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Europium complex of 5-(4-dodecyloxyphenyl)-2,2′-bipyridine-6′-carboxylic acid

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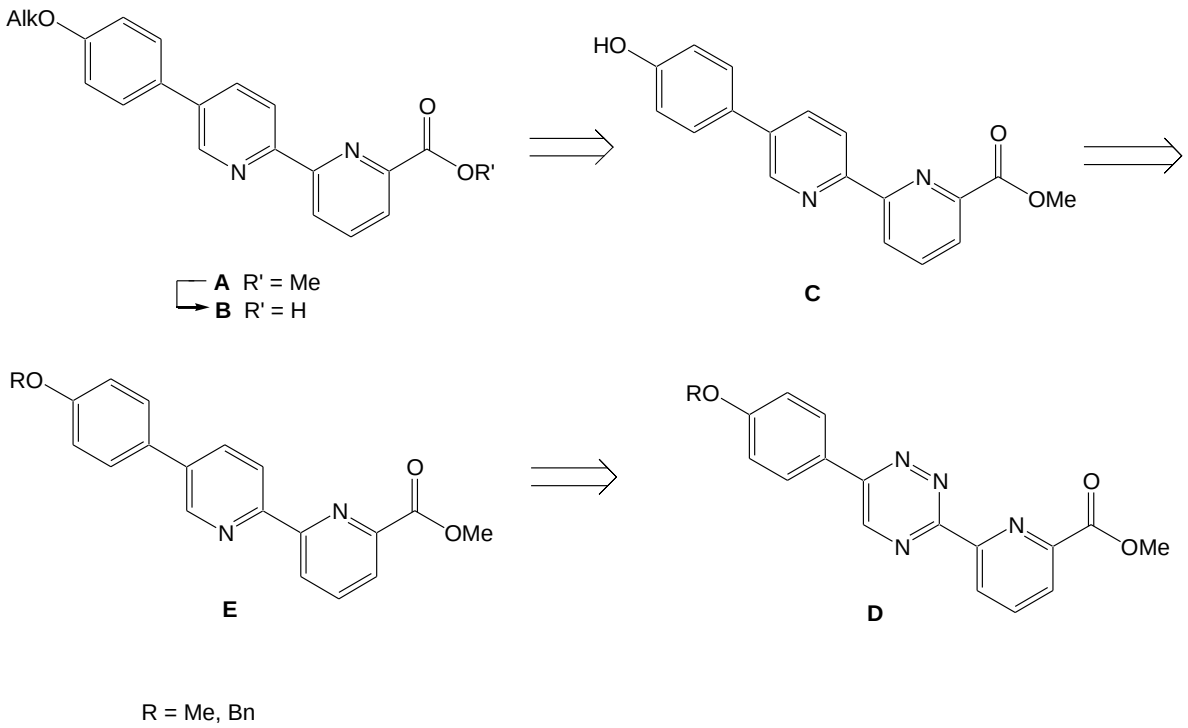
General. All reagents were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Bruker Avance-400 spectrometer, 298 K, digital resolution ± 0.01 ppm, using TMS as internal standard for ^{1}H NMR. UV–Vis spectra were recorded on Lambda 45 spectrophotometer (Perkin Elmer). Luminescence spectra were recorded on a Cary Eclipse spectrofluorometer (Varian). Mass spectra were recorded on a MicrOTOF-Q II mass spectrometer (Bruker Daltonics) with electrospray ionization. Elemental analysis were performed on a PE 2400 II CHN-analyzer (Perkin Elmer).

1-[4-(Benzyloxy)phenyl]ethanone **2**,[1] 6-(methoxycarbonyl)pyridine-2-carbaldehyde[2] and dodecyl benzenesulfonate[3] were synthesized as described in literature.

Retrosynthetic analysis towards the target ligand

In order to obtain the target ligand, like in previous cases, the 1,2,4-triazine-based methodology[4] was used. The retrosynthetic analysis towards the target ligand is outlined on Scheme S1. Obviously, synthesis of ester **A**, which is the direct precursor of the ligand **B**, can be performed through a preparation of phenol-substituted intermediate **C**. The synthesis of **C**, in turn, can be performed from 1,2,4-triazine precursor **D**, whose phenol group should be protected. The main issue was the choice of a suitable protective group. In principle, methyl group could be used for that purpose as it can be removed with boron tribromide. However, the obtaining of the appropriate bipyridine **E** (R = Me) was not an easy task due to significant difficulties on the step of the preparation of the corresponding 1,2,4-triazine **D** by heterocyclization reaction[5] (the yield of the desired 1,2,4-triazine **D** was in this case as low as 22%). Moreover, the required 6-(methoxycarbonyl)pyridine-2-carboxylic acid hydrazide is hardly available. In addition, the undesirable cleavage of the ester group during the demethylation reaction with BBr_3 was reported in some cases.[6] The use of benzyl protective group (which can be easy cleaved under the reductive conditions without the affecting ester groups) was considered as an alternative

approach. Anyway, in order to use the 1,2,4-triazine-based approach (compound **D**, R = Bn) it was necessary to develop a suitable method for the preparation of 1,2,4-triazine **D**, as this compound so far was not reported in a literature.



Scheme S1 The retrosynthetic approach of the target ligand.

2-[4-(Benzyloxy)phenyl]-2-oxoacetaldehyde oxime (3). The synthesis was fulfilled according to the optimized method[4]. 1-[4-(Benzyloxy)phenyl]ethanone **2** (55.78 g, 245.6 mmol) was dissolved in benzene (400 ml), then solution of sodium (11.33 g, 493 mmol) in ethanol (150 ml) and isopropyl nitrite (51.7 ml, 493 mmol) were added and the resulting mixture was stirred at room temperature overnight. The precipitate of sodium salt formed was filtered off, washed with benzene and ethanol and dried. Yield of the sodium salt was 45 g (162.3 mmol, 66%). Then this salt was suspended in water (250 ml). Glacial acetic acid (9.3 ml, 162.3 mmol) was added slowly under stirring at room temperature and then the resulting mixture was stirred for more 30 min. The precipitate formed was filtered off, washed with water and dried. The product was used in the next step without additional purification. Yield 39.42 g (154.4 mmol, total yield 63%). **ESI-MS**, *m/z*: found 256.10, calculated 256.10 $(M+H)^+$.

2-[4-(Benzyloxy)phenyl]-2-hydrazonoacetaldehyde oxime (4). The product **3** (25 g, 97.93 mmol) was suspended in ethanol (150 ml). Hydrazine hydrate (9.55 ml, 195.9 mmol) was added and the resulting mixture was stirred at 70 ºC for 3 h. Then precipitate was filtered off, water (1000 ml) was added slowly to the filtrate under stirring at room temperature. The precipitate formed was filtered off, washed with water and dried. The product was used in the next step without additional purification. Yield 14.49 g (53.86 mmol, 55%). **ESI-MS**, *m/z*: found 270.12, calculated 270.12 $(M+H)^+$.

Methyl 6-[6-(4-benzyloxyphenyl)-1,2,4-triazine-3-yl]picolinate (5). To the solution of hydrazone **4** (1.5 g, 5.57 mmol) in ethanol (25 ml) the solution of 6-(methoxycarbonyl)pyridine-2-carbaldehyde (0.92 g, 5.57 mmol) in ethanol (25 ml) was added and the resulting mixture was stored at room temperature for 10 h. Ethanol was removed under reduced pressure. Glacial acetic acid (40 ml) was added to the residue, the resulting mixture was heated to reflux 5 times. Then the resulting mixture was cooled to room temperature. The precipitate formed was filtered off. The filtrate was concentrated under reduced pressure. The residue was triturated with ethanol. The solid thus formed was filtered off, washed with ethanol and dried. The product was used in the next step without additional purification. Yield 1.11 g (2.79 mmol, 50%). **^{1}H NMR** (DMSO-d_6, δ, ppm): 3.98 (s, 3H, COOMe), 5.22 (s, 2H, Ph-C$\underline{H}_2$), 7.22 (m, 2H, C-H_{arom}), 7.30-7.50 (m, 5H, Ph), 8.22 (m, 2H, H-3,4), 8.28 (m, 2H, C-H_{arom}), 8.70 (d, 1H, ^3J = 7.8 Hz, H-5), 9.49 (s, 1H, H-5 (triazine)). **ESI-MS**, *m/z*: found 399.15, calculated 399.15 $(M+H)^+$.

Methyl 5'-(4-benzyloxyphenyl)-2,2'-bipyridine-6-carboxylate (6). The triazine **5** (1.11 g, 2.79 mmol) was suspended in *o*-xylene (30 ml), 2,5-norbornadiene (0.85 ml, 8.37 mmol) was added and the resulting mixture was refluxed for 19 h with addition of 2,5-norbornadiene every 7 h (each portion 0.85 ml, 8.37 mmol). The solvent was removed under reduced pressure. The residue was triturated with ethanol, the solid thus formed was filtered off and dried. The product was recrystallized from acetonitrile. Yield 0.55 g (1.4 mmol, 50%). M.p. 185-187 °C. **^{1}H NMR** ($CDCl_3$, δ, ppm): 4.05 (s, 3H, COOMe), 5.15 (s, 2H, Ph-C$\underline{H}_2$), 7.11 (m, 2H, C-H_{arom}), 7.32-7.50 (m, 5H, Ph), 7.60 (m, 2H, C-H_{arom}), 7.98 (m, 2H, H-4,4'), 8.14 (d, 1H, ^3J = 7.8 Hz, H-3), 8.58 (d, 1H, ^3J = 8.0 Hz, H-3'), 8.63 (d, 1H, ^3J = 7.8 Hz, H-5), 8.89 (d, 1H, ^4J = 2.1 Hz, H-6'). **ESI-MS**, *m/z*: found 397.16, calculated 397.16 $(M+H)^+$. Calcd for **$C_{25}H_{20}N_2O_3$**: C 75.74, H 5.08, N 7.07. Found: C 75.82, H 4.89, N 6.87.

Methyl 5'-(4-hydroxyphenyl)-2,2'-bipyridine-6-carboxylate (7). The mixture of benzyloxy derivative **6** (0.51 g, 1.28 mmol), ammonium formate (0.41 g, 6.43 mmol) and

palladium on charcoal (10%, 51 mg) in MeOH – THF mixture (1:1, 60 ml) was refluxed for 50 min under argon atmosphere. The catalyst was filtered off, the filtrate was evaporated under reduced pressure, the residue was purified by column chromatography (Silica gel, mixture of chloroform and methanol (20:1) as eluent, R_f 0.6). The product was used in the next step without additional purification. Yield 0.31 g (1.01 mmol, 79%). M.p. 201-203 °C. **^{1}H NMR** (DMSO-d_6, δ, ppm): 3.97 (s, 3H, COOMe), 6.88 (m, 2H, C-H_{arom}), 7.54 (m, 2H, C-H_{arom}), 8.06 (m, 3H, H-4',3,4), 8.51 (d, 1H, ^3J = 8.6 Hz, H-3'), 8.62 (m, 1H, H-5), 8.85 (d, 1H, ^4J = 2.3 Hz, H-6'), 9.48 (br. s., 1H, OH). **ESI-MS**, *m/z*: found 307.11, calculated 307.11 $(M+H)^+$.

Methyl 5'-(4-dodecyloxyphenyl)-2,2'-bipyridine-6-carboxylate (8). The compound **7** (0.46 g, 1.5 mmol) was dissolved in dry DMF (35 ml). Dodecyl benzenesulfonate (0.73 g, 2.25 mmol) and anhydrous potassium carbonate (1.04 g, 7.51 mmol) were added, and the mixture was stirred at 100 °C for 10 h. Water (50 ml) was added, the precipitate formed was filtered off, washed with water and dried. The product was purified by recrystallization (DMF). Yield 0.3 g (0.63 mmol, 40%). M.p. 145-147 °C. **^{1}H NMR** ($CDCl_3$, δ, ppm): 0.88 (m, 3H, $CH_2C\underline{H}_3$), 1.20-1.42 (m, 16H, $(C\underline{H}_2)_8CH_3$), 1.47 (m, 2H, $OCH_2CH_2C\underline{H}_2$), 1.82 (m, 2H, $OCH_2C\underline{H}_2$), 4.02 (t, 2H, ^3J = 6.8 Hz, $OC\underline{H}_2$), 4.05 (s, 3H, COOMe), 7.03 (m, 2H, C-H_{arom}), 7.59 (m, 2H, C-H_{arom}), 7.99 (m, 2H, H-4,4'), 8.14 (d, 1H, ^3J = 7.8 Hz, H-3), 8.58 (d, 1H, ^3J = 8.4 Hz, H-3'), 8.63 (d, 1H, ^3J = 7.8 Hz, H-5), 8.89 (d, 1H, ^4J = 2.1 Hz, H-6'). **ESI-MS**, *m/z*: found 475.30, calculated 475.30 $(M+H)^+$. Calcd for **$C_{30}H_{38}N_2O_3$**: C 75.92, H 8.07, N 5.90. Found: C 75.80, H 7.92, N 5.99.

5'-(4-Dodecyloxyphenyl)-2,2'-bipyridine-6-carboxylic acid (9). The ester **8** (240 mg, 0.51 mmol) and NaOH (41 mg, 1.02 mmol) were suspended in ethanol (30 ml) and the mixture was refluxed for 30 min and then kept at room temperature for 3 h. Ethanol (20 ml) was removed under reduced pressure, hydrochloric acid (5 *N*) was added to adjust pH = 2. The precipitate was filtered off, washed with ethanol and water, dried in vacuum. Yield 176 mg (0.38 mmol, 75%). M.p. 187-189 °C. **^{1}H NMR** ($CDCl_3$, δ, ppm): 0.88 (m, 3H, $CH_2C\underline{H}_3$), 1.20-1.42 (m, 16H, $(C\underline{H}_2)_8CH_3$), 1.47 (m, 2H, $OCH_2CH_2C\underline{H}_2$), 1.83 (m, 2H, $OCH_2C\underline{H}_2$), 4.02 (t, 2H, ^3J = 6.8 Hz, $OC\underline{H}_2$), 7.04 (m, 2H, C-H_{arom}), 7.60 (м, 2H, C-H_{arom}), 8.04 (dd, 1H, ^3J = 8.2 Hz, ^4J = 2.3 Hz, H-4'), 8.11 (dd, 1H, ^3J = 7.8 Hz, H-4), 8.27 (d, 1H, ^3J = 7.8 Hz, H-3), 8.40 (d, 1H, ^3J = 8.2 Hz, H-3'), 8.75 (d, 1H, ^3J = 7.8 Hz, H-5), 8.93 (d, 1H, ^4J = 2.1 Hz, H-6'). **ESI-MS**, *m/z*: found 459.26, calculated 459.26 $(M-H)^-$.

Complex Eu·9. The acid **9** (100 mg, 0.22 mmol) was suspended in methanol (35 ml), sodium hydroxide (9 mg, 0.22 mmol) was added and the mixture was refluxed until clear

solution was formed. Then mixture was cooled to room temperature and europium chloride hexahydrate (27 mg, 0.073 mmol) was added. The resulting mixture was kept at room temperature for 2 h. The solvent was removed under reduced pressure, water (20 ml) was added to the residue. The precipitate was filtered off, washed with water, dried in vacuum and solved in mixture methanol – dichloromethane (1:1, 20 ml). Unsolved part was filtered off, the solvents were removed from filtrate under reduced pressure. The product was dried in vacuum. Yield 62 mg (0.04 mmol, 55%). **ESI-MS**, *m/z*: found 1531.74, calculated 1531.74 $(M+H)^+$. Calcd for **$C_{87}H_{105}EuN_6O_9 \cdot CH_2Cl_2$**: C 65.42, H 7.34, N 5.19. Found: C 65.42, H 6.68, N 5.20.

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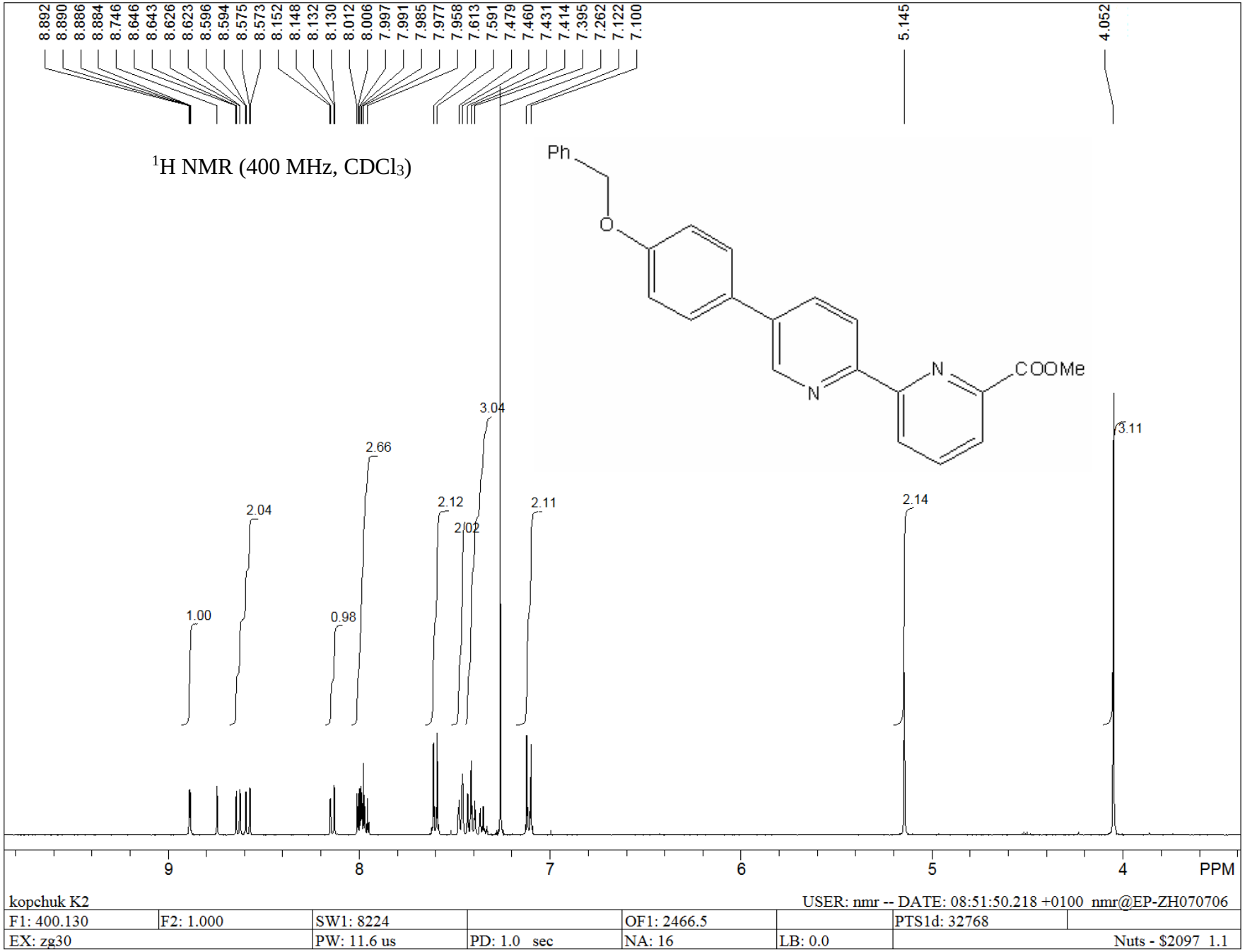
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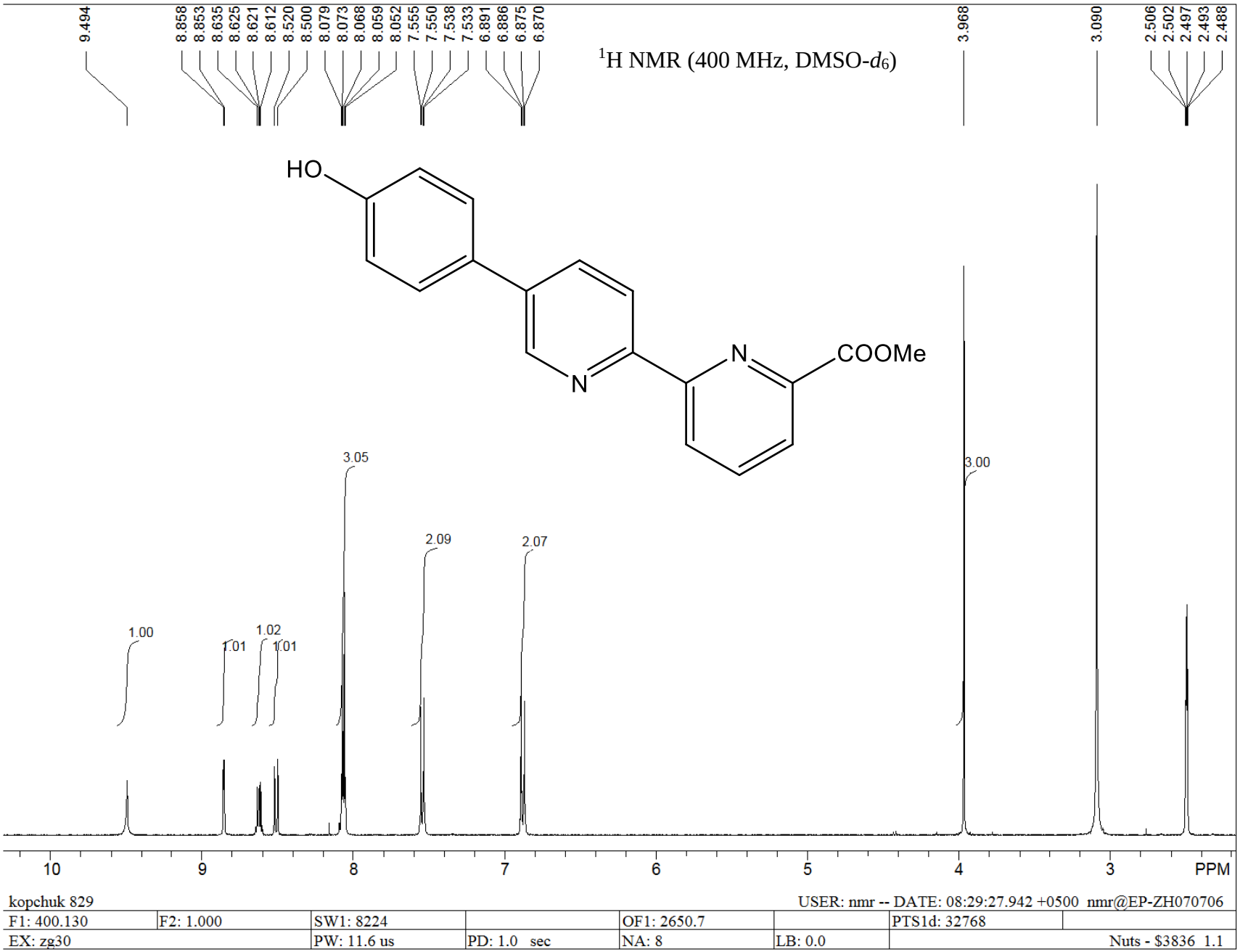
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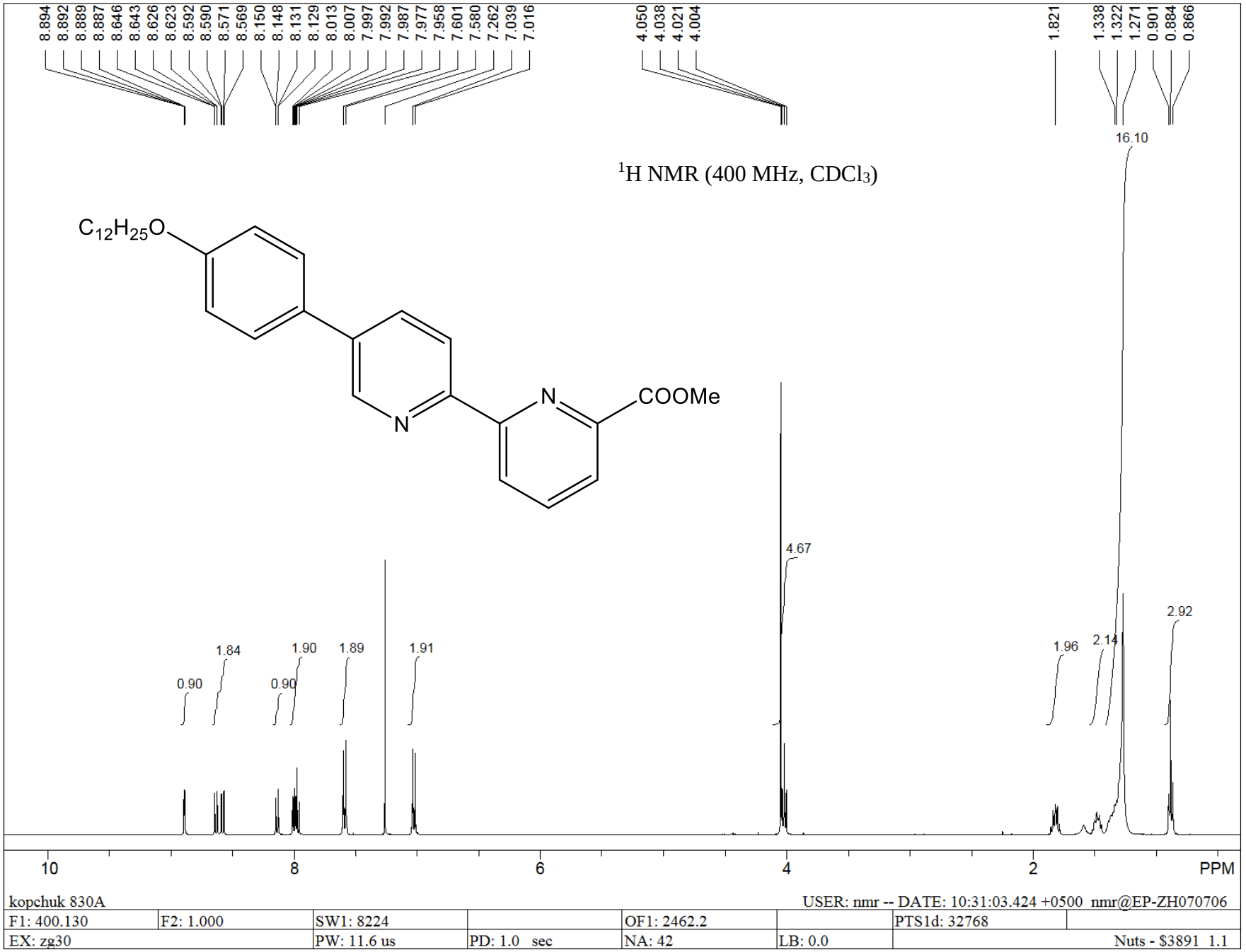
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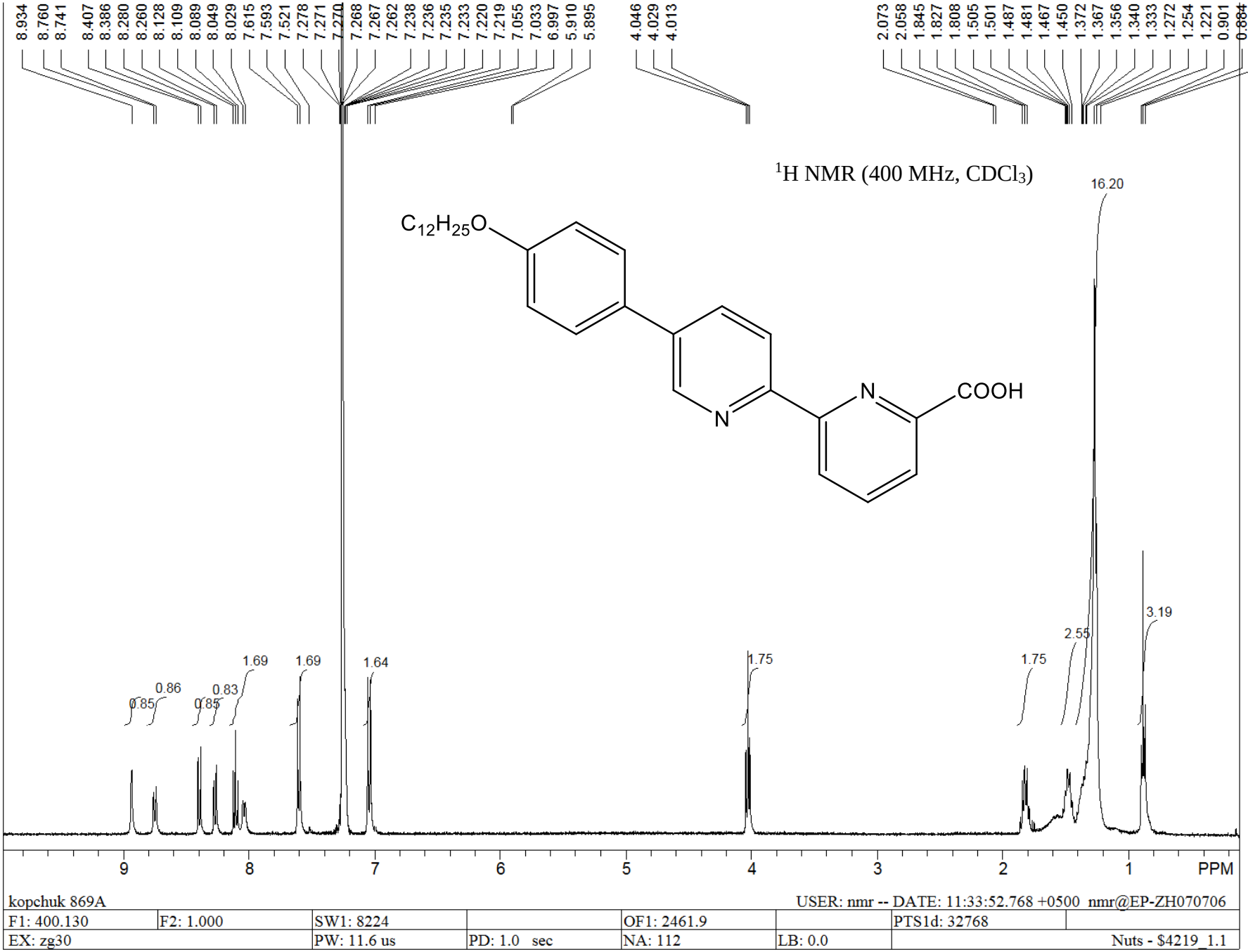
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