molbank

MDPI

Short Note

(2*E*,2′*E*)-3,3′-(2,2′-Bipyridine-6,6′-diyl)diacrylic Acid

Tristan Hergot [1], Mihayl Varbanov [1,2,*] and Florence Dumarçay-Charbonnier [1,*]

[1] L2CM, CNRS, Université de Lorraine, 54000 Nancy, France
[2] Laboratoire de Virologie, Centres Hospitaliers Régionaux Universitaires (CHRU) de Nancy Brabois, 54500 Vandœuvre-lès-Nancy, France
* Correspondence: mihayl.varbanov@univ-lorraine.fr (M.V.); florence.dumarcay@univ-lorraine.fr (F.D.-C.)

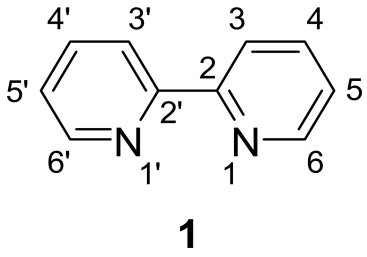
Abstract

A new carboxylic acid-functionalized 2,2′-bipyridine derivative, (2*E*,2′*E*)-3,3′-(2,2′-bipyridine-6,6′-diyl)diacrylic acid (**3**), was synthesized in two steps from 6,6′-dibromo-2,2′-bipyridine. A palladium-catalyzed double Heck coupling with tert-butyl acrylate afforded the corresponding protected diester intermediate, which was then deprotected under acidic conditions to give the target dicarboxylic acid. The compound was fully characterized by ^{1}H and ^{13}C NMR spectroscopy and HRMS. The combination of a 2,2′-bipyridine core with two conjugated carboxylic acid functionalities provides a bifunctional molecular building block potentially suitable for further derivatization.

Keywords: bipyridine; diacrylic acid; building block; microwave; Heck reaction

1. Introduction

2,2′-Bipyridine (bipy) is a widely known bidentate ligand [1] coordinating metal ions through its two nitrogen atoms on the 1 and 1′ positions (Figure 1). This scaffold and its derivatives constitute an essential building block in coordination chemistry for the design of a wide variety of ligands.



1

Figure 1. 2,2′-bipyridine (**1**) with atom numbering.

One of the most extensively studied bipyridine complex is the Ruthenium (II) tris bipy: $[Ru(bpy)_3]^{2+}$ [2,3] for its applications as a photosensitizer.

Over time, increasingly sophisticated ligands have been developed [4] making the bipyridine scaffold a versatile platform for the design of complex molecular architectures. A cryptand made of three bipy units linked on their 6 and 6′ positions to a central tri-methyl amine have been synthesized by Lehn [5] and its coordination properties with lanthanides have been studied [6].

Our group has developed such ligands based on this bipy motif. We have previously reported the synthesis of *N*-heterocyclic macrocycles [7,8] showing promising properties for potential application as photosensitizer.

Check for updates

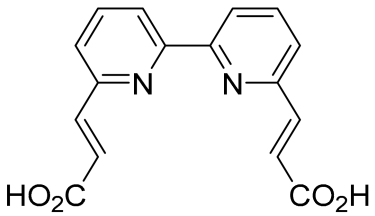
Academic Editor: Zhanhui Yang

Received: 11 September 2026
Revised: 25 September 2026
Accepted: 28 September 2026
Published: 2 October 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

This 2,2′-bipyridine motif can be modified with functional groups to access a wide range of derivatives opening the way to tunable ligands. In this work, our goal was to synthesize a symmetrical ligand based on a 2,2′-bipyridine bearing anchoring groups suitable for further functionalization. We also aimed to extend the bipyridine π-conjugated system on the 6 and 6′ positions inspiring our work on the synthesis of 6,6′-divinyl-2,2′-bipyridine reported by Newkome [9].

In this context, we report the synthesis and full characterization of the previously unreported (2E,2′E)-3,3′-(2,2′-bipyridine-6,6′-diyl)diacrylic acid (**3**). The target compound (Figure 2) was obtained through a palladium-catalyzed double Heck coupling followed by acid-mediated deprotection of the tert-butyl protecting groups.



3

Figure 2. (2E,2′E)-3,3′-(2,2′-bipyridine-6,6′-diyl)diacrylic acid (**3**).

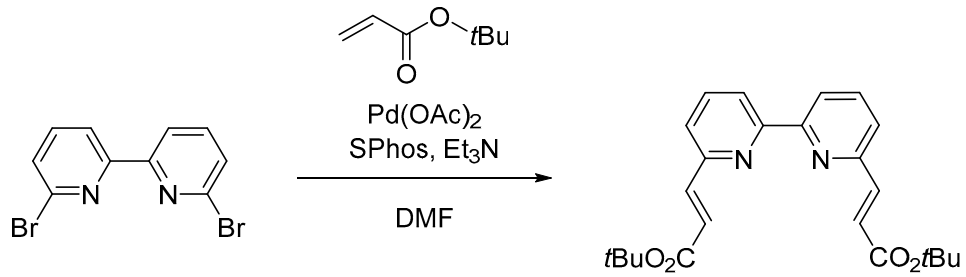
This short synthetic sequence provides access to a bifunctional bipyridine building block bearing two terminal carboxylic acid groups available for further functionalization.

2. Results and Discussion

The synthesis started with a double Heck coupling implying the 6 and 6′ bromine of the commercially available 6,6′-dibromo-2,2′-bipyridine. For this reaction, the first try was inspired by the conditions described by Ali et al. [10] on various halogeno-pyridines using palladium acetate with different phosphines and triethyl amine.

We conducted our first attempt as described in the literature: with SPhos as the phosphine (10 mol%), $Pd(OAc)_2$ (5 mol%), Et_3N (8 eq), 6,6′-Dibromo-2,2′-bipyridyl (1 eq) and the acrylate: tert-butyl acrylate (2.5 eq), in a ratio of 1.25 equivalent per halogen, in DMF at 120 °C for 48 h (Table 1, Entry 1).

Table 1. Double Heck coupling condition screening.



1 **2**

Entry	Activation	Temperature (°C)	Time (h)	Isolated Yield (%)
1	Thermal	120	48	8
2	MW	190	0.5	38
3	MW	160	1	78

These reaction conditions led to the formation of the desired product in a mixture with the mono-coupled by-product and the starting material. Indeed, this reaction can be

easily monitored by TLC with the solvent mixture: Cyclohexane/EtOAc 90:10. Under these conditions, the R_f were: 0.5 (desired product), 0.65 (mono-coupled product), 0.8 (starting material). The different products were then isolated by flash chromatography leading to the desired product (**2**) in 8% isolated yield, the mono-coupled (**2′**) product in 8% isolated yield, and 10% of starting material (**1**) (Figure 3).

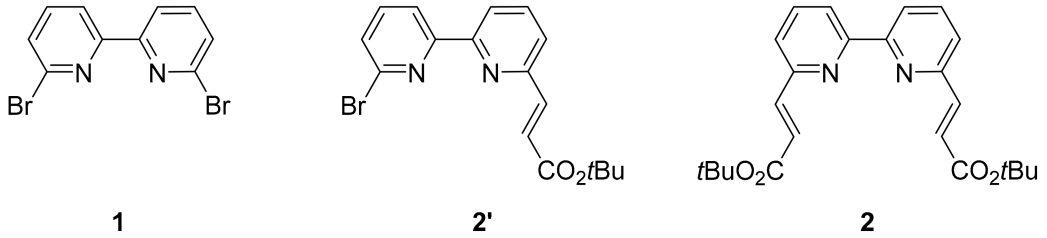


Figure 3. By-products resulting from the thermal double Heck coupling.

In order to increase the yield of product (**2**), we investigated microwave-assisted heating as an alternative to conventional thermal heating.

Under these conditions, compound (**2**) was the only product detected by TLC. (Table 1, Entries 2 and 3). No other by-products, as previously described, were observed with TLC monitoring. It can be noticed that lowering the temperature from 190 °C to 160 °C and extending the reaction time from 30 min to 1 h led to an increase in the isolated yield of the desired product (**2**).

The compound (**2**) was then fully characterized (Figures S1–S7) and the *E* configuration of the double bond was confirmed by ^{1}H NMR. Indeed, the coupling constant value of the two vinylic protons is 15.6 Hz. This large vicinal coupling constant between the two vinylic protons is consistent with an *E* configuration of the two double bonds.

The tert-butyl esters were deprotected under acidic conditions to form the diacrylic acid (**3**). This reaction was carried out in a 1:1 *v*/*v* mixture of trifluoroacetic acid (TFA) in dichloromethane (DCM). The addition of TFA occurred dropwise at 0 °C, then the reaction mixture was allowed to warm up to room temperature for 2 h (Figure 4).

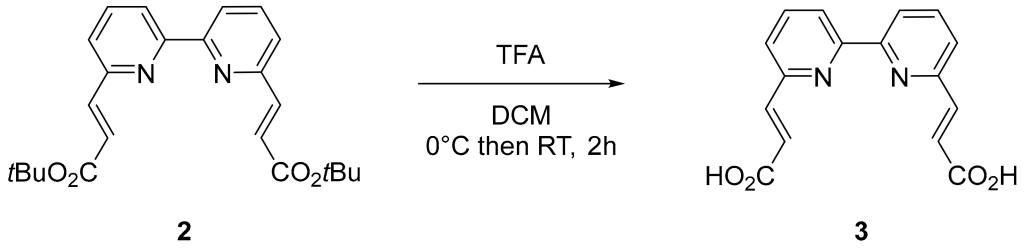


Figure 4. Deprotection of the tert-butyl esters.

Successful deprotection was highlighted by ^{1}H NMR: the complete disappearance of the tert-butyl signal at 1.56 ppm and the appearance of a broad carboxylic acid proton signal at 12.61 ppm is observed (Figures 5 and 6).

The reaction was complete, and compound (**3**) was isolated after several co-evaporations with DCM to remove the residual TFA, affording the final product (**3**) in 95% yield.

The final compound (**3**) was then fully characterized (Figures S8–S14) and the retention of the *E* configuration was confirmed by ^{1}H NMR. Indeed, the coupling constant value of the two vinylic protons is 15.7 Hz, which confirms retention of the *E* configuration after this reaction step.

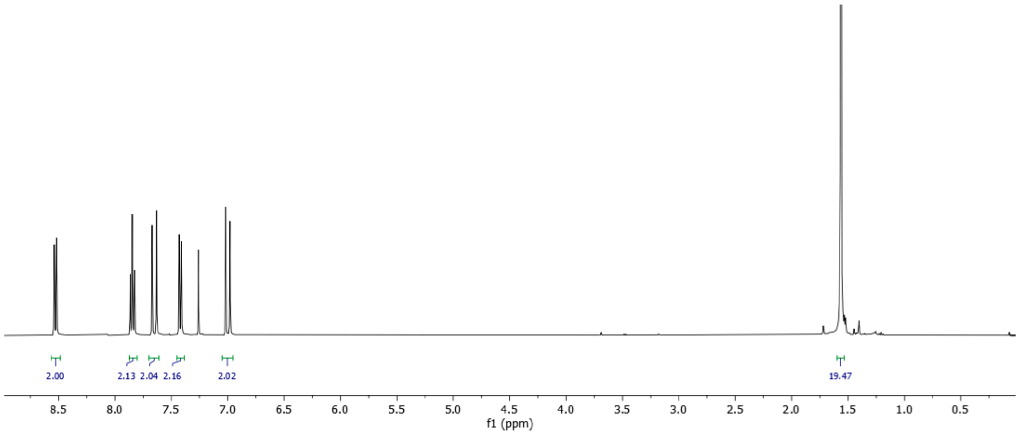


Figure 5. ^{1}H NMR spectrum of compounds (**2**) in $CDCl_3$.

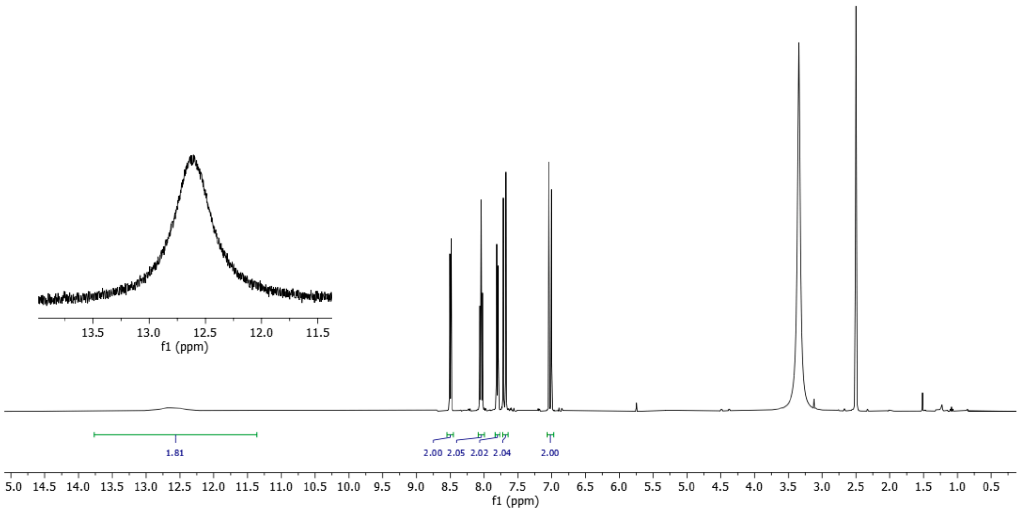


Figure 6. ^{1}H NMR spectrum of compounds (**3**) in DMSO-d_6.

Finally, the diacrylic acid (**3**) was obtained after optimization of the double Heck coupling reaction in an overall yield of 74%.

3. Materials and Methods

Solvents and liquid reagents were purified and dried according to the recommended procedures. Chemical reagents were purchased from BLDpharmatech GmbH (Reinbek, Germany) and were used as received. Analytical thin-layer chromatography was performed with silica gel 60 F254, 0.25 mm precoated TLC plates Sigma-Aldrich (Saint-Quentin-Fallavier, France). Compounds were visualized using UV light at 254 nm, IST Metz GmbH & Co. KG. (Nürtingen-Zizishausen, Germany). Microwave-assisted reactions were carried out using an Anton Paar France S.A.S. 450 single-mode microwave reactor (Les Ullis, France) under temperature-controlled conditions. The microwave power was automatically adjusted by the instrument to maintain the set temperature and was limited to a maximum of 60 W. Column chromatography was performed using a Grace Reveleris® equipment (BUCHI SARL, Villebon-sur-Yvette, France) using 40–50 µm silica gel. NMR spectra were recorded at 298K on a Bruker DRX400 (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) spectrometer (Bruker France SAS, Wissembourg, France). The chemical shifts are reported in ppm (δ) relative to residual solvent peak and coupling constant are reported in Hz. NMR assignments were made using additional 2D NMR (COSY, HSQC and HMBC). The FTIR spectra were recorded on a IRAffinity 1—SHIMADZU FTIR spectrometer (Shimadzu

France, Marne-la-Vallée, France). High-Resolution Mass Spectrometry (HRMS) data were obtained by using Bruker micrOTOF-Q spectrometer (Champs-sur-Marne, France).

*3.1. Di-tert-butyl 3,3′-(2,2′-Bipyridine-6,6′-diyl)(2E,2′E)-diacrylate (**2**)*

In a G10 microwave tube, $Pd(OAc)_2$ (4 mg, 0.02 mmol, 0.05 eq) and 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl, SPhos (13 mg, 0.03 mmol, 0.1 eq), 6,6′-dibromo-2,2′-bipyridyl (100 mg, 0.32 mmol, 1 eq), Et_3N (0.35 mL, 2.55 mmol, 8 eq) and tert-butyl acrylate (0.1 mL, 0.80 mmol, 2.5 eq) were dissolved in dry DMF (1.6 mL). The reaction mixture was heated at 160 °C, for 1 h under microwave irradiation (60 W). The reaction mixture was then diluted in CH_2Cl_2 and filtered over a celite pad. The solvent was removed under reduced pressure to yield a yellow powder. The crude mixture was purified by flash chromatography (SiO_2 12 g, solid deposit, 1:0 to 95:05 Cyclohexane/DCM) to yield (**2**) as a yellowish solid (102 mg, 78% yield).

R_f (Cyclohexane/EtOAc 90:10) = 0.5

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.53 (d, *J* = 7.9 Hz, 2H, $H_{3,3'}$), 7.84 (t, *J* = 7.8 Hz, 2H, $H_{4,4'}$), 7.65 (d, *J* = 15.6 Hz, 2H, $H_{7,7'}$), 7.42 (d, *J* = 7.6 Hz, 2H, $H_{5,5'}$), 7.00 (d, *J* = 15.6 Hz, 2H, $H_{8,8'}$), 1.56 (s, 18H, $H_{11–13,11'–13'}$)

^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.27 ($C_{9,9'}$), 155.98 ($C_{2,2'}$), 152.53 ($C_{6,6'}$), 142.46 ($C_{8,8'}$), 137.77 ($C_{4,4'}$), 124.60 ($C_{7,7'}$), 124.42 ($C_{5,5'}$), 121.76 ($C_{3,3'}$), 80.93 ($C_{10,10'}$), 28.35 ($C_{11–13,11'–13'}$).

FTIR (cm^{-1}): 2790–3030 (C-H_{arom}), 1700 (C=O)

HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{24}H_{29}N_2O_4$ 409.2127; found, 409.2134

*3.2. (2E,2′E)-3,3′-(2,2′-Bipyridine-6,6′-diyl)diacrylic Acid (**3**)*

To an ice-cooled solution of di-tert-butyl 3,3′-(2,2′-bipyridine-6,6′-diyl)(2*E*,2′*E*)-diacrylate (**2**) (102 mg, 0.25 mmol, 1 eq) in CH_2Cl_2 (1.5 mL), TFA (1.5 mL) was added dropwise. The reaction was stirred and allowed to warm to room temperature for 2 h. The solvent was then removed under reduced pressure. The crude mixture was diluted in CH_2Cl_2 and evaporated 5 times to afford (**3**) as a yellowish powder (70 mg, 95% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.61 (s, 2H, $H_{10,10'}$), 8.50 (d, *J* = 7.9 Hz, 2H, $H_{3,3'}$), 8.04 (t, *J* = 7.8 Hz, 2H, $H_{4,4'}$), 7.81 (d, *J* = 7.6 Hz, 2H, $H_{5,5'}$), 7.70 (d, *J* = 15.7 Hz, 2H, $H_{7,7'}$), 7.02 (d, *J* = 15.7 Hz, 2H, $H_{8,8'}$).

^{13}C NMR (101 MHz, DMSO-d_6) δ: 167.27 ($C_{9,9'}$), 154.90 ($C_{2,2'}$), 151.95 ($C_{6,6'}$), 142.79 ($C_{7,7'}$), 138.56 ($C_{4,4'}$), 125.08 ($C_{5,5'}$), 123.18 ($C_{8,8'}$), 121.42 ($C_{3,3'}$).

FTIR (cm^{-1}): 2700–3200 (O-H), 2330–2680 (C-H_{arom}), 1677 (C=O)

HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{13}N_2O_4$ 297.0875; found, 297.0874

4. Conclusions

In this work, a new building block for ligand design was synthesized and fully characterized by ^{1}H NMR, ^{13}C NMR, COSY, HSQC, HMBC, FTIR spectroscopy, and HRMS.

The two carboxylic acid groups provide convenient handles for further functionalization, making compound (**3**) a new bifunctional building block for the preparation of functionalized bipyridine derivatives and, consequently, more elaborate ligands.

Supplementary Materials: The following supporting information can be downloaded online. Figure S1: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound (**2**); Figure S2: ^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound (**2**); Figure S3: COSY spectrum (^{1}H- ^{1}H, $CDCl_3$) of compound (**2**); Figure S4: HSQC spectrum (^{1}H- ^{13}C, $CDCl_3$) of compound (**2**); Figure S5: HMBC spectrum (^{1}H- ^{13}C, $CDCl_3$) of compound (**2**); Figure S6: HRMS spectrum (ESI-TOF) of compound (**2**); Figure S7: FTIR spectrum of compound (**2**); Figure S8: ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound (**3**); Figure S9: ^{13}C NMR spectrum (101 MHz, DMSO-d_6) of compound (**3**); Figure S10: COSY spectrum (^{1}H- ^{1}H, DMSO-d_6) of compound (**3**); Figure S11: HSQC spectrum (^{1}H- ^{13}C, DMSO-d_6) of compound (**3**);

Figure S12: HMBC spectrum (^{1}H- ^{13}C, DMSO-d_6) of compound (**3**); Figure S13: HRMS spectrum (ESI-TOF) of compound (**3**); Figure S14: FTIR spectrum of compound (**3**).

Author Contributions: Conceptualization, M.V. and F.D.-C.; investigation, T.H.; writing—original draft preparation, T.H.; writing—review and editing, M.V. and F.D.-C.; supervision, M.V. and F.D.-C.; funding acquisition, M.V. and F.D.-C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Lorraine Université d'Excellence (LUE) program of Université de Lorraine, which supported the project and associated research activities.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding authors.

Acknowledgments: The authors gratefully acknowledge the CPM NMR facility of Université de Lorraine. The authors greatly acknowledge the Plateforme PhotoNS of the L2CM Laboratory, University of Lorraine. We thank François Dupire from the mass spectrometry MassLor platform of Lorraine University and Philippe Pierrat for the introduction and training on microwave-assisted organic synthesis.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

SPhos	2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
DMF	*N*,*N*-Dimethylformamide
TLC	Thin Layer Chromatography
MW	Microwave
HRMS	High-Resolution Mass Spectrometry
FT-IR	Fourier-transform infrared spectroscopy

References

1. Constable, E.C.; Housecroft, C.E. The Early Years of 2,2′-Bipyridine—A Ligand in Its Own Lifetime. *Molecules* **2019**, *24*, 3951. [CrossRef] [PubMed]
2. Balzani, V.; Ceroni, P.; Credi, A.; Venturi, M. Ruthenium Tris(Bipyridine) Complexes: Interchange between Photons and Electrons in Molecular-Scale Devices and Machines. *Coord. Chem. Rev.* **2021**, *433*, 213758. [CrossRef]
3. Bourgois, C.; Troian-Gautier, L.; Kitzmann, W.R. $[Ru(Bpy)_3]^{2+}$: The Ongoing Story of a Photochemical Icon. *Inorg. Chem.* **2026**, *65*, 7549–7577. [CrossRef] [PubMed]
4. Kaes, C.; Katz, A.; Hosseini, M.W. Bipyridine: The Most Widely Used Ligand. A Review of Molecules Comprising at Least Two 2,2′-Bipyridine Units. *Chem. Rev.* **2000**, *100*, 3553–3590. [CrossRef] [PubMed]
5. Rodriguz-Ubis, J.; Alpha, B.; Plancherel, D.; Lehn, J. Photoactive Cryptands. Synthesis of the Sodium Cryptates of Macrobicyclic Ligands Containing Bipyridine and Phenoanthroline Groups. *Helv. Chim. Acta* **1984**, *67*, 2264–2269. [CrossRef]
6. Bkouche-Waksman, I.; Guilhem, J.; Pascard, C.; Alpha, B.; Deschenaux, R.; Lehn, J.-M. Crystal Structures of the Lanthanum(III), Europium(III), and Terbium(III) Cryptates of Tris(Bipyridine) Macrobicyclic Ligands. *Helv. Chim. Acta* **1991**, *74*, 1163–1170. [CrossRef]
7. Hussein, H.; Varbanov, M.; Fournier, B.; Dumarçay-Charbonnier, F. Towards the Design, Synthesis and Preliminary Biological Evaluation of Potential Corono and Clipcarbenes: Novel *Bis*-Imidazolium-*Bis*-Heterocycle Macrocyclic Ligands. *Tetrahedron Lett.* **2021**, *79*, 153288. [CrossRef]
8. Hussein, H.; Wang, M.; Kunstek, H.; Hergot, T.; Philippot, S.; Frochot, C.; Arnoux, P.; Fournier, B.; Varbanov, M.; Dumarçay-Charbonnier, F. New Corono Asymmetrical N-Bis-Heterocyclic Bis-Imidazolium Macrocycle Salt, Preliminary Physicochemical Studies, X-Ray Structures, and Biological Evaluation. *J. Heterocycl. Chem.* **2025**, *62*, 1840–1846. [CrossRef]

9. Newkome, G.R.; Kiefer, G.E.; Matsumura, N.; Puckett, W.E. Chemistry of Heterocyclic Compounds Series. 110. Synthesis of Vinyl Derivatives of Phenanthroline and Bipyridine. *J. Org. Chem.* **1985**, *50*, 3807–3810. [CrossRef]
10. Ali, A.; Hussain, M.; Malik, I.; Villinger, A.; Fischer, C.; Langer, P. Double *Heck* Cross-Coupling Reactions of Dibrominated Pyridines. *Helv. Chim. Acta* **2010**, *93*, 1764–1772. [CrossRef]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.