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BENZO[*b*]-1,10-PHENANTHROLINES. V.[1] SYNTHESIS AND PROPERTIES OF 3,3'-POLYMETHYLENE-2-(PYRID-2'-YL)BENZO[*b*]-1,10-PHENANTHROLINES

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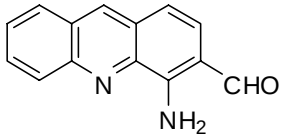
Abstract – A series of 3,3'-polymethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines were prepared by the Friedländer reactions of 4-aminoacridine-3-carbaldehyde with pyrido[*b*]cycloalkanones as potential tridentate ligands. Dehydrogenation of dimethylene-bridged system afforded the corresponding fully aromatized system. Flexibility of annulated bridges is highly dependent on the length of the carbon chain, where the tetramethylene-bridge is rigid enough to differentiate eight bridge protons in ^{1}H NMR time scale at rt.

INTRODUCTION

In earlier reports,[2] we described a synthesis of 4-aminoacridine-3-carbaldehyde (**1**) and its utility as a Friedländer synthon for the preparation of benzo[*b*]-1,10-phenanthroline-derived polydentates including 2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline (**2a**). As a ligand, the molecule **2a** is a fused form of the *N*,*N*-bidentate, 1,10-phenanthroline and the *N*,*N*-bidentate, 2,2'-bipyridine, and thus can be a good unsymmetrical *N*,*N*,*N*-tridentate.[3] Although a plethora of chemistry dealing with metal complexes of *N*,*N*,*N*-tridentates have been pursued,[4] only very limited numbers of unsymmetrical pyridine-derived *N*,*N*,*N*-tridentates such as 2-(pyrid-2'-yl)-1,10-phenanthroline (**3a**),[5] 2-(quinol-2'-yl)-1,10-phenanthroline (**3b**)[6] and 2-(isoquinol-1'-yl)-1,10-phenanthroline (**3c**)[6b] as well as their related analogues,[7] and their metal complex chemistry have only been studied.

As a part of our interest in the design and synthesis of new polydentates, especially unsymmetrical pyrdine-derived *N*,*N*,*N*-tridentates, we herein described the synthesis and properties of 3,3'-polymethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines and related compounds, in which the dihedral angles between the two aromatic rings, benzo[*b*]-1,10-phenanthroline and pyridine, were

controlled in a regular fashion depending on the length of the bridge methylene units as has been observed previously.[2c,8]



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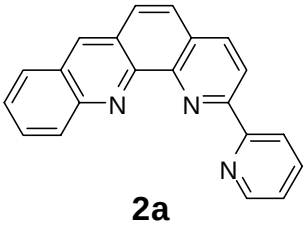
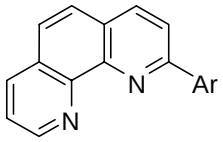


2a

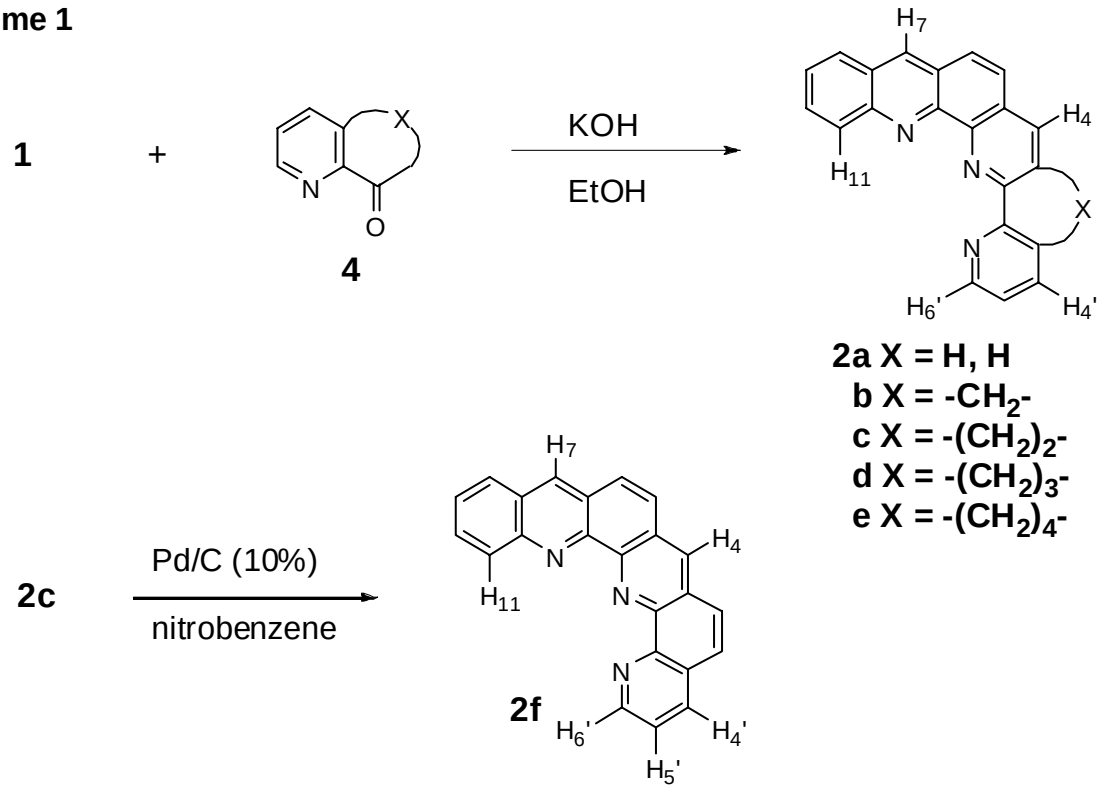


3a Ar = pyrid-2-yl
b Ar = quinol-2-yl
c Ar = isoquinol-1-yl

RESULTS AND DISCUSSION

Synthesis of designed ligands was straight forward as shown in Scheme 1. Friedländer condensations of 4-aminoacridine-3-carbaldehyde (**1**) with pyrido[*b*]cycloalkanones (**4c**-**e**)[9] afforded a series of 3,3'-polymethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines (**2c**-**e**) in 67-90% yields. Dehydrogenation of **2c** with Pd/C (10%) in nitrobenzene at 200 °C[10] led a fully aromatic, acridine-derived tridentate **2f** in 98% yield. Reaction of **1** with **4b** was, however, too sluggish to afford monomethylene-bridged ligand **2b**.

Scheme 1



Each proton resonance of the ligands was well resolved enough to be assigned by comparing previously reported data on the related compounds such as 2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline (**2a**)[1a] and confirmed by modern NMR techniques such as a COSY and DEPT experiments. The H6' of the ligand **2**

has characteristic coupling constant ($J_{5,6}$ = 4.8-5.5 and $J_{4,6}$ = 0.8-1.2 Hz) and been resonanced in the region of δ 8.63-9.20. H11's were resonanced in the region of δ 8.53-8.88 as a doublet of doublet with $J_{10,11}$ = 8.5-9.0 Hz and $J_{9,11}$ = 0.8-1.2 Hz. The resonances of H7's are an additional signature of the ligands and appeared in the region of δ 8.65-9.19. The resonances of the less planar ligands **2d** and **2e** were at δ 8.73 while that of the fully aromatized one (**2f**) at δ 9.19. ^{13}C NMR of **2e** showed 25 carbon resonances, of which DEPT (θ = 135^{o}) study showed 11 CH-carbons and 10-quaternary carbons in the aromatic region and 4 CH_2-carbons in the aliphatic region that confirmed a single component in 62.5 MHz ^{13}C NMR scale.

Table 1. Chemical shifts of selected H's of the ligands **2**

Compound	**2a**	**2c**	**2d**	**2e**	**2f** [a)]
H6'	8.75	8.63	8.85	8.73	9.20
H11	8.88	8.54	8.61	8.56	8.53
H7	8.88	8.65	8.73	8.73	9.19
H4	7.65	7.96	8.06	8.10	9.19

[a)] Each proton refers the same proton as in compound **2a**-**e** for consistency as shown in the Scheme 1 although the numbering pattern is not matched to **2f** based on the IUPAC systematic nomenclature.

The splitting pattern of the bridge protons generally affords conformational information of the ligands as has been reported.[1,6] The bridges of **2c** and **2d** in their ^{1}H NMR spectra showed two triplets for **2c**, and two triplets and a quintet for **2d** implying that the di- and trimethylene-bridges are flexible. ^{1}H NMR of **2e**, however, showed two one-proton doublets of doublets at δ 3.01 (^{2}J = 13.7 Hz, ^{3}J = 8.2 Hz) and δ 2.77 (^{2}J = 13.7 Hz, ^{3}J = 8.0 Hz), a one-proton triplet (J = 12.5 Hz) at δ 2.45, a two-proton multiplet in the region of δ 2.34-2.24, a one-proton triplet (J = 8.4 Hz) at δ 2.16, and a two-proton multiplet δ 1.83-1.58 in the aliphatic region. This implies that the tetramethylene bridge of **2e** is rigid enough to differentiate all eight protons in NMR time scale at rt. Such a conformational rigidity may induce enantiomerism through twisting the 2,2'-bond between the two aromatic rings, benzo[*b*]-1,10- phenanthroline and pyridine. Attempts to resolve each enantiomer were not successful as yet.

UV absorption spectra of the ligands **2** were taken from 4 x 10^{-3} M in CH_3CN and maxima and molar extinction coefficients summarized in Table 2. Four major absorption maxima originated from the π-π* transition were observed in the region of 241-268, 290-315, 305-329, and 334-365 nm. The absorption maximum in the region of 305-329 nm and 347-365 nm increases in energy and decreases in intensity as

the length of the bridge 3,3'-polymethylene bridge increases. Such trend reflects a decrease in the electronic interaction between the two aromatic halves of the molecule as the dihedral angle between them increases. Those of the planar and fully conjugated ligand **2f** were shifted to longer wavelength and shown high intensity, which reflected the better delocalization of the electrons.

Table 2. UV-Visible absorption spectral data for **2** (4×10^{-3} M)

Compound	λ_{max} nm (ε, $cm^{-1}M^{-1}$)			
2a	256 (106,600)	297 (51,300)	318 (62,400)	355 (39,200)
2c	268 (105,300)	315 (60,800)	329 (94,100)	365 (30,100)
2d	260 (103,700)	297 (63,000)	310 (86,800)	347 (20,200)
2e	260 (76,000)	294 (65,300)	305 (81,600)	334 (20,200)
2f	241 (115,600)	290 (58,100)	322 (103,300)	351 (41,500)

In conclusion, a series of 3,3'-polymethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines were prepared by the Friedländer reactions of 4-aminoacridine-3-carbaldehyde with pyrido[*b*]cycloalkanones. Dehydrogenation of dimethylene-bridged system afforded the corresponding fully aromatized one. The tetramethylene-bridge of 3,3'-tetramethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline is rigid enough to magnetically differentiate all the eight protons at rt in NMR time scale. Studies on the metal complexes of the ligands and their properties are ongoing and results will be reported in due course.

EXPERIMENTAL

Melting points were determined using a Fischer-Jones melting points apparatus and are not corrected. IR spectra were obtained using a Perkin-Elmer 1330 spectrophotometer. NMR spectra were obtained using a Bruker-250 spectrometer 250 MHz for ^{1}H NMR and 62.5 MHz for ^{13}C NMR and are reported as ppm from the internal standard tetramethylsilane. Chemicals and solvents were commercial reagent grade and used without further purification. The compounds **1**,[1a] **2a**,[1a] and **4**[9] were prepared by employing previously reported methods. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on a LCQ advantage-trap mass spectrometer (Thermo Finnigan, San Jose, CA, USA). Elemental analyses were taken on a Hewlett-Packard Model 185B elemental analyzer.

3,3'-Dimethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline (2c) (General procedure)

A mixture of 4-aminoacridine-3-carbaldedyde (**1**, 180 mg, 0.81 mmol) and pyrido[*b*]cyclohexanone (119 mg, 0.81 mmol) in absolute EtOH (20 mL) with saturated ethanolic KOH (1.5 mL) was refluxed for 12 h. The solvent was removed under reduced pressure and resulting brown solid was chromatographed on silica gel, eluting with CH_2Cl_2:EtOAc (1:1) and EtOAc. The latter fractions of EtOAc afforded pale yellow solid which was chromatographed on silica gel eluting with 1% MeOH in CH_2Cl_2 to give 181 mg (67%) of pale yellow needles after recrystallization from $CHCl_3$: mp 260-262 ^oC. ^1H NMR ($CDCl_3$, 250 MHz) δ 8.65 (s, 1H, H7), 8.63 (d, 1H, *J* = 4.6 Hz, H6'), 8.54 (d, 1H, *J* = 8.5 Hz, H11), 7.96 (s, 1H, H4), 7.95 (d, 1H, *J* = 7.8 Hz, H8), 7.78-7.69 (m, 2H), 7.58-7.51 (m, 3H), 7.22 (dd, 1H, *J* = 7.6, 4.8 Hz, H5'), 3.16 (t, 2H, *J* = 7.0 Hz), 3.04 (t, 2H, *J* = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 151.40, 150.90, 148.51, 147.83, 146.84, 145.44, 136.39, 136.11, 134.83, 134.65, 134.18, 130.45, 129.78, 129.37, 127.55, 127.48, 127.25, 126.72, 126.60, 125.40, 124.15, 27.59, 27.32. Mass (ESI) Calcd. for $C_{23}H_{15}N_3$ $[M+H]^+$ 334, found 334. *Anal.* Cald for $C_{23}H_{15}N_3 \cdot 0.5H_2O$: C, 80.68; H, 4.71; N, 12.27. Found: C, 80.75; H, 4.73; N, 12.26.

3,3'-Trimethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline (2d)

Yield (80%): mp 251-253 ^oC. ^1H NMR ($CDCl_3$, 250 MHz) δ 8.85 (dd, 1H, *J* = 4.6, 1.5 Hz, H6'), 8.73 (s, 1H, H7), 8.61 (d, 1H, *J* = 8.8 Hz, H11), 8.06 (s, 1H, H4), 8.04 (d, 1H, *J* = 8.5 Hz, H4'), 7.88 (d, 1H, *J* = 9.0 Hz, H5/H6), 7.81 (ddd, 1H, *J* = 8.3, 1.5, 1.0 Hz, H8), 7.70 (d, 1H, *J* = 9.0 Hz, H6/H5), 7.63-7.57 (m, 2H, H9 and H10), 7.35 (dd, 1H, *J* = 7.6, 4.8 Hz, H5'), 2.79 (t, 2H, *J* = 7.0 Hz), 2.60 (t, 2H, *J* = 7.0 Hz), 2.34 (quintet, 2H, *J* = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 157.48, 157.43, 148.88 (two C's), 148.65, 147.53, 146.04, 137.09, 136.25, 136.12 (two C's), 135.88, 131.32, 130.50, 129.51, 127.96, 127.93, 127.79, 127.11, 125.90, 124.10, 32.48, 30.47, 30.22. Mass (ESI) Calcd for $C_{24}H_{17}N_3$ $[M+H]^+$ 348, found 348. *Anal.* Calcd for $C_{24}H_{17}N_3 \cdot H_2O$: C, 78.88; H, 5.24; N, 11.50. Found: C, 78.95; H, 5.30; N, 11.63.

3,3'-Tetramethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthroline (2e)

Yield (90%): mp 186 ^oC. ^1H NMR ($CDCl_3$, 250 MHz) δ 8.73 (br. s, 2H, H7 and H6'), 8.56 (d, 1H, *J* = 8.7 Hz, H11), 8.10 (s, 1H, H4), 8.03 (d, 1H, *J* = 8.3 Hz, H8), 7.86 (d, 1H, *J* = 9.0 Hz, H5/H6), 7.79 (dd, 1H, *J* = 8.3, 7.8, 1.5 Hz, H10), 7.69 (d, 1H, *J* = 9.0 Hz, H6/H5), 7.64-7.58 (m, 2H, H4' and H9), 7.37 (dd, 1H, *J* = 7.7, 4.8 Hz, H5'), 3.01 (dd, 1H, *J* = 13.7, 8.2 Hz), 2.77 (dd, 1H, *J* = 13.7, 8.0 Hz), 2.45 (t, 1H, *J* = 12.5 Hz), 2.34-2.24 (m, 2H), 2.16 (t, 1H, *J* = 8.4 Hz), 1.83-1.58 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 156.47, 156.14, 148.14, 147.52, 147.04, 144.90, 138.53, 138.18, 137.67, 136.67, 135.85, 130.85, 130.01, 129.42, 127.50, 127.36 (two C's), 126.73, 126.66, 125.48, 123.96, 31.74, 31.71, 29.81, 28.84. Mass (ESI) Calcd for $C_{25}H_{19}N_3$ $[M+H]^+$ 362, found 362. *Anal.* Calcd for $C_{25}H_{19}N_3 \cdot 0.75H_2O$: C, 80.08; H, 5.51; N, 11.21. Found: C, 80.09; H, 5.50; N, 11.18.

Benzo[*b*]quino[7,8-*j*]-1,10-phenanthroline (2f)

A mixture of **2c** (33.3 mg, 0.1 mmol) and 10% Pd-C (33.2 mg, 100 wt %) in nitrobenzene (5 mL) was heated at 200 ^{o}C for 20 h. Resulting mixture was filtered through Celite® and chromatographed on silica gel eluting with CH_2Cl_2. The latter fractions [R_f = 0.1 (CH_2Cl_2)] afforded 33 mg (98%) of pale yellow solid: mp 185 ^{o}C. ^{1}H NMR (DMSO-d_6, 250 MHz) δ 9.20 (dd, 1H, *J* = 4.6, 1.5 Hz), 9.19 (s, 2H), 8.61 (d, 1H, *J* = 8.3 Hz), 8.53 (d, 1H, *J* = 8.5 Hz), 8.32 (d, 1H, *J* = 8.5 Hz), 8.24 (d, 1H, *J* = 8.8 Hz), 8.12 (d, 1H, *J* = 8.8 Hz), 8.11 (AB quartet, 2H), 8.13 (td, 1H, *J* = 8.3, 1.0 Hz), 7.89 (dd, 1H, *J* = 7.6, 4.8 Hz), 7.81 (t, 1H, *J* = 7.5 Hz). Mass (ESI) Calcd for $C_{23}H_{13}N_3$ $[M+H]^+$ 332, found 332. *Anal.* Calcd for $C_{23}H_{13}N_3 \cdot H_2O$: C, 79.07; H, 4.33; N, 12.03. Found: C, 79.05; H, 4.30; N, 12.03.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

1. Parts I, II, III, and IV are references 2a,b,c, and 2d, respectively.
2. (a) J. K. Son, J. K. Son, and Y. Jahng, *Heterocycles*, 2002, **57**, 1109. (b) A. F. M. M. Rahman and Y. Jahng, *Heteroatom Chem*., 2007, **18**, 650. (c) A. F. M. M. Rahman and Y. Jahng, *Heterocycles*, 2007, **71**, 2003. (d) A. F. M. M. Rahman and Y. Jahng, *Heterocycles*, 2008, **75**, 871.
3. Although all attempts to prepare bis-complexes of **2a** with various d_6 metals were failed, but instead afforded a complex mixture of products that were neither isolable nor characterizable, annulated analogues, **2c**-**f**, afforded ML_2-type metal complexes with various d_6 metals.
4. (a) K. Kalyanasundaram, *Photochemistry of Polypyridines and Phorphyrin Complexes*; Academic Press: San Diego, CA, 1992. (b) Y. Jahng and R. P. Thummel, *J. Org. Chem.*, 1987, **52**, 87. (c) R. P. Thummel, *Synthesis*, 1992, 1.
5. (a) F. H. Case and R. Sabin, *J. Org. Chem.*, 1955, **20**, 1330. (b) F. Wu, E. Riesgo, A. Pavalova, R. A. Kipp, R. H. Schmehl, and R. P. Thummel, *Inorg. Chem.*, 1999, **38**, 5620. (c) C. Bonnefous, A. Chouai, and R. P. Thummel, *Inorg. Chem*., 2001, **40**, 5851.
6. (a) F. H. Case and A. A. Schilt, *J. Heterocycl. Chem.*, 1979, **16**, 1135. (b) Y. Jahng, R. P. Thummel, and S. G. Bott, *Inorg. Chem.*, 1997, **36**, 3133.
7. J. G. Park and Y. Jahng, *Bull. Korean Chem. Soc*., 1998, **19**, 436.
8. (a) R. P. Thummel and F. Lefoulon, *J. Org. Chem*., 1985, **50**, 666. (c) R. P. Thummel, F. Lefoulon, and R. Mahadevan, *J. Org. Chem*., 1985, **50**, 3824.
9. R. P. Thummel, F. Lefoulon, D. Cantu, and R. Mahadevan, *J. Org. Chem*., 1984, **49**, 2208.
10. Y. Amemiya, D. D. Miller, and F.-L. Hsu, *Synth. Commun*., 1990, **20**, 2483.