3D Coumarin Systems Based on [2.2]Paracyclophane Synthesis, Spectroscopic Characterization, and Chiroptical Properties

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3D Coumarin systems based on [2.2]paracyclophane: synthesis, spectroscopic characterization and chiroptical properties

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ABSTRACT: In this article we report the preparation of a series of [2.2]paracyclophane-fused coumarin systems through a simple and general procedure involving a transition-metal catalysed cyclization of aryl alkynoates as the key step. We also highlight the influence of the [2.2]paracyclophane (pCp) motif and its "*phane*" interactions on the spectroscopic properties of the newly synthesized fluorophores, which emit in the blue-green region of the visible spectrum (λ_{em} up to 560 nm), and show extremely large Stokes shifts (up to 230 nm). Finally, we demonstrate that our straightforward approach can easily be used to access optically active planar chiral 3D coumarins. Compared to previously described fluorescent paracyclophanes and other organic dyes, our compact heteroaromatic derivatives show promising chiroptical properties, both in term of circular dichroism ($g_{abs} \sim 8 \times 10^{-3}$) and circularly polarized luminescence ($g_{lum} = 5 \times 10^{-3}$), thus demonstrating a practical application of our synthetic method.

INTRODUCTION

[2.2]Paracyclophane (pCp)[1] and its derivatives constitute a well-known class of aromatic compounds characterized by a unique three-dimensional (3D) framework. These substrates incorporate two benzene rings, called "*decks*", covalently linked together at their *para* positions by two ethylene bridges.[2] The conformational stiffness and proximity of the two π systems engender transannular through-space and through-bond interactions that confer on paracyclophanes intriguing spectroscopic properties. In fact, the pCp molecule exhibits an atypical absorbance spectrum compared to simple benzene derivatives, with a characteristic long-wavelength absorption band at 302 nm.[3] The fluorescence spectrum of pCp is also unexpected in comparison with those of more common aromatic compounds, as a broad emission band is observed at 356 nm.[4] These characteristics have been extensively exploited in material sciences for the development of organic light-emitting diodes (OLEDs),[5] and nonlinear optical materials.[6]

Most of the paracyclophane-based fluorophores developed so far present a "branched" π-extended structure functionalized with differently substituted stilbene subunits (Figure 1a). The photophysical behaviour of such compounds is generally tuned by introducing electron-donating or electron-withdrawing groups on their phenylethene moieties.[7] Paracyclophanes are also frequently used as central motifs to obtain fluorescent compounds showing complex secondary-ordered structures (Figure 1b).[8] The absorption and emission properties of such molecules can vary significantly based on their three-dimensional shape.

A different, scarcely exploited, approach to modulate the spectroscopic characteristics of fluorescent pCps consists in selectively functionalizing one of their benzene rings to form polycondensed (hetero)aromatic compounds.[9] In our ongoing work on paracyclophanes,[10] we envisaged using the last strategy for accessing new dyes with more compact 3D structures. This feature should be particularly important for several "in solution" applications, including catalytic processes, supramolecular recognition events, or non-planar biological probes.

Interestingly, depending on their substitution patterns, the pCp-based fluorophores can show planar chirality, and consequently display strong circular dichroism (CD) and circularly polarized luminescence (CPL). In this context, while the chiroptical properties of "branched" or "complex" pCps have been extensively investigated,[7,8] the behaviour of compact polycondensed (hetero)aromatic paracyclophanes has scarcely been described to date. The development of versatile synthetic pathways leading to such compounds would therefore be highly valuable in order to widen the chemical space of pCps and in fine develop new circularly polarized light-emitting organic dyes. On the basis of these considerations, we recently become interested in the

synthesis of [2.2]paracyclophanepyranones, a series of compact pCp-fused coumarin systems (Figure 1c).

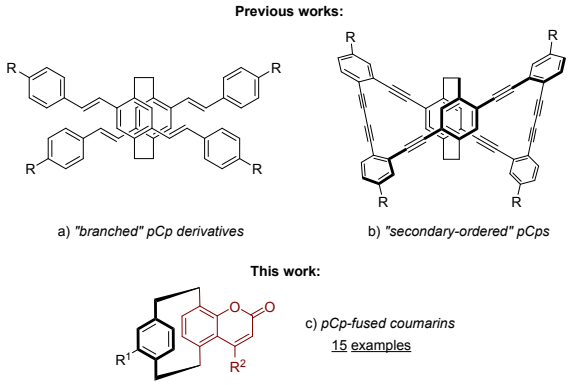


Figure 1. Different classes of pCp-based organic fluorophores

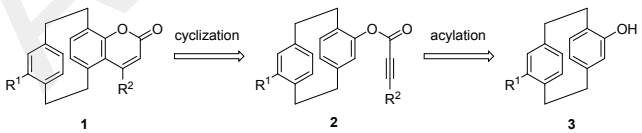
In this article, we will detail a versatile three-step procedure for preparing these fluorophores, and describe their photophysical properties (UV-Vis absorption and fluorescence emission). We will also demonstrate that our synthetic approach can be easily employed to access enantiopure (hetero)aromatic planar chiral dyes with promising chiroptical behaviors.

RESULTS AND DISCUSSION

Synthesis of [2.2]paracyclophane-fused coumarins

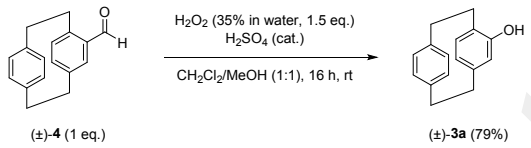
Since the discovery of the parent compound in 1820,[11] different routes have been described to prepare coumarin derivatives. The classical method, reported by Pechmann in 1884, involves the condensation between phenols and β-keto esters under acidic conditions.[12] Other processes are based on Knoevenagel, Reformatsky or Wittig reactions.[13] More recently, new synthetic procedures have been developed to construct the coumarin core via transition metal-catalysed intramolecular cyclizations of aryl alkynoates.[14] This approach proved to be particularly useful to access chiral coumarin-fused [6]helicenes.[15] We therefore envisaged to extend such versatile strategy to [2.2]paracyclophanes and thus form the desired 3D coumarin systems starting from precursors incorporating alkynyl ester moieties. These compounds can, in turn, be prepared via the acylation of 4-hydroxy[2.2]paracyclophanes with different propiolic acid derivatives (Scheme 1). To the best of our knowledge, this approach has never been followed to access [2.2]paracyclophane-fused coumarin systems.[16]

Scheme 1. Retrosynthetic pathway to pCp-fused coumarin systems



We started our investigations by synthetizing 4-hydroxy[2.2]paracyclophane (compound (±)-**3a**) via a Dakin oxidation of 4-formyl[2.2]paracyclophane (±)-**4** (Scheme 2).[17]

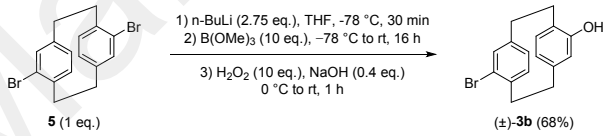
Scheme 2. Synthesis of 4-hydroxy[2.2]paracyclophane (±)-3a



The reaction was performed at room temperature, using H_2O_2 (1.5 eq.) and catalytic quantities of H_2SO_4 in a 1:1 mixture of CH_2Cl_2/MeOH. After 16 h, the desired pCp-based phenol (±)-**3a** was isolated in 79% yield (Scheme 2).

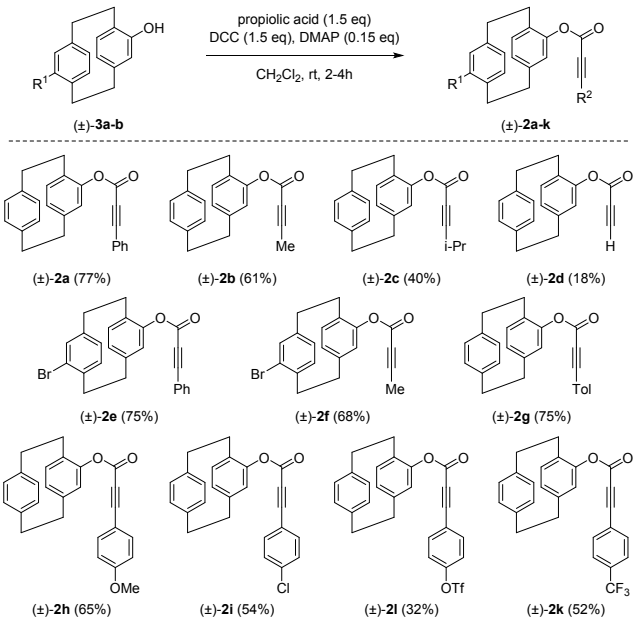
4-Bromo-16-hydroxy[2.2]paracyclophane (compound (±)-**3b**) was then prepared starting from commercially available 4,16-dibromo[2.2]paracyclophane **5** via a bromine-lithium exchange and subsequent addition of trimethyl borate (3 eq.). The resulting boronic ester could be directly oxidized into the corresponding phenol derivative using H_2O_2 (10 eq.) and NaOH (0.4 eq.). Following this procedure,[18] compound (±)-**3b** was isolated in 68% yield (Scheme 3).

Scheme 3. Synthesis of 4-bromo-16-hydroxy[2.2]paracyclophane (±)-3b



Phenols (±)-**3a** and (±)-**3b** were then submitted to a series of acylation reactions with different propiolic acid derivatives (Scheme 4).

Scheme 4. Acylation reaction leading to pCp-derived esters (±)-2a-k

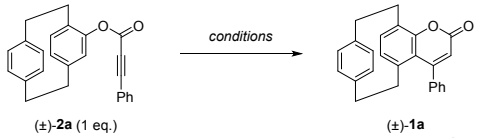


Paracyclophane esters (±)-**2a-k** could be isolated in moderate to good yields using DCC (1.5 eq.) as the coupling agent, and catalytic amounts of DMAP (0.15 eq.), in CH_2Cl_2 at room temperature under an inert atmosphere (Scheme 4).

We next focused our attention on the cyclization key step leading to the pCp-fused coumarins. This transformation is not trivial due to the congested molecular structure of [2.2]paracyclophane. Derivative (±)-**2a** was therefore selected as a model compound to optimize the reaction conditions (Table 1).

By taking inspiration from a previously reported procedure,[14a] a first cyclization assay was performed using $Pd(OAc)_2$ (3 mol %) as the catalyst, in a 1:1 mixture of CH_2Cl_2/TFA at –20 °C. Under these conditions, the desired 3D coumarin (±)-**1a** was obtained in 44% yield (Table 1, entry 1). All reaction partners proved to be essential for the cyclization to proceed. Indeed, in the absence of the catalyst or TFA no conversion of the starting material could be detected by ^1H NMR of the crude product (Table 1, entries 2 and 3). On the other hand, better yields were observed for the formation of compound (±)-**1a** when the cyclization was conducted at higher temperatures (46% and 58% yield at 0 °C and 20 °C respectively, Table 1, entries 4 and 5).

Table 1. Optimization of the cyclization key step



(±)-**2a** (1 eq.) (±)-**1a**

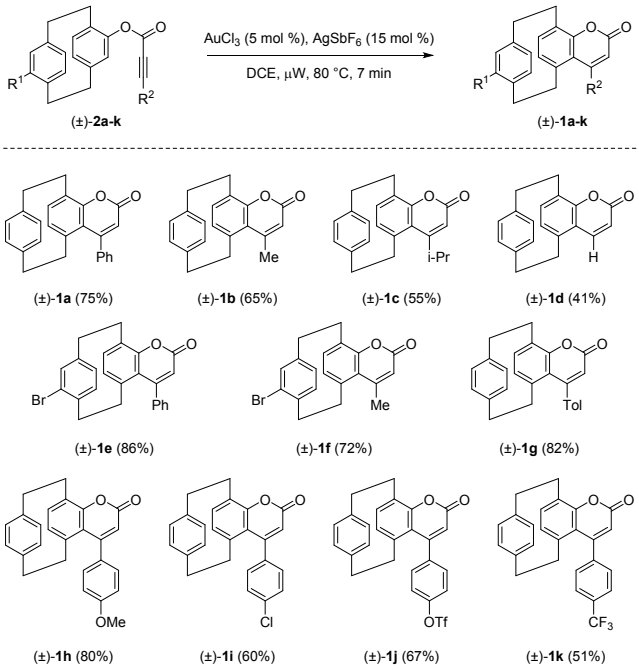
Entry	Catalyst[a]	Solvent	T (°C)	t (min)	Yield (%)
1	$Pd(OAc)_2$	CH_2Cl_2/TFA (1:1)	–20	30	44
2	/	CH_2Cl_2/TFA (1:1)	–20	30	n.d.
3	$Pd(OAc)_2$	CH_2Cl_2	–20	30	n.d.
4	$Pd(OAc)_2$	CH_2Cl_2/TFA (1:1)	0	30	46
5	$Pd(OAc)_2$	CH_2Cl_2/TFA (1:1)	20	30	58
6[b]	$AuCl_3$ $AgSbF_6$	DCE	50	60	63
7[b]	$AuCl_3$ $AgSbF_6$	DCE	80 (μW)	7	75
8[b]	$AuCl_3$ $AgSbF_6$	DCE	90 (μW)	4	69
9[b]	$AgSbF_6$	DCE	80 (μW)	7	n.d.
10[b]	$AuCl_3$	DCE	80 (μW)	7	70

[a] Catalytic charge: $Pd(OAc)_2$ = 3 mol%, $AuCl_3$ = 5mol %; $AgSbF_6$ = 15 mol %. [b] Reaction preformed under inert atmosphere

To further improve the reaction outcome, we ultimately decided to change the catalytic system and test an intramolecular hydroarylation promoted by gold and silver salts.[14d] Compound (±)-**2a** was thus submitted to a reaction in the presence of $AuCl_3$ (5 mol %), and $AgSbF_6$ (15 mol %), in DCE, under inert atmosphere. In this case, after stirring the mixture at 50 °C for 1 h, coumarin (±)-**1a** was isolated in 63% yield (Table 1, entry 6). Interestingly, this product could be rapidly obtained in a better 75% yield while running the same reaction for only 7 minutes, at 80 °C, under microwave irradiation (Table 1, entry 7). Heating the solution at a higher temperature (90 °C) had a detrimental impact on the reaction efficiency since coumarin (±)-**1a** was isolated in a lower 69% yield (Table 1, entry 8). Finally, while no reaction was observed using $AgSbF_6$ (15 mol %) as the sole catalyst (Table 1, entry 9), only a slight difference in term of efficiency could be observed while performing the cyclization in the absence of the silver salt. In this last case, product (±)-**1a** was indeed obtained in 70% yield (Table 1, entry 10). Nonetheless, since better yields were obtained in the presence of $AgSbF_6$ (Table 2, entry 7), we chose to use both the gold and silver catalysts to study the scope of the reaction. The short reaction time of this transformation could help prevent any undesired thermolysis of the pCp motif.

The optimized cyclization tolerated various alkyl and aryl substituents on the alkyne moieties of the pCp esters, and 3D coumarins (±)-**1b-k** could be isolated in moderate to good yields (Scheme 5). It is worth noting that better conversions were generally achieved when the triple bond terminal position was functionalized with electron-donating aromatic groups.

Scheme 5. Scope of the cyclization leading to 3D coumarins



(±)-**2a-k** (±)-**1a-k**

(±)-**1a** (75%) (±)-**1b** (65%) (±)-**1c** (55%) (±)-**1d** (41%)

(±)-**1e** (86%) (±)-**1f** (72%) (±)-**1g** (82%)

(±)-**1h** (80%) (±)-**1i** (60%) (±)-**1j** (67%) (±)-**1k** (51%)

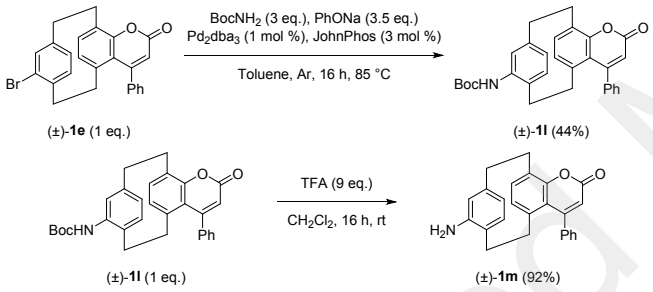
As such, electron-rich compounds (±)-**1g** and (±)-**1h** were obtained in 82% and 80% yields, while electron-poor derivatives (±)-**1i** and (±)-**1k** were isolated in 60% and 51% yields respectively (Scheme 5). Remarkably, the reaction could also be conducted starting from precursors with a terminal alkyne, as well as halogen atoms on the second ring of the pCp core (substrates (±)-**1d**, (±)-**1e** and (±)-**1f**, Scheme 5).

Late-stage functionalization

To access fluorescent 3D coumarins bearing stronger electron-donating groups, we submitted the halogenated compounds (±)-**1e** and (±)-**1i** to a series of Buchwald–Hartwig cross-couplings, and introduced on the molecules an amine substituent at different positions.

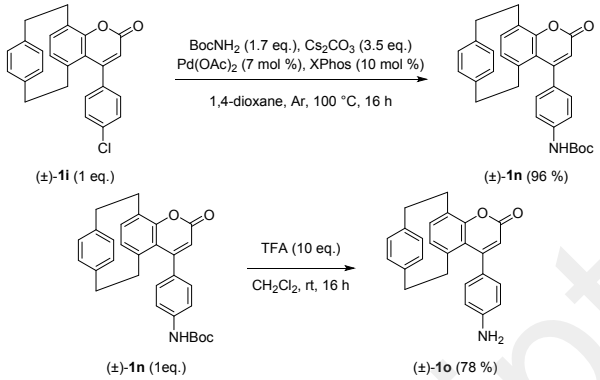
Coumarin (±)-**1e** successfully underwent a reaction with *tert*-butyl carbamate (3 eq.) in the presence of Pd_2dba_3 (1 mol %), JohnPhos (3 mol %), and sodium phenoxide (3.5 eq.), in toluene, at 85 °C under inert atmosphere. After 16 h, the corresponding product (±)-**1l** was isolated in 44% yield (Scheme 6). A cleavage of the Boc protecting group with TFA (10 eq.) subsequently leaded to the pCp-fused coumarin (±)-**1m**, incorporating a primary amine on its "out-of-plane" aromatic ring (Scheme 6).

Scheme 6. Synthesis of coumarin (±)-1m.



Coumarin (±)-**1i** could also react with *tert*-butyl carbamate (1.7 eq.). In this case, the cross-coupling was performed using $Pd(OAc)_2$ (7 mol %) as the catalyst, XPhos (10 mol %) as the ligand, and Cs_2CO_3 (3.5 eq.) as the base, in 1,4-dioxane at 100 °C. Under these conditions, coumarin (±)-**1n** was obtained in 96% yield (Scheme 7). After deprotection of the Boc group with TFA (10 eq.), derivative (±)-**1o** was finally isolated in 78% yield (Scheme 7).

Scheme 7. Synthesis of coumarin (±)-1o.



Shape considerations

Recently, increasing attention has been drawn to analysing and visualizing the diversity of chemical space, and several methods have been reported to highlight the 3D character of molecules.[19] One of these approaches consists in classifying the shape of different compounds according to their normalized principal moment of inertia (PMI). Such values are generally plotted in a ternary diagram with rods (*i.e.* diacetylene), disks (*i.e.* benzene), and spheres (*i.e.* adamantane) as the apexes.[19c] We used this method to compare the shapes of our pCp-based coumarin systems with those of more common, commercially available coumarins. As expected, paracyclophanes (±)-**1a-o** proved to possess rather distinctive three-dimensional shapes (Figure 2).[20] Interestingly, the more substituted compounds showed the tendency to diverge toward the linear apex. As a result, compounds (±)-**1b**, (±)-**1c**, (±)-**1d**, and (±)-**1l** exhibited the most pronounced 3D character for this series of molecules. This feature may reveal to be useful in the future for the development of probes and biosensors showing different physicochemical properties (i.e. solubility) in comparison with classical planar fluorophores.

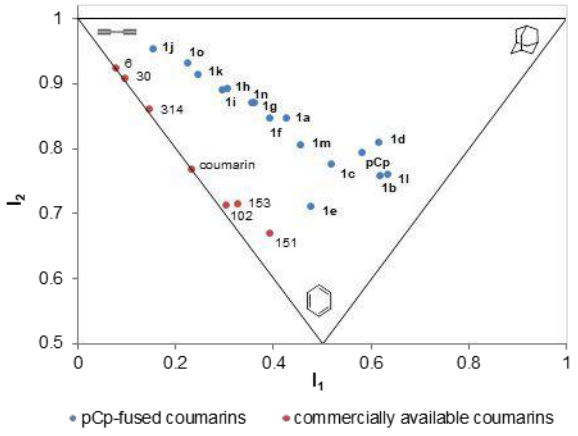


Figure 2. Shape comparison between pCp-fused coumarin and commercially available coumarins

UV-Vis absorption and fluorescence emission spectroscopy

Having the 3D coumarin systems in hand, we undertook a photophysical study to investigate the influence of the pCp motif and its "*phane*" interaction on the spectroscopic properties of fluorophores (±)-**1a-o**.

As a general trend, the 3D coumarins showed red-shifted absorption and emission bands when compared to [2.2]paracyclophane (Figure 3, Table 2). In addition, a bathochromic shift of the absorption and emission maxima was observed in comparison with previously described 4-amino[2.2]paracyclophane[21] (Table 2, entry 18) and paracyclophane-deprived model compounds **7a,b**[22] (Figure 3, Table 2, entries 19 and 20). This behavior can be attributed to an extension of the π-conjugation between the pCp and coumarin motifs in the novel fluorophores.

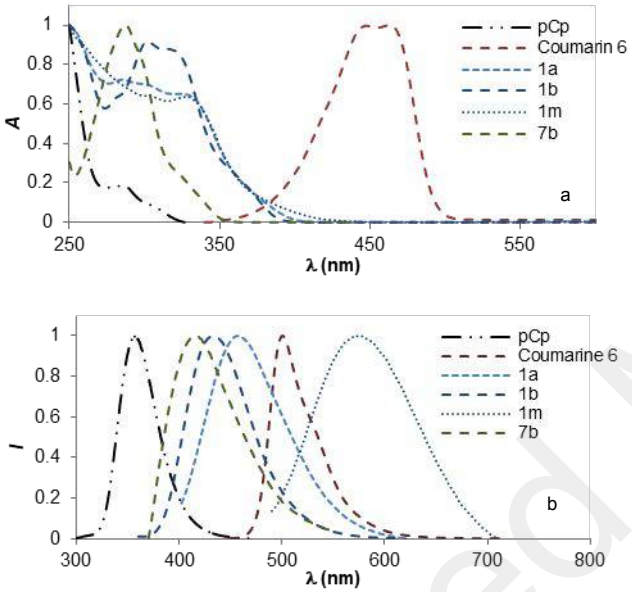
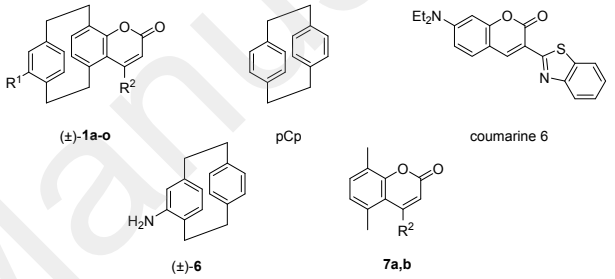


Figure 3. Normalized UV-Vis absorption (a) and fluorescence emission (b) spectra of selected 3D coumarins in comparison with unsubstituted [2.2]paracyclophane, model compound **7b**, and coumarin 6 (10^{-4}M solutions in DCE)

The UV-vis absorption spectra of fluorophores (±)-**1a-o** yet resulted to be shifted toward shorter wavelengths in comparison with commercially available coumarin 6 (Figure 3, Table 2), a compound which shows substantial intramolecular charge transfer (ICT).

With regard to fluorescence spectroscopy, the alkyl substituted derivatives (±)-**1b**, (±)-**1c**, and (±)-**1f** presented an emission band around 425-435 nm in DCE (Table 2, entries 2, 3 and 6). On the other hand, the fluorescence maxima of all aryl-containing 3D coumarins were found between 450 and 475 nm (Table 2, entries 1, 4-5, and 7-14). Interestingly, the introduction of different substituents on the "out-of-plane" *deck* of pCp significantly influenced the photophysical properties of these fluorescent molecules. Indeed, for the 3D coumarins (±)-**1e**, and (±)-**1f**, showing bromine atoms, a hypsochromic shift of the emission bands was observed in comparison with the behavior of their unsubstituted analogs (±)-**1a**, and (±)-**1b** (Table 2, entries 5, and 6 vs entries 1, and 2). However, the incorporation of an amine substituent at the same position induced, for compound (±)-**1m**, a further displacement of its band towards the longer wavelengths. The emission maximum of this fluorophore (560 nm, Table 2 entry 15) resulted to be significantly red-shifted in comparison with its Boc-protected analog (±)-**1l** (450 nm, Table 2 entry 14). The Boc protecting group is therefore supposed to prevent conjugation of the nitrogen lone pair and diminish the ITC character of compound (±)-**1l**. The emission band of coumarin (±)-**1m** was even found to be more red-shifted compared to that of coumarin 6 (Table 2, entry 17). In addition, given the fact that coumarin (±)-**1m** showed an absorption band around 300-330 nm, this molecule was found to possess a remarkably large Stokes shift (230 nm).

Table 2. Spectroscopic characterization of 3D coumarins (±)-1a-o



Entry	Compound	R^1,R^2	λ_{abs} (nm)	λ_{em} (nm)[d]
1[a]	(±)-**1a**	H , Ph	265, 300, 330	460
2[a]	(±)-**1b**	H, Me	301, 319	435
3[a]	(±)-**1c**	H, *i*-Pr	300,320	432
4[a]	(±)-**1d**	H, H	304, 320	445
5[a]	(±)-**1e**	Br, Ph	307, 325	450
6[a]	(±)-**1f**	Br, Me	306, 320	425
7[a]	(±)-**1g**	H, *p*-MePh	315	455
8[a]	(±)-**1h**	H, *p*-OMePh	300, 330	455
9[a]	(±)-**1i**	H, *p*-ClPh,	288, 310, 335	465
10[a]	(±)-**1j**	H, *p*-OTfPh,	280, 330	470
11[a]	(±)-**1k**	H, *p*-CF_3Ph	270, 335	475
12[a]	(±)-**1l**	NHBoc, Ph	317	450

13[a]	(±)-**1m**	NH_2, Ph	300, 330	560
14[a]	(±)-**1n**	H, *p*-NHBocPh	317	450
15[a]	(±)-**1o**	H, *p*-NH_2Ph	330	470
16[b]	pCp	/	286, 302	356
17[c]	Coumarin 6	/	455	498
18[e]	(±)-**6**	/	274, 324	386
19	**7a**	/,Ph	294	418
20	**7b**	/, Me	286	413

[a] 10^{-4} M solutions in DCE. [b] 10^{-5} M solution in DCM. [c] 10^{-5} M solution in DCE. [d] No significant effects were observed on the emission spectra while changing the excitation wavelength or the concentration of the samples. [e] 10^{-4} M solution in DCM.

These results clearly indicate that through-space interactions significantly influence the photophysical properties of pCp-fused coumarins.

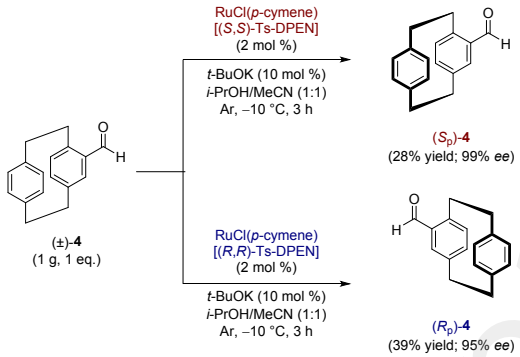
All compounds (±)-**1a-o** showed a good photostability.[23] Nonetheless, as in the case of several classical coumarin derivatives, low fluorescence quantum yields were observed for this series of pCp-based fluorophores (< 5%, see SI). This behavior may in part be explained by a non-optimal spatial disposition of the electron-donor and electron-withdrawing substituents of the molecules.

Enantioenriched planar chiral 3D coumarins

Starting from optically active precursors, our synthetic approach can easily be employed to access enantioenriched 3D coumarin systems. To illustrate this possibility, compounds (R_p)-**1b** and (S_p)-**1b** were rapidly prepared as a proof of concept.

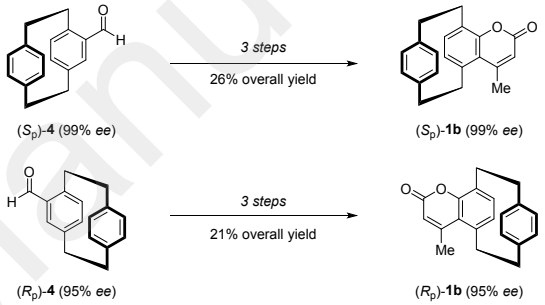
The enantioenriched aldehyde precursors (R_p)-**4** and (S_p)-**4** were first synthesized through a kinetic resolution of racemic 4-formyl[2.2]paracyclophane previously developed in our laboratory.[10a] Such reaction, which was run on a one gram scale, involved an asymmetric transfer hydrogenation catalysed by commercially available chiral ruthenium complexes (Scheme 8).

Scheme 8. Kinetic resolution of 4-formyl[2.2]paracyclophane



Precursors (R_p)-**4** and (S_p)-**4** were then converted into the corresponding 3D coumarins via the oxidation-acylation-cyclization pathway, as described above. Compounds (S_p)-**1b** and (R_p)-**1b** could eventually be isolated in 26% and 21% overall yields respectively (Scheme 9).

Scheme 9. Access to enantiopure coumarins (R_p)-1b and (S_p)-1b



No loss in term of enantiomeric excess was observed during the derivatization process.

Chiroptical properties of enantiopure pCp-fused coumarins

Circularly polarized light-emitting molecules have the ability to generate optical signals, which include not only wavelength and intensity but also chirality information.[24] These compounds are therefore currently receiving great attention for their potential applications in material chemistry, biochemistry, and for chirality induction in the field of organic synthesis and optical cryptography.

In recent years, planar chiral pCps were found to possess excellent characteristics both for circular dichroism (CD) and circularly polarized luminescence (CPL). In most cases, however, the [2.2]paracyclophane unit was used as building block to obtain optically active second-ordered structures of different shapes.[8] Given the fact that, up to now, only few studies have described the chiroptical properties of simple pCp derivatives,[7f,25] we finally decided to investigate the behavior of enantiopure 3D coumarins (S_p)-**1b** and (R_p)-**1b**.

The circular dichroism spectra of compounds (S_p)-**1b** and (R_p)-**1b** were recorded in CH_2Cl_2 (10^{-5} M solutions), and interesting mirror-image Cotton effect could be observed (Figure 4).

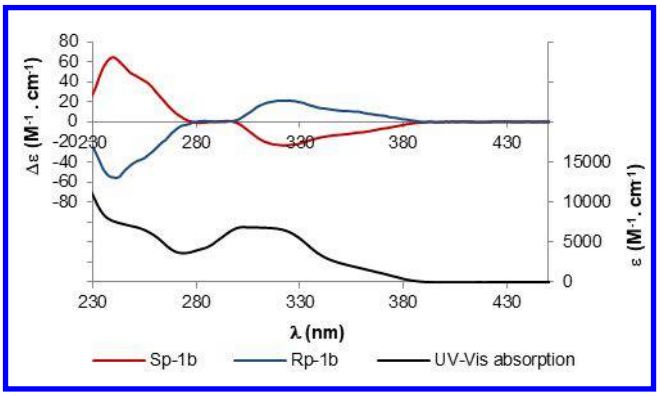


Figure 4. CD spectra and UV-Vis absorption of compounds (S_p)-**1b** and (R_p)-**1b**

Indeed, for coumarin (S_p)-**1b** a positive response was observed at 240 nm ($\Delta\varepsilon$ = +64 M^{-1}/cm^{-1}) and a negative at 320 nm ($\Delta\varepsilon$ = −23 M^{-1}/cm^{-1}). Coumarin (R_p)-**1b**, as expected, showed a negative response at 240 nm ($\Delta\varepsilon$ = −55 M^{-1}/cm^{-1}), and a positive at 320 nm ($\Delta\varepsilon$ = +21 M^{-1}/cm^{-1}). Furthermore, the two molecules showed good absorption dissymmetry factors (g_{abs} ~ 8 x 10^{-3} at 240 nm, see SI).

The circularly polarized luminescence (CPL) spectra of coumarins (S_p)-**1b** and (R_p)-**1b** were also recorded in DCM (10^{-5} M solutions, λ_{ex} = 330 nm), using a home-built CPL spectrofluoropolarimeter.[26] Here again, the two enantiomers gave mirror-image CPL signatures at the same wavelength as observed for unpolarised fluorescence (Figure 5). The obtained signals allowed us to determine a luminescence dissymmetry factor (g_{lum}) of 5 x 10^{-3}. Interestingly, the absorption and emission dissymmetry factors of compounds (S_p)-**1b** and (R_p)-**1b** are nearly equal to each other (g_{lum} ~ g_{abs}), thus suggesting that no significant changes occur in the chiral geometry of the excited state.

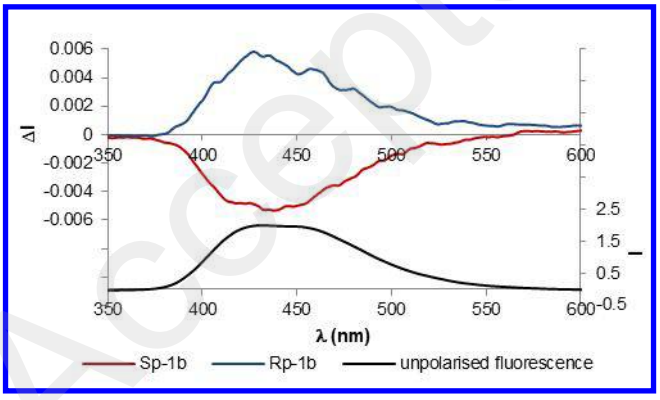


Figure 5. CPL spectra and unpolarised fluorescence of compounds (S_p)-**1b** and (R_p)-**1b**.

The observed g_{lum} value is comparable to the dissymmetry factors previously reported for more complex chiral pCps, and other organic dyes (10^{-4} - 10^{-2}).[8,27] This last result thus clearly proves that our synthetic approach can be particularly useful to rapidly obtain compact heteroaromatic paracyclophanes with promising chiroptical properties.

CONCLUSION

We developed a novel straightforward three-step procedure for preparing a series of pCp-based coumarin fluorophores by using an intramolecular cyclization of aryl alkynoates as the key step. This practical and simple method allowed us to rapidly explore new regions of chemical space by synthesizing compact heteroaromatic pCp dyes with unique three-dimensional structures. The photophysical properties of the newly synthesized compounds were also investigated. All 3D coumarin derivatives showed red-shifted absorption and emission bands in comparison with unsubstituted [2.2]paracyclophane.

The blue-green fluorescence emission (λ_{em} up to 560 nm) of the dyes could easily be tuned by varying their substitution pattern and proved to be strongly influenced by the "*phane*" motif. In addition, the pCp-based fluorophores showed extremely large Stokes shifts (up to 230 nm), especially if compared to more common or commercially available coumarin derivatives. Our approach finally proved to be particularly useful for synthesizing optically active planar chiral coumarins. Such enantioenriched derivatives showed promising chiroptical properties, both in term of circular dichroism and circularly polarized luminescence (g_{abs} ~ 8 x 10^{-3}; g_{lum} ~ 5 x 10^{-3}).

Studies are currently ongoing in our laboratory to prepare other families of compact pCp-based dyes with finely-tuned photophysical properties and increased fluorescence quantum yields.

EXPERIMENTAL SECTION

General remarks: All reactions were carried out under inert atmosphere, (in oven-dried glassware, using dry solvents unless otherwise specified. All commercially available compounds were purchased from Aldrich Chemical Co., Acros Organics or Alfa Aesar and used as received. Analytical thin layer chromatography (TLC) was performed on silica gel plates (Merck 60F254) visualized with a UV lamp (254 nm). Flash chromatography was performed on silica gel (60-230 mesh) unless otherwise specified. Organic extracts were dried over anhydrous $MgSO_4$. NMR spectra (^1H and $^{13}C\{^1H\}$) were recorded on Bruker Avancell 500 spectrometer, at 500 MHz (H value) in $CDCl_3$. Spectra were referenced to residual chloroform (7.26 ppm, ^1H; 77.0 ppm, $^{13}C\{^1H\}$). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), and m (multiplet or overlap of nonequivalent resonances), dd (doublet of doublet), td (triplet of doublet), and br (broad signal). Coupling constants, *J*, are reported in hertz (Hz). DEPT-135 experiments were used to assign ^{13}C NMR spectra. All NMR spectra were obtained at 300K unless otherwise specified. All microwave-mediated reactions were carried out using a Biotage Initiator™ Exp or an Anton Paar Monowave

microwave synthesizer. The microwave reactions were carried out in 2 - 5 mL vials. Optical rotations (αD) were measured on a Perkin Elmer polarimeter (model 341) at 20 °C. IR spectra were obtained using a spectrum one FT-IR spectrometer (Perkin Elmer). High Resolution mass spectra were recorded on a ThermoFischer Exactive Orbitrap spectrometer. HPLC analyses were performed on a Shimadzu chromatograph equipped with a diode array UV/VIS detector. Absorption and fluorescence spectra were recorded on UV-2700 spectrophotometer (Shimadzu) and F-7000 fluorescence spectrometer (Hitachi), respectively. The photophysical measurements were performed on air-equilibrated solutions, using quarts cuvettes with 1 cm optical path length. Electronic circular dichroism (ECD, in M^{-1} cm^{-1}) was measured on a Jasco J-815 Circular Dichroism Spectrometer (IFR140 facility - Biosit - Université de Rennes 1). Propiolic acid derivatives, as well as compounds (±)-**4**, (S_p)-**4**, (R_p)-**4**, and (±)-**6** were prepared according to previously reported procedures.[10a,21,28]

*Representative procedure for the Dakin oxidation: synthesis of compound (±)-**3a***. 4-Formyl[2.2]paracyclophane (527 mg, 2.23 mmol, 1eq.) was dissolved in a 1:1 mixture of DCM/MeOH. To this solution, 10 drops conc. H_2SO_4 and H_2O_2 (35% in water, 145 µL, 2.99 mmol, 1.4 eq.) were added subsequently and the reaction was stirred at rt overnight. The solvent was removed under reduced pressure and the residue was taken up in DCM (30 mL) and water (40 mL). The two phases were separated and the aqueous phase extracted with DCM (2x20 mL). The combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, gravity filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/Cy (1:14) as the eluent to afford compound (±)-**3a** (395 mg, 1.76 mmol, 79 % yield) an amorphous pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.00 (dd, J = 7.8, 1.9 Hz, 1H), 6.55 (dd, J = 7.8, 1.9 Hz, 1H), 6.45 (dd, J = 7.8, 1.9 Hz, 1H), 6.41-6.34 (m, 2H), 6.26 (dd, J = 7.7, 1.6 Hz, 1H), 5.54 (d, J = 1.5 Hz, 1H), 4.43 (s, 1H), 3.33 (ddd, J = 13.6, 7.7, 4.4 Hz, 1H), 3.18-2.80 (m, 6H), 2.74-2.58 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.6 (C), 141.9 (C), 139.6 (C), 138.8 (C), 135.4 (CH), 133.6 (CH), 132.7 (CH), 131.8 (CH), 127.9 (CH), 125.4 (C), 125.0 (CH), 122.6 (CH), 35.3 (CH_2), 34.8 (CH_2), 33.8 (CH_2), 31.1 (CH_2) ppm. Spectroscopic data were consistent with the literature data for this compound.[17]

*Compound (S_p)-**3a***: According to the representative procedure, starting from compound (S_p)-**4** (180 mg, 0.76 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:14) gave compound (S_p)-**3a** (140 mg, 82% yield, 99% *ee*) as amorphous white solid.

*Compound (R_p)-**3a***: According to the representative procedure, starting from compound (R_p)-**4** (180 mg, 0.76 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:14) gave compound (R_p)-**3a** (132 mg, 77% yield, 95% *ee*) as amorphous white solid.

*Synthesis of compound (±)-**3b**:* To a solution of 4-16-dibromo-[2.2]paracyclophane (1 g, 2.73 mmol, 1 eq.) in dry THF (100 mL) was slowly added *n*-BuLi (2.5 M in hexanes, 3 mL, 7.5 mmol, 2.75 eq.) at −78 °C under an argon atmosphere. The mixture was stirred at −78 °C for 30 min, then $B(OMe)_3$ (3 mL, 26.4 mmol, 9.7 eq.) was added. The reaction was allowed to warm up to rt and stirred overnight. After cooling to 0 °C, NaOH (1M in H_2O, 1.2 mL, 1.2 mmol, 0.4 eq.) and H_2O_2 (30 wt. % in H_2O, 3 mL, 26.5 mmol, 9.7 eq.) were added and the resulting mixture was stirred for 1h at rt. A saturated NH_4Cl aq solution (30 mL) was then added. The aqueous phase was extracted with DCM (3 x 30 mL), the combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using Cy/EtOAc (14:1) as the eluent to afford compound (±)-**3b** (558 mg, 1.84 mmol, 68 % yield) as an amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (dd, J = 7.8, 1.7 Hz, 1H), 6.81 (dd, J = 7.7, 1.7 Hz, 1H), 6.47 (d, J = 1.5 Hz, 1H), 6.42 (d, J = 7.8 Hz, 1H), 6.35 (d, J = 7.7 Hz, 1H), 5.58 (d, J = 1.6 Hz, 1H), 4.44 (br, s, 1H), 3.49 (ddd, J = 13.0, 10.4, 2.2 Hz, 1H), 3.36 (ddd, J = 13.3, 10.2, 2.8 Hz, 1H), 3.14–3.05 (m, 2H), 3.02–2.87 (m, 2H), 2.80 (ddd, J = 13.3, 10.7, 5.4 Hz, 1H), 2.68 (ddd, J = 13.6, 10.7, 5.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.6 (C), 141.5 (C), 141.1 (C), 138.4 (C), 137.5 (CH), 134.5 (CH), 133.8 (CH), 127.7 (CH), 126.5 (C), 124.8 (C), 122.9 (CH), 122.3 (CH), 35.4 (CH_2), 33.2 (CH_2), 32.8 (CH_2), 30.4 (CH_2) ppm. IR (neat):3351, 2932, 1573, 1417, 1320, 1268, 1093, 1033, 869, 830 cm^{-1}. HRMS (ESI): m/z $[M–H]^-$ calcd for $C_{16}H_{14}OBr$: 301.0234; found: 301.0228.

*Representative procedure for the acylation reaction: synthesis of compound (±)-**2a**.* Compound (±)-**3a** (400 mg, 1.78 mmol, 1 eq.), DMAP (33 mg, 0.27 mmol, 0.15 eq.), and phenylpropiolic acid (390 mg, 2.69 mmol, 1.5 eq.) were dissolved in dry DCM (15 mL) under an argon atmosphere. DCC (1 M in DCM, 2.7 mL, 2.7 mmol, 1.5 eq.) was added turning the reactions dark yellow and cloudy. The mixture was stirred at rt for 16 h, followed by filtration through a short plug of silica gel with DCM washings. The filtrates were concentrated under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: Cy/EtOAc 14:1) to afford compound (±)-**2a** (487 mg, 1.38 mmol, 77 %) as an amorphous yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69-7.61 (m, 2H), 7.55-7.47 (m, 1H), 7.46-7.38 (m, 2H), 7.03 (dd, J = 7.8, 1.8 Hz, 1H), 6.61-6.50 (m, 4H), 6.48 (dd, J = 7.8, 1.7 Hz, 1H), 6.20-6.10 (m, 1H), 3.28 (ddd, J = 13.0, 9.9, 2.6 Hz, 1H), 3.22-3.15 (m, 1H), 3.16-2.96 (m, 5H), 2.77 (ddd, J = 13.4, 10.3, 5.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.9 (C), 148.5 (C), 141.8 (C), 139.5 (C), 139.1 (C), 135.1 (CH), 133.4 (CH), 133.2 (2CH), 132.8 (CH), 132.4 (CH), 131.3 (C), 130.9 (CH), 130.9 (CH), 129.7 (CH), 128.6 (2CH), 127.6 (CH), 119.4 (C), 88.6 (C), 80.4 (C), 35.2 (CH_2), 34.8 (CH_2), 34.2 (CH_2), 31.5 (CH_2) ppm. IR (neat): 2928, 2852, 2219, 1721, 1490, 1281, 1153, 1084, 918, 758 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{21}O_2$: 353.1536; found: 353.1544.

*Compound (±)-**2b**:* According to the representative procedure, starting from compound (±)-**3a** (150 mg, 0.67 mmol); flash chromatography on silica gel (DCM/Cy, 1:2) gave compound (±)-**2b** (119 mg, 61% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (dd, J = 7.8, 1.9 Hz, 1H), 6.56-6.41 (m, 5H), 6.06 (d, J = 1.3 Hz, 1H), 3.23-2.93 (m, 7H), 2.72 (ddd, J = 12.6, 10.1, 5.4 Hz, 1H), 2.09 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.6 (C), 148.4 (C), 141.8 (C), 139.5 (C), 139.1 (C), 135.4 (CH), 133.4 (CH), 132.9 (CH), 132.4 (CH), 131.2 (C), 130.7 (CH), 129.7 (CH), 127.6 (CH), 87.7 (C), 72.3 (C), 35.3 (CH_2), 34.9 (CH_2), 34.2 (CH_2), 31.5 (CH_2), 4.1 (CH_3) ppm. IR (neat): 2987, 2959, 2929, 2900, 2856, 2234, 1721, 1412, 1240, 1222, 1103, 1086, 1043, 899, 740, 716 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{19}O_2$: 291.1380; found: 291.1386.

*Compound (S_p)-**2b***: According to the representative procedure, starting from compound (S_p)-**3a** (108 mg, 0.48

mmol); flash chromatography on silica gel (DCM/Cy, 1:2 to 1:1) gave compound (S_p)-**2b** (66 mg, 47% yield, 99% *ee*) as amorphous white solid. $[\alpha]_D^{20}$ +205 (c 0.21, $CHCl_3$).

*Compound (R_p)-**2b***: According to the representative procedure, starting from compound (R_p)-**3a** (113 mg, 0.50 mmol); flash chromatography on silica gel (DCM/Cy, 3:7 to 6:4) gave compound (R_p)-**2b** (85 mg, 58% yield, 95% *ee*) as amorphous white solid. $[\alpha]_D^{20}$ -189 (c 0.16, $CHCl_3$).

*Compound (±)-**2c***: According to the representative procedure, starting from compound (±)-**3a** (101 mg, 0.45 mmol); flash chromatography on silica gel (DCM/Cy, 1:1) gave compound (±)-**2c** (58 mg, 40% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.97 (dd, J = 7.8, 1.6 Hz, 1H), 6.61-6.38 (m, 5H), 6.08 (s, 1H), 3.30-2.90 (m, 7H), 2.87-2.63 (m, 2H), 1.30 (d, J = 6.9 Hz, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.8 (C), 148.5 (C), 141.7 (C), 139.5 (C), 139.0 (C), 135.3 (CH), 133.3 (CH), 132.8 (CH), 132.3 (CH), 131.2 (C), 130.6 (CH), 129.7 (CH), 127.6 (CH), 96.5 (C), 72.1 (C), 35.2 (CH_2), 34.8 (CH_2), 34.2 (CH_2), 31.5 (CH_2), 21.7 ($2CH_3$), 20.6 (CH) ppm. IR (neat): 2978, 2931, 2855, 2246, 1723, 1219, 1161, 1003, 716 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{23}O_2$: 319.1693; found: 319.1698.

*Compound (±)-**2d***: According to the representative procedure, starting from compound (±)-**3a** (150 mg, 0.67 mmol); flash chromatography on silica gel (DCM/Cy, 1:1) gave compound (±)-**2d** (34 mg, 18% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.94 (dd, J = 7.8, 1.7 Hz, 1H), 6.61-6.38 (m, 5H), 6.09 (s, 1H), 3.26-2.92 (m, 8H), 2.73 (ddd, J = 13.0, 9.6, 6.1 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.5 (C), 148.2 (C), 142.0 (C), 139.4 (C), 139.1 (C), 135.5 (CH), 133.4 (CH), 132.9 (CH), 132.3 (CH), 131.0 (C), 130.9 (CH), 129.6 (CH), 127.5 (CH), 76.5 (CH), 74.5 (C), 35.3 (CH_2), 34.9 (CH_2), 34.2 (CH_2), 31.5 (CH_2) ppm. IR (neat): 3257, 2930, 200, 2121, 1728, 1412, 1201, 1083, 912, 716 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{17}O_2$: 277.1223; found: 277.1229.

*Compound (±)-**2e***: According to the representative procedure, starting from compound (±)-**3b** (294 mg, 0.97 mmol); flash chromatography on silica gel (DCM/Cy, 1:2) gave compound (±)-**2e** (315 mg, 75% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): 7.63 (d, J = 7.4 Hz, 2H), 7.51-7.49 (m, 1H), 7.44-7.41 (m, 2H), 7.13 (dd, J = 7.8, 1.1 Hz, 1H), 7.00 (dd, J = 7.8, 1.0 Hz, 1H), 6.53-6.49 (m, 3H), 6.15 (s, 1H), 3.54-3.48 (m, 1H), 3.30-3.12 (m, 1H), 3.04-2.93 (m, 2H), 2.88-2.75 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1 (C), 149.0 (C), 141.5 (C), 141.3 (C), 138.8 (C), 137.6 (CH), 134.6 (CH), 134.5 (CH), 133.4 (2CH), 131.2 (CH), 131.0 (C), 129.2 (CH), 128.8 (2CH), 127.9 (CH), 127.8 (CH), 126.9 (C), 119.5 (C), 89.0 (C), 80.5 (C), 35.5 (CH_2), 33.7 (CH_2), 32.9 (CH_2), 31.0 (CH_2) ppm. IR (neat): 3044, 2964, 2934, 2856, 2219, 1719, 1489, 1284, 1227, 1182, 1156, 1034, 919, 823, 759 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{20}O_2Br$: 431.0641; found: 431.0646.

*Compound (±)-**2f***: According to the representative procedure, starting from compound (±)-**3b** (146 mg, 0.48 mmol); flash chromatography on silica gel (DCM/Cy, 3:7 to 1:1) gave compound (±)-**2f** (121 mg, 68% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09 (dd, J = 7.9, 1.7 Hz, 1H), 6.94 (dd, J = 7.8, 1.7 Hz, 1H), 6.60-6.34 (m, 3H), 6.08 (d, J = 1.6 Hz, 1H), 3.49 (ddd, J = 13.1, 10.3, 2.3 Hz, 1H), 3.26-3.05 (m, 3H), 3.05-2.89 (m, 2H), 2.82 (ddd, J = 13.4, 10.7, 5.6 Hz, 1H), 2.74 (ddd, J = 13.4, 10.7, 4.6 Hz, 1H), 2.09 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5 (C), 148.7 (C), 141.4 (C), 141.1 (C), 138.6 (C), 137.4 (CH), 134.3 (2CH), 130.7 (C), 129.0 (CH), 127.7 (CH), 127.6 (CH), 126.7 (C), 87.9 (C), 72.2 (C), 35.4 (CH_2), 33.5 (CH_2), 32.8 (CH_2), 30.9 (CH_2), 4.0 (CH_3) ppm. IR (neat): 2987, 2901, 2236, 1730, 1410, 1393, 1252, 1226, 1075, 1066, 1051, 905, 742 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{18}O_2Br$: 369.0485; found: 369.0492.

*Compound (±)-**2g***: According to the representative procedure, starting from compound (±)-**3a** (150 mg, 0.67 mmol); flash chromatography on silica gel (DCM/Cy, 1:1) gave compound (±)-**2g** (183 mg, 75% yield) as amorphous yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, J = 8.1 Hz, 2H), 7.25-7.18 (m, 2H), 7.01 (dd, J = 7.8, 1.9 Hz, 1H), 6.60-6.49 (m, 4H), 6.46 (dd, J = 7.8, 1.7 Hz, 1H), 6.13 (s, 1H), 3.26 (ddd, J = 13.1, 9.9, 2.7 Hz, 1H), 3.17 (ddd, J = 13.0, 10.0, 5.5 Hz, 1H), 3.13-3.04 (m, 4H), 3.00 (td, J = 11.6, 8.5 Hz, 1H), 2.75 (ddd, J = 13.2, 10.3, 5.5 Hz, 1H), 2.41 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1 (C), 148.6 (C), 141.8 (C), 141.7 (C), 139.6 (C), 139.1 (C), 135.4 (CH), 133.4 (CH), 133.2 (2CH), 132.9 (CH), 132.4 (CH), 131.3 (C), 130.8 (CH), 129.7 (CH), 129.4 (2CH), 127.7 (CH), 116.3 (C), 89.2 (C), 80.1 (C), 35.3 (CH_2), 34.9 (CH_2), 34.3 (CH_2), 31.6 (CH_2), 21.8 (CH_3) ppm. IR (neat): 2929, 900, 2217, 1721, 1286, 1149, 1084, 817, 716 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{26}H_{23}O_2$: 367.1693; found: 367.1701.

*Compound (±)-**2h***: According to the representative procedure, starting from compound (±)-**3a** (120 mg, 0.54 mmol); flash chromatography on silica gel (DCM/Pentane, 4:6) gave compound (±)-**2h** (134 mg, 65% yield) as amorphous pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.43 (m, 2H), 6.93 (dd, J = 7.9, 1.9 Hz, 1H), 6.89-6.79 (m, 2H), 6.50-6.42 (m, 4H), 6.39 (dd, J = 7.8, 1.8 Hz, 1H), 6.05 (br, d, J = 1.4 Hz, 1H), 3.79 (s, 3H), 3.18 (ddd, J = 12.9, 9.9, 2.6 Hz, 1H), 3.13-3.06 (m, 1H), 3.06-2.97 (m, 4H), 2.97-2.88 (m, 1H), 2.67 (ddd, J = 13.2, 10.3, 5.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.8 (C), 152.3 (C), 148.6 (C), 141.8 (C), 139.6 (C), 139.1 (C), 135.4 (CH), 135.2 (2CH), 133.4 (CH), 132.9 (CH), 132.4 (CH), 131.4 (C), 130.7 (CH), 129.8 (CH), 127.7 (CH), 114.4 (2CH), 111.2 (C), 89.7 (C), 80.0 (C), 55.4 (CH_3), 35.3 (CH_2), 34.9 (CH_2), 34.3 (CH_2), 31.6 (CH_2) ppm. IR (neat): 3009, 2931, 2853, 2211, 1718, 1603, 1509, 1284, 1254, 1145, 1028, 834 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{26}H_{23}O_3$: 383.1642; found: 383.1660.

*Compound (±)-**2i***: According to the representative procedure, starting from compound (±)-**3a** (153 mg, 0.68 mmol); flash chromatography on silica gel (DCM/Cy, 1:2) gave compound (±)-**2i** (142 mg, 54% yield) as amorphous yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61-7.49 (m, 2H), 7.49-7.33 (m, 2H), 6.99 (dd, J = 7.8, 1.9 Hz, 1H), 6.58-6.49 (m, 4H), 6.47 (dd, J = 7.8, 1.8 Hz, 1H), 6.13 (d, J = 1.3 Hz, 1H), 3.24 (ddd, J = 13.0, 9.8, 2.8 Hz, 1H), 3.20-2.96 (m, 6H), 2.76 (ddd, J = 13.2, 10.2, 5.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.8 (C), 148.5 (C), 141.9 (C), 139.5 (C), 139.1 (C), 137.4 (C), 135.4 (CH), 134.4 (2CH), 133.4 (CH), 132.9 (CH), 132.4 (CH), 131.3 (C), 130.9 (CH), 129.7 (CH), 129.2 (2CH), 127.6 (CH), 117.9 (C), 87.3 (C), 81.2 (C), 35.3 (CH_2), 34.9 (CH_2), 34.3 (CH_2), 31.5 (CH_2) ppm. IR (neat): 2968, 2930, 2900, 2221, 1721, 1489, 1284, 1156, 1090, 1014, 909, 830, 732 cm^{-1}. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{20}O_2Cl$: 387.1146; found: 387.1155.

*Compound (±)-**2j***: According to the representative procedure, starting from compound (±)-**3a** (150 mg, 0.67 mmol); flash chromatography on silica gel (DCM/Cy, 1:2 to 1:1) gave compound (±)-**2j** (106 mg, 32% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75-7.66 (m, 2H), 7.39-7.30 (m, 2H), 6.98 (dd, J = 7.8, 1.8 Hz, 1H), 6.60-6.44 (m, 5H), 6.13 (s, 1H), 3.24 (ddd, J = 13.0, 9.6, 2.9 Hz, 1H), 3.19-2.95 (m, 6H), 2.76 (ddd, J = 13.2, 10.1, 5.7 Hz, 1H) ppm. ^{13}C NMR (125

MHz, $CDCl_3$): δ 151.5 (C), 150.7 (C), 148.4 (C), 142.0 (C), 139.5 (C), 139.1 (C), 135.4 (CH), 135.1 (2CH), 133.4 (CH), 132.9 (CH), 132.4 (CH), 131.2 (C), 131.0 (CH), 129.7 (CH), 127.5 (CH), 121.9 (2CH), 120.1 (C), 118.7 (q, *J* = 318 Hz, CF_3), 85.8 (C), 81.7 (C), 35.3 (CH_2), 34.9 (CH_2), 34.2 (CH_2), 31.5 (CH_2) ppm. IR (neat): 2932, 2856, 2227, 1725, 1498, 147, 1214, 1160, 1139, 884 cm^{-1}. HRMS (ESI): *m/z* $[M-H]^-$ calcd for $C_{26}H_{18}O_5F_3S$: 499.0833; found: 499.0847.

*Compound (±)-**2k***: According to the representative procedure, starting from compound (±)-**3a** (100 mg, 0.45 mmol); flash chromatography on silica gel (DCM/Cy, 1:1) gave compound (±)-**2k** (98 mg, 52% yield) as amorphous white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.60-6.53 (m, 3H), 6.52 (dd, *J* = 7.7, 1.8 Hz, 1H), 6.48 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.15 (d, *J* = 1.2 Hz, 1H), 3.26 (ddd, *J* = 13.0, 9.8, 2.8 Hz, 1H), 3.21-2.96 (m, 6H), 2.78 (ddd, *J* = 13.3, 10.2, 5.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5 (C), 148.4 (C), 142.0 (C), 139.5 (C), 139.1 (C), 135.4 (CH), 133.4 (CH), 133.3 (2CH), 132.9 (CH), 132.5 (q, *J* = 32.7 Hz, C), 132.4 (CH), 131.2 (C), 130.9 (CH), 129.7 (CH), 127.5 (CH), 125.5 (q, *J* = 3.6 Hz, 2CH), 123.5 (q, *J* = 270.9 Hz, CF_3), 123.2 (C), 86.2 (C), 81.9 (C), 35.2 (CH_2), 34.8 (CH_2), 34.2 (CH_2), 31.5 (CH_2) ppm. IR (neat): 2932, 2856, 2231, 1725, 1322, 1280, 1157, 1130, 1066, 844, 734, 716 cm^{-1}. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{26}H_{20}O_2F_3$: 421.1410; found: 421.1421.

*Representative procedure for the gold-catalysed intramolecular cyclization: synthesis of compound (±)-**1a***. A 2-6 mL microwave vial was charged with $AuCl_3$ (4 mg, 0.013 mmol, 0.08 eq.) and $AgSbF_6$ (9 mg, 0.026 mmol, 0.16 eq.) under an Argon atmosphere. Dry DCE (1.5 mL) was then added and the resulting mixture was stirred at rt for 5 min. Compound (±)-**2a** (55 mg, 0.16 mmol, 1 eq.) was finally added. The tube was sealed, then evacuated and refilled with argon three times. The solution was irradiated in a microwave reactor at 80 °C for 7 min. At the end of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using Cy/EtOAc (17:3) as the eluent to afford compound (±)-**1a** (41 mg, 0.015 mmol, 75% yield) as an amorphous white solid ^1H NMR (500 MHz, $CDCl_3$): δ 7.80-7.18 (br m, 5H), 6.80 (d, *J* = 7.7 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 1H), 6.47 (s, 2H), 6.34 (s, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 3.69 (ddd, *J* = 13.3, 10.5, 2.8 Hz, 1H), 3.22 (ddd, *J* = 13.0, 10.5, 5.0 Hz, 1H), 3.10 (ddd, *J* = 13.3, 10.8, 2.9 Hz, 1H), 2.88-2.65 (m, 2H), 2.49 (ddd, *J* = 14.1, 9.7, 8.0 Hz, 1H), 2.40-2.25 (m, 1H), 2.18 (ddd, *J* = 13.3, 9.5, 8.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.9 (C), 156.1 (C), 154.2 (C), 141.3 (C), 139.5 (C), 138.4 (C), 138.0 (C), 136.6 (CH), 132.9 (CH), 132.2 (CH), 131.7 (CH), 129.6 (CH), 128.9 (br, 4CH), 128.3 (CH and C), 126.9 (CH), 120.6 (C), 115.9 (CH), 36.2 (CH_2), 35.1 (CH_2), 33.8 (CH_2), 30.0 (CH_2) ppm. IR (neat): 2938, 2856, 2248, 1716, 1568, 1446, 1415, 1355, 1183, 1038, 910, 730 cm^{-1}. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}O_2$: 353.1535; found: 353.1545.

*Compound (±)-**1b***: According to the representative procedure, starting from compound (±)-**2b** (40 mg, 0.14 mmol); flash chromatography on silica gel (EtOAc/Cy, 3:17) gave compound (±)-**1b** (26 mg, 65% yield) as amorphous white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 6.74 (d, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 1H), 6.56 (ddd, *J* = 9.9, 8.0, 1.8 Hz, 2H), 6.45 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.24 (d, *J* = 1.2 Hz, 1H), 6.20 (dd, *J* = 7.8, 2.0 Hz, 1H), 3.76-3.55 (m, 2H), 3.31-3.13 (m, 2H), 3.07 (ddd, *J* = 13.3, 10.8, 2.9 Hz, 1H), 2.95 (dt, *J* = 14.6, 9.2 Hz, 1H), 2.75 (ddd, *J* = 13.4, 10.8, 5.0 Hz, 1H), 2.63 (dt, *J* = 13.4, 9.3 Hz, 1H), 2.50 (d, *J* = 1.2 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7 (C), 153.3 (C), 153.1 (C), 139.8 (C), 139.7 (C), 137.7 (C), 135.9 (CH), 133.1 (CH), 132.2 (CH), 131.9 (CH), 129.0 (CH), 128.6 (C), 127.1 (CH), 121.9 (C), 116.0 (CH), 36.9 (CH_2), 35.3 (CH_2), 33.7 (CH_2), 30.1 (CH_2), 22.6 (CH_3) ppm. IR (neat): 2924, 2854, 2248, 1721, 1573, 1415, 1355, 1191, 1042, 914, 730, 720 cm^{-1}. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}O_2$: 291.1380; found: 291.1385.

*Compound (S_p)-**1b***: According to the representative procedure, starting from compound (S_p)-**2b** (45 mg, 0.16 mmol); flash chromatography on silica gel (EtOAc/Cy, 2:8) gave compound (S_p)-**1b** (30 mg, 67% yield, 99% *ee*) as amorphous white solid. $[\alpha]_D^{20}$ -513 (c 1, $CHCl_3$).

*Compound (R_p)-**1b***: According to the representative procedure, starting from compound (R_p)-**2b** (45 mg, 0.16 mmol); flash chromatography on silica gel (EtOAc/Cy, 2:8) gave compound (S_p)-**1b** (23 mg, 51% yield, 95% *ee*) as amorphous white solid. $[\alpha]_D^{20}$ +520 (c 0.05, $CHCl_3$).

*Compound (±)-**1c***: According to the representative procedure, starting from compound (±)-**2c** (40 mg, 0.13 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:9) gave compound (±)-**1c** (22 mg, 55% yield) as amorphous white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 6.72 (d, *J* = 7.7 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 6.56 (ddd, *J* = 7.2, 5.0, 1.8 Hz, 2H), 6.46 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.37 (d, *J* = 0.7 Hz, 1H), 6.16 (dd, *J* = 7.8, 1.9 Hz, 1H), 3.74-3.49 (m, 2H), 3.37 (p, *J* = 6.7 Hz, 1H), 3.26-3.12 (m, 2H), 3.07 (ddd, *J* = 13.2, 10.9, 2.8 Hz, 1H), 2.99 (dt, *J* = 14.8, 9.1 Hz, 1H), 2.72 (ddd, *J* = 13.4, 10.8, 5.1 Hz, 1H), 2.61 (dt, *J* = 13.4, 9.0 Hz, 1H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.11 (d, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (C), 161.5 (C), 153.7 (C), 139.7 (C), 139.2 (C), 137.5 (C), 135.5 (CH), 133.0 (CH), 132.1 (CH), 132.0 (CH), 128.9 (CH), 128.7 (C), 127.1 (CH), 120.3 (C), 111.7 (CH), 37.9 (CH_2), 35.5 (CH_2), 33.7 (CH_2), 30.3 (CH), 30.2 (CH_2), 24.1 (CH_3), 20.8 (CH_3) ppm. IR (neat): 2965, 2931, 2854, 1718, 1571, 1456, 1358, 1176, 1027, 918, 863, 682 cm^{-1}. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}O_2$: 319.1693; found: 319.1697.

*Compound (±)-**1d***: According to the representative procedure, starting from compound (±)-**2c** (32 mg, 0.12 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:9) gave compound (±)-**1d** (13 mg, 41% yield) as amorphous white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 9.7 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 6.55-6.33 (m, 4H), 6.23 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.67 (ddd, *J* = 13.3, 10.2, 3.0 Hz, 1H), 3.47 (ddd, *J* = 13.5, 10.5, 1.9 Hz, 1H), 3.25-3.04 (m, 3H), 2.98 (ddd, *J* = 13.9, 10.7, 5.9 Hz, 1H), 2.85-2.73 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.8 (C), 153.4 (C), 141.3 (CH), 139.8 (2C), 137.5 (C), 136.9 (CH), 133.1 (CH), 133.0 (CH), 129.4 (CH), 129.2 (CH), 127.9 (C), 126.5 (CH), 120.5 (C), 115.1 (CH), 34.8 (CH_2), 33.9 (CH_2), 31.9 (CH_2), 29.8 (CH_2) ppm. IR (neat): 2936, 2855, 2249n 1722, 1582, 1438, 1120, 907, 731 cm^{-1}. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{17}O_2$: 277.1223; found: 277.1229.

*Compound (±)-**1e***: According to the representative procedure, starting from compound (±)-**2e** (273 mg, 0.63 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:14 to 1:9) gave compound (±)-**1e** (234 mg, 86% yield) as amorphous white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.69-7.20 (br m, 5H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.62 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.56 (d, *J* = 1.5 Hz, 1H), 6.34 (s, 1H), 6.30 (d, *J* = 7.8 Hz, 1H), 3.73 (ddd, *J* = 13.4, 10.6, 2.8 Hz, 1H), 3.19 (ddd, *J* = 13.1, 10.7, 4.8 Hz, 1H), 3.03-2.97 (m, 2H), 2.90-2.81 (m, 1H), 2.81-

2.72 (m, 1H), 2.19 (dd, *J* = 13.9, 9.6 Hz, 1H), 2.04 (dt, *J* = 13.4, 9.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7 (C), 156.2 (C), 154.3 (C), 141.6 (C), 140.5 (C), 138.2 (C), 137.7 (C), 136.6 (CH), 136.0 (CH), 129.8 (CH), 129.7 (CH), 129.3 (br, CH), 128.9 (br, 2CH), 128.4 (CH), 127.6 (C), 126.8 (br, CH) 126.6 (CH), 126.3 (C), 120.8 (C), 116.0 (CH), 35.8 (CH_2), 33.2 (CH_2), 33.0 (CH_2), 29.7 (CH_2) ppm. IR (neat): 2934, 2857, 1719, 1568, 1415, 1355, 1265, 1250, 1185, 1158, 1031, 958, 865, 769, 736 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{25}H_{20}O_2Br$: 431.0641; found: 431.0648.

*Compound (±)-**1f***: According to the representative procedure, starting from compound (±)-**2f** (100 mg, 0.27 mmol); flash chromatography on silica gel (EtOAc/Cy, 3:17) gave compound (±)-**1f** (72 mg, 72% yield) as amorphous white solid.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (d, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 6.54-6.53 (m, 2H), 6.25 (br s, 1H), 6.18 (d, *J* = 7.6 Hz, 1H), 3.79-3.65 (m, 1H), 3.55 (dd, *J* = 14.4, 9.5 Hz, 1H), 3.43 (dd, *J* = 13.4, 9.5 Hz, 1H), 3.30 (dt, *J* = 14.3, 9.1 Hz, 1H), 3.14 (ddd, *J* = 12.9, 10.9, 4.9 Hz, 1H), 3.06-2.91 (m, 1H), 2.75 (ddd, *J* = 13.2, 11.0, 4.9 Hz, 1H), 2.63-2.42 (m, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6 (C), 153.5 (C), 153.0 (C), 142.0 (C), 138.9 (C), 137.5 (C), 136.7 (CH), 135.4 (CH), 130.7 (CH), 128.9 (CH), 127.9 (C), 126.8 (CH), 126.4 (C), 122.1 (C), 116.6 (CH), 36.1 (CH_2), 33.9 (CH_2), 32.9 (CH_2), 29.9 (CH_2), 22.6 (CH_3) ppm. IR (neat): 2936, 2248, 1723, 1573, 1416, 1390, 1191, 1032, 913, 730 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{20}H_{18}O_2Br$: 369.0485; found: 369.0494.

*Compound (±)-**1g***: According to the representative procedure, starting from compound (±)-**2g** (50 mg, 0.14 mmol); flash chromatography on silica gel (EtOAc/Cy, 3:17) gave compound (±)-**1g** (41 mg, 82% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.03 (br, m, 4H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 6.47 (s, 2H), 6.31 (d, *J* = 8.8 Hz, 2H), 3.68 (ddd, *J* = 13.3, 10.5, 2.8 Hz, 1H), 3.22 (ddd, *J* = 13.1, 10.5, 5.0 Hz, 1H), 3.10 (ddd, *J* = 13.2, 10.9, 2.8 Hz, 1H), 2.78 (dddd, *J* = 24.2, 15.8, 10.2, 3.2 Hz, 2H), 2.56-2.35 (m, 5H), 2.22-2.07 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (C), 156.2 (C), 154.2 (C), 141.3 (C), 139.8 (C), 139.4 (C), 138.0 (C), 136.5 (CH), 135.4 (C), 132.9 (CH), 132.2 (CH), 131.6 (CH), 129.5 (br, 4CH), 128.3 (CH), 128.2 (C), 126.9 (CH), 120.7 (C), 115.6 (CH), 36.3 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 29.9 (CH_2), 21.4 (CH_3) ppm. IR (neat): 2935, 2855, 2247, 1716, 1573, 1421, 1354, 1183, 1036, 911, 822, 730 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{26}H_{23}O_2$: 367.1693; found: 367.1695.

*Compound (±)-**1h***: According to the representative procedure, starting from compound (±)-**2h** (40 mg, 0.11 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:9) gave compound (±)-**1h** (32 mg, 80% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78–6.86 (br, m, 4H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.62 (dd, *J* = 16.9, 7.7 Hz, 2H), 6.47 (s, 2H), 6.30 (d, *J* = 7.3 Hz, 2H), 3.89 (s, 3H), 3.68 (ddd, *J* = 13.2, 10.5, 2.8 Hz, 1H), 3.22 (ddd, *J* = 13.1, 10.5, 5.0 Hz, 1H), 3.09 (ddd, *J* = 13.2, 10.8, 2.8 Hz, 1H), 2.89–2.64 (m, 2H), 2.62–2.38 (m, 2H), 2.15 (dt, *J* = 13.2, 9.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1 (C), 160.8 (C), 155.8 (C), 154.2 (C), 141.3 (C), 139.4 (C), 138.0 (C), 136.5 (CH), 132.9 (CH), 132.1 (CH), 131.6 (CH), 130.5 (C), 129.9 (br, 2CH), 128.2 (CH and C), 126.9 (CH), 120.7 (C), 115.1 (CH), 114.2 (br, 2CH), 55.4 (CH_3), 36.5 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 29.9 (CH_2) ppm. IR (neat): 2937, 1722, 1607, 1574, 1510, 1408, 1292, 1248, 1177, 1036, 913, 836, 731 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{26}H_{23}O_3$: 383.1642; found: 383.1646.

*Compound (±)-**1i***: According to the representative procedure, starting from compound (±)-**2i** (48 mg, 0.12 mmol); flash chromatography on silica gel (EtOAc/Cy, 3:17) gave compound (±)-**1i** (29 mg, 60% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72-7.09 (br m, 4H), 6.81 (d, *J* = 7.7 Hz, 1H), 6.63 (t, *J* = 8.1 Hz, 2H), 6.48 (s, 2H), 6.35-6.24 (m, 2H), 3.68 (ddd, *J* = 13.5, 10.5, 2.8 Hz, 1H), 3.22 (ddd, *J* = 13.2, 10.5, 5.0 Hz, 1H), 3.10 (ddd, *J* = 13.2, 10.9, 2.8 Hz, 1H), 2.89-2.80 (m, 1H), 2.76 (ddd, *J* = 13.5, 10.9, 5.0 Hz, 1H), 2.53 (ddd, *J* = 14.2, 9.6, 8.2 Hz, 1H), 2.37 (dd, *J* = 14.2, 9.6 Hz, 1H), 2.25-2.07 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6 (C), 154.8 (C), 154.2 (C), 140.9 (C), 139.5 (C), 137.8 (C), 136.8 (CH and C), 135.9 (C), 133.0 (CH), 132.2 (CH), 131.8 (CH), 129.4 (br, 4CH), 128.4 (C), 128.2 (CH), 126.9 (CH), 120.3 (C), 116.1 (CH), 36.3 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 29.9 (CH_2) ppm. IR (neat): 2935, 2854, 2248, 1721, 1572, 1491, 1420, 1354, 1183, 1090, 1035, 1012, 913, 834, 730 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{25}H_{20}O_2Cl$: 387.1146; found: 387.1156.

*Compound (±)-**1j***: According to the representative procedure, starting from compound (±)-**2j** (15 mg, 0.03 mmol); flash chromatography on silica gel (EtOAc/Cy, 2:8) gave compound (±)-**1j** (10 mg, 67% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93-7.17 (br, m, 4H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.63 (dd, *J* = 7.7, 4.6 Hz, 2H), 6.48 (s, 2H), 6.33 (s, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 3.68 (ddd, *J* = 13.3, 10.5, 2.8 Hz, 1H), 3.22 (ddd, *J* = 13.0, 10.5, 5.0 Hz, 1H), 3.11 (ddd, *J* = 13.3, 10.9, 2.8 Hz, 1H), 2.86 (dd, *J* = 13.1, 9.7 Hz, 1H), 2.77 (ddd, *J* = 13.4, 10.8, 5.0 Hz, 1H), 2.55 (ddd, *J* = 14.0, 9.7, 7.9 Hz, 1H), 2.22 (dd, *J* = 14.1, 9.7 Hz, 1H), 2.17-2.03 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3 (C), 154.2 (C), 153.9 (C), 150.1 (C), 140.6 (C), 139.6 (C), 138.7 (C), 137.7 (C), 137.0 (CH), 133.0 (CH), 132.3 (CH), 132.0 (CH), 130.4 (br, 2CH), 128.6 (C), 128.2 (CH), 126.9 (CH), 121.9 (br, 2CH), 120.1 (C), 118.7 (q, *J* = 318 Hz, CF_3), 116.5 (CH), 36.2 (CH_2), 35.1 (CH_2), 33.8 (CH_2), 29.9 (CH_2) ppm. IR (neat): 2937, 2858, 2249, 1721, 1570, 1500, 1423, 1212, 1138, 1036, 886, 846, 731 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{26}H_{20}O_5F_3S$: 501.0978; found: 501.0988.

*Compound (±)-**1k***: According to the representative procedure, starting from compound (±)-**2k** (45 mg, 0.11 mmol); flash chromatography on silica gel (EtOAc/Cy, 1:9) gave compound (±)-**1b** (23 mg, 51% yield) as amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94–7.31 (br m, 4H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.64 (t, *J* = 8.2 Hz, 2H), 6.49 (s, 2H), 6.34 (s, 1H), 6.30 (d, *J* = 8.0 Hz, 1H), 3.69 (ddd, *J* = 13.3, 10.4, 2.9 Hz, 1H), 3.23 (ddd, *J* = 13.1, 10.5, 5.1 Hz, 1H), 3.12 (ddd, *J* = 13.3, 10.8, 2.9 Hz, 1H), 2.90–2.82 (m, 1H), 2.78 (ddd, *J* = 13.4, 10.8, 5.1 Hz, 1H), 2.54 (ddd, *J* = 14.1, 9.8, 7.8 Hz, 1H), 2.25 (dd, *J* = 14.4, 9.9 Hz, 1H), 2.16 (ddd, *J* = 13.3, 9.6, 8.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.4 (C), 154.5 (C), 154.3 (C), 142.0 (C), 140.8 (C), 139.6 (C), 137.7 (C), 137.0 (CH), 133.0 (CH), 132.3 (CH), 131.9 (CH), 131.7 (q, *J* = 33 Hz, C), 128.6 (C), 128.3 (CH), 126.9 (CH), 126.1 (br, 4CH), 123.8 (q, *J* = 271 Hz, CF_3), 120.1 (C), 116.7 (CH), 36.2 (CH_2), 35.1 (CH_2), 33.8 (CH_2), 30.0 (CH_2) ppm. IR (neat): 2933, 2856, 1723, 1569, 1323, 1167, 1127, 1068, 845, 733 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{26}H_{20}O_2F_3$: 421.1410; found: 421.1418.

Late stage functionalization

*Synthesis of compound (±)-**1l***: An oven dried vial was charged with compound (±)-**1e** (40 mg, 0.093 mmol, 1 eq.), *tert*-butyl carbamate (33 mg, 0.278 mmol, 3 eq.), $Pd_2(dba)_3$ (0.8 mg, 0.001 mmol, 0.01 eq.), JohnPhos (0.7 mg, 0.002 mmol, 0.03 eq.), and sodium phenoxide (38 mg, 0.325 mmol, 3.5 eq.). The vial was sealed with a septum, then evacuated and refilled

with argon three times through a needle. Dry toluene (0.2 mL) was added via syringe and the resulting solution was heated at 85 °C in an oil bath overnight. The mixture was then cooled to rt, diluted with H_2O (15 mL), and extracted with AcOEt (3 x 10 mL). The combined organic layers (EtOAc) were filtered over Celite® and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/Cy (9:1 to 8:2) as the eluent to afford compound (±)-**1l** (18 mg, 0.041 mmol, 44% yield) as an amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74-7.33 (br m, 5H), 6.93 (s, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.43 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.33 (s, 1H), 6.25 (d, *J* = 7.8 Hz, 1H), 6.09 (s, 1H), 3.72-3.67 (m, 1H), 3.17-3.13 (m, 1H), 3.09-2.99 (m, 1H), 2.87-2.71 (m, 2H), 2.62 (dt, *J* = 14.2, 9.1 Hz, 1H), 2.25 (dd, *J* = 14.1, 9.3 Hz, 1H), 2.03 (dt, *J* = 14.3, 9.3 Hz, 1H), 1.53 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (C), 156.2 (C), 154. 5 (C), 152.6 (C), 141.2 (C), 140.1 (C), 138.4 (C), 137.7 (C), 136.5 (CH), 130.0 (CH), 129.8 (CH), 129.5 (br, CH), 129.0 (CH), 128.7 (br, CH), 128.4 (br, CH), 128.0 (C), 127.1 (CH), 126.8 (C), 123.7 (CH), 123.6 (CH), 120.6 (C), 116.2 (CH), 80.7 (C), 33.9 (CH_2), 33.5 (CH_2), 33.1 (CH_2),29.8 (CH_2), 28.5 ($3CH_3$) ppm. IR (neat): 2970, 1724, 1569, 1523, 1446, 1416, 1366, 1230, 1217, 1158, 1043, 977, 866, 768 750 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{30}H_{30}O_4N$: 468.2169; found: 468.2178.

*Synthesis of compound (±)-**1m**:* Compound (±)-**1l** (20 mg, 0.044 mmol, 1 eq.) was placed in a 10 mL round-bottomed flask and dissolved in DCM (0.5 mL). TFA (0.03 mL, 0.40 mmol, 9 eq.) was added and the reaction was stirred at rt overnight. The mixture was quenched with a saturated aq. $NaHCO_3$ solution (15 mL), and extracted with DCM (3 x 10 mL). The combined organic layers (DCM) were washed with H_2O (2 x 10 mL), and brine (2 x 10 mL), then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: EtOAc/pentane 3:7) to afford compound (±)-**1m** (15 mg, 0.041 mmol, 92% yield) as an amorphous yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (br s, 1H), 7.56 (br s, 1H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.38 (br s, 1H), 7.27 (br s, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 1H), 6.20-6.08 (m, 2H), 5.52 (s, 1H), 3.71 (ddd, *J* = 13.4, 10.7, 2.8 Hz, 1H), 3.47 (br s, 2H), 3.11 (ddd, *J* = 12.8, 10.7, 4.6 Hz, 1H), 2.94-2.87 (m, 1H), 2.85-2.61 (m, 3H), 2.26-2.07 (m, 2H), 2.01-1.87 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1 (C), 156.2 (C), 154.2 (C), 145.2 (C), 140.7 (C), 140.2 (C), 138.5 (C), 135.6 (CH), 129.9 (CH), 129.5 (CH), 129.2 (br, CH), 128.6 (br, CH), 128.2 (br, 2CH), 127.6 (C), 126.9 (br, CH), 122.8 (C), 120.8 (C), 120.7 (CH), 119.5 (CH), 116.0 (CH), 33.3 (CH_2), 32.6 (CH_2), 32.4 (CH_2), 29.6 (CH_2) ppm. IR (neat): 3464, 3370, 2930, 2854, 1709, 1622, 1567, 1498, 1446, 1416, 1355, 1263, 1186, 1040, 978, 868, 767, 736 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{25}H_{22}O_2N$: 368.1645; found: 368.1646.

*Synthesis of compound (±)-**1n***: An oven dried round-bottomed flask was charged with compound (±)-**3i** (30 mg, 0.076 mmol, 1 eq.), *tert*-butyl carbamate (14 mg, 0.13 mmol, 1.7 eq.), $Pd(OAc)_2$ (1.2 mg, 0.005 mmol, 0.07 eq.), XPhos (3.9 mg, 0.008 mmol, 0.1 eq.), and Cs_2CO_3 (86 mg, 0.26 mmol, 3.5 eq.). The flask was sealed with a septum, then evacuated and refilled with argon three times through a needle. Dry 1,4-dioxane (1 mL) was added via syringe and the resulting solution was heated at 100 °C in an oil bath overnight. The mixture was then cooled to rt, diluted with H_2O (15 mL), and extracted with AcOEt (3 x 10 mL). The combined organic layers (EtOAc) were filtered over Celite® and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/Cy (9:1 to 8:2) as the eluent to afford compound (±)-**1n** (34 mg, 0.073 mmol, 96 % yield) as an amorphous white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.06 (br m, 4H), 6.79 (d, J = 7.6 Hz, 1H), 6.74-6.55 (m, 3H), 6.46 (s, 2H), 6.30 (d, J = 10.8 Hz, 2H), 3.74-3.59 (m, 1H), 3.26-3.18 (m, 1H), 3.16-3.03 (m, 1H), 2.85-2.70 (m, 2H), 2.59-2.40 (m, 2H), 2.19-2.13 (m, 1H), 1.55 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (C), 155.7 (C), 154.2 (C), 152.4 (C), 141.3 (C), 139.9 (C), 139.4 (C), 138.0 (C), 136.5 (CH), 132.9 (CH), 132.6 (C), 132.2 (CH), 131.7 (CH), 128.2 (2CH), 127.4 (br, 2CH) 126.9 (CH), 120.6 (C), 118.2 (br, 2CH), 115.4 (CH), 81.1 (C), 36.5 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 29.9 (CH_2), 28.3 ($3CH_3$) ppm. IR (neat): 2970, 1720, 1592, 1524, 1405, 1366, 1316, 1231, 1217, 1160, 1053, 842, 739 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{30}H_{30}O_4N$: 468.2169; found: 468.2179.

*Synthesis of compound (±)-**1o**:* Compound (±)-**1m** (19 mg, 0.041 mmol, 1 eq.) was placed in a 10 mL round-bottomed flask and dissolved in DCM (0.5 mL). TFA (0.03 mL, 0.40 mmol, 10 eq.) was added and the reaction was stirred at rt overnight. The mixture was quenched with a saturated aq. $NaHCO_3$ solution (15 mL), and extracted with DCM (3 x 10 mL). The combined organic layers (DCM) were washed with H_2O (2 x 10 mL), and brine (2 x 10 mL), then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/pentane (2:8 to 4:6) as the eluent to afford compound (±)-**1o** (12 mg, 0.032 mmol, 78% yield) as an amorphous yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61-6.88 (m, 3H), 6.77 (d, *J* = 7.7 Hz, 2H), 6.62 (dd, *J* = 16.4, 7.8 Hz, 2H), 6.46 (s, 2H), 6.34-6.12 (m, 2H), 3.67 (ddd, *J* = 13.3, 10.5, 2.8 Hz, 1H), 3.21 (ddd, *J* = 13.1, 10.5, 5.0 Hz, 1H), 3.08 (td, *J* = 13.2, 12.1, 2.8 Hz, 1H), 2.81 (dd, *J* = 13.1, 9.6 Hz, 1H), 2.74 (ddd, *J* = 13.4, 10.9, 5.0 Hz, 1H), 2.62 (dd, *J* = 13.4, 9.2 Hz, 1H), 2.57-2.46 (m, 1H), 2.24-2.12 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.3 (C), 156.3 (C), 154.3 (C), 148.0 (C), 141.5 (C), 139.4 (C), 138.1 (C), 136.3 (CH), 132.8 (2CH), 132.1 (CH), 131.6 (CH), 128.2 (2CH), 128.1 (C), 128.0 (C), 126.9 (CH), 120.9 (C), 114.8 (2CH), 114.4 (CH), 36.6 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 29.9 (CH_2) ppm. IR (neat): 3362, 3223, 2928, 2854, 1708, 1621, 1605, 1573, 1515, 1437, 1412, 1355, 1286, 1247, 1180, 1155, 1035, 918, 832, 736 cm^{-1}. HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{25}H_{22}O_2N$: 368.1645; found: 368.1645.

ASSOCIATED CONTENT

Supporting Information. The Supporting Information is available free of charge on the ACS Publications website at DOI:

Synthetic procedures for the preparation of model compounds **7a** and **7b**; HPLC chromatograms of enantioenriched compounds; absorption and emission spectra of fluorophores **(±)-1a-o**, compound (±)-**6** and model compounds **7a,b**; g_{abs} and g_{lum} values form compounds (S_p)-**1b** and (R_p)-**1b**; ^{1}H NMR and ^{13}C NMR spectra of all new compounds (PDF).

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Notes

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REFERENCES

(1) Brown, C. J.; Farthing, A. C. Preparation and Structure of Di-*p*-Xylylene. *Nature* **1949**, *164*, 915-916

(2) Hope, H.; Bernstein, J.; Trueblood, K. N. The crystal and molecular structure of 1,1,2,2,9,9,10,10-octafluoro-[2,2]paracyclophane and a reinvestigation of the structure of [2,2]paracyclophane. *Acta Cryst.* **1972**, *B28*, 1733-1743.

(3) Cram, D. J.; Allinger, N. L.; Steinberg, H. Macro Rings. VII. The Spectral Consequences of Bringing Two Benzene Rings Face to Face. *J. Am. Chem. Soc.* **1954**, *76*, 6132-6141.

(4) Klee, D.; Weiss, N.; Lahann J. in *Modern Cyclophane Chemistry* (Eds.: R. Gleiter, H. Hopf), Wiley-VCH, Weinheim, **2004**.

(5) Chen, J. P.; Ueno, K.; Suzuki, K. Patent No: US 6869698, **2005**.

(6) (a) Goromaru, H.; Shigeiwa, N.; Murata, M.; Maeda, S.; Patent No: JP 4918803, **2012**; (b) Bartholomew, G. P.; Ledoux, I.; Mukamel, S.; Bazan, G. C.; Zyss, J. Three-Dimensional Nonlinear Optical Chromophores Based on Through-Space Delocalization. *J. Am. Chem. Soc.* **2002**, *124*, 13480-13485; (c) Zyss, J.; Ledoux, I.; Volkov, S.; Chernyak, V.; Mukamel, S.; Bartholomew, G. P.; Bazan, G. C. Through-Space Charge Transfer and Nonlinear Optical Properties of Substituted Paracyclophane. *J. Am. Chem. Soc.* **2000**, *122*, 11956-11962.

(7) (a) Zafra, J. L.; Molina, A.; Ontoria, P.; Mayorga Burrezo, M.; Pena-Alvarez, M.; Samoc, J.; Szeremeta, F. J.; Ramirez Lovander, M. D.; Droske, C. J.; Pappenfus, T. M.; Echegoyen, L.; Lopez Navarrete, J. T.; Martin, N.; Casado, J. Fingerprints of Through-Bond and Through-Space Exciton and Charge π-Electron Delocalization in Linearly Extended [2.2]Paracyclophanes. *J. Am. Chem. Soc.* **2017**, *139*, 3095-3105; (b) Hong, J. W.; Woo, H. Y.; Liu, B.; Bazan, G. C. Solvatochromism of Distyrylbenzene Pairs Bound Together by [2.2]Paracyclophane: Evidence for a Polarizable "Through-Space" Delocalized State. *J. Am. Chem. Soc.* **2005**, *127*, 7435-7443; (c) Woo, H. Y.; Hong, J. W.; Liu, B.; Mikhailovsky, A.; Korystov, D.; Bazan, G. C. Water-Soluble [2.2]Paracyclophane Chromophores with Large Two-Photon Action Cross Sections. *J. Am. Chem. Soc.* **2005**, *127*, 820-821; (d) Bartholomew, G. P.; Rumi, M.; Pond, S. J. K.; Perry, J. W.; Tretiak, S.; Bazan, G. C. Two-Photon Absorption in Three-Dimensional Chromophores Based on [2.2]-Paracyclophane. *J. Am. Chem. Soc.* **2004**, *126*, 11529-11542; (e) Hong, J. W.; Benmansour, H.; Bazan, G C. Through-Space Delocalized Water-Soluble Paracyclophane Bichromophores: New Fluorescent Optical Reporters. *Chem. Eur. J.* **2003**, *9*, 3186-3192; (f) Gon, M.; Morisaki, Y.; Chujo, Y. Optically Active Phenylethene Dimers Based on Planar Chiral Tetrasubstituted [2.2]Paracyclophane. *Chem. Eur. J.* **2017**, *23*, 6323-6329.

(8) (a) Morisaki, Y.; Gon, M.; Sasamori, T.; Tokitoh, N.; Chujo, Y. Planar Chiral Tetrasubstituted [2.2]Paracyclophane: Optical Resolution and Functionalization. *J. Am. Chem. Soc.* **2014**, *136*, 3350-3353; (b) Morisaki, Y.; Inoshita, K.; Chujo, Y. Planar-Chiral Through-Space Conjugated Oligomers: Synthesis and Characterization of Chiroptical Properties. *Chem. Eur. J.* **2014**, *20*, 8386–8390; (c) Gon, M.; Morisaki, Y.; Chujo, Y. Optically active cyclic compounds based on planar chiral [2.2]paracyclophane: extension of the conjugated systems and chiroptical properties. *J. Mater. Chem. C* **2015**, *3*, 521-529; (d) Gon, M.; Morisaki, Y.; Chujo, Y. Highly Emissive Optically Active Conjugated Dimers Consisting of a Planar Chiral [2.2]Paracyclophane Showing Circularly Polarized Luminescence. *Eur. J. Org. Chem.* **2015**, 7756-7762; (e) Morisaki, Y.; Sawada, R.; Gon, M.; Chujo, Y. New Types of Planar Chiral [2.2]Paracyclophanes and Construction of One-Handed Double Helices. *Chem. Asian J.* **2016**, *11*, 2524-2527.

(9) Hopf, H.; Hucker, J.; Ernst, L. On the Functionalization of [2.2](1,4)Phenanthrenoparacyclophane. *Eur. J. Org. Chem.* **2007**, 1891-1904.

(10) (a) Delcourt, M.-L.; Turcaud, S.; Benedetti, E.; Micouin, L. Efficient and Scalable Kinetic Resolution of Racemic 4-Formyl[2.2]paracyclophane via Asymmetric Transfer Hydrogenation. *Adv. Synth. Catal.* **2016**, *358*, 1213-1218; (b) Benedetti, E.; Delcourt, M.-L.; Gatin-Fraudet, B.; Turcaud, S.; Micouin, L. Synthesis and photophysical studies of through-space conjugated [2.2]paracyclophane-based naphthalene fluorophores. *RSC Adv.* **2017**, *7*, 50472-5047; (c) Delcourt, M.-L.; Felder, S.; Benedetti, E.; Micouin, L. Highly Enantioselective Desymmetrization of Centrosymmetric pseudo-para-Diformyl[2.2]paracyclophane via Asymmetric Transfer Hydrogenation. *ACS Catal.* **2018**, *8*, 6612-6616.

(11) Clark, G. S. Coumarin. *Perfumer & flavorist* **1995**, *20*, 23-34.

(12) (a) Pechmann, H. V. Neue Bildungsweise der Cumarine. Synthese des Daphnetins. I. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 929-936; (b) Woods, L. L.; Snapp, J. A. A New One-Step Synthesis of Substituted Coumarins. *J. Org. Chem.* **1962**, *27*, 3703-3705; (c) De, S. K.; Gibbs, R. A. An Efficient and Practical Procedure for the Synthesis of 4-Substituted Coumarins. *Synthesis* **2005**, *6*, 1231-1233.

(13) (a) Bogdak, D. Coumarins: Fast Synthesis by Knoevenagel Condensation under Microwave Irradiation. *J. Chem. Research (S)* **1998**, 468-469; (b) Fuson, R. C.; Thomas, N. Extension of the Reformatsky Reaction to new Types of Compounds. *J. Org. Chem.* **1953**, *18*, 1762-1766; (c) Yavari, I.; Hekmat-Shoar, R.; Zonouzi, A. A new and efficient route to 4-carboxymethylcoumarins mediated by vinyltriphenylphosphonium salt. *Tetrahedron Lett.* **1998**, *39*, 2391-2392.

(14) (a) Jia, C.; Piao, D.; Kitamura, T.; Fujiwara, Y. New Method for Preparation of Coumarins and Quinolinones via Pd-Catalyzed Intramolecular Hydroarylation of C–C Triple Bonds. *J. Org. Chem.* **2000**, *65*, 7516-7522; (b) Jia, C.; Piao, D.: Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. Efficient activation of aromatic C-H bonds for addition to C-C multiple bonds. *Science* **2000**, *287*, 1992-1995; (c) Menon, R. S.; Findlay, A. D.; Bissember, A. C.; Banwell, M. G. The Au(I)-Catalyzed Intramolecular Hydroarylation of Terminal Alkynes Under Mild Conditions: Application to the Synthesis of 2H-Chromenes, Coumarins, Benzofurans, and Dihydroquinolines. *J. Org. Chem.* **2009**, *74*, 8901–8903; (d) Shi, Z.; He, C. Efficient Functionalization of Aromatic C–H Bonds Catalyzed by Gold(III) under Mild and Solvent-Free Conditions. *J. Org. Chem.* **2004**, 69, 3669-3671; (e) Pastine, S. J.; Youn, S. W.; Sames, D. Pt(IV)-catalyzed cyclization of arene–alkyne substrates via C–H bond functionalizatio. *Tetrahedron* **2003**, *59*, 8859-8868; (f) Li, R.; Wang, S. R.; Lu, W. FeCl3-Catalyzed Alkenylation of Simple Arenes with Aryl-Substituted Alkynes. *Org. Lett.* **2007**, *9*, 2219-2222.

(15) Usui, K.; Yamamoto, K.; Ueno, Y.; Igawa, K.; Hagihara, R.; Masuda, T.; Ojida, A.; Karasawa, S.; Tomooka, K.; Hirai, G.; Suemune, H. Internal-Edge-Substituted Coumarin-Fused

[6]Helicenes: Asymmetric Synthesis, Structural Features, and Control of Self-Assembly; *Chem. Eur. J.* **2018**, *24*, 14617-14621.

(16) Only one example of pCp-based coumarin was reported prior to this study, see: Minuti, L.; Marrocchi, A.; Teseia, I.; Gacs-Baitz, E. 5-Nitro[2.2]paracyclophanepyran-6-one—building block for the synthesis of [2.2]paracyclophanes containing condensed benzofuran subunits. *Tetrahedron Lett.* **2005**, *46*, 8789-8792.

(17) Friedmann, C. J.; Ay, S.; Bräse, S. Improved Synthesis of Enantiopure 4-Hydroxy[2.2]paracyclophane. *J. Org. Chem.* **2010**, *75*, 4612-4614.

(18) (a) Kane, V. V.; Gerdes, A.; Grahn, W.; Ernst, L.; Dix, I.; Jones, P. G.; Hopf, H. A novel entry into a new class of cyclophane derivatives: synthesis of (±)-[2.2]paracyclophane-4-thiol. *Tetrahedron Lett.* **2001**, *42*, 373-376; (b) Ma, Q. ; Ma, Y.; Liu, X.; Duan, W.; Qu, B.; Song C. Planar chiral imidazolium salts based on [2.2]paracyclophane in the asymmetric rhodium-catalyzed 1,2-addition of arylboronic acids to aldehydes. *Tetrahedron: Asymm.* **2010**, *21*, 292-298.

(19) For selected examples, see: (a) Meyer, A. Y. Molecular mechanics and molecular shape. III. Surface area and cross-sectional areas of organic molecules. *J. Comput. Chem.* **1986**, 7, 144 – 152; (b) Todeschini, R.; Consonni, V. in *Molecular Descriptors for Chemoinformatics*; Wiley-VCH: Germany, **2009**; (c) Sauer, W. H. B.; Schwarz, M. K. Molecular Shape Diversity of Combinatorial Libraries: A Prerequisite for Broad Bioactivity. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 987-1003.

(20) The three-dimensional PMI plot was generated using LLAMA, see, Colomer, I.; Empson, C. J.; Craven, P.; Owen, Z.; Doveston, R. G.; Churcher, I.; Marsden, S. P.; Nelson, A. A divergent synthetic approach to diverse molecular scaffolds: assessment of lead-likeness using LLAMA, an open-access computational tool. *Chem. Commun.* **2016**, *52*, 7209-7212.

(21) Schneider, J. F.; Fröhlich, R.; Paradies J. Synthesis of Enantiopure Planar-Chiral Thiourea Derivatives. *Synthesis* **2010**, *20*, 3486-3492.

(22) For the synthesis of model substrate **7a,b**, see the SI.

(23) See the SI for more details.

(24) (a) Riehl, J. P.; Richardson, F. S. Circularly polarized luminescence spectroscopy. *Chem. Rev.* **1986**, *86*, 1-16; (b) Sánchez-Carnerero, E. M.; Agarrabeitia, A. R.; Moreno, F.; Maroto, B. L.; Muller, G.; Ortiz, M. J.; de la Moya, S. Circularly Polarized Luminescence from Simple Organic Molecules. *Chem. Eur. J.* **2015**, *21*, 13488-13500.

(25) Hassan, Z.; Spuling, E.; Knoll, D. M.; Lahann, J.; Bräse, S. Planar chiral [2.2]paracyclophanes: from synthetic curiosity to applications in asymmetric synthesis and materials. *Chem. Soc. Rev.* **2018**, *47*, 6947-6963.

(26) The samples were excited using a 90° geometry with a Xenon ozone-free lamp 150 W LS. The following parameters were used: emission slit width ≈ 2 mm, integration time = 4 sec, scan speed = 50 nm/min, accumulations = 5.

(27) For a recent review, see: (a) Tanaka, H.; Inoue, Y.; Mori, T. Circularly Polarized Luminescence and Circular Dichroisms in Small Organic Molecules: Correlation between Excitation and Emission Dissymmetry Factors. *ChemPhotoChem* **2018**, *2*, 386-402. For some recent contributions in this field, see: (b) Dhbaibi, K.; Favereau, L.; Srebro-Hooper, M.; Jean, M.; Vanthuyne, N.; Zinna, F.; Jamoussi, B.; Di Bari, L.; Autschbach, J.; Crassous, J. Exciton coupling in diketopyrrolopyrrole–helicene derivatives leads to red and near-infrared circularly polarized luminescence. *Chem. Sci.* **2018**, *9*, 735-742; (c) Saleh, N.; Moore, B.; Srebro, M.; Vanthuyne, N.; Toupet, L.; Williams, J. A. G.; Roussel, C.; Deol, K. K.; Muller, G.; Autschbach, J.; Crassous, J. Acid/Base-Triggered Switching of Circularly Polarized Luminescence and Electronic Circular Dichroism in Organic and Organometallic Helicenes. *Chem. Eur. J.* **2015**, *21*, 1673-1681; (d) Shen, C.; Srebro-Hooper, M.; Jean, M.; Vanthuyne, N.; Toupet, L.; Williams, J. A.; Torres, A. R.; Riives, A. J.; Muller, G.; Autschbach, J.; Crassous, J. Synthesis and Chiroptical Properties of Hexa-, Octa-, and Deca-azaborahelicenes: Influence of Helicene Size and of the Number of Boron Atoms. *Chem. Eur. J.* **2017**, *23*, 407-418.

(28) (a) Yonemoto-Kobayashi, M.; Inamoto, K.; Tanaka, Y.; Kondo, Y. Carboxylation of alkynylsilanes with carbon dioxide mediated by cesium fluoride in DMSO. *Org. Biomol. Chem.* **2013**, *11*, 3773-3775; (b) Zhang, X.; Zhang, W.-Z.; Ren, X.; Zhang, L.-L.; Lu, X.-B. Ligand-Free Ag(I)-Catalyzed Carboxylation of Terminal Alkynes with CO2. *Org. Lett.* **2011**, *13*, 2402-2405.

TOC graphic.