Useful Preparation of 6-Phenyl-2,2′-Bipyridine Ligands Bearing Di-*n*-butylaminophenyl or Gallate Derivatives Substituted in the 3- or 4-Positions

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Dedicated to the memory of Dr. Charles Mioskowski

Abstract: A simple protocol for the efficient preparation of substituted 6-phenyl-2,2′-bipyridine derivatives is described. A reverse type of Diels–Alder reaction between a 6-phenyl-2-pyridyl-1,3,4-triazine and 4-*N*,*N*-di-*n*-butylaminophenyl- or gallate-ethynyl derivatives at high temperature provide a mixture of two products easily separable by column chromatography. A variety of ligands suitable for the synthesis of cyclometalated platinum complexes have been produced. Additional substitution of the Pt–Cl by various donor–acceptor ethynyl fragments is feasible by mean of copper(I) catalysis.

Key words: triazine, retro-Diels–Alder, gallate, fluorescence, platinum

The construction of useful luminescent complexes generally requires the engineering of ligands so that the tailoring of the spectroscopic properties or even the redox properties corresponds to the envisaged applications. Phosphorescent transition-metal complexes find applications as chemical sensors,[1] electron[2] or photon[3] donors, light harvesters[4] and electrogenerated luminescent centres.[5]

Much effort is being extended to develop synthetic protocols able to produce stable, cheap, and versatile ligands capable to complex transition metals. Bipyridine, terpyridine, and phenyl analogues have found prominent use in a wide variety of photo-activated molecular systems.[6–9]

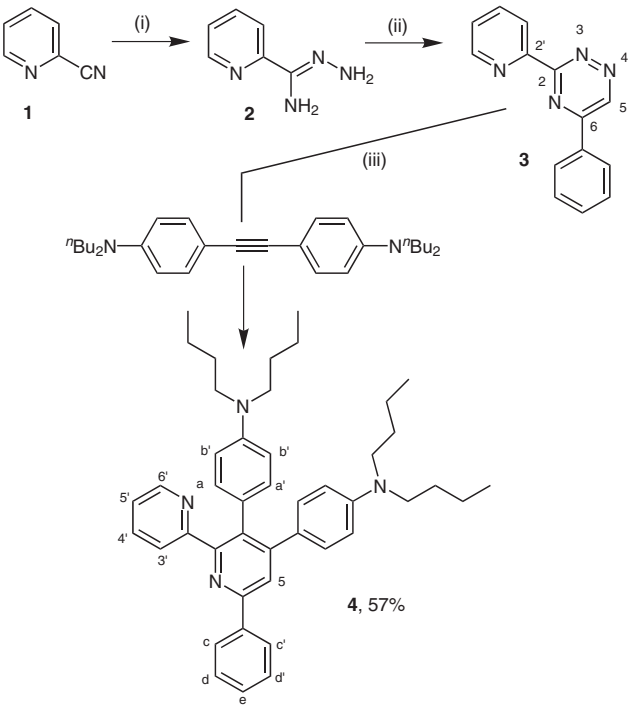
In many cases, these materials are luminescent in fluid solution at ambient temperature and the photophysical properties are sensitive to temperature, nuclearity, and the nature of the polypyridine ligand.[10] Attaching aryl hydrocarbon residues[11,12] close to the metal centre provides a means by which to prolong the triplet lifetime of the complex whilst the addition of electron-donating or electron-withdrawing units opens up the possibility to involve the metal complex in intramolecular charge-transfer states.[13,14] Attaching conjugated substituents to the metal complex introduces the likelihood that ligand-localised excited states will figure in the triplet manifold.[15]

Most of these ligands were produced by classical methods and recently in an alternative approach towards the same purposes sophisticated polytopic ligands (quarter-, quinque-, hexapyridine….) were prepared by controlled reverse Diels–Alder reactions.[16,17]

In this paper we report a method for the synthesis of a class of 6-phenyl-2,2′-bipyridine analogues starting from a common triazine starting material. The method is general and it allows for the convenient synthesis of a series of ligands in which the substituents on the central pyridine can be varied.

The target triazine was prepared in two steps from 2-cyanopyridine and hydrazine followed by condensation with phenylglyoxal (Scheme 1). Condensation of **1** with hydrazine hydrate was carried out as described in the literature.[18]

The condensation of the 1,3,4-triazine **3** with bis(4-*N*,*N*-di-*n*-butylphenyl)acetylene in *o*-dichlorobenzene at high temperature provides the trisubstituted bipyridine derivative **4** in acceptable yield (Scheme 1).[19]



Scheme 1 *Reagents and conditions*: (i) N_2H_4 hydrate, EtOH, r.t.; (ii) 2-phenylglyoxal, EtOH, reflux; (iii) disubstituted ethynyl compound, *o*-dichlorobenzene, 180 °C.

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Crystal structure determination for **4** (Figure 1)[20] confirms the stoichiometry and connectivity deduced from the NMR spectra. As expected the nitrogen atoms of the bipyridine moiety lie in a transoidal position that minimises electrostatic interactions between the neighbouring lone pairs, a situation frequently found in oligopyridine ligands.[21] The two 4-*N*,*N*-di-*n*-butylaminophenyl rings are tilted versus the central pyridine ring by 47.28° (3-position) and 46.27° (4-position). Besides, the nonsubstituted phenyl fragment in the 6-position is titled by 39.37°.

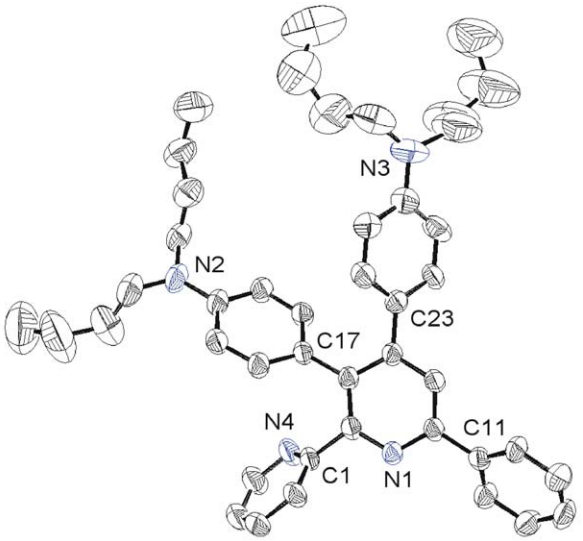
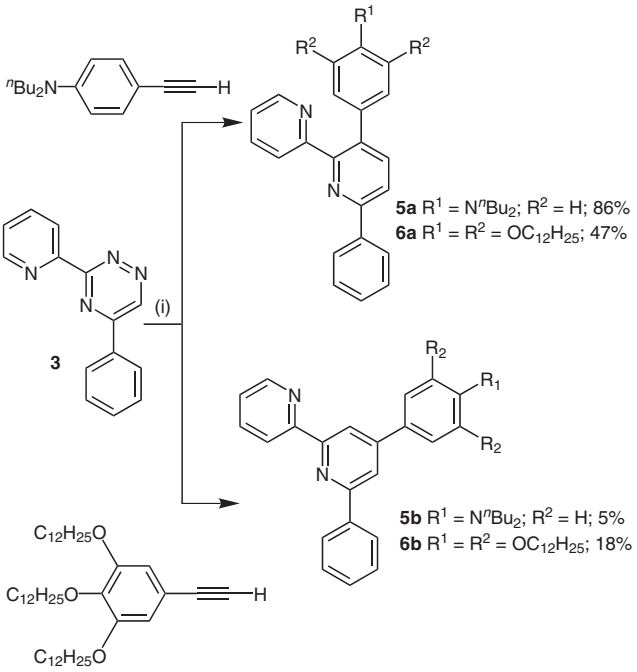


Figure 1 An ORTEP view of ligand **4** with atoms labelled. Probability displacement ellipsoids are shown at the 30% level.

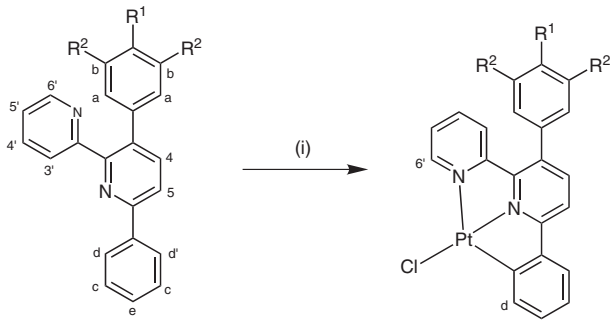
When the same condensation is carried out with 4-*N*,*N*-di-*n*-butylaminophenylacetylene or 3,4,5-dodecaalkoxy phenylacetylene the reaction proceeds smoothly but two regioisomers are formed which can be easily separated by a combination of chromatography and crystallization (Scheme 2). The *meta*-isomers **5a** and **6a** are identified by the multiplicities and chemical shifts of the 3,5- or 4,5-protons of the central pyridine. For the *meta*-isomers the protons 4 and 5 are presented by an AB system (J_{AB} = 8.1 Hz, $\nu_0\delta$ = 12.5 and 21.1 Hz, respectively) whereas for the *para*-isomers **5b** and **6b** the 3- and 5-protons are split into two weakly coupled doublets (^4J = 1.5 Hz, Figure 2). Also worth noting is the protons 3′ of the outer pyridine rings of the *para*-isomers which are notably shifted upfield in the *meta* cases **5a** (Figure 3) and **6a** due to the proximity of the substituted phenyl ring in the cisoid orientation.

The ratio of regioisomers is not influenced by temperature and reaction times. At lower temperature, the reaction is very slow and product conversion very modest. At higher temperature, the addition product of the acetylene to the triazine leads to the preferential decomposition of the compounds. It appears that the reverse Diels–Alder condensation takes place readily around 180 °C even with fairly hindered acetylene derivatives and provides a useful method for the incorporation of various substituents on the central pyridine residue.



Scheme 2 *Reagents and conditions*: (i) arylethynyl derivative, *o*-dichlorobenzene, 180 °C.

In order to test the coordination abilities of some of these novel ligands towards Pt(II) we allow these to react with K_2PtCl_4 in a refluxing mixture of acetonitrile (or THF) and water. Analysis of the crude reaction mixture indicate complete consumption of the ligands resulting in formation of deep-red complexes which were easily isolated in fair yields by column chromatography on silica gel eluting with dichloromethane (Scheme 3).



Scheme 3 *Reagents and conditions*: (i) K_2PtCl_4, H_2O–MeCN (for **5a**) or H_2O–THF (for **6a**), reflux.

The identity of complexes **7** and **8** was ascertained from their ^{1}H NMR which revealed a noticeable shift of proton 6′ (α to the nitrogen) toward low field when ligands were coordinated to metal centre (from δ = 8.6 to ca. 9.1 ppm). Another key feature in the spectra is the apparition of ^{195}Pt satellites, testifying of weak coupling of protons 6′ and d with the platinum atom.

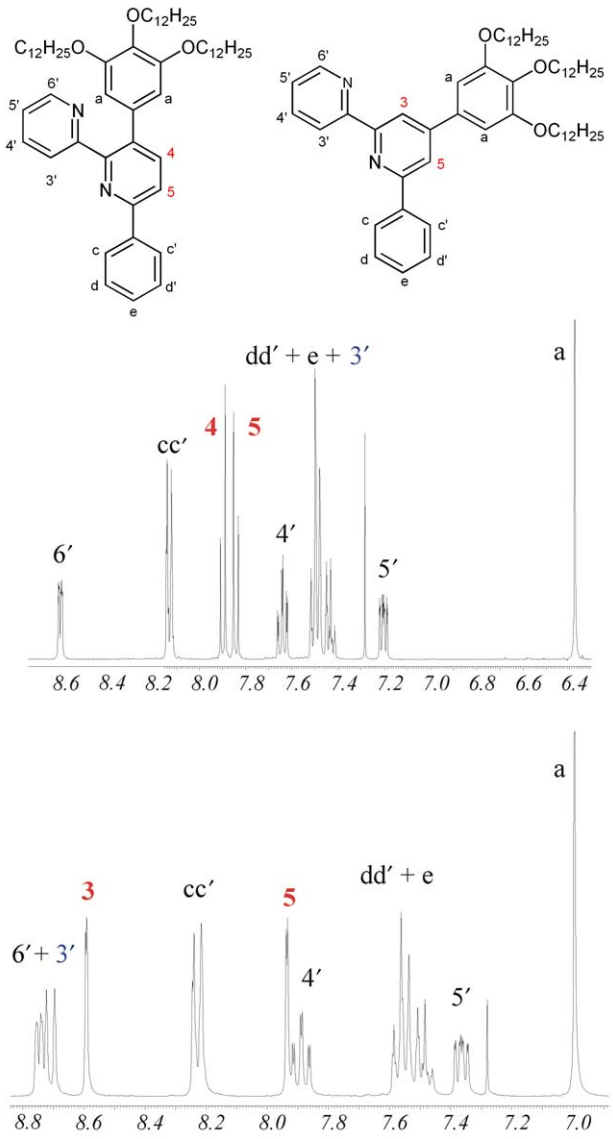


Figure 2 ^{1}H NMR (300 MHz, $CDCl_3$) of **6a** (*meta*-isomer, top) and **6b** (*para*-isomer, bottom). For the sake of clarity only the aromatic region of the spectra is shown.

Furthermore, complex **7** was adequately characterized by an X-ray molecular structure on single crystals (Figure 4).[22] The tridendate cyclometalated ligand and the chlorine are arranged in a distorted square-planar geometry about the platinum atom. The chelating ligand is almost flat with dihedral angles between the central pyridine and the outer cycles; 12.55° with the outer pyridine and 4.60° with the phenyl ring. The 4-*N*,*N*-di-*n*-butylaminophenyl fragment is severely tilted from the main platinum plane by 61.33°, a situation highlighting the steric congestion at the 3-substitution position. The platinum–nitrogen bond length *trans* to the phenyl group [Pt(1)–N(1) = 2.099 Å] is noticeably longer than that *trans* to the chlorine ligand [Pt(1)–N(2) = 1.966 Å] which is consistent with the greater *trans* influence exerted by the phenyl substituent.

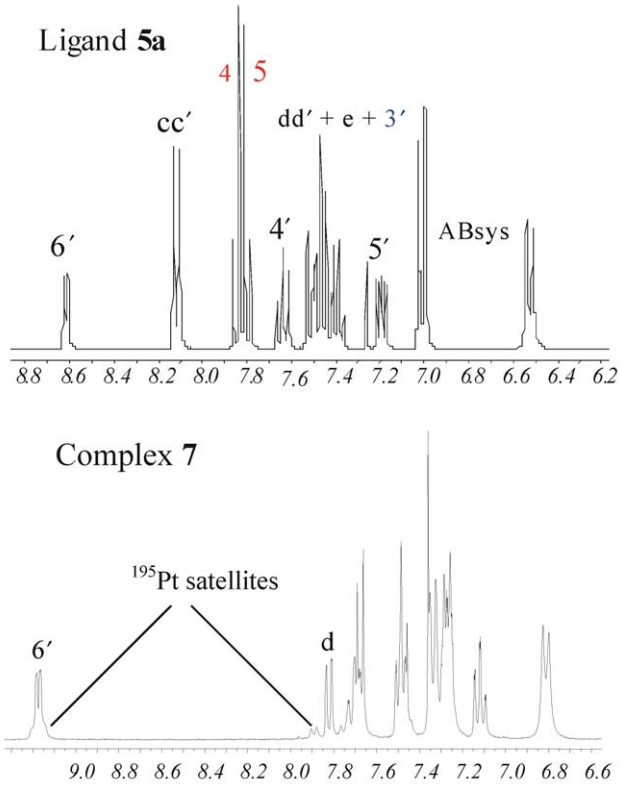


Figure 3 ^{1}H NMR (300 MHz, $CDCl_3$) of **5a** (top) and **7** (bottom). For the sake of clarity only the aromatic region is shown.

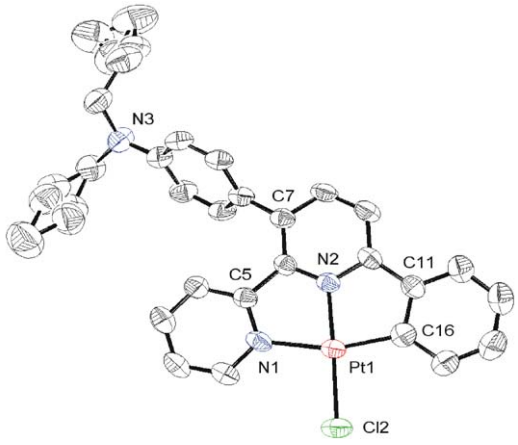
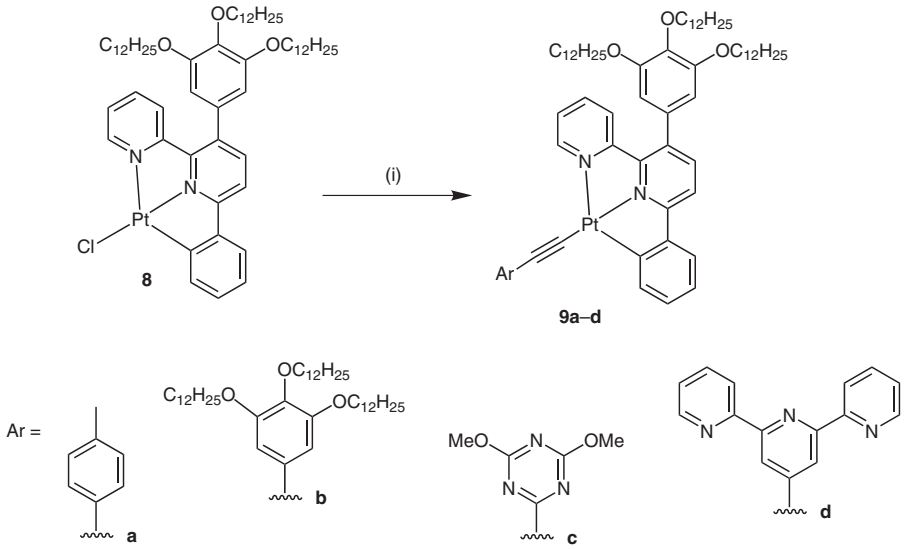


Figure 4 An ORTEP view of complex **7** with atoms labelled. Probability displacement ellipsoids are shown at the 50% level. Selected distances (Å) and angles (°): Pt(1)–N(1), 2.099; Pt(1)–N(2), 1.966; Pt(1)–C(16), 1.969; Pt(1)–Cl(2), 2.312; N(1)–Pt(1)–N(2), 78.92; N(1)–Pt(1)–C(16), 162.03; N(2)–Pt(1)–Cl(2), 177.67.

Displacement of the chloride ligands in complex **8** can be achieved under smooth conditions by using CuI as a catalyst (10 mol%). Although we made no attempt to systematically optimise the reaction conditions, displacement of the halide on the platinum centre is kinetically controlled and required fairly lengthy reaction times (1–3 d) at room temperature. Higher temperatures are not suitable here due to the instability of the platinum precursor in the presence of triethylamine and the solvent.



Scheme 4 *Reagents and conditions*: (i) arylethynyl derivative, CuI (10%mol), TEA, CH_2Cl_2, r.t.

Despite the fact that highly deactivated acetylene sources are used (e.g., derivative **c** in Scheme 4), the copper-promoted cross-coupling reaction is effective and there is little difference in the yields of the substituted platinum complexes from an electron-rich acetylene (a and b) versus electron-poor acetylene source (like c and d). Inasmuch, use of 4-ethynyl-terpyridine (d) does not induce ligand scrambling around the platinum metal (C^N^N versus N^N^N coordination mode), which testify to the high stability of the *ortho*-metalated metal centre under the used experimental conditions.

The proton NMR spectra of complexes **9a–d** presented the same features as previously discussed for complexes **7** and **8** with characteristic low-field shifting and ^{195}Pt satellites for the protons 6′ and d. Furthermore, the ^{13}C NMR spectra for the co-ligand part exhibit two signals between δ = 103 and 107 ppm unambiguously assigned to the sp-hybridised carbons of the ethynyl bond.

Selected spectroscopic data are gathered for all compounds in Table 1. The absorption spectra of most compounds exhibit an intense band between 270 and 360 nm (ε in the range 21000–46000 M^{-1} cm^{-1}), which can be assigned to the spin-allowed π–π* transitions involving the pyridyl/phenyl/ancillary aryl rings. All platinum complexes display an additional large absorption band at low energy (around 430–480 nm) assigned to spin-allowed metal-to-ligand charge transfer. The shape and position of these MLCT band is weakly affected by the nature of the ethynylaryl residues. All the compounds exhibit a relatively intense emission (Table 1) in solution at room temperature. The emission spectrum is similar in shape and the emission is significantly red shifted compared to the absorption spectrum, indicating a strong Stokes shift, which suggests a reorganization occurring in the excited state. For the *meta*-derivatives **5a** and **6a** the emission is red shifted, respectively, by 26 nm and 16 nm with respect to the *para*-isomers. Notice that for the complexes excitation in the MLCT or π–π* transition resulted in an emission in the range of 580 to 640 nm due to the phosphorescence of the MLCT triplet state.[23] Complex **9b** bearing an ethynylgallate fragment is completely quenched, likely due to a photo-induced electron-transfer process provided by the appended alkoxy fragments.[24]

Table 1 Selected Data for the Novel Ligands and Complexes

Compd	Yield (%)	MS–FAB (*m/z*)[a]	λ_{max} (nm), ε ($M^{-1}cm^{-1}$)[b]		λ_{em} (nm)[c]
			π–π*	MLCT	
4	57	639.3	332 (28600)	–	468
5a	86	436.2	350 (21900)	–	487
5b	5	436.2	356 (28200)	–	461
6a	47	861.4	306 (21000)	–	451
6b	18	861.4	285 (29500)	–	435
7	65	666.2	271 (45500)	484 (2000)	642
8	85	1055.1	279 (27500)	440 (1500)	589
9a	69	1171.0	280 (44700)	450 (5300)	608
9b	68	1709.2	283 (45500)	440 (5700)	–
9c	41	1220.0	283 (46000)	428 (5100)	579
9d	80	1312.0	288 (61500)	426 (7700)	583

[a] FAB mass spectroscopy, the molecular peak correspond to $[M + H]^+$ except for **8** where *m/z* accounts for $[M - Cl]^+$.
[b] Averaged value determined from at least two different solutions of nondegassed CH_2Cl_2 solution.
[c] Emission in CH_2Cl_2 solution at room temperature.

This study has shown that reverse Diels–Alder reaction provides unsymmetrically substituted ligands prepared in a single step as sketched in Scheme 1. It should be stressed that these highly substituted phenyl-bipyridine ligands are mostly inaccessible by any other known syn-

thetic route. The rate of the condensation is heavily dependent upon steric hindrance near the acetylene function. Nevertheless, even congested alkynes such as 1,2-di(4-*N*,*N*-dibutylaminophenyl)ethyne can be converted, albeit in low yield, into the desired target compounds. When two positional isomers are possible the regioselectivity is dictated by particular aryl–aryl interaction in the transition state. The *meta*-isomer is always favoured versus the *para*-isomer. The ratio of isomers cannot be regulated by varying the temperature or reaction rate excluding a kinetic and thermodynamic control. The coordination potential of these ligands have been tested by complexation with Pt(II) salts. Nonetheless, *ortho* metalation is feasible despite the fact that the *meta*-substitution position induces some steric constraints. High solubility has been ensured by the use of butyl or dodecaalkoxy solubilising chains. Under controlled conditions, this protocol is well suited to the production of novel phenyl/bipyridine ligands. This finding expands the synthetic scope of this reaction and makes readily accessible a class of previously rare ligands.

Acknowledgment

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(19) **3,4-Bis(*N*,*N*-dibutyl-4-aminophenyl)-6-phenyl-2,2′-bipyridine(4)**
A Schlenk tube was charged with 6-phenyl-2-pyridyl-1,3,4-triazine (**1**, 125 mg, 0.53 mmol), *N*,*N*-dibutyl-4-{2-[4 (dibutylamino)phenyl]ethynyl}benzenamine (230 mg, 0.53 mmol) and *o*-dichlorobenzene (1 mL). The mixture was argon-degassed via at least three freeze-pump-thaw cycles, heated to 190 °C and finally stirred in the dark for 1–3 d. The solvent was removed under high vacuum. The residue was treated with H_2O and extracted with CH_2Cl_2. The organic extracts were washed with H_2O, then with sat. brine and filtered through cotton wool. The solvent was removed by rotary evaporation, and the residue was purified by chromatography on aluminium oxide eluting with CH_2Cl_2–PE (v/v 0:1 to 50:50) to afford 194 mg (57%) of **4** as a white to light pink powder. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (d, 1 H, ^3J = 4.5 Hz), 8.11 (d, 2 H, ^3J = 7.0 Hz), 7.80 (s, 1 H), 7.49–7.35 (m, 4 H), 7.19 (d, 1 H, ^3J = 8.0 Hz), 7.09 (ddd, 1 H, J = 7.5, 4.8, 1.3 Hz), 6.78 (ABsys, 4 H, J_{AB} = 9.0 Hz, $\nu_0\delta$ = 220.6 Hz), 6.55 (ABsys, 4 H, J_{AB} = 8.8 Hz, $\nu_0\delta$ = 144.5 Hz), 3.24 (t, 4 H, ^3J = 7.5 Hz), 3.17 (t, 4 H, ^3J = 7.5 Hz), 1.59–1.44 (m, 8 H), 1.38–1.24 (m, 8 H), 0.95 (t, 6 H, ^3J = 7.3 Hz), 0.92 (t, 6 H, ^3J = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 157.7, 155.3, 150.5, 149.0, 147.5, 146.9, 139.9, 135.3, 133.3, 132.2, 130.7, 128.6, 128.5, 127.3, 126.3, 125.2, 124.7, 121.6, 121.5, 111.7, 111.1, 50.8, 50.7, 29.5, 29.4, 20.5, 20.4, 14.2, 14.1. UV/Vis (CH_2Cl_2): λ nm (ε, M^{-1} cm^{-1}) = 355 (sh, 19200), 331 (2860), 263 (30600). IR (KBr): ν = 3039 (w), 2955 (m), 2929 (m), 2870 (m), 1605 (s), 1517 (s), 1463 (m), 1364 (s), 1285 (m), 1198 (s), 1095 (m), 818 (s) cm^{-1}. MS–FAB$^+$: *m/z* (nature of the peak, relative intensity) = 639.3 (100) $[M + H]^+$. Anal. Calcd for $C_{44}H_{54}N_4$: C, 82.71; H, 8.52; N, 8.77. Found: C, 82.54; H, 8.29; N, 8.47.
(20) Crystal data for **4** at 293 K: $C_{44}H_{54}N_4$, M = 638.91, monoclinic, space group $P2_1/c$, a = 15.161(5) Å, b = 25.720(5) Å, c = 10.503(5) Å, α = 90.000(5)°, β = 107.245(5)°, γ = 90.000(5)° V = 3911.44(10) Å^3, Z = 4, λ = 0.71069 Å, D_c = 1.085 g cm^{-3}, μ = 0.063 mm^{-1}, 23064 reflections collected with θ ≤ 18.91°, 3085 unique, R(int) = 0.1214, and 1926 observed reflections [I ≥ 2σ(I)], 433 parameters, $R1$ = 0.0830, $wR2$ = 0.2397 refined on F^2. CCDC 649879.
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(22) Crystal data for **7** at 293 K: $C_{30}H_{32}ClN_3Pt$, M = 665.13, triclinic, space group P–1, a = 9.147(1) Å, b = 9.979(1) Å, c = 15.290(2) Å, α = 80.500(3)°, β = 80.922(2)°, γ = 73.057(3)°, V = 1307.8(3) Å^3, Z = 2, λ = 0.71069 Å, D_c = 1.689 g cm^{-3}, μ = 5.49 mm^{-1}, 15122 reflections collected with θ ≤ 27.61°, 5869 unique, R(int) = 0.0501, and 4993 observed reflections [I ≥ 2σ(I)], 354 parameters, $R1$ = 0.0383, $wR2$ = 0.0919 refined on F^2. CCDC 649883.
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