Unsymmetrically functionalized 5,5''-diaryl- and 5,6,5''-triaryl-2,2':6',2''-terpyridines: an efficient synthetic route and photophysical properties

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Complete List of Authors:	Krinochkin, Aleksey; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Kopchuk, Dmitry; I. Ya. Postovskiy Institute of Organic Synthesis Ural Division of the Russian Academy of Sciences 22 S. Kovalevskoy Str., Yekaterinburg 620219, Russian Federation; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Khasanov, Albert; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Chepchugov, Nikolay; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Kovalev, Igor; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Santra, Sougata ; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002 Zyryanov, Grigory; I. Ya. Postovskiy Institute of Organic Synthesis Ural Division of the Russian Academy of Sciences 22 S. Kovalevskoy Str., Yekaterinburg 620219, Russian Federation; Chemical Engineering Institute, Mira Street 19, Ural Federal University, Yekaterinburg, RU Majee, Adinath; Visva-Bharati University, Rusinov, Vladimir; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002; I. Ya. Postovskiy Institute of Organic Synthesis Ural Division of the Russian Academy of Sciences 22 S. Kovalevskoy Str., Yekaterinburg 620219, Russian Federation, Chupakhin, Oleg; Chemical Engineering Institute, Ural Federal University, Mira Street 19, 620002; I. Ya. Postovskiy Institute of Organic Synthesis Ural Division of the Russian Academy of Sciences 22 S. Kovalevskoy Str., Yekaterinburg 620219, Russian Federation,
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Unsymmetrically functionalized 5,5''-diaryl- and 5,6,5''-triaryl-2,2':6',2''-terpyridines: an efficient synthetic route and photophysical properties

Alexey P. Krinochkin,^a Dmitry S. Kopchuk,^{a,b} Albert F. Khasanov^a, Nikolay V. Chepchugov,^a
Igor S. Kovalev,^a Sougata Santra,^a Grigory V. Zyryanov,^{a,b*} Adinath Majee,^c
Vladimir L. Rusinov,^{a,b} and Oleg N. Chupakhin^{a,b}

^a Ural Federal University, 19, Mira St., Yekaterinburg, 62000, Russian Federation

^b I. Ya. Postovsky Institute of Organic Synthesis of RAS (Ural Division), 22/20, S. Kovalevskoy/Akademicheskaya St., Yekaterinburg, 62099, Russian Federation

^c Department of Chemistry, Visva-Bharati (A Central University), Santiniketan 731235, India

* Corresponding author. Tel.: +7-343-375-4501; fax: +7-343-374-0458; e-mail: gvzyryanov@gmail.com

Abstract

An efficient approach for the synthesis of 5,5"- or 5,6,5"-arylsubstituted 2,2':6',2"-terpyridines, bearing an anneleted cyclopentene unit in one of the side-chain pyridine ring for the improved solubility in organic solvents, *via* their 1,2,4-triazine analogues has been developed. By using this approach, various aromatic substituents were introduced in the 2,2':6',2"-terpyridine core. Depending on the nature of the aromatic substituents the obtained terpyridines exhibited an intense emission in a range of *ca.* 344–394 nm in acetonitrile solutions. For the most representative compounds a pronounced bathochromic shifts in both absorption and emission spectra were observed compare to previously reported substituted terpyridines.

Key words: 2,2':6',2"-terpyridines, 1,2,4-triazines, aza-Diels-Alder reaction, fluorescence.

Introduction

2,2':6',2'' - Terpyridines and their substituted derivatives are of wide interest due to their intriguing metal chelating and prospective photophysical properties of the ligands themselves¹ and their metal complexes.^{2,3} Thus, many examples were reported of using these compounds as chromophores in phosphorescent europium complexes,⁴ as well as chemosensors for metal cations.⁵ In addition, some terpyridine-based liquid crystal materials were described.⁶

In literature, there are several approaches towards 5,5'-diaryl 2,2':6',2''- terpyridines: *via* the transformations of their 1,2,4-triazine precursors by means of *aza*-Diels-Alder reactions with various dienophiles;^{1,7,8} Suzuki cross-coupling reactions of phenantrolines,⁹ 2,6-dibromopyridine,⁹ or terpyridine,¹⁰ Stille cross-coupling reaction of 2,6-bis-trimetilstannylpyridine,¹¹ cross-coupling between functionalized mono- and bipyridines.¹² In some cases the Krenke method was used, wherein the starting 2-acetyl-5-arylpyridines were synthesized by the combinations of cross-coupling reactions (for the introduction of aryl substituents), and the subsequent reactions of pyridyl-lithium intermediates with acetyl chloride for the introduction of acetyl group.^{2,13} It is worthy to mention that among these reported methods only few of them^{12,14} afforded the unsymmetrically functionalized 5,5''-diaryl-2,2':6',2''-terpyridines.

And only one case is reported for the synthesis of 5,6''-diaryl-2,2':6',2''-terpyridine and its analog, namely by means of sequential cross-coupling reactions of accordingly substituted terpyridines.¹⁵

In this paper, we wish to report a convenient synthetic approach towards unsymmetrically functionalized 5,5'-diaryl- and 5,6,5''-triaryl-2,2':6',2''-terpyridines starting from inexpensive and readily available reagents. Due to the absence of aromatic substituents

in α -positions of one or both side-chain pyridine rings the improved coordination properties, as well as photophysical properties, of these ligands are expected.

Experimental Section

General

Unless otherwise mentioned, all common reagents and solvents were used from commercial suppliers without further purification. Melting points were measured on the instrument Boetius. ^1H and ^{13}C NMR spectra were recorded with Bruker DRX-400 spectrometer using Me_4Si as an internal standard. Mass-spectra were recorded on MicrOTOF-Q II (Bruker Daltonics), electrospray as a method of ionization. Microanalyses (C, H, N) were performed using a Perkin–Elmer 2400 elemental analyzer. UV–Vis. spectra were recorded on a Lambda 45 spectrophotometer (Perkin Elmer). Luminescence spectra were recorded on a Horiba Fluoromax-4 Spectrofluorometer.

Hydrazones of isonitrosoacetophenones,¹⁶ (6-methylpyridin-2-yl)-5,6-diphenyl-1,2,4-triazine **13b**,²⁵ 6'-methyl-5-phenyl-2,2'-bipyridine **15a**,²⁴ 6'-bromomethyl-5-phenyl-2,2'-bipyridine **11a**²⁴ were synthesized as reported previously.

6'-Methyl-5,6-diphenyl-2,2'-bipyridine (15b). Triazine **13b** (3.31 g, 10.2 mmol) was suspended in *o*-xylene (45 ml), 2,5-norbornadiene (3.63 ml, 35.71 mmol) was added and the resulting mixture was refluxed for 9 hrs. An additional portion of 2,5-norbornadiene (1.815 ml, 18.36 mmol) was added and the mixture was refluxed for additional 9 hrs. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography using DCM and ethylacetate (10:1) as eluent. The analytical sample was obtained by the recrystallization from methanol. Yield 2.49 g (76%). M.p. 129–131 °C. NMR ^1H , δ , ppm ($\text{DMSO}-d_6$): 2.61 (3H, s, Me), 7.16–7.33 (9H, m, Ph, H-5'), 7.40 (2H, m, Ph), 7.75 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 7.87 (1H, d, $^3J = 7.8$ Hz, H-3), 8.31 (1H, d, $^3J = 7.8$ Hz, H-3'), 8.45 (1H, d, $^3J = 7.8$ Hz, H-4). **ESI-MS**, m/z : found 323.15 $[\text{M}+\text{H}]^+$, required 323.15. Found, %: C 85.77, H 5.70, N 8.81. **C₂₃H₁₈N₂**. Required, %: C 85.68, H 5.63, N 8.69.

General method for the synthesis of mono- and dibromomethylbipyridines 11, 12

Methylbipyridine **15b** (1 g, 3.1 mmol) was dissolved in dry CCl_4 (60 ml), *N*-bromosuccinimide (550 mg, 3.1 mmol) and the catalytic amount of benzoyl peroxide were added, and the resulting mixture was refluxed for 8 hrs. The precipitate formed was filtered off, and the mother liquid was evaporated under reduced pressure. The residue was separated

by column chromatography using the mixture of DCM and ethylacetate (200:1) as eluent. The obtained products were used for the next step without an additional purification.

6'-Bromomethyl-5,6-diphenyl-2,2'-bipyridine (11b). Rf 0.45. Yield 650 mg (52%). M.p. 177-179 °C. NMR ^1H , δ , ppm (DMSO- d_6): 4.73 (2H, s, CH_2Br), 7.18-7.33 (8H, m, Ph), 7.40 (2H, m, Ph), 7.75 (1H, dd, $^3J = 7.8$ Hz, $^4J = 0.7$ Hz, H-5'), 7.92 (2H, m, H-3,4'), 8.44 (1H, dd, $^3J = 7.8$ Hz, $^4J = 0.7$ Hz, H-3'), 8.47 (1H, d, $^3J = 8.0$ Hz, H-4). **ESI-MS**, m/z : found 401.17 $[\text{M}+\text{H}]^+$, required 401.17.

6'-Dibromomethyl-5,6-diphenyl-2,2'-bipyridine (12b). Rf 0.7. Yield 300 mg (20%). M.p. 189-191 °C. NMR ^1H , δ , ppm (DMSO- d_6): 7.19-7.33 (9H, m, Ph, CHBr_2), 7.39 (2H, m, Ph), 7.78 (1H, d, $^3J = 7.8$ Hz, H-5'), 7.94 (1H, d, $^3J = 8.0$ Hz, H-3), 8.00 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 8.48 (1H, d, $^3J = 7.8$ Hz, H-3'), 8.51 (1H, d, $^3J = 8.0$ Hz, H-4). **ESI-MS**, m/z : found 478.99 $[\text{M}+\text{H}]^+$, required 478.98.

6'-Dibromomethyl-5-phenyl-2,2'-bipyridine (12a). Methylbipyridine **15a** (0.5 g, 2.03 mmol) was dissolved in dry CCl_4 (60 ml), *N*-bromosuccinimide (360 mg, 2.03 mmol) and benzoyl peroxide in catalytic amount were added and the resulting mixture was refluxed for 8 hrs. An additional portion of *N*-bromosuccinimide (360 mg, 2.03 mmol) and benzoyl peroxide in catalytic amount were added and the resulting mixture was refluxed for additional 8 hrs. The precipitate formed was filtered off, and the mother liquid was evaporated under reduced pressure. The residue was purified by recrystallization (ethanol). Yield 410 mg (50%). M.p. 149-151 °C. NMR ^1H , δ , ppm (CDCl_3): 6.77 (1H, s, CHBr_2), 7.40-7.47 (1H, m, Ph), 7.48-7.55 (2H, m, Ph), 7.66 (2H, m, Ph), 7.84 (1H, d, $^3J = 7.8$ Hz), 7.93 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 8.04 (1H, dd, $^3J = 8.4$ Hz, $^4J = 2.4$ Hz, H-4), 8.41 (1H, d, $^3J = 7.8$ Hz), 8.53 (1H, d, $^3J = 8.4$ Hz, H-3), 8.93 (d, 1H, $^4J = 2.4$ Hz, H-6). **ESI-MS**, m/z : found 402.94 $[\text{M}+\text{H}]^+$, required 402.94.

General method for the synthesis of acetoxymethylbipyridines 16

The corresponding bromomethyl-substituted bipyridine **11** (1.2 mmol) was dissolved in dry DMF (70 ml), sodium acetate (985 mg, 12 mmol) was added and the resulting mixture was stirred at 130 °C for 10 h. The solvent was evaporated under reduced pressure. Water (20 ml) was added to the residue, and the reaction mixture was extracted with DCM (3 x 25 ml). The combined extracts were dried over anhydrous sodium sulfate, filtered and the solvent was removed under reduced pressure. The products were used in the next step without an additional purification.

6'-Acetoxymethyl-5-phenyl-2,2'-bipyridine (16a). Yield 330 mg (90%). NMR ^1H , δ , ppm (DMSO- d_6): 2.17 (3H, s, Ac), 5.23 (2H, s, CH_2OAc), 7.37-7.44 (2H, m, Ph, H-3'),

7.46-7.53 (2H, m, Ph), 7.72 (2H, m, Ph), 7.92 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 8.12 (1H, dd, $^3J = 8.3$, $^4J = 2.1$ Hz, H-4), 8.38 (1H, d, $^3J = 7.8$ Hz, H-3'), 8.48 (1H, d, $^3J = 8.3$ Hz, H-3), 8.91 (1H, d, $^4J = 2.1$ Hz, H-6). **ESI-MS**, m/z : found 381.16 $[M+H]^+$, required 381.16.

6'-Acetoxymethyl-5,6-diphenyl-2,2'-bipyridine (16b). Yield 400 mg (88%). NMR 1H , δ , ppm (DMSO- d_6): 2.19 (3H, s, Ac), 5.27 (2H, s, CH_2OAc), 7.19-7.32 (8H, m, Ph), 7.40 (2H, m, Ph), 7.43 (1H, dd, $^3J = 7.5$ Hz, H-5'), 7.89-7.95 (2H, m, H-3,4'), 8.42-8.47 (2H, m, H-4,3'). **ESI-MS**, m/z : found 305.13 $[M+H]^+$, required 305.13.

General method for the synthesis of hydroxymethylbipyridines 17

The corresponding acetoxymethylbipyridine **16** (1 mmol) was dissolved in methanol (25 ml). The solution of NaOH (200 mg, 5 mmol) in water (10 ml) was added and the resulting mixture was refluxed for 30 min. The methanol was removed under reduced pressure, and the residue was extracted with DCM (3 x 25 ml). The combined extracts were dried over anhydrous sodium sulfate, filtered, and the solvent was removed under reduced pressure. The obtained products were used for the next step without an additional purification.

6'-Hydroxymethyl-5-phenyl-2,2'-bipyridine (17a). Yield 210 mg (80%). NMR 1H , δ , ppm (DMSO- d_6): 4.66 (2H, d, $^3J = 5.5$ Hz, CH_2OH), 5.24 (1H, t, $^3J = 5.5$ Hz, OH), 7.38-7.43 (1H, m, Ph), 7.46-7.53 (2H, m, Ph), 7.72 (2H, m, Ph), 7.88 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 8.10 (1H, dd, $^3J = 8.3$, $^4J = 2.1$ Hz, H-4), 8.29 (1H, d, $^3J = 7.8$ Hz, H-3'), 8.49 (1H, d, $^3J = 8.3$ Hz, H-3), 8.90 (1H, d, $^4J = 2.1$ Hz, H-6). **ESI-MS**, m/z : found 263.12 $[M+H]^+$, required 263.12.

6'-Hydroxymethyl-5,6-diphenyl-2,2'-bipyridine (17b). Yield 280 mg (82%). NMR 1H , δ , ppm (DMSO- d_6): 4.68 (2H, d, $^3J = 5.7$ Hz, CH_2OH), 5.29 (1H, t, $^3J = 5.7$ Hz, OH), 7.19-7.32 (8H, m, Ph), 7.40 (2H, m, Ph), 7.53 (1H, d, $^3J = 7.8$ Hz, H-5'), 7.86-7.92 (2H, m, H-3,4'), 8.35 (1H, d, $^3J = 7.8$ Hz, H-3'), 8.44 (1H, d, $^3J = 8.0$ Hz, H-4). **ESI-MS**, m/z : found 339.15 $[M+H]^+$, required 339.15.

General method for the synthesis of bipyridinecarbaldehydes 7

The corresponding hydroxymethylbipyridine **17** (0.8 mmol) was dissolved in 1,2-dichloroethane (25 ml), activated MnO_2 (0.7 g, 8 mmol) was added and the resulting mixture was stirred at 50 °C for 5 hrs. Then precipitate was filtered off, washed with hot ethanol. Mother liquid was removed under reduced pressure, and the product was used in the next step without addition purification.

5-Phenyl-2,2'-bipyridine-6'-carbaldehyde (7a). Yield 145 mg (70%). NMR 1H , δ , ppm (DMSO- d_6): 7.39-7.46 (1H, m, Ph), 7.47-7.56 (2H, m, Ph), 7.75 (2H, m, Ph), 7.97 (1H, d, $^3J = 7.2$ Hz, H-3'), 8.12-8.23 (2H, m, H-4,4'), 8.61 (1H, d, $^3J = 8.0$ Hz, H-3), 8.72 (1H, d,

$^3J = 7.2$ Hz, H-5'), 8.97 (1H, d, $^4J = 2.1$ Hz, H-6), 10.11 (1H, s, CHO). **ESI-MS**, m/z : found 261.10 $[M+H]^+$, required 261.10.

5,6-Diphenyl-2,2'-bipyridine-6'-carbaldehyde (7b). Yield 215 mg (80%). NMR 1H , δ , ppm (DMSO- d_6): 7.19-7.35 (8H, m, Ph), 7.42 (2H, m, Ph), 7.97 (2H, m, H-3,3'), 8.15 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4'), 8.58 (1H, d, $^3J = 8.0$ Hz, H-4), 8.79 (1H, d, $^3J = 7.8$ Hz, H-5'), 10.13 (1H, s, CHO). **ESI-MS**, m/z : found 337.13 $[M+H]^+$, required 337.13.

General method for the synthesis of (2,2'-bipyridin-6-yl)-1,2,4-triazines 5

The corresponding aldehyde **7** (0.5 mmol) was dissolved in ethanol (20 ml). The solution of the corresponding isonitrosoacetophenone hydrazone (0.5 mmol) in ethanol (20 ml) was added and the resulting mixture was left at room temperature overnight. Then the solvent was removed under reduced pressure, the glacial acetic acid (10 ml) was added, and the resulting mixture was reflux for 2-5 minutes. The solvent was removed under reduced pressure, and the residue was triturated with ethanol. The precipitate formed was filtered off, washed with ethanol and dried. The analytical samples were obtained by recrystallization from ethanol.

3-(5'-Phenyl-2,2'-bipyridin-6-yl)-6-tolyl-1,2,4-triazine (5a). Yield 112 mg (56%). M.p. 244-246 °C. NMR 1H , δ , ppm (DMSO- d_6): 2.48 (3H, s, Me), 7.39-7.46 (3H, m, Tol, Ph), 7.49-7.55 (2H, m, Ph), 7.75 (2H, m, Ph), 8.12-8.24 (m, 4H, Tol, H-4,4' (bipy)), 8.56 (1H, d, $^3J = 7.4$ Hz, H-3 (bipy)), 8.65 (1H, d, $^3J = 7.4$ Hz, H-5 (bipy)), 8.74 (1H, d, $^3J = 8.3$ Hz, H-3' (bipy)), 8.96 (1H, d, $^4J = 2.1$ Hz, H-6' (bipy)), 9.48 (1H, s, H-5). **ESI-MS**, m/z : found 402.17 $[M+H]^+$, required 402.17. Found, %: C 77.61, H 4.64, N 17.29. $C_{26}H_{19}N_5$. Required, %: C 77.79, H 4.77, N 17.44.

6-(4-Methoxyphenyl)-3-(5'-phenyl-2,2'-bipyridin-6-yl)-1,2,4-triazine (5b). Yield 104 mg (50%). M.p. 244-246 °C. NMR 1H , δ , ppm (DMSO- d_6): 3.91 (3H, s, OMe), 7.14 (2H, m, 4-methoxyphenyl), 7.39-7.46 (1H, m, Ph), 7.48-7.56 (2H, m, Ph), 7.76 (2H, m, Ph), 8.15 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4 (bipy)), 8.22 (1H, dd, $^3J = 8.3$, $^4J = 2.1$ Hz, H-4), 8.29 (2H, m, 4-methoxyphenyl), 8.55 (1H, d, $^3J = 7.4$ Hz, H-3 (bipy)), 8.64 (1H, dd, $^3J = 7.4$ Hz, H-5 (bipy)), 8.73 (1H, d, $^3J = 8.3$ Hz, H-3' (bipy)), 8.97 (1H, d, $^4J = 2.1$ Hz, H-6 (bipy)), 9.48 (1H, s, H-5). **ESI-MS**, m/z : found 418.17 $[M+H]^+$, required 418.17. Found, %: C 74.68, H 4.50, N 16.55. $C_{26}H_{19}N_5O$. Required, %: C 74.80, H 4.59, N 16.78.

6-Phenyl-3-(5',6'-diphenyl-2,2'-bipyridin-6-yl)-1,2,4-triazine (5c). Yield 172 mg (74%). M.p. 174-176 °C. NMR 1H , δ , ppm (DMSO- d_6): 7.21-7.34 (8H, m, Ph), 7.44 (2H, m, Ph), 7.58-7.67 (3H, m, Ph (triazine)), 7.99 (1H, d, $^3J = 8.3$ Hz, H-3 (bipy)), 8.17 (1H, dd, $^3J = 7.8$, 7.8 Hz, H-4 (bipy)), 8.33 (2H, m, Ph (triazine)), 8.60 (1H, d, $^3J = 7.8$ Hz, H-3 (bipy)),

8.70 (1H, d, $^3J = 8.3$ Hz, H-4 (bipy)), 8.73 (1H, dd, $^3J = 7.8$ Hz, H-5 (bipy)), 9.55 (1H, s, H-5). **ESI-MS**, m/z : found 464.19 $[M+H]^+$, required 464.19. Found, %: C 80.13, H 4.43, N 14.93. **C₃₁H₂₁N₅**. Required, %: C 80.32, H 4.57, N 15.11.

General method for the synthesis of (2,2'-bipyridin-6-yl)-6,7-dihydro-5H-cyclopenta[c]pyridines 1

A mixture of the corresponding 1,2,4-triazine **5** (0.25 mmol) and 1-morpholinocyclopentene (0.2 ml, 1.25 mmol) was heated at 200 °C under argon atmosphere for 2 hrs. An additional portion of 1-morpholinocyclopentene (0.1 ml, 0.625 mmol) was added and the resulting mixture was stirred under the same conditions for 1 hr. The reaction mixture was cooled to room temperature and triturated with acetonitrile. The precipitate formed was filtered off, washed with acetonitrile and dried. An analytical sample was obtained by recrystallization.

1-(5'-Phenyl-2,2'-bipyridin-6-yl)-4-tolyl-6,7-dihydro-5H-cyclopenta[c]pyridine

(1a). Yield 82 mg (75%). M.p. 189-191 °C. NMR 1H , δ , ppm (DMSO- d_6): 2.15 (2H, m, CH₂-6), 2.42 (3H, s, Me), 3.07 (2H, t, $^3J = 7.3$ Hz, CH₂-7), 3.69 (2H, t, $^3J = 7.3$ Hz, CH₂-5), 7.29 (2H, m, Tol), 7.39-7.45 (3H, m, Ph), 7.48-7.55 (2H, m, Ph), 7.74 (2H, m, Tol), 8.03 (1H, dd, $^3J = 7.4$, 7.4 Hz, H-4 (bipy)), 8.18 (1H, dd, $^3J = 8.3$, $^4J = 2.1$ Hz, H-4' (bipy)), 8.40 (1H, d, $^3J = 7.4$ Hz, bipy), 8.44-8.49 (2H, m, H-3, bipy), 8.57 (1H, d, $^3J = 8.3$ Hz, H-3' (bipy)), 8.95 (1H, d, $^4J = 2.1$ Hz, H-6' (bipy)). NMR ^{13}C , δ , ppm (CDCl₃): 21.2, 25.6, 32.6, 34.2, 120.0, 121.1, 123.0, 127.1, 128.2, 128.5, 129.1, 129.4, 133.8, 135.0, 135.2, 136.4, 137.5, 137.6, 137.8, 139.2, 146.7, 147.6, 150.5, 153.1, 154.8, 155.5, 157.7. **ESI-MS**, m/z : found 440.21 $[M+H]^+$, required 440.21. Found, %: C 84.88, H 5.87, N 9.41. **C₃₁H₂₅N₃**. Required, %: C 84.71, H 5.73, N 9.56.

4-(4-Methoxyphenyl)-1-(5'-phenyl-2,2'-bipyridin-6-yl)-6,7-dihydro-5H-

cyclopenta[c]pyridine (1b). Yield 89 mg (78%). M.p. 204-206 °C. NMR 1H , δ , ppm (CDCl₃): 2.16 (2H, m, CH₂-6), 3.09 (2H, t, $^3J = 7.3$ Hz, CH₂-7), 3.69 (2H, t, $^3J = 7.3$ Hz, CH₂-5), 7.04 (2H, m, 4-methoxyphenyl), 7.41-7.55 (5H, m, Ph), 7.68 (2H, m, 4-methoxyphenyl), 7.98 (1H, dd, $^3J = 7.4$, 7.4 Hz, H-4 (bipy)), 8.40 (1H, dd, $^3J = 8.3$, $^4J = 2.1$ Hz, H-4' (bipy)), 8.37 (1H, d, $^3J = 7.4$ Hz, bipy), 8.48 (1H, d, $^3J = 7.4$ Hz, bipy), 8.56 (1H, s, H-3), 8.95 (1H, d, $^4J = 2.1$ Hz, H-6' (bipy)). NMR ^{13}C , δ , ppm (CDCl₃): 25.6, 32.7, 34.2, 55.4, 114.2, 119.9, 121.1, 123.0, 127.1, 128.2, 129.1, 129.7, 130.3, 133.5, 135.2, 136.4, 136.5, 137.8, 139.2, 146.5, 147.6, 150.2, 153.0, 154.8, 155.5, 157.7, 159.4. **ESI-MS**, m/z : found 456.21 $[M+H]^+$, required 456.21. Found, %: C 81.81, H 5.40, N 8.99. **C₃₁H₂₅N₃O**. Required, %: C 81.73, H 5.53, N 9.22.

1-(5',6'-Diphenyl-2,2'-bipyridin-6-yl)-4-phenyl-6,7-dihydro-5H-cyclopenta[c]pyridine (1c). Yield 90 mg (72%). M.p. 204-206 °C. NMR ^1H , δ , ppm (CDCl_3): 2.17 (2H, m, CH_2 -6), 3.10 (2H, t, $^3J = 7.3$ Hz, CH_2 -7), 3.72 (2H, t, $^3J = 7.3$ Hz, CH_2 -5), 7.23-7.33 (8H, m, Ph), 7.39-7.45 (1H, m, Ph), 7.47-7.55 (6H, m, Ph), 7.90 (1H, d, $^3J = 8.1$ Hz, H-3' (bipy)), 7.97 (1H, dd, $^3J = 7.4$, 7.4 Hz, H-4 (bipy)), 8.37 (1H, dd, $^3J = 7.4$, $^4J = 0.8$ Hz, bipy), 8.56 (1H, d, $^3J = 8.1$ Hz, H-4' (bipy)), 8.58 (1H, s, H-3), 8.62 (1H, dd, $^3J = 7.4$, $^4J = 0.8$ Hz, bipy). NMR ^{13}C , δ , ppm ($\text{DMSO}-d_6$): 24.9, 32.0, 33.8, 99.5, 119.1, 120.0, 122.8, 127.3, 127.7, 127.8, 128.3, 128.4, 128.6, 129.3, 129.7, 133.5, 135.8, 137.3, 137.8, 138.7, 139.4, 139.8, 140.2, 146.3, 149.8, 153.0, 154.2, 154.4, 155.7, 157.3. **ESI-MS**, m/z : found 502.23 $[\text{M}+\text{H}]^+$, required 502.23. Found, %: C 86.02, H 5.28, N 8.11. $\text{C}_{36}\text{H}_{27}\text{N}_3$. Required, %: C 86.20, H 5.43, N 8.38.

Results and discussion

Chemistry

Retro synthetic approaches

Initially, the two alternative synthetic approaches towards unsymmetrically arylated terpyridine core were considered, namely the Krenke method¹⁷ and the "1,2,4-triazine" methodology.¹⁸ In the first case, the proper location of aryl substituents in a terpyridine moiety can be achieved starting from two different (di)aryl-substituted 2-acetylpyridines (Scheme 1, route I). However, for the implementation of this method it is necessary to introduce an additional group in the position of 4' of terpyridine core, which is beyond the scope of this work, and the 2-acetylpyridines **2**, **3** are not easily available compounds. Besides, in the Krenke method the direct condensation of cycloalkane moiety to one of the side-chain pyridine ring of terpyridine core (from the standpoint of increasing the solubility of both the resulting terpyridines and their metal complexes in organic solvents^{19,20}) could not be performed.

On the other hand, in the "1,2,4-triazine" methodology (Scheme 1, route II) the direct condensation of cycloalkane moiety, for instance, cyclopentane one, to one pyridine ring of terpyridine core can be easily performed by means of aza-Diels-Alder reactions with

enamines as dienophiles,²¹ and the introduction of an additional substituent at the C4' position of terpyridine core is not needed. Additionally, this approach involves the use of only readily available reagents (as opposed to a Krenke method), and simple synthetic procedures. Considering the importance of all these factors, this pathway was chosen as a key methodology for the synthesis of our target terpyridines.

Implementation of "1,2,4-triazine" approach requires the synthesis of corresponding 1,2,4-triazine analogs **5** of desired terpyridines (Scheme 1, route II). Based on the literature, the reaction of 2,6-pyridine-biscarbaldehyde with hydrazones of isonitrosoacetophenones **6** (see Scheme S1 in Supplementary information) could be used for the preparation of such 1,2,4-triazines, which was successfully demonstrated earlier for the preparation of symmetrical terpyridines.^{7,8} However, obtaining unsymmetrically substituted terpyridines by using this method seems unlikely, since this reaction should be carried out between 2,6-pyridine-biscarbaldehyde and two different acetophenone hydrazones, whereby quite expectedly the reaction will afford a mixture of three products with approximately the same characteristics, and their separation is non-trivial. Thus, the sequential construction of two side-chain pyridine rings (bearing different aromatic substituents) on the central pyridine core by the "1,2,4-triazine" methodology (Scheme 1, route II) could be the most convenient approach.

Scheme 1. The retrosynthetic analysis for the synthesis of unsymmetrically functionalized 5,5"-diaryl-2,2':6',2"-terpyridines

Mono-1,2,4-triazine analogue **5** (Scheme 1) looks as the most probable precursor of the desired ligand **1**, and the most appropriate method for the preparation of 6-aryl-5*H*-1,2,4-

triazine is the condensation of hydrazones isonitrosoacetophenones **6** with the corresponding bipyridine-6-carbaldehyde **7**²² (see Scheme S1 in Supplementary information). Another alternative method is the reaction of 2-bromacetophenone **8** with two equivalents of hydrazides of the carboxylic acids **9**,²³ but this option obviously less desirable since it requires two equivalents of the less available bipyridine-6-carboxylic acid hydrazide. Thus, our further search has been directed to find a convenient method for the preparation of aldehydes **7**. Based on the literature the aldehyde group can be introduced in the bipyridine core through a series of transformations of mono- or dibromomethyl group, as well as ester groups. Obviously, the preparation of bipyridines **10-13** is also possible by means of “1,2,4-triazine” methodology. In the case of 6-aryl-5*H*-1,2,4-triazines **14**, **15** the pyridine residue can be modified by either the ester group¹⁹ or methyl group,²⁴ which can be brominated further. As for the 5,6-diaryl-1,2,4-triazines, the direct introduction of the ester group is not described in the literature, while the carboxyl group can be obtained by the oxidation of the methyl group.²⁵ In addition, it was reported earlier that the preparation of 6-aryl-5*H*-1,2,4-triazines **11** bearing the ester group in the α -position of the pyridine substituent.

Thus, the synthesis of aldehyde **7** (see Scheme S1 in Supplementary information) starting from 1,2,4-triazines bearing the α -methylsubstituted pyridine substituent was chosen as the most convenient approach.

Targeted approaches

In the first step 3-(6'-methylpyridyl-2')-1,2,4-triazines **13** were obtained according to described procedures.^{23,24} Next, these compounds were converted into the corresponding bipyridines **15** by means of aza-Diels-Alder reaction with 2,5-norbornadiene (Scheme 2). The following radical bromination of the methyl group in compound **15** initially resulted in a mixture of mono- and dibromomethyl-substituted products **11**, **12**, but during the more

prolonged reaction the dibromo-derivative **12a** was isolated as a major product. The further conversion of product **12a** via the transformation of dibromomethyl group in refluxing in aqueous solution formic acid or pyridine resulted in the desired product **7a** in very low yield due to the intensive tarring of the reaction mixture. Therefore, the alternative approach²⁶ (Scheme 2) was proposed where the bromomethyl group in compounds **11** was transformed into acetoxymethyl **16**. The subsequent hydrolysis of esters **16** afforded alcohols **17**, and their oxidation with activated manganese dioxide afforded the desired aldehydes **5** in good yields.

Scheme 2. The synthesis of non-symmetrically 5,5"-functionalized terpyridines. Reagents and conditions: i) 2,5-norbornadiene, *o*-xylene, 143 °C, 18 h; ii) NBS, CCl₄, 77 °C, 8 h; iii) NBS, CCl₄, benzoyl peroxide, 77 °C, 16 h; iv) NaOAc, DMF, 130 °C, 10 h; v) HCOOH-H₂O (85:15), reflux, 10 h; vi) NaOH, methanol, 65 °C, 30 min; vii) activated MnO₂, 1,2-dichloroethane, 50 °C, 5 h; viii) corresponding hydrazone of isonitrosoacetophenone, ethanol, r.t., overnight, then glacial acetic acid, reflux, 5 min; ix) 1-morpholinocyclopentene, neat, 200 °C, 3 h.

The subsequent heterocyclization according to the optimized procedure⁷ led to mono-1,2,4-triazinyl substituted precursors **8** of target terpyridine ligands **9**. At the final step the *aza*-Diels-Alder reaction between **8** and neat 1-morpholinocyclopentene led to the desired unsymmetrically substituted terpyridines **9**, which possessed an annealed cyclopentene unit in one of the side-chain pyridine ring for increased solubility, *vide supra*.

Photophysical studies of the resulted terpyridines **1**

For all new terpyridines we have investigated the photophysical properties, and their absorption and emission spectra are presented in Fig. 1-2. As illustrated in Table 1 acetonitrile solutions of terpyridines **1** exhibited the intensive emission in the range of 353-394 nm. A very pronounced bathochromic shift in both the absorption and emission spectra was observed for terpyridine **1c**, due to the contribution of three phenyl residues

simultaneously introduced into the terpyridine core, and, thus, the improvement of the conjugation of the poly(hetero)aromatic system. However, the quantum yield for the compound **1c** was significantly lower compared to terpyridines **1a-b**. Probably, the lowering of the quantum yield is due to the large contribution of $n-\pi^*$ excited state in the fluorescence, *i.e.* a large contribution of the non-radiative transitions.

Fig. 1. Absorbance spectra of terpyridines **1a-c** in CH_3CN at room temperature

Fig. 2. Fluorescence spectra of terpyridines **1a-c** in CH_3CN at room temperature

Draft

Table 1. The photophysical properties of newly obtained terpyridines **1a-c** and some previously reported terpyridines

^aAbsorption maxima at room temperature, ^bLuminescence maxima at room temperature,

^cAbsolute fluorescence quantum yields were measured in CH₃CN according to a reported procedure²⁷ by using Horiba-Fluoromax-4 spectrofluorimeter equipped with integrated sphere

We also compared the photophysical properties of new compounds with previously published data of similar structure. According to literature¹ the introduction of two cyclopentene fragments into the terpyridine core had limited affect on the absorption and emission spectra, while only a slight increase in the fluorescence quantum yield was observed (Table 1, entry 4). On the other hand, a significant bathochromic shift of the emission maximum (533 nm) was observed upon the introduction of the 4-methoxyphenyl residue in the position of C4' of terpyridine core (Table 1, entry 5). In addition, less significant hypsochromic shifts in the absorption spectra maxima were observed for the 5,5'-diaryl-6,6'-dicyanoterpyridines (302-313 nm), and bathochromic shifts in the emission spectra maxima were observed for *p*-tolyl- and 4-methoxyphenyl-substituted terpyridines (Table 1, entries 6-8). Additionally, an increase in electron donor properties of the aromatic substituent in the β -position of 2,2'-bipyridine upon the introduction of strong electron donating methoxy group instead of methyl group causes a bathochromic shift of the emission maxima⁸. The same situation we have observed for the compounds **1a** and **1b** (Table 1, entries 1-2): the introduction of strong electron donating 4-methoxy group instead of 4-methyl group caused a bathochromic shift of the fluorescence emission maxima by 39 nm (from 344 to 383 nm), and the quantum yields also increase from 27% to 31%, while the positions of the absorption maxima remained virtually unchanged.

It is worthy to mention, that some authors⁹ reported that the introduction of both sterically-constrained and electron-donating manisyl (2,6-dimethyl-4-methoxyphenyl) residues into the positions of C5- and C5'-, and C6- and C6'- of terpyridine core resulted in a slight hypsochromic shift in the absorption spectra maxima (284-286 nm), while in the emission spectra the values of bathochromic shifts were somehow greater in comparison with herein reported compounds (408-412 nm) (Table 1, entries 9-10).

Conclusion

In summary, in this paper we proposed an effective synthetic approach towards functionalized unsymmetrical 2,2':6',2"-terpyridines bearing aromatic substituents at positions 5, 5" or 5,6,5" of terpyridine core, and possessing an anneleted cyclopentene unit in one of the side-chain pyridine ring for the improved solubility in organic solvents. The herein reported synthetic approach is based on using inexpensive and readily available reagents, as well as simple synthetic protocols. The photophysical properties of new compounds were studied. For the most representative compounds pronounced bathochromic shifts in both absorption and emission spectra were observed compare to previously described substituted terpyridines.

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Scheme 1. The retrosynthetic analysis for the synthesis of unsymmetrically functionalized 5,5''-diaryl-2,2':6',2''-terpyridines

254x190mm (96 x 96 DPI)

Scheme 2. The synthesis of non-symmetrically 5,5''-functionalized terpyridines. Reagents and conditions: i) 2,5-norbornadiene, o-xylene, 143 °C, 18 h; ii) NBS, CCl₄, 77 °C, 8 h; iii) NBS, CCl₄, benzoyl peroxide, 77 °C, 16 h; iv) NaOAc, DMF, 130 °C, 10 h; v) HCOOH-H₂O (85:15), reflux, 10 h; vi) NaOH, methanol, 65 °C, 30 min; vii) activated MnO₂, 1,2-dichloroethane, 50 °C, 5 h; viii) corresponding hydrazone of isonitrosoacetophenone, ethanol, r.t., overnight, then glacial acetic acid, reflux, 5 min; ix) 1-morpholinocyclopentene, neat, 200 °C, 3 h.

254x190mm (96 x 96 DPI)

Therefore, the alternative approach (Scheme 2) was proposed

254x190mm (96 x 96 DPI)

Fig. 2. Fluorescence spectra of terpyridines 1a-c in CH₃CN at room temperature

254x190mm (96 x 96 DPI)

Table 1. The photophysical properties of newly obtained terpyridines **1a-c** and some previously reported terpyridines

Entry	# or Ref	R ¹	R ²	R ³	R ⁴	R ⁵	n	m	Solvent	λ_{abs} , nm ^a	λ_{em} , nm ^b	Φ , % ^c
1	1a	Tol	H	H	Ph	H	3	0	CH ₃ CN	322, 350 _{sh}	344, 353	27.4
2	1b	4-MeO C ₆ H ₄	H	H	Ph	H	3	0	CH ₃ CN	321	383	31.1
3	1c	Ph	H	H	Ph	Ph	3	0	CH ₃ CN	307, 353	394	6.0
4	¹	Ph	H	H	Ph	H	3	3	CH ₃ CN	247, 306, 331	389	56.6
5	¹	Ph	H	4-MeOC ₆ H ₄	Ph	H	3	3	CH ₃ CN	215, 245, 313, 328 _{sh}	533	4.4
6	⁸	Ph	CN	H	Ph	CN	0	0	EtOH	302	355	40
7	⁸	Tol	CN	H	Tol	CN	0	0	EtOH	305	363	50
8	⁸	4-MeO C ₆ H ₄	CN	H	4-MeOC ₆ H ₄	CN	0	0	EtOH	313	402	60
9	⁹	Mani syl	H	H	Manisyl	H	0	0	CH ₃ CN	286	408	85
10	⁹	H	Mani syl	H	H	Manisyl	0	0	CH ₃ CN	284	412	8

^aAbsorbtion maxima at room temperature, ^bLuminescence maxima at room temperature,

^cAbsolute fluorescence quantum yields were measured in CH₃CN according to a reported procedureⁱ by using Horiba-Fluoromax-4 spectrofluorimeter equipped with integrated sphere

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