HETEROCYCLES, Vol. 75, No. 4, 2008, pp. 871 - 877. © The Japan Institute of Heterocyclic Chemistry
Received, 28th November, 2007, Accepted, 15th January, 2008, Published online, 18th January, 2008. COM-07-11281

SYNTHESIS AND PROPERTIES OF 3,3'-POLYMETHYLENE-2,2'-BIBENZO[*b*]-1,10-PHENANTHROLINES

A. F. M. Motiur Rahman and Yurngdong Jahng*

College of Pharmacy, Yeungnam University, Gyeongsan 712-749, Korea, ydjahng@ynu.ac.kr

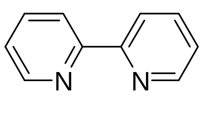
Abstract – The Friedländer reactions of 4-aminoacridine-3-carbaldehyde with cyclcoalkane-1,2-diones were examined. The reactions of cycloheptane- and cycloocatane-1,2-diones afforded 3,3'-tri- and 3,3'-tetramethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines in 20% and 80%, respectively, while reactions with butane-2,3-dione, cyclopentane-1,2-dione and cyclohexane-1,2-dione afforded only unexpected benzo[*b*]-1,10-phenanthroline. The trimethylene-bridge is flexible at room temperature while the tetramethylene units are rigid enough to magnetically differentiate all the 8 aliphatic protons at room temperature in NMR time scale even though showing two aliphatic carbon resonaces as expected.

INTRODUCTION

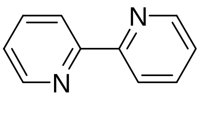
Creating a new bond at C2 positions of the heterocycles would lead 2,2'-biheterocycles, which have been attractive not only due to the potentials for conjugated organic π-electron materials[1] but also the potentials for metal complex formation. Among them, 2,2'-bipyridine has been mostly studied because of its potential to form metal complexes as a bidentate ligand and their various properties.[2] In fact, 2,2'-bipyridine can exist as two conformational isomers such as *cis*- (**1a**) and *trans*-isomer (**1b**), of which *cis*-isomer can only form metal complexes while the *trans*-conformation is more stable conformer in solid[3] as well as in solution.[4]

Murrell and coworkers studied the ^{1}H NMR spectra of 2,2'-bipyridine at various temperatures and they observed no major changes in the temperature range of -65 °C to 150 °C.[4c] These observations imply that a cisoid conformational rigidity can only be imposed either by the introduction of polymethylene units at C3 and C3'-positions of 2,2'-bipyridine[5a] or by metal coordinations. Same situation would be applied for 2,2'-biquinoline[5b] and 2,2'-bi-1,10-phenanthroline[5c] and so controlled conformations in a regular fashion.

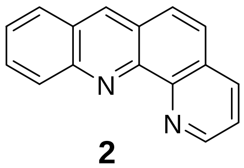
We have been involved in studies on the preparation and properties of benzo[*b*]-1,10-phenanthroline (**2**) and related polydentates.[6] When two molecules of benzo[*b*]-1,10-phenanthroline are connected at C2-positions to lead 2,2'-bibenzo[*b*]-1,10-phenanthroline (**3**), which can also exist as two conformational isomers as shown. The cisoid conformation (*cis*-**3a**) is expected to be less favorable, but responsible for coordination. Connection of C3 and C3'-positions by a polymethylene bridge would force tetradentate to have coordination-favored cisoid conformation.



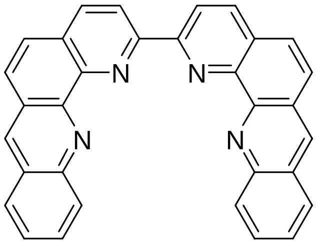
1a (*cis*-2,2'-bipyridine)



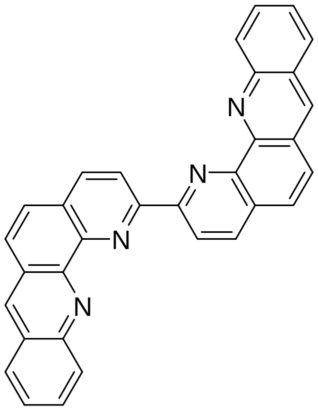
1b (*trans*-2,2'-bipyridine)



2

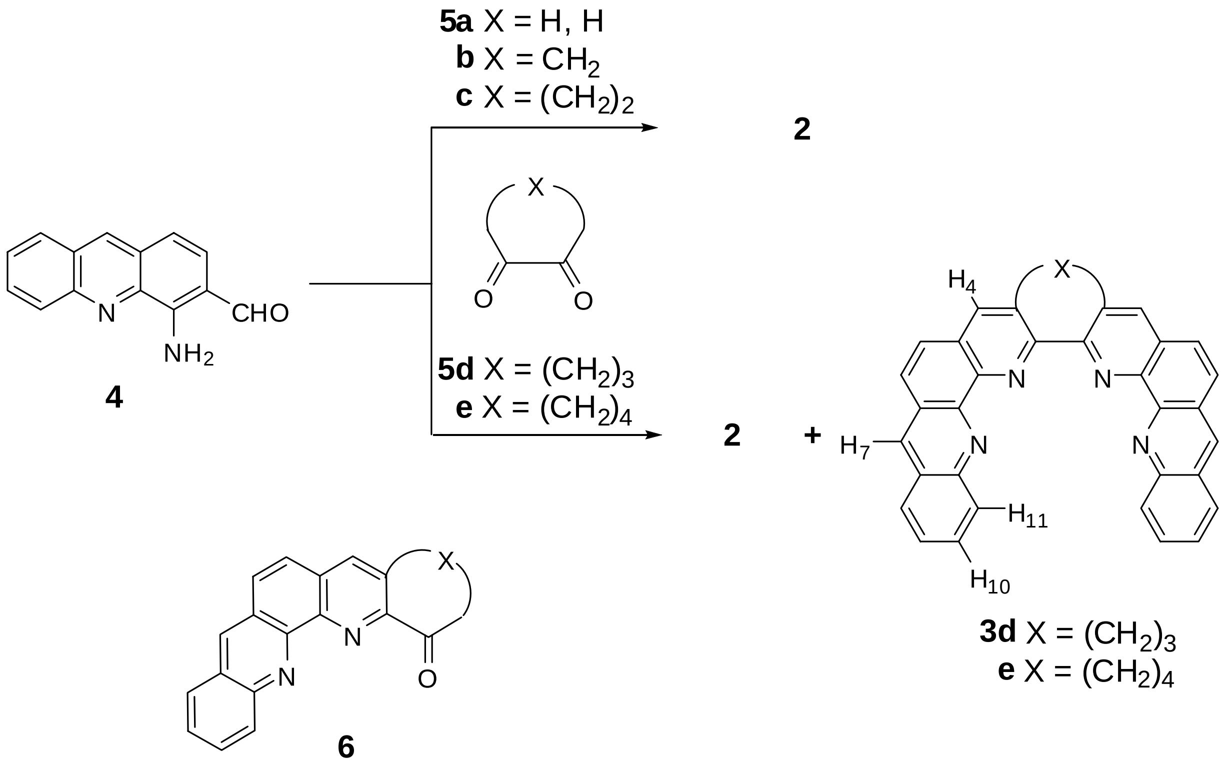


cis-**3a**



trans-**3a**

We reasoned that double Friedländer reactions of **4** with cycloalkane-1,2-diones (**5**) would lead a series of 3,3'-carbocycle-annulated 2,2'-bibenzo[*b*]-1,10-phenanthrolines (**3**). Two equivalents of the Friedländer synthon **4** was thus condensed with cycloheptane-1,2-dione (**5d**) and cyclooctane-1,2-dione (**5e**) in the presence of catalytic amount of KOH in EtOH to lead the corresponding 3,3'-tri- and 3,3'-tetramethylene-2,2'-bibenzo[*b*]-1,10-phenanthrolines (**3d** and **3e**) in 20% and 80% yield, respectively. Low yield of **3d** could be explained by formation of benzo[*b*]-1,10-phenanthroline (**2**) in 52% yield. However, the reactions of **4** with cyclopentane- and cyclohexane-1,2-diones (**5b**,**c**) did not provide the corresponding 3,3'-polymethylene-2,2'-bibenzo[*b*]-1,10-phenanthrolines (**3b**,**c**) or mono-condensed products (**6**), but instead led complex reaction mixtures. Careful and repeated column chromatography of the reaction mixtures afforded **2** in approximately 50% yield. Reactions under acidic (*p*-TsOH) or various basic (*i.e.* piperidine) condition[7] would not affect the distribution of the products. Similarly, the reaction of **4** with butane-2,3-dione (**5a**) also afforded benzo[*b*]-1,10-phenanthroline (**2**) in 75% yield instead of expected parent non-bridged 2,2'-bibenzo[*b*]-1,10-phenanthroline (**3a**) regardless of the equivalencies of **4**. Such results could be explained that the mono-condensed reaction intermediate, 2-acetylbenzo[*b*]-1,10-phenanthroline, would undergo base-catalyzed deacetylation to lead **2** in the reaction of **4** with **5a**. The similar results were previously reported in the Friedländer reactions of pentane-2,4-dione and triacetylmethane with various *ortho*-aminoaldehydes.[8] In addition, base-catalyzed deacetylation of pentane-2,4-dione[9] has also been previously reported. A step-wise condensation of **4** with butane-2,3-dione (**5a**) in the presence of either *p*-TsOH or KOH was also failed to afford corresponding 2-acetylbenzo[*b*]-1,10-phenanthroline, but to give **2** in 35% yield. However, formation of **2** from the reactions of **4** with **5b**,**c**,**d** can not be explained in a similar reaction pattern, which is remained to be explored.



^{13}C NMR spectra of the ligands showed all the carbon resonances as expected except **3d**, in which two α-carbons in the methylene bridge were coincidently resonanced at δ 29.93. ^{1}H NMR spectra of the ligands showed one-set of proton resonances, which could be readily assigned by comparing previous data on benzo[*b*]-1,10-phenanthroline and related compounds. An examination of the upfield-region of the ^{1}H NMR spectra for **3c** and **3d** gives information on the conformation of the ligands. The trimethylene-bridge protons of the ligand **3d** were resonanced at δ 2.86 as a four-proton triplet (J = 7.5 Hz) and δ 2.41 as a two-proton quintet (J = 7.5 Hz) implying that the bridge is flexible at room temperature in the ^{1}H NMR time scale, thus showing equivalency of the geminal protons on α- or β-methylene groups. However, the geminal protons on the methylene groups of tetramethylene-bridge of **3e** showed non-equivalency, thus a doublet of doublet at δ 3.04 with coupling constants of J_{gem} = 13.7 Hz and J_{vic} = 8.0 Hz, a doublet of doublet at δ 2.53 (J_{gem} = 13.7 Hz and J_{vic} = 11.3 Hz), two multiplets at δ 2.34-2.27 and δ 1.89-1.80. Conformational rigidity of the tetramethylene-bridge has been observed in most of the annulated heterocycles.

It is worthy to noting that such a rigidity of the bridge creates a chiral axis through 2,2'-bond of the molecule, thus compound **3e** exists as a mixture of two enantiomers. Attempts to separate each conformational enantiomer were not as yet successful.

In conclusion, double Friedländer reactions of 4-aminoacridine-3-carbaldehyde with cycloheptane- and cycloocatane-1,2-diones afforded 3,3'-tri- and 3,3'-tetramethylene-2-(pyrid-2'-yl)benzo[*b*]-1,10-phenanthrolines, respectively, while reactions with butane-2,3-dione, cyclopentane-1,2-dione and cyclohexane-1,2-dione afforded only unexpected benzo[*b*]-1,10-phenanthroline. The trimethylene-bridge is flexible at room temperature to show a 4-proton triplet and a 2-proton quintet while the tetramethylene unit is rigid enough to magnetically differentiate all the 8 aliphatic protons at room temperature in NMR time scale. Synthesis of designed ligands by an alternative route, resolution of enantiomers of tetramethylene-bridged system and studies on the metal complexes of the ligands 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. 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 TMS. Chemicals and solvents were commercial reagent grade and used without further purification. The starting 4-aminoacridine-3-carbaldehyde,[6a] cycloalkane-1,2-diones[10] 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.

Reaction of **4** with **5a**

A mixture of **4** (0.90 g, 4.0 mmol) and butane-2,3-dione (**5a**) (0.17 g, 1.98 mmol) in absolute EtOH (20 mL) with saturated alcoholic KOH (1.0 mL) was refluxed for 20 h. Evaporation of the solvent under reduce pressure gave a brown oily material, which was chromatographed on silica gel eluting with CH_2Cl_2, followed by CH_2Cl_2:MeOH (9:1). The early fractions (R_f = 0.80) of CH_2Cl_2:MeOH (9:1) afforded 0.34 g (75%) of **2** as pale yellow needles after recrystallization from petroleum ether:CH_2Cl_2 (1:1): mp 113-114 °C (lit.,[8] mp 113-114 °C, lit.,[11] mp 113 °C). All spectral data are identical to those in the literatures.

Reaction of **4** with **5b**

The same procedure described above for the reaction of **4** and **5a** was applied to **4** (0.45 g, 2.0 mmol) and cyclopentane-1,2-dione (**5b**) (0.10 g, 1.0 mmol) afforded 0.12 g (52%) of **2**: mp 113-114 °C.

Reaction of **4** with **5c**

The same procedure described above for the reaction of **4** and **5a** was applied to **4** (0.45 g, 2.0 mmol) and cyclohexane-1,2-dione (**5c**) (0.11 g, 0.98 mmol) afforded 0.11 g (49%) of **2**: mp 113-114 °C.

3,3'-Trimethylene-2,2'-bibenzo[*b*]-1,10-phenanthroline (3d). A mixture of **4** (0.45 g, 2.0 mmol) and cycloheptane-1,2-dione (**5d**) (0.13 g, 1.0 mmol) in absolute EtOH (20 mL) with saturated alcoholic KOH (1 mL) was refluxed for 20 h. Evaporation of the solvent under reduce pressure gave brown solid, which was chromatographed on silica gel eluting with CH_2Cl_2 followed by CH_2Cl_2:MeOH (9:1). The early fractions (R_f = 0.80) of CH_2Cl_2:CH_3OH (9:1) afforded of **2** as pale yellow needles (0.12 g, 52%): mp 113-114 °C (petroleum ether:CH_2Cl_2 = 1:1) (lit.,[8] mp 113-114 °C). All spectral data are identical to those in the literatures. The latter fractions (R_f = 0.20) afforded 0.10 g (20%) of **3d** as yellow needles: mp 240 °C. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.78 (s, 2H, H7), 8.70 (d, 2H, *J* = 8.5 Hz, H11), 8.13 (s, 2H, H4), 8.04 (d, 2H, *J* = 8.3 Hz, H8), 7.88 (d, 2H, *J* = 9.0 Hz, H5/H6), 7.78 (t, 2H, *J* = 8.3 Hz, H10), 7.74 (d, 2H, *J* = 9.0 Hz, H6/H5), 7.60 (t, 2H, *J* = 8.3 Hz, H9), 2.86 (t, 4H, *J* = 7.5 Hz), 2.41 (quintet, 2H, *J* = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 157.32, 148.37, 146.92, 145.76, 135.95, 135.89, 135.62, 130.94, 130.38, 129.27, 127.59, 127.53, 127.41, 126.79, 126.62, 125.40, 31.58, 29.93 (two C's). Mass (ESI) calcd. for $C_{35}H_{22}N_4$ $[M+H]^+$ 499, found 499. *Anal.* Calcd for $C_{35}H_{22}N_4 \cdot 1.0H_2O$: C, 81.37; H, 4.68; N, 10.85. Found: C, 81.32; H, 4.64; N, 10.92.

3,3'-Tetramethylene-2,2'-dibenzo[*b*]-1,10-phenanthroline (3e). A mixture of **4** (0.1 g, 0.71 mmol) and cyclooctane-1,2-dione (**5e**, 0.38 g, 2.1 mmol) in absolute EtOH (50 mL) with saturated alcoholic KOH (1 mL) was refluxed for 20 h. Evaporation of the solvent under reduced pressure gave brown solid was recrystallized in CH_2Cl_2:*n*-hexane (1:1) afforded 0.30 g (80 %) of **3e** as ash solid: mp >320 °C. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.75 (s, 2H, H7), 8.59 (d, *J* = 8.7 Hz, 2H, H11), 8.16 (s, 2H, H4), 8.01 (d, *J* = 8.2 Hz, 2H, H8), 7.88 (d, *J* = 9.0 Hz, 2H, H5/H6), 7.72 (ddd, *J* = 8.7, 7.2 Hz, 2H, H10), 7.71 (d, *J* = 9.0 Hz, 2H, H6/H5), 7.56 (td, *J* = 7.2, 0.7 Hz, 2H, H9), 3.04 (dd, 1H, *J* = 13.8, 8.0 Hz, 2H), 2.54 (dd, *J* = 13.7, 8.0 Hz, 2H), 2.34-2.26 (m, 2H), 1.89-1.76 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.50 MHz) δ 156.69, 148.35, 146.91, 144.94, 139.04 (two C's), 136.68 (CH), 135.82 (CH), 131.09 (CH), 130.16 (CH), 129.51, 127.54, 127.43 (CH), 127.38 (CH), 126.69 (CH), 125.38 (CH), 31.94 (CH_2), 29.85 (CH_2). Mass (ESI) calcd. for $C_{36}H_{24}N_4$ $[M+H]^+$ 513, found 513. *Anal.* Calcd for $C_{36}H_{24}N_4$: C, 84.35; H, 4.72; N, 10.93. Found: C, 84.38; H, 4.73; N, 10.89.

ACKNOWLEDGEMENT

Financial support from the *Korean Research Foundation Grant* (KRF-2006–005-J01101) is gratefully acknowledged.

REFERENCES AND NOTES

1. (a) G. R. Hutchison, M. A. Ratner, and T. J. Marks, *J. Am. Chem. Soc.*, 2005, **127**, 2339. (b) P. K. H. Ho, J.-S. Kim, J. H. Burroughes, H. Becker, S. F. Y. Li, T. M. Brown, F. Cacialli, and R. H. Friend, *Nature*, 2000, **404**, 481.
2. (a) G. R. Newkome, A. K. Patri, E. Holder, and U. S. Schubert, *Eur. J. Org. Chem.*, 2004, 235. (b) Lee, K. W. Lee, J. D. Slinker, A. A. Gorodetsky, S. Flores-Torres, H. D. Abruna, P. L. Houston, and G. G. Malliaras, *Phys. Chem. Chem. Phys.*, 2003, **5**, 2706. (c) K. Kalyanasundaram, Photochemistry of Polypyridine and Porphyrin Complexes, Academic Press, San Diego, 1992. (d) A. Juris, V. Balzani, F. Barigelletti, S. Campagna, P. Belser, and A. von Zelewsky, *Coord. Chem. Rev.*, 1988, **84**, 85.
3. (a) F. W. Cagle, Jr., *Acta Cryst.*, 1948, **1**, 158. (b) L. L. Merritt, Jr. and E. D. Schröder, *Acta Cryst.*, 1956, **9**, 801.
4. (a) C. W. N. Cumper, R. F. A. Ginman, and A. I. Vogel, *J. Chem. Soc.*, 1962, 1188. (b) S. Castellano, H. Günther, and S. Ebersole, *J. Phys. Chem.*, 1965, **69**, 4166. (c) J. N. Murrell, V. M. S. Gil, and F. B. Van Duijineveldt, *Rec. Trav. Chim. Pays-Bas*, 1965, **84**, 1399.
5. (a) R. P. Thummel, F. Lefoulon, and R. Mahadevan, *J. Org. Chem.*, 1985, **50**, 3824. (b) R. P. Thummel and F. Lefoulon, *J. Org. Chem.*, 1985, **50**, 666. (c) F. H. Case, *J. Heterocycl. Chem.*, 1964, **1**, 112.
6. (a) J. K. Son, J. K. Son, and Y. Jahng, *Heterocycles*, 2002, **57**, 1109. (b) A. F. M. M. Rahman and Y. Jahng, *Heterocycles*, 2007, **71**, 2003. (c) A. F. M. M. Rahman and Y. Jahng, *Heteroatom Chem.*, 2007, **18**, 650.
7. E. C. Riesgo, Y.-Z. Hu, and R. P. Thummel, *Inorg. Chem.*, 2003, **42**, 6648.
8. A. F. M. Motiur, Y. Kwon, and Y. Jahng, *Heterocycles*, 2005, **65**, 2777.
9. Recent example of base-catalyzed deacetylation: O. A. Attanasi, P. Filippone, C. Fiorucci, E. Foresti, and F. Mantellini, *J. Org. Chem.*, 1998, **63**, 9880. Strong alkali-catalyzed predeacetylation of 2,4-pentanedione to acetone was also reported, see: G. Stefanovic, M. Pavicic-Woss, L. Lorenc, and M. L. Mihailovic, *Tetrahedron*, 1959, **6**, 97. Examples of base-catalyzed deacetylation of acylacetone to methyl ketone: (a) F. Fischer and C. Bülow, *Ber.*, 1885, **18**, 2132. (b) R. Connor and

H. Adkins, *J. Am. Chem. Soc.*, 1932, **54**, 3420.

10. (a) J. Wrobel and J. M. Cook, *Synth. Commun*., 1980, **10**, 337. (b) M. C. Carre and P. Caubere, *Tetrahedron Lett.*, 1985, **26**, 3103. (c) C. C. Hach, C. V. Banks, and H. Diehl, *Org. Syn*, *Col. Vol. IV*, 1963, 229. (d) W. Haar, V. Voter, C. Roger, and C. V. Banks, *J. Org. Chem.*, 1949, **14**, 836. (e) G. Wittig and A. Krebs, *Chem. Ber*., 1961, **44**, 3760.
11. E. Koft and F. H. Case, *J. Org. Chem*., 1962, **27**, 865.