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Push–pull structures with a pyrazine core and hexatriene chain: synthesis and light-emitting properties

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ABSTRACT

In this paper, we describe the synthesis of various push–pull molecules with a central pyrazine unit connected to a hexatriene chain terminated by various *p*-substituted phenyl groups. The key steps involve metallation and subsequent transmetallation of 2-chloro and 2,6-dichloropyrazine followed by a Negishi cross-coupling reaction of the intermediate organozinc derivative with (2*E*,4*E*)-5-bromopentadienal. The aldehydes are then submitted to a Wittig reaction with the appropriate phosphonium salts readily obtained from various substituted benzyl alcohols. The light-emitting properties of the so obtained molecules are then investigated in terms of absorption and emission spectra and non-linear optics experiments have been carried out in two cases.

1. Introduction

In the past two decades, π-conjugated organic compounds have attracted much attention due to their potential applications in various fields such as liquid crystals,[1] components of organic light-emitting devices (OLEDs) for display and lighting,[2] field effect transistors (FETs),[3] single molecular electronics[4] and non-linear optical materials.[5] The fluorescent chromophores, generally known to have planar and rigid π-conjugated systems, are also of interest as functional materials in the molecular probes.[6] The advantages of molecular fluorescence for sensing and switching are very important:[7] indeed they enable a high sensitivity of detection, an 'on-off' switchability, a subnanometer spatial resolution and a submillisecond temporal resolution.

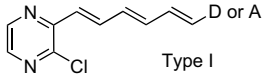
Among them, push–pull polyenes are of particular interest, generally, these compounds have a symmetrical structure (D–π–D or A–π–A) or an asymmetrical one (D–π–A), where A and D are electron acceptor or donor groups. The A and D substituents are connected with a polymethine chain (PC) containing alternating single and double bonds playing the role of electron transmitters for the internal charge transfer (ICT).

Asymmetrical push–pull polyenes with electron donor–acceptor π-conjugated system have received much attention due to their high polarizability and thus are promising compounds for non-linear optics (NLOs), harmonics generation, optical limitation, two-photon absorption (TPA) and optical imaging of biological materials. Moreover, such compounds can be used as convenient precursors for electron-transport materials (or emitter materials) in organic electroluminescent devices.

The introduction of a heteroaryl moiety into extended π-systems is of interest to bring considerable effect onto optical properties such as molar extinction, band position absorption and fluorescence spectra. The π-deficient character of the pyrazine ring allows us to use it as a π-electron acceptor.

Previously, a theoretical investigation and molecular design of chromophores containing ethylene–pyrazine bridge and donor or acceptor groups has been performed and has established that such compounds are good candidates for NLO properties with large molecular first hyperpolarizabilities (β). This preliminary study urged us to synthesize new donor/acceptor substituted pyrazines with a large π-extended conjugation, which could have potential interesting applications in NLO and fluorescence.

Herein, we report the synthesis of various linear compounds (type I) with a pyrazine moiety connected to a donor or an acceptor group though an oligoene chain as a bridge (Scheme 1).



Scheme 1.

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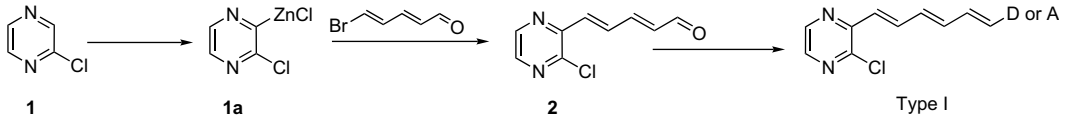
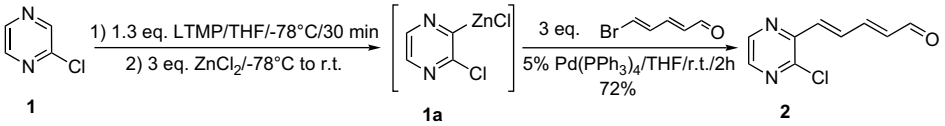
2. Results and discussion

2.1. Synthesis

The synthesis of compounds of type I was initiated from commercially available 2-chloropyrazine **1** using metallation and cross-coupling reactions, according to the following general synthetic way (Scheme 2).



Scheme 2.



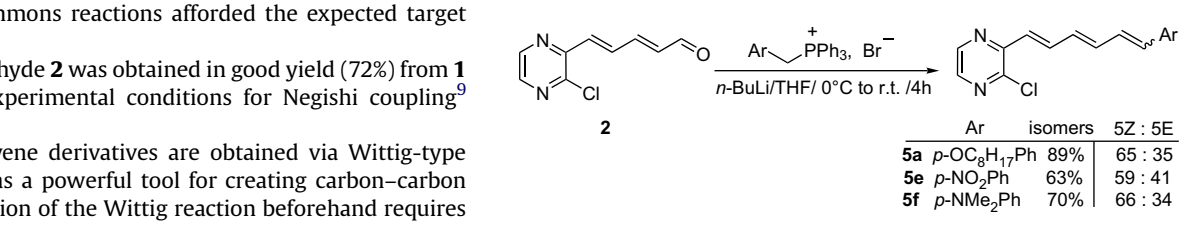
Scheme 3.

The key compound of this synthesis is the aldehyde **2**, readily obtained via a Negishi coupling reaction between the (2*E*,4*E*)-5-bromopentadienal[8] and the organozinc pyrazine **1a**.[9a] This last intermediate results from an *ortho*-lithiation of the chloropyrazine[9a] followed by reaction with zinc chloride. The choice of an organozinc intermediate, which is at once more stable and less reactive towards electrophiles than analogous lithio derivatives, allowed us to carry out the Negishi coupling reaction without protection of the aldehyde group. The last step using both Wittig and Wadsworth–Emmons reactions afforded the expected target polyenes.

The all *trans* aldehyde **2** was obtained in good yield (72%) from **1** according to the experimental conditions for Negishi coupling[9] (Scheme 3).

The various polyene derivatives are obtained via Wittig-type olefination known as a powerful tool for creating carbon–carbon bonds. Implementation of the Wittig reaction beforehand requires the preparation of phosphonium salts **3**, which were obtained in moderate to good yields from corresponding benzyl alcohols by reaction with commercial triphenylphosphonium bromide.[10] To evaluate the potential of a polyenal in a Wittig reaction, the phosphonium salts **3** were reacted with 5-bromopentadienal with *n*-butyllithium or potassium *tert*-butoxide as bases, leading to corresponding 6-arylbromohexatrienes **4** as a mixture of isomers (1*E*,3*E*,5*Z*) and (1*E*,3*E*,5*E*) where the 5*Z* isomer was the major product (Scheme 4). It must be noticed that compound **4b** was obtained as a sole isomer *E*. We have no real explanation for this difference of stereoselectivity in the case of **4b**, but it could be noticed that this compound contains the best electron donating group allowing a better conjugation. The stereomers (1*E*,3*E*,5*Z*) and (1*E*,3*E*,5*E*) were purified using flash column chromatography but not separated even by recrystallization.

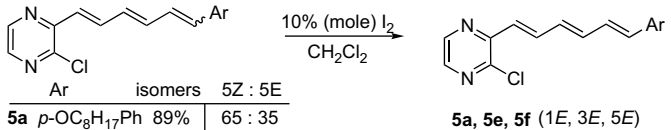
This result allowed us then to carry out the Wittig reaction of compound **2** with phosphonium salts **3a**, **3e** and **3f** using *n*-butyllithium as a base. The chromophores of type I were obtained in moderate to good yields as a mixture of isomers 5*Z* and 5*E*, which were inseparable (Scheme 5).



	Ar	isomers	5Z : 5E
5a	*p*-OC_8H_{17}Ph	89%	65 : 35
5e	*p*-NO_2Ph	63%	59 : 41
5f	*p*-NMe_2Ph	70%	66 : 34

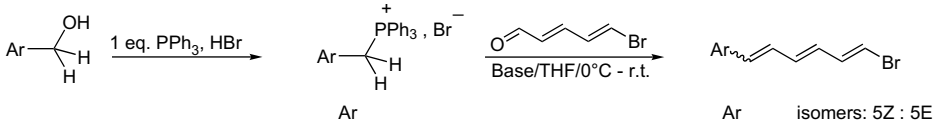
Scheme 5.

Chromophores of type I with all trans configuration and a better extended conjugation would have higher absorption wavelengths and extinction coefficients in UV spectra as well as better hyperpolarizability making them more attractive. A method to transform *cis*-stilbenes into *trans*-stilbenes has previously been described using iodine catalyzed isomerization.[11] Under these conditions, the isomer mixtures **5a**,**e**,**f** led to the corresponding (1*E*,3*E*,5*E*) configuration in quantitative yields (Scheme 6).



	Ar	isomers	5Z : 5E
5a	*p*-OC_8H_{17}Ph	89%	65 : 35
5e	*p*-NO_2Ph	63%	59 : 41
5f	*p*-NMe_2Ph	70%	66 : 34

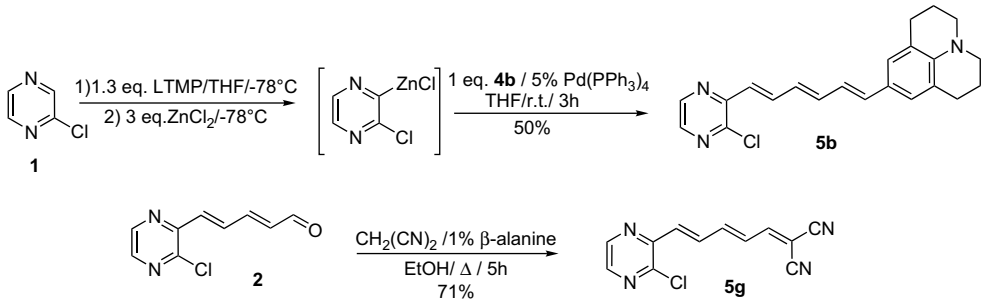
Scheme 6.



	Ar	
3a	*p* OC_8H_{17}Ph	92%
3b	Julolidinyl	93%
3c	2-Thienyl	80%
3d	*p*CF_3Ph	67%
3e	*p*NO_2Ph	95%
3f	*p*NMe_2Ph	100%

	Ar	isomers: 5Z : 5E
4a	*p* OC_8H_{17}Ph	93% / 55 : 45
4b	Julolidinyl	92% / 0 : 100
4c	2-Thienyl	99% / 58 : 42
4d	*p*CF_3Ph	54% / 68 : 32
4e	*p*NO_2Ph	67% / 56 : 44

Scheme 4.



Scheme 7.

Two other chromophores **5b** and **5g** were synthesized in all trans configuration using another way. So compound **5b** was obtained in one step by a Negishi coupling reaction of the bromo derivative **4b** with chloropyrazine via the organozinc pyrazine. Alternatively compound **5g** was obtained via Knoevenagel condensation of malononitrile with aldehyde **2** under base catalysis involving β-alanine (Scheme 7).

To extend the conjugation along the chromophores, in order to increase their optical properties, a second arm, constituted by aryl- or heteroaryl group and/or polyenic chain, could be connected at the 5′ position of the pyrazine ring, to afford D–π–A–π–D structures. Introduction of such substituents requires the presence of a halogen atom or a stannyl group at this position to perform cross-coupling reactions.

Regioselective functionalization at the C_5 or C_6 position of 2-halogenopyrazines has been previously described using metallation and subsequent reaction with electrophiles.[12]

The metallation was carried out with the acetal derivative **6** resulting from protection of the aldehyde group of compound **2** with triethyl orthoformate and catalytic amounts of NBS in ethanol.

Lithiation of compound **6** was achieved with 1.3 equiv of LTMP at −78 °C in THF for 15 min followed by reaction with various electrophiles for a time *t* leading, after deprotection of the aldehyde group, to the trisubstituted pyrazines **7**–**12** (Scheme 8, Table 1).

To determine unambiguously the position of substituents *E* on the pyrazine ring, compound **11** was compared with **11b** obtained via a Negishi coupling reaction between the (2*E*,4*E*)-5-bromopentadienal and the organozinc pyrazine **1b** resulting from metallation and transmetallation of the 2,6-dichloropyrazine (Scheme 9).

The melting points and NMR spectra (^{1}H, ^{13}C) of compounds **11** and **11b** are identical, allowing to assign the same structure for both compounds, with insertion of the second chlorine atom at the C_5 position.

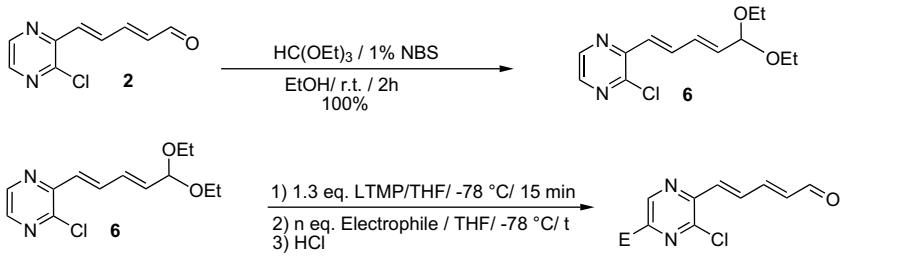
Table 1
Selected correlations from HMBC ^{1}H–^{13}C spectrum of compound **7**

	$C_{2'}$, δ=148.1 ppm	$C_{3'}$, δ=148.8 ppm	$C_{5'}$, δ=143.3 ppm	$C_{6'}$, δ=142.9 ppm
H_4, δ=7.67 ppm	^3J	—	—	—
H_5, δ=7.36 ppm	^2J	^3J	—	^4J
H_{pyr}, δ=8.45 ppm	^3J	—	^2J	—

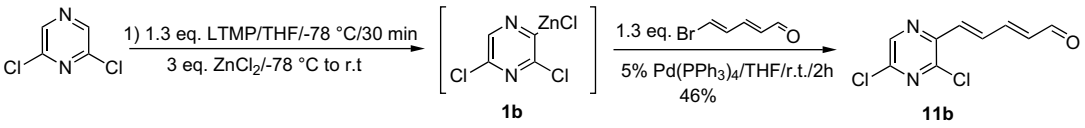
On the other hand, to confirm this result, a structure elucidation of the deuterated compound **7** has been carried out by applying various NMR experiments (^{1}H, ^{13}C, COSY, HMQC, HMBC).

The ^{1}H and COSY H–H spectra allow determination of chemical shifts and *J*-coupling constants of every hydrogen atom. The *J*-mod ^{13}C spectrum highlights six CH (δ: 193.8, 149.8, 142.9, 135.6, 135.0, 133.7 ppm) and three quaternary carbons (δ: 148.8, 148.1, 143.3 ppm); the triplet at 143.3 ppm indicates that this carbon is linked with the deuterium atom. The correlations observed with an experiment HMQC ^{1}H–^{13}C allow the assignment of every ethylenic carbon and the pyrazine carbon $C_{5'}$ with a chemical shift at 142.9 ppm.

To determine the chemical shifts of the quaternary carbons $C_{2'}$ and $C_{3'}$ an experiment HMBC ^{1}H–^{13}C with an evolution delay of 7 Hz (corresponding to two or three bond coupling) has been performed. The signal at 148.1 ppm has two correlations with H_4 (δ=7.67 ppm) and H_5 (δ=7.36 ppm) corresponding to the coupling constants: $^3J_{C2',H4}$ and $^2J_{C2',H5}$ can be assigned to $C_{2'}$, whereas only one correlation was determined between the signal at 148.8 ppm and H_5 ($^3J_{C3',H5}$) allowing an assignment to the carbon $C_{3'}$. Moreover, on the 2D HMBC ^{1}H–^{13}C map three other correlation peaks must be taken in consideration: first a weak correlation peak between the ethylenic H_5 and the $C_{6'}$ of the pyrazine ring according to a $^4J_{H5,C6'}$ and two correlations between the pyrazine $H_{5'}$ (δ=8.45) and the quaternary carbons $C_{2'}$ (δ=148.1 ppm) and $C_{5'}$ (δ=143.3 ppm) linked to the deuterium atom (Table 1, Fig. 1).



Scheme 8.



Scheme 9.

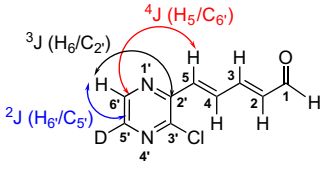
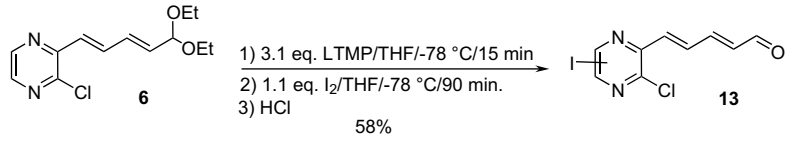


Figure 1.

These results allowed us to determine unambiguously the structure of compound **7** as the (2*E*,4*E*)-5-(3′-chloro-5′-deutero-pyrazin-2′-yl)penta-2,4-dienal (Fig. 1).

When the metallation of **6** was carried out under previous conditions (1.3 equiv; LTMP/−78 °C/THF/15 min) followed by reaction with iodine (1 equiv) as the electrophile, a mixture of inseparable mono and diiodo derivatives was obtained in a 1:1 ratio determined by ^{1}H NMR spectroscopy. Such results have been previously reported with the 2-fluoro-3-phenylpyrazine and it was highlighted that the ratio between monoiodo and diiodo derivatives depended on the amounts of base and iodine. Use of an excess of LTMP (3.1 equiv) and 1.1 equiv of iodine led to a single monoiodopyrazine **13** in 58% yield (Scheme 10).



Scheme 10.

As previously, various NMR experiments (^{1}H, ^{13}C, COSY, HMQC, HMBC) were performed to determine unambiguously the position of the iodine atom on the pyrazine ring. The ^{1}H, ^{13}C, COSY H–H experiments afforded assignment of every hydrogen of the aliphatic chain and $H_{5'}$ or $H_{6'}$ (δ=8.44 ppm) of pyrazine. The NMR ^{13}C spin echo spectrum allowed the differentiation of the six CH and the three quaternary carbons (δ=149.7, 148.1, 114.8 ppm), this latter with the upfield chemical shift being connected to the iodine atom. A further HMQC ^{1}H–^{13}C experiment allowed the assignment of the aliphatic carbons and the pyrazine carbon (δ=151.3 ppm). A HMBC ^{1}H–^{13}C experiment was achieved with a long range delay optimized for a coupling constant of 7 Hz to identify the two quaternary carbons $C_{2'}$ and $C_{3'}$ and the position of the carbon bearing the iodine atom (Table 2 and Fig. 2).

The correlated peaks observed in the HMBC ^{1}H–^{13}C spectrum of **13** led unequivocally to place the iodine atom at the $C_{6'}$ position (Fig. 2).

This unexpected iodination occurring at $C_{6'}$ whereas the other electrophiles take place at $C_{5'}$ requires some comments. It could be assumed that lithiation led first to the 5′-lithioderivative, which reacted with iodine to give the 5-iodo derivative. This compound underwent a further isomerization involving intermediate formation of the diiodo derivative leading to compound **13**. Such isomerizations resulting from a halogen migration have been previously reported in pyridine, pyrimidine and pyrazine[12,13] series, it is known as a 'halogen-dance' mechanism, which implies a halogen–lithium exchange.

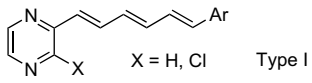
Two other chromophores with a bromine atom or a chloropyrazine as substituent at the $C_{5'}$ position have been synthesized using compound **12** as starting material (Scheme 11).

This synthetic way involved first a Wittig condensation performed with aldehyde **12** and phosphonium **3b** leading to compound **14** in good yield (89%). In a second step a Stille cross-coupling reaction of **14** with 2-chloro-6-tributylstannylpyrazine[12c] afforded compound **15** with a more efficient electro-attractive bispyrazine as the substituent. This enhancement of the electron-withdrawing character would cause an important red-shift for the absorption and emission maxima.

2.2. Geometrical, electronic, spectral and NLO properties

2.2.1. Geometry

Since a twisted structure could be induced by the steric hindrance of a chlorine atom at the $C_{3'}$ position, we performed quantum mechanical calculations of the geometry and electronic structure using the ab-initio DFT method at the B3LYP level of theory[14] with 6-31G* basis set[15] for various compounds of type I bearing an hydrogen or a chlorine atom at C_2 position.



In all cases, the geometry reveals a null dihedral angle between the pyrazine ring and the polyenic chain. As a consequence, the planarity of the structures could allow a high charge transfer between the electron-withdrawing pyrazine ring and the methoxy, julolidinyl or dimethylamino donating groups involved in A–π–D structures. This ICT could be more intensive with compound **15** and

Table 2
Selected correlations from HMBC ^{1}H–^{13}C experiment spectrum of **13**

	$C_{2'}$, δ=149.7	$C_{3'}$, δ=148.1	$C_{6'}$, δ=114.8
H_5, δ=7.19	^{2}J	^{3}J	^{4}J
H_{pyr}, δ=8.44	^{4}J	^{3}J	^{2}J

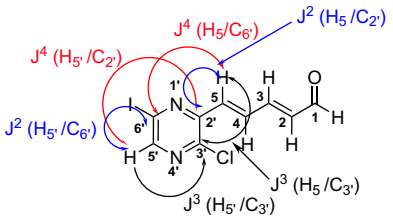
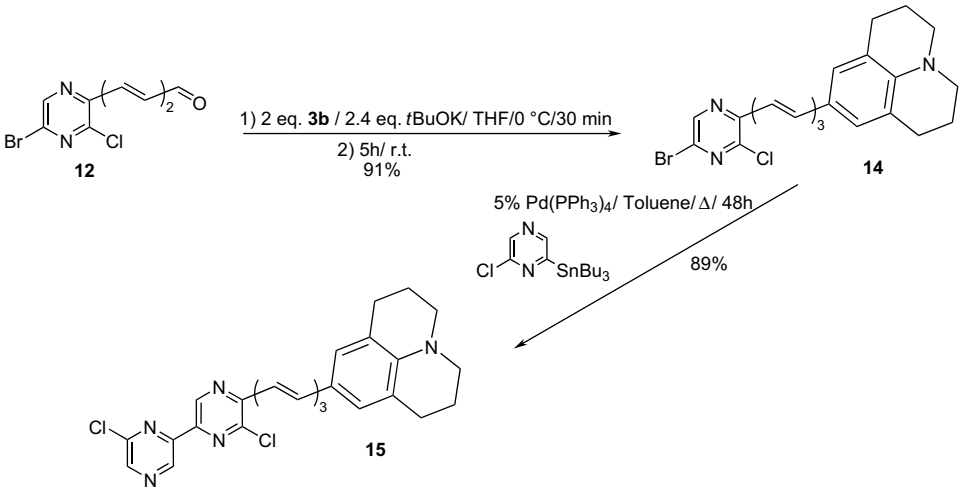


Figure 2.



Scheme 11.

Table 3
HOMO/LUMO energy levels in pyrazine and chloropyrazine series from DFT calculations

Ar	X=H			X=Cl		
	HOMO (eV)	LUMO (eV)	$\Delta E_{HOMO-LUMO}$ (eV)	HOMO (eV)	LUMO (eV)	$\Delta E_{HOMO-LUMO}$ (eV)
p-OMePh	−5.390	−2.373	3.017	−5.430	−2.485	2.945
p-NMe_2Ph	−5.027	−2.210	2.817	−5.059	−2.325	2.734
Julolidinyl	−4.796	−2.112	2.684	−4.830	−2.231	2.559
p-NO_2Ph	−6.111	−3.256	2.856	−6.156	−3.229	2.857

it would be also interesting to observe the properties of compound **5e** with an A–π–A structure.

2.2.2. Electronic properties

The HOMO and LUMO levels have been calculated in pyrazine and chloropyrazine series to appreciate the influence of the chlorine atom (Table 3). While the values obtained for the analogous compounds in each series, are similar, the presence of the chorine atom induces a slight decrease of the HOMO–LUMO gap values ($\Delta E_{HOMO-LUMO}$).

Absorption and fluorescence properties. The UV–vis and fluorescence spectroscopic data of various oligomers performed in chloroform at 25 °C are summarized in Table 4.

Table 4
Optical absorption and emission spectroscopic data for compounds **5a**,**b**, **5e**,**f**,**g**, **14** and **15** in chloroform solution (10^{-4} to 10^{-7} M) at 25 °C

Compound	λ_{abs}max (nm)	ε (M^{-1} cm^{-1})	λ_{em}max (nm)	Φ_F[a]	Stokes shift (cm^{-1})
5a	401	28,770	536	0.17[b]	6280
5b	474	34,787	653	0.20[c]	5783
5e	399	53,630	534	0.43[d]	6336
5f	445	11,447	629	0.07[e]	6574
5g	376	18,478	457	0.03[d]	4720
14	489	20,884	713	0.09[c]	6425
15	528	29,556	780	0.02[e]	6120

[a] ±10%. Quantum yields are determined by comparison with references selected according to the excitation wavelength of the studied compound.
[b] Quantum yield of fluorescence determined using harmane in 0.1 M H_2SO_4 as a standard (Φ_F=0.83), excitation at 381 nm.
[c] Quantum yield of fluorescence determined using cyanine **5** in PBS as a standard (Φ_F=0.20), excitation at 560 nm.
[d] Quantum yield of fluorescence determined using fluorescein in 0.1 M NaOH as a standard (Φ_F=0.90), excitation at 422 nm.
[e] Quantum yield of fluorescence determined using Rodamin 6G in water as a standard (Φ_F=0.76), excitation at 500 nm.

All the compounds of Table 3 absorb in UV–vis (376–428 nm) and display visible emission (457–780 nm) with low to moderate quantum yields.

Comparison of spectroscopic data of compounds **5a**–**g** highlights that compound **5g** possessing two electron-attractor groups (cyano groups) directly connected to the polyenic chain has the weakest spectroscopic data. For compounds **5a**, **5b** and **5f** with an electron-donor group linked though a phenyl ring to the polyenic chain, the absorption maxima are in agreement with the calculated HOMO–LUMO gaps (Table 3 and Table 4). The julolidinyl group known to be a better electron-donor group than dimethylamino group or than alkoxy group gives to compound **5b** the better absorption, emission maxima and quantum yield (Φ_F=0.20). Comparison of compounds **5b**, **14** and **15** shows that introduction of a substituent at $C_{5'}$ position such as a bromine atom or a pyrazine ring increases significantly the absorption and emission wavelengths. These results could be due to the electron-withdrawing character of the two substituents, the pyrazine ring being more efficient than the bromine leading to the most important modifications. However it could be emphasized that substitution at $C_{5'}$ leads also to a decrease of the quantum yield.

2.2.3. NLO properties

Compounds of type I, which are asymmetrical push–pull polyenes with electron donor–acceptor π-conjugated system could have a high polarizability and potential applications in quadratic non-linear optics. The NLO measurements of the $\mu\beta$ values of compounds **5a** and **5b** were determined by using the EFISH (Electric field Induced Second Harmonic) method[16] and assessed by comparison of the **DANS** (dimethylaminonitrostilbene) as reference[17] (Table 5). In the scalar $\mu\beta$ product, μ is the ground-state dipole moment and β the vector part of the hyperpolarizability tensor of the molecule.

These preliminary results indicate that compounds of type I have appreciable non-linear properties, comparable with those of the **DANS**. It can be noticed that replacement of the electron-donor

Table 5
Longest wavelength absorption maxima λ_{max} in $CHCl_3$ and $\mu\beta$ (EFISH measurement at 1907 nm in $CHCl_3$)

Compound	λ_{max} (nm)	$\mu\beta\times10^{-48}$ esu	μ (D)
DANS	427	350	6.6
5a	401	220	4.0
5b	474	1040	8.0

alkoxy group by julolidyl group improves significantly the quadratic hyperpolarizability, which is multiplied by a factor five.

3. Conclusion

Metallation and transmetallation of the commercial chloropyrazine, followed by Negishi coupling reaction or Wittig condensation allowed synthesis of a series of push–pull compounds. These compounds have a pyrazine moiety as electron-drawing group, an all trans hexatriene chain as conjugated link substituted by an aromatic bearing electron donating or withdrawing group. A compound with a bispyrazine group as also been synthesized.

A study of functionalization of the aldehyde **2** via metallation has been performed highlighting a regioselectivity at the C_5 position with various electrophiles and at C_6 position with the iodine as the electrophile. The push–pull compounds have interesting light-emitting properties and high Stokes shifts, two of them have been tested for their NLO properties and promising results have been observed.

4. Experimental section

4.1. General

Melting points were determined on a Reichert-Jung microscope apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 300 (300 MHz ^{1}H, 75 MHz ^{13}C) instrument. $CDCl_3$ was used as a solvent. Microanalyses were performed on a Carlo Erba CHNOS 1160 apparatus. The IR spectra were obtained as potassium bromide pellets with a Perkin Elmer Paragon 500 spectrometer. Absorption bands are given in cm^{-1}. Mass spectra were recorded with a Jeol JMS-AX500 spectrometer or an ATI Unicam Automass, under electron impact conditions (EI) at 70 eV ionizing potential, fitted (or not) with a GC-mass coupling.

4.2. General procedure for the metallation reaction followed by a Negishi coupling. Procedure A

To THF (V mL) under an argon atmosphere and previously cooled at −20 °C were successively added a solution of *n*-butyllithium (1.6 M or 2.5 M, in hexanes, concentration determined with a solution of diphenylacetic acid) and 2,2,6,6-tetramethylpiperidine (TMPH). The reaction mixture was allowed to warm at 0 °C and stirred for 30 min.

To this previously prepared solution of LTMP in THF cooled at θ_1, the appropriate pyrazine derivative dissolved in anhydrous THF was added and the resulting mixture was allowed to react at θ_1 for t_1 min. A solution of zinc dichloride (previously dried under vacuum with a drying gun) in THF (V_1 mL) was then added. The mixture was allowed to warm to room temperature and a solution of the appropriate halogeno derivative and tetrakis (triphenylphosphine)palladium[0] (5 mol %) in THF (V_2 mL) was then added. The reaction mixture was stirred at room temperature for t_2 min. Hydrolysis was carried out with a 20% aqueous solution of EDTA. The reaction mixture was then neutralized with a saturated aqueous solution of sodium hydrogencarbonate and extracted with dichloromethane (3×20 mL). The collected organic layers were dried on magnesium sulfate and evaporated under reduced pressure. The crude product was purified by chromatography on silica gel.

4.3. General procedure for the metallation reaction followed by quenching with an electrophile. Procedure B

The solution of LTMP was prepared as above and cooled at θ_1. The reagent was then added in THF. The reaction mixture was stirred for t_1 min at θ_1. After introduction of the appropriate electrophile, the mixture was stirred for t_2 min at θ_2. Hydrolysis was then carried out at this temperature. When the electrophile was iodine, a solution of sodium thiosulphate was used to remove the excess of iodine. The resulting mixture was allowed to warm to 0 °C and a saturated aqueous solution of sodium hydrogencarbonate was added in order to obtain a slightly basic medium. THF was partially removed and the residue extracted with dichloromethane (4×20 mL). The collected organic layers were dried on $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by chromatography on silica gel.

4.3.1. (2E,4E)-5-(3′-chloropyrazin-2′-yl)penta-2,4-dienal (**2**)

This compound was obtained according to the general procedure A.

LTMP was prepared from anhydrous THF (50 mL), 2,2,6,6-tetramethylpiperidine (0.63 mL, 3.67 mmol, 1.4 equiv) and *n*-BuLi (2.13 mL, 3.41 mmol, 1.3 equiv, 1.6 M in hexanes) cooled at θ_1=−78 °C and reacted with 2-chloropyrazine (0.23 mL, 2.62 mmol, 1 equiv) in THF (10 mL) for t_1=30 min, $ZnCl_2$ (1.070 g, 7.86 mmol, 3 equiv) in anhydrous THF (20 mL), (2*E*,4*E*)-5-bromopenta-2,4-dienal (0.422 g, 2.62 mmol, 1 equiv) and $Pd(PPh_3)_4$ (0.151 g, 0.13 mmol, 5 mol %) in V_2=THF (20 mL) for t_2=2 h. Eluent: pentane/ethyl acetate (70/30). Yield: 367 mg (72%) of a yellow solid. Mp 172 °C. ^{1}H NMR ($CDCl_3$): δ 9.63 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.44 (d, 1H, $J_{6'-5'}$=2.3 Hz, H$^{6'}$), 8.22 (d, 1H, $J_{5'-6'}$=2.3 Hz, H$^{5'}$), 7.66 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.34 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.30 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.35 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.4 Hz, H^2). ^{13}C NMR ($CDCl_3$): δ 193.7 (C^1), 149.8 (C^3), 148.7 (C$^{3'}$), 148.0 (C$^{2'}$), 143.6 (C$^{5'}$), 143.2 (C$^{6'}$), 135.5 (C^2), 134.9 (C^4), 133.7 (C^5). IR: 2831, 1675, 1589, 1446, 1376, 1170, 991, 862 cm^{-1}. MS (EI) *m*/*z*: 194–196 (M$^{+\bullet}$, 38%, 12%), 165–167 (M$^{+\bullet}$−CHO, 100%, 40%), 81 (55%), 65 (34%). Anal. Calcd for $C_9H_7ClN_2O$ (194.45): C, 55.54; H, 3.60; N, 14.40. Found: C, 55.77; H, 3.68; N, 14.53.

4.4. General procedure for the synthesis of 6-arylbromohexatriene 4 by Wittig reaction. Procedure C

To a solution of phosphonium salt **3** (2.14 mmol, 1.2 equiv) in THF (80 mL) at 0 °C under an argon atmosphere was slowly added *n*-BuLi (2.5 M in hexane, 2.14 mmol, 1.2 equiv) for **3a** and **3f** or *t*-BuOK (3.12 mmol, 1.8 equiv) for **3b**–**3e** in THF (30 mL). After 30 min stirring at −78 °C, (2*E*,4*E*)-5-bromopentadienal (1.71 mmol, 1.0 equiv) in THF (15 mL) was slowly added. The mixture was stirred for 10 min at −78 °C and then for 3 h at room temperature. The reaction mixture was quenched with a 10% aqueous solution of $NaHCO_3$ (20 mL). The resulting solution was then extracted with dichloromethane (3×15 mL). The combined organic extracts were washed with saturated brine (10 mL) and dried over $MgSO_4$. After evaporation the crude product was further purified by silica gel column chromatography to give a mixture of two isomers **4** (5*Z*,5*E*).

4.4.1. 1-Bromo-6-(p-n-octyloxyphenyl)hexa-1,3,5-triene (**4a**)

Yield: 1.04 g (93%) as a yellow solid. Mp >230 °C. IR: 3067, 3005, 2922, 2851, 1598, 1472, 1340, 1178, 995, 847 cm^{-1}. MS (CI, isobutane) *m*/*z*: 363–365 (M+1, 78%), 362–364 (M$^{+\bullet}$, 93%), 283 (M$^{+\bullet}$−Br, 100%), 279 (23%), 219 (19%), 167 (22%), 113 (45%), 97 (14%). Anal. Calcd for $C_{20}H_{27}BrO$ (362.9): C, 66.13; H, 7.44. Found: C, 66.17; H, 7.52.

4.4.2. (1E,3E,5E)-1-Bromo-6-(p-n-octyloxyphenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.32 (d, 2H, J=9.0 Hz, H^{arom}), 6.84 (d, 2H, J=9.0 Hz, H^{arom}), 6.78 (dd, 1H, J_{2-3}=10.9 Hz and J_{2-1}=13.6 Hz, H^2), 6.64 (dd, 1H, J_{5-4}=9.4 Hz and J_{5-6}=15.1 Hz, H^5), 6.56 (d, 1H, J_{6-5}=15.1 Hz, H^6), 6.38 (dd, 1H, J_{4-5}=9.4 Hz and J_{4-3}=14.7 Hz, H^4), 6.31 (d,

1H, J_{1-2}=13.6 Hz, H^1), 6.18 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=14.7 Hz, H^3), 3.95 (t, 2H, J=6.4 Hz), 1.77 (m, 2H), 1.47–1.28 (m, 10H), 0.88 (t, 3H, J=6.4 Hz). ^{13}C NMR ($CDCl_3$): δ 159.7 (C^{arom}), 138.2 (C^2), 134.7 (C^4), 134.2 (C^6), 130.0 (C^{arom}), 129.1 (C^3), 128.1 (C^{arom}), 126.5 (C^5), 115.1 (C^{arom}), 108.4 (C^1), 68.5, 32.3, 29.8, 29.7, 26.5, 23.1, 14.6.

4.4.3. (1E,3E,5Z)-1-Bromo-6-(p-n-octyloxyphenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.23 (d, 2H, J=8.7 Hz, H^{arom}), 6.82 (d, 2H, J=8.7 Hz, H^{arom}), 6.83 (dd, 1H, J_{4-5}=9.4 Hz and J_{4-3}=15.4 Hz, H^4), 6.31 (dd, 1H, J_{2-3}=10.9 Hz and J_{2-1}=13.6 Hz, H^2), 6.21 (d, 1H, J_{6-5}=6.8 Hz, H^6), 6.18 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.13 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=15.1 Hz, H^3), 3.95 (t, 2H, J=6.4 Hz), 1.77 (m, 2H), 1.47–1.28 (m, 10H), 0.88 (t, 3H, J=6.4 Hz). ^{13}C NMR ($CDCl_3$): δ 158.8 (C^{arom}), 138.1 (C^2), 131.7 (C^4), 131.4 (C^6), 130.6 (C^5), 130.1 (C^{arom}), 129.0 (C^3), 128.1 (C^{arom}), 114.7 (C^{arom}), 109.1 (C^1), 68.5, 32.2, 29.7, 29.6, 26.4, 23.0, 14.5.

*4.4.4. (1E,3E,5E)-1-Bromo-6-(9′-julolidinyl)hexa-1,3,5-triene (**4b**)*

Yield: 0.52 g (92%) as a brown solid. Mp >260 °C. ^{1}H NMR ($CDCl_3$): δ 6.86 (s, 2H, H^{arom}), 6.77 (dd, 1H, J_{2-1}=13.6 Hz and J_{2-3}=11.3 Hz, H^2), 6.54 (dd, 1H, J_{5-4}=9.8 Hz and J_{5-6}=15.1 Hz, H^5), 6.45 (d, 1H, J_{6-5}=15.1 Hz, H^6), 6.36 (dd, 1H, J_{4-3}=14.7 Hz and J_{4-5}=9.8 Hz, H^4), 6.23 (d, 1H, J_{1-2}=15.1 Hz, H^1), 6.10 (dd, 1H, J_{3-4}=14.7 Hz and J_{3-2}=11.3 Hz, H^3), 3.17 (t, 4H, J=5.7 Hz), 2.74 (t, 4H, J=6.4 Hz), 1.96 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 143.2 (C^{arom}), 138.4 (C^2), 135.5 (C^4 or C^6), 135.3 (C^4 or C^6), 127.1 (C^3), 125.8 ($2C^{arom}$), 124.7 (C^{arom}), 123.5 (C^5), 121.6 ($2C^{arom}$), 106.9 (C^1), 50.3, 28.0, 22.2. IR: 3056, 3014, 2930, 2838, 2789, 1611, 1588, 1351, 1310, 1205, 1179, 986 cm^{-1}. MS (EI) *m*/*z*: 329–331 ($M^{+\bullet}$, 5%), 285 (13%), 269 (16%), 222 (22%), 207 (31%), 186 (28%), 168 (13%), 144 (75%), 130 (30%), 116 (58%), 97 (48%), 89 (48%), 73 (63%), 64 (100%). Anal. Calcd for $C_{18}H_{20}BrN$ (329.9): C, 65.47; H, 6.06; N, 4.24. Found: C, 65.44; H, 6.12; N, 4.28.

*4.4.5. 1-Bromo-6-(2′-thienyl)hexa-1,3,5-triene (**4c**)*

Yield: 0.297 g (99%) as a brown solid. IR: 3076, 3054, 3032, 3020, 1600, 1286, 982, 852, 843, 822, 810, 700 cm^{-1}. MS (EI) *m*/*z*: 240–242 ($M^{+\bullet}$, 28%), 207 (41%), 203 (36%), 185 (52%), 175 (74%), 139 (24%), 131 (42%), 207 (41%), 118 (100%), 111 (39%), 110 (66%), 91 (71%), 55 (76%). Anal. Calcd for $C_{10}H_9BrS$ (241.15): C, 49.79; H, 3.73; S, 13.28. Found: C, 49.87; H, 3.81; S, 13.36.

4.4.6. (1E,3E,5E)-1-Bromo-6-(2′-thienyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.19 (d, 1H, J=5.0 Hz, H^{arom}), 6.98 (d, 1H, J=3.4 Hz, H^{arom}), 6.93 (dd, 1H, J=5.0 Hz and J=3.4 Hz, H^{arom}), 6.78 (m, 3H, H^2, H^5, H^6), 6.35 (dd, 1H, J_{4-5}=10.7 Hz and J_{4-3}=15.1 Hz, H^4), 6.27 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.18 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=14.7 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 142.3 (C^{arom}), 135.3 (C^2), 132.5 (C^4), 130.8 (C^6), 128.5 (C^5 or C^3), 128.1 (C^3 or C^5), 127.3 (C^{arom}), 126.8 (C^{arom}), 125.7 (C^{arom}), 108.8 (C^1).

4.4.7. (1E,3E,5Z)-1-Bromo-6-(2′-thienyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.21 (d, 1H, J=5.0 Hz, H^{arom}), 7.01–6.97 (m, 2H, H^{arom}), 6.83–6.73 (m, 2H, H^2, H^5), 6.57 (dd, 1H, J_{4-5}=10.2 Hz and J_{4-3}=15.1 Hz, H^4), 6.36 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.30 (d, 1H, J_{6-5}=7.5 Hz, H^6), 6.20 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=15.1 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 142.9 (C^{arom}), 137.9 (C^2), 133.7 (C^4), 130.0 (C^6), 128.4 (C^5 or C^3), 128.1 (C^3 or C^5), 127.1 (C^{arom}), 126.7 (C^{arom}), 125.0 (C^{arom}), 109.2 (C^1).

*4.4.8. 1-Bromo-6-(p-trifluoromethylphenyl)hexa-1,3,5-triene (**4d**)*

Yield: 1.04 g (54%) as a yellow solid. IR: 3054, 3019, 2024, 1612, 1562, 1414, 1331, 1068, 991, 735 cm^{-1}. MS (EI) *m*/*z*: 303–304 ($M^{+\bullet}$, 64%), 267 (31%), 247 (31%), 221 (19%), 207 (33%), 200 (40%), 165 (68%), 147 (43%), 122 (42%), 109 (38%), 97 (54%), 84 (100%), 71 (83%), 55 (81%). Anal. Calcd for $C_{13}H_{10}BrF_3$ (303.12): C, 51.49; H, 3.30. Found: C, 51.56; H, 3.34.

4.4.9. (1E,3E,5E)-1-Bromo-6-(p-trifluoromethylphenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.56 (d, 2H, J=8.3 Hz, H^{arom}), 7.48 (d, 2H, J=8.3 Hz, H^{arom}), 6.72 (dd, 1H, J_{2-3}=10.9 Hz and J_{2-1}=13.6 Hz, H^2), 6.66 (dd, 1H, J_{5-4}=9.4 Hz and J_{5-6}=15.1 Hz, H^5), 6.61–6.49 (m, 2H, H^6, H^4), 6.32 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.20 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=14.7 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 140.8 (C^{arom}), 136.1 (C^2), 133.1 (C^4), 132.8 (C^6), 131.3 (C^3), 130.3 (C^5), 129.9 (C^{arom}), 126.8 (C^{arom}), 126.0 (C^{arom}), 122.67 (C^{CF}_3), 110.4 (C^1). ^{19}F NMR ($CDCl_3$): δ −62.9.

4.4.10. (1E,3E,5Z)-1-Bromo-6-(p-trifluoromethylphenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 7.56 (d, 2H, J=8.3 Hz, H^{arom}), 7.48 (d, 2H, J=8.3 Hz, H^{arom}), 6.98 (dd, 1H, J_{4-5}=10.2 Hz and J_{4-3}=15.4 Hz, H^4), 6.75 (dd, 1H, J_{5-4}=10.6 Hz and J_{5-6}=7.2 Hz, H^5), 6.75 (dd, 1H, J_{2-3}=10.6 Hz and J_{2-1}=13.6 Hz, H^2), 6.43 (d, 1H, J_{6-5}=7.2 Hz, H^6), 6.34 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.33 (dd, 1H, J_{3-2}=10.6 Hz and J_{3-4}=15.1 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 140.8 (C^{arom}), 137.7 (C^2), 133.5 (C^4), 132.6 (C^6), 131.8 (C^5), 131.3 (C^3), 126.7 (C^{arom}), 125.9 (C^{arom}), 122.67 (C^{CF}_3), 110.4 (C^1). ^{19}F NMR ($CDCl_3$): δ −62.9.

*4.4.11. 1-Bromo-6-(p-nitrophenyl)hexa-1,3,5-triene (**4e**)*

Yield: 0.23 g (67%) as a yellow solid. IR: 3054, 2030, 2858, 1728, 1588, 1511, 1342, 1175, 861, 747 cm^{-1}. MS (EI) *m*/*z*: 281–279 ($M^{+\bullet}$, 26%), 223 (26%), 207 (29%), 170 (21%), 154 (26%), 149 (81%), 125 (24%), 109 (18%), 97 (25%), 84 (100%), 66 (49%), 57 (60%). Anal. Calcd for $C_{12}H_{10}BrNO_2$ (280.12): C, 51.45; H, 3.57; N, 5.00. Found: C, 51.54; H, 3.72; N, 5.28.

4.4.12. (1E,3E,5E)-1-Bromo-6-(p-nitrophenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 8.18 (d, 2H, J=8.7 Hz, H^{arom}), 7.45 (d, 2H, J=8.7 Hz, H^{arom}), 6.91 (dd, 1H, J_{2-3}=10.9 Hz and J_{2-1}=13.6 Hz, H^2), 6.66 (dd, 1H, J_{5-4}=10.9 Hz and J_{5-6}=15.4 Hz, H^5), 6.58 (dd, 1H, J_{4-5}=9.4 Hz and J_{4-3}=15.4 Hz, H^4), 6.50 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.33 (d, 1H, J_{6-5}=15.4 Hz, H^6), 6.26 (dd, 1H, J_{3-2}=10.2 Hz and J_{3-4}=15.1 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 147.1 (C^{arom}), 143.9 (C^{arom}), 135.7 (C^2), 133.4 (C^4 or C5 or C^6), 132.6 (C^4 or C5 or C^6), 132.1 (C^4 or C5 or C^6), 129.7 (C^3), 127.2 (C^{arom}), 124.1 (C^{arom}), 110.9 (C^1).

4.4.13. (1E,3E,5Z)-1-Bromo-6-(p-nitrophenyl)hexa-1,3,5-triene

^{1}H NMR ($CDCl_3$): δ 8.17 (d, 2H, J=8.7 Hz, H^{arom}), 7.51 (d, 2H, J=8.7 Hz, H^{arom}), 6.91 (dd, 1H, J_{4-5}=9.4 Hz and J_{4-3}=15.4 Hz, H^4), 6.82 (dd, 1H, J_{5-4}=10.9 Hz and J_{5-6}=6.9 Hz, H^5), 6.75 (dd, 1H, J_{2-3}=10.9 Hz and J_{2-1}=13.6 Hz, H^2), 6.47 (d, 1H, J_{1-2}=13.6 Hz, H^1), 6.43 (d, 1H, J_{6-5}=6.8 Hz, H^6), 6.33 (dd, 1H, J_{3-2}=10.9 Hz and J_{3-4}=15.1 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 147.1 (C^{arom}), 143.9 (C^{arom}), 137.6 (C^2), 133.2 (C^4 or C5 or C^6), 133.1 (C^4 or C5 or C^6), 133.0 (C^4 or C5 or C^6), 131.7 (C^3), 127.1 (C^{arom}), 124.5 (C^{arom}), 111.5 (C^1).

4.5. General procedure for the synthesis of the chromophores of type I (5) by Wittig reaction. Procedure D

To a solution of phosphonium salts **3a**, **3e** or **3f** (2.42 mmol, 1.1 equiv) in THF (80 mL) at 0 °C under an argon atmosphere, was slowly added *n*-BuLi (1.6 M in hexane, 2.42 mmol, 1.1 equiv). After 30 min stirring, aldehyde **2** (2.41 mmol, 1.0 equiv) in THF (15 mL) was slowly added. The mixture was stirred for 10 min at 0 °C and 4 h at room temperature. The reaction mixture was quenched with a 10% aqueous solution of $NaHCO_3$ (20 mL). The resulting solution was then extracted with dichloromethane (3×15 mL). The combined organic extracts were washed with saturated brine (10 mL) and dried over $MgSO_4$. After evaporation the crude product was further purified by silica gel column chromatography to give a mixture of two isomers **5** (5*Z*,5*E*). The isomerization was realized by 10 mol % of iodine in refluxing dichloromethane or toluene during 4 h. A solution of sodium thiosulfate was added and after

extraction with dichloromethane (2×15 mL) the combined organic extracts were dried over $MgSO_4$. After evaporation, only isomer all *E* was obtained with good purity.

4.5.1. (1E,3E,5E)-1-(3′-Chloropyrazin-2′-yl)-6-(p-n-octyloxyphenyl)hexa-1,3,5-triene (**5a**)

Yield: 0.844 g (89%) as a yellow solid. Mp 165 °C. ^{1}H NMR ($CDCl_3$): δ 8.41 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.13 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.63 (dd, 1H, J_{2-3}=11.3 Hz and J_{2-1}=15.1 Hz, H^2), 7.37 (d, 2H, J=8.7 Hz, H^{arom}), 6.97 (d, 1H, J_{1-2}=15.1 Hz, H^1), 6.86 (d, 2H, J=8.7 Hz, H^{arom}), 6.78 (d, 1H, J_{6-5}=15.1 Hz, H^6), 6.74 (dd, 1H, J_{4-3}=15.1 Hz and J_{4-5}=11.3 Hz, H^4), 6.65 (d, 1H, J_{5-4}=11.3 Hz and J_{5-6}=15.1 Hz, H^5), 6.58 (dd, 1H, J_{3-4}=14.7 Hz and J_{3-2}=11.3 Hz, H^3), 3.97 (t, 2H, J=6.4 Hz), 1.78 (m, 2H), 1.45–1.29 (m, 10H), 0.89 (t, 3H, J=6.4 Hz). ^{13}C NMR ($CDCl_3$): δ 159.7 (C^{arom}), 150.1 ($C^{2'}$), 147.5 ($C^{3'}$), 142.7 ($C^{6'}$), 141.3 ($C^{5'}$), 139.7 (C^4), 138.9 (C^2), 135.7 (C^5), 131.4 (C^3), 129.8 (C^{arom}), 128.4 (C^{arom}), 126.7 (C^6), 124.0 (C^1), 115.1 (C^{arom}), 68.4, 32.2, 29.7, 29.6, 26.4, 23.0, 14.6. IR: 3075, 3020, 2936, 2923, 1591, 1386, 1240, 1173, 1082, 871, 641 cm^{-1}. MS (EI) *m*/*z*: 396–398 ($M^{+\bullet}$, 21%, 6%), 375 (15%), 370 (20%), 350 (27%), 337 (53%), 324 (42%), 284 (37%), 281 (65%), 269 (27%), 250 (32%), 238 (56%), 226 (43%), 208 (40%), 198 (71%), 149 (70%), 132 (51%), 121 (48%), 106 (96%), 69 (97%), 57 (100%). Anal. Calcd for $C_{24}H_{29}ClN_2O$ (396.45): C, 33.71; H, 1.87; N, 8.74. Found: C, 33.79; H, 1.89; N, 8.73.

4.5.2. (1E,3E,5E)-1-(3′-Chloropyrazin-2′-yl)-6-(p-nitrophenyl)hexa-1,3,5-triene (**5e**)

Yield: 0.305 g (63%) as a yellow solid. Mp >260 °C. ^{1}H NMR ($CDCl_3$): δ 8.45 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.20 (d, 2H, J=9.0 Hz, H^{arom}), 8.19 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.65 (dd, 1H, J_{2-3}=10.6 Hz and J_{2-1}=15.1 Hz, H^2), 7.56 (d, 2H, J=9.0 Hz, H^{arom}), 7.08 (d, 1H, J_{1-2}=14.7 Hz, H^1), 7.05 (dd, 1H, J_{3-4}=15.1 Hz and J_{3-2}=11.7 Hz, H^3), 6.76–6.71 (m, 3H, H^4, H^5, H^6). ^{13}C NMR ($CDCl_3$): δ 149.5 (C^{arom}), 147.9 ($C^{2'}$), 147.2 ($C^{3'}$), 143.7 (C^{arom}), 142.8 ($C^{5'}$), 142.0 ($C^{6'}$), 137.8 (C^4 or C^2), 137.7 (C^2 or C^4), 135.4 (C^5), 133.2 (C^3 or C^6), 132.8 (C^6 or C^3), 127.3 (C^{arom}), 126.6 (C^1), 124.5 (C^{arom}). IR: 1600, 1584, 1513, 1446, 1379, 1345, 1258, 1174, 1133, 1080, 1049, 1001, 868, 831, 803, 629 cm^{-1}. MS (EI) *m*/*z*: 313–315 ($M^{+\bullet}$, 32%, 13%), 279 (47%), 259 (12%), 256 (31%), 229 (36%), 207 (34%), 185 (34%), 167 (51%), 149 (100%), 139 (20%), 129 (43%), 99 (34%), 97 (53%), 71 (64%), 57 (83%). Anal. Calcd for $C_{16}H_{12}ClN_3O_2$ (313.45): C, 61.25; H, 3.83; N, 13.40. Found: C, 61.49; H, 4.09; N, 13.63.

4.5.3. (1E,3E,5E)-1-(3′-Chloropyrazin-2′-yl)-6-(p-N,N-dimethylaminophenyl)hexa-1,3,5-triene (**5f**)

Yield: 0.481 g (70%) as a brown solid. Mp 207 °C. ^{1}H NMR ($CDCl_3$): δ 8.40 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.11 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.64 (dd, 1H, J_{2-3}=11.3 Hz and J_{2-1}=15.1 Hz, H^2), 7.34 (d, 2H, J=8.7 Hz, H^{arom}), 6.93 (d, 1H, J_{1-2}=15.1 Hz, H^1), 6.74 (d, 1H, J_{6-5}=15.1 Hz, H^6), 6.72 (dd, 1H, J_{4-3}=15.1 Hz and J_{4-5}=11.3 Hz, H^4), 6.68 (d, 2H, J=8.7 Hz, H^{arom}), 6.58 (dd, 1H, J_{5-4}=11.3 Hz and J_{5-6}=15.0 Hz, H^5), 6.53 (dd, 1H, J_{3-4}=15.1 Hz and J_{3-2}=11.3 Hz, H^3), 2.30 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$): δ 150.8 ($C^{1''}$), 150.3 ($C^{3'}$), 147.4 ($C^{2'}$), 142.7 ($C^{5'}$), 141.0 ($C^{6'}$), 140.4 (C^4), 139.2 (C^2), 136.6 (C^5), 130.1 (C^3), 128.4 ($C^{3''}$), 125.5 ($C^{4''}$), 124.7 (C^6), 123.1 (C^1), 112.6 ($C^{2''}$), 40.7 (CH_3). IR: 3081, 3048, 3015, 2889, 2807, 1614, 1582, 1550, 1362, 1273, 1251, 1010, 948, 884, 860, 810, 743 cm^{-1}. MS (EI) *m*/*z*: 311–313 ($M^{+\bullet}$, 84%, 39%), 276 (M−Cl, 5%), 231 (10%), 197 (100%), 196 (25%), 184 (16%), 165–167 (20%, 7%), 158 (22%), 134 (73%), 121 (28%). Anal. Calcd for $C_{18}H_{18}ClN_3$ (311.45): C, 69.35; H, 5.78; N, 13.48. Found: C, 69.34; H, 5.35; N, 13.28.

4.5.4. (1E,3E,5E)-1-(3′-Chloropyrazin-2′-yl)-6-(9″-julolidinyl)hexa-1,3,5-triene (**5b**)

Yield: 0.285 g (50%) as a purple solid. Mp 225 °C. ^{1}H NMR ($CDCl_3$): δ 8.39 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.09 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.63 (dd, 1H, J_{2-3}=11.3 Hz and J_{2-1}=15.1 Hz, H^2), 6.91 (s, 2H, H^{arom}), 6.90 (d, 1H, J_{1-2}=15.1 Hz, H^1), 6.70 (d, 1H, J_{6-5}=15.1 Hz, H^6), 6.69 (dd, 1H, J_{4-3}=14.3 Hz and J_{4-5}=10.6 Hz, H^4), 6.59–6.46 (m, 2H, H^5 and H^3), 3.19 (t, 4H, J=5.7 Hz, CH_2), 2.75 (t, 4H, J=6.4 Hz, CH_2), 1.96 (m, 4H, CH_2). ^{13}C NMR ($CDCl_3$): δ 150.3 ($C^{2'}$), 147.0 ($C^{3'}$), 143.6 ($C^{6''}$), 142.7 ($C^{6'}$), 140.8 ($C^{5'}$ or C^4), 140.7 ($C^{5'}$ or C^4), 139.4 (C^2), 137.2 (C^5), 129.5 (C^3), 126.2 ($C^{8''}$ and $C^{10''}$), 124.5 ($C^{9''}$), 123.8 (C^6), 122.5 (C^1), 121.6 ($C^{5''}$ and $C^{7''}$), 50.3 ($C^{2''}$), 28.0 ($C^{4''}$), 22.2 ($C^{3''}$). IR: 3143, 3016, 2958, 2926, 2869, 1612, 1573, 1273, 1242, 1203, 1160, 1130, 1048, 1001, 963, 880, 850, 745, 719 cm^{-1}. MS (EI) *m*/*z*: 363–365 ($M^{+\bullet}$, 96%, 31%), 249 (100%), 236 (7%), 222 (12%), 210 (8%), 186 (36%), 181 (31%), 168 (22%), 154 (8%), 137 (6%), 109 (10%), 97 (13%), 69 (14%), 57 (18%). Anal. Calcd for $C_{22}H_{22}ClN_3$ (363.45): C, 72.64; H, 6.05; N, 11.55. Found: C, 72.51; H, 5.98; N, 11.29.

4.5.5. (3E,5E)-1,1-Dicyano-6-(3′-chloropyrazin-2′-yl)hexa-1,3,5-triene (**5g**)

A mixture of aldehyde **2** (200 mg, 1.03 mmol, 1.00 equiv), malononitrile (68 mg, 1.03 mmol, 1.00 equiv) and β-alanine (0.92 mg, 0.01 mmol, 0.01 equiv) was stirred for 5 h in refluxing ethanol (60 mL) under argon atmosphere. The ethanol was removed under vacuum and water was added (20 mL). The resulting solution was then extracted with dichloromethane (3×15 mL) and the combined organic extracts were dried over $MgSO_4$. After evaporation the crude product was further purified by silica gel column chromatography.

Yield: 0.177 g (71%) as a yellow solid. Mp 218 °C. ^{1}H NMR ($CDCl_3$): δ 8.53 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.31 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.72 (dd, 1H, J_{5-4}=11.3 Hz and J_{5-6}=14.7 Hz, H^5), 7.55 (d, 1H, J_{2-3}=11.7 Hz, H^2), 7.42 (d, 1H, J_{6-5}=15.1 Hz, H^6), 7.15 (dd, 1H, J_{4-3}=14.7 Hz and J_{4-5}=11.3 Hz, H^4), 7.00 (dd, 1H, J_{3-4}=14.7 Hz and J_{3-2}=11.3 Hz, H^3). ^{13}C NMR ($CDCl_3$): δ 158.9 (C^2), 147.0 ($C^{3'}$), 148.0 (C^4), 147.8 ($C^{2'}$), 148.8 ($C^{5'}$), 143.2 ($C^{6'}$), 135.2 (C^5 or C^6), 135.1 (C^6 or C^5), 130.2 (C^3), 113.6 (C^{CN}), 111.6 (C^{CN}), 85.2 (C^1). IR: 3071, 3037, 3011, 2230, 1592, 1385, 1341, 1189, 1175, 1147, 859, 740, 611 cm^{-1}. MS (EI) *m*/*z*: 242–244 ($M^{+\bullet}$, 100%, 34%), 207 (M−Cl, 29%), 180 (24%), 165–167 (55%, 13%), 153 (2%), 129 (5%), 102 (27%), 76 (19%), 52 (32%). Anal. Calcd for $C_{12}H_7ClN_4$ (242.45): C, 59.39; H, 2.89; N, 23.10. Found: C, 59.67; H, 2.92; N, 23.38.

4.5.6. (2E,4E)-1,1-Diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**)

A solution of aldehyde **2** (321 mg, 1.65 mmol, 1.0 equiv), *N*-bromosuccinimide (3.00 mg, 0.02 mmol, 0.01 equiv) and ethyl orthoformate (0.50 mL, 2.48 mmol, 1.5 equiv) in ethanol (40 mL) was stirred for 2 h at room temperature. The reaction mixture was quenched with a 10% aqueous solution of NaOH (25 mL) and the ethanol was removed under vacuum. The resulting solution was then extracted with dichloromethane (2×20 mL). The combined organic extracts were washed with water (20 mL) and dried over Na_2SO_4. After evaporation, the crude product was obtained in good purity.

Yield: 0.443 g (100%) as a brown oil. ^{1}H NMR ($CDCl_3$): δ 8.41 (d, 1H, $J_{6'-5'}$=2.3 Hz, $H^{6'}$), 8.16 (d, 1H, $J_{5'-6'}$=2.3 Hz, $H^{5'}$), 7.51 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.02 (d, 1H, J_{5-4}=15.1 Hz, H^5), 6.63 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.02 (dd, 1H, J_{2-3}=15.4 Hz and J_{2-1}=4.9 Hz, H^2), 5.04 (d, 1H, J_{1-2}=4.9 Hz, H^1), 3.61 (m, 4H, CH_2), 1.22 (t, 6H, J=6.8 Hz, CH_3). ^{13}C NMR ($CDCl_3$): δ 149.4 ($C^{2'}$), 147.7 ($C^{3'}$), 142.8 ($C^{6'}$), 142.1 ($C^{5'}$), 137.3 (C^4), 136.4 (C^2), 132.3 (C^3), 126.3 (C^5), 100.7 (C^1), 61.3 (C^{CH2}), 15.6 (C^{CH3}). IR: 2975, 2931, 2877, 1609, 1512, 1441, 1379, 1343, 1132, 1051, 997, 874, 739 cm^{-1}. MS (EI) *m*/*z*: 268–270 ($M^{+\bullet}$, 36%, 12%), 241 (29%), 239 (78%), 223 (100%), 209 (26%), 195 (74%), 167 (97%), 152 (18%), 131 (22%), 103 (15%), 77 (38%), 53 (49%). Anal. Calcd for $C_{13}H_{17}ClN_2O_2$ (268.45): C, 58.11; H, 6.33; N, 10.43. Found: C, 58.06; H, 5.92; N, 10.45.

*4.5.7. (2E,4E)-5-(3′-Chloro-5′-deuteriopyrazin-2′-yl)penta-2,4-dienal (**7**)*

This compound has been obtained according to general procedure B. LTMP was prepared from TMPH (0.18 mL, 1.04 mmol, 1.4 equiv), *n*-BuLi (1.6 M in hexanes, 0.61 mL, 0.97 mmol, 1.3 equiv) in THF (40 mL), cooled at −78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (200 mg, 0.75 mmol, 1.0 equiv) in THF (15 mL) for t_1=15 min. The electrophile was EtOD (0.44 mL, 7.45 mmol, 10.0 equiv) in THF (10 mL) at −78 °C for 30 min. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/ethyl acetate (70/30). Yield: 0.080 g (54%) of a yellow solid. Mp 173 °C. ^{1}H NMR ($CDCl_3$): δ 9.63 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.45 (s, 1H, H$^{6'}$), 7.67 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.36 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.30 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.36 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.4 Hz, H^2). ^{13}C NMR ($CDCl_3$): δ 193.8 (C^1), 149.8 (C^3), 148.8 (C$^{3'}$), 148.1 (C$^{2'}$), 143.3 (C$^{5'}$), 142.9 (C$^{6'}$), 135.6 (C^2), 135.0 (C^4), 133.7 (C^5). IR: 2832, 1675, 1622, 1423, 1334, 1305, 1262, 990 cm^{-1}. MS (EI) *m*/*z*: 195–197 (M$^{+\bullet}$, 43%, 17%), 166–168 (M$^{+\bullet}$−CHO, 100%, 40%), 81 (43%), 65 (34%), 53 (32%). Anal. Calcd for $C_9H_6DClN_2O$ (195.45): C, 55.26; H, 3.07; N, 14.33. Found: C, 55.29; H, 3.11; N, 14.36.

*4.5.8. (2E,4E)-5-[3′-Chloro-5′-(p-methoxyphenylhydroxymethyl)-pyrazin-2′yl]penta-2,4-dienal (**8**)*

This compound has been obtained according to general procedure B. LTMP was prepared from TMPH (0.18 mL, 1.04 mmol, 1.4 equiv), *n*-BuLi (1.6 M in hexanes, 0.61 mL, 0.97 mmol, 1.3 equiv) in THF (40 mL), cooled at −78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (200 mg, 0.75 mmol, 1.0 equiv) in THF (15 mL) for t_1=15 min. The electrophile was 4-methoxybenzaldehyde (0.13 mL, 1.05 mmol, 1.3 equiv) in THF (10 mL) at −78 °C for 90 min. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/ethyl acetate (2:1). Yield: 0.195 g (73%) of a brown solid. Mp 137 °C. ^{1}H NMR ($CDCl_3$): δ 9.67 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.51 (s, 1H, H$^{6'}$), 7.66 (dd, 1H, J_{4-3}=11.7 Hz and J_{4-5}=14.7 Hz, H^4), 7.41–7.29 (m, 4H, H^3, H^5, 2H^{arom}), 6.89 (d, 2H, J=8.7 Hz, H^{arom}), 6.39 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.1 Hz, H^2), 5.82 (s, 1H, C*H*OH), 3.79 (s, 3H, CH_3), 3.51 (s, 1H, O*H*). ^{13}C NMR ($CDCl_3$): δ 193.9 (C^1), 160.1 (C$^{5''}$), 157.3 (C$^{2''}$), 150.1 (C^3), 147.1 (C$^{2'}$ or C$^{5'}$), 146.2 (C$^{2'}$ or C$^{5'}$), 141.3 (C$^{6'}$), 135.4 (C^2), 134.5 (C^4), 133.7 (C^5), 135.5 (C$^{3'}$), 128.6 (C$^{3''}$), 114.7 (C$^{4''}$), 74.2 (C$^{1''}$), 55.7 (C$^{6''}$). IR: 3427, 2846, 1675, 1620, 1514, 1341, 1253, 1169, 1126, 833 cm^{-1}. MS (EI) *m*/*z*: 330–332 (M$^{+\bullet}$, 3%, 1%), 301–303 (M−CHO, 10%, 3%), 195 (16%), 137 (100%), 109 (35%), 77 (69%). Anal. Calcd for $C_{17}H_{15}ClN_2O_3$ (330.45): C, 76.92; H, 9.40; N, 8.47. Found: C, 76.96; H, 9.65; N, 8.51.

*4.5.9. (2E,4E)-5-[3′-Chloro-5′-(1″-hydroxyethyl)pyrazin-2′-yl]penta-2,4-dienal (**9**)*

This compound has been obtained according to general procedure B. LTMP was prepared from TMPH (0.18 mL, 1.04 mmol, 1.4 equiv), *n*-BuLi (1.6 M in hexanes, 0.61 mL, 0.97 mmol, 1.3 equiv) in THF (40 mL), cooled at −78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (200 mg, 0.75 mmol, 1.0 equiv) in THF (15 mL) for t_1=15 min. The electrophile was acetaldehyde (0.44 mL, 7.71 mmol, 10.0 equiv) in THF (10 mL) at −78 °C for 90 min. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/ethyl acetate (2:1). Yield: 0.126 g (69%) of a brown solid. Mp 202 °C. ^{1}H NMR ($CDCl_3$): δ 9.63 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.55 (s, 1H, H$^{6'}$), 7.63 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.35 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.29 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.35 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.1 Hz, H^2), 4.93 (m, 1H, C*H*OH), 2.82 (d 1H, O*H*), 1.53 (d, 3H, J=6.4 Hz, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.0 (C^1), 159.1 (C$^{5'}$), 150.2 (C^3), 147.3 (C$^{3'}$), 146.2 (C$^{2'}$), 140.4 (C$^{6'}$), 135.2 (C^2), 134.3 (C^4), 133.8 (C^5), 68.6 (C$^{1''}$), 24.1 (C$^{2''}$). IR: 3476, 1667, 2981, 2838, 1677, 1617, 1550, 1341, 990, 943 cm^{-1}. MS (EI) *m*/*z*: 238–240 (M$^{+\bullet}$, 42%, 13%), 301–303 (M−CHO, 47%, 16%), 195 (16%), 137 (100%), 109 (35%), 77 (69%). Anal. Calcd for $C_{11}H_{11}ClN_2O_2$ (238.67): C, 55.35; H, 4.61; N, 11.74. Found: C, 55.32; H, 4.68; N, 11.75.

*4.5.10. (2E,4E)-5-[3′-Chloro-5′-(tri-n-butylstannyl)pyrazin-2′-yl]penta-2,4-dienal (**10**)*

This compound has been obtained according to general procedure B. LTMP was prepared from TMPH (0.20 mL, 1.17 mmol, 1.4 equiv), *n*-BuLi (1.6 M in hexanes, 0.68 mL, 1.08 mmol, 1.3 equiv) in THF (40 mL), cooled at −78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (224 mg, 0.83 mmol, 1.0 equiv) in THF (15 mL) for t_1=15 min. The electrophile was tributyltin chloride (0.29 mL, 1.08 mmol, 1.3 equiv) in THF (15 mL) at −78 °C for 2 h. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/ethyl acetate (14:1). Yield: 0.253 g (63%) of a colourless oil. ^{1}H NMR ($CDCl_3$): δ 9.64 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.41 (s, 1H, H$^{6'}$), 7.67 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.36 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.31 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.1 Hz, H^3), 6.35 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.1 Hz, H^2), 1.51 (m, 6H, CH_2), 1.28 (m, 6H, CH_2), 1.14 (t, 6H, J=8.1 Hz, CH_2), 0.84 (t, 9H, J=7.5 Hz, CH_3). ^{13}C NMR ($CDCl_3$): δ 193.9 (C^1), 172.0 (C$^{5'}$), 150.3 (C^3), 150.1 (C$^{3'}$), 149.3 (C$^{6'}$), 145.5 (C$^{2'}$), 135.1 (C^2 or C^5), 135.0 (C^5 or C^2),133.9 (C^4), 29.4 (C$^{2''}$), 27.6 (C$^{3''}$), 14.0 (C$^{4''}$), 12.8 (C$^{1''}$). IR: 2955, 2923, 2851, 1687, 1619, 1416, 1006; 988 cm^{-1}. MS (EI) *m*/*z*: 481–483–485–487–489 (M$^{+\bullet}$, 8%, 16%, 21%, 10%, 3%), 423–425–427–429–431 (15%, 39%, 55%, 22%, 10%), 367–369–371–373–374 (22%, 32%, 30%, 12%, 5%), 309–311–313–315–317 (32%, 70%, 100%, 48%, 20%), 284 (25%), 232 (12%), 177 (20%), 155 (25%), 129 (72%), 121 (12%), 104 (14%), 77 (15%), 57 (20%). Anal. Calcd for $C_{21}H_{33}ClN_2OSn$ (483.16): C, 52.16; H, 6.83; N, 5.80. Found: C, 52.31; H, 7.05; N, 6.10.

*4.5.11. (2E,4E)-5-(3′,5′-Dichloropyrazin-2′yl)penta-2,4-dienal (**11**)*

This compound has been prepared according to procedures A and B.

4.5.11.1. Procedure A. LTMP was prepared from anhydrous THF (50 mL), 2,2,6,6-tetramethylpiperidine (0.48 mL, 2.82 mmol, 1.4 equiv) and *n*-BuLi (1.05 mL, 2.62 mmol, 1.3 equiv, 2.5 M in hexanes) cooled at θ_1=−78 °C and reacted with 2,6-dichloropyrazine (300 mg, 2.01 mmol, 1 equiv) in THF (15 mL) for t_1=2 h, $ZnCl_2$ (830 mg, 6.04 mmol, 3 equiv) in anhydrous THF (20 mL), (2*E*,4*E*)-5-bromopenta-2,4-dienal (0.324 g, 2.01 mmol, 1 equiv) and $Pd(PPh_3)_4$ (0.116 g, 0.10 mmol, 5 mol %) in V_2=THF (20 mL) for t_2=20 h. Eluent for chromatography: pentane/ethyl acetate (70:30). Yield: 0.322 g (46%) as a pale yellow solid.

4.5.11.2. Procedure B. LTMP was prepared from TMPH (0.27 mL, 1.45 mmol, 1.2 equiv) and *n*-BuLi (2.5 M in hexanes, 0.58 mL, 1.45 mmol, 1.1 equiv) in THF (40 mL). LTMP was cooled at θ_1=−78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (353 mg, 1.45 mmol, 1.1 equiv) in THF (15 mL) for t_1=15 min. The electrophile was hexachloroethane (933 mg, 3.96 mmol, 3.0 equiv) in THF (20 mL) at θ_2=−78 °C for t_2=3 h. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/diethylether (70:30). Yield: 0.171 g (57%) as a yellow solid.

Mp 171 °C. ^{1}H NMR ($CDCl_3$): δ 9.63 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.43 (s, 1H, H$^{6'}$), 7.63 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.29 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.28 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.36 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.4 Hz, H^2). ^{13}C NMR ($CDCl_3$): δ 193.7 (C^1), 149.5 (C^3), 146.6 (C$^{3'}$ or C$^{5'}$), 146.5 (C$^{5'}$ or C$^{3'}$), 146.1 (C$^{2'}$), 142.9 (C$^{6'}$), 135.8 (C^2), 135.2 (C^4), 132.5 (C^5). IR: 3072, 2841, 1678, 1424, 1308, 1152, 1063,

993, 895, 789 cm^{-1}. MS (EI) *m/z*: 228–230–232 ($M^{+\bullet}$, 38%, 20%, 4%), 199–201–203 (M−CHO, 100%, 69%, 15%), 149 (40%), 129 (23%), 102 (24%), 81 (38%). Anal. Calcd for $C_9H_6Cl_2N_2O$ (228.90): C, 47.18; H, 2.62; N, 12.23. Found: C, 47.09; H, 2.47; N, 12.02.

4.5.12. (2E,4E)-5-(5′-Bromo-3′-chloropyrazin-2′-yl)penta-2,4-dienal (12)

This compound has been obtained according to procedure B. LTMP was prepared from TMPH (0.14 mL, 0.78 mmol, 1.2 equiv) and *n*-BuLi (1.6 M in hexanes, 0.45 mL, 0.72 mmol, 1.1 equiv) in THF (40 mL). LTMP was cooled at θ_1=−78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (188 mg, 0.65 mmol, 1.0 equiv) in THF (15 mL) for t_1=15 min, 1.2-dibromoethane (0.17 mL, 1.96 mmol, 3 equiv) in THF (10 mL) at θ_2=−78 °C for t_2=3 h. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/diethylether (80:20). Yield: 0.116 g (60%) as a yellow solid. Mp 197 °C. ^{1}H NMR ($CDCl_3$): δ 9.64 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.52 (s, 1H, $H^{6'}$), 7.66 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.30 (d, 1H, J_{5-4}=15.1 Hz, H^5), 7.25 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 6.40 (dd, 1H, J_{2-1}=7.9 Hz and J_{2-3}=15.4 Hz, H^2). ^{13}C NMR ($CDCl_3$): δ 193.7 (C^1), 149.5 (C^3), 146.9 ($C^{3'}$), 146.3 ($C^{2'}$), 145.8 ($C^{6'}$), 137.7 ($C^{5'}$), 135.8 (C^2), 135.3 (C^4), 132.6 (C^5). IR: 3067, 2839, 1674, 1619, 1521, 1420, 1307, 1257, 994, 885, 775 cm^{-1}. MS (EI) *m/z*: 272–274–276 ($M^{+\bullet}$, 20%, 45%, 5%), 243–245–247 (M−CHO, 75%, 70%, 36%), 167 (27%), 149 (54%), 129 (52%), 102 (32%), 81 (81%), 75 (41%), 51 (100%). Anal. Calcd for $C_9H_6BrClN_2O$ (273.35): C, 39.51; H, 2.20; N, 10.24. Found: C, 39.46; H, 2.22; N, 10.17.

4.5.13. (2E,4E)-5-(3′-Chloro-6′-iodopyrazin-2′-yl)penta-2,4-dienal (13)

This compound has been obtained according to procedure B. LTMP was prepared from TMPH (0.41 mL, 2.4 mmol, 3.2 equiv) in THF (40 mL), *n*-BuLi (1.6 M in hexanes, 1.44 mL, 2.3 mmol, 3.1 equiv), cooled at θ_1=−78 °C and treated with (2*E*,4*E*)-1,1-diethoxy-5-(3′-chloropyrazin-2′-yl)penta-2,4-diene (**6**) (200 mg, 0.75 mmol, 1.0 equiv) THF (15 mL) for t_1=15 min, iodine (213 mg, 0.84 mmol, 1.1 equiv) THF (20 mL) at θ_2=−78 °C for t_2=90 min. Hydrolysis was carried out with a 10% aqueous solution of HCl (20 mL). Eluent for chromatography: pentane/ethyl acetate (85:15). Yield: 0.143 g (58%) as a brown solid. Mp 198 °C. ^{1}H NMR ($CDCl_3$): δ 9.64 (d, 1H, J_{1-2}=7.9 Hz, H^1), 8.44 (s, 1H, $H^{5'}$), 7.66 (dd, 1H, J_{4-3}=11.3 Hz and J_{4-5}=15.1 Hz, H^4), 7.25 (dd, 1H, J_{3-4}=11.3 Hz and J_{3-2}=15.4 Hz, H^3), 7.19 (d, 1H, J_{5-4}=15.1 Hz, H^5), 6.40 (dd, 1H, J_{2-1}=7.5 Hz and J_{2-3}=15.4 Hz, H^2). ^{13}C NMR ($CDCl_3$): δ 193.7 (C^1), 151.3 ($C^{5'}$), 149.7 ($C^{2'}$), 149.2 (C^3), 148.1 ($C^{3'}$), 136.2 (C^2 or C^4), 136.1 (C^4 or C^2), 132.4 (C^5), 114.8 ($C^{6'}$). IR: 3063, 2836, 1683, 1596, 1487, 1387, 1295, 1211, 995, 584, 473 cm^{-1}. MS (EI) *m/z*: 320–322 ($M^{+\bullet}$, 39%, 15%), 291293 (M−CHO, 72%, 50%), 262 (23%), 255 (19%), 223–225 (18%, 3%), 193–195 (M−I, 45%, 10%), 164–166 (M−(CHO+I), 29%, 8%), 149 (54%), 129 (69%), 111 (34%), 98 (46%), 86 (100%), 74 (54%), 51 (58%). Anal. Calcd for $C_9H_6ClIN_2O$ (320.35): C, 33.71; H, 1.87; N, 8.74. Found: C, 33.79; H, 1.89; N, 8.73.

4.5.14. (1′E,3′E,5′E)-6-Bromo-2-chloro-3-[6′-(9″-julolidinyl)-hexa-1′,3′,5′-trienyl]pyrazine (14)

To a solution of phosphonium salt **3b** (2.88 g, 5.46 mmol, 2.0 equiv) in THF (100 mL) at 0 °C under an argon atmosphere was slowly added potassium *tert*-butoxide (0.735 g, 6.55 mmol, 2.4 equiv) in THF (40 mL). After 30 min stirring, aldehyde **12** (0.746 g, 2.73 mmol, 1.0 equiv) in THF (20 mL) was slowly added. The mixture was stirred for 10 min at 0 °C and 5 h at room temperature. The reaction mixture was quenched with a 10% aqueous solution of $NaHCO_3$ (20 mL). The resulting solution was then extracted with dichloromethane (3×15 mL). The combined organic extracts were washed with saturated brine (10 mL) and dried over $MgSO_4$. The isomerization was realized by 10 mol % of iodide in refluxing dichloromethane or toluene during 4 h. A solution of sodium thiosulfate was added and after extraction with dichloromethane (2×15 mL) the combined organic extracts were dried over $MgSO_4$. Yield: 1.10 g (91%) as a purple solid. Mp 225 °C (ethanol). ^{1}H NMR ($CDCl_3$): δ 8.45 (s, 1H, H^5), 7.62 (dd, 1H, $J_{2'-3'}$=11.3 Hz and $J_{2'-1'}$=15.1 Hz, $H^{2'}$), 6.90 (s, 2H, $H^{8''}$ and $H^{10''}$), 6.79 (d, 1H, $J_{1'-2'}$=15.1 Hz, $H^{1'}$), 6.70 (dd, 1H, $J_{4'-5'}$=10.6 Hz and $J_{4'-3'}$=14.3 Hz, $H^{4'}$), 6.60 (d, 1H, $J_{6'-5'}$=15.1 Hz, $H^{6'}$), 6.52 (dd, 1H, $J_{5'-4'}$=10.6 Hz and $J_{5'-6'}$=15.1 Hz, $H^{5'}$), 6.47 (dd, 1H, $J_{3'-2'}$=11.3 Hz and $J_{3'-4'}$=14.3 Hz, $H^{3'}$), 3.19 (t, 4H, $J_{2''-3''}$=5.7 Hz, $H^{2''}$), 2.74 (t, 4H, $J_{4''-3''}$=6.4 Hz, $H^{4''}$), 1.96 (m, 4H, $H^{3''}$). ^{13}C NMR ($CDCl_3$): δ 148.7 (C^3), 145.1 (C^2), 145.0 (C^5), 143.7 ($C^{6''}$), 141.4 ($C^{4'}$), 139.9 ($C^{2'}$), 137.6 ($C^{5'}$), 133.8 (C^6), 129.3 ($C^{3'}$), 126.3 ($C^{8''}$ and $C^{10''}$), 124.4 ($C^{9''}$), 123.7 ($C^{6'}$), 121.6 ($C^{5''}$ and $C^{7''}$), 121.3 ($C^{1'}$), 50.3 ($C^{2''}$), 28.0 ($C^{4''}$), 22.1 ($C^{3''}$). IR: 3043, 3019, 2936, 2839, 1609, 1573, 1516, 1488, 1313, 1267, 1205, 1135, 1057, 997, 880, 742, 722, 641 cm^{-1}. MS (EI) *m/z*: 441–443–445 ($M^{+\bullet}$, 74%, 96%, 20%), 250 (44%), 249 (100%), 236 (46%), 222 (5%), 191 (27%), 186 (59%), 173 (17%), 146 (24%), 107 (83%), 106 (90%), 86 (42%), 77 (26%), 72 (35%), 69 (17%), 58 (26%), 51 (16%). Anal. Calcd for $C_{22}H_{21}BrClN_3$ (442.35): C, 59.68; H, 4.75; N, 9.49. Found: C, 59.57; H, 4.72; N, 9.27.

4.5.15. (1″E,3″E,5″E)-6,6′-Dichloro-5-[6″-(9‴-julolidinyl)-hexa-1″,3″,5″-trienyl]-2,2′-bipyrazine (15)

A solution of (1′*E*,3′*E*,5′*E*)-6-bromo-2-chloro-3-[6′-(9″-julolidinyl)-hexa-1′,3′,5′- trienyl]pyrazine (**14**) (329 mg, 0.75 mmol) and 2-chloro-6-tributylstannylpyrazine (331 mg, 0.75 mmol) in anhydrous toluene (100 mL) was degassed and placed under an argon atmosphere. Tetrakis(triphenylphosphine)palladium[0] (43 mg, 5 mol %) was quickly added and the mixture was heated to reflux for 48 h. The mixture was cooled and diluted with diethyl ether (10 mL), filtered on a Celite pad and washed with dichloromethane. The collected organic layers were dried on $MgSO_4$ and evaporated under reduced pressure. The crude product was recrystallized from ethanol. Yield: 0.315 g (89%) as a purple solid. Mp >260 °C. ^{1}H NMR ($CDCl_3$): δ 9.39 (s, 1H, H^3), 9.32 (s, 1H, $H^{3'}$), 8.59 (s, 1H, H^5), 7.75 (dd, 1H, $J_{2''-3''}$=11.7 Hz and $J_{2''-1''}$=15.1 Hz, $H^{2''}$), 6.93 (d, 1H, $J_{1''-2''}$=15.1 Hz, $H^{1''}$), 6.70 (dd, 1H, $J_{4''-5''}$=10.6 Hz and $J_{4''3''}$=14.3 Hz, $H^{4''}$), 6.61 (d, 1H, $J_{6''-5''}$=15.1 Hz, $H^{6''}$), 6.66 (dd, 1H, $J_{5''-4''}$=10.6 Hz and $J_{5''-6''}$=15.1 Hz, $H^{5''}$), 6.55 (dd, 1H, $J_{3''-2''}$=11.3 Hz and $J_{3''-4''}$=14.3 Hz, $H^{3''}$), 3.19 (t, 4H, $J_{2'''-3'''}$=5.7 Hz, $H^{2'''}$), 2.74 (t, 4H, $J_{4'''-3'''}$=6.4 Hz, $H^{4'''}$), 1.96 (m, 4H, $H^{3'''}$). ^{13}C NMR ($CDCl_3$): δ 151.0 (C^5), 148.9 (C^6 or $C^{6'}$), 148.6 (C^6 or $C^{6'}$), 146.1 ($C^{6'''}$), 144.8 ($C^{5'}$), 143.9 (C^2 or $C^{2'}$), 143.8 (C^2 or $C^{2'}$), 142.1 ($C^{4''}$), 141.3 ($C^{2''}$), 141.0 (C^3 or $C^{3'}$), 140.9 (C^3 or $C^{3'}$), 138.0 ($C^{5''}$), 129.5 ($C^{3''}$), 126.4 ($C^{8'''}$ and $C^{10'''}$), 124.3 ($C^{9'''}$), 123.7 ($C^{6''}$), 122.2 ($C^{1''}$), 121.6 ($C^{5'''}$ and $C^{7'''}$), 50.3 ($C^{2'''}$), 28.0 ($C^{4'''}$), 22.1 ($C^{3'''}$). IR: 3048, 3009, 2943, 2830, 1569, 1313, 1265, 1139, 803, 745, 695 cm^{-1}. MS (EI) *m/z*: 475–477–479 ($M^{+\bullet}$, 60%, 41%, 6%), 408 (8%), 396 (14%), 350 (10%), 319 (21%), 281 (19%), 262 (40%), 228 (24%), 207 (20%), 183 (26%), 162 (16%), 149 (65%), 119 (40%), 107 (76%), 83 (58%), 64 (100%), 57 (81%). Anal. Calcd for $C_{26}H_{23}Cl_2N_5$ (475.90): C, 65.56; H, 4.83; N, 14.71. Found: C, 65.61; H, 4.98; N, 14.87.

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