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Synthesis of new bis(2-[1,8]naphthyridinyl) bridging ligands with multidentate binding sites

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Abstract

A series of new 2-[1,8]naphthyridinyl and bis(2-[1,8]naphthyridinyl) bridging ligands with multidentate binding sites were prepared using 2-amino-5-cyano-6-ethoxy-4-phenyl-3-carbaldehyde pyridine as excellent Friedländer synthon. Condensation with a series of acetyl(heteroaryl)-aromatics provides the corresponding 2-aryl(heteroaryl)-1,8-naphthyridines. Reaction with 1,3-diacetylbenzene, 2,6-diacetylpyridine or 4-*tert*-butyl-2,6-diacetylpyridine provides the expected Friedländer product. Similar 2:1 condensation with 1,4-diacetylbenzene, 4,4′-diacetylbiphenyl, 1,4- and 1,6-diacetylpyrene, 2,6-diacetylpyrazine or 2,3-butanedione leads to a family of six new bis-1,8-nap ligands. The reaction with cyclic 1,2- or 1,3-diketones affords 3,3′-annelated derivatives of all-*syn* or all-trans planar 2,2′-nap, respectively. Examination of the electronic absorption and emission spectra of the bridging ligands was realized.

1. Introduction

Bridging ligands have received much interest recently due to their ability to couple metal centres in a covalent manner resulting in polymetallic complexes that often possess new and interesting properties as, for example, photosynthetic mimics, molecular devices and electrocatalysts. Heteroaromatic nitrogen ligands find extended applications in several important research and technological fields, including asymmetric catalysis, DNA binding, use as diagnostic agents and drugs, tumour targeting, nonlinear optical materials and other applications in electrooptical and photonic devices.[1] Currently, there is enormous interest in the design and preparation of polydentate ligands capable of self-assembly processes.[2] Among the polydentate ligands, the 1,8-naphthyridine molecule has received wide attention because of its ability to function as an effective ligand. The naphthyridines and their derivatives exhibit various types of biological activity, and their organic chemistry has been frequently reviewed.[3] 1,8-Naphthyridine (nap), although less basic than 2,2′-bipyridine (bpy), can also function as a bidentate ligand where the nitrogen lone pairs are now fixed nearly parallel and coplanar in a 1,3 relationship. The functionalized derivatives of nap at positions 2 and 7 with, at least, a donor atom or group (X=O, N, P), such as X-nap **I** and X_2-nap **II**, introduce multiple coordination possibilities, and the ability to act as polynucleating ligands gathering several metal centres (Fig. 1).[4] Coordinating substituents on positions 2 and 7 of the napy ring, such as **III** (pynap) and **IV** (bpnap) (Fig. 1), gave rise to polydentate, cavity-shaped molecules able to coordinate two metal centres in the cavity.[5] Novel multidentate dinucleating ligands based

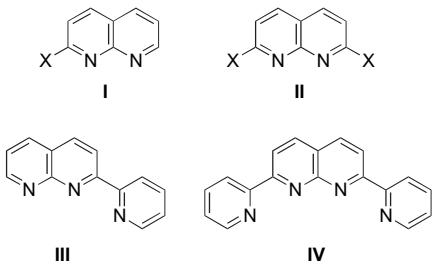

Figure 1.

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on 1,8-naphthyridine have been prepared with the aim of mimicking the coordination environment of dinuclear metallohydrolases that perform the hydrolysis of biologically important substrates such as DNA, RNA and peptides.[6]

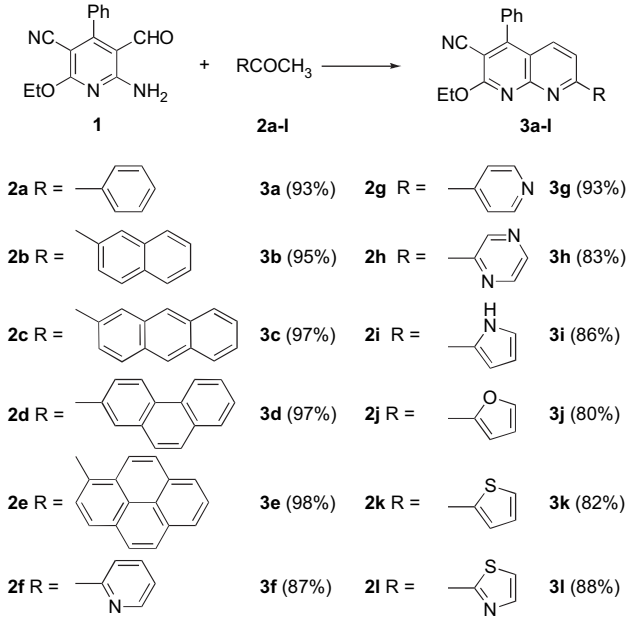
The Friedländer condensation, in which an aromatic α,β-unsaturated β-aminoaldehyde or ketone is condensed with an aldehyde or ketone containing at least one methylene group α to the carbonyl, represents a versatile and straightforward approach to the pyridine nucleus especially when it is incorporated into annulated derivatives such as quinoline and 1,8-naphthyridine.[7] The Friedländer reaction of *o*-aminoaldehydes to prepare quinolines was extensively reviewed by Cheng and Yan in 1982.[8] Caluwe et al.[9] and Thummel et al.[10] have demonstrated the use of this method for the regioselective introduction of 1,8-naphthyridine units. Friedländer reactions are generally carried out either by refluxing an aqueous or alcoholic solution of reactants in the presence of acids or bases or may take place by heating the reactants at high temperatures in the absence of catalyst. In recent years, modified methods have been employed and chlorotrimethylsilane,[11] Lewis acids,[12] iodine,[13] a combination of acidic catalysts and microwave irradiation[14] and ionic liquids[15] have all been found to be effective for this conversion.

We previously reported a highly efficient and regioselective synthesis of substituted pyrazinothienopyrimidinones and bis-(pyrazinothienopyrimidinyl)benzenes of interest as potential biologically active compounds or pharmaceuticals, as well as in their use as appropriate phenanthroline-like ligands.[16] In this context, as part of a programme of investigating the synthesis and study of new bridging ligands and their use as chelating ligands, we directed our attention to the synthesis of novel multidentate nitrogen based ligands and, herein, we disclose that the β-enaminoaldehyde **1** is an excellent Friedländer building block[17] for the preparation of a variety of functionalized derivatives of nap at positions 2 and 7, including annelated cavity-shaped molecules derivatives of substituted bis-1,8-naphthyridines.

2. Results and discussion

The prerequisite heterocyclic aminoaldehyde used as starting material for the preparation of the title condensed 1,8-naphthyridine derivatives can be readily prepared by $LiAlH_4$ reduction of 2-amino-3,5-dicyano-6-ethoxy-4-phenylpyridine,[18] which is easily accessible from malononitrile and benzaldehyde.[19] First, the initial objective was the synthesis of 2-aryl and 2-heteroaryl derivatives **3a–l**. Thus, the base-catalyzed reaction of the β-aminoaldehyde **1** with aryl and heteroaryl methyl ketones **2a–l** provides the corresponding 2-aryl and 2-heteroaryl-1,8-naphthyridines in very good yields of 80–98% (Scheme 1). The series of 2-aryl(heteroaryl) derivatives **3a–l** would help to investigate the π-stacking effect of this aromatic substituent with a pyridine of one of the auxiliary bpy ligands in $Ru(bpy)_2$ complexes.[10b,20]

The Friedländer reaction of **1** with a variety of diketones occurs readily under basic conditions leading polyaza cavities of bis-1,8-naphthyridine. Thus, we have prepared 1,4-bis-



Scheme 1.

(2′-nap)benzene **4** and the 4,4′-disubstituted biphenyl analogue ligand **5**. In fact, the aminoaldehyde **1** then undergoes double Friedländer condensation with 1,4-diacetylbenzene to provide 1,4-di(1,8-naphthyridyn-2′-yl)-benzene **4** (Fig. 2). In an analogous fashion, the condensation of **1** with 4,4′-diacetylbiphenyl provides the homologated biphenyl-bridged system **5** in 77% yield. Other diketones will condense in a similar 2:1 fashion, and thus, when 1,4-diacetylpyrene or 1,6-diacetylpyrene,

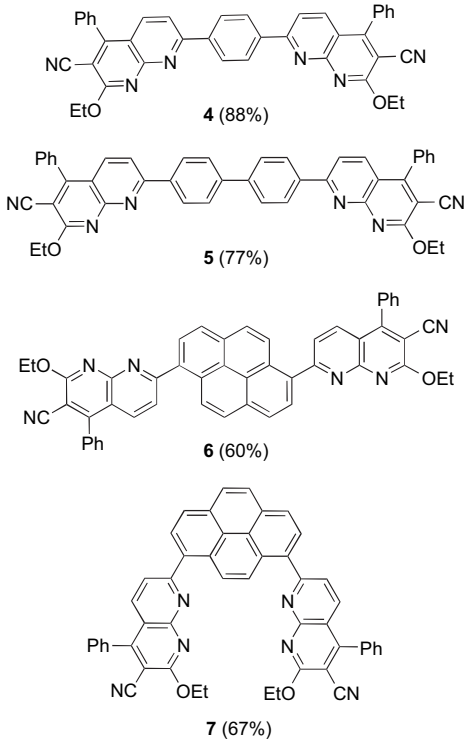
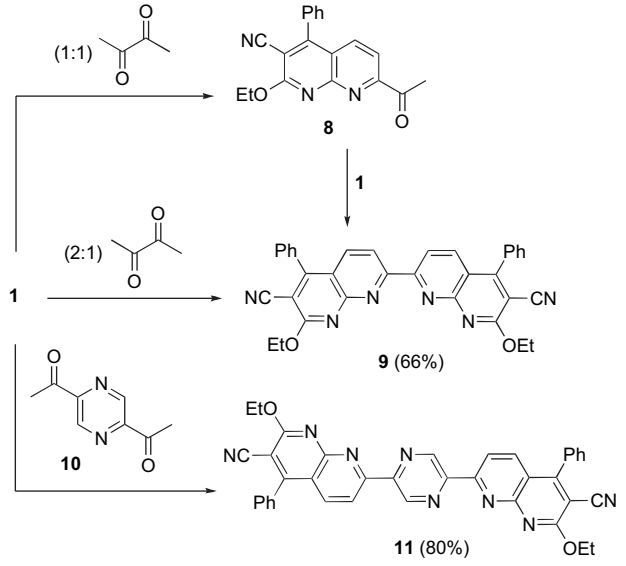


Figure 2.

accomplished according to a published procedures,[21] is condensed with the β-enaminoaldehyde **1**, the analogous corresponding 1,4- or 1,6-di(1,8-naphthyridyn-2′-yl)-pyrenes, **6** and **7**, are prepared in 60 and 67% yield, respectively. These four systems provide an interesting series of ligands wherein the orientation between metals bound at the two 1,8-naphthyridine sites will be controlled by the bridging group. This group will also strongly influence any electronic communication between the metal centres through the π-framework.[10b]

This synthesis could also be adapted to the preparation of analogues having their terminal 1,8-naphthyridine groups linked. Thus, 2,3-butanedione condenses in a similar 2:1 fashion, and provides 2,2′-bis[1,8]-naphthyridine **9** as a multidentate ligand (Scheme 2). The reaction of 2,3-butanedione with **1** in a 1:1 molar ratio in ethanol, under a catalytic alkaline conditions (10% ethanolic potassium hydroxide), gives 2-acetyl-1,8-naphthyridine **8**. Formation of **9** was confirmed by using an alternative way involving Friedländer condensation of acetylnaphthyridine **8** with **1** under the same reaction conditions. Similarly, the dinap-pyrazine **11** was synthesized by a double Friedländer condensation using an appropriate diacetyl diazine precursor and 2 equiv of α,β-enaminonitrile **1** (Scheme 2). The diacetylpyrazine **10** was prepared by the free radical acetylation of pyrazine using acetaldehyde and *tert*-butylhydroperoxide in the presence of ferric sulfate.[22] The condensation with **1** proceeded smoothly to afford 80% of the expected 2,5-dinappyridazine **11**.

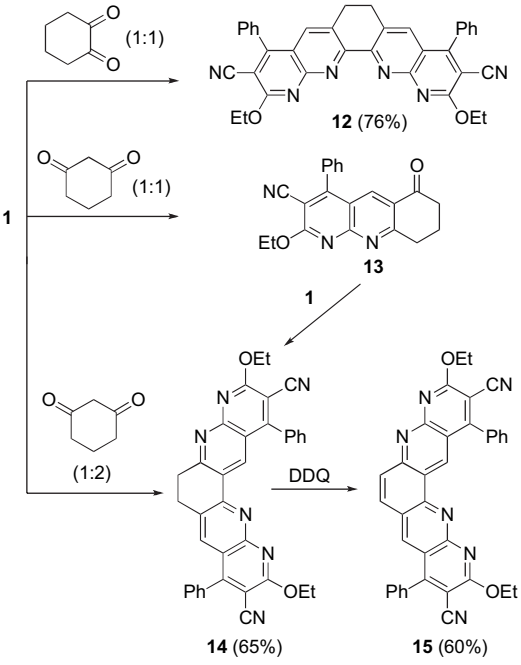


Scheme 2.

All bridging ligands **4**, **5**, **9** and **11** were readily characterized by ^{1}H NMR. The 2-nap moieties gave very similar and characteristic patterns in the aromatic region. Thus, the ^{1}H NMR spectra show two doublets at δ=8.04–8.17 and 8.20–8.86 (J=8.4–8.6) due to either one protons of the naphthyridine skeletons. The central ring was distinguished by either one singlet, δ=8.40 for **4** and 10.02 for **11**, or one multiplet, δ=7.85–7.92 for **5**. The deshielding of these protons was consistent with their proximities to nitrogen.[23] For the ligands **6** and **7**, the pyrene protons may be explained by their characteristic coupling patterns and chemical shifts. For the isomer **7** H4=H5 and H9=H10 and the signals of these protons appear as a singlets at δ=8.48 and 8.20, respectively. For this isomer, H3=H6≠H2=H7 and thus H3 and H6, as well as H2 and H7, appear as doublets at δ=8.39 and 8.35, respectively. For the isomer **6**, H4=H9≠H3=H8≠H2=H7≠H5=H10 appear as doublets at δ=8.50 (J=9.3 Hz), 8.36 (J=8.0 Hz), 8.32 (J=8.0 Hz) and 8.16 (J=9.3 Hz), respectively.

All the ligands are shown in their all-*syn* planar conformation, which would be the one providing the greatest interaction between two bond metal centres and emphasize potential cooperativity on metal binding. The free ligands in solution, however, more likely exist in conformations that would minimize H–H and nitrogen lone pair–lone pair repulsions about single bonds.[24] Rotation about the single bond connecting the terminal nap to the linker would provide other conformations of the ligands. Furthermore, molecule **5** has other single bonds in the linker, which would afford additional conformational freedom. Binding two metals will, in every case, restrict this rotational freedom. The fused pyridine rings serve to sterically congest the coordinating pocket of the molecule in its *syn* conformation and limit the types of complexation which can occur.[25]

Reactions of heterocyclic aminoaldehydes with cyclic diketones are especially valuable for the construction of polycondensed heterocyclic compounds for which in many cases alternate annelation methods are not readily available. The direction of annelation and the position of the heteroatom(s) are in general uniquely defined by the participating functional groups. As shown in Scheme 3, 1,2-cyclohexanedione provides direct accessibility of the 3,3′-annelated 2,2′-bis[1,8]-naphthyridine **12**. This 3,3′-ethylene-bridged system **12** is a cavity-shaped molecule with sp^2-hybridized nitrogen atoms



Scheme 3.

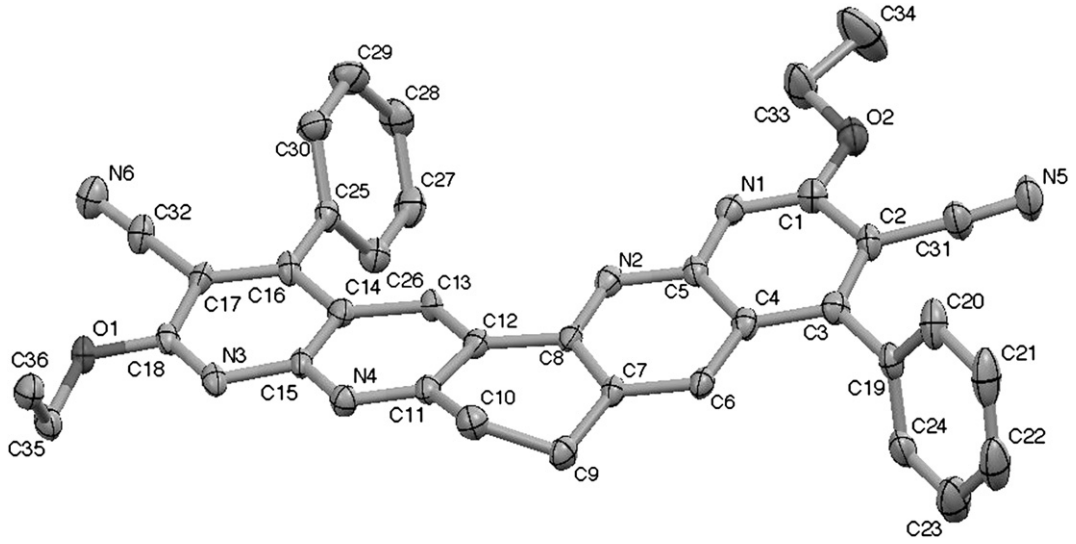


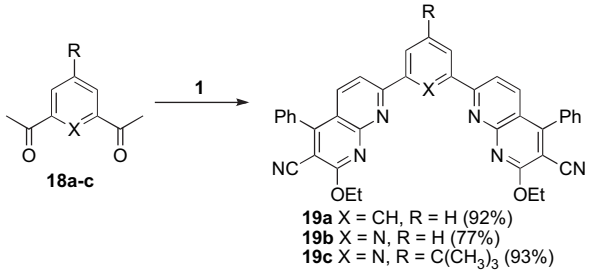
Figure 3. Crystal structure of compound **14** showing the atom labelling scheme and 50% probability thermal ellipsoids. Solvent molecules and hydrogen atoms have been omitted for clarity.

at every nonbridgehead position on the 'bay region'. Thus, the double condensation reaction of 1,2-cyclohexanedione with **1** in a 1:2 molar ratio proceeds to form exclusively polyaza cavity-shaped molecule **12** in a good manner. However, the analogous reaction with 1,2-cyclopentanedione has thus far been unsuccessful.

Annelation reactions of β-diketones with **1** are greatly facilitated by the presence of a double activated α-methylene group and, as expected, only one directed ring closure is observed. Thus, the base-catalyzed condensation of nicotinaldehyde **1** with 1,3-cyclohexanedione provides tricyclic ketone **13** or annelated bisnap **14**, depending on the molar ratio of the reactants. Treatment of the annelated ketone **13** with nicotinaldehyde **1** likewise resulted in the formation of the pentacyclic bisnaphthyrine **14** in 65% yield. Compound **14** could be oxidized to the fully aromatic derivative **15** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing THF. Bisnap molecule **12** can be considered as a 3,3′-ethylene-bridged derivative of all-*syn* planar 2,2′-bis[1,8]-naphthyrine **9**, and the latter ligands **14** and **15** as a 3,3′-dimethylene-bridged or a 3,3′-ethene-bridged derivative of all-trans planar 2,2′-nap **9**, respectively. The steric requirements of both ligands **9** and **12** are very similar, and differences in the properties of their metal complexes could be mostly attributed to electronic differences from the greater electronegativity of 2,2′-bis[1,8]-naphthyridine **12**.[26]

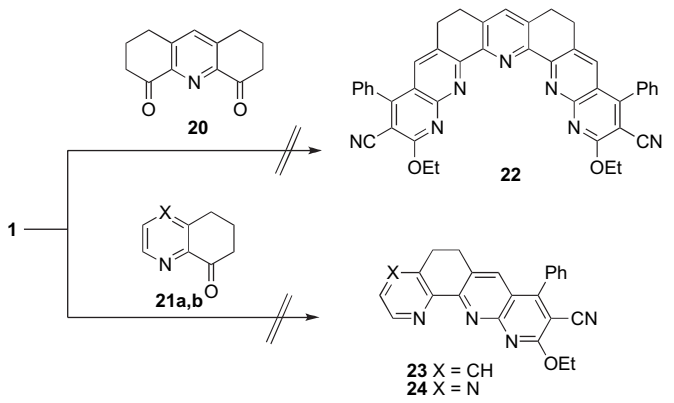
Further unambiguous identification for **12**–**15** was obtained from ^{1}H NMR, ^{13}C NMR, MS and elemental analyses. It should be noted that when the bridge contains more than one methylene unit a conformational inversion of the non-planar ring is possible, providing an interconvertible pair of enantiomers via twisting about the 3,3′-bond.[10a] As has been previously noted for other bridged similar compounds,[10] the 3,3′-ethylene system of **12** is conformationally mobile on the NMR time scale and a singlet is observed at δ=3.80 as expected for 4 equiv protons flanked by two napthyridine groups. For the ethylene bridge of **14**, the CH_2 groups are non-equivalent and two signals are observed. The structural determination of **14** was unequivocally established by the X-ray structure determination of a monocrystal (Fig. 3).

With a view towards modifying the size, shape and denticity of the binding pocket, we have undertaken in the preparation of polyaza ligands in which nitrogens are situated inside a molecular cavity potentially capable of polynuclear metal coordination. These ligands consist of two terminal moieties of 1,8-naphthyridine connected by an intervening aromatic or heteroaromatic species. Thus, the cavity-shaped molecules **19a**–**c** were synthesized by a double Friedländer condensation using 1,3-diacetylbenzene (**18a**), 2,6-diacetylpyridine (**18b**) or 4-*tert*-butyl-2,6-diacetylpyridine (**18c**)[27] precursors and 2 equiv of 2-amino-3-pyridinecarbaldehyde **1** (Scheme 4).



Scheme 4.

1,2,3,4,5,6,7,8-Octahydroacridine-2,8-dione **20**[28] may be considered as a bridged derivative of **19a**. Although it could be condense with **1** to provide the highly congested naphthyridine derivative **22**, solubility problems thwarted the characterization of this compound. That compound was detected in the ^{1}H NMR and mass spectra of the crude material but unfortunately separation and purification have been unsuccessful (Scheme 5). Also, an analogous 2:1 reaction with 5,6,7,8-tetrahydro-8-quinolone **21a** or 5,6,7,8-tetrahydro-8-quinazolone **21b**[29] to provide the ethylene bridged parent ligands **23** and



Scheme 5.

24 was also unsuccessful (Scheme 5). Once again, by solubility problems we have never been able to isolate such interesting bridged bisnaphthyridines although these compounds were detected in the ^{1}H NMR spectra of the crude materials.

The functionalized derivatives of 1,8-naphthyridine and 1,8-bisnaphthyridines prepared in this work introduce multiple coordination possibilities, and the ability to act as polynucleating ligands gathering by binding two or more metal atoms. On the other hand, several of the prepared ligands have a variety of different denticities available. Although it is possible for 1,8-naphthyridine to act as a chelating bidentate ligand, for the 2-(pyrid-2′-yl)-1,8-naphthyridine motif found in molecules as, for example, **3f** or **11** it is far more likely that bidentate metal binding will involve N1 of naphthyridine and the pyridine (or pyridazine) nitrogen. This would leave one nitrogen of the naphthyridine uncomplexed and available to facilitate other chemistry. This property has been exploited by Thummel et al. in studies aimed at the photooxidation of water assisted by photosensitized intramolecular proton transfer.[30]

To attain better electronic communication between linked ligands, substantial attention has been paid to the conjugating ability of the linker. Linkers with one or more π-bonds are common, while the inclusion of a tetrahedral centre such as an sp^3-carbon atom can serve as an insulating junction.[32] Conjugated π-systems as linkers pose further problems, the most important of which is the potential orthogonality between any two adjacent π-links. Such an orthogonal junction can also behave as an insulator, as has been noted with polyene and polyphenylene linkers.[32] In this context, the pyrene nucleus is of considerable current interest as part of a ligand system due to the promising symmetry and electronic structure of this polynuclear aromatic compound.[33] Consequently, we sought to use of benzene, pyrene, phenylene, pyridine or pyrazine molecule as a linker in bridging ligand design. The availability of diacetylbenzenes, 2,6-diacetylpyridine, 2,6-diacetylpyrazine, 4,4′-diacetylbiphenyl, 2,3-butanedione and several isomers of diacetylpyrene led us to prepare and study the family of bridging ligands **4**–**7**, **9**, **11** and **19** reported here. Although the ligands experience free rotation about the bond connecting nap to the linker, the incorporation of a metal centre unit rigidifies the system, for example, as $[Ru(bpy)_2]^{2+}$ by inhibiting this rotation. Nevertheless, the dinuclear complex of **7** can still rotate freely about the biphenyl linkage. In addition, we have also compared rigid cavity-shaped molecules, as **12**, and the mononuclear pyrene analogue **3f** of the compounds **6** and **7**.

Since the spectroscopic and electronic properties of metal complexes will depend to a great extent on ligand structure, it was of interest to measure their absorption and emission properties for these systems. These properties were recorded in CH_2Cl_2, and that data are compiled in Tables 1 and 2, and several interesting correlations can be made involving the energies of these absorptions and structure. The strongest correlation in these data involves different compounds aryl or heteroaryl substituted or with different central linkers between the terminal napy moieties.

Table 1
Photophysical data for naphthyridine derivatives **3**[a]

	Absorption[a] λ_{max} [nm] (log ε)	Emission[b] λ_{cm} [nm] 298 K
3a	234 (5.07), 350 (4.85), 365 (4.91)	380
3b	232 (5.39), 372 (5.04)	410
3c	241 (4.43), 266 (4.41), 366 (4.32), 410 (4.57)	440, 490
3d	235 (5.41), 264 (5.50), 375 (5.18)	420, 470
3e	236 (5.04), 271 (4.65), 351 (4.53), 400 (4.68)	440, 480
3f	235 (4.99), 277 (5.06), 350 (4.61), 366 (4.72)	390, 480
3g	274 (4.37), 370 (4.31), 387 (4.22)	420
3h	236 (5.34), 287 (5.22), 350 (5.00)	330, 480
3i	236 (4.67), 393 (4.75)	475
3j	275 (5.05), 367 (4.47), 379 (4.62)	410
3k	230 (5.40), 365 (5.38), 383 (5.50)	420
3l	274 (5.56), 372 (5.21), 388 (5.31)	420

[a] CH_2Cl_2 (10^{-5} M) at 25 °C.
[b] Excited to the long-wavelength absorption maximum.

The phenyl derivative **3a** shows a long-wavelength absorption at 365 nm, while the heteroaryl species show absorptions at somewhat lower energies consistent with increased electronegativity due to the additional heteroatom(s). The aryl derivatives **3a**–**e** show long-wavelength absorptions in the range 365–410 nm, and this long-wavelength region of the UV absorption spectra of **3a**, **3c** and **3d** is shown in Figure 4.

Table 2
Photophysical data for bisnaphthyridine derivatives[a]

	Absorption[a] λ_{max} [nm] (log ε)	Emission[b] λ_{cm} [nm] 298 K
4	233 (5.31), 291 (3.87), 386 (5.84)	410
5	232 (5.40), 333 (5.49), 384 (5.54)	410, 440
6	231 (5.63), 288 (4.57), 328 (4.50), 418 (4.68)	530
7	230 (5.56), 294 (4.51), 372 (4.52), 416 (4.59)	480
9	369 (3.74), 376 (3.83), 388 (3.85)	390
11	232 (5.11), 378 (5.10), 394 (5.13)	450
12	249 (4.60), 377 (4.34), 391 (4.37), 415 (4.37)	450
14	248 (4.98), 378 (4.89), 398 (5.06)	440
15	232 (5.25), 391 (5.11)	410
19a	235 (5.10), 286 (4.72), 353 (4.91), 369 (5.05)	495
19b	242 (5.58), 352 (5.37), 371 (5.54)	430

[a] CH_2Cl_2 (10^{-6} M) at 25 °C.
[b] Excited to the long-wavelength absorption maximum.

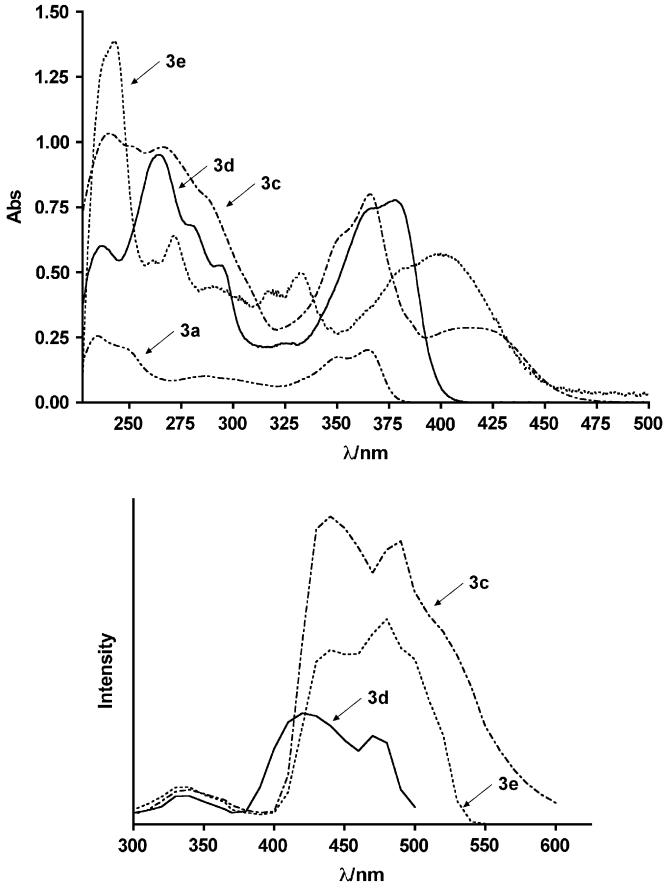


Figure 4. Absorption spectra (top) of **3a**,**c**–**e** measured in 10^{-5} M CH_2Cl_2 solutions at room temperature and the emission spectra (bottom) for **3c**–**e**.

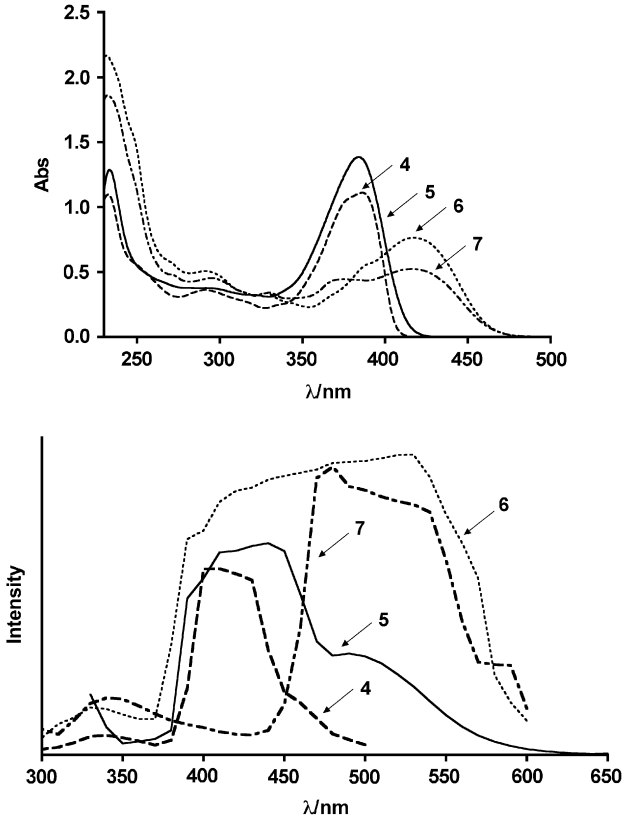


Figure 5. Absorption spectra (top) of **4**–**7** measured in 10^{-6} M CH_2Cl_2 solutions at room temperature and the emission spectra (bottom) for **4**–**7**.

Increasing delocalization causes a bathochromic shift and increase in intensity. Where the absorption spectrum gives information about the excited-state population of a molecule, the emission spectrum addresses the depopulation of this state. The long emission shifts to 380 nm for **3a**, 410 nm for **3b**, 490 nm for **3c**, 470 nm for **3d** and 480 nm for **3e** reflecting a steady progression to lower energy with increasing delocalization of the system. The shortest maximum emission for **3d** is consistent with the angular structure of the phenanthrene moiety. Figure 4 shows the emission spectra for **3c**–**e**.

The ligands **4**–**7**, **9** and **11** show low energy absorption bands in the range of 386–418 nm and several interesting correlations can be made involving the energies of these absorptions and structure. The strongest correlation that one finds in these data involves ligands having similar linkers between the terminal nap moieties. First, the bisnap derivative **4** shows long-wavelength absorption at 386 nm while the dimeric pyrene species **6** and **7** show absorptions at somewhat lower energies (418 and 416 nm, respectively), consistent with the symmetry and electronic structure of the pyrene moiety.[31] The ligand involving pyridazine **11** absorbs at longer wavelength (394 nm) than their benzene counterparts **4**, which agrees with increased electronegativity due to the additional nitrogen atoms. Figure 5 compares electronic absorption spectra for systems having an aromatic linker between the nap moieties. The existence of the pyridazine subunit causes a bathochromic shift and an increase in intensity. The emission shifts (Fig. 5) to 410 nm for **4**, 440 nm for **5** and 530 nm for **6**, in the fluorescence spectra, newly reflects a steady progression to lower energy with increasing delocalization of the system with the 16π-electron of the central pyrene ring providing better delocalization of the excited state. The Stokes shift is the difference between the absorption and emission maxima and, to some extent, provides a measure of geometric changes that occur upon electronic excitation. For **4**–**7**, and **11** we observe values of 24–112 nm, which are consistent with the more longitudinal organization of the molecule.[31]

For the two ligands involving 1,8-naphthyridine **9** and **12**, the one 2,2′-bis[1,8]-naphthyrine **9** absorbs at 27 nm shorter wavelength than their one all-*syn* planar 3,3′-dimethylene-bridged derivative **12**. This difference can be explained by considering the planar conformations available for the ligands. Conformational mobility about the 2,2′ bond provides less delocalization and the least coplanar system **9** absorbs at shortest wavelength. Finally, rotation about the single bonds connecting the terminal nap to the linker that would minimize nitrogen–nitrogen lone pair repulsions could explain shortest wavelength emission for **19b** than their isoster derivative **19a**.

Future work will investigate the metal binding properties of these new ligands. Preliminary results indicate an interesting Ru and Pt complexes.

3. Experimental section

3.1. General

All reagents used were commercial grade chemicals from freshly opened containers. Merk 60 $HF_{254+366}$ foils were used for thin layer chromatography and Merk 60 (230–400 mesh) silica gel for flash chromatography. NMR spectra were obtained in a Bruker Avance 500 equipped with a dual cryoprobe for ^1H and ^{13}C and a Bruker Avance 300 spectrometers. TMS was used as an internal reference. IR spectra were recorded as potassium bromide disks. Mass spectrometry experiments were carried out in a Fision VG-Quattro spectrometer. Electronic spectra were measured on a Perkin Elmer Lambda 900 spectrophotometer. Fluorescence spectra were obtained with a Hitachi F-2000 luminescence spectrometer. Melting points were measured using Stuart Scientific SMP3 apparatus and are uncorrected. Microanalyses were performed by the elemental analyses general service of the University of A Coruña.

3.2. 7-Aryl (or heteroaryl)-3-cyano-2-ethoxy-4-phenyl-1,8-naphthyridines **3a–l**. General procedure

A solution of **1** (0.75 mmol), a suitable aryl or heteroaryl methyl ketone **2** (0.75 mmol) and a catalytic amount of 10% ethanolic potassium hydroxide in ethanol (10 mL) was refluxed until all starting material had disappeared as checked by TLC (15 min–24 h). After cooling, the precipitates were collected by filtration and recrystallized from ethanol or purified by medium-pressure chromatography on silica gel.

3.2.1. 3-Cyano-2-ethoxy-4,7-diphenyl-1,8-naphthyridine (**3a**)

CH_2Cl_2–hexane, 1:1; yield (93%); white solid; mp: 204–206 °C. IR (KBr) 2231 (CN), 1587, 1382 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.56 (t, 3H, J=7.1 Hz, CH_3), 4.82 (q, 2H, J=7.1 Hz, $2OCH_2$), 7.48–7.63 (m, 8H, ArH), 7.80 (d, 1H, J=8.6 Hz, H-6), 8.01 (d, 1H, J=8.6 Hz, H-5), 8.2–8.23 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.7, 64.4, 98.9, 114.8, 116.9, 118.8, 128.4, 128.8, 130.4, 130.8, 133.5, 137.4, 138.4, 156.2, 158.5, 163.0. MS (FAB) m/z 352 [$(MH)^+$, 14], 341 (8), 308 (8), 289 (15). Anal. Calcd for $C_{23}H_{17}N_3O$: C, 78.61; H, 4.88; N, 11.96. Found: C, 78.43; H, 4.91; N, 12.06.

3.2.2. 3-Cyano-2-ethoxy-7-(naphth-2′-yl)-4-phenyl-1,8-naphthyridine (**3b**)

CH_2Cl_2–hexane, 3:7; yield (95%); orange solid; mp: 215–217 °C. IR (KBr) 2231 (CN), 1573, 1424 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.55 (t, 3H, J=7.1 Hz, CH_3), 4.82 (q, 2H, J=7.1 Hz, OCH_2), 7.49–7.64 (m, 12H, ArH), 7.67 (d, 1H, J=8.4 Hz, H-6), 8.10 (d, 1H, J=8.4 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.2, 99.0, 114.4, 116.5, 122.9, 125.2, 126.0, 126.8, 128.3, 128.4, 128.5, 128.6, 129.0, 129.3, 129.8, 130.2, 130.8, 133.1, 136.3, 137.4, 155.8, 158.4, 162.6, 164.9. MS (FAB) m/z 402 [$(MH)^+$, 100], 391 (9), 375 (14), 372 (22), 219 (18). Anal. Calcd for $C_{27}H_{19}N_3O$: C, 80.78; H, 4.77; N, 10.47. Found: C, 80.89; H, 4.66; N, 10.36.

3.2.3. 7-(Anthracen-2′-yl)-3-cyano-2-ethoxy-4-phenyl-1,8-naphthyridine (**3c**)

Recrystallized from ethanol; yield (93%); yellow crystals; mp: 285–287 °C. IR (KBr) 2226 (CN), 1583, 1486 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.58 (t, 3H, J=7.1 Hz, CH_3), 4.87 (q, 2H, J=7.1 Hz, OCH_2), 7.50–7.64 (m, 7H, ArH), 7.98–8.08 (m, 4H, ArH), 8.17 (d, 1H, J=9.0 Hz), 8.36 (dd, 1H, J=1.7, 7.2 Hz), 8.47 (s, 1H), 8.60 (s, 1H), 8.90 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.0, 63.7, 114.1, 116.3, 118.2, 128.6, 130.8, 131.5, 131.6, 132.2, 134.3, 136.6, 157.8, 160.0, 162.4. MS (FAB) m/z 452 [$(MH)^+$, 100], 451 (52), 424 (24), 391 (33), 341 (19), 289 (25). Anal. Calcd for $C_{31}H_{21}N_3O$: C, 82.46; H, 4.69; N, 9.31. Found: C, 82.59; H, 4.66; N, 9.26.

3.2.4. 3-Cyano-2-ethoxy-7-(phenanthren-2′-yl)-4-phenyl-1,8-naphthyridine (**3d**)

CH_2Cl_2–hexane, 8:2; yield (97%); white solid; mp: 284–285 °C. IR (KBr) 2226 (CN), 1583, 1480, 1414 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.59 (t, 3H, J=7.1 Hz, CH_3), 4.86 (q, 2H, J=7.1 Hz, OCH_2), 7.49–8.09 (m, 11H), 8.47–8.54 (m, 1H), 8.73–8.88 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 13.0, 64.0, 98.9, 115.0, 124.5, 128.5, 128.7, 128.9, 130.6, 130.8, 131.9, 132.0, 135.4, 137.3, 155.0, 163.3, 163.6. MS (FAB) m/z 452 [$(MH)^+$, 90], 391 (35). Anal. Calcd for $C_{31}H_{21}N_3O$: C, 82.46; H, 4.69; N, 9.31. Found: C, 82.79; H, 4.76; N, 9.16.

3.2.5. 3-Cyano-2-ethoxy-4-phenyl-7-(pyren-1′-yl)-1,8-naphthyridine (**3e**)

Recrystallized from ethanol; yield (98%); yellow crystals; mp: 275–276 °C. IR (KBr) 2936, 2854, 2224 (CN), 1584, 1481, 1409 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.59 (t, 3H, J=7.1 Hz, CH_3), 4.89 (q, 2H, J=7.1 Hz, OCH_2), 7.49–7.71 (m, 5H, ArH), 7.81 (d, 1H, J=8.0 Hz, H-6), 8.03–8.46 (m, 9H, ArH), 8.47 (d, 1H, J=8.0 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.5, 64.0, 98.8, 115.0, 118.2, 123.5, 124.8, 125.5, 127.5, 129.1, 129.2, 129.4, 129.8, 132.6, 136.6, 156.9, 158.1, 164.3. MS (FAB) m/z 476 [$(MH)^+$, 100], 446 (30), 391 (20). Anal. Calcd for $C_{33}H_{21}N_3O$: C, 83.35; H, 4.45; N, 8.84. Found: C, 83.49; H, 4.36; N, 9.01.

3.2.6. 3-Cyano-2-ethoxy-4-phenyl-7-(pyrid-2′-yl)-1,8-naphthyridine (**3f**)

Recrystallized from ethanol; yield (94%); yellow solid; mp: 244–246 °C. IR (KBr) 2991, 2229 (CN), 1593, 1474, 1440 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.60 (t, 3H, J=7.1 Hz, CH_3), 4.83 (q, 2H, J=7.1 Hz, OCH_2), 7.38–7.65 (m, 6H, ArH+Py), 7.85–7.98 (m, 1H, Py), 8.09 (d, 1H, J=7.8 Hz, H-6), 8.53 (d, 1H, J=7.8 Hz, H-5), 8.74–8.82 (m, 2H, Py). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.0, 98.9, 114.3, 117.6, 118.5, 122.7, 124.9, 128.9, 129.2, 130.0, 132.9, 136.8, 137.0, 148.7, 154.7, 155.9, 158.2, 161.0, 162.4. MS (FAB) m/z 353 [$(MH)^+$, 100], 325 (26), 289 (10). Anal. Calcd for $C_{22}H_{16}N_4O$: C, 74.98; H, 4.58; N, 15.90. Found: C, 74.89; H, 4.76; N, 16.01.

*3.2.7. 3-Cyano-2-ethoxy-4-phenyl-7-(pyrid-4′-yl)-1,8-naphthyridine (**3g**)*

Recrystallized from ethanol; yield (93%); yellow crystals; mp: 227–228 °C. IR (KBr) 2220 (CN), 1590, 1565 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.60 (t, 3H, J=7.1 Hz, CH_3), 4.83 (q, 2H, J=7.1 Hz, OCH_2), 7.47–7.52 (m, 2H, ArH), 7.63–7.66 (m, 3H, ArH), 7.84 (d, 1H, J=7.8 Hz, H-6), 8.06–8.14 (m, 2H, Py), 8.53 (d, 1H, J=7.8 Hz, H-5), 8.80–8.83 (m, 2H, Py). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.4, 114.1, 117.7, 118.3, 121.9, 129.1, 129.3, 130.4, 132.9, 135.3, 139.9, 145.2, 150.6, 158.4, 160.0. MS (FAB) *m/z* 353 [$(MH)^+$, 100], 325 (53). Anal. Calcd for $C_{22}H_{16}N_4O$: C, 74.98; H, 4.58; N, 15.90. Found: C, 74.95; H, 4.61; N, 15.94.

*3.2.8. 3-Cyano-2-ethoxy-4-phenyl-7-(pyrazin-2′-yl)-1,8-naphthyridine (**3h**)*

Recrystallized from ethanol; yield (83%); white crystals; mp: 264–265 °C. IR (KBr) 2986, 2225 (CN), 1591, 1474 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.58 (t, 3H, J=7.1 Hz, CH_3), 4.80 (q, 2H, J=7.1 Hz, OCH_2), 7.52–7.74 (m, 5H, ArH), 7.85 (d, 1H, J=7.8 Hz, H-6), 8.47 (d, 1H, J=7.8 Hz, H-5), 8.78–8.80 (m, 2H, Py), 9.8 (s, 1H, Py). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.4, 114.0, 117.7, 118.3, 121.9, 129.1, 130.4, 132.9, 135.5, 139.9, 145.2, 150.6, 158.4, 161.2. MS (EI) *m/z* 354 (M^+, 19), 326 (4), 289 (16), 219 (5). Anal. Calcd for $C_{21}H_{15}N_5O$: C, 71.38; H, 4.28; N, 19.82. Found: C, 71.35; H, 4.41; N, 19.72.

*3.2.9. 3-Cyano-2-ethoxy-4-phenyl-7-(pyrrol-2′-yl)-1,8-naphthyridine (**3i**)*

CH_2Cl_2–hexane, 1:1; yield (85%); yellow solid; mp: 180–182 °C. IR (KBr) 2982, 2232 (CN), 1583, 1525, 1374 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.54 (t, 3H, J=7.1 Hz, CH_3), 4.73 (q, 2H, J=7.1 Hz, OCH_2), 6.34–6.38 (m, 1H, pyrrolyl), 6.94–6.99 (m, 1H, pyrrolyl), 7.04–7.07 (m, 1H, pyrrolyl), 7.43–7.61 (m, 6H, ArH+H-5), 7.72 (d, 1H, J=8.7 Hz, H-6), 10.3 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 63.9, 97.0, 111.2, 114.7, 115.7, 117.0, 122.9, 128.9, 129.3, 130.7, 133.2, 154.8, 156.1, 157.8, 163.0. MS (EI) *m/z* 340 (M^+, 100), 325 (12), 312 (67), 295 (7), 284 (16). Anal. Calcd for $C_{21}H_{16}N_4O$: C, 74.10; H, 4.74; N, 16.46. Found: C, 74.15; H, 4.61; N, 16.51.

*3.2.10. 3-Cyano-2-ethoxy-7-(fur-2′-yl)-4-phenyl-4-1,8-naphthyridine (**3j**)*

Recrystallized from ethanol; yield (80%); yellow crystals; mp: 233–235 °C. IR (KBr) 3140, 2229 (CN), 1581, 1492 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.55 (t, 3H, J=7.1 Hz, CH_3), 4.81 (q, 2H, J=7.1 Hz, OCH_2), 6.63 (1H, dd, J=3.5, 1.7 Hz, furyl), 7.45–7.65 (m, 7H, ArH+furyl), 7.76 (d, 1H, J=8.6 Hz, H-6), 7.96 (d, 1H, J=8.6 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.1, 97.3, 112.8, 113.2, 116.7, 129.0, 129.3, 130.1, 137.0, 145.2, 152.7, 153.7, 155.9, 157.6, 160.7, 162.8, 163.3, 167.5. MS (FAB) *m/z* 342 [(MH^+), 100], 341 (21), 314 (15), 289 (20). Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.75; H, 4.41; N, 12.52.

*3.2.11. 3-Cyano-2-ethoxy-4-phenyl-7-(thien-2′-yl)-1,8-naphthyridine (**3k**)*

CH_2Cl_2–EtOH, 9:1; yield (82%); yellow solid; mp: 218–220 °C. IR (KBr) 2982, 2232 (CN), 1583, 1525, 1374 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.56 (t, 3H, J=7.1 Hz, CH_3), 4.85 (q, 2H, J=7.1 Hz, OCH_2), 7.16–7.21 (m, 1H, thienyl), 7.47–7.67 (m, 7H, ArH+thienyl+H-6), 7.70–7.93 (m, 2H, thienyl+H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.4, 63.9, 98.0, 114.3, 116.5, 128.1, 128.4, 129.0, 129.3, 130.1, 131.2, 134.5, 137.8, 144.2, 156.3, 163.1. MS (FAB) *m/z* 358 [(MH^+), 100], 330 (27), 289 (47). Anal. Calcd for $C_{21}H_{15}N_3OS$: C, 70.57; H, 4.23; N, 11.76. Found: C, 70.75; H, 4.11; N, 11.72.

*3.2.12. 3-Cyano-2-ethoxy-4-phenyl-7-(thiazol-2′-yl)-1,8-naphthyridine (**3l**)*

Recrystallized from ethanol; yield (88%); yellow crystals; mp: 248–250 °C. IR (KBr) 3106, 2972, 2222 (CN), 1574, 1425, 1327 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.59 (t, 3H, J=7.1 Hz, CH_3), 4.83 (q, 2H, J=7.1 Hz, OCH_2), 7.47–7.66 (m, 6H, ArH+thiazolyl), 8.02–8.11 (2H, m, thiazolyl+H-6), 8.28 (d, 1H, J=8.0 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 64.2, 97.0, 111.2, 114.7, 115.8, 117.0, 122.9, 124.0, 129.2, 129.3, 130.6, 137.0, 144.0, 154.8, 157.9, 163.6. MS (EI) *m/z* 358 (M^+, 90), 331 (30), 289 (55). Anal. Calcd for $C_{20}H_{14}N_4OS$: C, 67.02; H, 3.94; N, 15.63. Found: C, 67.15; H, 4.01; N, 15.74.

*3.3. 1,4-Di(1,8-naphthyridyn-2′-yl)-aryl(heteroaryl)ligands **4–7**, **9**, **11**, **12**, **14** and **19a–c**. General procedure*

A solution of **1** (0.90 mmol), a suitable diketone (0.45 mmol) and a catalytic amount of 10% ethanolic potassium hydroxide in ethanol (10 mL) was refluxed until all starting material had disappeared as checked by TLC (2–30 h). After cooling, the precipitates were collected by filtration and purified by medium-pressure chromatography on silica gel using CH_2Cl_2 as eluent. For **12**, **19a** and **19b**, the precipitate was filtered off and washed with EtOH. For **15**, the solid was purified by eluting with CH_2Cl_2–AcOEt 9:1.

*3.3.1. 1,4-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]benzene (**4**)*

From 1,4-diacetylbenzene. Reaction time 10 h; yield (88%); white solid; mp: >300 °C. IR (KBr) 2996, 2237 (CN), 1618, 1513, 1493, 1431, 1396 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.58 (t, 6H, J=7.1 Hz, $2CH_3$), 4.68 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.48–7.65 (m, 10H, $2C_6H_5$), 7.89 (d, 2H, J=7.8 Hz, H-3), 8.01 (d, 2H, J=7.8 Hz, H-4), 8.40 (s, 4H, C_6H_4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 63.8, 99.0, 115.0, 118.0, 125.5, 128.4, 129.1, 133.3, 136.6, 156.0, 158.2, 161.9, 163.1. MS (FAB) *m/z* 625 [$(MH)^+$, 20], 460 (14), 289 (50). Anal. Calcd for $C_{40}H_{28}N_6O_2$: C, 76.91; H, 4.52; N, 13.45. Found: C, 76.89; H, 4.63; N, 13.24.

*3.3.2. 4,4′-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]biphenyl (**5**)*

From 4,4′-diacetylbiphenyl. Reaction time 2 h; yield (77%); white solid; mp: >300 °C. IR (KBr) 2980, 2229

(CN), 1610, 1583, 1478, 1431, 1381 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.56 (t, 6H, J=7.1 Hz, $2CH_3$), 4.65 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.44–7.67 (m, 10H, $2C_6H_5$), 7.85–7.92 (m, 8H, biphenyl), 8.04 (d, 2H, J=7.8 Hz, H-3), 8.38 (d, 2H, J=7.8 Hz, H-4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 63.8, 99.0, 114.0, 117.0, 118.0, 125.5, 128.4, 129.1, 133.3, 136.6, 139.9, 142.1, 156.1, 158.4, 161.9, 163.1. MS (FAB) *m/z* 701 [$(MH)^+$, 14], 663 (98), 647 (70), 607 (13), 289 (64). Anal. Calcd for $C_{46}H_{32}N_6O_2$: C, 78.84; H, 4.60; N, 11.99. Found: C, 78.94; H, 4.71; N, 11.87.

*3.3.3. 1,6-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]pyrene (**6**)*

From 1,4-diacetylpyrene. Reaction time 10 h; yield (60%); yellow solid; mp: >300 °C. IR (KBr) 2226 (CN), 1583, 1329, 1294 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.57 (t, 6H, J=7.1 Hz, $2CH_3$), 4.85 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.56–7.68 (m, 10H, $2C_6H_5$), 7.84 (d, 2H, J=8.4 Hz, H-3), 8.16 (d, 2H, J=9.3 Hz, pyrene), 8.17 (d, 2H, J=8.4 Hz, H-4), 8.32 (d, 2H, J=8 Hz, pyrene), 8.36 (d, 2H, J=8 Hz, pyrene), 8.50 (d, 2H, J=9.3 Hz, pyrene). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.4, 64.3, 99.1, 114.4, 116.5, 123.6, 125.0, 125.2, 125.5, 128.3, 128.5, 129.0, 129.1, 129.3, 130.2, 131.7, 133.2, 135.2, 136.5, 155.9, 158.5, 162.8, 165.1. MS (EI) *m/z* 749 [$(MH)^+$, 40], 391 (30), 289 (55). Anal. Calcd for $C_{50}H_{34}N_6O_2$: C, 79.98; H, 4.56; N, 11.99. Found: C, 80.05; H, 4.51; N, 11.84.

*3.3.4. 1,8-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]pyrene (**7**)*

From 1,6-diacetylpyrene. Reaction time 3 h; yield (66%); yellow solid; mp: >260 °C (dec). IR (KBr) 2227 (CN), 1582, 1479, 1327 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.56 (t, 6H, J=7.1 Hz, $2CH_3$), 4.82 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.54–7.66 (m, 10H, $2C_6H_5$), 7.82 (d, 2H, J=8.4 Hz, H-3), 8.13 (d, 2H, J=8.4 Hz, H-4), 8.20 (s, 2H, pyrene), 8.35 (d, 2H, J=7.9 Hz, pyrene), 8.39 (d, 2H, J=7.9 Hz, pyrene), 8.48 (s, 2H, pyrene). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.5, 98.7, 114.3, 116.4, 123.7, 125.0, 125.2, 125.6, 128.1, 128.5, 129.0, 129.1, 130.3, 133.2, 134.2, 136.4, 156.0, 158.5, 162.8, 165.0. MS (EI) *m/z* 749 [$(MH)^+$, 25], 748 (9), 391 (20). Anal. Calcd for $C_{50}H_{34}N_6O_2$: C, 79.98; H, 4.56; N, 11.99. Found: C, 79.83; H, 4.74; N, 11.88.

*3.3.5. 6,6′-Dicyano-7,7′-diethoxy-5,5′-diphenyl-2,2′-bi-1,8-naphthyridine (**9**)*

From 1,3-butanedione. Reaction time 20 h; yield (66%); white solid; mp: >300 °C. IR (KBr) 2928, 2225 (CN), 1584, 1478, 1323 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.57 (t, 6H, J=7.1 Hz, $2CH_3$), 4.59 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.45–7.66 (m, 10H, $2C_6H_5$), 8.15 (d, 2H, J=8.6 Hz, H-3), 8.86 (d, 2H, J=8.6 Hz, H-4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 13.5, 63.0, 98.7, 115.0, 120.0, 129.3, 130.6, 136.2, 155.0, 159.6. MS (EI) *m/z* 549 [$(MH)^+$, 24], 460 (37), 391 (100). Anal. Calcd for $C_{34}H_{24}N_6O_2$: C, 74.44; H, 4.41; N, 15.32. Found: C, 74.40; H, 4.44; N, 15.38.

*3.3.6. 2,5-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]pyrazine (**11**)*

From 2,5-diacetylpyrazine. Reaction time 20 h; yield (78%); white solid; mp: >300 °C. IR (KBr) 2962, 2225 (CN), 1584, 1568, 1328 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.60 (t, 6H, J=7.1 Hz, $2CH_3$), 4.85 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.50–7.66 (m, 10H, $2C_6H_5$), 8.16 (d, 2H, J=8.6 Hz, H-3), 8.58 (d, 2H, J=8.6 Hz, H-4), 10.2 (s, 2H, pyrazine). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 64.1, 99.7, 114.0, 118.2, 119.0, 128.9, 129.1, 130.2, 132.7, 137.5, 143.3, 149.9, 155.3, 158.3, 158.9, 162.2. MS (EI) *m/z* 627 [$(MH)^+$, 10], 613 (15), 607 (15), 460 (50). Anal. Calcd for $C_{38}H_{26}N_8O_2$: C, 72.83; H, 4.18; N, 17.88. Found: C, 72.96; H, 4.21; N, 17.78.

*3.3.7. 6,6′-Dicyano-7,7′-diethoxy-3,3′-dimethylene-5,5′-diphenyl-2,2′-bi-1,8-naphthyridine (**12**)*

From 1,2-cyclohexanedione. Reaction time 2 h; yield (76%); yellow solid; mp: >300 °C. IR (KBr) 3323, 2227 (CN), 1586, 1476, 1412, 1331 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.56 (t, 6H, J=7.1 Hz, $2CH_3$), 3.08 (s, 4H, $2CH_2$), 4.83 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.47–7.64 (m, 10H, $2C_6H_5$), 7.85 (s, 2H, H-4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 14.4, 27.1, 31.8, 64.1, 64.4, 99.2, 99.5, 114.2, 114.3, 117.1, 129.1, 130.2, 155.0, 162.4, 165.8. MS (FAB) *m/z* 575 [$(MH)^+$, 33], 413 (26), 391 (83), 363 (60). Anal. Calcd for $C_{36}H_{26}N_6O_2$: C, 75.25; H, 4.56; N, 14.62. Found: C, 75.37; H, 4.57; N, 14.48.

*3.3.8. 3,11-Dicyano-2,10-diethoxy-4,12-diphenyl-6,7-dihydrobenzo[1,2-b:3,4-b′]1,8-binaphthyridine (**14**)*

From 1,3-cyclohexanedione. Reaction time 3 h; yield (65%); white solid; mp: 239–241 °C. IR (KBr), 2229 (CN), 1569, 1476, 1413, 1329 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.53 (t, 3H, J=7.1 Hz, CH_3), 1.55 (t, 3H, J=7.1 Hz, CH_3), 3.14 (t, 2H, J=6.9 Hz, CH_2), 3.43 (t, 2H, J=6.9 Hz, CH_2), 4.69 (q, 2H, J=7.1 Hz, CH_2), 4.78 (q, 2H, J=7.1 Hz, CH_2), 7.43–7.68 (m, 10H, $2C_6H_5$), 7.78 (s, 1H, H-4), 9.11 (s, 1H, H-13). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 14.4, 27.1, 31.8, 64.1, 64.4, 99.2, 99.5, 114.2, 114.3, 117.1, 117.5, 127.1, 129.1, 129.2, 129.6, 129.7, 130.2, 130.5, 132.9, 135.1, 155.0, 155.8, 156.2, 157.8, 159.5, 162.4, 163.1, 165.8. MS (FAB) *m/z* 575 [$(MH)^+$, 43], 391 (19), 307 (36), 289 (19). Anal. Calcd for $C_{36}H_{26}N_6O_2$: C, 75.25; H, 4.56; N, 14.62. Found: C, 75.38; H, 4.67; N, 14.78.

*3.3.9. 1,3-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]benzene (**19a**)*

From 1,3-diacetylbenzene. Reaction time 1 h; yield (92%); white solid; mp: >300 °C. IR (KBr) 2922, 2224 (CN), 1667, 1586, 1375 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.57 (t, 6H, J=7.1 Hz, $2CH_3$), 4.83 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.51–7.71 (m, 10H, $2C_6H_5$), 7.74 (1H, t, J=7.8 Hz, H-5), 7.97 (d, 2H, J=7.9 Hz, H-4, H-6), 8.08 (d, 2H, J=7.9 Hz, H-3′), 8.38 (d, 2H, J=7.9 Hz, H-4′), 9.01 (s, 1H, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 64.2, 98.9, 114.4, 116.8, 118.7, 127.8, 129.0, 129.3, 129.5, 130.2, 133.1, 137.3,

138.8, 155.9, 158.3, 162.1, 162.8. MS (EI) *m/z* 624 (M^+, 10), 623 (11), 424 (20), 262. Anal. Calcd for $C_{40}H_{28}N_6O_2$: C, 76.91; H, 4.52; N, 13.45. Found: C, 76.98; H, 4.41; N, 13.58.

*3.3.10. 2,6-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]pyridine (**19b**)*

From 2,6-diacetylpyridine. Reaction time 20 h; yield (77%); white solid; mp: >300 °C. IR (KBr) 2979, 2224 (CN), 1584, 1569, 1485, 1383 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.59 (t, 6H, J=7.1 Hz, $2CH_3$), 4.85 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.49–7.65 (m, 10H, $2C_6H_5$), 8.15 (m, 3H), 8.69 (d, 2H, J=7.8 Hz, H-3′), 8.93 (d, 2H, J=7.8 Hz, H-4′). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 63.6, 99.0, 114.0, 116.3, 118.0, 125.0, 128.4, 129.1, 130.6, 133.3, 136.6, 139.9, 154.2, 158.1, 163.4. MS (FAB) *m/z* 626 [$(MH)^+$, 100], 670 (23), 460 (14), 391 (52), 345 (8). Anal. Calcd for $C_{39}H_{27}N_7O_2$: C, 74.87; H, 4.32; N, 15.67. Found: C, 74.69; H, 4.50; N, 15.62.

*3.3.11. 2,6-Di[(6′-cyano-7′-ethoxy-5′-phenyl)-1,8-naphthyridin-2′-yl]-4-tert-butyl-pyridine (**19c**)*

From 4-*tert*-butyl-2,6-diacetylpyridine. Reaction time 30 h; yield (93%); mp: >300 °C. IR (KBr) 2980, 2226 (CN), 1585, 1571, 1330 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.57 (s, 9H, $3CH_3$), 1.60 (t, 6H, J=7.1 Hz, $2CH_3$), 4.82 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.51–7.64 (m, 10H, $2C_6H_5$), 8.11 (d, 2H, J=8.6 Hz, H-3′), 8.67 (d, 2H, J=8.6 Hz, H-4′), 8.87 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.2, 64.0, 98.9, 114.2, 117.6, 118.9, 121.2, 128.8, 129.2, 130.1, 132.9, 136.9, 139.9, 154.1, 154.4, 155.4, 163.8. MS (FAB) *m/z* 682 [$(MH)^+$, 100], 670 (23), 681 (12), 626 (7), 429 (8), 345 (12), 460. Anal. Calcd for $C_{44}H_{39}N_7O_2$: C, 75.73; H, 5.63; N, 14.05. Found: C, 75.88; H, 5.47; N, 14.21.

*3.4. 7-Acetyl-3-cyano-2-ethoxy-4-phenyl-1,8-naphthyridine (**8**)*

A catalytic amount of 10% ethanolic potassium hydroxide was added to a solution of **1** (0.27 g, 1 mmol) and 1,3-butanedione (103 mg, 1,2 mmol) in ethanol (10 mL) and the mixture was heated under reflux for 8 h until all starting material had disappeared as checked by TLC (2–30 h). After cooling, the precipitate was collected by filtration and washed with EtOH to give 160 mg (50%) of white solid. Mp: >300 °C (dec). IR (KBr) 2225 (CN), 1780 (CO), 1585, 1570, 1335 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.48 (t, 3H, J=7.1 Hz, CH_3), 3.49 (s, 3H, CH_3), 4.78 (q, 4H, J=7.1 Hz, $2OCH_2$), 7.47–7.78 (m, 5H, C_6H_5), 8.17 (d, 2H, J=8.6 Hz, H-6), 8.84 (d, 2H, J=8.6 Hz, H-5). Anal. Calcd for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.80; H, 4.74; N, 13.35.

*3.5. 3-Cyano-2-ethoxy-4-phenyl-6-oxo-6,7,8,9-tetrahydro-benzo[b]-1,8-naphthyridine (**13**)*

A catalytic amount of 10% ethanolic potassium hydroxide was added to a solution of **1** (0.27 g, 1 mmol) and 1,2-cyclohexanedione (123 mg, 1,11 mmol) in ethanol (10 mL) and the mixture was heated under reflux for 6 h. After cooling, the precipitate formed was filtered off and recrystallized from ethanol/acetone to give white crystals (0.28 g, 84%). Mp: 281–282 °C. IR (KBr) 2232 (CN), 1696 (CO), 1584, 1420, 1332 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.55 (t, 6H, J=7.1 Hz, CH_3), 2.22–2.30 (m, 2H, H-8), 2.75 (t, 2H, J=6.5 Hz, H-9), 3.37 (t, 2H, J=6.5 Hz, H-7), 4.81 (q, 4H, J=7.1 Hz, OCH_2), 7.45–7.64 (m, 5H, C_6H_5), 8.60 (s, 1H, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.3, 21.3, 33.1, 38.6, 64.7, 79.3, 99.8, 113.8, 116.7, 126.1, 129.2, 130.7, 132.4, 137.5, 157.0, 160.2, 163.8, 168.7, 196.4. MS (EI) *m/z* 343 (M^+, 39), 342 (100), 316 (18), 315 (79), 287 (47). Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 75.45; H, 4.99; N, 12.24. Found: C, 75.47; H, 5.10; N, 12.14.

*3.6. 3,11-Dicyano-2,10-diethoxy-4,12-diphenylbenzo-[1,2-b:3,4-b′]1,8-binaphthyridine (**15**)*

A solution of **14** (57 mg, 0.1 mmol) and DDQ (30 mg, 0.12 mmol) in THF (5 mL) was refluxed for 2 h. Alter cooling, the solid formed was filtered off and purified by flash chromatography on silica gel with CH_2Cl_2–AcOEt 9:1 to give a white solid (34 mg, 60%). Mp: >300 °C. IR (KBr) 2986, 2227 (CN), 1649, 1580, 1487, 1332 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.54–1.58 (m, 6H, $2CH_3$), 4.64 (q, 2H, J=7.0 Hz, OCH_2), 4.72 (q, 2H, J=7.0 Hz, OCH_2), 7.45–7.63 (m, 10H, $2C_6H_5$), 8.01 (d, 1H, J=8.6 Hz, H-6), 8.30 (d, 1H, J=8.6 Hz, H-7), 8.60 (s, 1H, H-5), 9.20 (s, 1H, H-13). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.2, 14.4, 27.1, 64.1, 64.9, 94.0, 99.5, 107.8, 114.1, 114.3, 117.4, 121.9, 129.0, 129.1, 129.4, 130.2, 132.5, 133.0, 136.5, 139.6, 139.8, 150.6, 157.9, 158.2, 161.2. Anal. Calcd for $C_{36}H_{24}N_6O_2$: C, 75.51; H, 4.22; N, 14.68. Found: C, 75.62; H, 4.17; N, 14.53.

4. Crystallographic material

Crystallographic data (excluding structural factors) for **14** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication number CCDC 674102. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 33603 or e-mail: deposit@ccdc.cam.ac.uk).

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