial cyclates are disfavoured in the first case and that a geometric factor prevents cyclate-formation in the second.

Introduction

Mixtures of 3,5-diarylpyridines (**35dpy**)[1] and 5-arylpyrimidines (**5apym**) are formed when solutions of diaminopropenium (vinamidinium) salts[2a-d] **1a** in diethyleneglycol are maintained at *ca.* 160° under a slow passage of anhydrous ammonia (Table 1 a).[3] Vinamidines **2a** (Scheme 1) appeared to be the reactive intermediates, cyclodimerising in highly orientation-selective and non-regiospecific manner forming 1-4' + 4-3' and 1-2' + 4-1' bonds[4] and giving initial cyclates that can undergo eliminative aromatisation[2c] (Scheme 2). Somewhat unexpectedly, the exposure of the C-2



Scheme 1

Table 1. Product Patterns from Reactions of Salts **1a** and **1b**.

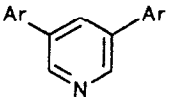
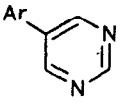
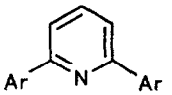
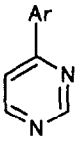
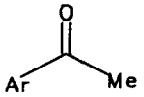
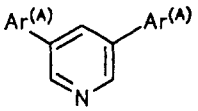
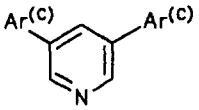
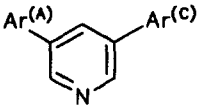
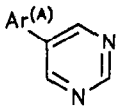
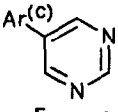
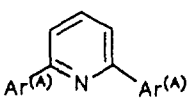
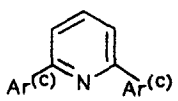
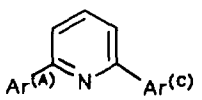
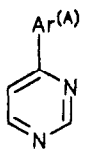
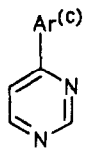
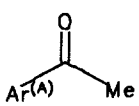
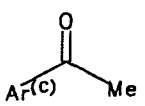
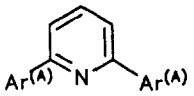
Reactants	Products (ratio in mixture)[a]
I. 'Sole' Reactions	
a) 1a + 1a A: Ar = Ph or B: Ar = *p*-MePh or C: Ar = *p*-MeOPh	 35dpy (0.8)  5apym (0.2)
b) 1b + 1b A: Ar = Ph or B: Ar = *p*-MePh or C: Ar = *p*-MeOPh	 26dpy (0.5)  4apym (0.5)  acp (+)[b]
II. 'Mixed' Reactions	
c) 1a A + 1a C A: Ar = Ph C: Ar = *p*-MeOPh	 35dpy (0.2)  35dpy (0.2)  35dpy (0.1)  5apym (0.25)  5apym (0.25)
d) 1b A + 1b C A: Ar = Ph C: Ar = *p*-MeOPh	 26dpy (0.2)  26dpy (0.2)  26dpy (0.2)  4apym (0.25)  4apym (0.25)  acp (+)[b]  acp (+)[b]

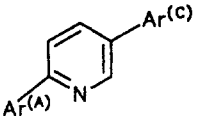
Table 1. (contd.)

III. 'Crossed' Reactions

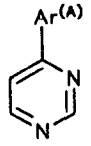
e) 1a C + 1b A
A: Ar = Ph
C: Ar = *p*-MeOPh



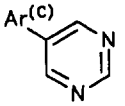
26dpy (0.2)



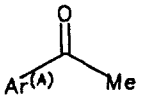
25dpy (0.25)



4apym (0.3)

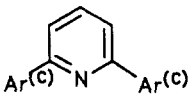


5apym (0.25)

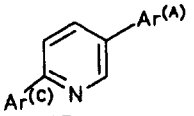


acp (+)[b]

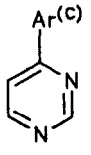
f) 1a A + 1b C
A: Ar = Ph
C: Ar = *p*-MeOPh



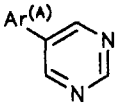
26dpy (0.2)



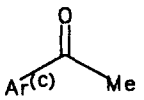
25dpy (0.25)



4apym (0.3)



5apym (0.25)

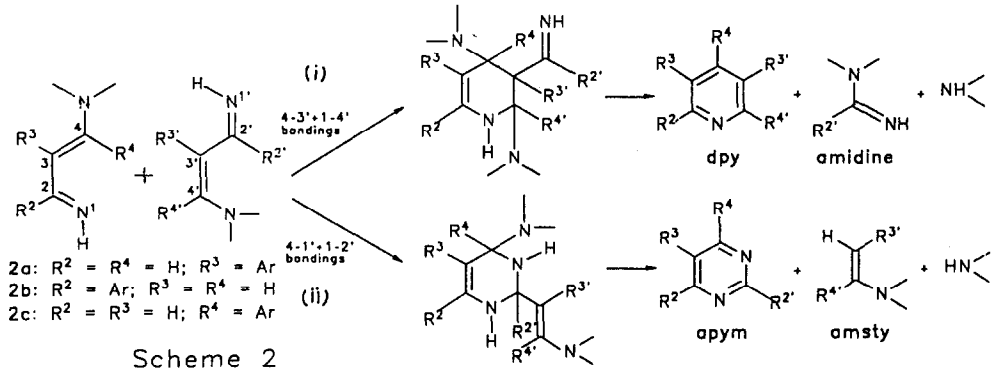


acp (+)[b]

[a] Approximate ratios of components averaged from different runs.

[b] Presence detected (see Experimental).

substituted salts **1b**[2b,c,e] to the cyclodimerising conditions gave mixtures of 2,6-diarylpyridines (**26dpy**) and 4-arylpyrimidines (**4apym**; Table 1 b), products whose structures constituted clear evidence that both of the isomeric vinamidines **2b** and **2c** (or their N,N-demethylated analogues)[5] were being cogenerated on exposure of salts **1b** to ammonia (Scheme 1); their cyclocondensations are as highly orientation selective and poorly regioselective as the cyclodimerisations of vinamidines **2a** (Scheme 2).[6] There was a further, and interesting, implication that vinamidines **2b** tended not to react as 2-centre participants and vinamidines **2c** not as 4-centre participants since none of the products from such participations (*e.g.* **4apy** or **24dpym** from **2c** + **2b** reactions, **2apy** or **24dpym** from **2b** + **2b** reactions or **24dpy** from **2c** + **2c** reactions)[7] were found. Since vinamidines **2a** had not shown any preference in their mode of participation in their 'sole' reactions, the simplest way to confirm the existence of a difference in behaviour on the part of vinamidines **2b** and **2c** was to carry out 'crossed' cyclocondensations employing 1:1 mixtures of salts **1a** and **1b** bearing different *p*-substituents on the phenyls and noting the origins of the cyclising moieties in the products.



Scheme 2

Results

Independent 'mixed' reactions, where the reactants were 1:1 mixtures of salts **1a** or of salts **1b** bearing dissimilar substituents, were conducted prior to the 'crossed' reactions since the identification of products exclusive to the latter was expected to be simplified when once those from concurrent 'mixed' reactions had been identified. The products formed in the 'mixed' reactions were as expected: 3,5-di-(*p*-anisyl)-, 3-*p*-anisyl-5-phenyl- and 3,5-diphenylpyridines as well as 5-*p*-anisyl- and 5-phenylpyrimidines from a mixture of salts **1a** with phenyl and *p*-anisyl as the substituents (Table 1 c) and, correspondingly, mixtures of 2,6-disubstituted pyridines and 4-substituted pyrimidines with the appropriate labels from a mixture of a similar pair of salts **1b** (Table 1 d). The production of **25dpy** *viz.* 2-phenyl-5-*p*-anisyl- and 2-*p*-anisyl-5-phenylpyridines, showing their origins to be, respectively, in **2b** + **2a** and **2a** + **2c** reactions, was realised in the 'crossed' reactions (Table 1 e & f),[8] together with all the products to be expected from concurrent 'mixed' reactions. There was, here again, no evidence of products from either **2a** + **2b** reactions (*e.g.* a **3apy** or a **25dpym**) or **2c** + **2a** reactions (*e.g.* a **34dpy**), reconfirming the aforementioned propensities of vinamidines **2b** and **2c**.

Acetophenone (**acp**) or a *p*-substituted acetophenone was found in traces[3d] (^{1}H NMR evidence) in the product mixtures whenever salts **1b** were included in the reactions (Table 1 b-f). While the **acp** were presumed as formed by hydrolysis (during workup) of α-aminostyrenes (**α-amsty**), eliminated during the aromatisation to the **4apym** (Scheme 2 ii), no similar evidence (*e.g.* the presence of an aryl acetaldehyde) could be had for β-aminostyrenes (**β-amsty**), expected to be eliminated during the formation of **5apym** (Scheme 2 ii). Reasons are suggested later for finding the **acp** in much less than molar equivalence of the **4apym** and no evidence at all of aryl acetaldehydes.

Discussion

Concerted and stepwise possibilities[9] had been considered for the formation of the initial cyclates leading to **35dpy** from salts **1a**.[3a] Even though the cyclising reactions of many 1-azabutadienes, seen earlier as concerted cycloadditions[10], are now thought not to be so,[10,11] the FMO method of simple prediction of orientations in [4 + 2] cycloadditions, employing Hückel coefficients and

FMO energies[12] was applied[13] to check whether the orientations favoured for the formation of the precursor cyclates (Scheme 2), initially bonding the softest centres,[12] would be the ones that would have led to the pyridines and pyrimidines found. The FMO method showed that the 1-4' + 4-3' and 1-2' + 4-1' bond formations, leading respectively not only to the pyridines and pyrimidines formed but also to certain other products not formed (examples above), would indeed be associated with high energies of stabilisation (E_{stab}'s).[12,14] However, it was found that the same predictions would follow from a consideration of simple Hückel net atomic charge distributions (Figure 1) which clearly reflect the alternate charge localisations to be expected in a dimethylamino-imino propene. The

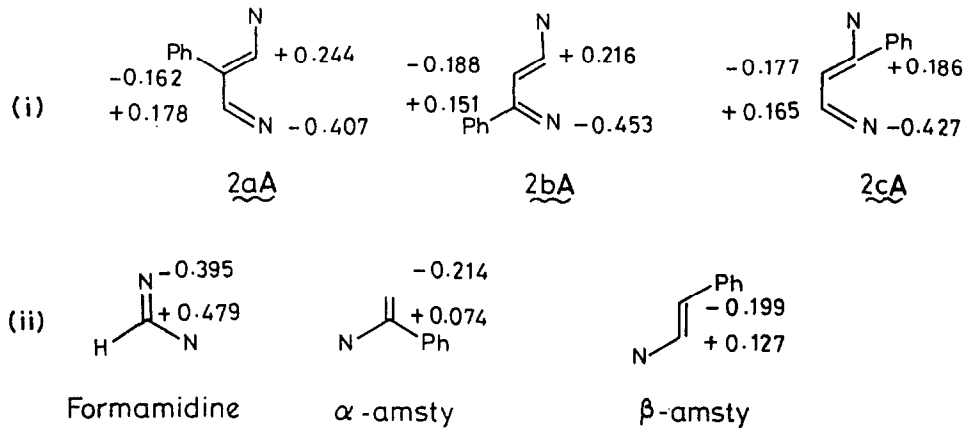


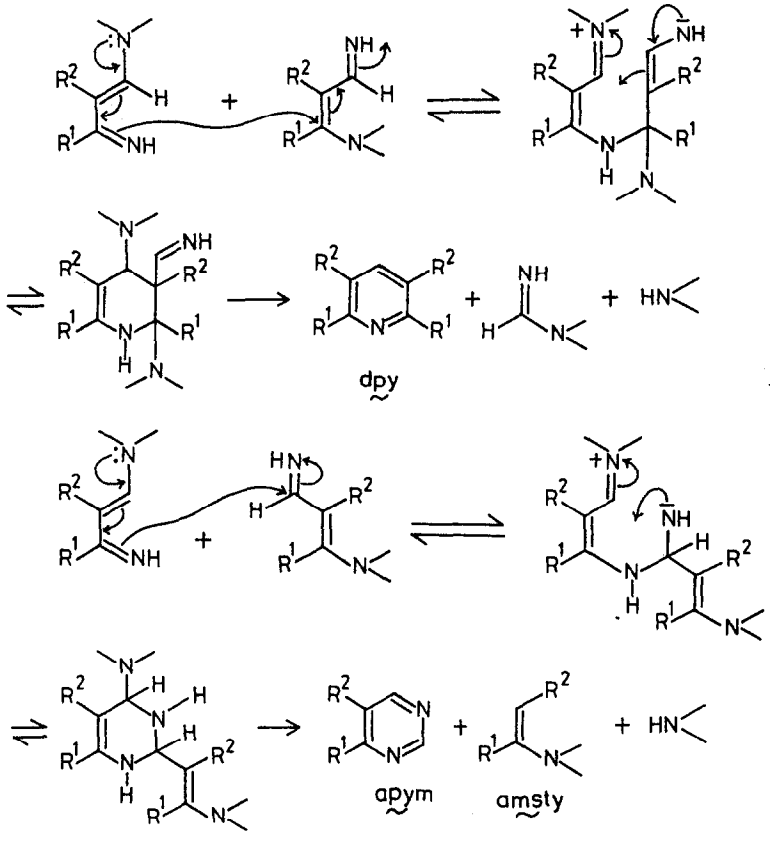
Figure 1

mechanism could, then, very well have been a stepwise one,[15] involving only the probable modes of charge transfers or relocations for forming the initial cyclates *via* zwitterions (Scheme 3), the orientations becoming electrostatically controlled.

Since neither the FMO E_{stab}'s nor electrostatic governance could account for the nonformation of products predicted by either as not disfavoured, the possible role of stereochemical factors in engendering specific discriminations was examined. An immediately apparent one was that vinamidine **2c** could prefer the s-*E* conformation about its C-2-C-3 formal single bond (Scheme 4) and were it to act as a 4-centre participant, the zwitterionic intermediate (Figure 2 i) would have its "C-2-C-3" double bond in the *E*-configuration, not conducive to collapse into a cyclate.

A test for the presence of conformational biases in vinamidines **2a-c** by the method of molecular mechanics,[16] while confirming that vinamidine **2a** is relatively unbiased (s-*E* vs s-*Z*; Table 2), showed a pronounced preference for the s-*E* conformation on the part of vinamidine **2c**, accounting, as just argued, for its reluctance to participate as a 4-centre reactant.[17] But the similarly high preference for the s-*Z* conformation on the part of vinamidine **2b**[18] could not be advanced as a reason for its not having participated as a 2-centre reactant. The raising of steric congestion in the transition states pertinent to the modes of Schemes 2 i and ii could not be sustained[19] as a significant factor since molecular models indicated (particularly clearly with two examples, Figures

2 ii and iii) that a **2b** + **2c** reaction would be likely as disfavoured as a **2b** + **2b** reaction. The first of these would have led to **26dpy** which is formed, and the second to **24dpym** which is not formed.

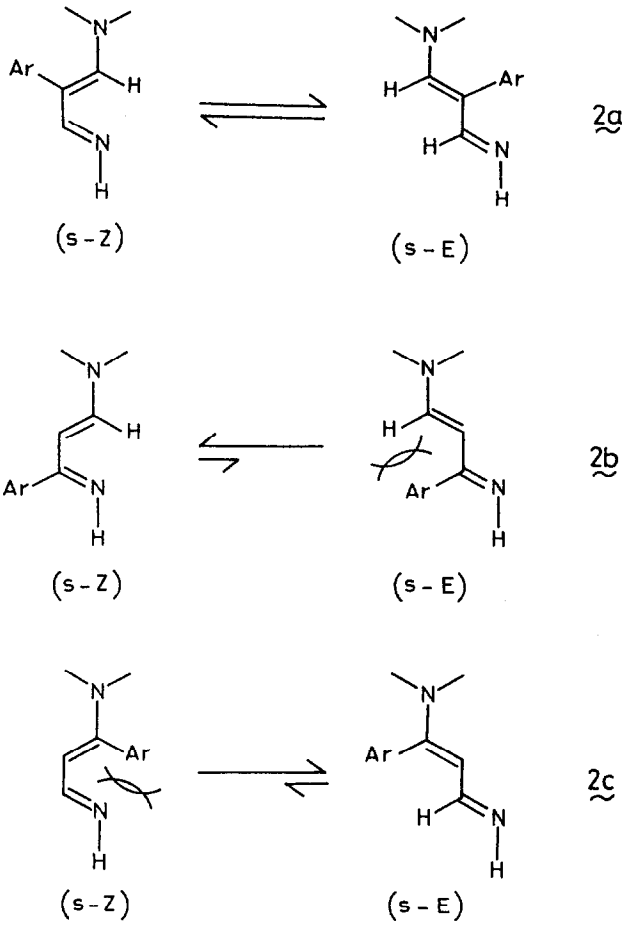


Scheme 3

Table 2. Stabilisation Parameters (k. Cal/mole) and Torsional Angles (°) from Molecular Mechanics

System	Nominal configuration[a]	Heat of formation	Steric energy	Strain energy	Torsional angles N_1-C_4[b]	Ph[c]
2a	s-*Z*, *Z*	21.92	24.37	23.90	20.64	82.24
2a	s-*E*, *Z*	22.22	24.60	24.12	179.94	88.18
2b	s-*Z*, *E*	20.79	21.15	20.65	26.19	33.57
2b	s-*E*, *E*	26.75	22.05	21.57	144.47	39.65
2c	s-*Z*, *E*	56.46	23.36	22.88	40.36	73.07
2c	s-*E*, *E*	47.16	21.32	20.84	177.97	85.05

[a] Of C-2-C-3 and C-3=C-4. [b] The N-1=C-2-C-3=C-4 dihedral angle. [c] The dihedral angles: **2a**: C-4-C-3-*ipso*-*ortho*; **2b**: C-3-C-2-*ipso*-*ortho*; and, **2c**: C-3-C-4-*ipso*-*ortho*.



Scheme 4

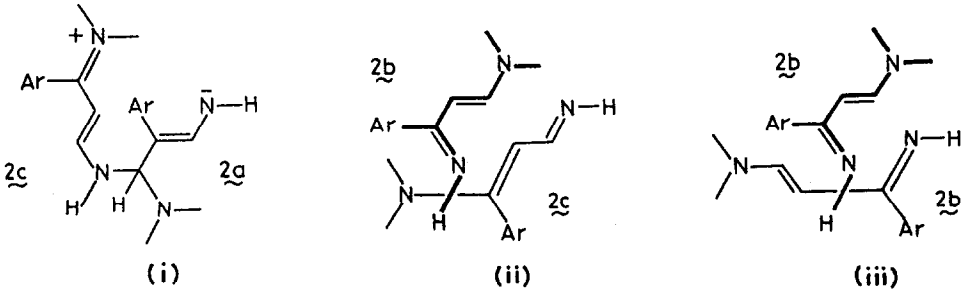
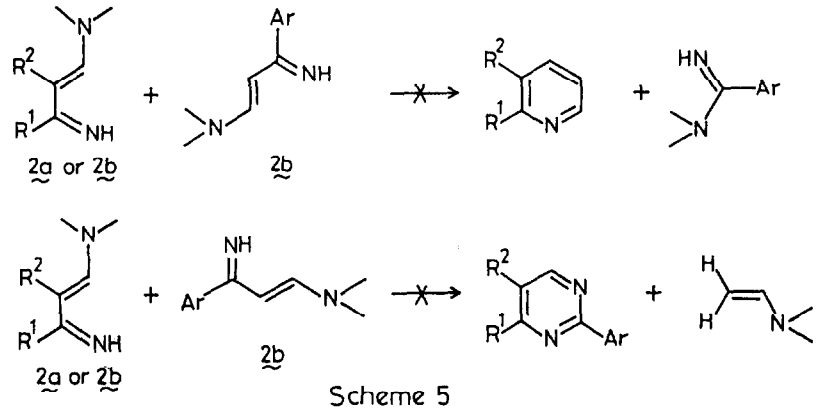


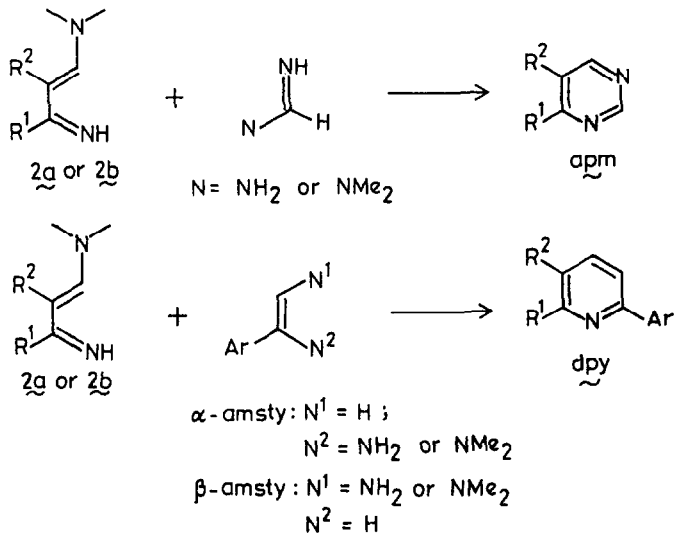
Figure 2

The possibility that a difference in the nature of the eliminations taking place during the aromatisation of the initially formed cyclates could underlie the difference in behaviour of vinamidine **2b** and the other two vinamidines was examined.[20] With vinamidines **2a** and **2c** as the 2-centre



Scheme 5

participants, the eliminants would have been formamidine[21] in the pyridine-forming reactions and α- or β-aminostyrene in the pyrimidine-forming reactions (Scheme 2), apart from ammonia. Had vinamidine **2b** participated as a 2-centre reactant, the eliminants would have been, respectively,



Scheme 6

benzamidine and aminoethylene for the two cases, with the elimination of ammonia turning into a 1,4-reaction (Scheme 5). While it is doubtful if the elimination of benzamidine or aminoethylene could have been anticipated as more difficult than that of formamidine or the aminostyrenes, the existence of such a difference could have made vinamidine **2b** appear not to have reacted as a 2-centre participant.

Both formamidine and the aminostyrenes can stand in for vinamidine **2a** or **2c** as 2-centre participants in the cyclisations, complementary to the main ones: formamidine, eliminated during pyridine-formation (Scheme 2 i), to produce the pyrimidines[22] and the styrenes, eliminated during pyrimidine-formation (Scheme 2 ii), to produce the pyridines (Scheme 6). The net electron density distributions in both formamidine and the aminostyrenes (Figure 1 ii) indicate that the favoured orientations relative to the vinamidine **2a** or **2b** would be just the ones that would have led to the pyrimidines and pyridines found in the main cyclisations (Table 1). While the reactivity of the α-aminostyrenes could be a reason for not finding the acetophenones in the appropriate abundance of molar equivalence of the 4-arylpyrimidines, a somewhat higher reactivity could be that for lack of evidence of β-aminostyrenes (*e.g.* in the form of aryl acetaldehydes) which can undergo various condensations under the reaction conditions.

Conclusion

Vinamidinium salts have been employed for the construction of various pyridines and other aza-aromatics.[2c,3e,23] The cyclocondensations of two similar or different pairs of mono-arylvinamidines leading to the formation of mixtures of diarylpyridines and arylpyrimidines through the eliminative aromatisation of the initially generated cyclates appears to have remained hitherto unreported, however. The cyclocondensations are more likely to be stepwise, involving the intermediacy of zwitterions, rather than concerted [4 + 2] processes, since the vinamidines cannot, apparently, meet various criteria of concertedness. High orientation selectivity seems ensured when the most negative centre (the imino nitrogen) on the vinamidine that acts as the 4-centre participant is seen as attacking the most positive centre on the molecule which acts as the 2-centre participant. The availability of two such centres on the latter leads to a lack of regiospecificity, allowing the formation of both diarylpyridines and arylpyrimidines.

An interesting further aspect of selectivity surfaces when it is noticed that no products are formed from the C-2 aryl substituted vinamidine **2b** having acted as a 2-centre reactant and from the C-4 aryl substituted vinamidine **2c** as a 4-centre reactant. Molecular mechanics have shown that the latter vinamidine has a high preference for the s-*E* conformation about its C-2–C-3 formal single bond. That preference can only lead to (reversibly formed) intermediates that are geometrically constrained from undergoing cyclisation. A high preference for the s-*Z* conformation about its C-2–C-3 formal single bond, shown to be the case for vinamidine **2b**, cannot prevent its acting as a 2-centre participant. However, the elimination of benzamidine or of aminoethylene, required to aromatise the initial cyclates formed whenever vinamidines **2b** participate as 2-centre reactants, may not be as favoured as the eliminations of formamidine and α- or β-aminostyrene when vinamidines **2a** or **2c** are the 2-centre participants and, under a clear possibility that initial cyclate-formation would be reversible, vinamidine **2b** would appear not to have acted as a 2-centre participant.

The eliminated formamidine and aminostyrenes can stand in for vinamidines **2a** or **2c** in reactions complementary to the main cyclocondensations.

Experimental

Melting points, determined for samples taken in open capillaries using a standardised thermometer, are reported as observed. Infrared spectra were recorded on a Perkin-Elmer Model 721 IR spectrophotometer. ^{1}H and ^{13}C (^{1}H decoupled and off-resonance irradiated) NMR spectra were recorded with a JEOL FX90-Q FT NMR instrument with TMS as the internal standard and $CDCl_3$ as the internal lock. Mass spectra, low and high resolution (LR and HR), were obtained under 70 eV EI conditions employing a JEOL JMX-DX 303 mass spectrometer equipped with a D-5000 data processor. TLC tests were carried out by standard procedures. Separation and isolation of components of the product mixtures were carried out by centrifugal TLC employing a Chromatotron^{R} (Harrison Research, USA) in conjunction with a precision fraction collector (Retriever IV, ISCO, USA). Diethylene glycol was a commercial product redistilled under reduced pressure prior to use. Solvents used for extractions, TLC separations and recrystallisations were purified by recommended methods.[24]

Procedure for the Cyclocondensations

A slow stream of anhydrous ammonia was passed through stirred solutions of the well-characterised perchlorate salts 1 prepared by known methods[2] (single materials in the 'sole' reactions and equimolar mixtures of the two components in the 'mixed' and 'crossed' reactions; see text; 20 mmol) in diethylene glycol (50 ml) while being brought to 155-165°. The solutions were maintained within this temperature range for 2 hr under continued slow streaming of ammonia, cooled thereafter, diluted with water and extracted with ether (2 × 100 ml). The combined ether extracts were re-extracted with dil. hydrochloric acid (2N; 2 x 100 ml). A light to deep yellow semisolid which separated on rendering the aqueous acidic extracts basic (pH 8) with 5N sodium hydroxide solution was isolated by extraction with ether (3 × 100 ml). The partly crystalline residues obtained on removal of the ether from the dried, combined extracts were taken to separation by the Chromatotron after preliminary TLC tests. The identity of products from different experiments in a series, thought to be the same, was always confirmed by infrared spectroscopy before any of the fractions were mixed.

The neutral residues, always obtained in small quantities on drying and concentrating the ether layers after extracting the basic components out, were analysed by TLC. Phenylacetaldehydes and acetophenones (acp) were expected as the respective products of hydrolysis of β- and α-aminostyrenes formed during the aromatisation of the initial cyclates (see text). Only the acetophenones (*p*-H, *p*-Me and *p*-OMe) were isolated and the evidence for their identification consisted in the presence of a carbonyl band in the infrared spectra and features in the ^{1}H NMR spectra attributable to ar-Me, acetyl Me or OMe (singlets in the appropriate regions) and the aryl ring (a broadened resonance or an AA'BB' pattern).[25]

Certain weak bases, notably the substituted pyridines, were not fully extracted out by aqueous acid. When once product profiles and patterns of separation by TLC were established, the extracts of TLC bands corresponding to the bases still present in the neutral fractions were mixed (after confirmation of the identification by infrared spectroscopy) with the corresponding materials isolated from separations using the Chromatotron, prior to repurification by crystallisation.

The components were well-separated by mixtures of 10-20% EtOAc with the 'hexane' fraction (b.p. 75-85°) of light petroleum. Diffuse, light yellow, bands remained near the starting positions in the initial chromatographic separations. Material balance based on the formation of the identified pyridines and pyrimidines accounted for conversions to extents of 80% on the average, neglecting losses during the extractions or separations.

Characterisation data on compounds identified have been gathered in Table 3-5.

Table 3 Melting Points and Molecular Weights of Diarylpyridines and Arylpyrimidines

		MP (°C)		MF	MW	
		lit.	obsvd.		calcd.	obsvd.[a]
A.	**Diarylpyridines**					
1.	**35dpy AA**[b]	136-7[c]	138-9	$C_{17}H_{13}N$	231.1048	231.1056
	35dpy BB	-	194-6	$C_{19}H_{17}N$	259.1361	259.1354
	35dpy CC	-	173-5	$C_{19}H_{17}NO_2$	291.1259	291.1256
2.	**26dpy AA**	82-3[d]	80-2	$C_{17}H_{13}N$	231.1048	231.1057
	26dpy BB	165-6[d]	163-4	$C_{19}H_{17}N$	259.1361	259.1337
	26dpy CC	197-8[d]	197-8	$C_{19}H_{17}NO_2$	291.1259	291.1263
3.	**26dpy CA**	125[d]	126	$C_{18}H_{15}NO$	261.1154	261.1155
	25dpy CA	-	154-5	$C_{18}H_{15}NO$	261.1154	261.1162
	36dpy CA	-	158	$C_{18}H_{15}NO$	261.1154	261.1155
	35dpy CA	-	167-8	$C_{18}H_{15}NO$	261.1154	261.1153
B.	**Arylpyrimidines**					
1.	**5apym A**	40[e]	40-1	$C_{10}H_8N_2$	156.0688	156.0697
	5apym B	-	78	$C_{11}H_{10}N_2$	170.0844	170.0015
	5apym C	-	84	$C_{11}H_{10}N_2O$	186.0793	186.0795
2.	**4apym A**	62-3[e]	62	$C_{10}H_8N_2$	156.0688	156.0689
	4apym B	-	76-7	$C_{11}H_{10}N_2$	170.0844	170.0830
	4apym C	-	109-11	$C_{11}H_{10}N_2O$	186.0793	186.0782

[a] By HRMS. [b] Refer to Table 1 and note 1 for abbreviations used. [c] Eliel, E.L.; McBride, R.T.; Kaufmann, St. *J.Am. Chem. Soc.*, **1953**, *75*, 4291. [d] Newkome, G.R.; Fisher, D.L. *J. Org. Chem.*, **1972**, *37*, 1329. [e] Wagner and Jutz in ref. 22.

Table 4 ^{1}H NMR Chemical Shifts (δ ex-TMS; 90 MHz; $CDCl_3$) on Diarylpyridines and Arylpyrimidines

		Heteroring and	Aryl	Me
A.	Diarylpyridines			
1.	35dpy AA	8.90 (br, 2H) 8.24 (br, 1H)[a]	7.55 (m, 10H)	–
	35dpy BB	8.76 (br, 2H) 8.00 (t, 1H)[a]	7.20 (AA'BB', 2 x 4H)	2.44 (s, 6H, 2 × C-Me)
	35dpy CC	8.69 (br, 2H) 7.89 (s, 1H)[a]	7.23 (AA'BB', 2 x 4H)	3.80 (s, 6H, 2 × OMe)
2.	26dpy AA	7.86-7.48 (AB_2, 3H)	8.24-8.00 (m, 4H) 7.48-7.27 (m, 6H)	–
	26dpy BB	7.85-7.63 (AB_2, 3H)	8.35-7.32 (AA'BB', 2 x 4H)	2.29 (s, 6H, 2 × C-Me)
	26dpy CC	7.85-7.30 (AB_2, 3H)	8.30-6.80 (AA'BB', 2 x 4H)	3.89 (s, 6H, 2 × OMe)
3.	26dpy CA	8.30-6.90 (AA'BB' & AB_2, 12H)		3.87 (s, 3H, OMe)
	25dpy CA	8.84 (br, 1H, H-6)[a] 7.95-6.85 (AA'BB'& AB_2, 11H)		3.83 (s, 3H, OMe)
	36dpy CA	8.82 (br, 1H, H-6) 8.05-6.86 (m, AB & AA'BB', 11H)		3.84 (s, 3H, OMe)
	35dpy CA	8.87 (br, 2H, H-2 & 6), 8.18 (br, 1H, H-4), 7.80-6.92 (m, 9H)		3.85 (s, 3H, OMe)
B.	Arylpyrimidines			
1.	5apym A	9.21 (br, 1H, H-2)[a] 8.93 (br, 2H, H-4&6)	7.60 (br, 5H)	–
	5apym B	9.20-8.94 (br, 3H)	7.40 (AA'BB', 4H)[b]	2.46 (s, 3H, C-Me)
	5apym C	9.16 (br, 1H, H-2)[a] 8.91 (br, 2H, H-4&6)	7.27 (AA'BB', 4H)[b]	3.86 (s, 3H, OMe)
2.	4apym A	9.30 ('s', 1H)[c] 8.76 ('d', 1H) 7.74 (dd, 1H)	8.15 (m, 2H) 7.53 (m, 3H)	–
	4apym B	9.26 ('s', 1H)[c] 8.74 ('d', 1H) 7.72 (dd, 1H)	8.04-7.29 (AA'BB', 4H)	2.46 (s, 3H, C-Me)
	4apym C	9.21 ('s', 1H)[c] 8.70 ('d', 1H) 7.70 (dd, 1H)	8.11-7.03 (AA'BB', 4H)	3.90 (s, 3H, OMe)

[a] Not evident as AB_2 spectrum. [b] Centre of AA'BB' system. [c] ABX or AMX pattern.

Table 5 ^{13}C NMR Chemical Shifts (δ ex-TMS; 22.49 MHz; $CDCl_3$) on Diarylpyridines and Arylpyrimidines

A. Diarylpyridines

		2	3	4	1'	2'	3'	4'	Me
1.	**35dpy AA**	147.04	137.86	132.85	136.75	127.38	129.16	128.33	–
	35dpy BB	146.22	138.31	132.78	134.84	127.15	129.96	138.31	21.29
	35dpy CC	145.18	135.04	130.70[a]	130.50[a]	127.96	114.39	159.34	55.04
2.	**26dpy AA**	156.51	118.48	137.33	139.39	126.93	128.67	128.88	–
	26dpy BB	156.73	118.05	137.33	138.85	126.93	129.42	136.90	21.40
	26dpy CC	155.22	116.54	131.27	137.12	127.48	113.72	159.98	54.78

		2	3	4	5	6	1' / 1"	2' / 2"	3' / 3"	4' / 4"	Me
3.	**26dpy CA**	156.34[b]	117.72	137.27	117.72	156.34[b]	139.53 / 132.02	126.90 / 128.21	128.57 / 114.03	127.50 / 160.51	55.27
	25dpy CA	156.40	117.18[b]	135.06	137.87	148.06	137.33 / 132.46	127.04 / 128.23	129.21 / 114.15	117.18[b] / 160.63	55.42
	36dpy CA	159.90	120.50	134.73	139.22	147.89	130.25[b] / 130.25[b]	126.93 / 128.97	128.20 / 114.74	-[c] / 159.89	55.55
	35dpy CA	146.27	136.48[b]	132.40	136.48[b]	146.05	137.71 / 157.43	127.20 / 129.04	128.18 / 114.52	129.37 / 159.81	55.26

B. Arylpyrimidines

		2	4[d]	5	6[d]	1'	2'	3'	4'	Me
1.	**5apym A**	157.27	154.56	133.97[b]		133.97[b]	126.71	129.20	128.77	–
	5apym B	157.02	154.37	138.78		131.15	126.51	129.94	133.92	21.04
	5apym C	156.62	154.02	133.54		126.17	127.80	114.69	160.19	55.10
2.	**4apym A**	158.57	163.01	116.42	156.84	135.92	126.61	128.45	130.51	–
	4apym B	158.72	163.49	116.29	156.93	133.45	126.78	129.52	141.20	21.18
	4apym C	158.60	161.94	115.81	156.81	129.75	128.45	114.04	163.01	55.10

[a] May be interchanged. [b] Accidentally isochronous. [c] line not seen. [d] C-4 = C-6 in **5apym**.

Computational

Computation of simple Hückel net atomic charge distributions[13] (Figure 1) was carried out by implementing a published[26] Fortran program after suitable updating and including a subroutine capable of diagonalising nonsymmetric square matrices (DIRNM).[27] The complete modified program was tested with pyridine and 1- and 2-azabutadienes as examples.[3a,b]

The molecular mechanics calculations were carried out using an available version of the MMPMI[28] program which employs a well-tested force field (termed MM2) together with the VESCF procedure for the π-energy calculations. Geometry optimisations were started with N-1-C-2-C-3-C-4 as a planar array (s-*Z* and s-*E*) in each case, taking into account that pairs of possibilities arise when the s-*Z* and s-*E* conformations about the C-2-C-3 formal single bond are combined with the *E*- and *Z*-configurations of the C-3-C-4 double bond (with reference to C-2-C-3-C-4-NMe_2). Results gathered in Table 2 (from which data pertinent to the highly destabilised forms with the *Z*-configuration about the C-3-C-4 double bond have been omitted) show that local minima are reached at the roughly planar s-*Z* and s-*E* conformations. The absence of a crossover from an s-*Z* to an s-*E* conformation or *vice versa* in any of the cases during the geometry optimisations was taken as indicating that the pertinent energy minima are separated by high barriers. The s-*Z* and s-*E* conformations, conjectured as respectively favoured by vinamidines **2b** and **2c** before the calculations (Scheme 4), are the ones stabilised in terms of both steric and strain energies, the two parameters significant when the relative stabilities of different conformations are compared.[28b] The differences in the heats of formation follow the same trend and appear sharper. Interestingly, the departure of the N-1-C-2-C-3-C-4 array from uniplanarity, small in others, is large for the s-*E* conformation of **2b** and the s-*Z* conformation of **2c**, indicating that the conjugative stabilisation at uniplanarity is mostly lost in them for steric reasons. The phenyl groups tend to get twisted out of conjugation[6] in all the cases, even coming into near orthogonality in systems **2a** and **2c**.

Acknowledgements

The authors wish to thank Dr. A.J. Boulton, University of East Anglia, England for directing their attention to the chemistry of vinamidinium systems and Prof. J. Chandrasekhar for helpful discussions. BJ and INNN thank the Director, IISc, and the UGC (India) for research fellowships. SNB thanks the CSIR (India) for support under an Emeritus Scientists' scheme.

References and Notes

1. It has been found convenient to designate structures/compound types using the following abbreviations: **a** - aryl; **d** - diaryl; **py** - pyridine; **pym** - pyrimidine; **amsty** - aminostyrene and **acp** - acetophenone. The numbers preceding the letters indicate positions of the aryl substituents on the heterorings; aryl groups, phenyl, *p*-tolyl, *p*-anisyl are indicated in order by **A**, **B** and **C**.

2. a. Arnold, Z. *Coll. Czech. Chem. Commun.* **1961**, *26*, 3051; b. Holy, A.; Krupicka, J.; Arnold, Z. *Coll. Czech. Chem. Commun.* **1965**, *30*, 4127; c. Jutz, C. *Topics in Current Chemistry* **1978**, *73*, 125; d. Balasubrahmanyam, S.N.; Radhakrishna, A.S. *J.C.S. Perkin II* **1977**, 1388; e. Balasubrahmanyam, S.N.; Mallick, I.M. *Org. Magn. Reson.* **1982**, *19*, 160.

3. a. Jeyashri, B.; Balasubrahmanyam, S.N. *Ind. J. Chem.* **1985**, *24B*, 341; b. Jeyashri, B. *Ph.D. thesis*, Indian Institute of Science, **1987**; c. Narayanan Namboothiri, I.N. *Ph.D. Thesis*, Indian Institute of Science, **1993**; d. **5apym** were detected subsequent to the work reported in ref. 3a, the methods of separation employed at the time having been, probably, ineffectual. Since a wide variety of substituted diazapropenium salts can be prepared in facile manner (refs. 2), it appeared that the cyclodimerisation method could be complementary to the ones reported for substituted pyridines by Komatsu *et al.* (Komatsu, M.; Takematsu, S.; Ueseka, M.; Yamamoto, S.; Ohshiro, Y.; Agawa, T. *J. Org. Chem.* **1984**, *49*, 2691). But as a preparative procedure it was compromised when **5apym**

were found to be coformed with the **35dpy**, making a separation step necessary; e. The methods of separation and analysis adopted later (refs. 3b, 3c, Balasubrahmanyam, S.N.; Jeyashri, B. *Indian J. Chem.* **1988**, *27B*, 559 and Experimental) are believed to have been capable of isolation/detection of components constituting at least 2% of the product mixtures.

4. The numbers indicate the positions on the vinamidines **2**, the primed ones referring to those on the 2-centre participant.

5. It appeared that only one of the dimethylamino goups would be replaced, the replacement of the other, believed to require a vinylogous displacement, seeming not very likely under the experimental conditions. Because such replacement would be necessary for the isomeric vinamidines **2b** and **2c** to enter equilibrium, the initial compositions of the reaction mixture from salts **1b** could be taken to have been kinetically controlled, with the two vinamidines not necessarily formed in equal amounts. The term "vinamidine" has been used to designate vinylogous amidines with one dimethylamino group and one imino group (structures **2**).

6. Both ultraviolet absorption data (Kucera, J.; Arnold, Z. *Coll. Czech. Chem. Commun.* **1967**, *32*, 1704) and ^{1}H dynamic NMR behaviour (ref. 2d) have shown that the vinamidinic and aryl moieties maintain a high dihedral angle in the aryl monosubstituted vinamidiniums **1** (also, Filleux-Blanchard, M.-L.; le Botlan, D. *Org. Magn. Reson.* **1977**, *9*, 618 and refs. to previous work). Since a similar situation may obtain in the derived vinamidines **2**, attenuated passage of information between the two moieties may cause the behaviour of the vinamidinic part not to be too responsive to the position of the aryl substituent.

7. **4apym** can, in principle, be formed in **2c** + **2c**, **2c** + **2b** or **2b** + **2c** reactions but the behaviour of vinamidines **2b** and **2c** would restrict the pathway to that mentioned last.

8. No evidence could be had for the formation of **35dpy**, to be expected from concurrent 'sole' reactions of salts **1a**. A possible explanation could lie in the **2a** + **2a** reactions being the slowest under the 'crossed' conditions.

9. Evidence said to show a change in the mechanism from concerted to stepwise depending on the nature of the "dienophile" in the cyclocondensations of 1-(N,N-dimethyl)aminobuta-1,3-dienes has been discussed: Sustmann, R.; Rogge, M.; Nüchter, U.; Bandmann, H. *Chem. Ber.* **1992**, *125*, 1647 and 1657; Rogge, M.; Nüchter, U.; Harvey, J. *Chem. Ber.* **1992**, *125*, 1665.

10. Boger, D.L. *Chem. Rev.* **1986**, *86*, 781.

11. Barluenga, J.; Rubio, V.; Gotor, V. *J. Org. Chem.* **1980**, *45*, 2592. Systems studied by these authors, 1,2,3-triaryl substituted diiminopropylidenes (cognate in structure *via* tautomerism with vinamidines **2a-c**), do not undergo cyclo self-condensations, possibly for steric reasons. The mechanism suggested for their cyclising reactions with systems containing activated multiple bonds to form dihydropyrimidines is a stepwise one, resembling that given in Scheme 3.

12. Eisenstein, O.; Lefour, J.M.; Anh, N.-T.; Hudson, R.F. *Tetrahedron* **1977**, *33*, 523; also, Eisenstein, O.; Lefour, J.M.; Anh, N.-T. *J. Chem. Soc. Chem. Commun.* **1971**, 969.

13. Details of the parameters assumed, methods of calculation and results are available from the authors (also ref. 3b and 3c).

14. Systems closely analogous to vinamidines **2**, known to participate in self-condensative cyclodimerisations involving heteroatoms, are substituted acraldehydes and thioacraldehydes. The reason ascribed for the opposite orientation selectivities found with the latter two systems (in reactions regarded as concerted but asynchronous) is that FMO interactions oppose and overcome electrostatic repulsions in the first but act additively in the second (first citation in ref. 12).

15. Criteria for concertedness of [4 + 2] reactions in which 1-azabutadienes may participate have been detailed: the $LUMO_{diene}$-controlled cycloadditions to N-benzenesulphonylated enamine of 1-acetylcyclohexene: Boger, D.L.; Kasper, A.M. *J. Am. Chem. Soc.* **1989**, *111*, 1517. Vinamidines **2** cannot meet most of these criteria in their cyclocondensations.

16. Clark, T. *Handbook of Computational Chemistry*, Wiley/Interscience, New York, **1985**, Chapter 2, p. 12-92 ff.

17. The Curtin-Hammett Principle requires that the ratio of intermediates/products, irreversibly formed from reactions in which the s-*E* and s-*Z* conformations of vinamidine **2c** had participated independently, reflect the ratio of the respective energies of activation. Our results, implying that vinamidine **2c** had not participated as a 4-centre reactant, may mean that the activation energies of reactions that could have provided evidence of its having participated as a 4-centre reactant are intrinsically higher than those in which it had actually participated as a 2-centre reactant.

18. The preference for the s-*Z* conformation by vinamidine **2b** may be seen as facilitating its participation as a 4-centre reactant in a concerted process. A basis for this is a suggestion that an increase in the population of the s-*Z* conformation in the N,N-dimethylhydrazone of methacrolein promotes its dienic reactivity in ($HOMO_{diene}$-controlled) cycloadditions: -Poncin, B.S.; -Frisque, A.-M. H.; Ghosez, L. *Tetrahedron Lett.* **1982**, 3261.

19. Steric congestion in the transition state does not in, any case, deter Diels-Alder reactions *e.g.* the cycloaddition of methyl methacrylate to 2,2-dimethylhexa-3,5-diene: Inukai, T.; and Kojima, T. *J. Org. Chem.* **1971**, *36*, 924.

20. Reversibility of initial cyclate formation must be assumed (under either the concerted or the stepwise mode) if the nature of eliminations were to be a factor in making vinamidine **2b** appear not as a 2-centre participant. Similarly, reversibility of zwitterion formation (Figure 2 i) is a condition necessary if the s-*E* conformational bias in vinamidine **2c** is invoked as a factor that makes it appear not to have acted as a 4-centre participant in a stepwise process.

21. N,N-dimethylated analogues are intended to be included when the amidines or amines are mentioned by name (Scheme 1 and note 5).

22. Substituted pyrimidines are formed in high yield when vinamidinium salts of type **1** are allowed to react with various amidines in the presence of sodium methoxide (Wagner, R.M.; Jutz, C. *Chem. Ber.* **1971**, *104*, 2975; Shkurko, O.P.; Khmeleva, E.P.; Mamaev, V.P. *Izv. Sib. Otd. Akad. Nauk. SSSR, Ser. Khim. Nauk.* **1978**, 106; *Chem. Abstr. 90*, 12153s). The transient intermediates in this synthetically useful procedure could very well be vinamidines and their reactions with amidines non-concerted and electrostatically controlled. The energy differences between the FMOs of vinamidines **2** and formamidines are much larger than those between the former and the FMOs of aminostyrenes (note 13).

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(*Received in UK* 10 *March* 1994; *revised* 9 *May* 1994; *accepted* 13 *May* 1994)