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Vincent Gutierrez, Axel Arnault, Véronique Ferreira, Albert Artigas, Denis Hagebaum-Reignier, et al.. Synthesis, Photophysical Properties, and Aromaticity of Pyrazine-Fused Tetrazapentalenes. *Journal of Organic Chemistry*, 2022, 87 (21), pp.13653-13662. 10.1021/acs.joc.2c01308 . hal-03856904

HAL Id: hal-03856904

<https://hal.science/hal-03856904v1>

Submitted on 17 Nov 2022

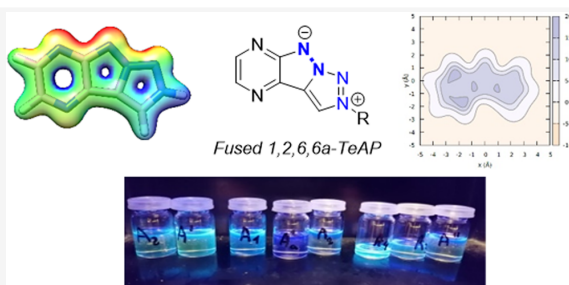
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Synthesis, Photophysical Properties, and Aromaticity of Pyrazine-Fused Tetrazapentalenes

Vincent S. Gutierrez, Axel Arnault, Véronique Ferreira, Albert Artigas, Denis Hagebaum-Reignier, Yannick Carissan, Yoann Coquerel,* Marie-Aude Hiebel,* and Franck Suzenet*

ABSTRACT: Pyrazine-fused 1,2,6,6a-tetrazapentalenes (PyTeAP) are zwitterionic tricyclic compounds exhibiting an original pattern with four consecutive nitrogen atoms. They were obtained by a challenging cyclization through the formation of a N–N bond under thermolytic conditions. Ten derivatives were synthesized, and the original scaffold of PyTeAP was confirmed by single-crystal X-ray diffraction analysis of one derivative. Examination of their photophysical properties in solution revealed blue fluorescence with $\lambda_{em} = 416\text{--}426\text{ nm}$. Theoretical investigations of the aromaticity in these compounds through magnetic criteria evidenced the presence of a dominant 14-electron circuit at the periphery.

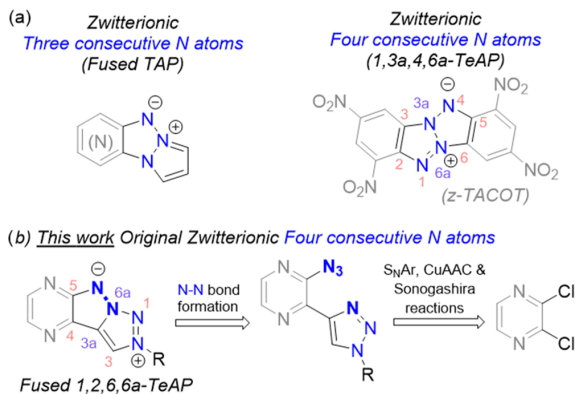


INTRODUCTION

Pentalene is an archetypal antiaromatic bicyclic hydrocarbon molecule, but its neutral nitrogen-containing analogues, the azapentalenes, can be aromatic according to Hückel's rules as a function of the number of nitrogen atoms introduced, their position and substitutions. For instance, the 1,3a,6a-triazapentalene (TAP) is a zwitterionic aromatic heterocycle with three consecutive nitrogen atoms of which two are at the bicyclic ring junction. The intramolecular charge transfer that can occur in this family of compounds has been particularly studied to produce compact organic fluorophores, either as simple bicyclic systems^{1–6} or as larger molecules when the azapentalene bicyclic system is fused to various heterocyclic scaffolds (Scheme 1a).^{7–11} They possess an amphiphilic character particularly interesting for biological imaging applications.^{12–15} With an additional nitrogen atom, zwitterionic tetrazapentalene analogue (TeAP) remains more confidential and were developed for energetic applications.^{16–19} Among them, z-TACOT and derivatives exhibit a unique pattern with four consecutive nitrogen atoms arranged in a Z shape, which was even recently flanked with various energy-rich fragments such as benzofuroxan or 1,2,3,4-tetrazine 1,3-dioxane.^{20–22}

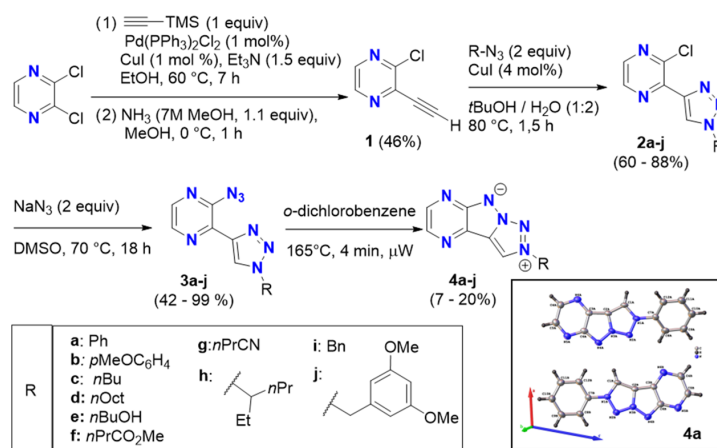
Herein, we propose the synthesis of tricyclic zwitterionic pyrazine-fused tetrazapentalene derivatives (PyTeAP) having four consecutive nitrogen atoms on one edge of the molecule, featuring a challenging cyclization step through formation of a N–N bond. The introduction of a pyrazine-fused ring rather than a phenyl, a pyridine, or a pyrimidine fused ring to enhance intramolecular charge transfer properties was guided by our

Scheme 1. (a) Known Zwitterionic Polyazapentalenes. (b) Retrosynthetic Approach to Pyrazine-Fused Tetrazapentalene Derivatives (PyTeAP)



recent work⁷ and using molecular electrostatic potential maps of some candidate molecules (see Figure S5 in the Supporting Information). A series of PyTeAP derivatives were obtained

Scheme 2. Synthesis of PyTeAP 4a–j and Single-Crystal X-ray Diffraction Analysis of 4a at 150 K (CCDC Registration Number 2168242)^a



^aEllipsoids are drawn at 50% probability.

Table 1. Fluorescence Properties

	$\lambda_{\text{Abs}}[\text{nm}]^a$	$\lambda_{\text{em}}[\text{nm}]^b$	$\Delta[\text{nm}]^c$	ϵ_{max}^d	ϕ_{F}^e
Ph (4a)	334	420	86	10755	0.12
<i>p</i> MeO-C ₆ H ₄ (4b)	292	426	134	21100	0.06
<i>n</i> Bu (4c)	374	423	49	7242	0.34
<i>n</i> Oct (4d)	374	421	47	4300	0.22
(4e)	373	424	51	9221	0.38
(4f)	372	419	47	3560	0.34
(4g)	364	419	55	5513	0.32
(4h)	374	422	48	9247	0.36
Bn (4i)	373	419	46	4938	0.38
(4j)	373	416	43	3728	0.19

^aApparent maxima of absorption bands. ^bApparent maxima of emission bands. ^cStokes Shift calculated as the difference between the maxima of absorption and emission bands. ^dUnits: L·mol⁻¹·cm⁻¹. ^e ϕ_{F} is the fluorescence quantum yield determined using anthracene ($\phi_{\text{F}} = 0.28$ in EtOH) as a reference standard.

and fully characterized, including their fluorescence properties. Aromaticity and π -electron delocalization in these molecules were analyzed theoretically through magnetic criteria.

RESULTS AND DISCUSSION

It was devised that the required azide precursors **3** for the key N–N bond forming step could be obtained by a Sonogashira cross-coupling/copper-catalyzed alkyne–azide cycloaddition (CuAAC)/S_NAr sequence from commercially available 2,3-dichloropyrazine (Scheme 1b). The nitrene chemistry developed from primary amine with a PIDA-mediated oxidative cyclization was attempted but led to a sulfoximine when dimethyl sulfoxide (DMSO) was used as solvent^{23,24} or to degradation in *N,N*-dimethylformamide confirming the need to introduce an azide as the nitrene precursor (see Supporting Information Section I for details). For this purpose,

an efficient Sonogashira cross-coupling reaction was performed on 2,3-dichloropyrazine with trimethylsilyl acetylene followed by a deprotection step of the alkyne and a CuAAC step with various alkyl and aryl azides to afford the chloropyrazine derivatives **2a–j** (Scheme 2). Using compound **2a** as a prototype, it was found that introduction of the required azide moiety can be achieved through an aromatic nucleophilic substitution of the chlorine atoms with sodium azide to afford **3a** in 59% yield. An alternative synthetic route to compound **3a** relying on an earlier introduction of its azide substituent was developed but was found less efficient (see Supporting Information Section II for details).

With compound **3a** in hand, the key cyclization step was performed. After some experimentation (see Supporting Information Section IV for details), it was found that heating a solution of **3a** at 165 °C for 4 min in *o*-dichlorobenzene

afforded the tricyclic PyTeAP product **4a** in 20% yield, the structure of which was secured by single-crystal X-ray diffraction analysis (see Supporting Information Section V). The low yield of formation of **4a** results, in part, from the thermal instability of **4a** under the reaction conditions. The options available for varying the nature of the substituent on the N2 nitrogen atom were explored. Several aromatic and aliphatic (linear or branched) substituents bearing electron-withdrawing (CO₂Me, CN) or electron-donating groups (OMe, OH) could be introduced on precursors **3a–j**. Thermolysis of these intermediates afforded the desired PyTeAP derivatives **4a–j**, albeit in consistently low yields.

The analysis of fluorescence properties (Table 1, see Supporting Information Section IX for details) highlights that this original PyTeAP family emits in blue wavelengths (416–426 nm) in dichloromethane (DCM) with a medium Stokes shift. The nature of the substituents on the triazole part barely affects the excitation and emission wavelengths but has a strong impact on the molar absorption coefficient (ϵ) and the quantum yields (ϕ_F). While aromatic substituents (**4a–b**) gave rise to the largest ϵ in agreement with the extended π -conjugation, their rather low ϕ_F moderates their global performance (brightness $\phi_F \cdot \epsilon_{\max}$ ca. 1200). The opposite observations are made when an alkyl chain is involved, and consequently, these compounds (**4c**, **4f**, **4g**, and **4i**) exhibit the same performance (brightness ca. 1800). The best results were obtained for **4e** and **4h** with a brightness of 3500 and 3300, respectively.

Electronic effects in the pyrazine-fused tetrapentalene derivative PyTeAP-H (R = H) were first evaluated by identifying some of its most relevant mesomeric resonance structures. Using the Hulis code,²⁵ the three resonance structures PyTeAP-Ha (14%), PyTeAP-Hb (41%), and PyTeAP-Hc (45%) were found to provide a satisfactory description of resonance in PyTeAP-H at Hückel level with a “trust factor” of 83.3% (Figure 1a). Notably, this suggests that the negative charge in PyTeAP-H can easily delocalize onto a nitrogen atom of the pyrazine ring, which is supported by its molecular electrostatic potential map (Figure 1b).

Aromaticity and π -electron delocalization in the pyrazine-fused tetrapentalene derivative PyTeAP-H and its individual cyclic constituents were evaluated by means of two popular magnetic criteria,²⁶ namely, the calculation of Nucleus Independent Chemical Shift (NICS)^{27,28} and the analysis of the Anisotropy of the Induced Current Density (AICD).^{29,30} Calculation of both isotropic NICS_{iso} and anisotropic NICS_{zz}, including π -only NICS _{π ,zz} calculations, as single points in PyTeAP-H indicated that all its three rings have an aromatic character, apparently comparable with the aromatic character of each individual cyclic or bicyclic constituents computed separately (Table 2). NICS calculations have proven of considerable value in the past, but they can be misinterpreted or overinterpreted, and it should be kept in mind that NICS is an indirect method that incurs a loss of information on the magnetic field it senses. This is thoroughly discussed in contemporaneous specialized literature, and the interested reader is invited to consult some of the excellent reviews available on the topic.^{26,28}

Apart from the standard single-point approach, richer pictures of NICS in molecules can be obtained by mapping NICS or the corresponding magnetic shielding σ (the negative of NICS), using two-dimensional (2D)^{31,32} and three-dimensional (3D) grids.^{33,34} Mapping isotropic magnetic shielding

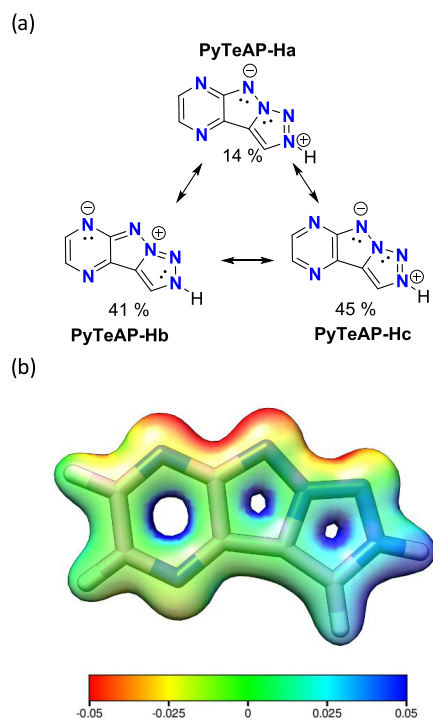
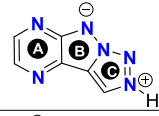
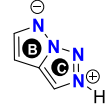





Figure 1. (a) Major resonance structures of PyTeAP-H (along with their relative weights). (b) Molecular electrostatic potential map of PyTeAP-H (isosurface with electron density = 0.07).

$[\sigma_{\text{iso}} = -\text{NICS}_{\text{iso}} = (\sigma_{xx} + \sigma_{yy} + \sigma_{zz})/3]$ in a plane located at 1 Å from the molecular plane provided the 2D σ_{iso} maps of PyTeAP-H and its individual cyclic constituents (Figure 2, left). The results for the corresponding anisotropic σ_{zz} ($= -\text{NICS}_{zz}$) maps are detailed in the Supporting Information (Figure S4 section VI). The 2D σ_{iso} maps offered a bird’s-eye view of the magnetic shielding in these systems, helping at perceiving their electron delocalization and aromaticity pattern.^{31,32,35} They should be interpreted as follows: blue areas indicate π electron delocalization with shades correlating with the intensity of the delocalization, and circular dark blue areas over a ring should be interpreted as intense circular delocalization over this ring attributed to plain aromaticity as in benzene (see Supporting Information example in Figure S3a). The 2D σ_{iso} map of PyTeAP-H indicates that moderate electron delocalization occurs over all of the tricyclic system and that somehow more intense aromaticity is localized over ring A. The 2D σ_{iso} maps of the individual cyclic (and bicyclic) constituents showed the patterns of their preferred 6-electron (and 10-electron) circuits, which are not comparable with the pattern visualized in the 2D σ_{iso} map of PyTeAP-H. While the single-point NICS analyses in Table 2 may lead to the conclusion that aromaticity in PyTeAP-H is resembling the sum of the “local aromaticity” of its individual components, the 2D σ_{iso} maps allow to visualize clearly it is not the case and to ascertain that aromaticity in PyTeAP-H is a global indivisible property of the molecule.

The AICD analysis^{29,30} of PyTeAP-H produced the corresponding isosurface (yellow color) and induced current density vectors (green arrows with red head) were plotted onto it (Figure 2). In the AICD representation of PyTeAP-H, an

Table 2. Single-Point NICS Calculations for PyTeAP-H and Its Individual Cyclic Constituents

	NICS _{iso} (0)	NICS _{iso} (1)	NICS _{zz} (0)	NICS _{zz} (1)	NICS _{π,zz} (1.7)
	A = -6.5 B = -12.6 C = -16.4	A = -10.1 B = -11.1 C = -12.0	A = -11.9 B = -9.6 C = -15.8	A = -27.1 B = -28.5 C = -33.1	A = -16.2 B = -14.4 C = -14.1
	B = -14.2 C = -15.4	B = -11.9 C = -11.2	B = -13.2 C = -12.8	B = -32.8 C = -31.4	B = -14.7 C = -13.6
	A = -5.3	A = -10.3	A = -12.7	A = -28.4	A = -15.9
	B = -13.6	B = -11.3	B = -15.1	B = -32.7	B = -13.1
	C = -14.1	C = -12.8	C = -19.6	C = -35.5	C = -12.8

inflate of the isosurface is visible at its edge indicating greater delocalization there, with a more pronounced effect over ring A. The current density analysis revealed a clear diatropic macrocyclic circuit of the 14 π electrons in the molecule.

Overall, the AICD and magnetic shielding analyses are consistent and indicate that PyTeAP-H is an aromatic tricyclic molecule with a macrocyclic 14-electron circuit preferred for the delocalization of its π electrons.

CONCLUSIONS

The tetraazapentalene (TeAP) class of molecules was enriched by the synthesis of 1,2,6a-TeAP isomers fused to a pyrazine ring, herein denominated PyTeAP. Their synthesis was conducted from 2,3-dichloropyrazine through a CuAAC and subsequent cyclization by N–N bond formation under thermolytic nitrene generation conditions. Ten derivatives were obtained and fully characterized including a structural analysis. These molecules exhibit an original planar tricyclic scaffold made of six carbon atoms and six nitrogen atoms, with four consecutive nitrogen atoms on one edge. The fluorescent properties of these small molecules in solution were established in the blue region of the visible spectra. Analysis of electron delocalization in these aromatic molecules was performed through magnetic criteria, which evidenced the presence of a dominant 14-electron circuit at their edges.

EXPERIMENTAL SECTION

General Remarks. Unless otherwise noted, all reagent-grade chemicals and commercially available solvents were used without further purification. Microwave-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by an IR sensor. Reactions were monitored by thin-layer chromatography (TLC) using aluminum sheets coated with silica gel 60 F254. Flash column chromatography was carried out using silica gel 60 Å (0.04–0.06 mm). Solvents mentioned as being dry were purified with a dry station GT S100 immediately prior to their use. PE refers to petroleum ether (bp: 40–60 °C) NMR spectra were recorded with a 250 MHz (¹H: 250 and ¹³C: 63 MHz), 300 MHz (¹H: 300 and ¹³C: 75 MHz), or 400 MHz (¹H: 400 and ¹³C: 100.7 MHz) Bruker spectrometer. Chemical shifts are given in parts per million (ppm) from tetramethylsilane (TMS), calibrated to the residual solvent peak. Coupling constants “J” are expressed in hertz (multiplicity: s = singlet, bs = broad singlet, d = doublet, dd = doublet,

doublet, dt = double triplet, t = triplet, q = quartet, m = multiplet). High-resolution accurate mass measurements (HRMS) were performed on a Bruker maXis (Q-TOF) mass spectrometer by the “Fédération de Recherche” ICOA/CBM (FR2708) platform, mass is given for the ³⁵Cl isotope. Melting points were measured in open capillary tubes.

All calculations were performed with the Gaussian16 package.³⁶ B3LYP hybrid density functional^{37,38} with the D3BJ correction for dispersion³⁹ and the def2-SVP basis set⁴⁰ without symmetry constraints. The corresponding .xyz files are provided in the Supporting Information. Analytical Hessians were computed to confirm that the optimized geometries are indeed minima (zero imaginary frequency). NMR-GIAO⁴¹ calculations of NICS or of the magnetic shielding σ were performed at the B3LYP-GIAO/6-311++G(d,p)⁴² level of theory, and the 2D σ_{iso} contour maps were generated as described previously.^{31,32} The NICS_{π,zz}(1.7) were calculated on ghost atoms located at 1.7 Å above the middle of each ring, as previously recommended^{43,44} within NBO6.0.⁴⁵ In this method, the contribution of the π electrons to the zz component of the chemical shift tensor is extracted from the canonic molecular orbitals.

For AICD calculations, the continuous set of gauge transformation (CSGT) method was used to calculate current densities,^{46,47} as implemented in the Gaussian16 package. The calculated current density was subsequently transformed in a rectangular grid and visualized as a cube-file with POVRAY.⁴⁸ The applied magnetic field is orthogonal to the molecular plane, pointing upward in all illustrations, with clockwise currents being diatropic.

Caution! Azide reagents are potentially hazardous.

General Procedure A for the Synthesis of 2a–j CuAAC Procedure.⁴⁹ 2-Chloro-3-ethynylpyrazine 1 (1 equiv) was dissolved into *t*BuOH/H₂O (1:2; 0.08 M) degassed. The azide reagent (2 equiv) and copper iodide (4 mol %) were added, respectively, and the media was stirred at 80 °C (using heating mantle) until the consumption of the starting material. *tert*-Butanol was concentrated under reduced pressure, and the crude compound was extracted three times with ethyl acetate. The organic layers were assembled, dried on MgSO₄, filtered, and concentrated. The desired compound was isolated after purification by flash chromatography.

General Procedure B for the Synthesis of 3a–j S_NAr Reaction.⁵⁰ Chlorinated compound (1 equiv) was dissolved in DMSO (1 M). Sodium azide (2 equiv) was added, and the reaction medium was stirred at 70 °C overnight (using heating mantle). After the consumption of the starting material, the reaction mixture was cooled down to room temperature, diluted with water (100 volumes), and the product was extracted three times with ethyl acetate. The organic

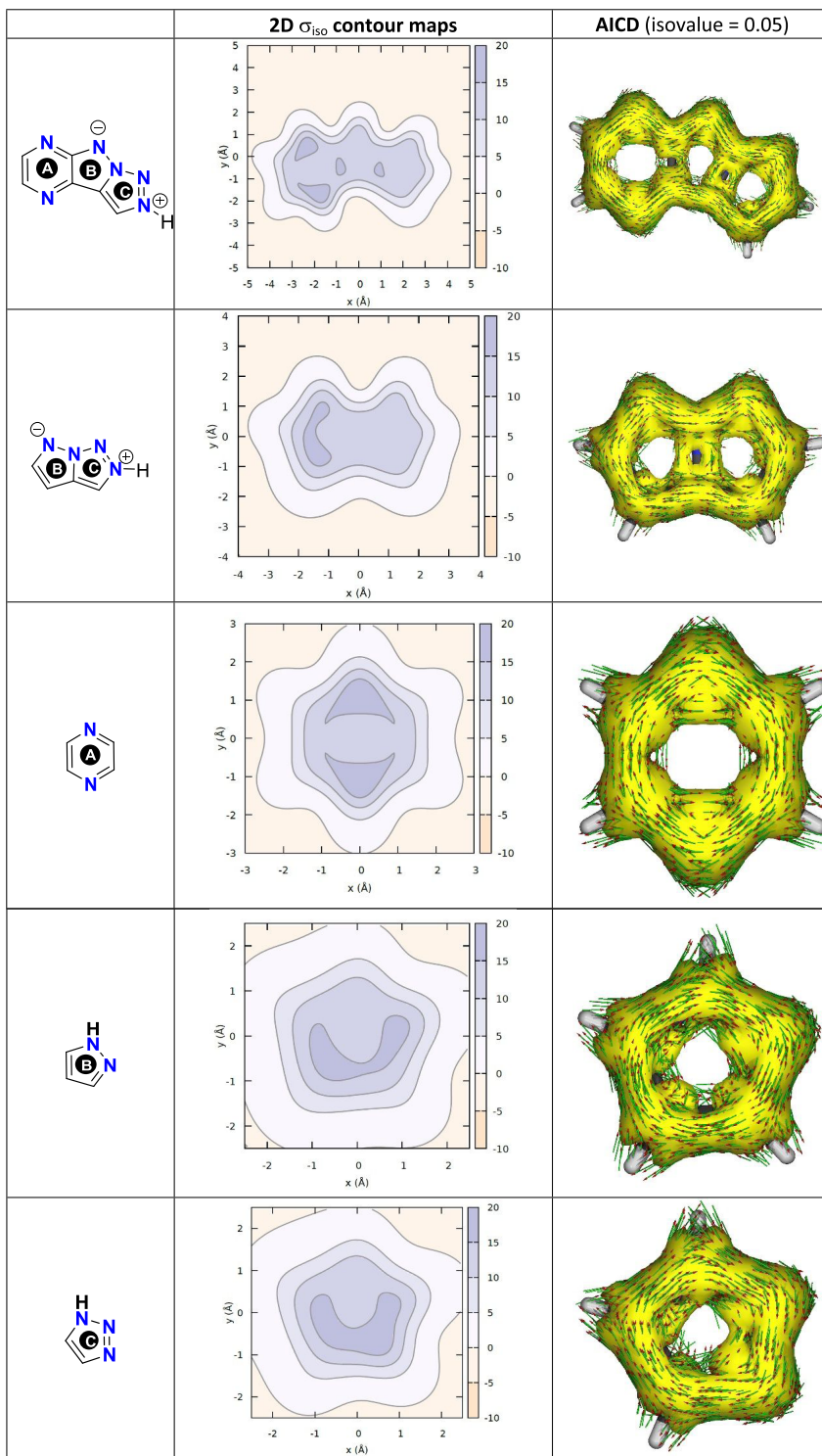


Figure 2. Magnetic shielding and AICD analyses of electron delocalization in PyTeAP-H and its individual cyclic constituents. For the current density analysis, the applied magnetic field is oriented perpendicular to the molecular plane pointing toward the observer.

layers were assembled and dried on MgSO₄. After filtration, the solvent was removed under pressure and the desired azide product was used without purification.

General Procedure C for the Synthesis of PyTeAP 4a–j. In a sealed tube, the azide derivative was dissolved into *o*-dichlorobenzene solution (0.05–0.08 M). The mixture was stirred at 165 °C for 4 min in a professional microwave reactor. The resulting material was directly purified by flash chromatography to give the corresponding tetrazapentane.

2-Chloro-3-ethynylpyrazine (1).⁵¹ 2,3-Dichloropyrazine (500 mg, 3.35 mmol, 1 equiv), Pd(PPh₃)₂Cl₂ (26 mg, 1 mol %), CuI (7 mg, 1 mol %), and NEt₃ (0.68 mL, 1.5 equiv) were dissolved in EtOH (11 mL). The reaction medium was degassed by argon sparging for 15 min at room temperature. Trimethylsilyl acetylene (0.50 mL, 1 equiv) was added dropwise, and the reaction was heated at 60 °C for 7 h (using heating mantle). The solvent was removed under vacuum, and the resulting material was dissolved in AcOEt and filtrated on celite. Water was added to the resulting filtrate (100 mL), and the mixture was extracted with ethyl acetate (3 × 50 mL). The organic layers were assembled, dried on MgSO₄, filtered, and concentrated under reduced pressure. The crude compound was purified by flash chromatography eluted with 98:2 PE/EtOAc to give the TMS compound as a yellow oil (402 mg, 1.91 mmol, 57%). Then, the product (1 equiv) was dissolved in methanol (0.15 M) and an ammonia solution (7 M in MeOH) (1.1 equiv) was added at 0 °C and stirred for 50 min. The solvent was concentrated under reduced pressure, water was added (100 mL), and the media was extracted with ethyl acetate (3 × 25 mL). The organic layers were assembled, dried on MgSO₄, filtered, and concentrated under reduced pressure to give the desired compound **1** as a beige solid (100 mg; 80%). *R*_f: 0.4 (9:1; PE/EtOAc). Mp: 54–55 °C. ¹H NMR (250 MHz, CDCl₃): δ_H 8.49 (d, *J* = 2.5 Hz, 1H), 8.33 (d, *J* = 2.5 Hz, 1H), 3.61 (s, 1H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 151.2 (C), 142.7 (CH), 142.4 (CH), 138.6 (C), 85.5 (CH), 78.5 (C). HRMS (ESI) *m/z*: [M + H]⁺ The molecular ion was not detected for this molecule. IR (neat): $\bar{\nu}$ (cm⁻¹) 3220, 2116, 1366, 1191, 1051, 869.

2-Chloro-3-(1-phenyl-1H-1,2,3-triazol-4-yl)pyrazine (2a). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (200 mg, 1.45 mmol) and azidophenyl (345 mg, 2.90 mmol), the title compound was obtained as a beige solid (282 mg, 1.1 mmol, 76%). *R*_f: 0.5 (3:7; PE/EtOAc). Mp: 97–98 °C. ¹H NMR (250 MHz, CDCl₃): δ_H 8.75 (s, 1H), 8.66 (d, *J* = 2.3 Hz, 1H), 8.37 (d, *J* = 2.3 Hz, 1H), 7.85–7.77 (m, 2H), 7.60–7.42 (m, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.3 (C), 144.2 (C), 144.0 (C), 142.7 (CH), 142.6 (CH), 136.7 (C), 130.0 (2CH), 129.4 (CH), 123.6 (CH), 121.0 (2CH). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₂H₉ClN₅, 258.0541; found 258.0540. IR (neat): $\bar{\nu}$ (cm⁻¹) 3174, 3050, 1503, 1411, 1240, 1064, 813.

2-Chloro-3-(1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)pyrazine (2b). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (200 mg, 1.45 mmol) and azidoanisole (432 mg, 2.90 mmol), the title compound was obtained as a beige solid (337 mg, 1.17 mmol, 81%). *R*_f: 0.5 (2:8; PE/EtOAc); Mp: 151–152 °C. ¹H NMR (250 MHz, CDCl₃): δ_H 8.66–8.65 (m, 2H), 8.36 (d, *J* = 2.3 Hz, 1H), 7.74–7.66 (m, 2H), 7.07–7.00 (m, 2H), 3.86 (s, 3H). ¹³C {¹H} NMR (63 MHz, CDCl₃): δ_C 160.3 (C), 146.2 (C), 144.3 (C), 143.7 (C), 142.7 (CH), 142.5 (CH), 130.1 (C), 123.7 (CH), 122.6 (2CH), 115.0 (2CH), 55.8 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₃H₁₁ClN₅O, 288.0646; found 288.0649. IR (neat): $\bar{\nu}$ (cm⁻¹) 2971, 1517, 1436, 1161, 1053, 988, 811.

2-Chloro-3-(1-butyl-1H-1,2,3-triazol-4-yl)pyrazine (2c). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (398 mg, 2.88 mmol) and azidobutane (571 mg, 5.76 mmol), the title compound was obtained as a light yellow solid (603 mg, 2.54 mmol, 88%). *R*_f: 0.5 (7:3; EtOAc/PE). Mp: 69–70 °C. ¹H NMR (400 MHz, CDCl₃): δ_H 8.62 (d, *J* = 2.3 Hz, 1H), 8.32 (d, *J* = 2.3 Hz, 1H), 8.31 (s, 1H), 4.46 (t, *J* = 7.2 Hz, 2H), 1.95 (tt, *J* = 9.2, 6.8 Hz, 2H), 1.48–1.31 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.0 (C), 144.5 (C), 143.1 (C), 142.7 (CH), 142.3 (CH), 125.3 (CH), 50.5 (CH₂), 32.4 (CH₂), 19.8 (CH₂), 13.5

(CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₃ClN₅, 238.0854; found 238.0854. IR (neat): $\bar{\nu}$ (cm⁻¹) 2959, 1464, 1233, 1059, 976, 862.

2-Chloro-3-(1-octyl-1H-1,2,3-triazol-4-yl)pyrazine (2d). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (400 mg, 2.90 mmol) and azidooctane (900 mg, 5.80 mmol), the title compound was obtained as a beige solid (755 mg, 2.58 mmol, 88%). *R*_f: 0.8 (7:3; EtOAc/PE). Mp: 75–76 °C. ¹H NMR (400 MHz, CDCl₃): δ_H 8.62 (d, *J* = 2.4 Hz, 1H), 8.32 (d, *J* = 2.4 Hz, 1H), 8.31 (s, 1H), 4.45 (t, *J* = 7.2 Hz, 2H), 1.97 (t, *J* = 7.2 Hz, 2H), 1.38–1.22 (m, 10H), 0.88–0.82 (m, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.1 (C), 144.6 (C), 143.1 (C), 142.7 (CH), 142.3 (CH), 125.3 (CH), 50.8 (CH₂), 31.8 (CH₂), 30.4 (CH₂), 29.1 (CH₂), 29.0 (CH₂), 26.5 (CH₂), 22.7 (CH₂), 14.1 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₄H₂₁ClN₅, 294.1480; found 294.1482. IR (neat): $\bar{\nu}$ (cm⁻¹) 2921, 1470, 1235, 1150, 1069, 985, 880, 745.

4-(4-(3-Chloropyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butan-1-ol (2e). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (400 mg, 2.90 mmol) and azidobutanol (670 mg, 5.80 mmol), the title compound was obtained as a yellow oil (414 mg, 1.64 mmol, 56%). *R*_f: 0.1 (7:3; EtOAc/PE). ¹H NMR (400 MHz, CDCl₃): δ_H 8.63 (br, 1H), 8.36 (s, 1H), 8.34 (br, 1H), 4.54 (t, *J* = 7.2 Hz, 2H), 3.71 (t, *J* = 6.1 Hz, 2H), 2.11 (dq, *J* = 9.2, 7.3 Hz, 2H), 1.66–1.62 (m, 2H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.1 (C), 144.5 (C), 143.2 (C), 142.7 (CH), 142.4 (CH), 125.6 (CH), 62.0 (CH₂), 50.6 (CH₂), 29.3 (CH₂), 27.2 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₃ClN₅O, 254.0803; found 254.0802. IR (neat): $\bar{\nu}$ (cm⁻¹) 3420, 1329, 1154, 1056, 980, 745.

Methyl 4-(4-(3-Chloropyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butanoate (2f). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (200 mg, 1.45 mmol) and methyl 4-azidobutanoate (415 mg, 2.90 mmol), the title compound was obtained as a yellow solid (339 mg, 1.21 mmol, 83%). *R*_f: 0.3 (2:8; PE/EtOAc). Mp: 80 °C. ¹H NMR (400 MHz, CDCl₃): δ_H 8.63 (d, *J* = 2.4 Hz, 1H), 8.35–8.32 (m, 2H), 4.56 (t, *J* = 6.9 Hz, 2H), 3.68 (s, 3H), 2.45–2.40 (m, 2H), 2.31 (pd, *J* = 6.9, 1.2 Hz, 2H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 172.8 (C), 146.1 (C), 144.4 (C), 143.3 (C), 142.7 (CH), 142.4 (CH), 125.7 (CH), 52 (CH₃), 49.6 (CH₂), 30.5 (CH₂), 25.6 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₁H₁₃ClN₅O₂, 282.0752; found 282.0748. IR (neat): $\bar{\nu}$ (cm⁻¹) 3158, 2957, 1716, 1428, 1222, 1047, 973.

4-(4-(3-Chloropyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butanenitrile (2g). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (400 mg, 2.90 mmol) and 4-azidobutanenitrile (638 mg, 5.80 mmol), the title compound was obtained as a beige solid (688 mg, 2.77 mmol, 87%). *R*_f: 0.3 (7:3; EtOAc/PE); Mp: 119–120 °C. ¹H NMR (400 MHz, CDCl₃): δ_H 8.64 (br, 1H), 8.40 (s, 1H), 8.36 (br, 1H), 4.64 (t, *J* = 6.5 Hz, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.40 (p, *J* = 6.7 Hz, 2H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.2 (C), 144.1 (C), 143.5 (C), 142.7 (2CH), 126.1 (CH), 118.1 (C), 48.7 (CH₂), 26.0 (CH₂), 14.7 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₀ClN₆, 249.0650; found 249.0654. IR (neat): $\bar{\nu}$ (cm⁻¹) 3131, 2245, 1543, 1400, 1120, 1061, 978, 857, 783.

2-Chloro-3-(1-(hexan-3-yl)-1H-1,2,3-triazol-4-yl)pyrazine (2h). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (400 mg, 2.90 mmol) and 3-azidohexane (552 mg, 5.80 mmol), the compound was obtained as a white solid (302 mg, 1.14 mmol, 39%). *R*_f: 0.6 (7:3; EtOAc/PE). Mp: 43–44 °C. ¹H NMR (400 MHz, CDCl₃): δ_H 8.63 (d, *J* = 2.3 Hz, 1H), 8.33 (d, *J* = 2.3 Hz, 1H), 8.26 (s, 1H), 4.56–4.49 (m, 1H), 2.01–1.84 (m, 4H), 1.32–1.14 (m, 2H), 0.92–0.84 (m, 6H). ¹³C {¹H} NMR (101 MHz, CDCl₃): δ_C 146.1 (C), 144.7 (C), 143.1 (C), 142.6 (CH), 142.3 (CH), 124.0 (CH), 64.1 (CH), 37.5 (CH₂), 29.0 (CH₂), 19.3 (CH₂), 13.7 (CH₃), 10.6 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₁H₁₇ClN₅, 266.1167; found 266.1170. IR (neat): $\bar{\nu}$ (cm⁻¹) 2961, 1364, 1250, 1149, 1086, 869, 760.

2-(1-Benzyl-1H-1,2,3-triazol-4-yl)-3-chloropyrazine (2i). Following **general procedure A** from 2-chloro-3-ethynylpyrazine **1** (400 mg, 2.90 mmol, 1 equiv) and azidobenzyle (772 mg, 5.80 mmol), the

title compound was obtained as a beige solid (688 mg, 2.54 mmol, 87%). R_f : 0.5 (1:1; PE/EtOAc). Mp: 114–115 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.61 (d, $J = 2.4$ Hz, 1H), 8.32 (d, $J = 2.4$ Hz, 1H), 8.24 (s, 1H), 7.39–7.36 (m, 3H), 7.33–7.30 (dd, $J = 7.5, 2.2$ Hz, 2H), 5.64 (s, 2H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 146.1 (C), 144.4 (C), 143.7 (C), 142.6 (CH), 142.4 (CH), 134.3 (C), 129.4 (2CH), 129.1 (CH), 128.2 (2CH), 125.5 (CH), 54.5 (CH_2). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{11}\text{ClN}_5$ 272.0697; found 272.0696. IR (neat): $\bar{\nu}$ (cm^{-1}) 2921, 1494, 1337, 1229, 1150, 982, 720.

2-Chloro-3-(1-(3,5-dimethoxybenzyl)-1H-1,2,3-triazol-4-yl)pyrazine (2j). Following **general procedure A** from 2-chloro-3-ethylpyrazine **1** (400 mg, 2.90 mmol) and 1-(azidomethyl)-3,5-dimethoxybenzene (1.11 g; 5.80 mmol), the title compound was obtained as a brown solid (665 mg, 2.01 mmol, 69%). R_f : 0.5 (3:7; PE/EtOAc). Mp: 121–122 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.63 (br, 1H), 8.33 (d, $J = 2.1$ Hz, 1H), 8.27 (s, 1H), 6.45–6.44 (m, 3H), 5.56 (s, 2H), 3.76 (s, 6H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 161.6 (C), 146.2 (C), 144.4 (C), 143.8 (C), 142.7 (CH), 142.5 (CH), 136.4 (C), 125.5 (CH), 106.3 (2CH), 100.8 (CH), 55.6 (2 CH_3), 54.6 (CH_2). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{15}\text{ClN}_5\text{O}_2$ 332.0909; found 332.0912. IR (neat): $\bar{\nu}$ (cm^{-1}) 2942, 1600, 1353, 1050, 861, 679.

2-Azido-3-(1-phenyl-1H-1,2,3-triazol-4-yl)pyrazine (3a). Following **general procedure B** from compound **2a** (99 mg, 0.38 mmol), the title compound was obtained as a white solid (59 mg, 0.22 mmol, 59%). R_f : 0.6 (1:1; DCM/EtOAc). Mp: 220 °C. ^1H NMR (250 MHz, $\text{DMSO}-d_6$): δ_{H} 9.77 (s, 1H), 9.44 (d, $J = 4.6$ Hz, 1H), 8.53 (d, $J = 4.6$ Hz, 1H), 8.10 (bd, $J = 7.4$ Hz, 2H), 7.67 (bdd, $J = 8.0, 7.1$ Hz, 2H), 7.57 (bdd, $J = 7.4, 7.1$ Hz, 1H). ^{13}C $\{^1\text{H}\}$ NMR (63 MHz, $\text{DMSO}-d_6$): δ_{C} 142.8 (C), 142.3 (C), 142.2 (C), 136.2 (C), 133.3 (CH), 130.0 (2CH), 129.3 (CH), 125.7 (CH), 120.7 (2CH); 118.7 (CH). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_9\text{N}_8$ 265.0944; found 265.0942. IR (neat): $\bar{\nu}$ (cm^{-1}) 3091, 1571, 1497, 1426, 1255, 1041, 809, 758.

2-Azido-3-(1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)pyrazine (3b). Following **general procedure B** from compound **2b** (279 mg, 0.97 mmol), the title compound was obtained as a white solid (121 mg, 0.41 mmol, 42%). R_f : 0.5 (1:1; DCM/EtOAc). Mp: 207 °C. ^1H NMR (250 MHz, $\text{DMSO}-d_6$): δ_{H} 9.65 (s, 1H), 9.42 (d, $J = 4.6$ Hz, 1H), 8.52 (d, $J = 4.6$ Hz, 1H), 8.00 (d, $J = 9.2$ Hz, 2H), 7.19 (d, $J = 9.2$ Hz, 2H), 3.86 (s, 3H). ^{13}C $\{^1\text{H}\}$ NMR (63 MHz, $\text{DMSO}-d_6$): δ_{C} 159.7 (C), 142.6 (C), 142.3 (C), 142.1 (C), 133.3 (CH), 129.5 (C), 125.5 (CH), 122.3 (2CH), 118.6 (CH), 114.9 (2CH), 55.6 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{11}\text{N}_8\text{O}$ 295.1050; found 295.1050. IR (neat): $\bar{\nu}$ (cm^{-1}) 3102, 1575, 1467, 1303, 1165, 1022, 835.

Azido-3-(1-butyl-1H-1,2,3-triazol-4-yl)pyrazine (3c). Following **general procedure B** from compound **2c** (100 mg, 0.42 mmol), the title compound was obtained as a white solid (74 mg, 0.30 mmol, 72%). R_f : 0.4 (7:3; EtOAc/PE). Mp: 119–120 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 9.04 (s, 1H), 8.72 (d, $J = 4.6$ Hz, 1H), 8.43 (d, $J = 4.6$ Hz, 1H), 4.56 (t, $J = 7.3$ Hz, 2H), 2.06–1.99 (m, 2H), 1.48–1.39 (m, 2H), 1.01 (t, $J = 7.4$ Hz, 3H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 143.5 (C), 142.2 (C), 141.6 (C), 133.8 (CH), 128.0 (CH), 116.7 (CH), 50.8 (CH_2), 32.3 (CH_2), 19.8 (CH_2), 13.6 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{13}\text{N}_8$ 245.1258; found 245.1262. IR (neat): $\bar{\nu}$ (cm^{-1}) 2933, 1599, 1427, 1148, 1064, 861, 795.

2-Azido-3-(1-octyl-1H-1,2,3-triazol-4-yl)pyrazine (3d). Following **general procedure B** from compound **2d** (200 mg, 0.68 mmol), the title compound was obtained as a white solid (182 mg, 0.61 mmol, 89%). R_f : 0.6 (6:4; DCM/EtOAc). Mp: 130 °C. ^1H NMR (250 MHz, CDCl_3): δ_{H} 9.03 (s, 1H), 8.72 (d, $J = 4.6$ Hz, 1H), 8.43 (d, $J = 4.6$ Hz, 1H), 4.54 (t, $J = 7.1$ Hz, 2H), 2.03 (pent, $J = 7.1$ Hz, 2H), 1.46–1.14 (m, 10H), 0.90–0.76 (m, 3H). ^{13}C $\{^1\text{H}\}$ NMR (63 MHz, CDCl_3): δ_{C} 143.5 (C), 142.2 (C), 141.6 (C), 133.8 (CH), 128.0 (CH), 116.7 (CH), 51.1 (CH_2), 31.8 (CH_2), 30.4 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 26.6 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI) m/z : $[\text{M}$

$+$ $\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{N}_8$ 301.1883; found 301.1885. IR (neat): $\bar{\nu}$ (cm^{-1}) 2922, 1567, 1462, 1042.

4-(4-(3-Azidopyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butan-1-ol (3e). Following **general procedure B** from compound **2e** (181 mg, 0.72 mmol), the title compound was obtained as a white solid (78 mg, 0.3 mmol, 42%). R_f : 0.2 (9:1; DCM/MeOH). Mp: 138–139 °C. ^1H NMR (250 MHz, $\text{DMSO}-d_6$): δ_{H} 9.37 (d, $J = 4.6$ Hz, 1H), 9.30 (s, 1H), 8.47 (d, $J = 4.6$ Hz, 1H), 4.60 (t, $J = 7$ Hz, 2H), 4.49 (br, 1H), 3.44 (t, $J = 6.1$ Hz, 2H), 2.06–1.87 (m, 2H), 1.53–1.34 (m, 2H). ^{13}C $\{^1\text{H}\}$ NMR (63 MHz, $\text{DMSO}-d_6$): δ_{C} 142.6 (C), 142.1 (C), 141.4 (C), 133.3 (CH), 128.3 (CH), 118.2 (CH), 60.0 (CH_2), 49.7 (CH_2), 29.2 (CH_3), 26.7 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{13}\text{N}_8\text{O}$ 261.1206; found 261.1209. IR (neat): $\bar{\nu}$ (cm^{-1}) 3371, 3105, 2941, 1568, 1463, 1240, 1063, 939.

Methyl 4-(4-(3-Azidopyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butanoate (3f). Following **general procedure B** from compound **2f** (370 mg, 1.32 mmol), the title compound was obtained as a white solid (306 mg, 1.06 mmol, 81%). R_f : 0.3 (1:1; DCM/EtOAc). Mp: 145–146 °C. ^1H NMR (250 MHz, $\text{DMSO}-d_6$): δ_{H} 9.37 (d, $J = 4.5$ Hz, 1H), 9.30 (s, 1H), 8.47 (d, $J = 4.5$ Hz, 1H), 4.62 (t, $J = 6.9$ Hz, 2H), 3.58 (s, 3H), 2.40 (t, $J = 7.3$ Hz, 2H), 2.32–2.18 (m, 2H). ^{13}C $\{^1\text{H}\}$ NMR (63 MHz, $\text{DMSO}-d_6$): δ_{C} 172.4 (C), 142.5 (C), 142.1 (C), 141.5 (C), 133.3 (CH), 128.4 (CH), 118.3 (CH), 51.4 (CH_3), 49.0 (CH_2), 30.2 (CH_2), 25.2 (CH_2). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{13}\text{N}_8\text{O}_2$ 289.1156; found 289.1156. IR (neat): $\bar{\nu}$ (cm^{-1}) 3124, 1720, 1568, 1426, 1352, 1219, 1050, 854.

4-(4-(3-Azidopyrazin-2-yl)-1H-1,2,3-triazol-1-yl)butanenitrile (3g). Following **general procedure B** from compound **2g** (300 mg, 1.21 mmol), the title compound was obtained as a white solid (240 mg, 0.94 mmol, 78%). R_f : 0.3 (1:1; PE/EtOAc). Mp: 147–148 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} 9.38 (d, $J = 4.6$ Hz, 1H), 9.35 (s, 1H), 8.48 (d, $J = 4.6$ Hz, 1H), 4.67 (t, $J = 6.9$ Hz, 2H), 2.60 (t, $J = 7.2$ Hz, 2H), 2.28 (p, $J = 6.9$ Hz, 2H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$): δ_{C} 142.5 (C), 142.1 (C), 141.6 (C), 133.3 (CH), 128.6 (CH), 119.7 (C), 118.3 (CH), 48.6 (CH_2), 25.6 (CH_2), 13.8 (CH_2). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{10}\text{N}_8$ 256.1054; found 256.1052. IR (neat): $\bar{\nu}$ (cm^{-1}) 3129, 2250, 1567, 1230, 1091, 860.

2-Azido-3-(1-(hexan-3-yl)-1H-1,2,3-triazol-4-yl)pyrazine (3h). Following **general procedure B** from compound **2h** (245 mg, 0.92 mmol), the title compound was obtained as a white solid (252 mg, 0.92 mmol, quant). R_f : 0.4 (1:1; PE/EtOAc). Mp: 81–82 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 9.00 (s, 1H), 8.72 (d, $J = 4.5$ Hz, 1H), 8.44 (d, $J = 4.5$ Hz, 1H), 4.65–4.58 (m, 1H), 2.07–1.89 (m, 4H), 1.34–1.15 (m, 2H), 0.89 (q, $J = 14.7, 7.3$ Hz, 6H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 143.6 (C), 142.2 (C), 141.5 (C), 133.8 (CH), 126.6 (CH), 116.6 (CH), 64.5 (CH), 37.5 (CH_2), 28.9 (CH_2), 19.3 (CH_2), 13.7 (CH_3), 10.6 (CH_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{N}_8$ 273.1570; found 273.1575. IR (neat): $\bar{\nu}$ (cm^{-1}) 2966; 1569; 1378; 1234; 1180; 1069; 933; 824; 678.

2-Azido-3-(1-benzyl-1H-1,2,3-triazol-4-yl)pyrazine (3i). Following **general procedure B** from compound **2i** (300 mg, 1.11 mmol), the title compound was obtained as a white solid (206 mg, 0.74 mmol, 65%). R_f : 0.4 (1:1; PE/EtOAc). Mp: 179–180 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.96 (s, 1H), 8.70 (d, $J = 4.5$ Hz, 1H), 8.42 (d, $J = 4.5$ Hz, 1H), 7.40–7.36 (m, 5H), 5.71 (s, 2H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 143.3 (C), 142.2 (C), 142.1 (C), 134 (C), 133.8 (CH), 129.5 (2CH), 129.3 (CH), 128.3 (2CH), 128.0 (CH), 116.8 (CH), 54.8 (CH_2). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{11}\text{N}_8$ 279.1101; found 279.1104. IR (neat): $\bar{\nu}$ (cm^{-1}) 3118, 1567, 1402, 1233, 1060, 864, 660.

2-Azido-3-(1-(3,5-dimethoxybenzyl)-1H-1,2,3-triazol-4-yl)pyrazine (3j). Following **general procedure B** from compound **2j** (300 mg, 0.91 mmol), the title compound was obtained as a white solid (210 mg, 0.62 mmol, 68%). R_f : 0.3 (1:1; PE/EtOAc); Mp: 182–183 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.97 (s, 1H), 8.70 (d, $J = 4.5$ Hz, 1H), 8.42 (d, $J = 4.5$ Hz, 1H), 8.42 (d, $J = 4.5$ Hz, 1H), 6.48 (d, $J = 2.2$ Hz, 2H), 6.44 (t, $J = 2.2$ Hz, 1H), 5.63 (s, 2H), 3.77 (s, 6H). ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): δ_{C} 161.6 (C), 143.4 (C), 142.1 (C), 136.1 (C), 133.8 (CH), 128.1 (CH), 116.8 (CH), 106.3 (2CH), 100.9 (CH), 55.6

(2CH₃), 54.9 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₅H₁₃N₆O₂ 339.1312; found 339.1313. IR (neat): ν (cm⁻¹) 2939, 1597, 1463, 1298, 1153, 1048, 855, 679.

2-Phenyl-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4a). Following **general procedure C** from compound **3a** (150 mg, 0.57 mmol), the title compound was obtained as a white solid (28 mg, 0.12 mmol, 20%). *R_f*: 0.5 (96:4; DCM/MeOH). Mp: 149–150 °C (degradation). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} 9.94 (s, 1H), 8.62 (d, *J* = 2.4 Hz, 1H), 8.45 (d, *J* = 2.4 Hz, 1H), 8.13–8.09 (m, 2H), 7.73–7.69 (m, 2H), 7.64–7.62 (m, 1H). ¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ_{C} 156.6 (C), 144.0 (CH), 136.6 (C), 136.3 (CH), 130.1 (2CH), 129.9 (CH), 126.9 (C), 123.9 (C), 121.0 (2CH), 116.9 (CH). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₂H₉N₆ 237.0883; found 237.0881. IR (neat): ν (cm⁻¹) 3071, 1529, 1372, 1196, 1074, 818.

2-(4-Methoxyphenyl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4b). Following **general procedure C** from compound **3b** (136 mg, 0.46 mmol), the title compound was obtained as a white solid (18 mg, 0.07 mmol, 18%). *R_f*: 0.4 (96:4; DCM/MeOH). Mp: 169–170 °C (degradation). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} 9.83 (s, 1H), 8.62 (d, *J* = 2.4 Hz, 1H), 8.45 (d, *J* = 2.4 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 2H), 7.25 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H). ¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ_{C} 160.3 (C), 156.5 (C), 143.9 (CH), 136.2 (CH), 129.8 (C), 126.7 (C), 123.9 (C), 122.9 (CH), 116.7 (CH), 115.2 (CH), 55.8 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₃H₁₁N₆O 267.0988; found 267.0986. IR (neat): ν (cm⁻¹) 2921, 1605, 1513, 1315, 1242, 1073, 848, 763.

2-Butyl-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4c). Following **general procedure C** from compound **3c** (140 mg, 0.57 mmol), the title compound was obtained as a yellowish-orange solid (9.2 mg, 0.04 mmol, 7%). *R_f*: 0.4 (96:4; DCM/MeOH). Mp: 147–148 °C. ¹H NMR (250 MHz, CDCl₃): δ_{H} 8.62 (d, *J* = 2.4 Hz, 1H), 8.36 (d, *J* = 2.4 Hz, 1H), 8.23 (s, 1H), 4.59 (t, *J* = 7.1 Hz, 2H), 2.08 (p, *J* = 7.1 Hz, 2H), 1.45 (q, *J* = 7.3 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H). ¹³C{¹H} NMR (63 MHz, CDCl₃): δ_{C} 157.2 (C), 144.5 (CH), 136.4 (CH), 126.7 (C), 123.8 (C), 115.8 (CH), 53.5 (CH₂), 32.2 (CH₂), 19.7 (CH₂), 13.5 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₃N₆ 217.1196; found 217.1201. IR (neat): ν (cm⁻¹) 2957, 1531, 1282, 1213, 1062, 837, 762.

2-Octyl-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4d). Following **general procedure C** from compound **3d** (134 mg, 0.45 mmol), the title compound was obtained as a white solid (23 mg, 0.08 mmol, 19%). *R_f*: 0.2 (96:4; DCM/MeOH). Mp: 146–147 °C. ¹H NMR (250 MHz, CDCl₃): δ_{H} 8.61 (d, *J* = 2.4 Hz, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.25 (s, 1H), 4.58 (t, *J* = 7.1 Hz, 2H), 2.09 (t, *J* = 7.1 Hz, 2H), 1.39–1.27 (m, 10H), 0.90–0.85 (m, 3H). ¹³C{¹H} NMR (63 MHz, CDCl₃): δ_{C} 144.4 (CH), 136.3 (CH), 126.7 (C), 123.8 (C), 115.9 (CH), 53.8 (CH₂), 31.8 (CH₂), 30.3 (CH₂), 29.1 (CH₂), 29.0 (CH₂), 26.5 (CH₂), 22.7 (CH₂), 14.1 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₄H₂₁N₆ 273.1822; found 273.1827. IR (neat): ν (cm⁻¹) 2923, 1530, 1377, 1213, 1063, 822, 767.

2-(4-Hydroxybutyl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4e). Following **general procedure C** from compound **3e** (140 mg, 0.54 mmol), the title compound was obtained as a yellow solid (13 mg, 0.05 mmol, 10%). *R_f*: 0.1 (94:6; DCM/MeOH). Mp: 152–153 °C (degradation). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} 9.27 (s, 1H), 8.58 (d, *J* = 2.4 Hz, 1H), 8.38 (d, *J* = 2.4 Hz, 1H), 4.67 (t, *J* = 7.1 Hz, 2H), 4.49 (br, 1H), 3.45 (t, *J* = 6.4 Hz, 2H), 2.09–2.01 (m, 2H), 1.50–1.43 (m, 2H). ¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ_{C} 156.1 (C), 143.6 (CH), 135.7 (CH), 125.5 (C), 123.4 (C), 118.6 (CH), 59.9 (CH₂), 52.7 (CH₂), 29.0 (CH₂), 26.4 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₃N₆O 233.1145; found 233.1150. IR (neat): ν (cm⁻¹) 3342, 1445, 1354, 1220, 1038, 827, 642.

2-(4-Methoxy-4-oxobutyl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4f). Following **general procedure C** from compound **3f** (100 mg, 0.35 mmol), the title compound was obtained as a white solid (10 mg, 0.04 mmol, 11%). *R_f*: 0.1 (96:4; DCM/MeOH). Mp: 140–141 °C. ¹H NMR (250 MHz, CDCl₃): δ_{H}

8.60 (d, *J* = 2.4 Hz, 1H), 8.36 (d, *J* = 2.4 Hz, 1H), 8.33 (s, 1H), 4.74–4.69 (m, 2H), 3.68 (s, 3H), 2.44–2.39 (m, 4H). ¹³C{¹H} NMR (63 MHz, CDCl₃): δ_{C} 172.6 (C), 157.2 (C), 144.5 (CH), 136.5 (CH), 126.7 (C), 123.8 (C), 116.5 (CH), 52.6 (CH₂), 52.1 (CH₃), 30.2 (CH₂), 25.4 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₁H₁₃N₆O₂ 261.1094; found 261.1101. IR (neat): ν (cm⁻¹) 3034, 1720, 1480, 1357, 1281, 1197, 913, 764, 645.

2-(3-Cyanopropyl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4g). Following **general procedure C** from compound **3g** (142 mg, 0.55 mmol), the title compound was obtained as a yellow solid (6.1 mg, 0.03 mmol, 5%). *R_f*: 0.3 (96:4; DCM/MeOH). Mp: 150–151 °C (degradation). ¹H NMR (250 MHz, DMSO-*d*₆): δ_{H} 9.28 (s, 1H), 8.58 (d, *J* = 2.4 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 4.74 (t, *J* = 6.7 Hz, 2H), 2.63 (t, *J* = 7.1 Hz, 2H), 2.37 (pent, *J* = 6.9 Hz, 2H). ¹³C{¹H} NMR (63 MHz, DMSO-*d*₆): δ_{C} 156.1 (C), 143.6 (CH), 135.7 (CH), 125.8 (C), 123.5 (C), 119.7 (CN), 119.0 (CH), 51.4 (CH₂), 25.3 (CH₂), 13.7 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₀H₁₀N₇ 228.0992; found 228.0996. IR (neat): ν (cm⁻¹) 3053, 2242, 1530, 1351, 1217, 1028, 845, 727.

2-(Hexan-3-yl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4h). Following **general procedure C** from compound **3h** (140 mg, 0.51 mmol), the title compound was obtained as a yellow solid (9.1 mg, 0.04 mmol, 7%). *R_f*: 0.3 (96:4; DCM/MeOH). Mp: 81–82 °C (degradation). ¹H NMR (250 MHz, CDCl₃): δ_{H} 8.62 (d, *J* = 2.4 Hz, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.21 (s, 1H), 4.51–4.44 (m, 1H), 2.19–1.92 (m, 4H), 1.36–1.15 (m, 2H), 0.94–0.85 (dt, *J* = 14.5, 7.4 Hz, 6H). ¹³C{¹H} NMR (63 MHz, CDCl₃): δ_{C} 157.2 (C), 144.4 (CH), 136.2 (CH), 126.3 (C), 123.9 (C), 115 (CH), 68.0 (CH), 37.3 (CH₂), 28.9 (CH₂), 19.3 (CH₂), 13.6 (CH₃), 10.6 (CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₂H₁₇N₆ 245.1509; found 245.1510. IR (neat): ν (cm⁻¹) 2965, 1528, 1373, 1210, 1027, 799.

2-Benzyl-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4i). Following **general procedure C** from compound **3i** (152 mg, 0.55 mmol), the title compound was obtained as a yellow solid (13 mg, 0.05 mmol, 9%). *R_f*: 0.2 (96:4; DCM/MeOH). Mp: 157–158 °C (degradation). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} 9.39 (s, 1H), 8.58 (d, *J* = 2.4 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 7.50–7.47 (m, 2H), 7.44–7.38 (m, 3H), 5.89 (s, 2H). ¹³C{¹H} NMR (101 MHz, DMSO-*d*₆): δ_{C} 156.1 (C), 143.7 (CH), 135.9 (CH), 134.7 (C), 128.9 (2CH), 128.7 (CH), 128.3 (2CH), 125.7 (C), 123.5 (C), 118.8 (CH), 55.9 (CH₂). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₃H₁₁N₆ 251.1039; found 251.1045. IR (neat): ν (cm⁻¹) 2919, 1477, 1310, 1204, 1028, 822, 651.

2-(3,5-Dimethoxybenzyl)-2H-[1,2,3]triazolo[1',5':1,5]pyrazolo[3,4-b]pyrazin-9-ium-8-ide (4j). Following **general procedure C** from compound **3j** (140 mg, 0.41 mmol), the title compound was obtained as a brown solid (10 mg, 0.03 mmol, 8%). *R_f*: 0.4 (96:4; DCM/MeOH). Mp: 125–126 °C (degradation). ¹H NMR (250 MHz, CDCl₃): δ_{H} 8.62 (d, *J* = 2.4 Hz, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.16 (s, 1H), 6.55–6.54 (m, 2H), 6.50–6.49 (m, 1H), 5.63 (s, 2H), 3.79 (s, 6H). ¹³C{¹H} NMR (63 MHz, CDCl₃): δ_{C} 161.8 (C), 144.6 (CH), 136.5 (CH), 134.5 (C), 115.9 (CH), 106.9 (2CH), 101.4 (CH), 57.3 (CH₂), 55.7 (2CH₃). HRMS (ESI) *m/z*: [M + H]⁺ calcd for C₁₃H₁₃N₆O₂ 311.1251; found 311.1254. IR (neat): ν (cm⁻¹) 2918, 152, 1311, 1207, 1052, 766, 711.

Accession Codes

CCDC 2168242 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors gratefully acknowledge major financial support from Région Centre Val de Loire (APR-IR Orgalight) and in part, from the French Agence Nationale de la Recherche—ANR (ANR-19-CE07-0041), which made this study possible, and also the projects CHemBio (FEDER-FSE 2014-2020-EX003677), Techsab (FEDER-FSE 2014-2020-EX011313), RTR Motivhealth (2019-00131403), and the Labex programs SYNORG (ANR-11-LABX-0029) and IRON (ANR-11-LABX-0018-01) for their financial support of ICOA, UMR 7311, University of Orléans, CNRS.

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