In conclusion, the concept of an accessible and controllable molecular program, even within the limited arena of metal coordination structures, seems premature. If one wants to "program" in the "machine language" of molecules, (s)he will receive the greatest insight from the firm fundamentals of thermodynamics and kinetics as opposed to distractions of sirenous supramolecular slogans.

Received: August 16, 2000 [Z15648]

[1] J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, **1995**.
[2] D. M. Bassani, J.-M. Lehn, K. Fromm, D. Fenske, *Angew. Chem.* **1998**, *110*, 2534; *Angew. Chem. Int. Ed.* **1998**, *37*, 2364.
[3] P. N. W. Baxter, J.-M. Lehn, B. O. Kneisel, D. Fenske, *Angew. Chem.* **1997**, *109*, 2067; *Angew. Chem. Int. Ed.* **1997**, *36*, 1978.
[4] D. Venkataraman, Y. Du, S. R. Wilson, K. A. Hirsch, P. Zhang, J. S. Moore, *J. Chem. Educ.* **1997**, *74*, 915.
[5] M. Fujita, *Acc. Chem. Res.* **1999**, *32*, 53.
[6] M. Fujita in *Comprehensive Supramolecular Chemistry*, *Vol. 9* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn), Pergamon, Oxford, **1996**, pp. 253 – 280.
[7] D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975.
[8] S. Leininger, B. Olenyuk, P. J. Stang, *Chem. Rev.* **2000**, *100*, 853.
[9] P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502.
[10] P. J. Stang, *Chem. Eur. J.* **1998**, *4*, 19.
[11] P. N. W. Baxter, J.-M. Lehn, J. Fischer, M.-T. Youinou, *Angew. Chem.* **1994**, *106*, 2432; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2284.
[12] G. S. Hanan, D. Volkmer, U. S. Schubert, J.-M. Lehn, G. Baum, D. Fenske, *Angew. Chem.* **1997**, *109*, 1929; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1842.
[13] J. Rojo, J.-M. Lehn, G. Baum, D. Fenske, O. Waldmann, P. Müller, *Eur. J. Inorg. Chem.* **1999**, 517.
[14] P. N. W. Baxter, J.-M. Lehn, B. O. Kneisel, D. Fenske, *Chem. Commun.* **1997**, 2231.
[15] J.-M. Lehn, *Angew. Chem.* **1990**, *102*, 1347; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1304.
[16] D. P. Funeriu, J.-M. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **1997**, *3*, 99.
[17] P. G. Sammes, G. Yahioglu, *Chem. Soc. Rev.* **1994**, *23*, 327.
[18] E. C. Constable in *Comprehensive Supramolecular Chemistry*, *Vol. 9* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn), Pergamon, Oxford, **1996**, pp. 213 – 252.
[19] C. O. Dietrich-Buchecker, J.-P. Sauvage in *Bioorganic Chemistry Frontiers*, *Vol. 2* (Ed.: H. Dugas), Springer, Berlin, **1991**, pp. 195 – 248.
[20] R. F. Carina, C. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1996**, *118*, 9110.
[21] S. Toyota, C. R. Woods, M. Benaglia, J. S. Siegel, *Tetrahedron Lett.* **1998**, *39*, 2697.
[22] J. Nasielski, A. Standaert, R. Nasielski-Hinkens, *Synth. Commun.* **1991**, *21*, 901.
[23] Crystal structure analysis: Bruker P4 four-circle diffractometer, rotating-anode generator, Hi-Star area detector, $Cu_{K\alpha}$ radiation ($\lambda =$ 1.54178 Å), graphite monochromator, Ω scans, $T = 295(2)$ K, cell determination with 3053 reflections ($18 < \theta < 45^\circ$), data collection, data reduction, Lorentz and polarization corrections carried out using FRAMBO and SAINT. Structure solution by direct methods, remaining non-H atoms by LS – ΔF syntheses, refinement against F^2 (SHELXH) with all H atoms included in idealized positions, BF_4^- ions disordered so B–F distances were restrained to be approximately 1.43 Å, all non-H atoms refined anisotropically except atoms in pendant anisole groups which were kept isotropic. Structure solution, refinements, graphics, and tables calculations performed with SHELXTL/PC. **1**. $C_{228}H_{156}B_4Cu_4F_{16}N_{24}O_{12}$, $M_r = 4025.17$, monoclinic, space group $P2_1/n$ (no. 14), $a = 17.5893(1)$, $b = 40.3378(9)$, $c =$ 30.5005(4) Å, $\beta = 94.590(1)^\circ$, $V = 21571.1(6)$ Å^3, $Z = 4$, $\rho_{calcd} =$ 1.239 g cm^{-3}, $\mu(Cu_{K\alpha}) = 1.083$ mm^{-1}, crystal dimensions ca. $0.063 \times 0.030 \times 0.030$ mm^3, $2\theta_{max} = 90.64^\circ$, 31168 reflections measured, 12441 unique reflections ($R_{int} = 0.197$), 1756 parameters, 23 restraints, $R_1(wR_2) = 0.1524(0.2278)$ for 6194 reflections with $I > 2\sigma(I)$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-148212. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
[24] F. Cozzi, M. Cinquini, R. Annunziata, T. Dwyer, J. S. Siegel, *J. Am. Chem. Soc.* **1992**, *114*, 5729.
[25] F. Cozzi, M. Cinquini, R. Annuziata, J. S. Siegel, *J. Am. Chem. Soc.* **1993**, *115*, 5330.
[26] F. Cozzi, J. S. Siegel, *Pure Appl. Chem.* **1995**, *67*, 683.
[27] F. Cozzi, F. Ponzini, R. Annunziata, M. Cinquini, J. S. Siegel, *Angew. Chem.* **1995**, *107*, 1092; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1019.
[28] W. L. Jorgensen, D. L. Severance, *J. Am. Chem. Soc.* **1990**, *112*, 4768.
[29] C. A. Hunter, J. K. M. Sanders, *J. Am. Chem. Soc.* **1990**, *112*, 5525.
[30] C. A. Hunter, *Angew. Chem.* **1993**, *105*, 1653; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1584.
[31] C. A. Hunter, *Chem. Soc. Rev.* **1994**, *23*, 101.
[32] J. Bernstein, M. C. Etter, L. Leiserowitz in *Structure Correlation*, *Vol. 2* (Eds.: H.-B. Bürgi, J. D. Dunitz), VCH, Weinheim, **1994**, pp. 431 – 507.
[33] A. Gavezzotti in *Structure Correlation*, *Vol. 2* (Eds.: H.-B. Bürgi, J. D. Dunitz), VCH, Weinheim, **1994**, pp. 509 – 542.
[34] J. D. Dunitz, A. Gavezzotti, *Acc. Chem. Res.* **1999**, *32*, 677.
[35] J. Sandström, *Dynamic NMR Spectroscopy*, Academic Press, New York, **1982**.

Synthesis and Fluorescence Properties of Manisyl-Substituted Terpyridine, Bipyridine, and Phenanthroline**

Jon C. Loren and Jay S. Siegel*

Cation affinity, solubility, and spectroscopy (e.g. fluorescence) are three characteristic physical properties of oligopyridine-based heterocycles (2,2′:6′,2″-terpyridines, 2,2′-bipyridines, and 1,10-phenanthrolines, in the following simply designated as terpyridines, bipyridines, and 1,10-phenanthrolines) that one would like to control through a simple synthesis scheme from common building blocks.[1] In particular, aryl-substituted heterocycles of this family have a rich history in metal coordination chemistry.[2, 3] Their conjugated backbones make them attractive chromophores and molecular "antennae";[4–7] however, the larger and fused analogues typically suffer from poor solubility and inefficient chemical syntheses. Among aryl substituents, *p*-anisyl (4-methoxyphenyl) has been extensively used where further structural elaboration was desired,[8–10] and mesityl has been noted for endowing superior solubility features.

A hybrid of these two aryl motifs, 4-methoxy-2,6-dimethylphenyl or "manisyl", offers both characteristics, but has been

[*] Prof. J. S. Siegel, J. C. Loren
Department of Chemistry, University of California, San Diego
La Jolla, CA 92093-0358 (USA)
Fax: (+1) 858-822-0386
E-mail: jss@chem.ucsd.edu

[**] Manisyl = 4-methoxy-2,6-dimethylphenyl. This work was supported by the US National Science Foundation (CHE-9904275).

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

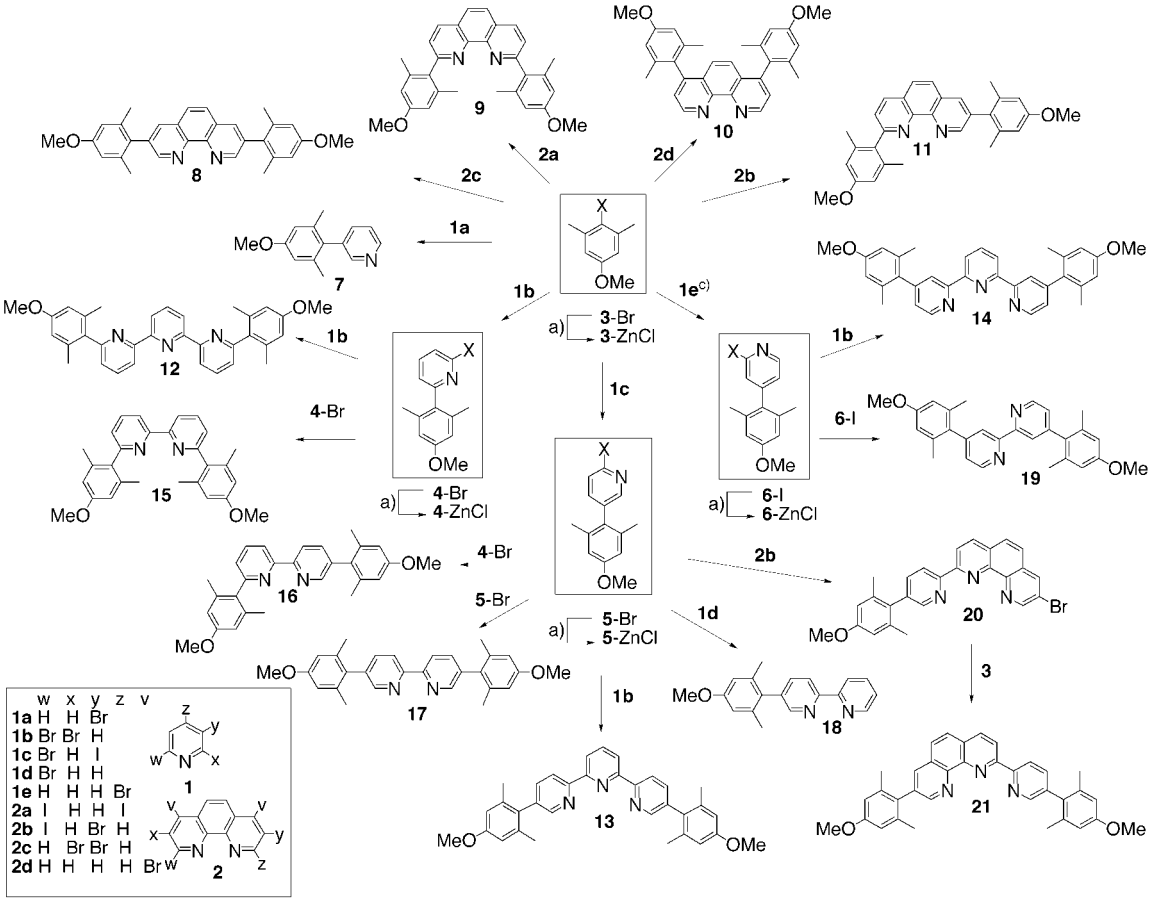
virtually absent as a substituent in this family of heterocyclic compounds. Here we present a general route to these aryl-substituted heterocycles using palladium-mediated coupling of organozinc halides with heterocyclic halides, and note an extraordinary suitability of zinc to complex with the in situ forming ligand, thus protecting the catalyst from poisoning and simplifying product purification. A further highlight of this work stems from the ability of the manisyl group to endow specific members of this family with high fluorescence quantum efficiency. Therefore, in one concentrated effort we have been able to address problems related to the chemical synthesis, physical manipulation, and photophysical properties of these versatile metal chelates.

Considering substitution at the α, β, and γ positions relative to the nitrogen atom of a pyridine and including the combinations of pyridine and phenanthroline up to tridentate chelates (pyridine, bipyridine, terpyridine, phenanthroline, and pyridylphenanthroline) generates a family of 42 structures, from which a representative subset of 17 were targeted for synthesis, with manisyl as the prototypical substituted arene. An appropriate set of halogenated pyridines (**1a**–**e**) and phenanthrolines (**2a**–**d**) were available either commercially or from literature procedures.[11–15] Starting from commercially available 3,5-dimethylanisole, the literature-known 4-methoxy-2,6-dimethylbromobenzene (**3**-Br) was prepared[16] and then converted into the organozinc reagent **3**-ZnCl by employing Negishi conditions.[17–19] Halopyridines **1a**–**c** and **1e** react smoothly with one molar equivalent of **3**-ZnCl to form the corresponding arylpyridines, of which **4**-Br, **5**-Br, and **6**-I can be converted to the organozinc analogue.[20] These six sets of building blocks can be permuted between organozinc and halide counterparts in a series of Negishi couplings to generate a large array of ligand patterns (Scheme 1). For example, symmetrical terpyridines (**12**–**14**) were prepared from two molar equivalents of an organozinc and **1b** in about 60% yield (Table 1).

Table 1. Substrates and yields for the synthesis of heterocycles **7**–**21**.

Aryl–ZnCl	Aryl–X	Product	Yield [%][a]	Melting range [°C][b]
3-ZnCl	**1b**	**4**-Br	61	75–77
3-ZnCl	**1c**	**5**-Br	85	78–80
3-ZnCl	**1e**	**6**-H	98	98–100
3-ZnCl	**1a**	**7**	75	53–54
3-ZnCl	**2c**	**8**	70	248–249
3-ZnCl	**2a**	**9**	69	234–235
3-ZnCl	**2d**	**10**	15	255 (decomp)
3-ZnCl	**2b**	**11**	67	244–245
4-ZnCl	**1b**	**12**	50	215–216
5-ZnCl	**1b**	**13**	62	224–225
6-ZnCl	**1b**	**14**	11	272–274
4-ZnCl	**4**-Br	**15**	59	231–233
5-ZnCl	**4**-Br	**16**	31	164–166
5-ZnCl	**5**-Br	**17**	59	257–258
5-ZnCl	**1d**	**18**	59	94–96
6-ZnCl	**6**-I	**19**	21	272–274
5-ZnCl	**2b**	**20**	77	112–118
3-ZnCl	**20**	**21**	81	130–134

[a] Yields based on isolated product after purification. [b] Melting points are uncorrected.



Scheme 1. a) *n*-Butyllithium, −78 °C, THF; $ZnCl_2$, THF, −78 °C → RT; b) Aryl–X, 5% $[Pd(PPh_3)_4]$, reflux, 12 h, THF; c) see ref. [20].

  1433-7851/01/4004-0755 $ 17.50+.50/0

A special highlight of the method was the ease with which the peculiar pyridylphenanthroline **21** was prepared as a highly soluble terpyridine analogue.[21] In some cases the zinc complex of the ligand precipitates at the end of the reaction. This solid can be readily separated from the organic by-products after which the zinc cation can be removed by an EDTA extraction to leave the pure ligand. In addition, all compounds prepared could be isolated in pure form by column chromatography on alumina with hexanes/dichloromethane. The transferability of reaction conditions across this series of derivatives indicates that this method is generally applicable to the synthesis of any aryl/alkyl cognate that will tolerate the formation/presence of organozinc halides.[22, 23]

The solubility of all manisyl derivatives in organic solvents is superior to that of the simple phenyl- or anisyl-substituted heterocycles (e.g., the solubility of dimanisyl terpyridine **13** compared to that of its anisyl cognate in chloroform, dichloromethane, tetrahydrofuran and acetone are 230, 210, 95, and 10 mg mL^{-1} versus 2, >1, >1, >1 mg mL^{-1}, respectively). Facile deprotection of the methoxy group by pyridinium hydrochloride has been demonstrated for terpyridine **13**, and the resulting phenolic derivative remains soluble. Realkylation of the phenolic oxygens occurred by standard methods (e.g. allyl bromide in the presence of potassium carbonate in acetonitrile) without problems, which makes it clear that these ligands will be directly applicable to the synthesis of larger supramolecular coordination complexes and will be instrumental in the elaboration of new topological stereoisomers[9, 24] and materials incorporating metal binding sites.[25]

Presumably the solubility of the manisyl derivatives stems from the orthogonal conformation at the aryl–pyridyl bond due to the proximal methyl groups. This conformation should also prohibit the effectiveness of normal planar conjugation. Curiously, terpyridine **13** displays a very bright fluorescence (λ_{em} 408 nm; λ_{max} 286 nm) with a quantum yield (Φ_f) of 0.85 in acetonitrile and retains fluorescence in water.[26, 27] The possibility of a type of spiroconjugation or twisted excited state electron transfer thus arises.[27, 28] The ease of the synthetic method provided access to a large swath of structural space and the ability to probe structural dependence of this fluorescence behavior. Classifying the quantum yields for the 17 representative ligands as high ($\Phi_f > 0.75$), medium ($0.25 < \Phi_f < 0.75$), and low ($\Phi_f < 0.25$), one immediately sees that manisyl substitution β to the nitrogen atom is a common structural feature of the high quantum yield group, **13**, **17**, and **18** (Figure 1).[29] The control comparison of pyridine **7** with bipyridine **18** shows low and high efficiency, respectively, and establishes the principal "minimum" chromophore. The compounds of medium quantum yield (**8**, **16**, and **21**) also bear a manisyl group in the β position. Substitution only α or only γ resulted in quantum yields significantly lower than 20%, with the γ set slightly more efficient than the α set. Protonation of the heterocycle results in a standard red shift of about 30–100 nm in the absorption spectrum and emission maxima. The presence of zinc as a complexing metal causes a shift in the spectra of the ligands in the high- and medium-efficiency group (Table 2). Protonation and metalation display clean isosbestic behavior. A full analysis of the fluorescence behavior as a function of aryl substitution is underway.

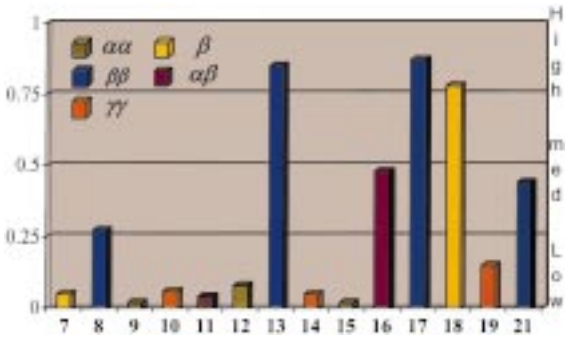


Figure 1. Bar graph of fluorescence quantum yield for heterocycles **7**–**21**.

Table 2. Excitation and emission wavelengths of free ligands (L), selected protonated ligands (L-H$^+$),[a] zinc-bound ligands (L-Zn^{2+}),[b] and fluorescence quantum yields (Φ_f)[c] recorded in CH_3CN.

	L λ_{ex} [nm]	L λ_{em} [nm]	Φ_f	L-H$^+$ λ_{ex} [nm]	L-H$^+$ λ_{em} [nm]	L-Zn^{2+} λ_{ex} [nm]	L-Zn^{2+} λ_{em} [nm]
7	285	358	0.05				
8	270	405	0.27	356	449	322	486
9	266	380	0.02				
10	267	412	0.06				
11	270	383	0.04				
12	284	412	0.08				
13	286	408	0.85	368	535	340	512
14	279	417	0.05				
15	282	408	0.02				
16	290	409	0.48	350	532	314	516
17	296	408	0.87	350	569	320	491
18	286	410	0.78	310	499	308	496
19	282	414	0.15				
21	296	443	0.44	368	541	366	537

[a] Excess CH_3SO_3H. [b] Excess $ZnCl_2$. [c] Measured relative to 9,10-diphenylanthracene.

In conclusion, a simple general procedure for the synthesis of α-, β-, and γ-substituted bipyridines, terpyridines, phenanthrolines, and pyridylphenanthrolines has been developed on the basis of palladium-mediated coupling of organozinc halides and halogenated heterocycles. The method has been showcased with the "manisyl" (4-methoxyl-2,6-dimethylphenyl) group as the aryl prototype. The manisyl group adds desirable functionality that results in facile chemical elaboration, superior solubility and high fluorescence quantum yield. The compounds prepared here are representative of a much larger class of imaginable aryl-substituted heterocycles that will be important ligands for metal chelation, supramolecular complexation, topological isomer construction and fluorophore generation.[30, 31] Such auspicious spectral and complexation features point to the use of such compounds in recognition,[32] sensor,[32] tagging,[33] and catalytic applications.[34]

Experimental Section

21:[35] To a solution of **3**-Br (0.206 g, 0.957 mmol) in THF (20 mL) at −78 °C was added *n*BuLi (0.60 mL of a 1.6 M solution in hexane, 0.96 mmol). To this mixture was added a 0 °C solution of zinc chloride (0.130 g, 0.96 mmol) in THF (5 mL) by cannula and allowed to warm to room temperature.

  1433-7851/01/4004-0756 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2001**, *40*, No. 4

Subsequently, a solution of **20** (0.300 g, 0.638 mmol) and $[Pd(PPh_3)_4]$ (0.055 g, 0.048 mmol) in THF (5 mL) was added to the organozinc intermediate by cannula. The mixture was heated at reflux for 20 h, cooled to room temperature, and placed in a freezer. The white precipitate was filtered, washed with cold THF, and dried. The precipitate was dissolved in dichloromethane and extracted vigorously with saturated aqueous EDTA and basified with saturated aqueous sodium bicarbonate. The organic layer was separated, dried over magnesium sulfate, filtered, and evaporated to afford a white crystalline solid (270 mg, 81 %), m.p. 130–134 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.05$ (d, $J = 2.0$ Hz, 1H), 9.04 (d, $J = 8.0$ Hz, 1H), 8.83 (d, $J = 8.5$ Hz, 1H), 8.53 (d, $J = 2.0$ Hz, 1H), 8.41 (d, $J = 8.5$ Hz, 1H), 8.06 (d, $J = 2.0$ Hz, 1H), 7.88 (d, $J = 9.0$ Hz, 1H), 7.81 (d, $J = 9.0$ Hz, 1H), 7.72 (dd, $J = 2.0$, 8.0 Hz, 1H), 6.74 (s, 2H), 6.70 (s, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 2.07 (s, 6H), 2.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.85$, 158.67, 156.12, 154.37, 151.80, 149.63, 145.51, 144.67, 138.38, 137.83, 137.67, 136.89, 136.41, 135.84, 130.23, 130.01, 128.66, 128.49, 126.62, 122.41, 120.56, 112.88, 112.82, 55.23, 55.20, 21.43, 21.34; UV/Vis (CH_3CN): λ_{max} (ε) = 240 (6.3×10^4), 296 (4.3×10^4), 354 (8.7×10^3) nm; HR-MS: *m/z*: calcd for $C_{35}H_{31}N_3O_2$: 525.2416; found: 525.2407.

Received: August 28, 2000 [Z15713]

[1] U. S. Schubert, C. Eschbaumer, *Org. Lett.* **1999**, *1*, 1027; O. Henze, U. Lehmann, A. D. Schlüter, *Synthesis* **1999**, 683; U. Lehmann, O. Henze, A. D. Schlüter, *Chem. Eur. J.* **1999**, *5*, 854; J.-P. Sauvage, M. Ward, *Inorg. Chem.* **1991**, *30*, 3869; and the classic work of F. Kröhnke, *Synthesis* **1976**, 1.

[2] A. von Zelewsky, *Stereochemistry of Coordination Compounds*, Wiley, Chichester, **1996**.

[3] E. C. Constable in *Comprehensive Supramolecular Chemistry*, *Vol. 9* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn), Pergamon, Oxford, **1996**, p. 165.

[4] T. Yamamoto, Y. Yoneda, K. Kizu, *Macromol. Rapid Commun.* **1995**, *16*, 549.

[5] B. Alpha, R. Ballardini, V. Balzani, J.-M. Lehn, S. Perathoner, N. Sabbatini, *Photochem. Photobiol.* **1990**, *52*, 299.

[6] B. Alpha, V. Balzani, J.-M. Lehn, S. Perathoner, N. Sabbatini, *Angew. Chem.* **1987**, *99*, 1310; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1266.

[7] B. Alpha, J.-M. Lehn, G. Mathis, *Angew. Chem.* **1987**, *99*, 259; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 266.

[8] C. Dietrich-Buchecker, J.-P. Sauvage, *New J. Chem.* **1992**, *16*, 277.

[9] J.-P. Sauvage, *Acc. Chem. Res.* **1990**, *23*, 319.

[10] J.-P. Sauvage, *Acc. Chem. Res.* **1998**, *31*, 611.

[11] Pyridine **1c** was prepared by lithiation of commercially available 2,5-dibromopyridine and quenching with elemental iodine.

[12] M. Schmittel, A. Ganz, *Synlett* **1997**, 710.

[13] M. Levis, U. Lüning, M. Müller, M. Schmittel, C. Wöhrle, *Z. Naturforsch. B* **1994**, *49*, 675.

[14] S. Toyota, C. R. Woods, M. Benaglia, J. S. Siegel, *Tetrahedron Lett.* **1998**, *39*, 2697.

[15] D. Tzalis, Y. Tor, S. Failla, J. S. Siegel, *Tetrahedron Lett.* **1995**, *36*, 3489.

[16] A. Pelter, R. Drake, *Tetrahedron* **1994**, *50*, 13775.

[17] I. Klement, M. Rottlander, C. E. Tucker, T. N. Majid, P. Knochel, P. Venegas, G. Cahiez, *Tetrahedron* **1996**, *52*, 7201.

[18] E. Negishi, *J. Org. Chem.* **1977**, *42*, 1821.

[19] E. Negishi, T. Takahashi, A. O. King, *Org. Synth.* **1988**, *66*, 67.

[20] Because of the instability of 4-halopyridines, the hydrochloride of **1e** was used in combination with 2 molar equivalents of **3**-ZnCl under otherwise analogous Negishi conditions to produce **6**-H. This intermediate is treated with sodium amide in dimethyl aniline (Chichibabin conditions) to produce the 2-aminopyridine, see: J.-C. Chambron, J.-P. Sauvage, *Tetrahedron* **1987**, *43*, 895. The 2-aminopyridine is converted to **6**-I by reaction with isoamylnitrite and iodine in toluene (non-aqueous Sandmeyer conditions), see: L. Friedman, J. F. Chlebowski, *J. Org. Chem.* **1968**, *33*, 1636.

[21] For recent reports of the parent heterocycle and an alkyl/aryl derivative see: C. Y. Hung, T. L. Wang, Z. Q. Shi, R. P. Thummel, *Tetrahedron* **1994**, *50*, 10685; J.-P. Collin, P. Gavina, J.-P. Sauvage, A. DeCian, J. Fischer, *Aust. J. Chem.* **1997**, *50*, 951, respectively; see also: F. Barigelletti, B. Ventura, J.-P. Collin, R. Kayhanian, P. Gaviña, J.-P. Sauvage, *Eur. J. Inorg. Chem.* **2000**, 113–119.

[22] S. A. Savage, A. P. Smith, C. L. Fraser, *J. Org. Chem.* **1998**, *63*, 10048.

[23] S. L. Hargreaves, B. L. Pilkington, S. E. Russell, P. A. Worthington, *Tetrahedron Lett.* **2000**, *41*, 1653.

[24] D. M. Walba, *Tetrahedron* **1985**, *41*, 3161.

[25] J.-M. Lehn, *Makromol. Chem. Macromol. Symp.* **1993**, *69*, 1.

[26] J. N. Demas, G. A. Crosby, *J. Phys. Chem.* **1971**, *75*, 991.

[27] J. R. Lakowicz, *Principles of Fluorescence Spectroscopy*, Kluwer, New York, **1999**.

[28] W. Rettig, *Top. Curr. Chem.* **1994**, *169*, 1.

[29] In a related set of 3,8-bis(phenethynyl)phenanthrolines, Tor and co-workers have seen high fluorescence quantum yields and emission tunability, see H. S. Joshi, R. Jamshidi, Y. Tor, *Angew. Chem.* **1999**, *111*, 2888; *Angew. Chem. Int. Ed.* **1999**, *38*, 2722.

[30] V. Balzani, A. Credi, M. Venturi, *Coord. Chem. Rev.* **1998**, *171*, 3.

[31] P. Belser, S. Bernhard, C. Blum, A. Beyeler, L. De Cola, V. Balzani, *Coord. Chem. Rev.* **1999**, *192*, 155.

[32] *Chemosensors of Ion and Molecular Recognition* (Eds.: J.-P. Desvergnes, A. Czarnik), Kluwer, Dordrecht, **1997**, 245 (492, N. ASI).

[33] V. M. Mukkala, M. Helenius, I. Hemmila, J. Kankare, H. Takalo, *Helv. Chim. Acta* **1993**, *76*, 1361.

[34] J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**.

[35] Although written explicitly for the novel heterocycle **21**, this exemplifies a general procedure for any of the compounds reported.

Parallel Reactions for Enantiomeric Quantification of Peptides by Mass Spectrometry**

W. Andy Tao and R. Graham Cooks*

The accelerating trend towards the use of enantiomerically pure compounds as drugs has underscored the need for new methods of enantioselective synthesis and chiral analysis.[1] The capabilities of mass spectrometry for the rapid analysis of complex mixtures have encouraged its exploration for gas-phase chiral recognition.[2] This has been achieved by direct measurement of the relative abundance of two diastereomeric ions formed by complexing enantiomers and a chiral reference,[2d,g–i] ion–molecule reactions of diastereomeric adducts,[2c,e] or collisional dissociation of diastereomers.[2b] Quantitative analysis, especially when one enantiomer comprises only a few percent of a mixture, remains a challenge. Competitive reactions of two enantiomers toward a chiral reference are unavoidably influenced by the relative concentrations of the enantiomers, which affects the accuracy of the measurement of the enantiomeric excess (*ee*) unless the selectivity factor *s* (the ratio of competing rate constants) is

[*] Prof. R. G. Cooks, W. A. Tao
Department of Chemistry
Purdue University
West Lafayette, IN 47907 (USA)
Fax: (+1) 765-494-9421
E-mail: cooks@purdue.edu

[**] This work was supported by the U.S. Department of Energy, Office of Energy Research. W.A.T. acknowledges fellowship support from Triangle Pharmaceuticals.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.