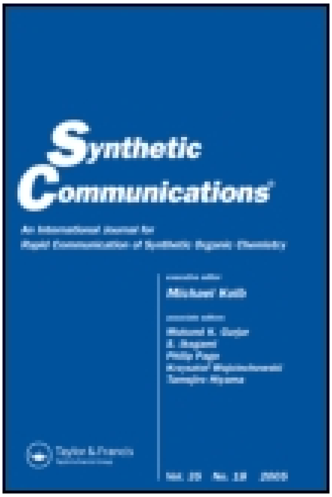


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of Novel Donor-π-Acceptor Chromophores with Dipicolinate as Acceptor

Haibo Xiao [a] , Xiaoming Tao [a] , Hui Li [a] & Guanghao Shi [a]

[a] Department of Chemistry , Shanghai Normal University , Shanghai, China

To cite this article: Haibo Xiao , Xiaoming Tao , Hui Li & Guanghao Shi (2009) Synthesis of Novel Donor-π-Acceptor Chromophores with Dipicolinate as Acceptor, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 39:8, 1472-1477, DOI: 10.1080/00397910802531963

To link to this article: http://dx.doi.org/10.1080/00397910802531963

Synthetic Communications®, 39: 1472–1477, 2009

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910802531963

Synthesis of Novel Donor–π–Acceptor Chromophores with Dipicolinate as Acceptor

Haibo Xiao, Xiaoming Tao, Hui Li, and Guanghao Shi
Department of Chemistry, Shanghai Normal University, Shanghai, China

Abstract: Three novel donor–π–acceptor (D–π–A) chromophores, with dipicolinate as acceptor, have been synthesized. All the compounds were characterized by ^1H NMR, infrared (IR) spectroscopy, mass spectrometry (MS), and elemental analysis.

Keywords: Acceptor, chromophore, dipicolinate, synthesis

INTRODUCTION

The luminescence of lanthanide (Ln^{III}) coordination complexes is unique because of their high color purity, long lifetimes, and insensitivity to environmental quenching.[1] The sensitization of Ln^{III} by the two-photon antenna effect may lead to less harmful and deep-penetrating bioimaging applications.[1–3] Although studies on biological imaging from lanthanides (by ultraviolet, UV, absorption) or induced by two-photon excited fluorescence (from organic systems) have been widely reported,[4] relatively few complexes that combine the advantages of two-photon sensitization and high-purity Ln^{III} emission can be found. Pyridine-2,6-dicarboxylic (dipicolinic) acid and its derivatives are highly useful tridentate ligands. Pyridine-2,6-dicarboxylic acid forms nine-coordinating luminescent complexes with lanthanides, providing high quantum yields of phosphorescence, and these are used as luminescent tags, labels, and barcodes.[5–9] Despite the simplicity of the preparation of tridentate ligands based on pyridine-2,6-dicarboxylic acid, fabrication

Received July 25, 2008.

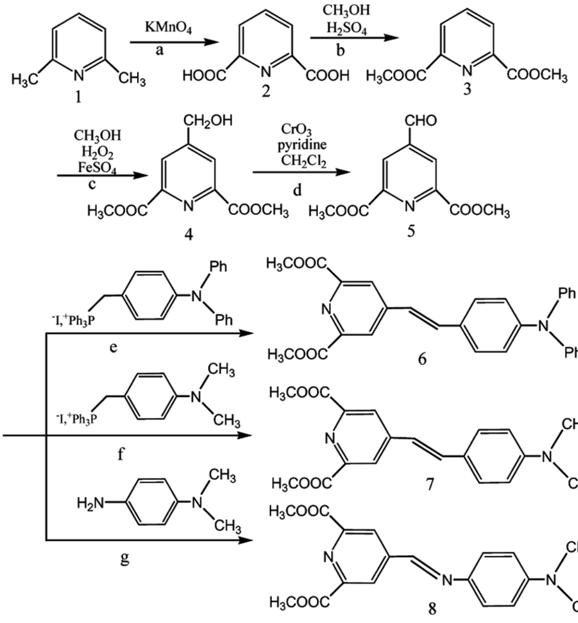
Address correspondence to Haibo Xiao, Department of Chemistry, Shanghai Normal University, Shanghai, China. E-mail: xiaohb@shnu.edu.cn

of complex systems based on its derivatives necessitates derivatization of the pyridine ring. Consequently, substantial efforts have been concentrated on the preparation of functionalized pyridine-2,6-dicarboxylic acid derivatives.[10,11] To the best of our knowledge, there has not been any report on dipicolinates or its derivatives as acceptors in donor–π–acceptor (D–π–A) chromophores.

In this article, we describe the synthesis of three novel D–π–A chromophores containing dipicolinate. The arylamine group in chromophore functions as an electron donor (D), the dipicolinate moiety acts as an electron acceptor (A), and the C=C or C=N double bond acts as a conjugation bridge. Therefore, a chromophore is a polar molecule that shows D–π–A character, which is known to be the structural basis for an efficient two-photon absorber.[12] The target compounds are the possible candidates to be used to sensitize Ln^{III} by the two-photon antenna effect.

RESULTS AND DISCUSSION

The target compounds **6, 7,** and **8** were synthesized according to the steps outlined in Scheme 1. Direct functionalization of pyridine-2,6-dicarboxylates cannot be performed by conventional substitution reactions, because



Scheme 1. Synthesis of three D–π–A chromophores containing dipicolinate.

of the resistance of the pyridine ring in pyridine-2,6-dicarboxylic acid derivatives to electrophilic and nucleophilic attacks.[8] Shelkov and Melman reported the synthesis of 4-(hydroxyalkyl) pyridine-2,6-dicarboxylates through free-radical reactions.[8] These reactions proceeded with complete regioselectivity, and no detectable amounts of isomeric products were observed, despite the presence of two electron-withdrawing methoxycarbonyl groups known to favor 3-substitution. The key intermediate, dimethyl 4-formylpyridine-2,6-dicarboxylate **5**, was synthesized by oxidation of 4-(hydroxymethyl) pyridine-2,6-dicarboxylate, and the formyl group was employed to synthesize a C=C or C=N double bond as the conjugation bridge. The synthesis of dimethyl 4-formylpyridine-2,6-dicarboxylate **5** from 4-(hydroxymethyl)pyridine-2,6-dicarboxylate using MnO_2 resulted in poor yield. The application of CrO_3 was used as an alternative for this reaction and gave **5** in 75% yield.

In conclusion, we have been successful in utilizing dimethyl 4-formylpyridine-2,6-dicarboxylate **5** for the syntheses of novel D–π–A chromophores. Compounds **5, 6, 7,** and **8** are new and have been characterized by spectral and analytical data.

EXPERIMENTAL

Melting points were determined with an XT4A apparatus and are uncorrected. Magnetic resonance spectra were recorded on a Bruker DRX 400 spectrometer, using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. Infrared (IR) spectra were obtained on a Nicolet Avatar 370 DTGS spectrometer. Mass spectra were obtained on a VG12-250 mass spectrometer. Elemental analyses were obtained on a Perkin-Elemer instrument.

All reagents and solvents were commercial reagents of analytical grade and were used as received. Further purification and drying by standard methods were employed and they were distilled prior to use when necessary. Reactions were monitored by thin-layer chromatography (TLC), on silica gel (grade 60 PF_{254})–protected glass sheets, and the spots were detected by exposure to a UV lamp at λ_{254} nm for a few seconds.

Compound **4** was prepared starting from 2,6-dimethylpyridin according to the literature method.[8,13]

Dimethyl 4-formyl-pyridine-2,6-dicarboxylate (5)

A mixture of CrO_3(1 g, 1 mmol), pyridine (1.58 g, 2 mmol), and CH_2Cl_2 (100 ml) was stirred at room temperature for 20 min. A solution of **4**

(0.45 g, 2 mmol) in CH_2Cl_2 (10 ml) was added dropwise over 30 min at 25–30°C. The mixture was stirred for 5 h at room temperature. The organic phase was washed with 1 mol/L HCl and water successively and dried over $MgSO_4$. The crude product was purified by silica-gel column chromatography, eluting with petroleum/ethyl acetate to afford **5** (0.33 g). Yield 75%. Mp 186–188 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 10.2 (s, 1H, CHO), 8.7 (s, 2H, PyH), 4.1 (s, 6H, OCH_3). EI-MS: m/z 223 (M^+). Anal. calcd. for $C_{10}H_9NO_5$: C, 53.82; H, 4.06; N, 6.28. Found: C, 53.79; H, 4.05; N, 6.25.

Trans-dimethyl-4-[4′-(N,N-diphenylamino)-styryl]-pyridin-2,6-dicarboxylate (6)

To a 50-ml, two-necked flask, 0.115 g **5** (0.5 mmol), 0.323 g phosphonium salt (0.6 mmol), and 100 ml anhydrous tetrahydrafuran (THF) were added under a nitrogen atmosphere. The reaction mixture was cooled to 0°C in an ice bath. A THF solution (15 ml) of 0.024 g NaH was dropped into the flask. After the reaction mixture had been stirred for 24 h at room temperature, the mixture was washed with water. The organic phase was dried over $MgSO_4$, then evaporated to give yellow solid. The crude product was purified by chromatography on silica gel, using CH_2Cl_2/hexane as the eluent, to give pure product in 50% yield (119 mg). Mp 193–195 °C. IR (KBr) 2953.9, 2925.3, 2851.7, 1711.6, 1585.0, 1491, 1356, 1278.5, 1249.9, 1115.1, 992.5, 967.9, 759.6, 694.2 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ ppm): 8.35 (s, 2H, PyH), 7.4–7.46 (m, 2H), 7.28–7.34 (m, 4H), 7.15 (d, $J = 8.4$ Hz, 4H), 7.03–7.13 (m, 4H), 6.95–7.0 (d, $J = 16.8$ Hz, 2H), 4.0 (s, 6H). EI-MS: m/z 464 (M^+). Anal. calcd. for $C_{29}H_{24}N_2O_4$: C, 74.98; H, 5.21; N, 6.03. Found: C, 75.03; H, 5.16; N, 6.06.

Trans-dimethyl-4-[4′-(N,N-dimethylamino)-styryl]-pyridin-2,6-dicarboxylate (7)

Compound **7** used the same method as **6**. Yield 45%, mp 200–202 °C. IR (KBr): 2953.9, 2921.2, 2855.8, 2802.7, 1752.5, 1711.6, 1609.5, 1589.1, 1446.1, 1258.1, 1237.7, 1184.6, 1155.9, 992.5,955.7, 804.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ ppm): 8.35 (s, 2H, PyH), 7.4–7.5(m, $J = 8.0$ Hz, 16.0 Hz, 3H), 6.90 (d, $J = 16.0$ Hz, 1H, Py–CH=), 6.75 (d, $J = 8.0$ Hz, 2H, ArH), 4.0 (s, 6H, OCH_3), 3.0 (s, 6H, NCH_3). EI-MS: m/z 340 (M^+). Anal. calcd. for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.04; H, 5.89; N, 8.23.

Dimethyl 4-((E)-[4-(dimethylamino]phenylimino]methyl)pyridine-2,6-dicarboxylate (8)

To a 100- ml flask, 50 mg (0.224 mmol) **5** and 30 ml anhydrous ethanol were added. After the mixture was stirred for 30 min at room temperature, 30.5 mg (0.224 mmol) N,N-dimethylaniline were added. The reaction mixture was refluxed for 4 h and then cooled to room temperature. The resulting precipitate was filtered and recrystallized from ethanol to give yellow crystals in 85% yield (65 mg). Mp 192–193 (C. IR (KBr): 2949.8, 2884.5, 2806.8, 1752.5, 1719.8, 1625.8, 1576.8, 1442.0, 1339.8, 1245.8, 1204.9, 1160.0, 996.6, 816.8, 780.0 cm^{-1}. ^{1}H NMR ($CDC1_3$, δ ppm): (8.8(s, 2H, PyH), 8.6 (s, 1H, –CH=N), 7.4 (d, $J = 8.8$ Hz, 4H, ArH), 4.1 (s, 6H, OCH_3), 3.1 (s, 6H, NCH_3). EI-MS: m/z 341 (M^+). Anal. calcd. for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31. Found: C, 63.34; H, 5.58; N, 12.30.

ACKNOWLEDGMENTS

This work was financially supported by the Shanghai Municipal Education Committee (No. 06DZ010) and Shanghai Normal University (No. SK200839).

REFERENCES

1. Fu, L.-M.; Zhang, J.-P.; Wang, Y.; et al. Efficient two-photon-sensitized luminescence of a europium(III) complex. *Angew. Chem. Int. Ed.* **2005**, *44*, 747–750.
2. D'Aléo, A.; Maury, O.; Andraud, C.; et al. Two-photon microscopy and spectroscopy of lanthanide bioprobes. *Chem. Phys. Chem.* **2007**, *8*, 2125–2132.
3. Picot, A.; Malvolti, F.; Le Guennic, B.; Baldeck, P. L.; Williams, J. A. G.; Andraud, C.; Maury, O. Two-photon antenna effect induced in octupolar Europium Complexes. *Inorg. Chem.* **2007**, *46*, 2659–2665.
4. Xiao, H. B.; Shen, H.; Tian, H.; et al. Spirosilabifluorene linked bistriphenylamine: Synthesis and application in hole transporting and two-photon fluorescent imaging. *Dyes and Pigments.* **2007**, *73*, 224–229.
5. Latva, M.; Takalo, H.; Simberg, K.; Kankare, J. Enhanced Eu^{III} ion luminescence and efficient energy transfer between lanthanide chelates within the polymeric structure in aqueous solutions. *J. Chem. Soc., Perkin Trans.* **1995**, *2*, 995–999.
6. Lamture, J. B.; Iverson, B.; Hogan, M. E. An intensely luminescent polymeric lanthanide chelator for multiple fluorescence labeling of biomolecules. *Tetrahedron Lett.* **1996**, *37*, 6483–6486.

7. Lamture, J. B.; Zhou, Z. H.; Wensel, T. G.; et al. Luminescence properties of terbium(III) complexes with 4-substituted dipicolinic acid analogs. *Inorg. Chem.* **1995**, *34*, 864–869.
8. Shelkov, R.; Melman, A. Free-radical approach to 4-substituted dipicolinates. *Eur. J. Org. Chem.* **2005**, 1397–1401.
9. Lu, Z.-J.; Wang, P.-N.; et al. Tracking of mercury ions in living cells with a fluorescent chemodosimeter under single- or two-photon excitation. *Anal. Chim. Acta.* **2007**, *597*, 306–312.
10. Schmidt, B.; Ehlert, D. K.; et al. Preparation of N-Boc-(2,6-bis-(ethoxycarbonyl) pyridin-4-yl)-L-alanines as tridentate ligands. *Tetrahedron Lett.* **1998**, *39*, 3999–4002.
11. Chauvin, A.-S.; Tripier, R.; et al. A new versatile methodology for the synthesis of 4-halogenated-6-diethylcarbamoylpyridine-2-carboxylic acids. *Tetrahedron Lett.* **2001**, *42*, 3089–3091.
12. Albota, M.; Beljonne, D.; Bredas, J.-L.; et al. Design of organic molecules with large two-photon absorption cross sections. *Science* **1998**, *281*, 1653–1656.
13. Tang, R. R.; Yan, Z. E.; Guo, C. C.; et al. Synthesis of Eu(III) and Tb(III) complexes with novel pyridine-2,6-dicarboxylic acid derivatives and their fluorescence properties. *Chem. J. Chin. Univ.* **2006**, *3*, 472.