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Friedländer Approach for the Incorporation of 6-Bromoquinoline into Novel Chelating Ligands

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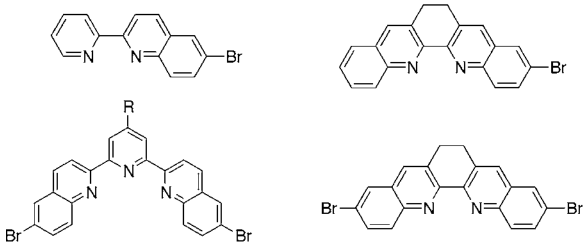
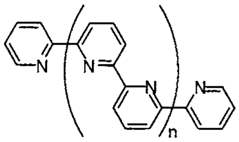
ABSTRACT

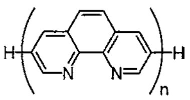


Nitration of 3-bromobenzaldehyde followed by sodium dithionite reduction provides 5-bromo-2-aminobenzaldehyde, which undergoes the Friedländer condensation with a variety of enolizable ketones to afford bidentate and tridentate 6-bromoquinoline derivatives. These species may be dimerized with Ni(0) to form biquinolines or treated under Sonogashira conditions to afford 6-alkynyl derivatives. Examination of optical properties indicate an unusually high emission quantum yield for 6,6′-biquinolines.

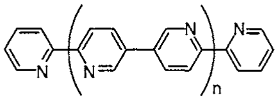
In the burgeoning field of nanoscale chemistry, the organized synthesis of polynuclear metal complexes holds considerable promise for the construction of useful molecular devices.[1] Early work centered on bridging ligands in which two, most often equivalent, metal binding centers were incorporated into a single molecule.[2] Often these metal binding centers were chelating groups, and the polypyridines have received considerable attention in this regard.[3] Molecules such as quaterpyridine or sexipyridine (**1**, $n = 1, 2$) have multiple binding sites that involve critical spacial demands since the pyridine rings are connected in a meta rather than a para fashion. These ligands form helical rather than linear complexes, and tertiary structural considerations are of considerable importance.[4]



1 (n = 1, 2)



3 (n = 1, 2)



2 (n = 1, 2)

To organize a polychelating ligand in a more linear fashion, it is preferable to join the binding units in an axial sense, as in polypyridine **2**, where 3,3′-bipyridine is the repeating unit.[5] Such systems still present concerns associated with the rotational mobility between adjacent pyridine rings. These concerns are addressed in molecules such as **3** where

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(1) (a) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853. (b) Fabbrizzi, L., Poggi, A., Eds. *Transition Metals in Supramolecular Chemistry*; Kluwer: Dordrecht, 1994. (c) Lehn, J.-M. *Supramolecular Chemistry*: *Concepts and Prospectives*; VCH: Weinheim, 1995. (d) Baxter, P. N. W.; Khoury, R. G.; Lehn, J.-M.; Baum, G.; Fenske, D. *Chem. Eur. J.* **2000**, *6*, 4140.

(2) (a) Balzani, V.; Juris, A.; Venturi, M.; Campagna, S.; Serroni, S. *Chem. Rev.* **1996**, *96*, 759. (b) Steel, P. J. *Coord. Chem. Rev.* **1990**, *106*, 227. (c) Sauvage, J.-P.; Collin, J.-P.; Chambron, J.-C.; Guillerez, S.; Coudret, C.; Balzani, V.; Barigelletti, F.; De Cola, L.; Flamigni, L. *Chem. Rev.* **1994**, *94*, 4, 993. (d) Kalyanasundaram, K.; Nazeeruddin, M. K. *Inorg. Chim. Acta* **1994**, *226*, 213.

(3) (a) Kaes, C.; Katz, A.; Hosseini, M.-W. *Chem. Rev.* **2000**, *100*, 3553. (b) Kalyanasundaram, K. *Photochemistry of Polypyridine and Porphyrin Complexes*; Academic Press: San Diego, 1992.

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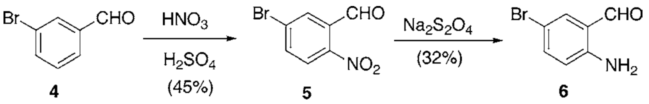
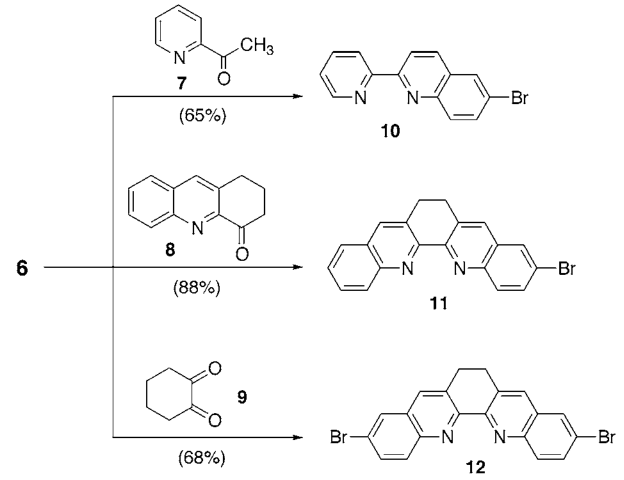
1,10-phenanthroline (phen) is the repeating unit.[6] The syn orientation of the two chelating pyridine moieties is enforced by fusion of the central benzo-ring.

Another serious problem in polychelating ligands is electronic communication between each subunit. Such communication is strongly affected by the dihedral angle between two adjacent aromatic units. These units normally prefer a more orthogonal conformation, which is unfavorable to the π-overlap required for effective communication. One solution is the incorporation of alkynyl linker groups that allow more efficient electronic communication.[7]

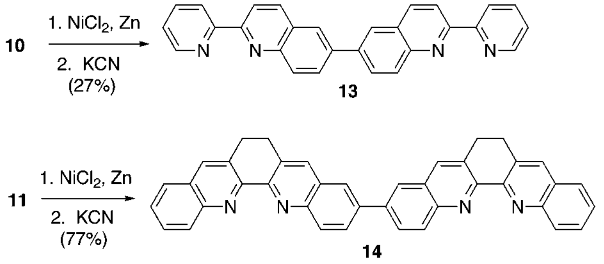
The ligand 2,2′-biquinoline (biq) is a benzalogue of 2,2′-bipyridine that presents some electronic advantages over its simpler counterpart. The extended π-system provides a more delocalized molecule whose π*-state provides a lower energy metal-to-ligand charge transfer (MLCT) for transition metal complexes. This MLCT results in a lower energy absorption that extends considerably further into the visible region of the spectrum. To incorporate quinoline into ligand systems, we have developed a simple synthesis of 6-bromoquinolines and report on the utility of this approach.



The nitration of 3-bromobenzaldehyde with nitric and sulfuric acids provides 5-bromo-2-nitrobenzaldehyde (**5**),[8] which may be reduced to **6** in modest yield with sodium dithionite. This reduction method is preferred over the more traditional method involving iron and HCl since it provides pure product directly without the need for chromatographic separation.[9] The aminoaldehyde **6** then undergoes Friedländer condensation[10] with 2-acetylpyridine (**7**) to provide 6-bromo-2-(2′pyridyl)-quinoline (**10**) in 65% yield. In an analogous fashion, the condensation of **6** with the tetrahydroacridone **8**[11] provides the 3,3′-dimethylene-6-bromobiq (**11**) in 88% yield. A similar 2:1 condensation of **6** with 1,2-cyclohexanedione (**9**)[12] provides a 68% yield of the dimethylene-bridged 6,6′-dibromobiq derivative **12**.



These bromoquinolines may be coupled with Ni(0) generated from the treatment of $NiCl_2$ with zinc and triphenylphosphine.[13] The 2,2′-di(2″-pyridyl)-6,6′-biquinoline (**13**) is obtained in 27% yield, while the dimer of **11** is obtained by a similar reaction in 77% yield. An important part of this coupling process involves sonication of the crude product with KCN to scavenge any Ni(II) byproduct that may have complexed with the desired ligand.[14]



The alkynyl-linked analogue **16** may be prepared by two sequential Sonogashira reactions. The first coupling between **11** and 2-methyl-3-butyn-2-ol, followed by base-promoted removal of the acetone protecting group, provides the 6-ethynyl derivative **15** in 92% overall yield.[7a] This species is then coupled with another equivalent of **11** to afford the bis-biq alkyne **16** in 71% yield. When the same coupling approach is applied to the dibromo derivative **12**, the bis-ethynyl species **17** may be prepared in 94% overall yield. Coupling this species with 2 equiv of the 6-bromobiq **11** affords a low yield of what appears by mass spectroscopy

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(4) (a) Potts, K. T.; Raiford, K. A. G.; Keshavarz-K., M. *J. Am. Chem. Soc.* **1993**, *115*, 2793. (b) Chotalia, R.; Constable, E. C.; Neuburger, M.; Smith, D. R.; Zehner, M. *J. Chem. Soc., Dalton Trans.* **1996**, *22*, 4207. (c) Constable, E. C.; Chotalia, R. *J. Chem. Soc., Chem. Commun.* **1992**, *1*, 64. (d) Constabel, E. C.; Ward, M. D.; Tocher, D. A. *J. Am. Chem. Soc.* **1990**, *112*, 1256.

(5) (a) Schwab, P. F. H.; Noll, B. C.; Michl, J. *J. Org. Chem.* **2002**, *67*, 5476. (b) Schwab, P. F. H.; Fleischer, F.; Michl, J. *J. Org. Chem.* **2002**, *67*, 443. (c) Khatyr, A.; Ziessel, R. *Org. Lett.* **2001**, *3*, 1857.

(6) (a) Hu, Y.-Z.; Xiang, Q.; Thummel, R. P. *Inorg. Chem.* **2002**, *41*, 3423. (b) Toyota, S.; Woods, C. R.; Benaglia, M.; Haldimann, R.; Wärnmark, K.; Hardcastle, K.; Siegel, J. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 751. (c) Liu, S.-X.; Michel, C.; Schmittel, M. *Org. Lett.* **2000**, *2*, 3959. (d) Heuft, M. A.; Fallis, A. G. *Angew. Chem., Int. Ed.* **2002**, *41*, 4520. (e) Dietrich-Buchecker, C.; Jiménez, M. C.; Sauvage, J.-P. *Tetrahedron Lett.* **1999**, *40*, 3395. (f) Joshi, H. S.; Jamshidi, R.; Tor, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 2722. (g) Hurley, D. J.; Tor, Y. *Tetrahedron Lett.* **2001**, *42*, 7217.

(7) (a) Khatyr, A.; Ziessel, R. *J. Org. Chem.* **2000**, *65*, 7814. (b) Khatyr, A.; Ziessel, R. *J. Org. Chem.* **2000**, *65*, 3126. (c) Ley, K. D.; Li, Y.; Johnson, J. V.; Powell, D. H.; Schanze, K. S. *Chem. Commun.* **1999**, 1749. (d) Walters, K. A.; Ley, K. D.; Cavalaheiro, C. S. P.; Miller, S. E.; Gosztola, D.; Wasielewski, M. R.; Bussandri, A. P.; van Willigen, H.; Schanze, K. S. *J. Am. Chem. Soc.* **2001**, *123*, 8329.

(8) Behr, L. C. *J. Am. Chem. Soc.* **1954**, *76*, 3674.

(9) Horner, J. K.; Henry, D. W. *J. Med. Chem.* **1968**, *11*, 946.

(10) (a) Riesgo, E. C.; Jin, X.; Thummel, R. P. *J. Org. Chem.* **1996**, *61*, 1, 3017. (b) Thummel, R. P. *Synlett* **1992**, 1. (c) Cheng, C.-C.; Yan, S.-J. *Org. React.* **1982**, *28*, 37.

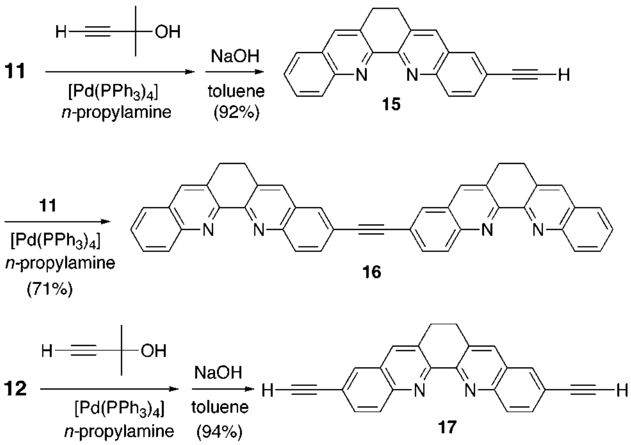
(11) Jahng, Y.; Thummel, R. P.; Bott, S. *Inorg. Chem.* **1997**, *36*, 3133.

(12) Thummel, R. P.; Lefoulon, F. *J. Org. Chem.* **1985**, *50*, 666.

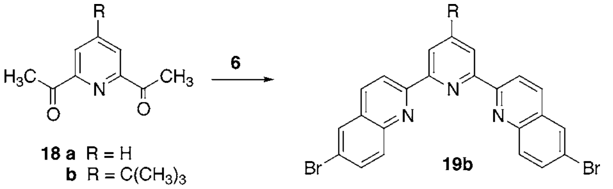
(13) Janiak, C.; Deblon, S.; Uehlin, L. *Synthesis* **1999**, 959.

(14) Constable, E. C.; Elder, S. M.; Healy, J.; Tocher, D. A. *J. Chem. Soc., Dalton Trans.* **1990**, 1669.

to be the trimeric ligand, but further characterization was prevented by poor solubility.



A tridentate system incorporating two 6-bromoquinoline moieties can be prepared in a similar fashion by the condensation of the aminoaldehyde **6** with 2,6-diacetylpyridine. Once again, solubility problems thwarted the complete characterization of the parent ligand **19a**, but the 4-*t*-butyl analogue was formed in 57% yield from the corresponding 4-*tert*-butyl-2,6-diacetylpyridine (**18b**).[15]

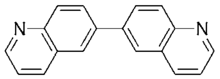


The bromo- and alkynyl-quinolines, as well as the coupled derivatives, were characterized by their NMR spectra, mass spectra, and elemental analyses (see Supporting Information). Since the prepared molecules were to be used as ligands for the preparation of potentially photoactive transition metal complexes, it was of interest to measure their absorption and emission properties. These properties were recorded in $CH_2Cl_2-CH_3OH$ (99:1), and the data are collected in Table 1. The 2,2′-biquinoline derivatives show long-wavelength absorptions in the range of 358−375 nm, while the dimeric species **14** and **16** show absorptions that are about twice as intense at somewhat lower energies (378 and 395 nm). All the monomeric species except **10** emit when excited into their long-wavelength band with quantum yields in the range of $1.66-13.5 \times 10^{-3}$. The dimeric species, however, show more intense emissions with quantum yields that are about 2 orders of magnitude greater. We suspected that the stronger emission might be due to the presence of the 6,6′-biquinoline moiety found in **14**. The very strong emission ($\phi = 0.658$) observed for **13** seems to bear out this premise. As a further test, we prepared the parent 6,6′-biquinoline (**20**) by the dimerization of 6-bromoquinoline[16] and found that it emitted at 352 and 372 nm with $\phi = 0.100$. Future work will report the coordination properties of these systems.

Table 1. Photophysical Data for Quinoline Derivatives[a]

compound	absorption λ_{max}, nm (ϵ, M^{-1} cm^{-1})	emission[b] λ_{EM}, nm	$10^3\phi_{EM}$[d]
biq-2[c]	227 (40 500), 261 (64 700), 343 (20 800), 358 (24 200)	422	4.33
10	254 (37 900), 324 (14 600), 339 (11 900)	none	
11	228 (39 000), 265 (58 500), 346 (20 900), 362 (27 900)	377, 389	1.66
12	230 (45 200), 268 (61 000), 349 (24 900), 364 (35 700)	379, 393	4.10
13	227 (33 500), 264 (55 500), 350 (49 100)	386, 396	658
14	228 (51 700), 277 (69 300), 378 (65 600)	405, 426	310
15	232 (34 800), 267 (54 500), 350 (22 000), 367 (29 000)	403	6.14
16	229 (54 700), 273 (57 800), 377 (72 500), 395 (67 700)	408, 430	350
17	234 (39 700), 274 (56 800), 357 (26 800), 375 (39 400)	389, 405	13.5
19	256 (90 600), 325 (40 200), 341 (34 600)	365	2.94
20	254 (77 600), 306 (14 300), 320 (sh, 12 900)	356, 372	100

[a] Solvent: CH_2Cl_2-MeOH (99:1), 25 °C. [b] Excited at the long-wavelength absorption maximum. [c] 3,3′-Dimethylene-2,2′-biquinoline. [d] Error: ±10%.



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Supporting Information Available: Full experimental details for the preparation of compounds **5**, **6**, **10**−**17**, **19**, and **20**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Nückel, S.; Burger, P. *Organometallics* **2001**, *20*, 4345.

(16) Benito, Y.; Canoira, L.; Rodriguez, J. G. *Appl. Organomet. Chem.* **1987**, *1*, 535.