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Aminoimidazo[1,2-*a*]pyridines: regioselective synthesis of substituted imidazonaphthyridines, azacarbolines and cyclazines

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Abstract—In order to study the regioselectivity of thermal cyclocondensation, aminoimidazo[1,2-*a*]pyridines (AIP) **5a**–**e** were prepared, further converted into iminophosphoranes **7a**–**e**, and ultimately converted regioselectively in angular annulated imidazonaphthyridines (IN) **8a**, **10a**, **11a**, **12a** or linear annulated dipyridoimidazole (DPI) **17a**. From 2-substituted derivative **23**, the *peri* annulated product **24a** was obtained. The starting amines **5a**–**f** reacted with aldehydes to yield regioselectively IN **8a**–**c**, **10a**–**c**, **11a**–**c**, **12a**,**b**, DPI **16a**–**e**, **17a**–**d** and TIBO like structures (±)-**13** and **24a**–**c**, as proved by X-ray analysis. The 1,2- or 1,4-addition between amines and α,β-unsaturated aldehydes concerning the pyridine and imidazole moieties is discussed in the light of these results. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Tricyclic dipyridoimidazoles show considerable pharmacological potential. Dipyridoimidazoles (GLU-P1, P2)[1,2] are azaisosteres of carbolines,[3] and are thus of pharmacological interest as potential anticancer compounds. On an other hand, some pyrido[4,3-*b*]indoles (Trp-P1 and P2) have been reported to have genotoxic activity.[4] Imidazonaphthyridines are analogs of methoxatin,[5] and have potential implications as inhibitors of bacterial coenzymes. Finally, pyridoimidazodiazepines can be regarded as isosteres of 4,5,6,7-tetrahydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-2(1*H*)-ones (TIBO),[6] and are therefore of great interest as potential anti-HIV agents.

As a continuation of our work on the synthesis and the applications of pyridoimidazoles,[7] we envisaged the preparation of dipyridoimidazoles, imidazonaphthyridines, and pyridoimidazodiazepines by heteroannulation of the appropriate aminoimidazo[1,2-*a*]pyridines **5** (Fig. 1). To our knowledge there are very few precedents for this kind of heteroannulation.[1,7b] From among the known methods for obtaining nitrogen heterocycles, we chose to study the heteroannulation via the iminophosphoranes,[8,9] and the direct thermal condensation of the AIPs with aldehydes. The use of acrolein would enable us to determine whether the reactions went to completion. If this were the case, the results obtained by using crotonaldehyde as a reactant would provide further insight into the reaction mechanism. In the case of thermal annulation, we decided to extend these studies to acetaldehyde and propanal because using the aldol condensation products would increase the potential for diversification, giving rise to small collections of the three families of compounds.

2. Results and discussion

Amines **5a** and **5c**–**e** were prepared as described previously.[7b,10–12] Multigram quantities of the required amines **5b** and **5f**[13] were obtained from esters **1b** and **1f**[14] as shown in Scheme 1. Thus, the esters were transformed to the corresponding carbohydrazides **2b**,**f**, treatment of which with NaN_3 and $NaNO_2$/HCl gave carbazides **3b**,**f**. Heating of compounds **3b**,**f** in EtOH gave the corresponding carbamates **4b**,**f** by a Curtius rearrangement. Saponification of the carbamates led to amines **5b** and **5f** in 55 and 47% overall yield, respectively.

Two routes to synthesis of iminophosphoranes **7a**–**e** were developed (Scheme 2). Diazotation of amines **5a**–**c** with $NaNO_2$/HCl followed by addition of NaN_3 yielded azides **6a**–**c** as stable solids, wich were then converted to **7a**–**c** by the Staudinger reaction using $P(C_6H_5)_3$ in CH_2Cl_2. However, this method was unsatisfactory with amines **5d**–**f**. Azide **6d**

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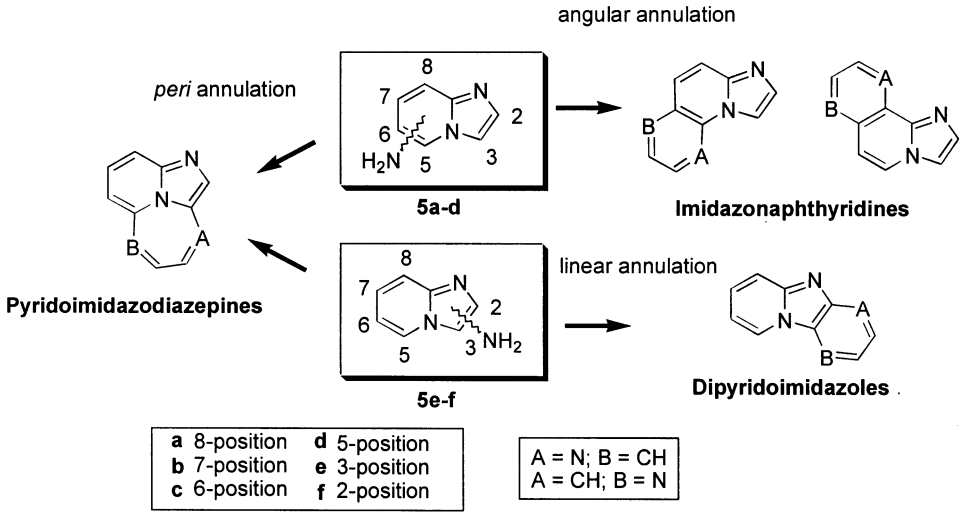
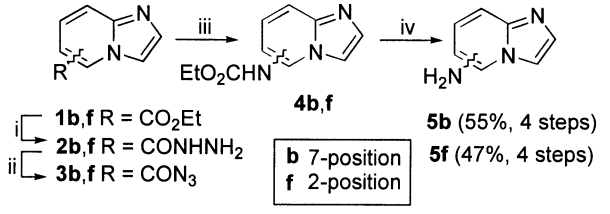


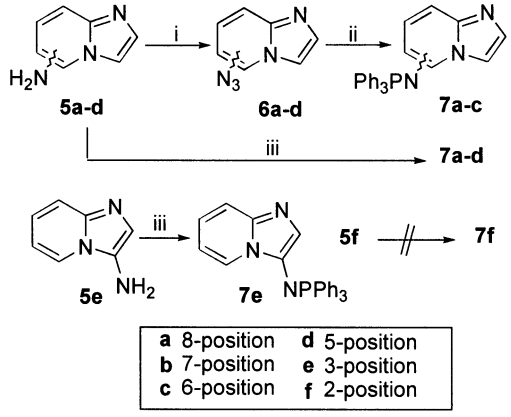
Figure 1.

was obtained in low yields, probably because the intermediate diazonium salt generated from **5d** is unstable.[15] Amine **5e** led to a complex mixture of products from which only 2-aminopyridine (8%) could be identified, indicating the presence of a ring opening process.[16] 2-AIP **5f** did not react.

The second method for obtaining iminophosphoranes **7a**–**c** consisted of treatment of amines **5a**–**c** with $P(C_6H_5)_3/CCl_4/NEt_3$ in CH_3CN. This was successful in yielding **7a**–**e**, but once again **5f** did not react.

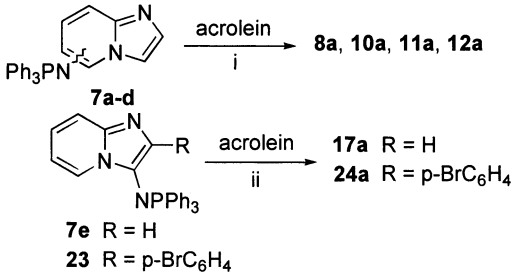


Scheme 1. *Reagents and conditions*: (i) NH_2NH_2, EtOH, Δ; (ii) $NaNO_2$/HCl, NaN_3; (iii) EtOH, Δ; (iv) NaOH (5N), Δ.



Scheme 2. *Reagents and conditions*: (i) $NaNO_2$/HCl, 0°C, NaN_3; (ii) PPh_3, CH_2Cl_2, rt; (iii) PPh_3, CCl_4, NEt_3, CH_3CN.

Iminophosphoranes **7a**–**e** reacted with acrolein in nitrobenzene or 1,2-dichlorobenzene to give the corresponding imidazonaphthyridines **8a**, **10a**, **11a**, **12a**, and dipyridoimidazole **17a** (Scheme 3, Table 1). Attempts to improve the cyclization by varying the temperature and the reaction times were unsuccessful.



Scheme 3. *Reagents and conditions*: (i) nitrobenzene, Δ; (ii) 1,2-dichlorobenzene, Δ; see Schemes 4, 6 and 8 for chemical structures.

Table 1. Reactions of iminophosphoranes **7a**–**e** and **23** with acrolein (3 equiv.)

Entry	Iminophosphorane	Method C (% yield)
1	**7a**	**8a** (17)[a]
2	**7b**	**10a** (3)[a]
3	**7c**	**11a** (9)[a]
4	**7d**	**12a** (9)[a]
5	**7e**	**17a** (16)[b]
6	**23**	**24a** (13)[b]

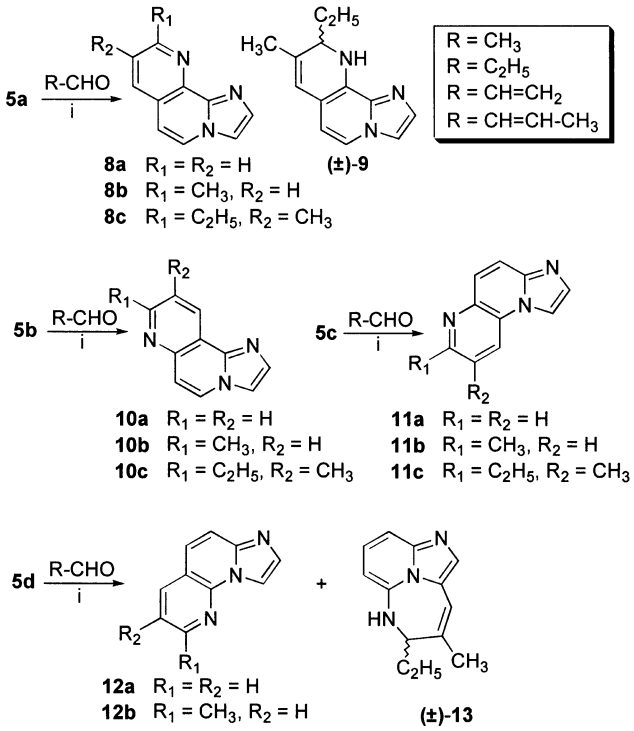
[a] Nitrobenzene, Δ.
[b] 1,2-Dichlorobenzene, Δ.

Thermal condensation of amine **5a** with acrolein, crotonaldehyde, or acetaldehyde, in refluxing 1,2-dichlorobenzene (method A) led to the desired [1,7]naphthyridines **8a**–**b** (Scheme 4, Table 2). The regioselectivity of the condensation with unsaturated aldehydes (or saturated aldehydes after aldolization/crotonization) indicated that the reaction proceeds via a conjugate 1,4-addition followed by ring closure and final aromatization (Scheme 7, entry 1). The

fact that compound (±)-**9**, the non-aromatic intermediate, was obtained together with naphthyridine **8c** in the condensation of **5a** with propanal proved the proposed mechanism. Addition of 10% Pd/C to the reaction mixture (method B) resulted in a considerable increase in the yields of the naphthyridines **8a**–**c**.

Under the conditions of method B, amines **5b** and **5c** yielded the corresponding isomeric [1,6] and [1,5]naphthyridines **10a**–**c**, **11a**–**c** by angular annulation (Scheme 4). The cyclization of 6-AIP **5c** on C5 rather than on C7 can be explained by the higher electron density of C5 (Fig. 2), and by the higher thermodynamic stability of compounds **11**. Theoretical calculations showed that compound **11b** is about 9.1 kcal mol^{-1} more stable than the linear naphthyridine **15**. Similar calculations allowed us to explain the preferred cyclization of compound **5b** on C8 rather than on C6, naphthyridine **10b** being more stable than compound **14** by 10.9 kcal mol^{-1}.

In the case of compound **5d**, both an angular and a *peri* annulation process can take place a priori. However, only the angular annulated compounds **12a** and **12b** were obtained using an excess of acrolein, crotonaldehyde or acetaldehyde, and the yields were extremely low. In contrast only the *peri* annulated structure (±)-**13** was detected in the reaction of **5d** with an excess of propanal.



Scheme 4. *Reagents and conditions*: (i) 1,2-dichlorobenzene, Δ (method A); 1,2-dichlorobenzene, 10% Pd/C, Δ (method B).

We then investigated the thermal condensation of the 2-AIP **5f** and 3-AIP **5e**, in which the amino group is at the more activated imidazole ring. Amine **5f** reacted with acrolein, crotonaldehyde, acetaldehyde, and propanal to yield

Table 2. Thermal condensation of amines **5a**–**f** and **22** with aldehydes

Entry	Amine	Aldehyde	Method A[a] (% yield)	Method B[b] (% yield)
1	**5a**	Acrolein	**8a** (17)	**8a** (32)
2	**5a**	Crotonaldehyde	**8b** (18)	**8b** (58)
3	**5a**	Acetaldehyde	**8b** (9)	**8b** (44)
4	**5a**	Propanal	(±)-**9** (24)–**8c** (17)	**8c** (48)
5	**5b**	Acrolein	**10a** (2)	**10a** (4)
6	**5b**	Crotonaldehyde	**10b** (12)	**10b** (18)
7	**5b**	Acetaldehyde	**10b** (4)	**10b** (5)
8	**5b**	Propanal	**10c** (20)	**10c** (13)
9	**5c**	Acrolein	**11a** (10)	**11a** (79)
10	**5c**	Crotonaldehyde	**11b** (4)	**11b** (39)
11	**5c**	Acetaldehyde	**11b** (31)	**11b** (58)
12	**5c**	Propanal	**11c** (25)	**11c** (53)
13	**5d**	Acrolein	**12a** (1)	**12a** (2)
14	**5d**	Crotonaldehyde	**12b** (1)	**12b** (14)
15	**5d**	Acetaldehyde	**12b** (5)	**12b** (2)
16	**5d**	Propanal	(±)-**13** (2)	ND[c]
17	**5e**	Acrolein	**17a** (6)	**17a** (30)
18	**5e**	Crotonaldehyde	**17b** (13)	(±)-**20** (23)
19	**5e**	Acetaldehyde	**17c** (23)	**17c** (41)
20	**5e**	Propanal	**17d** (8)	**16d** (48)
21	**5f**	Acrolein	**16a** (38)	**16a** (28)
22	**5f**	Crotonaldehyde	**16b** (17)	**16b** (27)
23	**5f**	Acetaldehyde	**16c** (40)	**16c** (28)
24	**5f**	Propanal	**16d** (8)	**16d** (17)–**16e** (18)
25	**22**	Acrolein	**24a** (30)	**24a** (27)
26	**22**	Crotonaldehyde	(±)-**24b** (18)–**25a** (8)	(±)-**24b** (42)
27	**22**	Acetaldehyde	(±)-**24b** (44)	(±)-**24b** (11)
28	**22**	Propanal	(±)-**24c** (53)	(±)-**24c** (27)

[a] 1,2-Dichlorobenzene, Δ.
[b] 1,2-Dichlorobenzene, 10% Pd/C, Δ.
[c] ND=not detected.

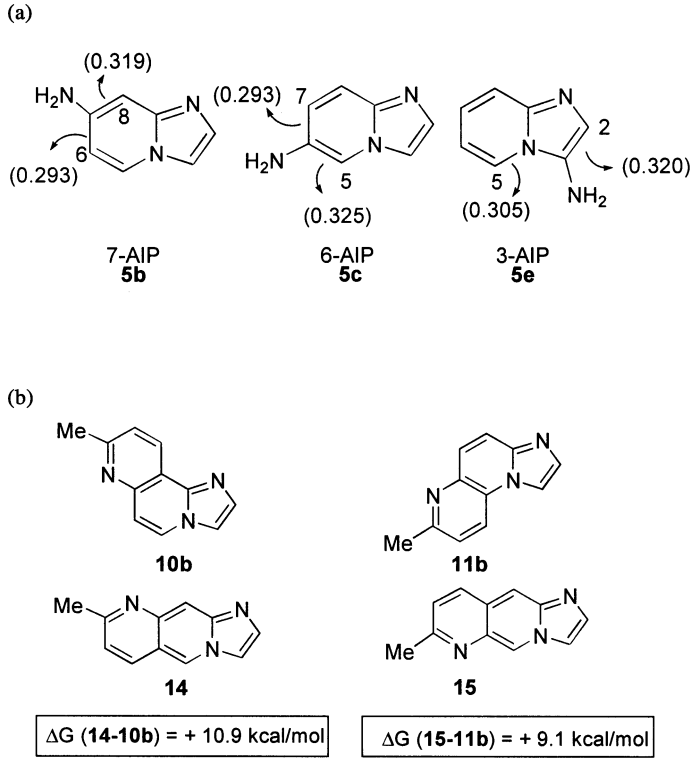
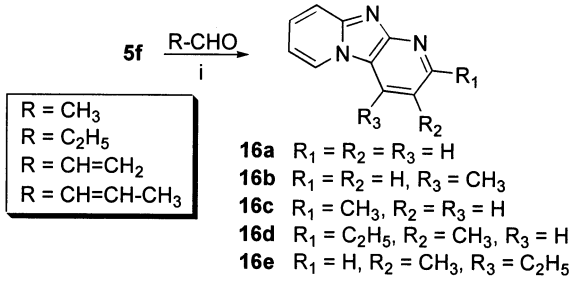


Figure 2. (a) Electron density at the bond critical point (in e); (b) energy differences of regioisomers.

α-azacarbolines **16a–e**. Interestingly, reaction of **5f** with crotonaldehyde gave compound **16b** (Scheme 5), indicating that the reaction is driven by a hard–hard and soft–soft affinity rather than by a 1,4-addition (Scheme 7, entry 2), which would have led to isomer **16c**. However, the fact that reaction of **5f** with acetaldehyde yielded azacarboline **16c** indicates that the reaction of acetaldehyde with the amine is faster than the aldol condensation. Accordingly, reaction of **5f** with propanal (Table 2, entry 24) provided compound **16d**. In the presence of 10% Pd/C (method B) the reaction with propanal afforded an equimolar mixture of isomers **16d** and **16e**, which indicated that the palladium can accelerate the aldol condensation.



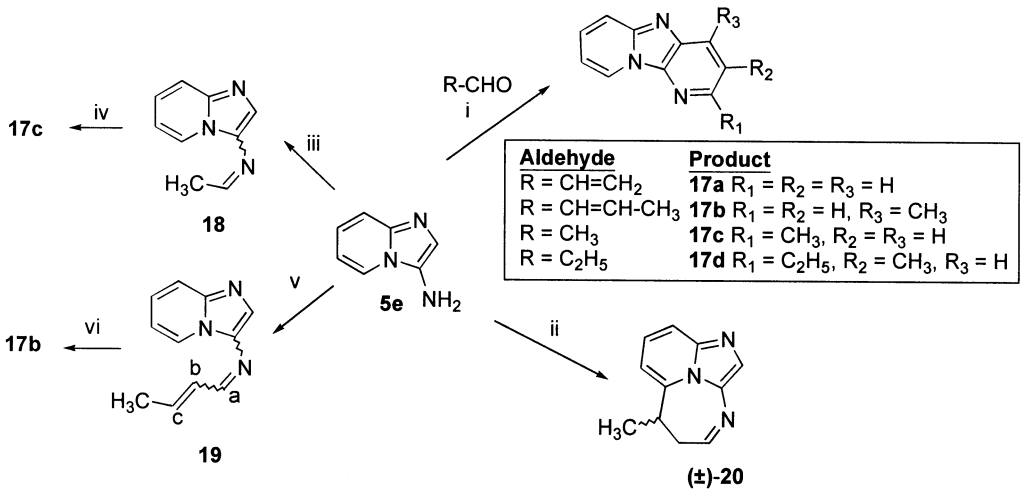
Scheme 5. *Reagents and conditions*: (i) 1,2-dicholoro benzene, Δ (method A); 1,2-dichlorobenzene, 10% Pd/C, Δ (method B).

The results of the thermal condensation of 3-AIP **5e** and the chosen aldehydes (Scheme 6) led to the expected azacarbolines **17a–d**, as a result of linear or *peri* annulation. The regioselectivity of these reactions was consistent with the above reasoning.

Condensation of **5e** with crotonaldehyde in toluene at 70°C yielded the expected enimine **19**, proving that the reaction occurs through a 1,2-addition followed by electrophilic aromatic substitution (SEAr) on the π-excessive imidazole ring (Scheme 7, entry 2). In addition, condensation of **5e** with 1.5 equiv. of acetaldehyde at rt gave imine **18**, and the thermal condensation of **18** with more acetaldehyde yielded the expected cyclization product **17c** (Scheme 7, entry 3). These results and the fact that compounds **17b** and **17c** have very similar stability ($\Delta G \approx 0.1$ kcal mol^{-1} according to theorical calculations), confirm that the condensation of saturated aldehydes with the amines **5** is faster than aldol condensation.

The role of palladium in the condensations remained to be clarified. Its addition was relevant in the case of **5b** and **5c**, in which the SEAr occurs on positions C8 and C5. In contrast, it was not significant for cyclizations on the C6 and C7 positions. Pertinent to this issue is the drastic effect of adding of 10% Pd/C on the outcome of the reaction of **5e** with crotonaldehyde (Table 2, entry 18). Thus, instead of the linear cyclization product **17c**, diazepine (±)-**20** was obtained in 23% yield. However, this was not observed using acetaldehyde or acrolein. This could be explained by considering that the Pd usually complexes the intermediate enimine on the exocyclic conjugated π-system, which then is fixed in its cisoid conformation, and cyclizes on the less hindered C2 position; however, in the presence of crotonaldehyde, the Pd complex seems to involve the heterocycle and renders position C5 more nucleophilic than C2.

In the light of the results that showed the nucleophilicity of position C5, which is consistent with the nucleophilicity of C5 that we had already observed in the 4-azaindole series,[7a]

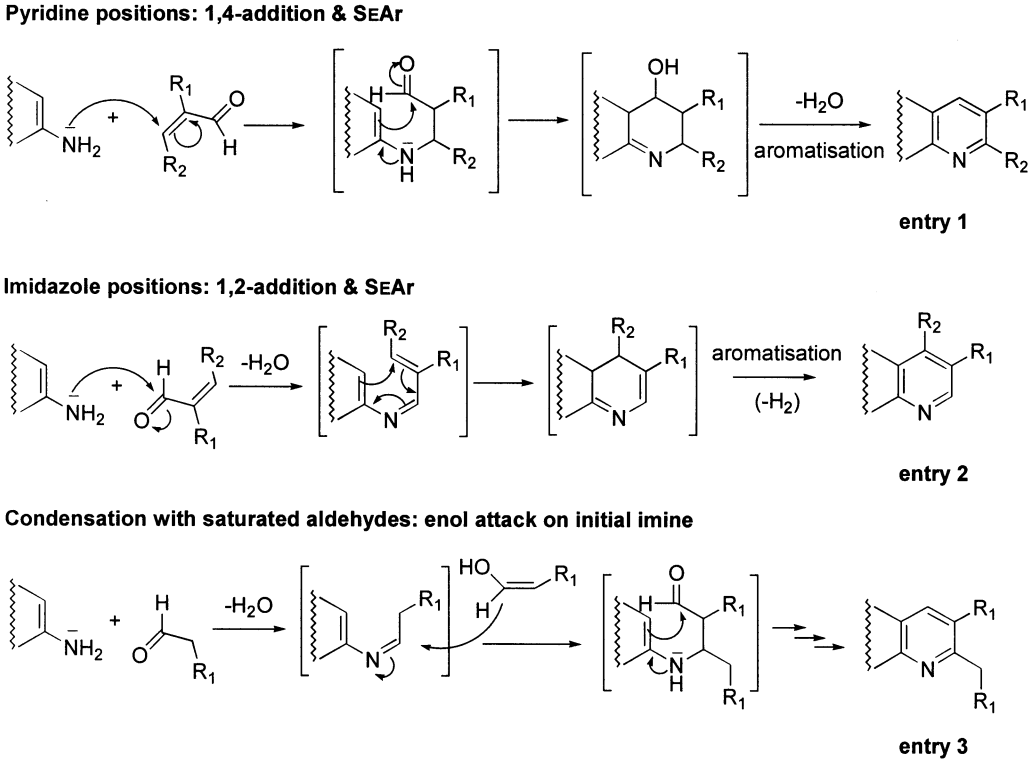


Scheme 6. *Reagents and conditions*: (i) Method A or B (except for crotonaldehyde) (cf Table 2); (ii) crotonaldehyde, method B; (iii) ethanal (1.5 equiv.), CH_2Cl_2, rt, 36 h; (iv) ethanal (1.1 equiv.) 1,2-dichlorobenzene, 10% Pd/C, Δ, 2.5 h; (v) crotonaldehyde, toluene, 70°C, 10 h; (vi) 1,2-dichlorobenzene, crotonaldehyde, 10% Pd/C, Δ.

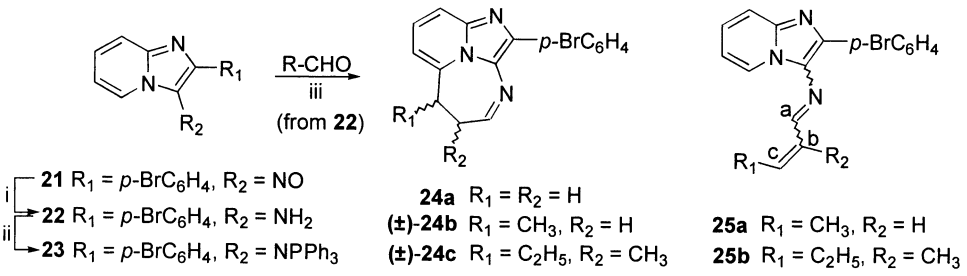
we focused our attention on the synthesis of cyclazines **24**. Cyclazines **24** are unprecedented isosteres of TIBO,[6] and therefore constitute a new class of potential non-competitive inhibitors of HIV-1 reverse transcriptase.

The suitable starting substrate, 2-substituted (and thus C2 blocked) 3-AIP **22**, was obtained by reduction[16] of the nitroso compound **21**[17] (Scheme 8). Since we wanted to assay both heteroannulation methods, amine **22** was treated with triphenylphosphine to yield iminophosphorane **23**, using the same procedure as for preparation of imino-phosphoranes **7**. The ^{13}C NMR spectrum of **23** displayed among other signals a doublet at 129.5 ppm with a coupling constant of $^1J_{P-C}=100$ Hz, characteristic of the methine carbon bonded to phosphor.

Condensation of iminophosphorane **23** with acrolein yielded the expected diazepine **24a** in 13% yield (Table 1). On the other hand, thermal condensation of amine **22** with the selection of aldehydes (Table 2) in 1,2-dichlorobenzene at 180°C, yielded the expected [1,3]diazepines **24a–c**. When using crotonaldehyde in the absence of 10% Pd/C, diazepine (±)-**24b** was produced together with the intermediate enimine **25a** (8%). In agreement with our previous



Scheme 7.



Scheme 8. *Reagents and conditions*: (i) HBr, Sn, 0°C; (ii) PPh_3, CCl_4, NEt_3; (iii) 1,2-dichlorobenzene, Δ (method A) or 1,2-dichlorobenzene, 10% Pd/C, Δ (method B).

observations (±)-**24b** was obtained in higher yield (42%) and as the only product in the presence of 10% Pd/C. Use of propanal resulted in isolation of the intermediate enimine **25b** which cyclized suitably when reaction times were extended.

Enimines **25a**,**b** were isolated by column chromatography and identified by their spectral data (see Section 4). The structure of azepines **24** was also determined from their ^1H and ^{13}C NMR data, and confirmed by an X-ray crystal structure determination on (±)-**24b** (Fig. 3).

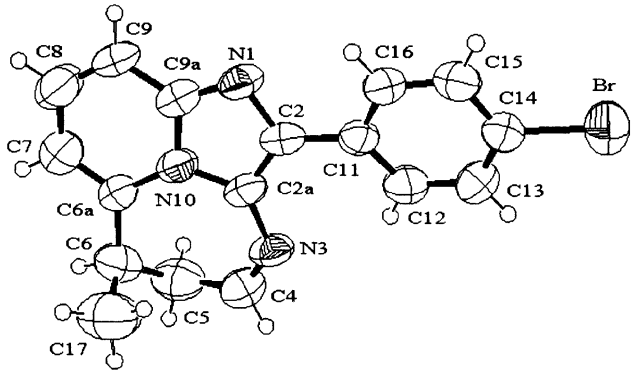


Figure 3. ORTEP[18] diagram of compound (±)-**24b** showing 50% probability displacements ellipsoids for non-H atoms. H-atoms are included with small arbitrary radii.

3. Conclusion

Aminoimidazopyridines have proved to be suitable building blocks for the preparation of imidazonaphthyridines, dipyridoimidazoles, and pyridoimidazodiazepines. Both the heteroannulation methods explored were successful for our purposes. However, the thermal condensation of the starting amines with aldehydes in the presence of 10% Pd/C was generally superior to their condensation with iminophosphoranes: the Staudinger step is unnecessary, the yields are often better, and the possibility of using saturated aldehydes offers a larger scope for diversification. In the reaction of 3-AIP with crotonaldehyde regioselectivity of the thermal cyclization was observed.

We have thus prepared a small collection of compounds within the three structural families considered, and we have applied the method to obtain compounds **24**, three new isosteres of TIBO.

4. Experimental

4.1. General procedures

Melting points were determined on an Electrothermal IA9300 (capillary) and are not corrected. NMR (proton 400 MHz or carbon 100 MHz) were recorded on a Bruker AC 400 spectrophotometer using $CDCl_3$, CD_3OD or DMSO-d_6 as solvent. Infrared spectra were recorded on a Beckman Acculab 2 spectrophotometer and on a FTIR Nicolet Impact 410. Mass spectral analyses were performed on a Hewlett–Packard 5985B or 5989A instrument. Toluene, 1,2-dichlorobenzene and nitrobenzene were dried over Na. Other solvents were stored over molecular sieves.

4.2. Single crystal X-ray diffraction analysis of (±)-24b $C_{17}H_{14}N_3Br$

Intensities were collected on an Enraf-Nonius CAD-4 diffractometer[19] using the $\omega-2\theta$ scan technique. $C_{17}H_{14}N_3Br$ crystallized in space group $P2_1/n$ with a=7.755(6), b=12.490(3), c=15.304(4) Å and β=96.05(4)°. Of the 4293 unique reflections measured (Mo Kα radiation), 1262 were considered observed ($I \geq 2\sigma(I)$). The final refinement residuals were R=0.066 (on F) and wR_2=0.146 (on F^2). The data reduction was processed using the XCAD4 program[20] and corrected for Lorentz and polarization effects. The structure was solved by direct methods[21] and all non-hydrogen atoms were refined anisotropically. All hydrogen atoms were treated as riding with $U_{iso}(H)=1.5U_{eq}(C)$ for methyl H atoms and $1.2U_{eq}(C)$ for others. All programs used for this study were performed using the WinGX package.[22]

4.3. Method for the theoretical calculations

Calculations have been performed at the Density Functional level of theory using the B3LYP[23] method and the 6-31G(d)[24] basis set. All the structures have been subjected to geometry optimization. The minimum-energy nature of the stationary points has been verified from inspection of the vibrational frequencies. These values were used to compute zero-point energy, thermal and entropy corrections to the free energy (at 298 K and 1 atm) using the standard procedure implemented in Gaussian 98.[25]

4.3.1. Ethyl (imidazo[1,2-*a*]pyridin-7-yl)carboxylate (1b). To a solution of 2-aminoisonicotinic acid ethyl ester[27] (5.81 g, 35 mmol) and $NaHCO_3$ (5.00 g, 59.5 mmol) in 250 mL of EtOH, chloroacetaldehyde (50% in

H_2O) (28.8 g, 158 mmol) was added. The mixture was refluxed for 9 h and the solvent was evaporated. 200 mL of H_2O were added and the residue was basified with Na_2CO_3 and extracted with CH_2Cl_2. The organic layers were dried over Na_2SO_4, filtered and evaporated under reduced pressure. Chromatography (neutral Al_2O_3, CH_2Cl_2) yield **1b** (5.38 g, 81%); mp 73–75°C; IR (KBr) 1740, 1350, 1250 cm^{-1}; MS *m/z* 190 (M^+, 91), 162 (58), 145 (100), 117 (40), 90 (24); ^1H NMR ($CDCl_3$) δ 1.43 (t, 3H, *J*=7 Hz), 4.41 (q, 2H, *J*=7 Hz), 7.38 (d, 1H, *J*=7 Hz), 7.70 (s, 1H), 7.79 (s, 1H), 8.18 (d, 1H, *J*=7 Hz), 8.37 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.2, 61.5, 111.6, 113.7, 120.5, 125.3, 126.2, 135.9, 144.4, 165.2. Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.91; H, 5.28; N, 14.68.

4.3.2. 7-Carbohydrazidoimidazo[1,2-*a*]pyridine (2b). A mixture of ester **1b** (17.5 g, 92.1 mmol) and hydrazine monohydrate (27.6 g, 553 mmol) in EtOH (180 mL) was refluxed for 60 h. After cooling at rt the solvent was concentrated under vacuo, the precipitate was filtred and washed with CH_2Cl_2 to give **2b** (15.0 g, 92.5%); mp 277–279°C; IR (KBr) 3305, 3251, 1647, 1550, 1342 cm^{-1}; MS *m/z* 176 (M^+, 22), 145 (100), 117 (64), 90 (49), 63 (24); ^1H NMR (DMSO-d_6) δ 4.61 (brs, 2H), 7.31 (d, 1H, *J*=7 Hz), 7.72 (s, 1H), 8.07 (s, 1H), 8.08 (s, 1H), 8.62 (d, 1H, *J*=7 Hz), 9.99 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 110.0, 114.2, 115.6, 126.6, 128.7, 134.9, 143.6, 164.3. Anal. Calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.68; H, 4.60; N, 31.69.

4.3.3. 2-Carbohydrazidoimidazo[1,2-*a*]pyridine (2f). This was prepared according to the procedure used for the synthesis of compound **2b**. From ester **1f**[14] (28.5 g, 150 mmol) using (18.8 g, 376 mmol) of hydrazine (reaction time 60 h). The precipitate was washed with a small quantity of EtOH and dried in vacuo to yield **2f** (24.1 g, 91%); mp 198–200°C; IR (KBr) 3430, 1679, 1568, 1475 cm^{-1}; MS *m/z* 176 (M^+, 87), 145 (100), 117 (50), 90 (57), 78 (88), 63 (38), 51 (33); ^1H NMR (DMSO-d_6) δ 4.30 (brs, 2H), 6.76 (t, 1H, *J*=7 Hz), 7.12 (brs, 1H), 7.38 (d, 1H, *J*=9 Hz), 8.17 (s, 1H), 8.37 (d, 1H, *J*=7 Hz), 9.35 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 113.0, 114.4, 117.3, 126.2, 127.5, 138.8, 144.0, 161.5. Anal. Calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.48; H, 4.56; N, 31.91.

4.3.4. 7-Carbazidoimidazo[1,2-*a*]pyridine (3b). A stirred solution of **2b** (24.1 g, 137 mmol) in 2N HCl (80 mL) was diluted with cold H_2O (500 mL). An aqueous solution of $NaNO_2$ (14.18 g, 206 mmol) was added dropwise, maintaining the temperature below 15°C. The solution was stirred at rt for 2 h, neutralized with Na_2CO_3 and extracted with CH_2Cl_2. After drying, the organic layers were concentrated under vacuo. The crude precipitate was washed with Et_2O (30 mL) to afford **3b** (19.6 g, 76%); mp 123–125°C (note: explosion hazards!);[26] IR (KBr) 2155, 1687, 1323, 1220, 1125 cm^{-1}; MS *m/z* 187 (M^+, 20), 159 (95), 131 (100), 104 (65), 77 (85), 52 (86); ^1H NMR ($CDCl_3$) δ 7.37 (d, 1H, *J*=7 Hz), 7.74 (s, 1H), 7.84 (s, 1H), 8.19 (d, 1H, *J*=7 Hz), 8.36 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 110.8, 114.4, 120.9, 125.6, 126.1, 136.70, 144.0, 170.9. Anal. Calcd for $C_8H_5N_5O$: C, 51.34; H, 2.69; N, 37.42. Found: C, 51.54; H, 2.70; N, 37.28.

4.3.5. 2-Carbazidoimidazo[1,2-*a*]pyridine (3f). This was prepared according to the procedure used for the synthesis of compound **3b**. From **2f** (reaction time 4 h) to yield **3f** (19.6 g, 76%); mp 138–140°C; (note: explosion hazards!);[26] IR (KBr) 2148, 1682 cm^{-1}; MS *m/z* 187 (M^+, 23), 159 (84), 145 (21), 104 (100), 90 (22), 77 (48), 63 (24), 51 (62); ^1H NMR ($CDCl_3$) δ 6.94 (t, 1H, *J*=6.5 Hz), 7.31 (m, 1H), 7.69 (d, 1H, *J*=9 Hz), 8.18 (d, 1H, *J*=6.5 Hz), 8.26 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 114.3, 117.6, 119.0, 126.3, 126.7, 136.9, 145.5, 168.2. Anal. Calcd for $C_8H_5N_5O$: C, 51.34; H, 2.69; N, 37.42. Found: C, 51.49; H, 2.68; N, 37.42.

4.3.6. 7-(Ethoxycarbonyl)aminoimidazo[1,2-*a*]pyridine (4b). A solution of **3b** (11.1 g, 59.3 mmol) in EtOH (200 mL) was refluxed for 4.5 h. The white precipitate was filtered and washed with EtOH (30 mL) to give amide **4b** (7.97 g). The filtrate was concentrated in vacuo and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2). The first fraction gave **1b** (3.20 g, 28%), The final elution gave amide *7-(ethoxycarbonyl)aminoimidazo[1,2-a]pyridine* (**4b**) (0.81 g) overall yield (72%); mp 162–164°C; IR (KBr) 3205, 1720, 1601, 1273, 1254, 1069 cm^{-1}; MS *m/z* 205 (M^+, 100), 177 (24), 159 (50), 132 (74), 105 (72), 79 (35), 52 (51); ^1H NMR (DMSO-d_6) δ 1.28 (t, 3H, *J*=7 Hz), 4.18 (q, 2H, *J*=7 Hz), 6.95 (d, 1H, *J*=7 Hz), 7.44 (s, 1H), 7.73 (s, 1H), 7.79 (s, 1H), 8.43 (d, 1H, *J*=7 Hz), 9.95 (brs, 1H); ^{13}C NMR (DMSO-d_6) δ 14.4, 60.6, 101.1, 106.4, 112.0, 127.0, 133.0, 136.2, 145.2, 153.5. Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.67; H, 5.39; N, 20.41.

4.3.7. 2-(Ethoxycarbonyl)aminoimidazo[1,2-*a*]pyridine (4f). This was prepared according to the procedure used for the synthesis of compound **4b**. From **3f** (19.6 g, 105 mmol) (reaction time 3.5 h) 17.8 g of amide **4f** was collected and chromatography gave in order of elution: **1f** (0.42 g, 3%) and *7-(ethoxycarbonyl)aminoimidazo[1,2-a]pyridine* (**4f**) (0.50 g) overall yield (85%); mp 223–225°C; IR (KBr) 3182, 1712, 1258 cm^{-1}; MS *m/z* 205 (M^+, 50), 159 (27), 133 (100), 105 (57), 78 (60), 51 (46); ^1H NMR (DMSO-d_6) δ 1.27 (t, 3H, *J*=7 Hz), 4.17 (q, 2H, *J*=7 Hz), 6.86 (t, 1H, *J*=6.5 Hz), 7.21 (m, 1H), 7.41 (d, 1H, *J*=9 Hz), 7.88 (s, 1H), 8.53 (d, 1H, *J*=6.5 Hz), 10.34 (brs, 1H); ^{13}C NMR (DMSO-d_6) δ 14.6, 60.4, 98.9, 111.5, 115.0, 124.1, 126.4, 141.2, 142.5, 153.4. Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.72; H, 5.41; N, 20.45.

4.3.8. 7-Aminoimidazo[1,2-*a*]pyridine (5b). A stirred solution of **4b** (2.00 g, 9.76 mmol) in 5N aqueous NaOH (100 mL) was heated under reflux for 7 h. The solution was diluted with H_2O (100 mL), extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated in vacuo. The crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2/EtOH, 99/1, v/v) to afford **5b** (1.21 g, 93%); mp 139–141°C; IR (KBr) 3421, 2924, 1656 cm^{-1}; MS *m/z* 133 (M^+, 100), 106 (18), 79 (37), 52 (35); ^1H NMR ($CDCl_3$) δ 4.55 (s, 2H), 6.20 (dd, 1H, *J*=2, 7 Hz), 6.54 (d, 1H, *J*=2 Hz), 7.19 (s, 1H), 7.24 (s, 1H), 7.69 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 94.5, 106.7, 110.3, 125.8, 131.4, 142.2, 147.2. Anal. Calcd for $C_7H_7N_3$: C, 63.14; H, 5.30; N, 31.56. Found: C, 62.91; H, 5.30; N, 31.45.

4.3.9. 2-Aminoimidazo[1,2-*a*]pyridine (5f).[13] This was prepared according to the procedure used for the synthesis of compound **5b**. From **4f** (0.50 g, 2.44 mmol) to afford **5f** (0.26 g, 80%) (note: these amine was unstable and decomposed at rt).

4.3.10. 3-Amino-2-(4-bromophenyl)imidazo[1,2-*a*]pyridine (22). To a cold solution (0°C) of 3-nitroso compound **21**[17] (4.00 g, 13.2 mmol) in concentrated HBr (48%, 50 mL), tin powder in small portion (4.00 g, 33.6 mmol) was added. The solution was stirred at rt for 3 h. After cooling, H_2O (100 mL) was added, the solution was neutralized with Na_2CO_3 and concentrated in vacuo. The crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to give **22** (2.40 g, 63%); mp 150–152°C; IR (KBr) 3200–2900, 1480 cm^{-1}; MS *m/z* 289 (M^++2, 96), 287 (M^+, 100), 261 (10), 259 (10), 181 (37), 104 (24), 79 (87), 78 (75), 51 (23); ^1H NMR ($CDCl_3$) δ 3.38 (brs, 2H), 6.83 (t, 1H, *J*=6.8 Hz), 7.14 (m, 1H), 7.53 (m, 3H), 7.89 (d, 2H, *J*=8.5 Hz), 7.96 (d, 1H, *J*=6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 111.9, 117.3, 121.1, 121.9, 123.6, 128.4, 128.5 (2C), 131.7 (2C), 132.4, 133.4, 141.1. Anal. Calcd for $C_{13}H_{10}N_3Br$: C, 54.19; H, 3.50; N, 14.58. Found: C, 54.21; H, 3.48; N, 14.62.

4.4. General procedure for the preparation of azido compounds 6a–d

To a cold solution (−5°C) of the appropriate amine (22.5 mmol) in mixture of H_2O (150 mL) and concentrated HCl (37%, 9 mL), a solution of $NaNO_2$ (1.72 g, 24.9 mmol) in H_2O (30 mL) was added dropwise, keeping the temperature of the reaction below 0°C. After 10 min, a solution of NaN_3 (3.66 g, 56.3 mmol) in H_2O (35 mL) was added dropwise to the cooled reaction mixture. The solution was stirred at rt until completion (1–12 h). The mixture was neutralized with Na_2CO_3, extracted with CH_2Cl_2, dried, and concentrated in vacuo. The residue was purified by chromatography (neutral Al_2O_3, CH_2Cl_2) to give azides **6a–d**. All azido compounds are light sensitive and must be kept cold under argon.

4.4.1. 8-Azidoimidazo[1,2-*a*]pyridine (6a). Reaction time 1 h, yield: 76%; mp 59–61°C; IR (KBr) 2060, 1720, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.72 (m, 2H), 7.63 (m, 2H), 7.95 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 111.7, 112.1, 113.6, 122.2, 129.0, 133.0, 140.1. Anal. Calcd for $C_7H_5N_5$: C, 52.83; H, 3.17; N, 44.00. Found: C, 52.65; H, 3.16; N, 43.99.

4.4.2. 7-Azidoimidazo[1,2-*a*]pyridine (6b). Reaction time 2 h, yield: 60%; mp 132–134°C; IR (KBr) 2110, 1644, 1522, 1471, 1308, 1278, 1143 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.38 (d, 1H, *J*=7 Hz), 7.12 (s, 1H), 7.46 (s, 1H), 7.50 (s, 1H), 7.98 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 104.7, 106.3, 112.0, 126.5, 134.1, 137.2, 145.2. Anal. Calcd for $C_7H_5N_5$: C, 52.83; H, 3.17; N, 44.00. Found: C, 53.02; H, 3.16; N, 44.08.

4.4.3. 6-Azidoimidazo[1,2-*a*]pyridine (6c). Reaction time 2 h, CH_2Cl_2/EtOH, 98/2, v/v, yield: 63%; mp 71–73°C; IR (KBr) 2110, 1530, 1310, 1260, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.97 (dd, 1H, *J*=2, 9.5 Hz), 7.56 (s, 1H), 7.62 (d, 1H, *J*=9.5 Hz), 7.65 (s, 1H), 7.90 (d, 1H, *J*=2 Hz); ^{13}C NMR ($CDCl_3$) δ 113.1, 115.4, 117.9, 118.6, 127.7, 134.5, 142.7. Anal. Calcd for $C_7H_5N_5$: C, 52.83; H, 3.17; N, 44.00. Found: C, 52.95; H, 3.17; N, 44.10.

4.4.4. 5-Azidoimidazo[1,2-*a*]pyridine (6d). Reaction time 12 h, yield: <1% as an brown oil; IR (KBr) 2140, 1500, 1290, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.59 (d, 1H, *J*=7.5 Hz), 7.25 (dd, 1H, *J*=9, 7.5 Hz), 7.47 (d, 1H, *J*=9 Hz), 7.62 (s, 1H), 7.66 (s, 1H). Anal. Calcd for $C_7H_5N_5$: C, 52.83; H, 3.17; N, 44.00. Found: C, 52.80; H, 3.18; N, 44.17.

4.5. Method A: General procedure for the preparation of iminophosphoranes using amino compounds

To a solution of the appropriate amine **5** (19.5 mmol) in CH_3CN (50 mL), Et_3N (33 mL), CCl_4 (21 mL) and PPh_3 (2 equiv.) were added. The solution was stirred at rt for 24 h, concentrated in vacuo, and chromatographed (neutral Al_2O_3, AcOEt/hexanes, 8/2, v/v) to afford **7a–e**, **23**.

4.6. Method B: General procedure for the preparation of iminophosphoranes using azido compounds

To a solution of the appropriate azide **6a–c** (1.26 mmol) in dry CH_2Cl_2 (20 mL), PPh_3 (0.36 g, 2.74 mmol) was added. The solution was stirred at rt for 4 h. The solvent was evapored and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to give iminophosphoranes **7a–c**.

4.6.1. 8-(Triphenylphosphoranylidene)aminoimidazo[1,2-*a*]pyridine (7a). *Method A*: yield: 23%; *Method B*: yield: 67%; mp 164–166°C; IR (KBr) 1517, 1482, 1341, 1127 cm^{-1}; MS *m/z* 393 (M^+, 100), 369 (45), 238 (12), 183 (33); ^1H NMR ($CDCl_3$) δ 6.00 (d, 1H, *J*=7 Hz), 6.35 (t, 1H, *J*=7 Hz), 7.53 (m, 12H), 7.92 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 108.1 (d, $^3J_{P-C}$=13 Hz), 112.5, 113.2, 115.1, 125.6 (d, $^3J_{P-C}$=11 Hz, 6C), 130.0 (d, $^1J_{P-C}$=100 Hz, 3C), 131.8, 131.8 (3C), 132.8 (d, $^2J_{P-C}$=10 Hz, 6C), 141.8, 146.1 (d, $^3J_{P-C}$=27 Hz). Anal. Calcd for $C_{25}H_{20}N_3P$: C, 76.32; H, 5.12; N, 10.68. Found: C, 76.35; H, 5.10; N, 10.68.

4.6.2. 7-(Triphenylphosphoranylidene)aminoimidazo[1,2-*a*]pyridine (7b). *Method A*: yield: 49%; *Method B*: yield: 61%; mp 161–163°C; IR (KBr) 1640, 1464, 1323, 1131 cm^{-1}; MS *m/z* 393 (M^+, 100), 316 (17), 208 (16), 183 (20); ^1H NMR ($CDCl_3$) δ 6.54 (s, 1H), 6.68 (d, 1H, *J*=7 Hz), 7.25 (s, 1H), 7.31 (s, 1H), 7.49 (m, 6H), 7.57 (t, 3H, *J*=7 Hz), 7.81 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 103.0 (d, $^3J_{P-C}$=13 Hz), 109.9, 116.1 (d, $^3J_{P-C}$=26 Hz), 124.8, 128.8 (d, $^3J_{P-C}$=12 Hz, 6C), 129.6 (d, $^1J_{P-C}$=99 Hz, 3C), 132.1 (4C), 132.6 (d, $^2J_{P-C}$=10 Hz, 6C), 148.2, 149.7. Anal. Calcd for $C_{25}H_{20}N_3P$: C, 76.32; H, 5.12; N, 10.68. Found: C, 76.44; H, 5.14; N, 10.66.

4.6.3. 6-(Triphenylphosphoranylidene)aminoimidazo[1,2-*a*]pyridine (7c). *Method A*: yield: 36%; *Method B*: yield: 50%; mp 152–154°C; IR (KBr) 1506, 1437, 1358, 1295, 1204 cm^{-1}; MS *m/z* 393 (M^+, 100), 208 (12), 183 (31); ^1H NMR ($CDCl_3$) δ 6.92 (d, 1H, *J*=9.5 Hz), 7.21 (s, 1H), 7.29 (d, 1H, *J*=9.5 Hz), 7.40 (s, 1H), 7.45 (m, 10H), 7.75 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 111.4, 115.1 (d, $^3J_{P-C}$=18 Hz), 116.1, 127.6 (d, $^3J_{P-C}$=16 Hz), 128.6 (d,

$^{3}J_{P-C}$=12 Hz, 6C), 130.2 (d, $^{1}J_{P-C}$=100 Hz, 3C), 131.8 (3C), 132.0, 132.3 (d, $^{2}J_{P-C}$=9.5 Hz, 6C), 137.9, 142.2. Anal. Calcd for $C_{25}H_{20}N_3P$: C, 76.32; H, 5.12; N, 10.68. Found: C, 76.12; H, 5.13; N, 10.71.

4.6.4. 5-(Triphenylphosphoranylidene)aminoimidazo-[1,2-*a*]pyridine (7d). *Method A*: yield: 48%; mp 193–195°C; IR (KBr) 1577, 1439, 1352, 1274, 1110 cm^{-1}; MS *m/z* 393 (M^+, 1), 369 (100), 292 (12), 260 (12), 183 (43), 109(12); ^{1}H NMR ($CDCl_3$) δ 5.78 (d, 1H, *J*=7.5 Hz), 6.32 (d, 1H, *J*=7.5 Hz), 7.18 (t, 1H, *J*=7.5 Hz), 7.46 (m, 8H), 7.53 (m, 3H), 7.86 (dd, 6H, *J*=7, 12 Hz); ^{13}C NMR ($CDCl_3$) δ 96.3, 106.9 (d, $^{3}J_{P-C}$=21.5 Hz), 128.3 (8C), 130.7 (d, $^{1}J_{P-C}$=100 Hz, 3C), 131.4 (3C), 133.1 (d, $^{2}J_{P-C}$=10 Hz, 6C), 138.6, 156.6, 162.6 (d, $^{3}J_{P-C}$=5 Hz). Anal. Calcd for $C_{25}H_{20}N_3P$: C, 76.32; H, 5.12; N, 10.68. Found: C, 76.28; H, 5.14; N, 10.69.

4.6.5. 3-(Triphenylphosphoranylidene)aminoimidazo-[1,2-*a*]pyridine (7e). *Method A*: yield: 36%; mp 129–131°C; IR (KBr) 1540, 1438, 1292, 1184, 1119 cm^{-1}; MS *m/z* 393 (M^+, 71), 288 (8), 262 (100), 183 (62), 108 (41), 78 (23), 51 (20); ^{1}H NMR ($CDCl_3$) δ 6.71 (t, 1H, *J*=7 Hz), 6.95 (m, 1H), 7.42 (d, 1H, *J*=9 Hz), 7.50 (m, 6H), 7.58 (t, 3H, *J*=7 Hz), 7.83 (m, 6H), 8.35 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 110.1, 115.7, 117.0, 120.8, 122.5, 128.8 (d, $^{3}J_{P-C}$=12 Hz, 6C), 129.7 (d, $^{1}J_{P-C}$=101 Hz, 3C), 132.2 (3C), 132.5 (d, $^{2}J_{P-C}$=10 Hz, 6C), 133.4 (d, $^{2}J_{P-C}$=9.5 Hz, C), 139.9. Anal. Calcd for $C_{25}H_{20}N_3P$: C, 76.32; H, 5.12; N, 10.68. Found: C, 76.59; H, 5.11; N, 10.66.

4.6.6. 3-(Triphenylphosphoranylidene)amino-2-(4-bromophenyl)imidazo[1,2-*a*]pyridine (23). *Method A*: yield: 99%; mp 197–199°C; IR (KBr) 1541, 1438, 1341, 1114 cm^{-1}; MS *m/z* 549 (M^++2, 43), 547 (M^+, 41), 288 (13), 262 (100), 183 (47), 108 (30), 78 (28); ^{1}H NMR ($CDCl_3$) δ 6.43 (t, 1H *J*=7 Hz), 6.89 (m, 1H), 7.21 (d, 2H, *J*=8 Hz), 7.41 (m, 7H), 7.50 (m, 3H), 7.59 (m, 6H), 7.78 (d, 1H, *J*=7 Hz), 7.83 (d, 2H, *J*=8 Hz); ^{13}C NMR ($CDCl_3$) δ 110.0, 116.6, 118.8, 121.4, 122.4, 128.2 (d, $^{3}J_{P-C}$=10 Hz, 6C), 128.4 (2C), 129.6 (d, $^{1}J_{P-C}$=100 Hz, 3C), 129.6 (d, $^{2}J_{P-C}$=8.5 Hz), 130.2 (2C), 131.7 (d, $^{4}J_{P-C}$=3 Hz, 3C), 131.9 (d, $^{2}J_{P-C}$=10 Hz, 6C), 133.0, 134.5 (d, $^{3}J_{P-C}$=3 Hz), 139.5 (d, $^{4}J_{P-C}$=1.5 Hz). Anal. Calcd for $C_{31}H_{23}N_3BrP$: C, 67.89; H, 4.23; N, 7.66. Found: C, 68.02; H, 4.22; N, 7.64.

4.7. Reactivity of amines with carbonyl compounds

Method A: General procedure in 1,2-dichlorobenzene. To a solution of the appropriate amine (7.52 mmol) in dry 1,2-dichlorobenzene (40 mL) a solution of the suitable carbonyl reagent in the same solvent (10 mL) was added. The mixture was refluxed until no more substrate was observed by TLC. The solvent was evapored and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2).

Method B: General procedure in 1,2-dichlorobenzene with 10% Pd/C. To a solution of the appropriate amine (7.52 mmol) in dry 1,2-dichlorobenzene (40 mL) a solution of the suitable carbonyl reagent (4 equiv. for acetaldehyde and propanal, and 2 equiv. for acrolein and crotonaldehyde) in the same solvent (10 mL), and a small quantity of 10% Pd/C were added. The mixture was refluxed until no more substrate was observed by TLC. The solvent was evaporated and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2).

Method C: General procedure using iminophosphoranes compounds. To a stirred solution of the appropriate iminophosphorane (2.03 mmol) in dry nitrobenzene (15 mL), acrolein (3 equiv.) in nitrobenzene (5 mL) was added. The solution was heated at 95°C for 20 h, and refluxed for 3 h. The solvent was removed under vacuo and the crude product was chromatographed (neutral Al_2O_3, AcOEt/hexanes, 9/1, v/v).

4.7.1. Imidazo[1,2-*h*][1,7]naphthyridine (8a). From acrolein: *Method A*: (4 equiv., reaction time 18 h), *Method B*: (reaction time 5 h), *Method C*: (eluate with CH_2Cl_2/EtOH, 99/1, v/v) as an oil; IR (KBr) 1520, 1480, 1410, 1390, 1330 cm^{-1}; MS *m/z* 169 (M^+, 100), 142 (29), 129 (14), 115 (17); ^{1}H NMR ($CDCl_3$) δ 6.99 (d, 1H, *J*=7.2 Hz), 7.49 (dd, 1H, *J*=4.3, 8 Hz), 7.65 (s, 1H), 7.72 (s, 1H), 8.00 (d, 1H, *J*=7.2 Hz), 8.02 (d, 1H, *J*=8 Hz), 8.97 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 111.5, 115.0, 122.8, 124.0, 124.7, 132.6, 134.5, 140.6, 142.8, 150.6. Anal. Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 70.73; H, 4.18; N, 24.85.

4.7.2. 9-Methylimidazo[1,2-*h*][1,7]naphthyridine (8b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 19 h), *Method B*: (reaction time 2.5 h); mp 132–134°C; IR (KBr) 1600, 1480, 1420, 1390, 1320, 1140 cm^{-1}; MS *m/z* 183 (M^+, 100), 182 (48), 157 (20); ^{1}H NMR ($CDCl_3$) δ 2.77 (s, 3H), 6.89 (d, 1H, *J*=7 Hz), 7.30 (d, 1H, *J*=8 Hz), 7.57 (s, 1H), 7.64 (s, 1H), 7.84 (d, 1H, *J*=8 Hz), 7.89 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 25.0, 111.4, 114.8, 122.4, 123.1, 123.2, 132.2, 134.7, 139.8, 142.7, 160.0. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 72.32; H, 4.96; N, 22.86.

From ethanal: *Method A*: (2 equiv., reaction time 19 h), *Method B*: (reaction time 3.5 h).

4.7.3. 9-Ethyl-8-methylimidazo[1,2-*h*][1,7]naphthyridine (8c). From propanal: *Method A*: (2.2 equiv., reaction time 19 h). The first fraction gave *(±)-9-ethyl-9,10-dihydro-8-methylimidazo[1,2-h][1,7]naphthyridine* (±)-(**9**) as an oil; IR (KBr) 3500, 1630, 1540, 1480, 1330 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3H, *J*=7.4 Hz), 1.39 (m, 1H), 1.59 (hept., 1H, *J*=7.2 Hz), 4.12 (m, 1H), 5.48 (s, 1H), 5.96 (s, 1H), 6.23 (d, 1H, *J*=6.7 Hz), 7.24 (d, 1H, *J*=6.7 Hz), 7.28 (s, 1H), 7.37 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.1, 20.5, 27.5, 57.1, 109.0, 111.83, 112.6, 113.2, 119.8, 130.3, 131.5, 137.9. Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.50; H, 7.06; N, 19.65. The second fraction gave *9-ethyl-8-methylimidazo[1,2-h][1,7]naphthyridine* (**8c**); mp 183–185°C; IR (KBr) 1510, 1480, 1410, 1390, 1320, 1140 cm^{-1}; MS *m/z* 211 (M^+, 96), 210 (100), 183 (44); ^{1}H NMR ($CDCl_3$) δ 1.44 (t, 3H, *J*=7.5 Hz), 2.51 (s, 3H), 3.09 (q, 2H, *J*=7.5 Hz), 6.93 (d, 1H, *J*=7 Hz), 7.60 (d, 1H, *J*=1 Hz), 7.68 (d, 1H, *J*=1 Hz), 7.73 (s, 1H), 7.93 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.9, 19.0, 29.3, 111.3, 114.9, 123.1, 123.2, 131.1, 132.2, 135.0, 138.4, 143.1, 164.0. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20;

N, 19.89. Found: C, 74.12; H, 6.22; N, 19.83. *Method B*: (reaction time 2.5 h) to give **8c**.

4.7.4. Imidazo[2,1-*f*][1,6]naphthyridine (10a). From acrolein: *Method A*: (4 equiv., reaction time 14 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v). *Method B* (reaction time 4 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v), *Method C*: (eluate with AcOEt/hexanes, 8/2, v/v) as a yellow oil; IR (KBr) 1635, 1522, 1320, 805 cm^{-1}; MS *m/z* 169 (M^+, 100), 142 (48), 129 (16), 115 (27); ^1H NMR ($CDCl_3$) δ 7.31 (d, 1H, *J*=7.5 Hz), 7.53 (dd, 1H, *J*=4.5, 8 Hz), 7.62 (s, 1H), 7.64 (s, 1H), 8.12 (d, 1H, *J*=7.5 Hz), 8.88 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 114.5, 114.6, 119.9, 122.8, 126.5, 131.1, 132.7, 142.1, 146.5, 150.7. Anal. Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 71.09; H, 4.18; N, 24.92.

4.7.5. 8-Methylimidazo[2,1-*f*][1,6]naphthyridine (10b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 36 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v). *Method B*: (reaction time 4 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v); mp 116–118°C; IR (KBr) 1638, 1560, 1321 cm^{-1}; MS *m/z* 183 (M^+, 100), 182 (22), 142 (16); ^1H NMR ($CDCl_3$) δ 2.57 (s, 3H), 7.04 (d, 1H, *J*=7.5 Hz), 7.22 (d, 1H, *J*=8 Hz), 7.43 (s, 1H), 7.45 (s, 1H), 7.92 (d, 1H, *J*=7.5 Hz), 8.58 (d, 1H, *J*=8 Hz); ^{13}C NMR ($CDCl_3$) δ 24.7, 113.9, 117.2, 122.8 (2C), 126.1, 130.9, 131.1, 142.0, 145.7, 159.8. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 72.22, H, 4.94; N, 22.86.

From ethanal: *Method A*: (8 equiv., reaction time 14 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v). *Method B*: (reaction time 5 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v).

4.7.6. 8-Ethyl-9-methylimidazo[2,1-*f*][1,6]naphthyridine (10c). From propanal: *Method A*: yield: (8 equiv., reaction time 14 h, eluate with CH_2Cl_2/EtOH 99/1, v/v). *Method B*: (reaction time 5 h, eluate with CH_2Cl_2/EtOH 99/1, v/v); mp 89–91°C; IR (KBr) 1639, 1546, 1321 cm^{-1}; MS *m/z* 211 (M^+, 94), 210 (100), 183 (25), 51 (12); ^1H NMR ($CDCl_3$) δ 1.40 (t, 3H, *J*=7.5 Hz), 2.55 (s, 3H), 3.00 (q, 2H, *J*=7.5 Hz), 7.29 (d, 1H, *J*=7.5 Hz), 7.59 (s, 1H), 7.62 (s, 1H), 8.07 (d, 1H, *J*=7.5 Hz), 8.63 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.8, 19.1, 29.3, 114.2, 114.5, 118.2, 125.4, 131.3, 131.5, 132.0, 142.5, 144.4, 163.8. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.61; H, 6.18; N, 19.97.

4.7.7. Imidazo[1,2-*a*][1,5]naphthyridine (11a). From acrolein: *Method A*: (5 equiv., reaction time 18 h), *Method B*: (reaction time 3 h); mp 145–147°C; IR (KBr) 1528, 1454, 1316 cm^{-1}; MS *m/z* 169 (M^+, 100), 142 (16), 129 (31), 115 (17); ^1H NMR ($CDCl_3$) δ 7.52 (dd, 1H, *J*=4.5, 8.5 Hz), 7.68 (s, 1H), 7.73 (AB system, 2H, *J*=9.5 Hz), 8.04 (s, 1H), 8.19 (d, 1H, *J*=8.5 Hz), 8.77 (d, 1H, *J*=4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 111.7, 120.9, 122.5, 122.6, 127.4, 128.9, 133.5, 141.0, 143.3, 147.3. Anal. Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 70.92; H, 4.16; N, 24.85.

4.7.8. 7-Methylimidazo[1,2-*a*][1,5]naphthyridine (11b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 7 h), *Method B*: (reaction time 3 h); mp 166–168°C; IR (KBr) 1520, 1450, 1420, 1310 cm^{-1}; MS *m/z* 183 (M^+, 100), 156 (11), 129 (10); ^1H NMR ($CDCl_3$) δ 2.72 (s, 3H), 7.38 (d, 1H, *J*=8.5 Hz), 7.67 (s, 1H), 7.70 (AB system, 2H, *J*=9.5 Hz), 8.00 (s, 1H), 8.08 (d, 1H, *J*=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 24.5, 111.5, 120.7, 122.9, 123.0, 127.0, 127.1, 133.3, 140.3, 143.3, 156.3. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 72.24; H, 4.94; N, 22.95.

From ethanal: *Method A*: (2 equiv., reaction time 9 h), *Method B*: (reaction time 3 h).

4.7.9. 7-Ethyl-8-methylimidazo[1,2-*a*][1,5]naphthyridine (11c). From propanal: *Method A*: (2 equiv., reaction time 20 h). *Method B*: (reaction time 3 h); mp 163–165°C; IR (KBr) 1600, 1510, 1310, 1280, 1210, 1180 cm^{-1}; MS *m/z* 211 (M^+, 100), 210 (98), 194 (9), 183 (23); ^1H NMR ($CDCl_3$) δ 1.39 (t, 3H, *J*=7.5 Hz), 2.56 (s, 3H), 2.98 (q, 2H, *J*=7.5 Hz), 7.69 (s, 1H), 7.72 (s, 2H), 7.93 (s, 1H), 8.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.8, 19.4, 28.8, 111.3, 119.5, 123.5, 127.3, 127.5, 131.5, 133.3, 138.5, 143.6, 160.1. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.63; H, 6.22; N, 19.82.

4.7.10. Imidazo[1,2-*a*][1,8]naphthyridine[7g] (12a). From acrolein: *Method A*: (5 equiv., reaction time 6 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v). *Method B*: (reaction time 19 h, eluate with CH_2Cl_2/EtOH, 99/1, v/v); mp 90–92°C (lit. 91–93°C).

4.7.11. 8-Methylimidazo[1,2-*a*][1,8]naphthyridine[7b] (12b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 24 h). *Method B*: (reaction time 20 h); mp 100–102°C (lit. 101–103°C).

From ethanal: *Method A*: (8 equiv., reaction time 35 h). *Method B*: (reaction time 23 h).

4.7.12. (±)-6-Ethyl-5,6-dihydro-4-methylpyrido[6,1,2-*cd*]-2,3a,5-triazaazulene (±)-(13). From propanal: *Method A*: (3 equiv., reaction time 20 h) as an oil; IR (KBr) 3290, 1634, 1540, 1456, 1379, 1274, 1149 cm^{-1}; MS *m/z* 213 (M^+, 63), 198 (33), 184 (100), 143 (30); ^1H NMR ($CDCl_3$) δ 1.04 (t, 3H, *J*=7 Hz), 1.38 (m, 1H), 1.70 (m, 1H), 2.02 (s, 3H), 3.68 (m, 1H), 5.45 (brs, 1H), 6.12 (d, 1H, *J*=7 Hz), 6.44 (s, 1H), 7.10 (t, 1H, *J*=7 Hz), 7.18 (d, 1H, *J*=7 Hz), 7.47 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 10.7, 24.07, 28.7, 64.4, 97.9, 108.6, 114.1, 123.3, 126.4, 133.5, 133.8, 143.1, 148.5. Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.33; H, 7.11; N, 19.74.

4.7.13. Dipyrido[1,2-*a*;2′,3′-*d*]imidazole (16a). From acrolein: *Method A*: (4 equiv., reaction time 20 h). *Method B*: (reaction time 20 h); mp 199–201°C; IR (KBr) 1497, 1408 cm^{-1}; MS *m/z* 169 (M^+, 100), 168 (22), 142 (11), 78 (44), 51 (37); ^1H NMR ($CDCl_3$) δ 6.96 (t, 1H, *J*=7 Hz), 7.30 (dd, 1H, *J*=4.5, 8 Hz), 7.54 (m, 1H), 7.80 (d, 1H, *J*=9 Hz), 8.23 (d, 1H, *J*=8 Hz), 8.51 (d, 1H, *J*=7 Hz), 8.83 (d, *J*=4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 111.3, 115.9, 118.3, 118.7, 121.1, 125.8, 130.7, 148.7, 149.6, 156.3. Anal. Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 71.22; H, 4.16; N, 24.79.

4.7.14. 4-Methyldipyrido[1,2-*a*;2′,3′-*d*]imidazole (16b). From crotonaldehyde: *Method A*: (5 equiv., reaction time 17 h). *Method B*: (reaction time 20 h); mp 192–194°C; IR

(KBr) 1500, 1483, 1278, 1124 cm^{-1}; MS *m/z* 183 (M^+, 100), 182 (34), 168 (8), 155 (12), 78 (37), 51 (33); ^1H NMR ($CDCl_3$) δ 2.81 (s, 3H), 6.80 (t, 1H, *J*=7 Hz), 6.88 (d, 1H, *J*=5 Hz), 7.37 (m, 1H), 7.64 (d, 1H, *J*=9 Hz), 8.50 (d, 1H, *J*=5 Hz), 8.52 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 18.7, 111.1, 117.9, 118.4, 120.5, 127.8, 130.8, 132.7, 147.9, 149.1, 155.7. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 71.88; H, 4.95; N, 22.99.

4.7.15. 2-Methyldipyrido[1,2-*a*;2′,3′-*d*]imidazole (16c). From ethanal: *Method A*: (6 equiv., reaction time 22 h). *Method B*: (reaction time 20 h); mp 220–222°C; IR (KBr) 3043, 1596, 1498, 1409, 1350, 1242 cm^{-1}; MS *m/z* 183 (M^+, 100), 182 (44), 155(11), 78 (29), 51 (26); ^1H NMR ($CDCl_3$) δ 2.77 (s, 3H), 6.89 (t, 1H, *J*=7 Hz), 7.14 (d, 1H, *J*=8 Hz), 7.47 (m, 1H), 7.74 (d, 1H, *J*=9 Hz), 8.03 (d, 1H, *J*=8 Hz), 8.44 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 25.1, 111.0, 116.0, 118.2, 118.7, 119.1, 125.6, 130.0, 149.3, 156.1, 157.9. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 72.08; H, 4.94; N, 23.01.

4.7.16. 2-Ethyl-3-methyldipyrido[1,2-*a*;2′,3′-*d*]imidazole (16d) and 3-ethyl-2-methyldipyrido[1,2-*a*;2′,3′-*d*]imidazole (16e). From propanal: *Method A*: (2.2 equiv., reaction time 17 h) gave compound **16d**; mp 219–221°C; IR (KBr) 1609, 1504, 1449, 1402, 1354, 1256 cm^{-1}; MS *m/z* 211 (M^+, 74), 210 (100), 183 (21), 78 (28), 51 (18); ^1H NMR ($CDCl_3$) δ 1.43 (t, 3H, *J*=7 Hz), 2.54 (s, 3H), 3.02 (q, 2H, *J*=7 Hz), 6.87 (t, 1H, *J*=6.5 Hz), 7.44 (m, 1H), 7.74 (d, 1H, *J*=9 Hz), 7.92 (s, 1H), 8.39 (d, 1H, *J*=6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 12.7, 19.4, 29.2, 110.6, 117.9, 119.2, 119.3, 123.9, 125.5, 129.2, 148.6, 154.5, 161.3. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.98; H, 6.21; N, 19.84. *Method B*: (reaction time 20 h) yield in order to elution **16d** and **16e**; mp 178–180°C; IR (KBr) 1639, 1495, 1357, 1321 cm^{-1}; MS *m/z* 211 (M^+, 100), 196 (29), 182 (23) 169 (7), 78 (2); ^1H NMR ($CDCl_3$) δ 1.28 (t, 3H, *J*=7.5 Hz), 2.40 (s, 3H), 3.07 (q, 2H, *J*=7.5 Hz), 6.81 (t, 1H, *J*=7 Hz), 7.36 (m, 1H), 7.67 (d, 1H, *J*=9 Hz), 8.46 (s, 1H), 8.48 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.7, 15.7, 21.2, 111.2, 118.3, 119.8, 124.0, 127.7, 129.2, 136.7, 149.1, 150.0, 155.1. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.98; H, 6.19; N, 19.92.

4.7.17. Dipyrido[1,2-*a*;3′,2′-*d*]imidazole[1] (17a). From acrolein: *Method A*: (4 equiv., reaction time 7 h) yield 6%. *Method B*: (reaction time 3.5 h). *Method C*: (using dry 1,2-dichlorobenzene (40 mL) as solvent, 90°C for 21 h and reflux for 3 h); mp 125–127°C (lit. 129–131°C).

4.7.18. 4-Methyldipyrido[1,2-*a*;3′,2′-*d*]imidazole[1] (17b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 23 h); mp 134–136°C (lit. 143–145°C). *Method B*: (reaction time 11 h) gave *(±)-5,6-dihydro-6-methylpyrido[6,1,2-cd]-2,3a,8-triazaazulene* (**20**) as an oil; IR (KBr) 1627, 1521, 1500, 1453, 1294 cm^{-1}; MS *m/z* 185 (M^+, 90), 170 (100), 157 (50), 104 (55), 78 (41), 63 (20), 51 (39); ^1H NMR ($CDCl_3$) δ 1.19 (d, 3H, *J*=6.5 Hz), 2.58 (d, 1H, *J*=16 Hz), 2.93 (td, 1H, *J*=6.5, 16 Hz), 3.52 (quint., *J*=6.5 Hz), 6.70 (d, 1H, *J*=7 Hz), 7.19 (dd, 1H, *J*=7, 8 Hz), 7.52 (m, 2H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1, 36.2, 40.0, 110.7, 116.0, 125.3, 132.5, 135.9, 143.3, 146.4, 152.7. Anal. Calcd for $C_{11}H_{11}N_3$: C, 71.33; H, 5.99; N, 22.69. Found: C, 71.21; H, 5.99; N, 22.77.

4.7.19. 2-Methyldipyrido[1,2-*a*;3′,2′-*d*]imidazole[1] (17c). From ethanal: *Method A*: (4 equiv., reaction time 16 h). *Method B*: (reaction time 2.5 h); mp 150–152°C (lit. 149–151°C).

4.7.20. 2-Ethyl-3-methyldipyrido[1,2-*a*;3′,2′-*d*]imidazole (17d). From propanal: *Method A*: (2.2 equiv., reaction time 7 h). *Method B* (reaction time 4 h); mp 108–110°C; IR (KBr) 1639, 1571, 1493, 1397, 1134 cm^{-1}; MS *m/z* 211 (M^+, 66), 196 (100), 149 (16), 78 (55), 51 (24); ^1H NMR ($CDCl_3$) δ 1.37 (t, 3H, *J*=7.5 Hz), 2.47 (s, 3H), 2.93 (q, 2H, *J*=7.5 Hz), 6.80 (t, 1H, *J*=7 Hz), 7.38 (m, 1H), 7.58 (d, 1H, *J*=9 Hz), 7.88 (s, 1H), 8.72 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.9, 19.6, 28.7, 110.2, 117.8, 124.4, 127.8, 129.5, 129.9, 135.1, 139.8, 147.9, 155.4. Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89. Found: C, 74.18; H, 6.22; N, 19.84.

4.7.21. 2-(4-Bromophenyl)-5,6-dihydropyrido[6,1,2-*cd*]-2,3a,8-triazaazulene (24a). From acrolein: *Method A*: (10 equiv., reaction time 24 h). *Method B*: (reaction time 30 h). *Method C*: (using dry 1,2-dichlorobenzene (40 mL) as solvent, 90°C for 20 h and reflux for 4 h) yield: 13%; mp 124–126°C; IR (KBr) 1470, 1340, 1010 cm^{-1}; MS *m/z* 327 (M^++2, 96), 325 (M^+, 100), 312 (8), 246 (12), 117 (16), 91 (43), 64 (13); ^1H NMR ($CDCl_3$) δ 2.96 (m, 2H), 3.19 (m, 2H), 6.65 (d, 1H, *J*=6.5 Hz), 7.22 (m, 1H), 7.55 (d, 1H, *J*=9 Hz), 7.61 (d, 2H, *J*=7.5 Hz), 7.70 (t, 1H, *J*=4 Hz), 8.38 (d, 2H, *J*=7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 30.8, 34.65, 112.1, 115.9, 122.3, 126.0, 128.5, 130.6 (2C), 131.3 (2C), 133.1, 139.0, 141.9, 144.8, 154.9. Anal. Calcd for $C_{16}H_{12}N_3Br$: C, 58.91; H, 3.71; N, 12.88. Found: C, 59.04; H, 3.70; N, 12.83.

4.7.22. (±)-2-(4-Bromophenyl)-5,6-dihydro-6-methylpyrido[6,1,2-*cd*]-2,3a,8-triazaazulene (24b). From crotonaldehyde: *Method A*: (4 equiv., reaction time 5 h) yield *2-(4-bromophenyl)-3-(but-2-eneimino)imidazo[1,2-a]pyridine* (**25a**); mp 108–110°C; IR (KBr) 1580, 1480, 1340, 1220 cm^{-1}; MS *m/z* 341 (M^++2, 27), 339 (M^+, 29), 325 (10), 261 (30), 78 (100), 51 (16); ^1H NMR ($CDCl_3$) δ 2.02 (dd, 3H, *J*=1.5, 7 Hz), 6.29 (sex., 1H, *J*=7, 15.5 Hz), 6.51 (ddd, 1H, *J*=15.5, 1.5, 9 Hz), 6.87 (t, 1H, *J*=7 Hz), 7.24 (m, 1H), 7.58 (d, 1H, *J*=9 Hz), 7.59 (d, 2H, *J*=8.5 Hz), 7.71 (d, 2H, *J*=8.5 Hz), 8.27 (d, 1H, *J*=7 Hz), 8.32 (d, 1H, *J*=9 Hz); ^{13}C NMR ($CDCl_3$) δ 18.9, 112.4, 117.4, 121.7, 123.10, 125.0, 129.8 (2C), 131.9 (2C), 132.9, 133.9, 142.8, 144.2, 161.9. Anal. Calcd for $C_{17}H_{14}N_3Br$: C, 60.02; H, 4.15; N, 12.35. Found: C, 59.96; H, 4.14; N, 12.38. *Method A*: (6 equiv., reaction time at 105°C for 7.5 h, and under reflux for 17 h). The first eluate gave (±)-**24b**; mp 155–157°C; IR (KBr) 1620, 1500, 1470, 1340, 1300, 1230 cm^{-1}; MS *m/z* 341 (M^++2, 100), 339 (M^+, 94), 326 (55), 324 (57), 244 (14), 123 (17), 104 (48), 78 (18); ^1H NMR ($CDCl_3$) δ 1.24 (d, 3H, *J*=7 Hz), 2.63 (d, 1H, *J*=15.5 Hz), 2.98 (dt, 1H, *J*=15.5, 6 Hz), 3.54 (m, 1H), 6.69 (d, 1H, *J*=7 Hz), 7.22 (dd, 1H, *J*=7, 9 Hz), 7.55 (d, 1H, *J*=9 Hz), 7.60 (d, 2H, *J*=8.5 Hz), 7.62 (m, 1H), 8.29 (d, 2H, *J*=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 20.4, 36.3, 40.1, 110.9, 115.7, 122.2, 125.9, 128.4, 130.6 (2C), 131.2 (2C), 133.1, 141.8, 143.6,

144.9, 152.7. Anal. Calcd for $C_{17}H_{14}N_3Br$: C, 60.02; H, 4.15; N, 12.35. Found: C, 60.21; H, 4.16; N, 12.33. The second eluate gave **25a**. *Method B*: (reaction time for 30 h) yields compound (±)-**24b**.

From acetaldehyde: *Method A*: (4 equiv., reaction time 28 h) gave (±)-**24b**. *Method B*: (reaction time 30 h) gave (±)-**24b**.

4.7.23. (±)-2-(4-Bromophenyl)-6-ethyl-5,6-dihydro-5-methylpyrido[6,1,2-*cd*]-2,3a,8-triazaazulene (±)-(24c). From propanal: *Method A*: (8 equiv., reaction time 31 h). The first eluate gave (±)-**24c** as an oil; yield: 6%; IR (KBr) 1620, 1500, 1470, 1350, 1300, 1240 cm^{-1}; MS *m/z* 369 (M^++2, 82), 367 (M^+, 82), 340 (97), 338 (100), 311 (16), 118 (21), 104 (18), 78 (13); ^1H NMR ($CDCl_3$) δ 0.82 (t, 3H, *J*=7 Hz), 1.10 (m, 1H), 1.55 (d, 3H, *J*=7.5 Hz), 1.64 (m, 1H), 2.27 (qd, 1H, *J*=7.5, 2 Hz), 3.05 (d, 1H, *J*=11.5 Hz), 6.65 (d, 1H, *J*=6.5 Hz), 7.24 (dd, 1H, *J*=6.5, 9 Hz), 7.37 (d, 1H, *J*=2 Hz), 7.58 (d, 1H, *J*=9 Hz), 7.61 (d, 2H, *J*=8.5 Hz), 8.30 (d, 2H, *J*=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 11.9, 17.8, 22.1, 42.3, 51.3, 112.8, 115.7, 122.3, 125.3, 128.1, 130.6 (2C), 131.3 (2C), 133.1, 140.8, 141.9, 145.1, 158.3. Anal. Calcd for $C_{19}H_{18}N_3Br$: C, 61.97; H, 4.93; N, 11.41. Found: C, 62.11; H, 4.94; N, 11.36. The second eluate gave *2-(4-bromophenyl)-3-(2-methylpent-2-ene-imino)imidazo[1,2-a]pyridine* (**25b**) as an oil; yield: 7%; IR (KBr) 1580, 1470, 1340, 1220 cm^{-1}; MS *m/z* 369 (M^++2, 18), 367 (M^+, 18), 354 (37), 352 (37), 289 (10), 261 (16), 259 (16), 78 (100), 51 (18); ^1H NMR ($CDCl_3$) δ 1.11 (t, 3H, *J*=7.5 Hz), 2.08 (s, 3H), 2.37 (m, 2H), 5.94 (t, 1H, *J*=7 Hz), 6.85 (t, 1H, *J*=6.6 Hz), 7.22 (m, 1H), 7.57 (m, 3H), 7.73 (d, 2H, *J*=8.5 Hz), 8.28 (d, 1H, *J*=6.6 Hz), 8.32 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 10.9, 13.4, 22.4, 112.3, 117.4, 121.5, 123.1, 124.8, 129.7 (2C), 131.0, 131.3, 131.8 (2C), 134.00, 142.7, 148.0, 136.3, 164.4. Anal. Calcd for $C_{19}H_{18}N_3Br$: C, 61.97; H, 4.93; N, 11.41. Found: C, 61.81; H, 4.91; N, 11.46. *Method A*: (18 equiv., reaction time 45 h) gave (±)-**24c**. *Method B*: (reaction time 30 h) gave (±)-**24c**.

4.7.24. 3-Ethaniminoimidazo[1,2-*a*]pyridine (18). To a solution of **5e** (0.40 g, 3.01 mmol) in dry CH_2Cl_2 (40 mL), a solution of acetaldehyde (0.20 g, 4.55 mmol) in the same solvent (10 mL) was added. The mixture was stirred at rt for 36 h. The solvent was evaporated and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to yield **18** (0.45 g, 94%) as an oil; IR (KBr) 1633, 1501, 1357 cm^{-1}; MS *m/z* 159 (M^+, 100), 105 (15), 79 (18); ^1H NMR ($CDCl_3$) δ 2.20 (d, 3H, *J*=5 Hz), 6.79 (t, 1H, *J*=7 Hz), 7.12 (m, 1H), 7.48 (s, 1H), 7.50 (d, 1H, *J*=9 Hz), 8.22 (q, 1H, *J*=5 Hz), 8.31 (d, 1H, *J*=7 Hz); ^{13}C NMR ($CDCl_3$) δ 23.2, 112.2, 117.5, 118.7, 122.7, 124.2, 134.1, 143.6, 158.7. Anal. Calcd for $C_9H_9N_3$: C, 67.91; H, 5.70; N, 26.40. Found: C, 68.11; H, 5.71; N, 26.32.

4.8. Thermolysis of 18

To a solution of **18** (0.45 g, 2.83 mmol) in dry 1,2-dichlorobenzene (20 mL), a solution of acetaldehyde (0.14 g, 3.18 mmol) in the same solvent (5 mL), and a small quantity of 10% Pd/C were added. The solution was refluxed for 2.5 h. The solvent was evapored and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to yield **17c** (70 mg, 14%).

4.8.1. 3-(But-2-eneimino)imidazo[1,2-*a*]pyridine (19). To a solution of **5e** (0.70 g, 5.26 mmol) in dry toluene (30 mL), a solution of crotonaldehyde (0.74 g, 10.6 mmol) in the same solvent (5 mL) was added. The mixture was stirred at 70°C for 10 h. The solvent was evaporated and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to yield **19** (0.75 g, 77%); mp 116–118°C; IR (KBr) 1637, 1583, 1485, 1338, 1302, 1250 cm^{-1}; MS *m/z* 185 (M^+, 32), 169 (16), 107 (34), 78 (100), 51 (42); ^1H NMR (CD_3OD) δ 1.92 (d, 3H, *J*=6 Hz), 6.42 (m, 2H), 6.90 (t, 1H, *J*=7 Hz), 7.24 (m, 1H), 7.43 (d, 1H, *J*=9 Hz), 7.59 (s, 1H), 8.33 (d, 1H, *J*=7 Hz), 8.38 (d, 1H, *J*=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 18.8, 112.2, 117.7, 119.2, 123.0, 124.5, 132.9, 134.4, 142.3, 144.1, 156.9. Anal. Calcd for $C_{11}H_{11}N_3$: C, 71.33; H, 5.99; N, 22.69. Found: C, 71.42; H, 5.97; N, 22.71.

4.9. Thermolysis of 19

To a solution of **19** (0.20 g, 1.08 mmol) in dry 1,2-dichlorobenzene (15 mL), a small quantity of 10% Pd/C was added. The solution was stirred under reflux for 20 h. The solvent was evaporated and the crude product was chromatographed (neutral Al_2O_3, CH_2Cl_2) to yield **17b** (22 mg, 11%).

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